



## Clinical trial results:

### A Phase 3 Open-label, Multicenter, Pharmacokinetics, Safety, and Efficacy Study of a Recombinant Fusion Protein Linking Coagulation Factor IX with Albumin (rIX-FP) in Previously Treated Children with Hemophilia B

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2011-006032-23  |
| Trial protocol           | AT ES CZ IT     |
| Global end of trial date | 05 October 2014 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 13 July 2016  |
| First version publication date | 21 April 2015 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | CSL654_3002 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01662531 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | CSL Behring GmbH  |
| Sponsor organisation address | Emil-von-Behring Strasse 76, Marburg, Germany, 35041                          |
| Public contact               | Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.com |
| Scientific contact           | Clinical Trial Disclosure Manager, CSL Behring, clinicaltrials@cslbehring.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001107-PIP01-10 |
| 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? | No                  |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 24 October 2014 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 05 October 2014 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

- To evaluate the pharmacokinetics (PK) of a single dose of rIX-FP.
- To evaluate the safety of rIX-FP with respect to the development of inhibitors to Factor IX (FIX) in patients with severe hemophilia B (FIX:  $\leq 2\%$ ).

Protection of trial subjects:

To ensure the safety of the subjects, this study did not start until after 50 exposure days (EDs) were accrued in at least 10 subjects  $\geq 12$  years of age in the rIX-FP clinical program. Study enrollment was limited to subjects 6 to  $<12$  years of age with at least 150 EDs to previous FIX products and subjects  $<6$  years of age with at least 50 EDs to previous FIX products. Subjects with a history (including family history) of inhibitors against FIX were excluded to further reduce the risk of inhibitor formation during the study.

This study was carried out in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice guidelines, the Declaration of Helsinki (2008), and standard operating procedures for clinical research and development at CSL Behring (CSLB).

The study protocol and all amendments were approved by the Independent Ethics Committee(s) (IECs) / Institutional Review Board(s) (IRBs) of the participating centers.

Before undergoing screening procedures for possible enrollment into the study, subjects and/or their legally acceptable representative were informed, in an understandable form, about the nature, scope, and possible consequences of the study. This information was given orally to subjects by a physician or medically qualified person; written information about the study was also provided in a Subject Information Sheet.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 16 January 2013 |
| 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 | Spain: 1          |
| Country: Number of subjects enrolled | Austria: 2        |
| Country: Number of subjects enrolled | Czech Republic: 3 |
| Country: Number of subjects enrolled | France: 6         |
| Country: Number of subjects enrolled | Germany: 3        |
| Country: Number of subjects enrolled | Italy: 3          |
| Country: Number of subjects enrolled | Australia: 2      |
| Country: Number of subjects enrolled | Canada: 1         |
| Country: Number of subjects enrolled | Israel: 4         |

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Russian Federation: 2 |
| Worldwide total number of subjects   | 27                    |
| EEA total number of subjects         | 18                    |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 3  |
| Children (2-11 years)                     | 24 |
| 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:

Of the 18 sites that were activated, subjects were enrolled from 17 sites in 10 countries.

### Pre-assignment

Screening details:

Patients <12 years of age with severe hemophilia B (FIX activity of  $\leq 2\%$ ) were planned to be enrolled in the study, including 11 to 12 subjects in each age group (6 to <12 years and <6 years of age).

Of 29 subjects screened, 27 subjects were enrolled and treated with rIX-FP.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |        |
|-----------|--------|
| Arm title | rIX-FP |
|-----------|--------|

Arm description:

All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.

Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | Recombinant Coagulation Factor IX Albumin Fusion Protein |
| Investigational medicinal product code | CSL654   |
| Other name                             | rIX-FP   |
| Pharmaceutical forms                   | Powder for concentrate for solution for infusion         |
| Routes of administration               | Intravenous use  |

Dosage and administration details:

Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria.

|                                       |        |
|---------------------------------------|--------|
| <b>Number of subjects in period 1</b> | rIX-FP |
| Started                               | 27     |
| Completed                             | 27     |

## Baseline characteristics

### Reporting groups

|   |        |
|---|--------|
| Reporting group title   | rIX-FP |
| Reporting group description:  |        |
| All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.  |        |
| Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria. |        |

| Reporting group values  | rIX-FP        | Total |  |
|---|---------------|-------|--|
| Number of subjects  | 27            | 27    |  |
| Age categorical<br>Units: Subjects                                      |               |       |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 5.9<br>± 2.93 | -     |  |
| Gender categorical<br>Units: Subjects                                   |               |       |  |
| Female  | 0             | 0     |  |
| Male  | 27            | 27    |  |

### Subject analysis sets

|   |                    |
|---|--------------------|
| Subject analysis set title  | Age < 6 Years      |
| Subject analysis set type   | Sub-group analysis |
| Subject analysis set description:   |                    |
| All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.  |                    |
| Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria. |                    |
| Subject analysis set title  | Age 6 to <12 Years |
| Subject analysis set type   | Sub-group analysis |
| Subject analysis set description:   |                    |
| All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.  |                    |
| Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria. |                    |

| Reporting group values  | Age < 6 Years | Age 6 to <12 Years |  |
|---|---------------|--------------------|--|
| Number of subjects  | 12            | 15                 |  |
| Age categorical<br>Units: Subjects                                      |               |                    |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 3.2<br>± 1.7  | 8.1<br>± 1.41      |  |

|                    |    |    |  |
|--------------------|----|----|--|
| Gender categorical |    |    |  |
| Units: Subjects    |    |    |  |
| Female             | 0  | 0  |  |
| Male               | 12 | 15 |  |

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## End points

### End points reporting groups

|  |                    |
|--|--------------------|
| Reporting group title  | rIX-FP             |
| Reporting group description:<br>All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.<br>Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria.      |                    |
| Subject analysis set title   | Age < 6 Years      |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:<br>All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.<br>Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria. |                    |
| Subject analysis set title   | Age 6 to <12 Years |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:<br>All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.<br>Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria. |                    |

### Primary: Incremental recovery following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product

|  |  |
|--|--|
| End point title  | Incremental recovery following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product <sup>[1]</sup> |
| End point description:<br>Incremental recovery (IU/dL/IU/kg) is defined as the FIX activity (IU/dL) obtained 30 minutes following infusion, per dose of (IU/kg) infusion.<br>FIX activity was measured at a central laboratory using validated one-stage clotting method.<br>Recovery values were baseline-corrected for pre-infusion plasma FIX activity.<br>Incremental recovery was measured following a single intravenous dose of 50 IU/kg rIX-FP on Day 1.<br>Analysis of previous FIX product was conducted at the beginning of the study in a subset of subjects who had no historical PK data of their previous FIX product. For the PK assessment, the previous FIX product was administered by IV infusion after approximately 4 days following the last FIX treatment, prior to any dosing of rIX-FP.<br>The formal PK population consisted of subjects who received at least 1 dose of rIX-FP for PK assessment and for whom a sufficient number of analyzable PK samples had been obtained to permit the evaluation of the PK profile of rIX-FP. |  |
| End point type   | Primary  |
| End point timeframe:<br>30 minutes after infusion  |  |

#### 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: No statistical analyses were conducted for this end point.

| End point values                     | rIX-FP             | Age < 6 Years        | Age 6 to <12 Years   |  |
|--------------------------------------|--------------------|----------------------|----------------------|--|
| Subject group type                   | Reporting group    | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed          | 27                 | 12                   | 15                   |  |
| Units: (IU/dL)/(IU/kg)               |                    |                      |                      |  |
| arithmetic mean (standard deviation) |                    |                      |                      |  |
| rIX-FP Assessment (n=27, 12, 15)     | 1.0114 (± 0.22711) | 0.9506 (± 0.20432)   | 1.06 (± 0.23934)     |  |

|                                      |                         |                        |                         |  |
|--------------------------------------|-------------------------|------------------------|-------------------------|--|
| Previous FIX Assessment (n=17, 8, 9) | 0.7379 ( $\pm$ 0.19768) | 0.6764 ( $\pm$ 0.1398) | 0.7925 ( $\pm$ 0.23219) |  |
|--------------------------------------|-------------------------|------------------------|-------------------------|--|

## Statistical analyses

No statistical analyses for this end point

### Primary: Half-life (t<sub>1/2</sub>) following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product

|                 |   |
|-----------------|---|
| End point title | Half-life (t <sub>1/2</sub> ) following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product <sup>[2]</sup> |
|-----------------|---|

End point description:

FIX activity was measured at a central laboratory using validated one-stage clotting method. FIX levels were not corrected for baseline values.

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

End point timeframe:

Pre-dose, 30 minutes, 3, 24, 48, 72 120, 168, 240 and 336 hours post-dose

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: No statistical analyses were conducted for this end point.

| End point values                     | rIX-FP                   | Age < 6 Years             | Age 6 to <12 Years        |  |
|--------------------------------------|--------------------------|---------------------------|---------------------------|--|
| Subject group type                   | Reporting group          | Subject analysis set      | Subject analysis set      |  |
| Number of subjects analysed          | 27                       | 12                        | 15                        |  |
| Units: hours                         |                          |                           |                           |  |
| arithmetic mean (standard deviation) |                          |                           |                           |  |
| rIX-FP Assessment (n=26, 11, 15)     | 91.4492 ( $\pm$ 15.9754) | 89.6124 ( $\pm$ 11.17364) | 92.7962 ( $\pm$ 19.02537) |  |
| Previous FIX Assessment (n=16, 7, 9) | 18.6291 ( $\pm$ 6.15551) | 19.8816 ( $\pm$ 8.01073)  | 17.655 ( $\pm$ 4.52497)   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Area under the concentration versus time curve from time point zero to the last sample with quantifiable drug concentration (AUClast)

|                 |  |
|-----------------|--|
| End point title | Area under the concentration versus time curve from time point zero to the last sample with quantifiable drug concentration (AUClast) <sup>[3]</sup> |
|-----------------|--|

End point description:

AUClast following a single intravenous dose of 50 IU/kg rIXFP or previous FIX product.

FIX activity was measured at a central laboratory using validated one-stage clotting method. FIX levels were not corrected for baseline values.

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

End point timeframe:

Pre-dose, 30 minutes, 3, 24, 48, 72 120, 168, 240 and 336 hours post-dose



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: No statistical analyses were conducted for this end point.

| End point values                     | rIX-FP                | Age < 6 Years         | Age 6 to <12 Years    |  |
|--------------------------------------|-----------------------|-----------------------|-----------------------|--|
| Subject group type                   | Reporting group       | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed          | 27                    | 12                    | 15                    |  |
| Units: IU*hr/dL                      |                       |                       |                       |  |
| arithmetic mean (standard deviation) |                       |                       |                       |  |
| rIX-FP Assessment (n=27, 12, 15)     | 4156.704 (± 1204.095) | 3891.482 (± 1252.994) | 4368.881 (± 1162.1)   |  |
| Previous FIX Assessment (n=16, 7, 9) | 718.9386 (± 230.5288) | 676.5414 (± 316.9138) | 751.9143 (± 146.7045) |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Clearance for FIX activity following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product

|                 |  |
|-----------------|--|
| End point title | Clearance for FIX activity following a single intravenous dose of 50 IU/kg rIX-FP or previous FIX product <sup>[4]</sup> |
|-----------------|--|

End point description:

FIX activity was measured at a central laboratory using validated one-stage clotting method. FIX levels were not corrected for baseline values. Clearance is normalized for body weight.

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

End point timeframe:

Pre-dose, 30 minutes, 3, 24, 48, 72 120, 168, 240 and 336 hours post-dose

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: No statistical analyses were conducted for this end point.

| End point values                     | rIX-FP             | Age < 6 Years        | Age 6 to <12 Years   |  |
|--------------------------------------|--------------------|----------------------|----------------------|--|
| Subject group type                   | Reporting group    | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed          | 27                 | 12                   | 15                   |  |
| Units: mL/hr/kg                      |                    |                      |                      |  |
| arithmetic mean (standard deviation) |                    |                      |                      |  |
| rIX-FP Assessment (n=26, 11, 15)     | 1.1119 (± 0.31373) | 1.1841 (± 0.32924)   | 1.0589 (± 0.30203)   |  |
| Previous FIX Assessment (n=16, 7, 9) | 6.4007 (± 2.14434) | 7.1576 (± 2.78944)   | 5.8119 (± 1.37641)   |  |

## Statistical analyses

No statistical analyses for this end point

**Primary: Number of subjects who developed inhibitors to FIX or antibodies to rIX-FP**

|  |   |
|--|---|
| End point title  | Number of subjects who developed inhibitors to FIX or antibodies to rIX-FP <sup>[5]</sup> |
| End point description:<br>Inhibitor formation was defined as any inhibitor ( $\geq 0.6$ BU/mL) identified and confirmed by retesting. Antibodies to rIX-FP were measured using a direct-binding enzyme-linked immunosorbent assay (ELISA).                 |   |
| End point type   | Primary   |
| End point timeframe:<br>12 months  |   |
| Notes:<br>[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.<br>Justification: No statistical analyses were conducted for this end point. |   |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | rIX-FP          |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 27              |  |  |  |
| Units: participants         |                 |  |  |  |
| FIX inhibitors              | 0               |  |  |  |
| Antibodies to rIX-FP        | 0               |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of subjects with treatment-related adverse events**

|                                   |  |
|-----------------------------------|--|
| End point title                   | Number of subjects with treatment-related adverse events |
| End point description:            |  |
| End point type                    | Secondary  |
| End point timeframe:<br>12 months |  |

|                                 |                 |  |  |  |
|---------------------------------|-----------------|--|--|--|
| <b>End point values</b>         | rIX-FP          |  |  |  |
| Subject group type              | Reporting group |  |  |  |
| Number of subjects analysed     | 27              |  |  |  |
| Units: participants             |                 |  |  |  |
| Any adverse event               | 26              |  |  |  |
| Treatment-related adverse event | 0               |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

### Secondary: Number of rIX-FP Infusions required to achieve hemostasis

|   |   |
|---|---|
| End point title   | Number of rIX-FP Infusions required to achieve hemostasis |
| End point description:<br>For each bleeding episode that required treatment, the number of episodes that required one, two or more than two infusions of rIX-FP to achieve hemostasis |   |
| End point type  | Secondary   |
| End point timeframe:<br>12 months   |   |

| End point values            | rIX-FP          | Age < 6 Years        | Age 6 to <12 Years   |  |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type          | Reporting group | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed | 27              | 12                   | 15                   |  |
| Units: bleeding episodes    |                 |                      |                      |  |
| 1 infusion                  | 94              | 40                   | 54                   |  |
| 2 infusions                 | 9               | 5                    | 4                    |  |
| > 2 infusions               | 3               | 0                    | 3                    |  |
| 1 or 2 infusions            | 103             | 45                   | 58                   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Consumption of rIX-FP during routine prophylaxis

|  |  |
|--|--|
| End point title  | Consumption of rIX-FP during routine prophylaxis |
| End point description:<br>Consumption of rIX-FP during routine prophylaxis is expressed as the total prophylaxis dose per month. |  |
| End point type   | Secondary  |
| End point timeframe:<br>12 months  |  |

| End point values                     | rIX-FP                  | Age < 6 Years            | Age 6 to <12 Years       |  |
|--------------------------------------|-------------------------|--------------------------|--------------------------|--|
| Subject group type                   | Reporting group         | Subject analysis set     | Subject analysis set     |  |
| Number of subjects analysed          | 27                      | 12                       | 15                       |  |
| Units: IU/kg/month                   |                         |                          |                          |  |
| arithmetic mean (standard deviation) | 205.071 ( $\pm$ 41.155) | 213.517 ( $\pm$ 44.3848) | 198.314 ( $\pm$ 38.5693) |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 months

Adverse event reporting additional description:

Treatment-emergent AEs (TEAEs), defined as AEs present prior to the first dose of rIX-FP that subsequently worsened in severity or those that were not present prior to the first dose but subsequently appeared are summarized.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | rIX-FP |
|-----------------------|--------|

Reporting group description:

All subjects received a single dose of 50 IU/kg rIX-FP on Day 1 during the pharmacokinetic phase of the study.

Subjects received weekly (7-day) routine prophylaxis treatment with an initial weekly dose of 35 to 50 IU/kg rIX-FP, which may have been adjusted based on protocol-specified criteria.

| Serious adverse events                            | rIX-FP          |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 4 / 27 (14.81%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |
| Injury, poisoning and procedural complications    |                 |  |  |
| Forearm fracture                                  |                 |  |  |
| subjects affected / exposed                       | 1 / 27 (3.70%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Head injury                                       |                 |  |  |
| subjects affected / exposed                       | 1 / 27 (3.70%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Tongue injury                                     |                 |  |  |
| subjects affected / exposed                       | 1 / 27 (3.70%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Musculoskeletal and connective tissue             |                 |  |  |

|   |                |  |  |
|---|----------------|--|--|
| disorders                                       |                |  |  |
| arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 1 / 27 (3.70%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Groin pain                                      |                |  |  |
| subjects affected / exposed                     | 1 / 27 (3.70%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | rIX-FP           |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 23 / 27 (85.19%) |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Contusion   |                  |  |  |
| subjects affected / exposed                           | 5 / 27 (18.52%)  |  |  |
| occurrences (all)                                     | 9                |  |  |
| Injury  |                  |  |  |
| subjects affected / exposed                           | 2 / 27 (7.41%)   |  |  |
| occurrences (all)                                     | 4                |  |  |
| Head injury   |                  |  |  |
| subjects affected / exposed                           | 2 / 27 (7.41%)   |  |  |
| occurrences (all)                                     | 2                |  |  |
| Nervous system disorders                              |                  |  |  |
| Headache  |                  |  |  |
| subjects affected / exposed                           | 2 / 27 (7.41%)   |  |  |
| occurrences (all)                                     | 4                |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Pyrexia   |                  |  |  |
| subjects affected / exposed                           | 9 / 27 (33.33%)  |  |  |
| occurrences (all)                                     | 14               |  |  |
| Blood and lymphatic system disorders                  |                  |  |  |

|   |  |  |  |
|---|--|--|--|
| Anaemia<br>subjects affected / exposed<br>occurrences (all)   | 2 / 27 (7.41%)<br>2  |  |  |
| Gastrointestinal disorders<br>Dental discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Toothache<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 2 / 27 (7.41%)<br>2<br><br>2 / 27 (7.41%)<br>2<br><br>2 / 27 (7.41%)<br>2<br><br>2 / 27 (7.41%)<br>2 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)  | 4 / 27 (14.81%)<br>4<br><br>2 / 27 (7.41%)<br>2  |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 3 / 27 (11.11%)<br>3<br><br>2 / 27 (7.41%)<br>2  |  |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Bronchitis  | 4 / 27 (14.81%)<br>6   |  |  |

|                                   |                 |  |  |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed       | 3 / 27 (11.11%) |  |  |
| occurrences (all)                 | 4               |  |  |
| Ear infection                     |                 |  |  |
| subjects affected / exposed       | 3 / 27 (11.11%) |  |  |
| occurrences (all)                 | 4               |  |  |
| Gastroenteritis                   |                 |  |  |
| subjects affected / exposed       | 3 / 27 (11.11%) |  |  |
| occurrences (all)                 | 3               |  |  |
| Pharyngitis                       |                 |  |  |
| subjects affected / exposed       | 2 / 27 (7.41%)  |  |  |
| occurrences (all)                 | 3               |  |  |
| Viral infection                   |                 |  |  |
| subjects affected / exposed       | 2 / 27 (7.41%)  |  |  |
| occurrences (all)                 | 3               |  |  |
| Molluscum contagiosum             |                 |  |  |
| subjects affected / exposed       | 2 / 27 (7.41%)  |  |  |
| occurrences (all)                 | 2               |  |  |
| Upper respiratory tract infection |                 |  |  |
| subjects affected / exposed       | 2 / 27 (7.41%)  |  |  |
| occurrences (all)                 | 2               |  |  |



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported