



## Clinical trial results:

**A randomized, parallel group, multi-centre phase-2 study of GX-G3 compared with pegfilgrastim as an adjunct to chemotherapy in patients with Non-Hodgkin's Lymphoma**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-002693-20 |
| Trial protocol           | BG             |
| Global end of trial date | 29 August 2019 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 22 January 2020 |
| First version publication date | 22 January 2020 |

### Trial information

#### Trial identification

|                       |                     |
|-----------------------|---------------------|
| Sponsor protocol code | GXG3_NHL_2/CGX14001 |
|-----------------------|---------------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                                                  |
|------------------------------|----------------------------------------------------------------------------------|
| Sponsor organisation name    | Ilkogen Ilac San. ve Tic. A.S.                                                   |
| Sponsor organisation address | Sanayi Mahallesi Teknopark Bulvari No: 1/3 A/411 Pendik, İstanbul, Turkey, 34906 |
| Public contact               | Burcu Bulut, Ilkogen Ilac San. ve Tic. A.S., +90 2165648000, byilmaz@ilko.com.tr |
| Scientific contact           | Burcu Bulut, Ilkogen Ilac San. ve Tic. A.S., +90 2165648000, byilmaz@ilko.com.tr |

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                       | 27 May 2019      |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 18 December 2018 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 29 August 2019   |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the present trial is to assess the efficacy, safety, and tolerability of three doses of GX-G3 with the aim of selecting the optimal dose by comparing each of the doses with the reference product (Neulasta®). The major aim for including one group with delayed administration (250 µg/kg of GX-G3 on day 3 after R-CHOP dosing) is to evaluate the optimal point in time for dosing of the test product.

Protection of trial subjects:

Continuous medical surveillance during the whole trial by means of: laboratory examinations, vital signs, check of exclusion/withdrawal criteria, adverse event questioning.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 14 February 2017 |
| 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 | Turkey: 19            |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Ukraine: 5            |
| Country: Number of subjects enrolled | Romania: 6            |
| Country: Number of subjects enrolled | Bulgaria: 26          |
| Country: Number of subjects enrolled | Germany: 4            |
| Worldwide total number of subjects   | 65                    |
| EEA total number of subjects         | 36                    |

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)      | 38 |
| From 65 to 84 years       | 27 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The results from screening and data collected during the study were recorded in the patient's case report

### Period 1

|                              |                               |
|------------------------------|-------------------------------|
| Period 1 title               | not provided (overall period) |
| Is this the baseline period? | Yes                           |
| Allocation method            | Randomised - controlled       |
| Blinding used                | Not blinded                   |

### Arms

|                              |          |
|------------------------------|----------|
| Are arms mutually exclusive? | Yes      |
| <b>Arm title</b>             | Cohort 1 |

Arm description:

150 µg/kg body weight 24 hrs after R-CHOP administration (treatment A)

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | GX-G3                  |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

150 µg/kg body weight 24 hrs after R-CHOP administration (treatment A)

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 2 |
|------------------|----------|

Arm description:

250 µg/kg body weight 24 hrs after R-CHOP administration (treatment B)

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | GX-G3                  |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

250 µg/kg body weight 24 hrs after R-CHOP administration (treatment B)

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 3 |
|------------------|----------|

Arm description:

350 µg/kg body weight 24 hrs after R-CHOP administration (treatment C)

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | GX-G3                  |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

350 µg/kg body weight 24 hrs after R-CHOP administration (treatment C)

|                                                                        |                               |
|------------------------------------------------------------------------|-------------------------------|
| <b>Arm title</b>                                                       | Cohort 4                      |
| Arm description:                                                       |                               |
| Reference product (Neulasta®) (Treatment D)                            |                               |
| Arm type                                                               | Experimental                  |
| Investigational medicinal product name                                 | Reference product (Neulasta®) |
| Investigational medicinal product code                                 |                               |
| Other name                                                             |                               |
| Pharmaceutical forms                                                   | Solution for injection        |
| Routes of administration                                               | Subcutaneous use              |
| Dosage and administration details:                                     |                               |
| Reference product (Neulasta®) (Treatment D)                            |                               |
| <b>Arm title</b>                                                       | Cohort 5                      |
| Arm description:                                                       |                               |
| 250 µg/kg body weight 72 hrs after R-CHOP administration (treatment E) |                               |
| Arm type                                                               | Experimental                  |
| Investigational medicinal product name                                 | GX-G3                         |
| Investigational medicinal product code                                 |                               |
| Other name                                                             |                               |
| Pharmaceutical forms                                                   | Solution for injection        |
| Routes of administration                                               | Subcutaneous use              |
| Dosage and administration details:                                     |                               |
| 250 µg/kg body weight 72 hrs after R-CHOP administration (treatment E) |                               |

| Number of subjects in period 1 | Cohort 1 | Cohort 2 | Cohort 3 |
|--------------------------------|----------|----------|----------|
| Started                        | 14       | 12       | 13       |
| Completed                      | 14       | 12       | 13       |

| Number of subjects in period 1 | Cohort 4 | Cohort 5 |
|--------------------------------|----------|----------|
| Started                        | 12       | 14       |
| Completed                      | 12       | 14       |

## Baseline characteristics

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cohort 1         |
| Reporting group description:<br>150 µg/kg body weight 24 hrs after R-CHOP administration (treatment A)                                                                                                                                                                                                                                                                                                                                                                |                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cohort 2         |
| Reporting group description:<br>250 µg/kg body weight 24 hrs after R-CHOP administration (treatment B)                                                                                                                                                                                                                                                                                                                                                                |                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cohort 3         |
| Reporting group description:<br>350 µg/kg body weight 24 hrs after R-CHOP administration (treatment C)                                                                                                                                                                                                                                                                                                                                                                |                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cohort 4         |
| Reporting group description:<br>Reference product (Neulasta®) (Treatment D)                                                                                                                                                                                                                                                                                                                                                                                           |                  |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Cohort 5         |
| Reporting group description:<br>250 µg/kg body weight 72 hrs after R-CHOP administration (treatment E)                                                                                                                                                                                                                                                                                                                                                                |                  |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                            | Primary Endpoint |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                             | Full analysis    |
| Subject analysis set description:<br>The primary objective of this study was to assess the efficacy, safety, and tolerability of three doses of GX-G3 with the aim of selecting the optimal dose by comparing each of the doses with the reference product (Neulasta®).<br>Furthermore, the optimal point in time for dosing of the test product by delayed administration of 250 µg/kg body weight (BW) of GX-G3 72 hours after R-CHOP administration was evaluated. |                  |

### Primary: Primary endpoint

|                                                                                                                                                                                                                |                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| End point title                                                                                                                                                                                                | Primary endpoint |
| End point description:                                                                                                                                                                                         |                  |
| End point type                                                                                                                                                                                                 | Primary          |
| End point timeframe:<br>Time to recover from severe neutropenia (defined as ANC $<0.5 \times 10^9/l$ ) to a target $\geq 0.5 \times 10^9/l$ after each administration of R-CHOP chemotherapy in cycles 1 and 2 |                  |

| End point values                     | Cohort 1        | Cohort 2        | Cohort 3        | Cohort 4        |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type                   | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed          | 14              | 12              | 13              | 12              |
| Units: number                        |                 |                 |                 |                 |
| arithmetic mean (standard deviation) | 3.833 (± 1.697) | 2.500 (± 1.000) | 3.375 (± 2.504) | 3.571 (± 2.936) |

| End point values            | Cohort 5        |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 14              |  |  |  |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Units: number                        |                      |  |  |  |
| arithmetic mean (standard deviation) | 2.636 ( $\pm$ 1.859) |  |  |  |

## Statistical analyses

|                                                                                                                                                                                                 |                                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                               | Primary endpoint Full Analysis Set                   |
| Statistical analysis description:<br>All randomized patients who received at least one dose of the study medication and who have at least one post-baseline assessment of the primary endpoint. |                                                      |
| Comparison groups                                                                                                                                                                               | Cohort 4 v Cohort 1 v Cohort 2 v Cohort 3 v Cohort 5 |
| Number of subjects included in analysis                                                                                                                                                         | 65                                                   |
| Analysis specification                                                                                                                                                                          | Post-hoc                                             |
| Analysis type                                                                                                                                                                                   | superiority                                          |
| P-value                                                                                                                                                                                         | < 0.5                                                |
| Method                                                                                                                                                                                          | ANCOVA                                               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The time of administration of the first cycle of treatment (study day 1) is designated as start of safety data collection. The data collection period ends with the final examination.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description: -

| Serious adverse events                            | Cohort 2      |  |  |
|---------------------------------------------------|---------------|--|--|
| Total subjects affected by serious adverse events |               |  |  |
| subjects affected / exposed                       | 0 / 1 (0.00%) |  |  |
| number of deaths (all causes)                     | 0             |  |  |
| number of deaths resulting from adverse events    | 0             |  |  |

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

| Non-serious adverse events                            | Cohort 2        |  |  |
|-------------------------------------------------------|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 1 / 1 (100.00%) |  |  |
| Skin and subcutaneous tissue disorders                |                 |  |  |
| itching                                               |                 |  |  |
| alternative assessment type: Non-systematic           |                 |  |  |
| subjects affected / exposed                           | 1 / 1 (100.00%) |  |  |
| occurrences (all)                                     | 1               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                        |
|-------------------|--------------------------------------------------|
| 13 April 2016     | Changes in study protocol                        |
| 28 September 2016 | Change of sponsor address and project management |
| 16 February 2018  | Inclusion of 2 other countries                   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported