



Clinical trial results:

Double-blind, placebo-controlled multicenter phase II trial to evaluate the efficacy and safety of romiplostim for the treatment of chemotherapy-induced thrombocytopenia in subjects with relapsed ovarian cancer (2nd or further line)

Summary

EudraCT number	2013-002564-69
Trial protocol	DE
Global end of trial date	26 February 2018

Results information

Result version number	v1 (current)
This version publication date	13 July 2022
First version publication date	13 July 2022

Trial information

Trial identification

Sponsor protocol code	410/56
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03622931
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GMIHO Gesellschaft für Medizinische Innovation - Hämatologie und Onkologie mbH
Sponsor organisation address	Almstadtstraße 7, Berlin, Germany, 10119
Public contact	Medical Consulting, GMIHO Gesellschaft für Medizinische Innovation - Hämatologie und Onkologie mbH, 0049 35125933100, info@gmiho.de
Scientific contact	Europäisches Kompetenzzentrum für Eierstockkrebs (EKZE) Stüdiensekretariat, Charité Campus Virchow-Klinikum Universitätsmedizin Berlin, 0049 30450564052, studiensekretariat.agovarialca@charite.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	20 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 February 2018
Global end of trial reached?	Yes
Global end of trial date	26 February 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of secondary chemotherapy-induced thrombocytopenia prophylaxis with romiplostim in ovarian cancer subjects receiving myelosuppressive chemotherapy, with respect to platelet suppression during the first romiplostim/placebo cycle.

Protection of trial subjects:

The conduct 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 carried out in keeping with applicable local law(s) and regulation(s). In order to assure adequate toxicity assessment, an independent DSMB was established for analysis of safety. The board met for the first time after ten patients were included in each arm

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 21
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	13
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From March 2015 until February 2018 a total of 23 patients was screened for inclusion at 8 study sites in Germany. It was planned to include 74 patients (approx. 37 patients each in experimental and placebo arm).

Pre-assignment

Screening details:

21 patients were registered; 11 patients were randomized to experimental arm A and 10 patients to placebo arm B.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

Patients were randomized by an online procedure at a 1:1 ratio to group A (experimental arm) and group B (control arm). The treatment allocation and the respective information regarding the vial number was obtained from computer-generated randomization lists (one per stratum) with permuted blocks of randomly variable size. Each block length was 4 and the number of blocks was 12 per stratum. Randomization was stratified according to combination-chemotherapy vs. monotherapy.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Standard chemotherapy + romiplostim

Arm type	Experimental
Investigational medicinal product name	Romiplostim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients received standard chemotherapy + romiplostim 750 µg. Romiplostim was administered on day 1, 8, 15 (+/- 1 day) of a three-weekly chemotherapy regimen, and in case of a four-weekly regime on day 1, 8, 15 with a break between day 22 – 28.

Arm title	Arm B
------------------	-------

Arm description:

Chemotherapy + placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients received standard chemotherapy + matching placebo. Placebo was administered on day 1, 8, 15 (+/- 1 day) of a three-weekly chemotherapy regimen, and in case of a four-weekly regime on day 1, 8, 15 with a break between day 22 – 28.

Number of subjects in period 1	Arm A	Arm B
Started	11	10
Completed	8	10
Not completed	3	0
randomized but no IMP administration	1	-
Protocol deviation	2	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A
Reporting group description: Standard chemotherapy + romiplostim	
Reporting group title	Arm B
Reporting group description: Chemotherapy + placebo	

Reporting group values	Arm A	Arm B	Total
Number of subjects	11	10	21
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	7	13
From 65-84 years	5	3	8
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	11	10	21
Male	0	0	0

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Standard chemotherapy + romiplostim	
Reporting group title	Arm B
Reporting group description:	
Chemotherapy + placebo	

Primary: Rate of grade 3/4 thrombocytopenia (nadir value)

End point title	Rate of grade 3/4 thrombocytopenia (nadir value)
End point description:	
End point type	Primary
End point timeframe:	
on days 8, 11 or 12, 15 and 18 or 19	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	10		
Units: percent				
number (confidence interval 95%)	0.00 (0.00 to 39.94)	60.00 (26.24 to 87.84)		

Statistical analyses

Statistical analysis title	Efficacy analysis
Comparison groups	Arm B v Arm A
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.0036
Method	One-sided Cochran-Armitage Trend Test

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

on days 8, 11 or 12, 15 and 18 or 19 (days 18 or 19 are optional after cycle 1) and 30 days after last application of study treatment

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

Dictionary used

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

Dictionary version	18.0
--------------------	------

Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: In total, 220 AEs were reported (104 in arm A and 116 in arm B). Platelet count decreased was the most frequently reported AE (arm A: n=5 [50%], arm B: n=9 [90%]). Platelet count decreased was severe or life-threatening (grade 3/4) in two of the five patients of arm A and in all nine patients of arm B. AEs were more frequently related to chemotherapy than to study treatment (romiplostim/placebo). Six patients (arm A: n=2, arm B: n=4) experienced SAEs.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2016	Amendment No. 01 dated 16/02/2016: change of study title from "2nd and 3rd line" to "2nd and further line"; change of exclusion criteria; specification of indication, change of time point of the first meeting of Data Safety and Monitoring Board (DSMB)

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.

Due to slow recruitment and the results of the interim analysis, the study was prematurely discontinued on 17 JAN 2019.

Notes: