



## Clinical trial results:

**A “window of opportunity” trial with Brentuximab Vedotin and Imatinib in patients with relapsed or refractory ALK+ anaplastic large cell lymphoma or patients ineligible for chemotherapy**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2013-003505-26   |
| Trial protocol           | AT               |
| Global end of trial date | 03 November 2021 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 16 July 2022 |
| First version publication date | 16 July 2022 |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | AGMT_ALCL1 |
|-----------------------|------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02462538 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AGMT  |
| Sponsor organisation address | Gentzgasse 60/21, Vienna, Austria, 1180                               |
| Public contact               | Daniela Wolkersdorfer, AGMT, 0043 6626404412, d.wolkersdorfer@agmt.at |
| Scientific contact           | Richard Greil, AGMT, 0043 5725525801, r.greil@salk.at                 |

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:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 03 November 2021 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 03 November 2021 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To determine the safety and tolerability of simultaneous administration of brentuximab vedotin and imatinib mesylate in substitution of conventional chemotherapeutic treatment.

Protection of trial subjects:

Safety measurements were assessed at screening, every 3 weeks during and at the end of treatment, and at final visit. All (serious) adverse events occurring during study treatment were collected from signing the informed consent form until 12 weeks after the end of study treatment.

In general, concomitant medications and therapies necessary for supportive care and safety of the patient are allowed: Because of the inherent risk of either reduced activity or enhanced toxicity of the concomitant medication and/or imatinib, drugs known to interact with the same CYP450 isoenzymes (2D and 3A4) as imatinib or MMAE should have been used with caution.

Background therapy:

None.

Evidence for comparator:

Not applicable.

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 16 March 2015 |
| 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 | Austria: 3 |
| Worldwide total number of subjects   | 3          |
| EEA total number of subjects         | 3          |

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) | 3 |
| From 65 to 84 years  | 0 |
| 85 years and over    | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Between 03-Nov-2015 and 26-September-2017 three patients were enrolled at one site in Austria.

### Pre-assignment

Screening details:

Due to low recruitment study was withdrawn prematurely after inclusion of three patients on 22-Mar-2018. At time of this decision, no patients were on study treatment. Planned follow up phase was conducted and ended on 03-Nov-2021.

### Period 1

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

### Arms

|  |  |
|--|--|
| <b>Arm title</b>                       | Overall trial                                    |
| Arm description:                       |  |
| Combination therapy                    |  |
| Arm type                               | Experimental                                     |
| Investigational medicinal product name | Brentuximab vedotin                              |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder for concentrate for solution for infusion |
| Routes of administration               | Intravenous use                                  |

Dosage and administration details:

Starting dose of brentuximab vedotin 1.8 mg/kg; cycles were repeated every 3 weeks up to 48 weeks (last administration: d1 week 45)

|  |                 |
|--|-----------------|
| Investigational medicinal product name | Imatinib        |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Capsule, Tablet |
| Routes of administration               | Oral use        |

Dosage and administration details:

100mg daily starting from day 1 of the first cycle; increased to 200mg daily starting from day 1 of the second cycle; continued at 200mg for 48 weeks

| Number of subjects in period 1 | Overall trial |
|--------------------------------|---------------|
| Started                        | 3             |
| Completed                      | 1             |
| Not completed                  | 2             |
| Adverse event, non-fatal       | 1             |
| Progressive disease            | 1             |



## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 3             | 3     |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  |               | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |               | 0     |  |
| Newborns (0-27 days)                                  |               | 0     |  |
| Infants and toddlers (28 days-23<br>months)           |               | 0     |  |
| Children (2-11 years)                                 |               | 0     |  |
| Adolescents (12-17 years)                             |               | 0     |  |
| Adults (18-64 years)                                  |               | 0     |  |
| From 65-84 years                                      |               | 0     |  |
| 85 years and over                                     |               | 0     |  |
| Age continuous  |               |       |  |
| Age at enrollment                                     |               |       |  |
| Units: years  |               |       |  |
| median  | 26            |       |  |
| full range (min-max)                                  | 24 to 47      | -     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 0             | 0     |  |
| Male  | 3             | 3     |  |
| Prior ALCL therapies                                  |               |       |  |
| Units: Subjects                                       |               |       |  |
| 1 prior therapy                                       | 2             | 2     |  |
| 3 prior therapies                                     | 1             | 1     |  |

## End points

### End points reporting groups

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

### Primary: Safety and tolerability

|                 |  |
|-----------------|--|
| End point title | Safety and tolerability <sup>[1]</sup> |
|-----------------|--|

End point description:

Due to small sample size, no evaluation of tolerability can be given, results are tabulated only.

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

End point timeframe:

60 weeks - from enrollment to final visit 12 weeks after discontinuing or completion of study treatment

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: Main aim of this phase I/II pilot study is feasibility and safety. No formal hypothesis testing was planned.

| End point values            | Overall trial   |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 3               |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Withdrawal due to AE        | 1               |  |  |  |
| No withdrawal due to AE     | 2               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical response rate

|                 |                        |
|-----------------|------------------------|
| End point title | Clinical response rate |
|-----------------|------------------------|

End point description:

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

End point timeframe:

Response at final visit (12 weeks after discontinuing or completion of study treatment)

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Overall trial   |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 3               |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Complete remission          | 2               |  |  |  |
| Partial remission           | 0               |  |  |  |
| Stable disease              | 0               |  |  |  |
| Progressive disease         | 1               |  |  |  |

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From inclusion of patient until final visit (12 weeks after completion or discontinuation of study treatment)

Adverse event reporting additional description:

According to protocol, an abnormal laboratory value was not assessed as an AE unless that value led to discontinuation or delay in treatment, dose modification, therapeutic intervention. Progression of disease was not to be regarded as SAE.

Relation to IMP brentuximab vedotin is given.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall trial |
|-----------------------|---------------|

Reporting group description:

All enrolled patients

| Serious adverse events                            | Overall trial  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 2 / 3 (66.67%) |  |  |
| number of deaths (all causes)                     | 1              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |
| Gastrointestinal disorders                        |                |  |  |
| Oesophagitis                                      |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Intestinal obstruction                            |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | Overall trial   |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 3 / 3 (100.00%) |  |  |
| Investigations  |                 |  |  |
| Gamma-glutamyltransferase increased                   |                 |  |  |
| subjects affected / exposed                           | 3 / 3 (100.00%) |  |  |
| occurrences (all)                                     | 7               |  |  |
| Neutrophil count decreased                            |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Nervous system disorders                              |                 |  |  |
| Seizure   |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Polyneuropathy  |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Blood and lymphatic system disorders                  |                 |  |  |
| Neutropenia   |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| General disorders and administration site conditions  |                 |  |  |
| Stenosis  |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Pyrexia   |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Generalised oedema                                    |                 |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Gastrointestinal disorders                            |                 |  |  |
| Vomiting  |                 |  |  |
| subjects affected / exposed                           | 2 / 3 (66.67%)  |  |  |
| occurrences (all)                                     | 2               |  |  |
| Diarrhoea   |                 |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 2 / 3 (66.67%) |  |  |
| occurrences (all)                               | 2              |  |  |
| Nausea  |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Ascites   |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Abdominal pain                                  |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholestasis                                     |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 2              |  |  |
| Psychiatric disorders                           |                |  |  |
| Anxiety   |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Joint swelling                                  |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Arthritis reactive                              |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Infections and infestations                     |                |  |  |
| Dermatophytosis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 2              |  |  |
| Nasopharyngitis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Influenza                                       |                |  |  |
| subjects affected / exposed                     | 2 / 3 (66.67%) |  |  |
| occurrences (all)                               | 2              |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| Metabolism and nutrition disorders |                |  |  |
| Hypokalaemia                       |                |  |  |
| subjects affected / exposed        | 1 / 3 (33.33%) |  |  |
| 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

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

|   |
|---|
| Recruitment was withdrawn prematurely due to very slow recruitment. Three patients were enrolled, planned sample size of 10 patients was not reached. |
|---|

Notes: