



## Clinical trial results:

### An Open-Label Phase II Study in anti-GBM disease (Goodpasture's disease) with Adverse Renal Prognosis to Evaluate the Efficacy and Safety of IdeS --GOOD-IDES

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-004082-39 |
| Trial protocol           | SE DK AT FR    |
| Global end of trial date | 24 July 2020   |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 11 January 2022 |
| First version publication date | 11 January 2022 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | GOOD-IDES-01 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03157037 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Linköping University   |
| Sponsor organisation address | Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden, SE-581 83 |
| Public contact               | Mårten Segelmark, Linköping University, +46 10103 2297 , marten.segelmark@liu.se                       |
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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? | No |

Notes:

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## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 23 November 2021 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 24 July 2020     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 24 July 2020     |
| Was the trial ended prematurely?                     | No               |

Notes:

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## General information about the trial

Main objective of the trial:

The primary efficacy objective is to evaluate the efficacy of an IdeS based regimen to salvage independent renal function defined as no need for dialysis at 6 months and after IdeS treatment.

Protection of trial subjects:

Details of the goals of the research and the risk and benefits of the protocol were reviewed with each potential study subject.

In the event of adverse effects from the study, full resources of the hospital were available to intervene as medically necessary.

Licensed physicians expert in the care of patients with vasculitis were available at all times at each study site.

To mitigate the risk of infections all patients received antibiotic prophylaxis.

Prophylactic medication against *Pneumocystis jiroveci* pneumonia (PCP) was strongly recommended.

Before administration of imlifidase all patients received solu-medrol and loratadine (or equivalent).

All patients received glucocorticoids as part of standard-of-care. Prophylaxis against peptic ulcers and osteoporosis was given at the discretion of the investigator.

All patients were treated with cyclophosphamide and were therefore monitored for full blood counts according to local practice with a minimum schedule recommended in the study protocol.

Background therapy:

All patients received standard-of-care consisting of plasma exchange (PLEX), glucocorticoids (GC) and cyclophosphamide (CYC), as detailed below:

PLEX: Administered according to local practice, and given at a dose considered necessary to keep anti-GBM antibodies below a toxic level. A standard session usually consisted of 60 ml/kg (based on actual body weight) using albumin (3-5% with or without crystalloid) as a replacement solution. More than 36 hours had to pass after administration of imlifidase before PLEX could be initiated. More than 15 hours following an IV dose of CYC had to pass before PLEX could be given and more than 12 hours if CYC was administered orally. On days when PLEX was given CYC was given after completed PLEX.

GC: Commenced with IV methylprednisolone as 3 daily pulse doses. Each pulse was between 0.5 g and 1 g at the discretion of the investigator. Any dose given to the patient prior to study inclusion was subtracted from the total dose. Additional pulses of methyl prednisolone were allowed to curb resistant pulmonary haemorrhage. Oral GC therapy with prednisolone (dosing according to local practice) was initiated after stopping methylprednisolone. Oral GC was given as a single daily dose. An equivalent daily IV dose applied for patients intolerant to oral GC or if oral GC was contraindicated.

CYC: Induction therapy with CYC was prescribed for at least 13 weeks in patients with independent renal function, but could be withdrawn earlier in patients considered to have reached end-stage renal disease. The study protocol allowed the use of either IV or oral CYC. Concomitant use of mesna was optional and at the discretion of the investigator.

Evidence for comparator:

N/A

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 16 June 2017 |
| 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 | Sweden: 4  |
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | France: 5  |
| Worldwide total number of subjects   | 15         |
| EEA total number of subjects         | 15         |

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)                 | 0 |
| Adults (18-64 years)                      | 8 |
| From 65 to 84 years                       | 7 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited between 16-Jun-2017 and 22-Jan-2020.

### Pre-assignment

Screening details:

A total of 26 patients were screened and 15 were enrolled in the study. Five patients were not eligible due to an eGFR above 15 mL/min/1.73 m<sup>2</sup> and another 6 patients were excluded based on one or more exclusion criteria.

### Period 1

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

Blinding implementation details:

N/A

### Arms

|           |              |
|-----------|--------------|
| Arm title | All patients |
|-----------|--------------|

Arm description:

All 15 patients (i.e., both patients who were dialysis dependent and patients who were dialysis independent at baseline)

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Imlifidase  |
| Investigational medicinal product code |   |
| Other name                             | IdeS, IgG endopeptidase   |
| Pharmaceutical forms                   | Concentrate for solution for infusion, Powder for solution for infusion |
| Routes of administration               | Intravenous use   |

Dosage and administration details:

After dilution imlifidase was administered as an IV infusion over 30 minutes using a syringe or an infusion bag, an infusion pump and a particle filter.

All patients received a dose of 0.25 mg/kg.

The protocol allowed slowing down or stopping and restarting the infusion if required.

|                                       |              |
|---------------------------------------|--------------|
| <b>Number of subjects in period 1</b> | All patients |
| Started                               | 15           |
| Completed                             | 14           |
| Not completed                         | 1            |
| Adverse event, serious fatal          | 1            |

## Baseline characteristics

### Reporting groups

| Reporting group title          | Overall trial |
|--------------------------------|---------------|
| Reporting group description: - |               |

| Reporting group values                             | Overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 15            | 15    |  |
| 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)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 8             | 8     |  |
| From 65-84 years                                   | 7             | 7     |  |
| 85 years and over                                  | 0             | 0     |  |
| Age continuous                                     |               |       |  |
| Units: years                                       |               |       |  |
| arithmetic mean                                    | 61            |       |  |
| full range (min-max)                               | 19 to 77      | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 6             | 6     |  |
| Male   | 9             | 9     |  |
| Dialysis status                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| Dialysis   | 10            | 10    |  |
| Not on dialysis but eGFR <15ml/min/1.73m2          | 5             | 5     |  |
| Occurrence of pulmonary symptoms                   |               |       |  |
| Units: Subjects                                    |               |       |  |
| Yes  | 9             | 9     |  |
| No   | 3             | 3     |  |
| Not reported                                       | 3             | 3     |  |
| Double positive for Anti-GBM antibodies and ANCA   |               |       |  |
| Units: Subjects                                    |               |       |  |
| Yes  | 6             | 6     |  |
| No   | 9             | 9     |  |
| Time since anti-GBM diagnosis                      |               |       |  |
| Units: Days  |               |       |  |
| median   | 2             |       |  |
| full range (min-max)                               | 0 to 40       | -     |  |
| Anti-GBM concentration                             |               |       |  |
| Units: U/mL  |               |       |  |

|   |                    |   |  |
|---|--------------------|---|--|
| median<br>full range (min-max)  | 130.0<br>2 to 1090 | - |  |
| Time since first renal symptom<br>Units: Days<br>median<br>full range (min-max)     | 10<br>4 to 76      | - |  |
| Time since first pulmonary symptom<br>Units: Days<br>median<br>full range (min-max) | 32<br>1 to 113     | - |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | All patients                              |
| Reporting group description:<br>All 15 patients (i.e., both patients who were dialysis dependent and patients who were dialysis independent at baseline) |   |
| Subject analysis set title   | Dialysis Dependent Patients at Baseline   |
| Subject analysis set type  | Sub-group analysis                        |
| Subject analysis set description:<br>Subgroup of all patients who were on dialysis at baseline   |   |
| Subject analysis set title   | Dialysis Independent Patients at Baseline |
| Subject analysis set type  | Sub-group analysis                        |
| Subject analysis set description:<br>Subgroup of all patients who were not on dialysis at baseline   |   |

### Primary: Proportion of Patients with Independent Renal Function at 6 Months

|  |   |
|--|---|
| End point title  | Proportion of Patients with Independent Renal Function at 6 Months <sup>[1]</sup> |
| End point description:<br>Number of patients without need for dialysis at 6 months. A patient with independent renal function is defined as a patient without need for dialysis.   |   |
| End point type   | Primary   |
| End point timeframe:<br>6 months after imlifidase administration   |   |
| Notes:<br>[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.<br>Justification: No statistical analysis was specified. This study is a single arm study. |   |

| End point values            | All patients    | Dialysis Dependent Patients at Baseline | Dialysis Independent Patients at Baseline |  |
|-----------------------------|-----------------|---|---|--|
| Subject group type          | Reporting group | Subject analysis set                    | Subject analysis set                      |  |
| Number of subjects analysed | 15              | 10                                      | 5   |  |
| Units: Patients             | 10              | 5                                       | 5   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of Patients with Independent Renal Function at 3 Months

|  |  |
|--|--|
| End point title  | Proportion of Patients with Independent Renal Function at 3 Months |
| End point description:<br>Number of patients without need for dialysis at 3 months. A patient with independent renal function is defined as a patient without need for dialysis. |  |

|  |           |
|--|-----------|
| End point type                           | Secondary |
| End point timeframe:                     |           |
| 3 months after imlifidase administration |           |

| End point values            | All patients    | Dialysis<br>Dependent<br>Patients at<br>Baseline | Dialysis<br>Independent<br>Patients at<br>Baseline |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group | Subject analysis set                             | Subject analysis set                               |  |
| Number of subjects analysed | 15              | 10   | 5  |  |
| Units: Patients             | 9               | 4  | 5  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Renal Function at 3 Months as Measured by eGFR

|   |  |
|---|--|
| End point title   | Renal Function at 3 Months as Measured by eGFR |
| End point description:  |  |
| eGFR is a measure of kidney function. eGFR has been calculated based on p-creatinine according to the modification of diet in renal disease (MDRD) equation. eGFR for a kidney with normal function is above 90 mL/min/1.73m <sup>2</sup> . Reduced kidney function is characterised by a decreased eGFR value. |  |
| End point type  | Secondary                                      |
| End point timeframe:  |  |
| 3 months after imlifidase administration  |  |

| End point values                     | All patients    | Dialysis<br>Dependent<br>Patients at<br>Baseline | Dialysis<br>Independent<br>Patients at<br>Baseline |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group | Subject analysis set                             | Subject analysis set                               |  |
| Number of subjects analysed          | 7               | 3  | 4  |  |
| Units: mL/min/1.73m <sup>2</sup>     |                 |  |  |  |
| arithmetic mean (standard deviation) | 23.8 (± 8.9)    | 20.3 (± 4.7)                                     | 26.5 (± 11.0)                                      |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Renal Function at 6 Months as Measured by eGFR

|  |  |
|--|--|
| End point title  | Renal Function at 6 Months as Measured by eGFR |
| End point description:   |  |
| eGFR is a measure of kidney function. eGFR has been calculated based on p-creatinine according to the modification of diet in renal disease (MDRD) equation. eGFR for a kidney with normal function is above |  |



90 mL/min/1.73m<sup>2</sup>. Reduced kidney function is characterised by a decreased eGFR value.

|  |           |
|--|-----------|
| End point type                           | Secondary |
| End point timeframe:                     |           |
| 6 months after imlifidase administration |           |

| End point values                     | All patients    | Dialysis Dependent Patients at Baseline | Dialysis Independent Patients at Baseline |  |
|--------------------------------------|-----------------|---|---|--|
| Subject group type                   | Reporting group | Subject analysis set                    | Subject analysis set                      |  |
| Number of subjects analysed          | 10              | 5                                       | 5   |  |
| Units: mL/min/1.73m <sup>2</sup>     |                 |   |   |  |
| arithmetic mean (standard deviation) | 30.9 (± 13.9)   | 24.8 (± 6.6)                            | 36.9 (± 17.3)                             |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Renal Function over Time as Measured by eGFR

|   |  |
|---|--|
| End point title   | Change in Renal Function over Time as Measured by eGFR |
| End point description:  |  |
| eGFR is a measure of kidney function. eGFR has been calculated based on p-creatinine according to the modification of diet in renal disease (MDRD) equation. Reduced kidney function is characterised by a decreased eGFR value. A positive change in eGFR from baseline indicates improved renal function. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Pre-implifidase up to 6 months  |  |

| End point values            | All patients      | Dialysis Dependent Patients at Baseline | Dialysis Independent Patients at Baseline |  |
|-----------------------------|-------------------|---|---|--|
| Subject group type          | Reporting group   | Subject analysis set                    | Subject analysis set                      |  |
| Number of subjects analysed | 10 <sup>[2]</sup> | 5 <sup>[3]</sup>                        | 5 <sup>[4]</sup>                          |  |
| Units: Patients             |                   |   |   |  |
| Pre-implifidase eGFR=0-15   | 6                 | 1                                       | 5   |  |
| Pre-implifidase eGFR=15-30  | 0                 | 0                                       | 0   |  |
| Pre-implifidase eGFR=30-60  | 0                 | 0                                       | 0   |  |
| Pre-implifidase eGFR ≥60    | 0                 | 0                                       | 0   |  |
| 1 month eGFR=0-15           | 2                 | 1                                       | 1   |  |
| 1 month eGFR=15-30          | 3                 | 1                                       | 2   |  |
| 1 month eGFR=30-60          | 2                 | 0                                       | 2   |  |
| 1 month eGFR ≥60            | 0                 | 0                                       | 0   |  |
| 3 month eGFR=0-15           | 0                 | 0                                       | 0   |  |
| 3 month eGFR=15-30          | 6                 | 3                                       | 3   |  |
| 3 month eGFR=30-60          | 1                 | 0                                       | 1   |  |

|                        |   |   |   |  |
|------------------------|---|---|---|--|
| 3 month eGFR $\geq$ 60 | 0 | 0 | 0 |  |
| 6 month eGFR=0-15      | 0 | 0 | 0 |  |
| 6 month eGFR=15-30     | 6 | 4 | 2 |  |
| 6 month eGFR=30-60     | 4 | 1 | 3 |  |
| 6 month eGFR $\geq$ 60 | 0 | 0 | 0 |  |

Notes:

[2] - Pre-implifidase: 6 patients

1 month: 7 patients

3 months: 7 patients

6 months: 10 patients

[3] - Pre-implifidase: 1 patients

1 month: 2 patients

3 months: 3 patients

6 months: 5 patients

[4] - Pre-implifidase: 5 patients

1 month: 5 patients

3 months: 4 patients

6 months: 5 patients

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Study Visits with Anti-GBM Antibodies Above a Toxic Level

|                 |   |
|-----------------|---|
| End point title | Number of Study Visits with Anti-GBM Antibodies Above a Toxic Level |
|-----------------|---|

End point description:

Very few patients had anti-GBM antibodies >20 U/mL on the assessment timepoints following imlifidase. PLEX was performed at any time throughout the study when the Investigator judged it necessary, without requirement of recording the anti-GBM antibody level prior to initiation. Hence it was not possible to analyse number of patient days with an anti-GBM level >20 U/mL as was the original plan. Instead number of study visits with a toxic level after imlifidase treatment are presented.

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

End point timeframe:

Pre-implifidase up to 6 months after imlifidase administration

| End point values            | All patients    | Dialysis Dependent Patients at Baseline | Dialysis Independent Patients at Baseline |  |
|-----------------------------|-----------------|---|---|--|
| Subject group type          | Reporting group | Subject analysis set                    | Subject analysis set                      |  |
| Number of subjects analysed | 15              | 10                                      | 5   |  |
| Units: Patients             |                 |   |   |  |
| 0 visits                    | 2               | 1                                       | 1   |  |
| 1 visit                     | 7               | 3                                       | 4   |  |
| 2 visits                    | 1               | 1                                       | 0   |  |
| 3 visits                    | 1               | 1                                       | 0   |  |
| 5 visits                    | 2               | 2                                       | 0   |  |
| 6 visits                    | 1               | 1                                       | 0   |  |
| 9 visits                    | 1               | 1                                       | 0   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Haematuria (Blood in urine)

|                 |                             |
|-----------------|-----------------------------|
| End point title | Haematuria (Blood in urine) |
|-----------------|-----------------------------|

End point description:

Haematuria was assessed using urine dipstick. The result was presented as: Negative/Trace/+1/+2/+3/+4. In the analysis results being +2 or above are considered as relevant. Haematuria was an inclusion criterion. All 15 patients had haematuria when included in the study.

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

End point timeframe:

At 6 months after imlifidase administration

| End point values            | All patients    |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 10              |  |  |  |
| Units: Positive             |                 |  |  |  |
| number (not applicable)     |                 |  |  |  |
| Day 180                     | 3               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Proteinuria During the Study

|                 |  |
|-----------------|--|
| End point title | Change in Proteinuria During the Study |
|-----------------|--|

End point description:

Change in proteinuria measured as u-albumin/creatinine (g/mol) in morning void during the study .

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

End point timeframe:

Up to 6 months after imlifidase administration

| End point values                     | All patients      | Dialysis<br>Dependent<br>Patients at<br>Baseline | Dialysis<br>Independent<br>Patients at<br>Baseline |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                             | Subject analysis set                               |  |
| Number of subjects analysed          | 14 <sup>[5]</sup> | 9 <sup>[6]</sup>                                 | 5 <sup>[7]</sup>                                   |  |
| Units: g/mol                         |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| Pre-implifidase                      | 700 (± 1197)      | 1117 (± 1544)                                    | 199 (± 166)  |  |
| 3 Months                             | 190 (± 178)       | 220 (± 197)                                      | 153 (± 172)  |  |
| 6 Months                             | 161 (± 198)       | 183 (± 231)                                      | 122 (± 133)  |  |

Notes:

[5] - Pre-implifidase: 11 patients  
3 Months: 9 patients  
6 Months: 14 patients  
[6] - Pre-implifidase: 6 patients  
3 Months: 5 patients  
6 Months: 9 patients  
[7] - Pre-implifidase: 5 patients  
3 Months: 4 patients  
6 Months: 5 patients

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of PLEXs Needed over Time

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Number of PLEXs Needed over Time |
|-----------------|----------------------------------|

End point description:

Number of PLEXs needed before anti-GBM antibodies are below toxic levels. PLEX was initiated at the discretion of the investigator throughout the study.

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

End point timeframe:

Before implifidase was administered and up to 3 months after implifidase was administered

| End point values                     | All patients    | Dialysis<br>Dependent<br>Patients at<br>Baseline | Dialysis<br>Independent<br>Patients at<br>Baseline |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group | Subject analysis set                             | Subject analysis set                               |  |
| Number of subjects analysed          | 15              | 10   | 5  |  |
| Units: Number of PLEX sessions       |                 |  |  |  |
| Pre-Screening                        | 33              | 10   | 23   |  |
| Post-Screening to Pre-implifidase    | 5               | 5  | 0  |  |
| Pre-implifidase to Day 3             | 1               | 0  | 1  |  |
| Day 3 to Day 7                       | 8               | 8  | 0  |  |
| Day 7 to Day 10                      | 14              | 14   | 0  |  |
| Day 10 to Day 15                     | 22              | 20   | 2  |  |
| Day 15 to Day 22                     | 23              | 18   | 5  |  |
| Day 22 to Day 29                     | 6               | 5  | 1  |  |
| Day 29 to Day 50                     | 8               | 5  | 3  |  |
| Day 50 to 3 Months                   | 1               | 0  | 1  |  |
| Total (Post-implifidase to 3 Months) | 83              | 70   | 13   |  |
| Total (Pre-Screening to 3 Months)    | 121             | 85   | 36   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics of Implifidase (AUC, Cmax, CL, Vz)

|  |  |
|--|--|
| End point title  | Pharmacokinetics of Imlifidase (AUC, Cmax, CL, Vz) |
| End point description:   |  |
| AUC=Area under the plasma concentration of imlifidase versus time curve              |  |
| Cmax=Maximum observed plasma concentration of imlifidase following dosing            |  |
| CL=Clearance is a measure of the ability of the body to clear imlifidase from plasma |  |
| Vz=Volume of distribution of imlifidase during the elimination phase                 |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Pre-implifidase to Day 14 after administration                                       |  |

|                                       |                     |  |  |  |
|---------------------------------------|---------------------|--|--|--|
| <b>End point values</b>               | All patients        |  |  |  |
| Subject group type                    | Reporting group     |  |  |  |
| Number of subjects analysed           | 15                  |  |  |  |
| Units: See below                      |                     |  |  |  |
| geometric mean (full range (min-max)) |                     |  |  |  |
| AUC (h x microgram/mL)                | 158 (73 to 304)     |  |  |  |
| Cmax (microgram/mL)                   | 4.7 (2.6 to 8.0)    |  |  |  |
| CL (mL/h/kg)                          | 1.6 (0.8 to 3.4)    |  |  |  |
| Vz (L/kg)                             | 0.13 (0.07 to 0.21) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics of Imlifidase (t1/2)

|  |                                       |
|--|---------------------------------------|
| End point title  | Pharmacokinetics of Imlifidase (t1/2) |
| End point description:   |                                       |
| The half-life is the time it takes for the concentration of the drug to be reduced by 50%.       |                                       |
| Half-life during distribution phase (Alpha-t1/2) Half-life during elimination phase (Beta-t1/2). |                                       |
| End point type   | Secondary                             |
| End point timeframe:   |                                       |
| Pre-dose to Day 14 after administration of imlifidase  |                                       |

|  |                   |  |  |  |
|--|-------------------|--|--|--|
| <b>End point values</b>                | All patients      |  |  |  |
| Subject group type                     | Reporting group   |  |  |  |
| Number of subjects analysed            | 15 <sup>[8]</sup> |  |  |  |
| Units: hours                           |                   |  |  |  |
| arithmetic mean (full range (min-max)) |                   |  |  |  |
| Alpha-t1/2                             | 2.6 (0.9 to 7.5)  |  |  |  |
| Beta-t1/2                              | 53 (26 to 115)    |  |  |  |

Notes:

[8] - The results refers to harmonic mean. Arithmetic was used since harmonic was not a selectable option.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics (IgG Degradation)

|                 |                                    |
|-----------------|------------------------------------|
| End point title | Pharmacodynamics (IgG Degradation) |
|-----------------|------------------------------------|

End point description:

Imlifidase specifically cleaves all subclasses of human IgG rapidly and efficiently. The cleaving process involves two steps: (i) intact IgG to single cleaved IgG followed by (ii) single cleaved IgG to completely cleaved IgG (one F(ab')<sub>2</sub>- and one homodimeric Fc-fragment) The electroluminescence analysis method used measures the sum of intact and single cleaved IgG in serum. The efficacy of imlifidase is evaluated as remaining concentration of intact and single cleaved IgG in serum after treatment.

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

End point timeframe:

Pre-implifidase up to 6 months after imlifidase administration

| End point values                     | All patients      |  |  |  |
|--------------------------------------|-------------------|--|--|--|
| Subject group type                   | Reporting group   |  |  |  |
| Number of subjects analysed          | 15 <sup>[9]</sup> |  |  |  |
| Units: mg/mL                         |                   |  |  |  |
| arithmetic mean (standard deviation) |                   |  |  |  |
| Pre-implifidase                      | 6.66 (± 2.94)     |  |  |  |
| 2 hours                              | 0.17 (± 0.12)     |  |  |  |
| 6 hours                              | 0.08 (± 0.05)     |  |  |  |
| 24 hours                             | 0.08 (± 0.05)     |  |  |  |
| Day 3                                | 0.09 (± 0.05)     |  |  |  |
| Day 7                                | 0.85 (± 1.56)     |  |  |  |
| Day 10                               | 1.58 (± 1.69)     |  |  |  |
| Day 15                               | 2.64 (± 2.42)     |  |  |  |
| Day 22                               | 2.94 (± 2.34)     |  |  |  |
| Day 29                               | 3.94 (± 2.18)     |  |  |  |
| Day 50                               | 4.29 (± 2.05)     |  |  |  |
| 6 Months                             | 6.76 (± 2.49)     |  |  |  |

Notes:

[9] - 15 patients at all time points except for 24h, Day 50 and 6 months when 14 patients were analysed

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-implifidase Antibodies

|                 |                             |
|-----------------|-----------------------------|
| End point title | Anti-implifidase Antibodies |
|-----------------|-----------------------------|

|   |           |
|---|-----------|
| End point description:  |           |
| Concentration of anti-implifidase antibodies                        |           |
| End point type  | Secondary |
| End point timeframe:  |           |
| Pre-implifidase up to 6 months following implifidase administration |           |

| End point values                     | All patients       |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 15 <sup>[10]</sup> |  |  |  |
| Units: mg/L                          |                    |  |  |  |
| arithmetic mean (standard deviation) |                    |  |  |  |
| Pre-implifidase                      | 9.00 (± 4.17)      |  |  |  |
| Day 7                                | 4.32 (± 5.29)      |  |  |  |
| Day 15                               | 752 (± 728)        |  |  |  |
| Day 22                               | 744 (± 736)        |  |  |  |
| Day 29                               | 609 (± 493)        |  |  |  |
| Day 50                               | 547 (± 580)        |  |  |  |
| 3 Months                             | 327 (± 263)        |  |  |  |
| 6 Months                             | 242 (± 280)        |  |  |  |

Notes:

[10] - Pre-implifidase, D7, D15, D22, D29: 15 patients

D50 and 6 Months: 14 patients

3 Months: 12 patients

## Statistical analyses

No statistical analyses for this end point

## Secondary: Renal Histology

|   |                 |
|---|-----------------|
| End point title   | Renal Histology |
| End point description:  |                 |
| Kidney biopsies classified according to Berden et al. 2010 (focal, crescentic, mixed and sclerotic) and provide information on the histological activity and kidney outcome. Focal class is associated with favourable kidney outcome, whereas sclerotic carries a poor outcome. Crescentic/mixed class could have an intermediate outcome between focal and sclerotic. Immunofluorescence performed at the local hospitals was also used to assess linear IgG deposits which is a hallmark of anti-GBM antibody disease. |                 |
| End point type  | Secondary       |
| End point timeframe:  |                 |
| Before administration of implifidase (0-33 days) and after administration of implifidase (3-6 days)   |                 |

| End point values            | All patients       |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 10 <sup>[11]</sup> |  |  |  |
| Units: Biopsies             |                    |  |  |  |
| Crescentic                  | 9                  |  |  |  |
| Mixed                       | 4                  |  |  |  |
| Sclerotic                   | 1                  |  |  |  |

|                     |    |  |  |  |
|---------------------|----|--|--|--|
| Linear IgG deposits | 11 |  |  |  |
|---------------------|----|--|--|--|

Notes:

[11] - 14 biopsies from 10 patients were analysed.  
10 biopsies were collected pre-implifidase and 4 after.

## Statistical analyses

---

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected for 6 months (i.e., from the timepoint the patient signed the informed consent form (ICF) until end of study.

Adverse event reporting additional description:

AEs were obtained if spontaneously reported by the patient, if reported in response to an open question from the study personnel, or if revealed by observation.

A TEAE is any AE occurring after imlifidase and within the time of the residual drug effect period i.e. 28 days.

All SAEs were post-TEAEs.

The listed non-serious AEs presents TEAEs only.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Safety Analysis Set |
|-----------------------|---------------------|

Reporting group description:

All patients who have received imlifidase.

| Serious adverse events                               | Safety Analysis Set |  |  |
|--|---------------------|--|--|
| Total subjects affected by serious adverse events    |                     |  |  |
| subjects affected / exposed                          | 5 / 15 (33.33%)     |  |  |
| number of deaths (all causes)                        | 1                   |  |  |
| number of deaths resulting from adverse events       | 1                   |  |  |
| Cardiac disorders                                    |                     |  |  |
| Cardiac failure                                      |                     |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)      |  |  |
| occurrences causally related to treatment / all      | 0 / 1               |  |  |
| deaths causally related to treatment / all           | 0 / 0               |  |  |
| General disorders and administration site conditions |                     |  |  |
| Pyrexia  |                     |  |  |
| subjects affected / exposed                          | 1 / 15 (6.67%)      |  |  |
| occurrences causally related to treatment / all      | 0 / 1               |  |  |
| deaths causally related to treatment / all           | 0 / 0               |  |  |
| Gastrointestinal disorders                           |                     |  |  |
| Diarrhoea  |                     |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Viral infection                                 |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 15 (6.67%) |  |  |
| 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>                     | Safety Analysis Set |  |  |
| Total subjects affected by non-serious adverse events |                     |  |  |
| subjects affected / exposed                           | 13 / 15 (86.67%)    |  |  |
| Vascular disorders                                    |                     |  |  |

|   |   |  |  |
|---|---|--|--|
| Hypertension<br>subjects affected / exposed<br>occurrences (all)  | 2 / 15 (13.33%)<br>2  |  |  |
| Pelvic venous thrombosis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Thrombophlebitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Immune system disorders<br>Cryoglobulinaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypogammaglobulinaemia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1                            |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Bronchial obstruction<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Sinus pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1 |  |  |
| Investigations<br>Blood iron decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Red blood cell count decreased  | 1 / 15 (6.67%)<br>1   |  |  |

|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   |  |  |
| Nervous system disorders<br>Cognitive disorder<br>subjects affected / exposed<br>occurrences (all)<br><br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1   |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)   | 6 / 15 (40.00%)<br>6  |  |  |
| Ear and labyrinth disorders<br>Tinnitus<br>subjects affected / exposed<br>occurrences (all)   | 2 / 15 (13.33%)<br>2  |  |  |
| Eye disorders<br>Foreign body sensation in eyes<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1   |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)           | 1 / 15 (6.67%)<br>1<br><br>4 / 15 (26.67%)<br>4<br><br>2 / 15 (13.33%)<br>2 |  |  |
| Skin and subcutaneous tissue disorders<br>Ecchymosis  |   |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hyperhidrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash erythematous</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> |  |  |
| <p>Renal and urinary disorders</p> <p>Haematuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 15 (6.67%)</p> <p>1</p>  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscle spasms</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p>   |  |  |
| <p>Infections and infestations</p> <p>Clostridium difficile infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Herpes zoster</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pneumonia klebsiella</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> <p>1 / 15 (6.67%)</p> <p>1</p> |  |  |
| <p>Metabolism and nutrition disorders</p>   |   |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  |  |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)     | 2 / 15 (13.33%)<br>2 |  |  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1  |  |  |
| Steroid diabetes<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|     |
|-----|
| N/A |
|-----|

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31563334>