



## Clinical trial results:

### An Open-label, Single Arm Study to Evaluate the Pharmacokinetics of a Single Dose of Intravenous Difelikefalin in Adolescents Aged 12 to 17 Years on Haemodialysis

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-000894-94 |
| Trial protocol           | IT             |
| Global end of trial date | 30 May 2023    |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 15 December 2023 |
| First version publication date | 15 December 2023 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | KOR-PED-201 |
|-----------------------|-------------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Vifor Fresenius Medical Care Renal Pharma Ltd.   |
| Sponsor organisation address | Rechenstrasse 37, St. Gallen, Switzerland, CH-9014   |
| Public contact               | Clinical Trial Information Desk, Vifor Fresenius Medical Care Renal Pharma Ltd., +41 588518000, clinicaltrials@csllbehring.com |
| Scientific contact           | Clinical Trial Information Desk, Vifor Fresenius Medical Care Renal Pharma Ltd., +41 588518000, clinicaltrials@csllbehring.com |

Notes:

##### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-002565-PIP02-19 |
| 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                       | 03 August 2023 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 30 May 2023    |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 30 May 2023    |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetic (PK) profile of a single dose of difelikefalin in adolescent subjects aged 12 to 17 years on haemodialysis (HD).

Protection of trial subjects:

The study was conducted according to the principles of the World Medical Association's Declaration of Helsinki, and the ICH guidelines for Good Clinical Practices (GCP) as amended.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 22 November 2021 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Lebanon: 5        |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Worldwide total number of subjects   | 8                 |
| EEA total number of subjects         | 0                 |

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)  | 0 |
| Children (2-11 years)                     | 0 |
| Adolescents (12-17 years)                 | 8 |
| 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:

The screening visit occurred within 21 calendar days prior to the start of study drug administration.

### Period 1

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

### Arms

|  |   |
|--|---|
| Arm title                              | Difelikefalin                           |
| Arm description: -                     |   |
| Arm type                               | Experimental                            |
| Investigational medicinal product name | Difelikefalin solution (IV formulation) |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Injection                               |
| Routes of administration               | Intravenous use                         |

Dosage and administration details:

Individual IV doses of difelikefalin were based on subject body weight (0.5 µg/kg dry body weight) and prepared by withdrawing subject-specific volume of study drug with sterile, single-use 1 ml Plastipak syringe (or equivalent) and sterile single-use needles.

Difelikefalin was administered by IV bolus injection within 15 minutes following the end of the dialysis on the scheduled drug administration day. Difelikefalin administration could be done by injection into the dialysis venous line (e.g., into the venous port) or by direct injection into a vein. If the dialysis line was used, following the bolus, the venous line was flushed with at least 10 ml of normal saline.

| Number of subjects in period 1 | Difelikefalin |
|--------------------------------|---------------|
| Started                        | 8             |
| Completed                      | 8             |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Difelikefalin |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                             | Difelikefalin | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 8             | 8     |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 8             | 8     |  |
| Adults (18-64 years)                               | 0             | 0     |  |
| From 65-84 years                                   | 0             | 0     |  |
| 85 years and over                                  | 0             | 0     |  |
| Age continuous                                     |               |       |  |
| Units: years                                       |               |       |  |
| arithmetic mean                                    | 15.0          |       |  |
| standard deviation                                 | ± 2.14        | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 5             | 5     |  |
| Male   | 3             | 3     |  |

### Subject analysis sets

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | Pharmacokinetic Analysis Population |
|----------------------------|-------------------------------------|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

The PK evaluable population includes all subjects who received the dose of study drug and have sufficient plasma concentrations for PK analysis

| Reporting group values                             | Pharmacokinetic Analysis Population |  |  |
|--|-------------------------------------|--|--|
| Number of subjects                                 | 7                                   |  |  |
| Age categorical                                    |                                     |  |  |
| Units: Subjects                                    |                                     |  |  |
| In utero   | 0                                   |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                                   |  |  |
| Newborns (0-27 days)                               | 0                                   |  |  |
| Infants and toddlers (28 days-23 months)           | 0                                   |  |  |
| Children (2-11 years)                              | 0                                   |  |  |
| Adolescents (12-17 years)                          | 7                                   |  |  |

|                      |        |  |  |
|----------------------|--------|--|--|
| Adults (18-64 years) | 0      |  |  |
| From 65-84 years     | 0      |  |  |
| 85 years and over    | 0      |  |  |
| Age continuous       |        |  |  |
| Units: years         |        |  |  |
| arithmetic mean      | 15.1   |  |  |
| standard deviation   | ± 2.27 |  |  |
| Gender categorical   |        |  |  |
| Units: Subjects      |        |  |  |
| Female               | 4      |  |  |
| Male                 | 3      |  |  |

## End points

### End points reporting groups

|   |                                     |
|---|-------------------------------------|
| Reporting group title   | Difelikefalin                       |
| Reporting group description: -  |                                     |
| Subject analysis set title  | Pharmacokinetic Analysis Population |
| Subject analysis set type   | Full analysis                       |
| Subject analysis set description:   |                                     |
| The PK evaluable population includes all subjects who received the dose of study drug and have sufficient plasma concentrations for PK analysis |                                     |

### Primary: Cmax

|                        |                     |
|------------------------|---------------------|
| End point title        | Cmax <sup>[1]</sup> |
| End point description: |                     |
| End point type         | Primary             |
| End point timeframe:   |                     |
| Day 1 to 3             |                     |

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 statistics were included for this PK parameter.

|                                      |                                     |  |  |  |
|--------------------------------------|-------------------------------------|--|--|--|
| <b>End point values</b>              | Pharmacokinetic Analysis Population |  |  |  |
| Subject group type                   | Subject analysis set                |  |  |  |
| Number of subjects analysed          | 7                                   |  |  |  |
| Units: ng/mL                         |                                     |  |  |  |
| arithmetic mean (standard deviation) | 6.03 (± 1.81)                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: AUC0-48

|                        |                        |
|------------------------|------------------------|
| End point title        | AUC0-48 <sup>[2]</sup> |
| End point description: |                        |
| End point type         | Primary                |
| End point timeframe:   |                        |
| Day 1 to 3             |                        |

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: Only descriptive statistics were included for this PK parameter.

| End point values                     | Pharmacokinetic Analysis Population |  |  |  |
|--------------------------------------|-------------------------------------|--|--|--|
| Subject group type                   | Subject analysis set                |  |  |  |
| Number of subjects analysed          | 7                                   |  |  |  |
| Units: h*ng/mL                       |                                     |  |  |  |
| arithmetic mean (standard deviation) | 63.4 (± 17.4)                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: AUCinf

|                 |                       |
|-----------------|-----------------------|
| End point title | AUCinf <sup>[3]</sup> |
|-----------------|-----------------------|

End point description:

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

End point timeframe:

Day 1 to 3

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 statistics were included for this PK parameter.

| End point values                     | Pharmacokinetic Analysis Population |  |  |  |
|--------------------------------------|-------------------------------------|--|--|--|
| Subject group type                   | Subject analysis set                |  |  |  |
| Number of subjects analysed          | 7                                   |  |  |  |
| Units: h*ng/mL                       |                                     |  |  |  |
| arithmetic mean (standard deviation) | 72.5 (± 23.7)                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

from Baseline to the End of the trial

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Difelikefalin |
|-----------------------|---------------|

Reporting group description: -

| Serious adverse events                            | Difelikefalin |  |  |
|---|---------------|--|--|
| Total subjects affected by serious adverse events |               |  |  |
| subjects affected / exposed                       | 0 / 8 (0.00%) |  |  |
| number of deaths (all causes)                     | 0             |  |  |
| number of deaths resulting from adverse events    | 0             |  |  |

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

| Non-serious adverse events                            | Difelikefalin  |  |  |
|---|----------------|--|--|
| Total subjects affected by non-serious adverse events |                |  |  |
| subjects affected / exposed                           | 1 / 8 (12.50%) |  |  |
| Nervous system disorders                              |                |  |  |
| Dizziness   |                |  |  |
| subjects affected / exposed                           | 1 / 8 (12.50%) |  |  |
| occurrences (all)                                     | 1              |  |  |
| Headache  |                |  |  |
| subjects affected / exposed                           | 1 / 8 (12.50%) |  |  |
| occurrences (all)                                     | 1              |  |  |



## 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