# Clinical trial results:
# SINGLE AGENT JNJ-56022473 IN MDS AND AML PATIENTS FAILING HYPOMETHYLATING AGENT BASED THERAPY

## Summary

| | |
|---|---|
| EudraCT number | 2016-000327-10 |
| Trial protocol | DE FR |
| Global end of trial date | 31 October 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 29 December 2019 |
| First version publication date | 29 December 2019 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SAMBA |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02992860 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GWT-TUD GmbH |
| Sponsor organisation address | Freiberger Straße 33, Dresden, Germany, 01067 |
| Public contact | Medical Consulting, GWT-TUD GmbH, +49 35125933193, martin.puttrich@gwtonline.de |
| Scientific contact | Medical Consulting, GWT-TUD GmbH, +49 35125933193, martin.puttrich@gwtonline.de |

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 | 25 October 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 July 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 October 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy of JNJ-56022473 for the treatment of MDS and AML patients who have relapsed after or are refractory to treatment with HMAs

Protection of trial subjects:

The conduct, evaluation, and documentation of this study, was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also be carried out in keeping with applicable local law(s) and regulation(s).
No further specific measures had to be put in place, because it had been assumed, that 9 mg/kg every 14 days is a well tolerated dose and would be the lowest dose that provides adequate exposure and sustained target saturation at the site of action throughout the entire dosing interval.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 23 November 2016 |
| 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 | Germany: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 0 |
| From 65 to 84 years | 23 |

| | |
|---|---|
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 6 study sites in Germany, whereas only 4 sites recruited patients into the study. From November 2016 on a total of 24 patients had been included in the study and treated with study medication before it was prematurely terminated.

### Pre-assignment

Screening details:

Screening period started with the patients consent and must completed within 28 days prior initiation of study treatment. Out of 28 screened patients 3 patient became a screening failure and 1 patient have had an SAE prior start of treatment.

### 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** | Talacotuzumab |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Talacotuzumab |
| Investigational medicinal product code | |
| Other name | JNJ-56022473 |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

9 mg / kg body weight every two weeks

| **Number of subjects in period 1** | Talacotuzumab |
|---|---|
| Started | 24 |
| Completed | 10 |
| Not completed | 14 |
| Adverse event, serious fatal | 6 |
| Consent withdrawn by subject | 2 |
| Physician decision | 1 |
| Adverse event, non-fatal | 1 |
| Lack of efficacy | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | overall trial |

Reporting group description: -

| Reporting group values | overall trial | Total | |
|---|---|---|---|
| Number of subjects | 24 | 24 | |
| Age categorical<br>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) | 0 | 0 | |
| From 65-84 years | 23 | 23 | |
| 85 years and over | 1 | 1 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 17 | 17 | |

## End points

### End points reporting groups

| Reporting group title | Talacotuzumab |
|---|---|

Reporting group description: -

### Primary: Overall hematological response rate at 3 months

| End point title | Overall hematological response rate at 3 months[1] |
|---|---|

End point description:

All patients with one of the following response states at the 3 months response assessment (V6) are defined as responder:
•Complete remission (CR), Partial remission (PR), marrow CR, Stable disease (SD) for MDS or
•Hematologic improvement for MDS or
•CR, Complete remission with incomplete recovery (CRi), morphologic leukemia free state, PR, Cytogenetic complete remission (CRc), Molecular complete remission (CRm), SD for AML

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

End point timeframe:

at 3 months (week 11)

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: As the study had been terminated prematurely, no formal statistical analysis on study endpoints was performed. Available data were only listed and summarized descriptively.

| End point values | Talacotuzumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 | | | |
| Units: number of patients | 24 | | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The observation phase for AEs started with signing the informed consent form and ended 28 days after the last intake of study drug, unless the investigator suspects a delayed adverse reaction to the study drug.

Adverse event reporting additional description:

In case of ongoing AEs after the last follow-up visit – especially when related to treatment with the study medication – the respective AE has been followed until resolution, if possible.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Talacotuzumab |

Reporting group description: -

| Serious adverse events | Talacotuzumab | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 24 / 24 (100.00%) | | |
| number of deaths (all causes) | 11 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related infection | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences causally related to treatment / all | 3 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subarachnoid haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vascular disorders | | | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Blood and lymphatic system disorders | | | |
| Anemia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypersensitivity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrointestinal angiectasia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal hemorrhage | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ulcer | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Decice related infection | | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia infection | | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutropenic infection | | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 6 / 24 (25.00%) | | | |
| occurrences causally related to treatment / all | 2 / 6 | | | |
| deaths causally related to treatment / all | 1 / 3 | | | |
| Pneumonia fungal | | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia staphylococcal | | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 3 | | | |
| Staphylococcal infection | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic hyperglycaemic coma | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Talacotuzumab | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 24 (100.00%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Haematoma | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | | |
| occurrences (all) | 6 | | |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Pallor | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Phlebitis | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Surgical and medical procedures | | | |
| Temporomandibular joint surgery | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Chills | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | | |
| occurrences (all) | 5 | | |
| Feeling hot | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Infusion site erythema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Injection site erythema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Mucosal haemorrhage | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Oedema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 4 | | |
| Pain | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 5 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 24 (29.17%) | | |
| occurrences (all) | 19 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Immune system disorders | | | |
| Decreased immune responsiveness | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |

| | | | |
|---|---|---|---|
| Testicular oedema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 24 (20.83%) | | |
| occurrences (all) | 5 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 4 | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Stridor | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Blood glucose decreased | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Fall | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 4 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| occurrences (all) | 7 | | |
| Wound haematoma | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Tachyarrhythmia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Dizziness<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Paraparesis<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Phantom pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 4 / 24 (16.67%)<br>4 | | |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Splenomegaly<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Eye disorders<br>Visual impairment<br>subjects affected / exposed<br>occurrences (all) | 1 / 24 (4.17%)<br>1 | | |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all) | 4 / 24 (16.67%)<br>4 | | |
| Constipation<br>subjects affected / exposed<br>occurrences (all) | 2 / 24 (8.33%)<br>2 | | |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all) | 7 / 24 (29.17%)<br>7 | | |
| Dysphagia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Gingival bleeding | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Intra-abdominal haematoma | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Lip swelling | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 5 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Tongue discolouration | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|---|---|---|
| Petechiae | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 2 | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 12 | | |
| Muscle tightness | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 3 | | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Aspergillus infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 4 | | |
| Wound sepsis | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Hyperkalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 2 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 24 (12.50%) | | |
| occurrences (all) | 3 | | |
| Type 3 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 February 2017 | Version 3.0 dated 10 Jan 2017 was issued to include new information from the updated safety reference document. |
| 13 September 2017 | Version 5.0 dated 28 Jul 2017 was issued to adjust the section "drug administration" according to updated safety information. |

Notes:

### 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 stopped in July 2017 due to results from a pivotal study which indicated added toxicity and lack of efficacy of talacotuzumab.

Notes: