# Clinical trial results:
# A Phase 2 Open-Label Study in Infants with Respiratory Syncytial Virus Lower Respiratory Tract Infection, Followed by a Double-blind, Placebo Controlled Part, to Evaluate the Safety, Tolerability, Pharmacokinetics and Antiviral Effect of RV521 (REVIRAL 1)

## Summary

| | |
|---|---|
| EudraCT number | 2018-001010-15 |
| Trial protocol | HU PL BE |
| Global end of trial date | 05 December 2022 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 21 June 2023 |
| First version publication date | 21 June 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | C5241003 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04225897 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | REVC003: Study ID |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 27 January 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 05 December 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

Part A and Part B: To evaluate the safety and tolerability of single (Part A) and multiple (Part B) oral doses of RV521 in infants hospitalised with Respiratory Syncytial Virus (RSV) lower respiratory tract infection (LRTI).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 13 November 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Hungary: 4 |
| Country: Number of subjects enrolled | Malaysia: 7 |
| Country: Number of subjects enrolled | Taiwan: 1 |
| Country: Number of subjects enrolled | Thailand: 9 |
| Country: Number of subjects enrolled | Panama: 3 |
| Country: Number of subjects enrolled | Spain: 27 |
| Worldwide total number of subjects | 51 |
| EEA total number of subjects | 31 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 43 |
| Children (2-11 years) | 8 |

| | |
|---|---|
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

This study was planned to be conducted in 3 parts: Part A, B and optional part C. Part C was not conducted as part of a reassessment of the clinical development plan for RV521 (sisunatovir); hence, data is not reported for Part C in any section of the results. A total of 51 subjects were enrolled in the study (Part A=19 and Part B=32).

### Period 1

| | |
|---|---|
| Period 1 title | Part A (Screening Visit to Day 7) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort 1: RV521 1.0 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 1.0 milligram per kilogram (mg/kg) of RV521 orally on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 1.0 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route on Day 1.

| | |
|---|---|
| **Arm title** | Cohort 1: RV521 2.0 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.0 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.0 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route on Day 1.

| | |
|---|---|
| **Arm title** | Cohort 1: RV521 2.5 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.5 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route on Day 1.

| | |
|---|---|
| **Arm title** | Cohort 2: RV521 2.0 mg/kg |

Arm description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received a single dose of 2 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.0 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route on Day 1.

| **Number of subjects in period 1[1]** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg |
|---|---|---|---|
| Started | 3 | 7 | 3 |
| Completed | 3 | 6 | 1 |
| Not completed | 0 | 1 | 2 |
| Adverse events | - | 1 | - |
| Parent/legal guardian request | - | - | 1 |
| Lost to follow-up | - | - | 1 |

| **Number of subjects in period 1[1]** | Cohort 2: RV521 2.0 mg/kg |
|---|---|
| Started | 6 |
| Completed | 6 |
| Not completed | 0 |
| Adverse events | - |
| Parent/legal guardian request | - |
| Lost to follow-up | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Total 51 subjects were enrolled (Part A=19 and Part B=32).

## Period 2

| | |
|---|---|
| Period 2 title | Part B (Screening Visit to Day 12) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | No |
| **Arm title** | Cohort 3: Placebo |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received placebo every 12 hours twice daily (BID) orally for 5 days.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered placebo dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of placebo separated by 12 hours orally for 5 days.

| | |
|---|---|
| **Arm title** | Cohort 3: RSV1 2.5 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of RV521 separated by 12 hours orally for 5 days.

| | |
|---|---|
| **Arm title** | Cohort 3: RV521 3.5 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 3.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 3.5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of RV521 separated by 12 hours orally for 5 days.

| | |
|---|---|
| **Arm title** | Cohort 3: RV521 5 mg/kg |

Arm description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of RV521 separated by 12 hours orally for 5 days.

| **Arm title** | Cohort 4: Placebo |
|---|---|

Arm description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| Arm type | Placebo |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered placebo dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of placebo separated by 12 hours orally for 5 days.

| **Arm title** | Cohort 4: RV521 2.5 mg/kg |
|---|---|

Arm description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of RV521 separated by 12 hours orally for 5 days.

| **Arm title** | Cohort 5: Placebo |
|---|---|

Arm description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| Arm type | Placebo |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered placebo dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of placebo separated by 12 hours orally for 5 days.

| **Arm title** | Cohort 5: RV521 2.5 mg/kg |
|---|---|

Arm description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Arm type | Experimental |
|---|---|

| | |
|---|---|
| Investigational medicinal product name | RV521 |
| Investigational medicinal product code | |
| Other name | Sisunatovir |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered RV521 2.5 mg/kg dispersed in a defined volume of permitted suspending diluent via the oral route. Subjects received BID of RV521 separated by 12 hours orally for 5 days.

| **Number of subjects in period 2** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg |
|---|---|---|---|
| Started | 3 | 3 | 4 |
| Completed | 3 | 3 | 4 |
| Not completed | 0 | 0 | 0 |
| Parent/legal guardian request | - | - | - |

| **Number of subjects in period 2** | Cohort 3: RV521 5 mg/kg | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|
| Started | 3 | 1 | 4 |
| Completed | 2 | 1 | 4 |
| Not completed | 1 | 0 | 0 |
| Parent/legal guardian request | 1 | - | - |

| **Number of subjects in period 2** | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|
| Started | 6 | 8 |
| Completed | 6 | 8 |
| Not completed | 0 | 0 |
| Parent/legal guardian request | - | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort 1: RV521 1.0 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 1.0 milligram per kilogram (mg/kg) of RV521 orally on Day 1. | |
| Reporting group title | Cohort 1: RV521 2.0 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.0 mg/kg of RV521 orally on Day 1. | |
| Reporting group title | Cohort 1: RV521 2.5 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.5 mg/kg of RV521 orally on Day 1. | |
| Reporting group title | Cohort 2: RV521 2.0 mg/kg |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received a single dose of 2 mg/kg of RV521 orally on Day 1. | |

| Reporting group values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg |
|---|---|---|---|
| Number of subjects | 3 | 7 | 3 |
| Age Categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 1 | 5 | 3 |
| Children (2-11 years) | 2 | 2 | 0 |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 27.8 | 18.1 | 9.4 |
| standard deviation | ± 5.90 | ± 7.25 | ± 2.46 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 0 | 4 | 2 |
| Male | 3 | 3 | 1 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asian | 0 | 7 | 0 |
| White | 3 | 0 | 3 |
| Black or African American | 0 | 0 | 0 |
| Unknown or Other | 0 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 3 |
| Not Hispanic or Latino | 3 | 7 | 0 |
| Unknown | 0 | 0 | 0 |

| Reporting group values | Cohort 2: RV521 2.0 mg/kg | Total | |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Number of subjects | 6 | 19 | |
| Age Categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 6 | 15 | |
| Children (2-11 years) | 0 | 4 | |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 2.7 | | |
| standard deviation | ± 1.69 | - | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 1 | 7 | |
| Male | 5 | 12 | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 1 | 1 | |
| Asian | 1 | 8 | |
| White | 4 | 10 | |
| Black or African American | 0 | 0 | |
| Unknown or Other | 0 | 0 | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 4 | |
| Not Hispanic or Latino | 5 | 15 | |
| Unknown | 0 | 0 | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Cohort 3: Placebo |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days. | |
| Subject analysis set title | Cohort 3: RSV1 2.5 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Subject analysis set title | Cohort 3: RV521 3.5 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 3.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Subject analysis set title | Cohort 3: RV521 5 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Subject analysis set title | Cohort 4: Placebo |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Subject analysis set title | Cohort 4: RV521 2.5 mg/kg |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Subject analysis set title | Cohort 5: Placebo |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Subject analysis set title | Cohort 5: RV521 2.5 mg/kg |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Subject analysis set title | Cohort 4 and 5 combined: RV521 2.5 mg/kg |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received BID of RV521 2.5 mg/kg separated by 12 hours orally for 5 days. Subjects from Cohort 4 and 5 were included.

| | |
|---|---|
| Subject analysis set title | Cohort 4 and 5 combined: Placebo |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received BID of placebo separated by 12 hours orally for 5 days. Subjects from Cohorts 4 and 5 were included.

| **Reporting group values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg |
|---|---|---|---|
| Number of subjects | 3 | 3 | 4 |
| Age Categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 3 | 3 | 2 |
| Children (2-11 years) | 0 | 0 | 2 |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 17.5 | 8.9 | 18.5 |
| standard deviation | ± 4.00 | ± 4.51 | ± 13.54 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 1 | 1 | 3 |
| Male | 2 | 2 | 1 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 1 | 0 | 0 |
| Asian | 1 | 3 | 1 |
| White | 1 | 0 | 3 |
| Black or African American | 0 | 0 | 0 |
| Unknown or Other | 0 | 0 | 0 |
| Ethnicity | | | |

| | | | |
|---|---|---|---|
| Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 0 |
| Not Hispanic or Latino | 2 | 3 | 4 |
| Unknown | 0 | 0 | 0 |

| **Reporting group values** | Cohort 3: RV521 5 mg/kg | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|
| Number of subjects | 3 | 1 | 4 |
| Age Categorical | | | |
| Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 1 | 1 | 4 |
| Children (2-11 years) | 2 | 0 | 0 |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 22.2 | 1.6 | 1.2 |
| standard deviation | ± 7.97 | ± 99999 | ± 0.43 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 0 | 0 |
| Male | 1 | 1 | 4 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asian | 1 | 0 | 0 |
| White | 1 | 1 | 4 |
| Black or African American | 0 | 0 | 0 |
| Unknown or Other | 1 | 0 | 0 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 1 |
| Not Hispanic or Latino | 3 | 1 | 3 |
| Unknown | 0 | 0 | 0 |

| **Reporting group values** | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg | Cohort 4 and 5 combined: RV521 2.5 mg/kg |
|---|---|---|---|
| Number of subjects | 5 | 8 | 12 |
| Age Categorical | | | |
| Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 5 | 8 | 12 |
| Children (2-11 years) | 0 | 0 | 0 |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 2.0 | 3.0 | 2.4 |
| standard deviation | ± 0.47 | ± 1.10 | ± 1.26 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 5 | 5 |
| Male | 5 | 3 | 7 |

| | | | |
|---|---|---|---|
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 1 | 1 |
| Asian | 1 | 1 | 1 |
| White | 2 | 6 | 10 |
| Black or African American | 1 | 0 | 0 |
| Unknown or Other | 1 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | 1 | 2 |
| Not Hispanic or Latino | 2 | 7 | 10 |
| Unknown | 1 | 0 | 0 |

| **Reporting group values** | Cohort 4 and 5 combined: Placebo | | |
|---|---|---|---|
| Number of subjects | 6 | | |
| Age Categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 6 | | |
| Children (2-11 years) | 0 | | |
| Age Continuous | | | |
| 99999 indicates standard deviation could not be calculated as a single subject was analysed. | | | |
| Units: months | | | |
| arithmetic mean | 1.9 | | |
| standard deviation | ± 0.45 | | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 0 | | |
| Male | 6 | | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | | |
| Asian | 1 | | |
| White | 3 | | |
| Black or African American | 1 | | |
| Unknown or Other | 1 | | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | | |
| Not Hispanic or Latino | 3 | | |
| Unknown | 1 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Cohort 1: RV521 1.0 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 1.0 milligram per kilogram (mg/kg) of RV521 orally on Day 1. | |
| Reporting group title | Cohort 1: RV521 2.0 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.0 mg/kg of RV521 orally on Day 1. | |
| Reporting group title | Cohort 1: RV521 2.5 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.5 mg/kg of RV521 orally on Day 1. | |
| Reporting group title | Cohort 2: RV521 2.0 mg/kg |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received a single dose of 2 mg/kg of RV521 orally on Day 1. | |
| Reporting group title | Cohort 3: Placebo |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received placebo every 12 hours twice daily (BID) orally for 5 days. | |
| Reporting group title | Cohort 3: RSV1 2.5 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 3: RV521 3.5 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 3.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 3: RV521 5 mg/kg |
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 4: Placebo |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 4: RV521 2.5 mg/kg |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 5: Placebo |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days. | |
| Reporting group title | Cohort 5: RV521 2.5 mg/kg |
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days. | |
| Subject analysis set title | Cohort 3: Placebo |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 3: RSV1 2.5 mg/kg |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 3: RV521 3.5 mg/kg |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 3.5 mg/kg every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 3: RV521 5 mg/kg |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 5 mg/kg every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 4: Placebo |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 4: RV521 2.5 mg/kg |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 5: Placebo |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 5: RV521 2.5 mg/kg |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Subject analysis set title | Cohort 4 and 5 combined: RV521 2.5 mg/kg |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received BID of RV521 2.5 mg/kg separated by 12 hours orally for 5 days. Subjects from Cohort 4 and 5 were included.

| Subject analysis set title | Cohort 4 and 5 combined: Placebo |
|---|---|
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received BID of placebo separated by 12 hours orally for 5 days. Subjects from Cohorts 4 and 5 were included.

## Primary: Part A: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Withdrawals due to TEAEs

| End point title | Part A: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Withdrawals due to TEAEs[1] |
|---|---|

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a clinical study subject

administered a medicinal product which did not necessarily have a causal relationship with the investigational medicinal product (IMP). TEAEs were defined as AEs which started, or worsened, after the first dose of IMP. An SAE was any untoward medical occurrence or effect that, at any dose, resulted in death; was life threatening; required or prolonged inpatient hospitalisation; resulted in persistent or significant disability/incapacity or other important medical event. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

From start of IMP on Day 1 up to Day 7

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| TEAEs | 2 | 5 | 3 | 1 |
| SAEs | 0 | 1 | 0 | 0 |
| Withdrawals due to TEAEs | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Withdrawals due to TEAEs

| End point title | Part B: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Withdrawals due to TEAEs[2] |
|---|---|

End point description:

An AE was defined as any untoward medical occurrence in a clinical study subject administered a medicinal product which did not necessarily have a causal relationship with the IMP. TEAEs were defined as AEs which started, or worsened, after the first dose of IMP. An SAE was any untoward medical occurrence or effect that, at any dose, resulted in death; was life threatening; required or prolonged inpatient hospitalisation; resulted in persistent or significant disability/incapacity or other important medical event. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

From start of IMP on Day 1 up to Day 12

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | | | | |
| TEAEs | 1 | 2 | 1 | 1 |
| SAEs | 0 | 0 | 0 | 0 |
| Withdrawal due to TEAEs | 0 | 0 | 0 | 1 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | | | | |
| TEAEs | 1 | 2 | 3 | 1 |
| SAEs | 0 | 0 | 0 | 0 |
| Withdrawal due to TEAEs | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Physical Examination Results at Baseline

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Physical Examination Results at Baseline[3] |
|---|---|

End point description:

Physical examination included general appearance; head, eyes, ears, nose and throat (HEENT); dermatologic; cardiovascular; respiratory; gastrointestinal; and neurological examination. Clinical significance of results were determined by the investigator. Safety population included all subjects who received at least 1 dose of IMP. Here, 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| General appearance; n=3,7,3,5 | 0 | 1 | 0 | 0 |
| HEENT; n=3,7,3,4 | 1 | 2 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Dermatologic; n=3,7,3,4 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=3,7,3,5 | 0 | 1 | 0 | 0 |
| Respiratory; n=3,7,3,5 | 3 | 6 | 2 | 1 |
| Gastrointestinal; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| Neurological; n=3,7,3,5 | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Physical Examination Results Anytime Between 18 to 24 Hours Post-dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Physical Examination Results Anytime Between 18 to 24 Hours Post-dose[4] |
|---|---|

End point description:

Physical examination included general appearance; HEENT; dermatologic; cardiovascular; respiratory; gastrointestinal; and neurological examination. Clinical significance of results were determined by the investigator. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 18 to 24 hours post-dose on Day 1

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | | | | |
| General appearance; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| HEENT; n=3,6,1,5 | 1 | 2 | 0 | 0 |
| Dermatologic; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| Respiratory; n=3,6,2,6 | 1 | 4 | 1 | 1 |
| Gastrointestinal; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| Neurological; n=3,6,2,6 | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Physical Examination Results at 48 Hours Post-dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant |
|---|---|

| | |
|---|---|
| | Physical Examination Results at 48 Hours Post-dose[5] |

End point description:

Physical examination included general appearance; HEENT; dermatologic; cardiovascular; respiratory; gastrointestinal; and neurological examination. Clinical significance of results were determined by the investigator. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

At 48 hours post-dose on Day 1

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | | | | |
| General appearance; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| HEENT; n=3,6,2,5 | 1 | 1 | 1 | 0 |
| Dermatologic; n=3,6,2,5 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| Respiratory; n=3,6,2,6 | 1 | 3 | 1 | 1 |
| Gastrointestinal; n=3,6,2,6 | 0 | 0 | 0 | 0 |
| Neurological; n=3,6,2,6 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Physical Examination Results at Baseline

| | |
|---|---|
| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Physical Examination Results at Baseline[6] |

End point description:

Physical examination included general appearance; dermatologic; cardiovascular; respiratory; gastrointestinal; and neurological examination. Clinical significance of results were determined by the investigator. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 3 | 4 | 3 |
| Units: Subjects | | | | |
| General Appearance; n=2,3,4,3,1,4,5,7 | 0 | 0 | 1 | 0 |
| HEENT; n=2,3,3,3,1,4,5,7 | 0 | 0 | 1 | 1 |
| Dermatologic; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=2,3,4,3,1,4,5,7 | 0 | 0 | 1 | 0 |
| Respiratory; n=2,3,4,3,1,4,5,7 | 1 | 2 | 3 | 3 |
| Gastrointestinal; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Neurological; n=2,3,4,3,1,4,5,7 | 0 | 0 | 1 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 7 |
| Units: Subjects | | | | |
| General Appearance; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 1 |
| HEENT; n=2,3,3,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Dermatologic; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Respiratory; n=2,3,4,3,1,4,5,7 | 1 | 2 | 4 | 3 |
| Gastrointestinal; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |
| Neurological; n=2,3,4,3,1,4,5,7 | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

### Primary: Part B: Number of Subjects With Abnormal Clinically Significant Physical Examination Results Anytime Between 40 to 48 Hours Post-dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Physical Examination Results Anytime Between 40 to 48 Hours Post-dose 10[7] |
|---|---|

End point description:

Physical examination included general appearance; HEENT; dermatologic; cardiovascular; respiratory; gastrointestinal; and neurological examination. Clinical significance of results were determined by the investigator. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | | | | |
| General appearance; n=3,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| HEENT; n=3,3,3,2,0,4,5,8 | 0 | 0 | 1 | 0 |
| Dermatologic; n=3,3,3,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Cardiovascular; n=3,3,3,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Respiratory; n=3,3,4,2,0,4,5,8 | 0 | 1 | 0 | 0 |
| Gastrointestinal; n=3,3,3,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Neurological; n=3,3,3,2,0,4,5,8 | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[8] | 4 | 5 | 8 |
| Units: Subjects | | | | |
| General appearance; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| HEENT; n=3,3,3,2,0,4,5,8 | | 0 | 0 | 0 |
| Dermatologic; n=3,3,3,2,0,4,5,8 | | 0 | 0 | 0 |
| Cardiovascular; n=3,3,3,2,0,4,5,8 | | 0 | 0 | 0 |
| Respiratory; n=3,3,4,2,0,4,5,8 | | 1 | 0 | 0 |
| Gastrointestinal; n=3,3,3,2,0,4,5,8 | | 0 | 0 | 0 |
| Neurological; n=3,3,3,2,0,4,5,8 | | 0 | 0 | 0 |

Notes:

[8] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Baseline

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Baseline[9] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | 0 | 2 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

### Primary: Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose[10] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose on Day 1

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | 0 | 1 | 1 | 0 |

### Statistical analyses

No statistical analyses for this end point

### Primary: Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at 12 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at 12 Hours Post-Dose[11] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

12 hours post-dose on Day 1

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 2 | 6 |
| Units: Subjects | 0 | 2 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 18 to 24 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 18 to 24 Hours Post-Dose[12] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 18 to 24 hours post-dose on Day 1

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | 0 | 2 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at 48 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant |
|---|---|

| | |
|---|---|
| | Vital Signs per Investigator’s Interpretation at 48 Hours Post-Dose[13] |

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

48 hours post-dose on Day 1

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | 0 | 1 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Vital Signs per Investigator’s Interpretation at Baseline

| | |
|---|---|
| End point title | Part B: Number of Subjects With Abnormal Vital Signs per Investigator’s Interpretation at Baseline[14] |

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 1

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 1[15] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose 1 (Day 1)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | 1 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs

## per Investigator’s Interpretation At Pre-dose 2

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation At Pre-dose 2[16] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 2 (Day 1)

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 1 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 3

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 3[17] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 3 (Day 2)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 4

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 4[18] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 4 (Day 2)

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 1 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Pre-dose 5

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Pre-dose 5[19] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 5 (Day 3)

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 1 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs

## per Investigator’s Interpretation at Pre-dose 6

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 6[20] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 6 (Day 3)

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 4 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation Anytime Between 4 to 5 Hours Post-Dose 6

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation Anytime Between 4 to 5 Hours Post-Dose 6[21] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose 6 (Day 3)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 4 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 7

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 7[22] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 7 (Day 4)

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 1 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Pre-dose 8

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator's Interpretation at Pre-dose 8[23] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 8 (Day 4)

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 2 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 4 | 6 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs

## per Investigator’s Interpretation at Pre-dose 9

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 9[24] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 9 (Day 5)

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 2 | 1 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 4 | 5 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation at Pre-dose 10[25] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 10 (Day 5)

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 1 | 1 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 4 | 4 |
| Units: Subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation Anytime Between 40 to 48 Hours Post-Dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Vital Signs per Investigator’s Interpretation Anytime Between 40 to 48 Hours Post-Dose 10[26] |
|---|---|

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, respiratory rate, heart rate and pulse oximetry. Number of subjects with abnormal clinically significant vital signs per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[27] | 4 | 5 | 8 |
| Units: Subjects | | 0 | 0 | 0 |

Notes:

[27] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Hematology Results at Baseline

| End point title | Part A: Number of Subjects With Abnormal Hematology Results at Baseline[28] |
|---|---|

End point description:

Haematology parameters included basophils, eosinophils, lymphocytes, monocytes, neutrophils, haemoglobin (Hb), haematocrit (HCT), white blood cell count (WBC), red blood cell count (RBC), platelet count, mean cell volume (MCV), mean cell haemoglobin (MCH), and MCH concentration (MCHC). Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Basophils; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Eosinophils; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Eosinophils; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCHC; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCHC; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCH; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCH; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCV; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| MCV; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| RBC; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| RBC; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| HCT; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| HCT; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Hb; below normal range; n=2,7,3,6 | 0 | 0 | 1 | 0 |
| Hb; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| WBC; below normal range; n=2,7,1,6 | 0 | 0 | 1 | 1 |
| WBC; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Lymphocytes; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Lymphocytes; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Monocytes; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Monocytes; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Neutrophils; below normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Neutrophils; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 0 |
| Platelets; below normal range; n=2,7,1,6 | 0 | 2 | 0 | 1 |
| Platelets; above normal range; n=2,7,1,6 | 0 | 0 | 0 | 1 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Hematology Results at 48 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Hematology Results at 48 Hours Post-Dose[29] |
|---|---|

End point description:

Haematology parameters included basophils, eosinophils, lymphocytes, monocytes, neutrophils, Hb, HCT, WBC, RBC, platelet count, MCV, MCH and MCHC. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

48 hours post-dose on Day 1

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 5 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Basophils; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Eosinophils; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Eosinophils; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCHC; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCHC; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCH; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCH; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCV; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| MCV; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| RBC; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| RBC; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| HCT; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| HCT; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Hb; below normal range; n=3,6,2,5 | 0 | 0 | 0 | 0 |
| Hb; above normal range; n=3,6,2,5 | 0 | 0 | 0 | 0 |
| WBC; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| WBC; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 1 |
| Lymphocytes; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Lymphocytes; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Monocytes; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Monocytes; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Neutrophils; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Neutrophils; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Platelets; below normal range; n=3,6,1,5 | 0 | 1 | 0 | 0 |
| Platelets; above normal range; n=3,6,1,5 | 1 | 1 | 1 | 1 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Hematology Results at Baseline

| | |
|---|---|
| End point title | Part B: Number of Subjects With Abnormal Hematology Results at Baseline[30] |

End point description:

Haematology parameters included basophils, eosinophils, lymphocytes, monocytes, neutrophils, Hb, HCT, WBC, RBC, platelet count, MCV, MCH and MCHC. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 1 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Basophils; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Eosinophils; below normal range; n=3,3,3,1,0,4,2,7 | 1 | 0 | 1 | 0 |
| Eosinophils; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| MCHC; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| MCHC; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| MCH; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| MCH; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| MCV; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 1 | 0 |
| MCV; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| RBC; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| RBC; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| HCT; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 1 |
| HCT; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Hb; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 1 | 0 |
| Hb; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| WBC; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| WBC; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Lymphocytes; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Lymphocytes; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Monocytes; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Monocytes; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Neutrophils; below normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Neutrophils; above normal range; n=3,3,3,1,0,4,2,7 | 0 | 0 | 0 | 0 |
| Platelets; below normal range; n=3,3,3,1,0,3,2,7 | 1 | 0 | 1 | 0 |

| | | | | |
|---|---|---|---|---|
| Platelets; above normal range; n=3,3,3,1,0,3,2,7 | 1 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[31] | 4 | 2 | 7 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Basophils; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Eosinophils; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 2 |
| Eosinophils; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| MCHC; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 1 |
| MCHC; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| MCH; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 1 |
| MCH; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| MCV; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| MCV; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| RBC; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| RBC; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| HCT; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 2 | 0 |
| HCT; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Hb; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 1 | 1 |
| Hb; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| WBC; below normal range; n=3,3,3,1,0,4,2,7 | | 2 | 1 | 0 |
| WBC; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Lymphocytes; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 1 | 0 |
| Lymphocytes; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Monocytes; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 1 |
| Monocytes; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 1 | 1 |
| Neutrophils; below normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |
| Neutrophils; above normal range; n=3,3,3,1,0,4,2,7 | | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Platelets; below normal range; n=3,3,3,1,0,3,2,7 | | 0 | 0 | 0 |
| Platelets; above normal range; n=3,3,3,1,0,3,2,7 | | 0 | 0 | 1 |

Notes:

[31] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Hematology Results Anytime Between 40 to 48 Hours Post-dose 10

| End point title | Part B: Number of Subjects With Abnormal Hematology Results Anytime Between 40 to 48 Hours Post-dose 10[32] |
|---|---|

End point description:

Haematology parameters included basophils, eosinophils, lymphocytes, monocytes, neutrophils, Hb, HCT, WBC, RBC, platelet count, MCV, MCH and MCHC. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 2 | 4 | 2 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Basophils; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Eosinophils; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Eosinophils; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| MCHC; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| MCHC; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 1 |
| MCH; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 1 |
| MCH; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| MCV; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 1 |
| MCV; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| RBC; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| RBC; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| HCT; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| HCT; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| Hb; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Hb; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| WBC; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| WBC; above normal range; n=3,2,4,2,0,1,3,7 | 1 | 0 | 0 | 0 |
| Lymphocytes; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Lymphocytes; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Monocytes; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| Monocytes; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| Neutrophils; below normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 0 | 0 |
| Neutrophils; above normal range; n=3,2,4,2,0,1,3,7 | 0 | 0 | 1 | 0 |
| Platelets; below normal range; n=3,2,3,1,0,1,3,7 | 0 | 0 | 0 | 0 |
| Platelets; above normal range; n=3,2,3,1,0,1,3,7 | 2 | 1 | 2 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[33] | 1 | 3 | 7 |
| Units: Subjects | | | | |
| Basophils; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| Basophils; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| Eosinophils; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| Eosinophils; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| MCHC; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 1 |
| MCHC; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| MCH; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 1 |
| MCH; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| MCV; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| MCV; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 0 |

| | | | | |
|---|---|---|---|---|
| RBC; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| RBC; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| HCT; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 2 | 0 |
| HCT; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 0 |
| Hb; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 1 |
| Hb; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 0 |
| WBC; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 1 |
| WBC; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| Lymphocytes; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 1 |
| Lymphocytes; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 0 | 0 |
| Monocytes; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 1 |
| Monocytes; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 1 |
| Neutrophils; below normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 1 |
| Neutrophils; above normal range; n=3,2,4,2,0,1,3,7 | | 0 | 1 | 0 |
| Platelets; below normal range; n=3,2,3,1,0,1,3,7 | | 0 | 0 | 0 |
| Platelets; above normal range; n=3,2,3,1,0,1,3,7 | | 0 | 2 | 6 |

Notes:

[33] - No subjects were evaluable

## Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinical Chemistry Results at Baseline

| End point title | Part A: Number of Subjects With Abnormal Clinical Chemistry Results at Baseline[34] |
|---|---|

End point description:

Clinical chemistry parameters included creatinine, urea (or blood urea nitrogen), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), total bilirubin, albumin, total protein, sodium, potassium, chloride, glucose, and calcium. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| ALT; above normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| Albumin; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Albumin; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| ALP; below normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| ALP; above normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| AST; below normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| AST; above normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Bilirubin; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Calcium; below normal range; n=3,7,3,6 | 0 | 1 | 0 | 0 |
| Calcium; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 1 |
| Chloride; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Chloride; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Creatinine; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Creatinine; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| GGT; below normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| GGT; above normal range; n=3,7,3,5 | 0 | 0 | 0 | 0 |
| Glucose; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Glucose; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| LDH; below normal range; n=3,7,3,3 | 0 | 0 | 0 | 0 |
| LDH; above normal range; n=3,7,3,3 | 0 | 0 | 0 | 0 |
| Potassium; below normal range; n=3,7,3,4 | 0 | 0 | 0 | 0 |
| Potassium; above normal range; n=3,7,3,4 | 0 | 0 | 0 | 1 |
| Protein; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Protein; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Sodium; below normal range; n=3,7,3,6 | 0 | 1 | 0 | 0 |
| Sodium; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Urea; below normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |
| Urea; above normal range; n=3,7,3,6 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinical Chemistry Results at 48 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinical Chemistry Results at 48 Hours Post-Dose[35] |
|---|---|

End point description:

Clinical chemistry parameters included creatinine, urea, AST, ALT, GGT, ALP, LDH, total bilirubin, albumin, total protein, sodium, potassium, chloride, glucose, and calcium. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

48 hours post-dose on Day 1

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| ALT; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Albumin; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Albumin; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| ALP; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| ALP; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| AST; below normal range; n=3,5,1,5 | 0 | 0 | 0 | 0 |
| AST; above normal range; n=3,5,1,5 | 0 | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Bilirubin; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Calcium; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Calcium; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 1 |
| Chloride; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Chloride; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Creatinine; below normal range; n=3,6,1,4 | 0 | 0 | 0 | 0 |
| Creatinine; above normal range; n=3,6,1,4 | 0 | 0 | 0 | 0 |
| GGT; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| GGT; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Glucose; below normal range; n=3,6,1,4 | 0 | 0 | 0 | 1 |
| Glucose; above normal range; n=3,6,1,4 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| LDH; below normal range; n=3,5,1,5 | 0 | 0 | 0 | 0 |
| LDH; above normal range; n=3,5,1,5 | 0 | 0 | 0 | 0 |
| Potassium; below normal range; n=3,5,1,4 | 0 | 0 | 0 | 0 |
| Potassium; above normal range; n=3,5,1,4 | 0 | 1 | 0 | 3 |
| Protein; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Protein; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Sodium; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Sodium; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Urea; below normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |
| Urea; above normal range; n=3,6,1,5 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinical Chemistry Results at Baseline

| End point title | Part B: Number of Subjects With Abnormal Clinical Chemistry Results at Baseline[36] |
|---|---|

End point description:

Clinical chemistry parameters included creatinine, urea, AST, ALT, GGT, ALP, LDH, total bilirubin, albumin, total protein, sodium, potassium, chloride, glucose, and calcium. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'n' signifies number of subjects evaluable for the specified categories. 99999 indicates data was not available as no subjects were evaluable.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,3,4,3,0,4,5,8 | 0 | 0 | 0 | 0 |
| ALT; above normal range; n=3,3,4,3,0,4,5,8 | 0 | 0 | 0 | 0 |
| Albumin; below normal range; n=2,3,3,3,1,4,4,8 | 0 | 0 | 0 | 1 |
| Albumin; above normal range; n=2,3,3,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| ALP; below normal range; n=2,3,3,3,1,4,4,5 | 0 | 0 | 0 | 0 |
| ALP; above normal range; n=2,3,3,3,1,4,4,5 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| AST; below normal range; n=3,3,4,3,0,4,5,7 | 0 | 0 | 0 | 0 |
| AST; above normal range; n=3,3,4,3,0,4,5,7 | 0 | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,3,4,3,1,4,4,8 | 1 | 0 | 2 | 1 |
| Bilirubin; above normal range; n=3,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Calcium; below normal range; n=2,3,2,3,1,4,3,6 | 0 | 0 | 0 | 0 |
| Calcium; above normal range; n=2,3,2,3,1,4,3,6 | 0 | 0 | 0 | 0 |
| Chloride; below normal range; n=3,3,4,3,1,4,5,8 | 1 | 0 | 0 | 0 |
| Chloride; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| Creatinine; below normal range; n=3,3,4,3,1,4,5,8 | 1 | 0 | 2 | 2 |
| Creatinine; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| GGT; below normal range; n=2,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| GGT; above normal range; n=2,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Glucose; below normal range; n=3,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Glucose; above normal range; n=3,3,4,3,1,4,4,8 | 1 | 0 | 3 | 0 |
| LDH; below normal range; n=0,3,2,3,0,2,2,3 | 99999 | 0 | 0 | 0 |
| LDH; above normal range; n=0,3,2,3,0,2,2,3 | 99999 | 0 | 0 | 1 |
| Potassium; below normal range; n=1,3,3,3,0,3,5,7 | 0 | 0 | 0 | 0 |
| Potassium; above normal range; n=1,3,3,3,0,3,5,7 | 0 | 1 | 0 | 1 |
| Protein; below normal range; n=3,3,4,3,1,4,4,7 | 0 | 0 | 0 | 0 |
| Protein; above normal range; n=3,3,4,3,1,4,4,7 | 0 | 0 | 0 | 0 |
| Sodium; below normal range; n=3,3,4,3,1,4,5,8 | 1 | 0 | 0 | 0 |
| Sodium; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 1 |
| Urea; below normal range; n=2,3,4,2,1,4,5,8 | 0 | 0 | 1 | 0 |
| Urea; above normal range; n=2,3,4,2,1,4,5,8 | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,3,4,3,0,4,5,8 | 99999 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| ALT; above normal range; n=3,3,4,3,0,4,5,8 | 99999 | 0 | 0 | 3 |
| Albumin; below normal range; n=2,3,3,3,1,4,4,8 | 0 | 0 | 1 | 0 |
| Albumin; above normal range; n=2,3,3,3,1,4,4,8 | 0 | 0 | 0 | 1 |
| ALP; below normal range; n=2,3,3,3,1,4,4,5 | 0 | 0 | 0 | 0 |
| ALP; above normal range; n=2,3,3,3,1,4,4,5 | 0 | 0 | 0 | 0 |
| AST; below normal range; n=3,3,4,3,0,4,5,7 | 99999 | 0 | 0 | 0 |
| AST; above normal range; n=3,3,4,3,0,4,5,7 | 99999 | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,3,4,3,1,4,4,8 | 0 | 0 | 0 | 2 |
| Bilirubin; above normal range; n=3,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Calcium; below normal range; n=2,3,2,3,1,4,3,6 | 0 | 0 | 0 | 1 |
| Calcium; above normal range; n=2,3,2,3,1,4,3,6 | 0 | 0 | 0 | 1 |
| Chloride; below normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| Chloride; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| Creatinine; below normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 1 | 4 |
| Creatinine; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| GGT; below normal range; n=2,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| GGT; above normal range; n=2,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Glucose; below normal range; n=3,3,4,3,1,4,4,8 | 0 | 0 | 0 | 0 |
| Glucose; above normal range; n=3,3,4,3,1,4,4,8 | 0 | 1 | 0 | 4 |
| LDH; below normal range; n=0,3,2,3,0,2,2,3 | 99999 | 0 | 0 | 0 |
| LDH; above normal range; n=0,3,2,3,0,2,2,3 | 99999 | 0 | 0 | 0 |
| Potassium; below normal range; n=1,3,3,3,0,3,5,7 | 99999 | 0 | 0 | 0 |
| Potassium; above normal range; n=1,3,3,3,0,3,5,7 | 99999 | 0 | 1 | 2 |
| Protein; below normal range; n=3,3,4,3,1,4,4,7 | 0 | 0 | 1 | 2 |
| Protein; above normal range; n=3,3,4,3,1,4,4,7 | 0 | 0 | 0 | 1 |
| Sodium; below normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 1 |
| Sodium; above normal range; n=3,3,4,3,1,4,5,8 | 0 | 0 | 0 | 0 |
| Urea; below normal range; n=2,3,4,2,1,4,5,8 | 0 | 0 | 0 | 3 |
| Urea; above normal range; n=2,3,4,2,1,4,5,8 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinical Chemistry Results Anytime Between 40 to 48 Hours Post-dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinical Chemistry Results Anytime Between 40 to 48 Hours Post-dose 10[37] |
|---|---|

End point description:

Clinical chemistry parameters included creatinine, urea, AST, ALT, GGT, ALP, LDH, total bilirubin, albumin, total protein, sodium, potassium, chloride, glucose, and calcium. Institutional laboratory normal ranges were used. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,3,3,2,0,3,5,6 | 0 | 0 | 0 | 0 |
| ALT; above normal range; n=3,3,3,2,0,3,5,6 | 0 | 0 | 0 | 0 |
| Albumin; below normal range; n=3,3,4,2,0,4,4,6 | 0 | 0 | 0 | 0 |
| Albumin; above normal range; n=3,3,4,2,0,4,4,6 | 0 | 0 | 0 | 0 |
| ALP; below normal range; n=3,3,3,2,0,4,4,7 | 0 | 0 | 0 | 0 |
| ALP; above normal range; n=3,3,3,2,0,4,4,7 | 0 | 0 | 1 | 0 |
| AST; below normal range; n=3,3,2,2,0,2,4,7 | 0 | 0 | 0 | 0 |
| AST; above normal range; n=3,3,2,2,0,2,4,7 | 0 | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,3,4,2,0,4,4,6 | 1 | 0 | 1 | 0 |
| Bilirubin; above normal range; n=3,3,4,2,0,4,4,6 | 0 | 0 | 0 | 0 |
| Calcium; below normal range; n=3,3,3,2,0,4,4,7 | 0 | 0 | 0 | 0 |
| Calcium; above normal range; n=3,3,3,2,0,4,4,7 | 0 | 1 | 1 | 0 |
| Chloride; below normal range; n=3,3,4,2,0,4,5,8 | 1 | 0 | 0 | 0 |
| Chloride; above normal range; n=3,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Creatinine; below normal range; n=2,3,4,2,0,4,5,8 | 1 | 0 | 0 | 1 |
| Creatinine; above normal range; n=2,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| GGT; below normal range; n=3,3,4,2,0,4,4,7 | 0 | 0 | 0 | 0 |
| GGT; above normal range; n=3,3,4,2,0,4,4,7 | 0 | 0 | 0 | 1 |
| Glucose; below normal range; n=2,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Glucose; above normal range; n=2,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| LDH; below normal range; n=2,3,2,1,0,2,3,6 | 0 | 0 | 0 | 0 |
| LDH; above normal range; n=2,3,2,1,0,2,3,6 | 0 | 0 | 0 | 0 |
| Potassium; below normal range; n=2,3,2,2,0,2,4,6 | 0 | 0 | 0 | 0 |
| Potassium; above normal range; n=2,3,2,2,0,2,4,6 | 0 | 1 | 0 | 1 |
| Protein; below normal range; n=3,3,4,2,0,4,4,7 | 0 | 0 | 0 | 0 |
| Protein; above normal range; n=3,3,4,2,0,4,4,7 | 0 | 0 | 0 | 0 |
| Sodium; below normal range; n=3,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |
| Sodium; above normal range; n=3,3,4,2,0,4,5,8 | 0 | 0 | 0 | 1 |
| Urea; below normal range; n=3,3,4,2,0,4,5,8 | 1 | 0 | 1 | 1 |
| Urea; above normal range; n=3,3,4,2,0,4,5,8 | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[38] | 4 | 5 | 8 |
| Units: Subjects | | | | |
| ALT; below normal range; n=3,3,3,2,0,3,5,6 | | 0 | 0 | 0 |
| ALT; above normal range; n=3,3,3,2,0,3,5,6 | | 0 | 0 | 1 |
| Albumin; below normal range; n=3,3,4,2,0,4,4,6 | | 0 | 0 | 1 |
| Albumin; above normal range; n=3,3,4,2,0,4,4,6 | | 0 | 0 | 1 |
| ALP; below normal range; n=3,3,3,2,0,4,4,7 | | 0 | 0 | 0 |
| ALP; above normal range; n=3,3,3,2,0,4,4,7 | | 0 | 0 | 0 |
| AST; below normal range; n=3,3,2,2,0,2,4,7 | | 0 | 0 | 0 |
| AST; above normal range; n=3,3,2,2,0,2,4,7 | | 0 | 0 | 0 |
| Bilirubin; below normal range; n=3,3,4,2,0,4,4,6 | | 0 | 0 | 1 |
| Bilirubin; above normal range; n=3,3,4,2,0,4,4,6 | | 0 | 0 | 0 |
| Calcium; below normal range; n=3,3,3,2,0,4,4,7 | | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Calcium; above normal range; n=3,3,3,2,0,4,4,7 | | 1 | 0 | 5 |
| Chloride; below normal range; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| Chloride; above normal range; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| Creatinine; below normal range; n=2,3,4,2,0,4,5,8 | | 0 | 1 | 4 |
| Creatinine; above normal range; n=2,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| GGT; below normal range; n=3,3,4,2,0,4,4,7 | | 0 | 0 | 0 |
| GGT; above normal range; n=3,3,4,2,0,4,4,7 | | 0 | 1 | 0 |
| Glucose; below normal range; n=2,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| Glucose; above normal range; n=2,3,4,2,0,4,5,8 | | 0 | 1 | 1 |
| LDH; below normal range; n=2,3,2,1,0,2,3,6 | | 0 | 0 | 0 |
| LDH; above normal range; n=2,3,2,1,0,2,3,6 | | 0 | 0 | 1 |
| Potassium; below normal range; n=2,3,2,2,0,2,4,6 | | 0 | 0 | 0 |
| Potassium; above normal range; n=2,3,2,2,0,2,4,6 | | 0 | 1 | 1 |
| Protein; below normal range; n=3,3,4,2,0,4,4,7 | | 0 | 1 | 1 |
| Protein; above normal range; n=3,3,4,2,0,4,4,7 | | 0 | 0 | 0 |
| Sodium; below normal range; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| Sodium; above normal range; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |
| Urea; below normal range; n=3,3,4,2,0,4,5,8 | | 0 | 1 | 0 |
| Urea; above normal range; n=3,3,4,2,0,4,5,8 | | 0 | 0 | 0 |

Notes:

[38] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Urinalysis Results at Baseline

| End point title | Part A: Number of Subjects With Abnormal Urinalysis Results at Baseline[39] |
|---|---|

End point description:

Following urine parameters were analysed: epithelial cells (normal range: 0 to 5 cells per high power field [hpf]), erythrocytes (0 to 2 per hpf), granular casts (0 per low power field [lpf]), hyaline casts (0 to 1 per lpf), leukocytes (0 to 5 per hpf), RBC casts (0 per lpf), WBC casts (0 per lpf), waxy casts (0 per lpf) and pH (5 to 8). Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 7 | 3 | 6 |
| Units: Subjects | | | | |
| Epithelial Cells; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Epithelial Cells; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Erythrocytes; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Erythrocytes; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Granular casts; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Granular casts; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Hyaline casts; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Hyaline casts; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Leukocytes; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Leukocytes; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| RBC cast; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| RBC cast; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| WBC cast; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| WBC cast; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Waxy cast; below normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| Waxy cast; above normal range; n=2,7,3,6 | 0 | 0 | 0 | 0 |
| pH; below normal range; n=2,7,3,4 | 0 | 0 | 0 | 0 |
| pH; above normal range; n=2,7,3,4 | 0 | 1 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Urinalysis Results at 48 Hours Post-dose

| End point title | Part A: Number of Subjects With Abnormal Urinalysis Results at 48 Hours Post-dose[40] |
|---|---|

End point description:

Following urine parameters were analysed: epithelial cells (normal range: 0 to 5 cells per hpf),

erythrocytes (0 to 2 per hpf), granular casts (0 per lpf), hyaline casts (0 to 1 per lpf), leukocytes (0 to 5 per hpf), RBC casts (0 per lpf), WBC casts (0 per lpf), waxy casts (0 per lpf) and pH (5 to 8). Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

48 hours post-dose on Day 1

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 0[41] | 6 |
| Units: Subjects | | | | |
| Epithelial Cells; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Epithelial Cells; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Erythrocytes; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Erythrocytes; above normal range; n=3,6,0,6 | 1 | 0 | | 1 |
| Granular casts; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Granular casts; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Hyaline casts; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Hyaline casts; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Leukocytes; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Leukocytes; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| RBC cast; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| RBC cast; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| WBC cast; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| WBC cast; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Waxy cast; below normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| Waxy cast; above normal range; n=3,6,0,6 | 0 | 0 | | 0 |
| pH; below normal range; n=2,6,0,5 | 0 | 0 | | 0 |
| pH; above normal range; n=2,6,0,5 | 0 | 2 | | 1 |

Notes:

[41] - No subjects were evaluable

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Urinalysis Results at Baseline

| End point title | Part B: Number of Subjects With Abnormal Urinalysis Results at Baseline[42] |
|---|---|

End point description:

Following urine parameters were analysed: epithelial cells (normal range: 0 to 5 cells per hpf), erythrocytes (0 to 2 per hpf), granular casts (0 per lpf), hyaline casts (0 to 1 per lpf), leukocytes (0 to 5 per hpf), RBC casts (0 per lpf), WBC casts (0 per lpf), waxy casts (0 per lpf) and pH (5 to 8). Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and ‘n’ signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 3 | 2 | 2 |
| Units: Subjects | | | | |
| Epi Cells; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Epi Cells; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Ery; below normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 0 |
| Ery; above normal range; n=2,3,2,2,1,2,4,3 | 0 | 1 | 1 | 0 |
| Gran casts; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Gran casts; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Hya casts; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Hya casts; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Leuko; below normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 0 |
| Leuko; above normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 0 |
| RBC cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| RBC cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| WBC cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| WBC cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Waxy cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Waxy cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| pH; below normal range; n=3,3,2,3,1,2,4,5 | 0 | 0 | 0 | 0 |
| pH; above normal range; n=3,3,2,3,1,2,4,5 | 0 | 0 | 1 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 4 | 5 |
| Units: Subjects | | | | |
| Epi Cells; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Epi Cells; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Ery; below normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 1 |
| Ery; above normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 0 |
| Gran casts; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Gran casts; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Hya casts; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Hya casts; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Leuko; below normal range; n=2,3,2,2,1,2,4,3 | 0 | 0 | 0 | 1 |
| Leuko; above normal range; n=2,3,2,2,1,2,4,3 | 0 | 1 | 2 | 1 |
| RBC cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| RBC cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| WBC cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| WBC cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Waxy cast; below normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| Waxy cast; above normal range; n=2,3,1,2,1,2,2,2 | 0 | 0 | 0 | 0 |
| pH; below normal range; n=3,3,2,3,1,2,4,5 | 0 | 0 | 0 | 0 |
| pH; above normal range; n=3,3,2,3,1,2,4,5 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Urinalysis Results Anytime Between 40 to 48 Hours Post-Dose 10

| End point title | Part B: Number of Subjects With Abnormal Urinalysis Results Anytime Between 40 to 48 Hours Post-Dose 10[43] |
|---|---|

End point description:

Following urine parameters were analysed: epithelial cells (normal range: 0 to 5 cells per hpf), erythrocytes (0 to 2 per hpf), granular casts (0 per lpf), hyaline casts (0 to 1 per lpf), leukocytes (0 to 5 per hpf), RBC casts (0 per lpf), WBC casts (0 per lpf), waxy casts (0 per lpf) and pH (5 to 8). Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and ‘n’ signifies number of subjects evaluable for the specified categories.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 3 | 2 | 1 |
| Units: Subjects | | | | |
| Epi Cells; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Epi Cells; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Ery; below normal range; n=2,3,2,1,0,0,3,2 | 0 | 0 | 0 | 0 |
| Ery; above normal range; n=2,3,2,1,0,0,3,2 | 0 | 0 | 1 | 0 |
| Gran casts; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Gran casts; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Hya casts; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Hya casts; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Leuko; below normal range; n=2,3,2,1,0,0,3,2 | 0 | 0 | 0 | 0 |
| Leuko; above normal range; n=2,3,2,1,0,0,3,2 | 0 | 0 | 0 | 0 |
| RBC cast; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| RBC cast; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| WBC cast; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| WBC cast; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Waxy cast; below normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| Waxy cast; above normal range; n=2,3,1,1,0,0,1,2 | 0 | 0 | 0 | 0 |
| pH; below normal range; n=2,3,2,1,0,0,3,5 | 0 | 0 | 0 | 0 |
| pH; above normal range; n=2,3,2,1,0,0,3,5 | 1 | 0 | 1 | 1 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[44] | 0[45] | 3 | 5 |
| Units: Subjects | | | | |
| Epi Cells; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Epi Cells; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Ery; below normal range; n=2,3,2,1,0,0,3,2 | | | 0 | 0 |
| Ery; above normal range; n=2,3,2,1,0,0,3,2 | | | 2 | 0 |
| Gran casts; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Gran casts; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Hya casts; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Hya casts; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Leuko; below normal range; n=2,3,2,1,0,0,3,2 | | | 0 | 0 |
| Leuko; above normal range; n=2,3,2,1,0,0,3,2 | | | 1 | 0 |
| RBC cast; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| RBC cast; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| WBC cast; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| WBC cast; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Waxy cast; below normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| Waxy cast; above normal range; n=2,3,1,1,0,0,1,2 | | | 0 | 0 |
| pH; below normal range; n=2,3,2,1,0,0,3,5 | | | 0 | 0 |
| pH; above normal range; n=2,3,2,1,0,0,3,5 | | | 0 | 2 |

Notes:

[44] - No subjects were evaluable

[45] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Baseline

| | |
|---|---|
| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Baseline[46] |

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QT interval corrected by Bazzett's formula (QTcB) interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator’s Interpretation Anytime Between 4 to 5 Hours Post-Dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator’s Interpretation Anytime Between 4 to 5 Hours Post-Dose[47] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose on Day 1

Notes:

[47] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 18 to 24 Hours Post-dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 18 to 24 Hours Post-dose[48] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 18 to 24 hours post-dose on Day 1

Notes:

[48] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Baseline

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Baseline[49] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP.

| End point type | Primary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1)

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 3 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at 48 Hours Post-dose

| End point title | Part A: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at 48 Hours Post-dose[50] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

48 hours post-dose on Day 1

Notes:

[50] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis was planned.

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 2 | 6 |
| Units: Subjects | 0 | 1 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 1

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 1[51] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose 1 on Day 1

Notes:

[51] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 3 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 3

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 3[52] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 3 (Day 2)

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 5

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 5[53] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 5 (Day 3)

Notes:

[53] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

### Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 6

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation Anytime Between 4 to 5 Hours Post-Dose 6[54] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours post-dose 6 (Day 3)

Notes:

[54] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 3 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 4 | 7 |
| Units: Subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 10[55] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose (Day 5)

Notes:

[55] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 1 | 0[56] |
| Units: Subjects | 0 | 0 | 0 | |

Notes:

[56] - No subjects were evaluable

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[57] | 3 | 3 | 4 |
| Units: Subjects | | 0 | 0 | 0 |

Notes:

[57] - No subjects were evaluable

## Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 8

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator's Interpretation at Pre-dose 8[58] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Pre-dose 8 (Day 4)

Notes:

[58] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| **End point values** | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 2 | 2 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| **End point values** | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 4 | 5 |
| Units: Subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator’s Interpretation Anytime Between 40 to 48 Hours Post-Dose 10

| End point title | Part B: Number of Subjects With Abnormal Clinically Significant Electrocardiogram (ECG) Results per Investigator’s Interpretation Anytime Between 40 to 48 Hours Post-Dose 10[59] |
|---|---|

End point description:

A 12-lead ECG was performed for assessment of following ECG parameters: ventricular heart rate, PR interval, QRS interval, QT interval and QTcB interval. Number of subjects with abnormal clinically significant results for any ECG parameter per investigators interpretation are reported in this outcome measure. Safety population included all subjects who received at least 1 dose of IMP. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Primary |
|---|---|

End point timeframe:

Anytime between 40 to 48 hours post-dose 10 on Day 5

Notes:

[59] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint is specific to Part B; hence, only arms for Part B are included.

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Subjects | 0 | 0 | 0 | 0 |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[60] | 4 | 5 | 8 |
| Units: Subjects | | 0 | 0 | 0 |

Notes:

[60] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Time to Maximum Plasma Concentration (tmax)

| End point title | Part A: Time to Maximum Plasma Concentration (tmax) |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement.

| End point type | Secondary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Hours | | | | |
| median (full range (min-max)) | 4.17 (4 to 4.5) | 4.58 (4.42 to 6.18) | 7 (4.87 to 48.3) | 4.78 (2 to 6.67) |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part B: Time to Maximum Plasma Concentration (tmax)

| End point title | Part B: Time to Maximum Plasma Concentration (tmax) |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| **End point values** | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 4 | 3 | 4 |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Dose 1; n=3,4,3,4,8 | 4.6 (4.33 to 4.63) | 4.32 (3.58 to 11.6) | 4.17 (2.5 to 4.17) | 4.03 (3.77 to 5.5) |
| Dose 6; n=3,3,2,3,8 | 4.43 (4.38 to 4.5) | 3.95 (3.67 to 4.88) | 4.53 (4.05 to 5) | 4.58 (3.58 to 11.5) |

| **End point values** | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Dose 1; n=3,4,3,4,8 | 4.31 (4.08 to 12) | | | |
| Dose 6; n=3,3,2,3,8 | 4.29 (0 to 11.8) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Maximum Observed Plasma Concentration (Cmax)

| End point title | Part A: Maximum Observed Plasma Concentration (Cmax) |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement.

| End point type | Secondary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 3 | 6 |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | 1.59 (± 2.76) | 8.08 (± 7.94) | 2.98 (± 3.09) | 28 (± 17.5) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Maximum Observed Plasma Concentration (Cmax)

| End point title | Part B: Maximum Observed Plasma Concentration (Cmax) |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'n' signifies number of subjects evaluable for the specified categories.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 4 | 3 | 4 |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=3,4,3,4,8 | 43.2 (± 36.7) | 24.9 (± 20) | 115 (± 182) | 39.3 (± 26.4) |
| Dose 6; n=3,3,2,3,8 | 30.9 (± 31.3) | 67.8 (± 86.3) | 212 (± 157) | 133 (± 64.8) |

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=3,4,3,4,8 | 56.5 (± 88.1) | | | |
| Dose 6; n=3,3,2,3,8 | 177 (± 151) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Plasma Concentration Time Curve From Time Zero to 12 Hours (AUC0-12)

| End point title | Part A: Area Under the Plasma Concentration Time Curve From Time Zero to 12 Hours (AUC0-12) |
|---|---|

End point description:

AUC(0 to 12) was calculated using the linear trapezoidal method. No sampling was done at 0 hour. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

0 hour, anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours post-dose on Day 1

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 7 | 2 | 6 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 9.22 (± 16) | 45 (± 48) | 6.46 (± 9.14) | 201 (± 143) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Area Under the Plasma Concentration Time Curve From Time Zero to 12 Hours (AUC0-12)

| End point title | Part B: Area Under the Plasma Concentration Time Curve From Time Zero to 12 Hours (AUC0-12) |
|---|---|

End point description:

AUC(0 to 12) was calculated using the linear trapezoidal method. No sampling was done at 0 hour on Day 1. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint and 'n' signifies number of subjects evaluable for the specified categories. 99999 indicates data could not be calculated due to insufficient number of subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (0 hour, anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 2 | 1 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=0,0,2,1,4 | 99999 (± 99999) | 99999 (± 99999) | 1170 (± 1460) | 127 (± 99999) |
| Dose 6; 1,1,0,1,1 | 87.9 (± 99999) | 184 (± 99999) | 99999 (± 99999) | 1110 (± 99999) |

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 4 | | | |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=0,0,2,1,4 | 160 (± 120) | | | |
| Dose 6; 1,1,0,1,1 | 1600 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Measurable Concentration (AUC[0 to t])

| End point title | Part A: Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Measurable Concentration (AUC[0 to t]) |
|---|---|

End point description:

Area under the plasma concentration-time curve from time 0 to the last measurable concentration was determined using the linear trapezoidal method. No sampling was done at 0 hour. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint. 99999 signifies data could not be calculated due to insufficient subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

0 hour, anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 6 | 2 | 6 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 23.1 (± 99999) | 48.1 (± 49.9) | 14 (± 1.46) | 287 (± 217) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Measurable Concentration (AUC[0 to t])

| End point title | Part B: Area Under the Plasma Concentration-Time Curve From Time 0 to the Last Measurable Concentration (AUC[0 to t]) |
|---|---|

End point description:

Area under the plasma concentration-time curve from time 0 to the last measurable concentration was determined using the linear trapezoidal method. No sampling was done at 0 hour on Day 1. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (0 hour, anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 4 | 2 | 4 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=3,4,2,4,8 | 288 (± 251) | 163 (± 132) | 1170 (± 1460) | 342 (± 240) |
| Dose 6; n=3,3,2,3,8 | 225 (± 233) | 477 (± 594) | 1560 (± 1010) | 1310 (± 802) |

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dose 1; n=3,4,2,4,8 | 315 (± 386) | | | |
| Dose 6; n=3,3,2,3,8 | 1140 (± 845) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Terminal Half-life (t1/2)

| End point title | Part B: Terminal Half-life (t1/2) |
|---|---|

End point description:

T1/2 was calculated as loge (2) divided by kel, where kel is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| **End point values** | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[61] | 0[62] | 0[63] | 0[64] |
| Units: Hours | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[61] - No subjects were evaluable

[62] - No subjects were evaluable

[63] - No subjects were evaluable

[64] - No subjects were evaluable

| **End point values** | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[65] | | | |
| Units: Hours | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[65] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Terminal Half-life (t1/2)

| End point title | Part A: Terminal Half-life (t1/2) |
|---|---|

End point description:

T1/2 was calculated as loge (2) divided by kel, where kel is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[66] | 0[67] | 0[68] | 5 |
| Units: Hours | | | | |
| arithmetic mean (standard deviation) | () | () | () | 6.22 (± 1.46) |

Notes:

[66] - No subjects were evaluable

[67] - No subjects were evaluable

[68] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC0 to inf)

| End point title | Part A: Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC0 to inf) |
|---|---|

End point description:

AUCinf was determined as AUC(0 to t) + (Clast/kel), where Clast was the plasma concentration at the last quantifiable timepoint estimated from the log-linear regression analysis and kel was the terminal phase rate. No sampling was done at 0 hour. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

0 hour, anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| **End point values** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[69] | 0[70] | 0[71] | 5 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | () | 231 (± 161) |

Notes:

[69] - No subjects were evaluable

[70] - No subjects were evaluable

[71] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC0 to inf)

| End point title | Part B: Area Under the Plasma Concentration Time Curve From Time Zero to Infinity (AUC0 to inf) |
|---|---|

End point description:

AUCinf was determined as AUC(0 to t) + (Clast/kel), where Clast was the plasma concentration at the last quantifiable timepoint estimated from the log-linear regression analysis and kel was the terminal phase rate. No sampling was done at 0 hour on Day 1. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (0 hour, anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[72] | 0[73] | 0[74] | 0[75] |
| Units: Hours*nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | () | () | () |

Notes:

[72] - No subjects were evaluable

[73] - No subjects were evaluable

[74] - No subjects were evaluable

[75] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[76] | | | |
| Units: Hours*nanogram per milliliter | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[76] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Trough Concentration at the end of First Dosing Interval (C12)

| End point title | Part A: Trough Concentration at the end of First Dosing Interval (C12) |
|---|---|

End point description:

PK Population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

At 12 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[77] | 0[78] | 0[79] | 0[80] |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[77] - No subjects were evaluable

[78] - No subjects were evaluable

[79] - No subjects were evaluable

[80] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Trough Concentration at the end of First Dosing Interval (C12)

| End point title | Part B: Trough Concentration at the end of First Dosing Interval (C12) |
|---|---|

End point description:

PK Population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

At 12 hours post-dose 6

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 2 | 3 |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | 7.6 (± 8.33) | 9.55 (± 9.75) | 36.9 (± 5.3) | 89.8 (± 99.1) |

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | 124 (± 167) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Predicted Plasma Clearance

| End point title | Part A: Predicted Plasma Clearance |
|---|---|

End point description:

Clearance was calculated as Dose divided by AUC(0 to inf). PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[81] | 0[82] | 0[83] | 5 |
| Units: Liters per hour per kilogram | | | | |
| arithmetic mean (standard deviation) | () | () | () | 12.7 (± 7.66) |

Notes:

[81] - No subjects were evaluable

[82] - No subjects were evaluable

[83] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Predicted Plasma Clearance

| End point title | Part B: Predicted Plasma Clearance |
|---|---|

End point description:

Clearance was calculated as Dose divided by AUC(0 to inf). PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| **End point values** | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[84] | 0[85] | 0[86] | 0[87] |
| Units: Liters per hour per kilogram | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[84] - No subjects were evaluable

[85] - No subjects were evaluable

[86] - No subjects were evaluable

[87] - No subjects were evaluable

| **End point values** | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[88] | | | |
| Units: Liters per hour per kilogram | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[88] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Apparent Volume of Distribution of the Drug After Extravascular Administration

| End point title | Part A: Apparent Volume of Distribution of the Drug After Extravascular Administration |
|---|---|

End point description:

Apparent volume of distribution was estimated as Dose/Kel*AUC(0 to inf), where Kel=apparent first-order terminal elimination rate constant. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Anytime between 4 to 5 hours, anytime between 6 to 8 hours, 12 hours, 18 to 24 hours and 48 hours post-dose on Day 1

| End point values | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg | Cohort 2: RV521 2.0 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[89] | 0[90] | 0[91] | 5 |
| Units: Litres per kilogram | | | | |
| arithmetic mean (standard deviation) | () | () | () | 119 (± 87.4) |

Notes:

[89] - No subjects were evaluable

[90] - No subjects were evaluable

[91] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Apparent Volume of Distribution of the Drug After Extravascular Administration

| End point title | Part B: Apparent Volume of Distribution of the Drug After Extravascular Administration |
|---|---|

End point description:

Apparent volume of distribution was estimated as Dose/Kel*AUC(0 to inf), where Kel=apparent first-order terminal elimination rate constant. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[92] | 0[93] | 0[94] | 0[95] |
| Units: Liters per kilogram | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[92] - No subjects were evaluable

[93] - No subjects were evaluable

[94] - No subjects were evaluable

[95] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[96] | | | |
| Units: Liters per kilogram | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[96] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Accumulation Ratio

| End point title | Part B: Accumulation Ratio |
|---|---|

End point description:

Accumulation ratio was calculated as ratio of the area under the curve (AUC) during a single dosing interval under steady state conditions to the AUC during a dosing interval after one singe dose. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[97] | 0[98] | 0[99] | 0[100] |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[97] - No subjects were evaluable

[98] - No subjects were evaluable

[99] - No subjects were evaluable

[100] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[101] | | | |
| Units: Ratio | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[101] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Percentage Fluctuation

| End point title | Part B: Percentage Fluctuation |
|---|---|

End point description:

Percentage fluctuation was calculated as 100*(Cmax-Cmin)/Cavg, where Cmin=minimum plasma concentration and Cmax measured over dosing interval. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint. 99999 indicates data could not be calculated due to insufficient number of subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| **End point values** | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 0[102] | 1 |
| Units: Percentage of fluctuation | | | | |
| arithmetic mean (standard deviation) | 132 (± 99999) | 123 (± 99999) | () | 8.63 (± 99999) |

Notes:

[102] - No subjects were evaluable

| **End point values** | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: Percentage of fluctuation | | | | |
| arithmetic mean (standard deviation) | 98.1 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Area Under the Plasma Concentration Time Curve From Time Zero to the end of Last Dosing Interval (AUC0-tau)

| End point title | Part B: Area Under the Plasma Concentration Time Curve From Time Zero to the end of Last Dosing Interval (AUC0-tau) |
|---|---|

End point description:

AUC(0 to tau) was determined using the linear trapezoidal method. No sampling was done at 0 hour. PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint. 99999 indicates data could not be calculated due to insufficient number of subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 0[103] | 1 |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 87.9 (± 99999) | 184 (± 99999) | () | 1110 (± 99999) |

Notes:

[103] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 | | | |
| Units: Hours*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 1600 (± 99999) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Average Plasma Concentration Over Dosing Interval (Cavg)

| End point title | Part B: Average Plasma Concentration Over Dosing Interval (Cavg) |
|---|---|

End point description:

Cavg was estimated as AUC(0 to tau)/tau, where tau=dosing interval (12 hours). PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint. 99999 indicates data could not be calculated due to insufficient number of subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 1 | 0[104] | 1 |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 7.32 (± 99999) | 15.3 (± 99999) | () | 92.7 (± 99999) |

Notes:

[104] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|

| Subject group type | Reporting group | | | |
|---|---|---|---|---|
| Number of subjects analysed | 1 | | | |
| Units: Nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | 133 (± 99999) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Minimum Observed Plasma Concentration

| End point title | Part B: Minimum Observed Plasma Concentration |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| End point values | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[105] | 0[106] | 0[107] | 0[108] |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[105] - No subjects were evaluable

[106] - No subjects were evaluable

[107] - No subjects were evaluable

[108] - No subjects were evaluable

| End point values | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[109] | | | |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[109] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Plasma Trough Concentration

| End point title | Part B: Plasma Trough Concentration |
|---|---|

End point description:

PK population included all subjects who received IMP and had at least 1 post-dose PK concentration measurement. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Day 1 Dose 1 (anytime between 4 to 5 hours post-dose, 12 hours post-dose), Day 3 Dose 6 (pre-dose, anytime between 4 to 5 hours post-dose, 12 hours post-dose)

| **End point values** | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[110] | 0[111] | 0[112] | 0[113] |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | () | () | () | () |

Notes:

[110] - No subjects were evaluable

[111] - No subjects were evaluable

[112] - No subjects were evaluable

[113] - No subjects were evaluable

| **End point values** | Cohort 5: RV521 2.5 mg/kg | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[114] | | | |
| Units: Nanograms per milliliter | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[114] - No subjects were evaluable

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Percent Change From Baseline in Logarithm to Base10 (Log10) Total RSV Viral Load by Quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR)

| End point title | Part B: Percent Change From Baseline in Logarithm to Base10 (Log10) Total RSV Viral Load by Quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR) |
|---|---|

End point description:

Percent change from baseline in log10 total RSV viral load was analysed using a mixed effects analysis of covariance (ANCOVA) model. The model was fitted to the subjects treated at the final doses selected for Cohort 5 as pre-planned in statistical analysis plan. Modified Intent to Treat (mITT) population included all subjects who received at least 1 dose of IMP (RV521 or placebo) and had a pre-treatment positive RSV nasopharyngeal swab confirmed by the central laboratory and agreed by the project team during blind data review meeting. Here, 'n' signifies subjects evaluable at the specified timepoints.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (pre-dose on Day 1), 60 hours and 156 hours after first dose on Day 1

| End point values | Cohort 4 and 5 combined: RV521 2.5 mg/kg | Cohort 4 and 5 combined: Placebo | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 | 6 | | |
| Units: Percent change | | | | |
| least squares mean (standard error) | | | | |
| 60 hours; n=5,11 | -31.29 (± 8.19) | -23.27 (± 10.48) | | |
| 156 hours; n=4,12 | -47.53 (± 8.03) | -32.31 (± 11.52) | | |

## Statistical analyses

| Statistical analysis title | Placebo versus RV521 2.5 mg/kg |
|---|---|

Statistical analysis description:

Analysis was performed using mixed effects analysis of covariance model on change from baseline in viral load, including a random effect for subject and fixed effects for treatment group, baseline human rhinovirus/enterovirus status (present or absent), visit, vist by treatment group interaction, and baseline viral load as a covariate.

| | |
|---|---|
| Comparison groups | Cohort 4 and 5 combined: Placebo v Cohort 4 and 5 combined: RV521 2.5 mg/kg |
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | other[115] |
| Parameter estimate | Mean difference (net) |
| Point estimate | -15.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -40.15 |
| upper limit | 9.7 |

Notes:

[115] - 156 hours

| Statistical analysis title | Placebo versus RV521 2.5 mg/kg |
|---|---|

Statistical analysis description:

Analysis was performed using mixed effects analysis of covariance model on change from baseline in viral load, including a random effect for subject and fixed effects for treatment group, baseline human rhinovirus/enterovirus status
(present or absent), visit, vist by treatment group interaction, and baseline viral load as a covariate.

| | |
|---|---|
| Comparison groups | Cohort 4 and 5 combined: Placebo v Cohort 4 and 5 combined: RV521 2.5 mg/kg |

| | |
|---|---|
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | other[116] |
| Parameter estimate | Mean difference (net) |
| Point estimate | -8.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -31.78 |
| upper limit | 15.74 |

Notes:

[116] - 60 hours

## Secondary: Part B: Percent Change From Baseline in Logarithm to Base10 (Log10) Total RSV Viral Load by Cell-Based Infectivity Assay (CBIA)

| | |
|---|---|
| End point title | Part B: Percent Change From Baseline in Logarithm to Base10 (Log10) Total RSV Viral Load by Cell-Based Infectivity Assay (CBIA) |

End point description:

Percent change from baseline in log10 total RSV viral load was analysed using a mixed effects ANCOVA model. The model was fitted to the subjects treated at the final doses selected for Cohort 5 as pre-planned in statistical analysis plan. mITT population included all subjects who received at least 1 dose of IMP (RV521 or placebo) and had a pre-treatment positive RSV nasopharyngeal swab confirmed by the central laboratory and agreed by the project team during blind data review meeting. Here, 'n' signifies subjects evaluable at the specified timepoints.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline (pre-dose on Day 1), 60 hours and 156 hours after first dose on Day 1

| **End point values** | Cohort 4 and 5 combined: RV521 2.5 mg/kg | Cohort 4 and 5 combined: Placebo | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 12 | 6 | | |
| Units: Percent change | | | | |
| least squares mean (standard error) | | | | |
| 60 hours; 5, 11 | -54.74 (± 34.87) | -69.56 (± 46.32) | | |
| 156 hours; 4, 12 | -41.20 (± 34.01) | -10.00 (± 51.88) | | |

### Statistical analyses

| **Statistical analysis title** | Placebo versus RV521 2.5 mg/kg |
|---|---|

Statistical analysis description:

Analysis was performed using mixed effects analysis of covariance model on change from baseline in viral load, including a random effect for subject and fixed effects for treatment group, baseline human rhinovirus/enterovirus status (present or absent), visit, vist by treatment group interaction, and baseline viral load as a covariate.

| | |
|---|---|
| Comparison groups | Cohort 4 and 5 combined: Placebo v Cohort 4 and 5 combined: RV521 2.5 mg/kg |
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | other[117] |
| Parameter estimate | Mean difference (net) |
| Point estimate | -31.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -143.96 |
| upper limit | 81.57 |

Notes:

[117] - 156 hours

| **Statistical analysis title** | Placebo versus RV521 2.5 mg/kg |
|---|---|

Statistical analysis description:

Analysis was performed using mixed effects analysis of covariance model on change from baseline in viral load, including a random effect for subject and fixed effects for treatment group, baseline human rhinovirus/enterovirus status (present or absent), visit, vist by treatment group interaction, and baseline viral load as a covariate.

| | |
|---|---|
| Comparison groups | Cohort 4 and 5 combined: Placebo v Cohort 4 and 5 combined: RV521 2.5 mg/kg |
| Number of subjects included in analysis | 18 |
| Analysis specification | Pre-specified |
| Analysis type | other[118] |
| Parameter estimate | Mean difference (net) |
| Point estimate | 14.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -91.68 |
| upper limit | 121.33 |

Notes:

[118] - 60 hours

## Secondary: Part B: Time to Resolution of RSV-Related Signs and Symptoms

| End point title | Part B: Time to Resolution of RSV-Related Signs and Symptoms |
|---|---|

End point description:

Time to resolution was calculated for RSV-related signs and symptoms that were present at study start and was defined as the time of randomisation to the time that RSV-related signs and symptoms were absent. mITT population included all subjects who received at least 1 dose of IMP (RV521 or placebo) and had a pre-treatment positive RSV nasopharyngeal swab confirmed by the central laboratory and agreed by the project team during blind data review meeting. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 days

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Days | | | | |
| median (full range (min-max)) | 6.20 (6.1 to 6.6) | 6.20 (6.2 to 6.3) | 6.45 (5.9 to 6.8) | 3.80 (2.6 to 5.0) |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Days | | | | |
| median (full range (min-max)) | 4.90 (4.9 to 4.9) | 6.30 (4.6 to 6.9) | 6.00 (2.5 to 6.7) | 6.10 (4.1 to 6.9) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: Time to Improvement in RSV-Related Signs and Symptoms

| End point title | Part B: Time to Improvement in RSV-Related Signs and Symptoms |
|---|---|

End point description:

Time to improvement was calculated for RSV-related signs and symptoms that were classified as moderate or severe during the course of the study and was defined as the time from randomisation to the time that RSV-related signs and symptoms were mild or absent. mITT population included all subjects who received at least 1 dose of IMP (RV521 or placebo) and had a pre-treatment positive RSV nasopharyngeal swab confirmed by the central laboratory and agreed by the project team during blind data review meeting. Here, 'Number of Subjects Analysed' signifies number of subjects evaluable for this endpoint.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to 13 days

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 3 | 4 | 2 |
| Units: Days | | | | |
| median (full range (min-max)) | 2.25 (1.5 to 3.0) | 0.50 (0.5 to 6.3) | 3.15 (2.1 to 5.9) | 2.55 (1.1 to 4.0) |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Days | | | | |
| median (full range (min-max)) | 1.90 (1.9 to 1.9) | 4.35 (3.6 to 6.9) | 3.00 (1.0 to 6.0) | 6.00 (1.5 to 6.9) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Part B: RSV Clinical Scoring System Scores

| End point title | Part B: RSV Clinical Scoring System Scores |
|---|---|

End point description:

RSV clinical score was a composite score for infants with RSV infection >= 1 month of age based on 4 items (respiratory rate, wheezing, retraction of respiratory muscles and general condition). Score for each item ranged from 0 to 3 where 0=none/normal and 3=severe. Total score was calculated as sum of individual items and ranged from 0 to 12, where higher score indicated severe disease. RSV symptoms were graded as mild: score <=5, moderate: score > 5 but < 9 and severe: score >=9. mITT population was analysed. Here, 'Number of Subjects Analysed' signifies subjects evaluable for this endpoint and 'n' signifies subjects evaluable at the specified timepoints. 99999 signifies data could not be calculated due to insufficient subjects.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (pre-dose 1 on Day 1), pre-dose 3, pre-dose 5, pre-dose 7, pre-dose 9, anytime between 40 to 48 hours post-dose 10 on Day 5

| End point values | Cohort 3: Placebo | Cohort 3: RSV1 2.5 mg/kg | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 3 | 4 | 2 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline; n=2,3,4,2,1,4,5,8 | 3.5 (± 2.12) | 5.0 (± 1.73) | 6.8 (± 2.50) | 4.5 (± 6.36) |
| pre-dose 3; n=3,3,4,2,1,4,5,8 | 2.0 (± 1.73) | 4.0 (± 2.65) | 2.5 (± 1.29) | 1.0 (± 1.41) |
| pre-dose 5; n=3,3,4,2,1,4,5,8 | 1.0 (± 1.00) | 2.7 (± 2.08) | 1.8 (± 1.50) | 2.5 (± 3.54) |
| pre-dose 7; n=3,3,4,2,1,3,5,8 | 0.7 (± 0.58) | 3.0 (± 1.73) | 1.3 (± 1.50) | 2.5 (± 3.54) |
| pre-dose 9; n=1,2,2,1,1,2,4,4 | 0.0 (± 99999) | 3.5 (± 2.12) | 1.5 (± 0.71) | 1.0 (± 99999) |
| 40 to 48 hours post-dose 10; n=3,3,4,2,0,3,5,8 | 0.3 (± 0.58) | 1.0 (± 1.00) | 0.5 (± 0.58) | 0.0 (± 0.00) |

| End point values | Cohort 4: Placebo | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|---|

| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
|---|---|---|---|---|
| Number of subjects analysed | 1 | 4 | 5 | 8 |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline; n=2,3,4,2,1,4,5,8 | 8.0 (± 99999) | 6.8 (± 2.22) | 6.2 (± 3.56) | 6.0 (± 2.73) |
| pre-dose 3; n=3,3,4,2,1,4,5,8 | 4.0 (± 99999) | 5.0 (± 0.00) | 1.8 (± 1.10) | 4.3 (± 2.38) |
| pre-dose 5; n=3,3,4,2,1,4,5,8 | 3.0 (± 99999) | 3.3 (± 0.96) | 1.4 (± 1.14) | 3.9 (± 2.75) |
| pre-dose 7; n=3,3,4,2,1,3,5,8 | 1.0 (± 99999) | 1.3 (± 0.58) | 1.6 (± 0.55) | 2.3 (± 2.12) |
| pre-dose 9; n=1,2,2,1,1,2,4,4 | 1.0 (± 99999) | 2.0 (± 1.41) | 1.8 (± 0.50) | 2.3 (± 0.96) |
| 40 to 48 hours post-dose 10; n=3,3,4,2,0,3,5,8 | 99999 (± 99999) | 1.0 (± 1.00) | 1.2 (± 1.10) | 0.6 (± 0.52) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of IMP on Day 1 up to Day 7 for Part A; From start of IMP on Day 1 up to Day 12 for Part B

Adverse event reporting additional description:

Same event may appear as SAE and non-SAE, what is presented are distinct events. Event may be categorised as serious in 1 subject and as non-serious in another or 1 subject may have experienced both serious and non-serious event during study.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Cohort 1: RV521 1.0 mg/kg |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 1.0 milligram per kilogram (mg/kg) of RV521 orally on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 1: RV521 2.0 mg/kg |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.0 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 1: RV521 2.5 mg/kg |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received a single dose of 2.5 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 2: RV521 2.0 mg/kg |

Reporting group description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received a single dose of 2 mg/kg of RV521 orally on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 3: Placebo |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Reporting group title | Cohort 5: RV521 2.5 mg/kg |

Reporting group description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Reporting group title | Cohort 3: RV521 3.5 mg/kg |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 3.5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Reporting group title | Cohort 3: RV521 5 mg/kg |

Reporting group description:

Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 5 mg/kg every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Reporting group title | Cohort 4: Placebo |

Reporting group description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days.

| | |
|---|---|
| Reporting group title | Cohort 4: RV521 2.5 mg/kg |

Reporting group description:

Infants aged >=1 month to <6 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days.

| Reporting group title | Cohort 5: Placebo |
|---|---|
| Reporting group description: | |
| Infants aged >=1 month to <6 months hospitalised with RSV LRTI received placebo every 12 hours (BID) orally for 5 days. | |

| Reporting group title | Cohort 3: RSV1 2.5 mg/kg |
|---|---|
| Reporting group description: | |
| Infants aged >=6 months to <=36 months hospitalised with RSV LRTI received RV521 2.5 mg/kg every 12 hours (BID) orally for 5 days. | |

| **Serious adverse events** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Cohort 2: RV521 2.0 mg/kg | Cohort 3: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 3: RSV1 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | Cohort 1: RV521 1.0 mg/kg | Cohort 1: RV521 2.0 mg/kg | Cohort 1: RV521 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 4 / 7 (57.14%) | 3 / 3 (100.00%) |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cyanosis central | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monocyte count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Otorrhoea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 3 / 3 (100.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Post-tussive vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Anal erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 7 (14.29%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash macular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Renal and urinary disorders | | | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 7 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Cohort 2: RV521 2.0 mg/kg | Cohort 3: Placebo | Cohort 5: RV521 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 3 (33.33%) | 1 / 8 (12.50%) |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 3 (33.33%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cyanosis central | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monocyte count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post-tussive vomiting | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash macular | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 1 / 8 (12.50%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 3 (0.00%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 3 (33.33%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 3 (33.33%) | 0 / 8 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| **Non-serious adverse events** | Cohort 3: RV521 3.5 mg/kg | Cohort 3: RV521 5 mg/kg | Cohort 4: Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 1 / 1 (100.00%) |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cyanosis central | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|---|---|---|
| Post-tussive vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Rash macular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Cohort 4: RV521 2.5 mg/kg | Cohort 5: Placebo | Cohort 3: RSV1 2.5 mg/kg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 3 / 5 (60.00%) | 2 / 3 (66.67%) |
| Vascular disorders | | | |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Withdrawal syndrome | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cyanosis central | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Bacterial test positive | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Monocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Leukocytosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Post-tussive vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anal erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash macular | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Oliguria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 13 May 2019 | Inclusion of optional Study Part C.<br>Change in dosage form to dry powder blend requiring dispersal in water prior to administration and inclusion of text concerning information provided to parents/carers as to how to prepare and record administration of IMP at home.<br>Adjustment of minimum hospital stay to at least 3 days.<br>Adjustment to RSV signs and symptoms to be monitored and how these will be analysed.<br>Update to permitted concomitant medications.<br>Update to assessments to include evaluation of hydration status.<br>Clarification of duration of SAE reporting and SUSAR reporting commitment. |
| 15 January 2020 | Addition of central laboratory (ECG analysis).<br>Addition of respiratory pathogen screen of baseline nasopharyngeal swabs using BioFire assay. |
| 01 March 2021 | Change to central laboratory responsible for viral resistance emergence testing.<br>Reduction in nasopharyngeal swab sampling timepoints and rationalisation of PK sampling.<br>Clarification of subject replacement parameters in all study parts.<br>Update to study analysis populations and their definitions. |
| 31 January 2022 | Amendment to Part C study design, objectives, and endpoints.<br>Clarification of requirements for opening Cohort 5.<br>Clarification of informed consent requirements in line with local regulations.<br>Adjustment to inclusion and exclusion criteria.<br>Amendment to Part C duration of hospitalisation.<br>Revision of stopping criteria, correction of adverse reaction definition, clarification of AE severity grading and AE Part C follow-up duration in response to regulatory request.<br>Amendment to prior and concomitant medication section to clarify permitted medications/therapy and update to list of drugs affecting CYP3A4 and P-gp.<br>Introduction of ReSVinet Scale for Clinicians in Part C.<br>Clarification of study procedures and permitted time windows.<br>Clarification of information to be provided to the parent/carer at discharge.<br>Clarification of local laboratory and central laboratory safety testing.<br>Updated monitoring section to reflect changes in monitoring during COVID-19 pandemic. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported