



## Clinical trial results:

### Allogeneic Transplantation of Haematopoietic Stem Cells Following Non-myeloablative Conditioning With Melphalan, Fludarabine, Thiotepa, Rituximab and Ibritumomab Tiuxetan (Zevalin) in Patients With Aggressive Non-Hodgkin's B-cell Lymphoma

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2007-003302-10   |
| Trial protocol           | ES               |
| Global end of trial date | 04 February 2013 |

#### Results information

|                                   |                                               |
|-----------------------------------|-----------------------------------------------|
| Result version number             | v1 (current)                                  |
| This version publication date     | 15 July 2021                                  |
| First version publication date    | 15 July 2021                                  |
| Summary attachment (see zip file) | Z-RIC (ZRIC_30abril2015_corregidoLola_MC.pdf) |

#### Trial information

##### Trial identification

|                       |                       |
|-----------------------|-----------------------|
| Sponsor protocol code | GELTAMO- Z-RIC - Allo |
|-----------------------|-----------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00644371 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                          |
|------------------------------|----------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GELTAMO                                                                                                  |
| Sponsor organisation address | H. MARQUES DE VALDECILLA SERVICIO DE HEMATOLOGIA, SANTANDER, Spain, 39008                                |
| Public contact               | GELTAMO, Grupo Español de Linfomas y Transplante Autólogo de Médula Ósea, 0034 913195780, dm@geltamo.com |
| Scientific contact           | GELTAMO, Grupo Español de Linfomas y Transplante Autólogo de Médula Ósea, 0034 913195780, sc@geltamo.com |

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                       | 04 February 2013 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 21 February 2011 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 04 February 2013 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Progression-free survival

Protection of trial subjects:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was  $\leq 2$  and no major organ dysfunction was present (serum bilirubin  $< 2$  mg/dL with AST, ALT, GGT and AP  $< 2$  times ULN, left ventricular ejection fraction  $> 40\%$  and serum creatinine  $< 2$  mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 30 November 2007 |
| 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 | Spain: 18 |
| Worldwide total number of subjects   | 18        |
| EEA total number of subjects         | 18        |

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)                        | 18 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study.

Patients were eligible if they were between 18 and 65 years old, ECOG performance status was  $\leq 2$

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 18 |
| Number of subjects completed | 18 |

### Period 1

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

### Arms

|           |              |
|-----------|--------------|
| Arm title | Experimental |
|-----------|--------------|

Arm description:

Experimental arm

|                                        |                                |
|----------------------------------------|--------------------------------|
| Arm type                               | Experimental                   |
| Investigational medicinal product name | Ibritumomab Tiuxetan (Zevalin) |
| Investigational medicinal product code |                                |
| Other name                             |                                |
| Pharmaceutical forms                   | Injection                      |
| Routes of administration               | Injection                      |

Dosage and administration details:

0.4 mCi/kg (14.8 MBq/kg). Maximum: 32 mCi on day -14.

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Rituximab       |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

250 mg/m<sup>2</sup> on days -21 and -14 and 0.4 mCi/kg of Y-90-IB was administered after rituximab dose

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Fludarabine     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

30 mg/m<sup>2</sup>/day on days -7, -6, -5, -4 and -3 as a 30-min infusion.

|                                        |           |
|----------------------------------------|-----------|
| Investigational medicinal product name | Melphalan |
| Investigational medicinal product code |           |
| Other name                             |           |

|                                                      |                    |
|------------------------------------------------------|--------------------|
| Pharmaceutical forms                                 | Injection/infusion |
| Routes of administration                             | Intravenous use    |
| Dosage and administration details:                   |                    |
| 70 mg/m2/day on days -3 and -2 as a 15-min infusion. |                    |
| Investigational medicinal product name               | Thiotepa           |
| Investigational medicinal product code               |                    |
| Other name                                           |                    |
| Pharmaceutical forms                                 | Injection          |
| Routes of administration                             | Intravenous use    |
| Dosage and administration details:                   |                    |
| 5 mg/kg over 4 hours every 12 hours on day -8.       |                    |

| <b>Number of subjects in period 1</b> | Experimental |
|---------------------------------------|--------------|
| Started                               | 18           |
| Completed                             | 18           |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | OVERALL TRIAL |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                             | OVERALL TRIAL | Total |  |
|----------------------------------------------------|---------------|-------|--|
| Number of subjects                                 | 18            | 18    |  |
| 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)                               | 18            | 18    |  |
| From 65-84 years                                   | 0             | 0     |  |
| 85 years and over                                  | 0             | 0     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female                                             | 3             | 3     |  |
| Male                                               | 15            | 15    |  |

### Subject analysis sets

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | Overall trial |
|----------------------------|---------------|

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

Subject analysis set description:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was  $\leq 2$  and no major organ dysfunction was present (serum bilirubin < 2 mg/dL with AST, ALT, GGT and AP < 2 times ULN, left ventricular ejection fraction > 40% and serum creatinine < 2 mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

| Reporting group values                             | Overall trial |  |  |
|----------------------------------------------------|---------------|--|--|
| Number of subjects                                 | 18            |  |  |
| Age categorical                                    |               |  |  |
| Units: Subjects                                    |               |  |  |
| In utero                                           |               |  |  |
| Preterm newborn infants (gestational age < 37 wks) |               |  |  |
| Newborns (0-27 days)                               |               |  |  |
| Infants and toddlers (28 days-23 months)           |               |  |  |
| Children (2-11 years)                              |               |  |  |

|                           |    |  |  |
|---------------------------|----|--|--|
| Adolescents (12-17 years) | 18 |  |  |
| Adults (18-64 years)      |    |  |  |
| From 65-84 years          |    |  |  |
| 85 years and over         |    |  |  |
| Gender categorical        |    |  |  |
| Units: Subjects           |    |  |  |
| Female                    | 3  |  |  |
| Male                      | 15 |  |  |

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## End points

### End points reporting groups

|                              |               |
|------------------------------|---------------|
| Reporting group title        | Experimental  |
| Reporting group description: |               |
| Experimental arm             |               |
| Subject analysis set title   | Overall trial |
| Subject analysis set type    | Full analysis |

Subject analysis set description:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was  $\leq 2$  and no major organ dysfunction was present (serum bilirubin  $< 2$  mg/dL with AST, ALT, GGT and AP  $< 2$  times ULN, left ventricular ejection fraction  $> 40\%$  and serum creatinine  $< 2$  mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

### Primary: Primary

|                           |         |
|---------------------------|---------|
| End point title           | Primary |
| End point description:    |         |
| Progression-free survival |         |
| End point type            | Primary |
| End point timeframe:      |         |
| 12-months                 |         |

| End point values            | Experimental    | Overall trial        |  |  |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type          | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed | 18              | 18                   |  |  |
| Units: pfs                  | 18              | 18                   |  |  |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| Statistical analysis title              | Progression free survival    |
| Comparison groups                       | Experimental v Overall trial |
| Number of subjects included in analysis | 36                           |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[1]</sup>         |
| P-value                                 | = 50                         |
| Method                                  | Logrank                      |
| Parameter estimate                      | TTP                          |

Notes:

[1] - PFS

### Secondary: Secondary

|                                                                                                              |           |
|--------------------------------------------------------------------------------------------------------------|-----------|
| End point title                                                                                              | Secondary |
| End point description:                                                                                       |           |
| safety (toxicity, transplantation- and graft-related mortality)                                              |           |
| response to treatment according to the Cheson's criteria (Cheson B, et al. JCO 25, 570, 2007).               |           |
| overall survival                                                                                             |           |
| relapse rate                                                                                                 |           |
| acute and chronic Graft-versus-Host Disease                                                                  |           |
| haematological and immunological reconstitution, and chimerism.                                              |           |
| the impact of Complete Clinical Response, determined by flow cytometry and PET, on progression-free survival |           |
| End point type                                                                                               | Secondary |
| End point timeframe:                                                                                         |           |
| 36 months                                                                                                    |           |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Experimental    |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 18              |  |  |  |
| Units: pfs                  | 18              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On 4-year estimated PFS

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 3.0 |
|--------------------|-----|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events                            | All patients    |  |  |
|---------------------------------------------------|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 7 / 18 (38.89%) |  |  |
| number of deaths (all causes)                     | 7               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |
| Cardiac disorders                                 |                 |  |  |
| Septic shock                                      |                 |  |  |
| subjects affected / exposed                       | 2 / 18 (11.11%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders   |                 |  |  |
| Pneumonia                                         |                 |  |  |
| subjects affected / exposed                       | 2 / 18 (11.11%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Pleural effusion                                  |                 |  |  |
| subjects affected / exposed                       | 3 / 18 (16.67%) |  |  |
| 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>                     | All patients     |  |  |
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 11 / 18 (61.11%) |  |  |
| Blood and lymphatic system disorders                  |                  |  |  |
| Infection                                             |                  |  |  |
| subjects affected / exposed                           | 5 / 18 (27.78%)  |  |  |
| occurrences (all)                                     | 1                |  |  |
| Gastrointestinal disorders                            |                  |  |  |
| Diarrhoea                                             |                  |  |  |
| subjects affected / exposed                           | 6 / 18 (33.33%)  |  |  |
| occurrences (all)                                     | 1                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported