Clinical trial results:
Multicenter, Double-Blind, Randomized, Comparative Efficacy and Safety Study of MYL 1401H and European Sourced Neulasta® in Stage II/III Breast Cancer Patients Receiving Neoadjuvant or Adjuvant Chemotherapy

Summary

EudraCT number	2014-002324-27
Trial protocol	HU DE BG PL
Global end of trial date	09 February 2016

Results information

Result version number	v1 (current)
This version publication date	12 January 2024
First version publication date	12 January 2024

Trial information

Trial identification

Sponsor protocol code	MYL-1401H-3001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Mylan GmbH
Sponsor organisation address	Thurgauerstrasse 40, 8050 Zürich, Switzerland, Switzerland, 8010
Public contact	Eduardo J. Pennella, Mylan GmbH, 724 514-2369, Eduardo.Pennella@mylan.com
Scientific contact	Eduardo J. Pennella, Mylan GmbH, 724 514-2369, Eduardo.Pennella@mylan.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	15 September 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2016
Global end of trial reached?	Yes
Global end of trial date	09 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the efficacy of MYL-1401H versus Neulasta® for the prophylactic treatment of chemotherapy-induced neutropenia in patients with stage II/III breast cancer receiving TAC anti-cancer chemotherapy.

Protection of trial subjects:

Informed consent was obtained before a patient was enrolled in the study and prior to the commencement of any protocol-driven activities. The investigator (or designated staff member) met with the patient and explained the study in sufficient detail to permit an informed decision to participate. The investigator (or designated staff member), patient, and a witness signed an ICF. The original signed and dated ICF for each patient was kept with the patient's chart, and a copy was provided to the patient.
The ICF was written in compliance with ICH guidelines and other national regulations as appropriate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 January 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	Bulgaria: 15
Country: Number of subjects enrolled	Georgia: 56
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Ukraine: 110
Worldwide total number of subjects	194
EEA total number of subjects	28

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	194
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter, randomized, double-blind, parallel-group study with 2 treatment arms. Patients underwent 6 chemotherapy cycles planned every 3 weeks (Cycle 1 through Cycle 6), each cycle beginning on Day 1, when the chemotherapy dose was administered, with the administration of either MYL-1401H or EU-Neulasta® on Day 2 of each cycle.

Pre-assignment

Screening details:

The planned duration for the entire study was approximately 28 weeks (from Screening to follow-up [24 weeks from the first dose of study drug]), assuming no delays in dosing. The planned duration of patient treatment during the entire study was approximately 18 weeks (from the first day of chemotherapy [Day 1 Cycle 1] to the last scheduled asses

Period 1

Period 1 title	Test product- MYL-1401H
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The oncology pharmacist who prepared the doses and the person administering the drug (eg, study nurse, physician [other than the principal investigator or sub-principal investigator]) were the only individuals who had access or knowledge of the actual drug delivered. Other unblinded personnel in the study included the clinical research associate (CRA) who audited the drug dispensation log and drug accountability. There were 2 CRAs assigned to each site: with the CRA monitoring the study

Arms

Arm title	Test arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Test Product
Investigational medicinal product code	MYL-1401H
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Test Product, Dose, Mode of Administration, and Batch Number: MYL-1401H 6 mg injection administered as a single sc dose, on Day 2 of each cycle, ie, 24 h (+ 2 h after) after the end of chemotherapy. Each prefilled syringe (PFS) contained 6 mg of MYL-1401H in 0.6 mL solution for injection. The concentration was 10 mg/mL based on protein only. Batch S14DBPEGI-0003 of MYL-1401H was used.

Number of subjects in period 1[1]	Test arm
Started	127
Completed	120
Not completed	7
Physician decision	1
Consent withdrawn by subject	2
Adverse event, non-fatal	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Number of Patients (Planned and Analyzed):
Planned: Approximately 189 patients were planned for enrolment into the study in a 2:1 ratio of the 2 treatment
groups (126:63 in the MYL-1401H and EU-Neulasta® arm, respectively).
Actual: 194 patients were randomized and received study treatment; 127 patients were randomized to receive
MYL-1401H and 67 patients were randomized to receive EU-Neulasta®.
Completed: 186 patients completed the study.
Analyzed: 194 patients were included in the data an

Period 2

Period 2 title	Reference product, US-Neulasta®
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The oncology pharmacist who prepared the doses and the person administering the drug (eg, study nurse, physician [other than the principal investigator or sub-principal investigator]) were the only individuals who had access or knowledge of the actual drug delivered.
Other unblinded personnel in the study included the clinical research associate (CRA) who audited the drug dispensation log and drug accountability. There were 2 CRAs assigned to each site: with the CRA monitoring the study bei

Arms

Arm title	Reference Product- EU-Neulasta®

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Reference
Investigational medicinal product code	EU-Neulasta®
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Reference Product, Dose, Mode of Administration, and Batch Numbers: EU-Neulasta® 6 mg injection administered as a single sc dose, on Day 2 of each cycle, ie, 24 h (+ 2 h) after the end of chemotherapy. Each PFS
contained 6 mg of pegfilgrastim in 0.6 mL solution for injection. The concentration was 10 mg/mL based on
protein only. Batches 1048603D and 1053573B of EU-Neulasta® were used.

Number of subjects in period 2[2]	Reference Product-EU-Neulasta®
Started	67
Completed	66
Not completed	1
Other	1

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Number of Patients (Planned and Analyzed):
Planned: Approximately 189 patients were planned for enrolment into the study in a 2:1 ratio of the 2 treatment
groups (126:63 in the MYL-1401H and EU-Neulasta® arm, respectively).
Actual: 194 patients were randomized and received study treatment; 127 patients were randomized to receive
MYL-1401H and 67 patients were randomized to receive EU-Neulasta®.
Completed: 186 patients completed the study.
Analyzed: 194 patients were included in the data an

Baseline characteristics

End points

End points reporting groups

Reporting group title	Test arm
Reporting group description: -	
Reporting group title	Reference Product- EU-Neulasta®
Reporting group description: -	

Primary: Primary Efficacy Endpoint:

End point title	Primary Efficacy Endpoint:[1]
End point description:	
End point type	Primary
End point timeframe:	

Primary Efficacy Endpoint:
The primary efficacy endpoint was the duration of severe neutropenia (DSN) in Cycle 1, defined as days with
ANC <0.5 × 109/L.

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: Primary Efficacy Analysis: An analysis of variance (ANOVA) model, with treatment as an independent variable,
and a 2-sided 95% confidence interval (CI) for the difference in least squares mean (LS Mean) of the DSN for the 2 treatments, was employed. Equivalence between the 2 treatments was declared if the CI was completely within the range of ± 1 day.

End point values	Test arm			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: ANC <0.5 × 109/L.				
least squares mean (confidence interval 95%)				
MYL-1401H	131 (1 to 148)			
EU-Neulasta®	130 (1 to 148)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

A total of 1220 TEAEs were reported in the safety population. A total of 806 TEAEs were reported in 114 (89.8%) patients in the MYL-1401H group and 414 TEAEs were reported in 58 (86.6%) patients in the EU-Neulasta® group (Table 14.3.1.1.2). Refer to Tab

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Test- MYL-1401H
Reporting group description: -	
Reporting group title	Reference arm- EU-Neulasta®

Reporting group description: -

Serious adverse events	Test- MYL-1401H	Reference arm- EU-Neulasta®	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 127 (6.30%)	1 / 67 (1.49%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 127 (0.79%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	6 / 127 (4.72%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 127 (0.79%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	1 / 127 (0.79%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Test- MYL-1401H	Reference arm- EU-Neulasta®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 127 (26.77%)	13 / 67 (19.40%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 127 (5.51%)	8 / 67 (11.94%)	
occurrences (all)	7	8	
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 127 (5.51%)	7 / 67 (10.45%)	
occurrences (all)	7	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 127 (2.36%)	2 / 67 (2.99%)	
occurrences (all)	3	2	
Platelet count decreased			
subjects affected / exposed	7 / 127 (5.51%)	5 / 67 (7.46%)	
occurrences (all)	7	5	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 127 (2.36%)	2 / 67 (2.99%)	
occurrences (all)	3	2	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 127 (9.45%)	8 / 67 (11.94%)	
occurrences (all)	12	8	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 127 (3.15%)	1 / 67 (1.49%)	
occurrences (all)	4	1	
Blood and lymphatic system disorders			

Anemia			
subjects affected / exposed	14 / 127 (11.02%)	9 / 67 (13.43%)	
occurrences (all)	14	9	
Febrile neutropenia			
subjects affected / exposed	7 / 127 (5.51%)	1 / 67 (1.49%)	
occurrences (all)	7	1	
Thrombocytopenia			
subjects affected / exposed	14 / 127 (11.02%)	6 / 67 (8.96%)	
occurrences (all)	14	6	
Thrombocytosis			
subjects affected / exposed	8 / 127 (6.30%)	0 / 67 (0.00%)	
occurrences (all)	8	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	23 / 127 (18.11%)	10 / 67 (14.93%)	
occurrences (all)	23	10	
Fatigue			
subjects affected / exposed	19 / 127 (14.96%)	13 / 67 (19.40%)	
occurrences (all)	19	16	
Pyrexia			
subjects affected / exposed	3 / 127 (2.36%)	5 / 67 (7.46%)	
occurrences (all)	3	5	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	3 / 127 (2.36%)	1 / 67 (1.49%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 127 (2.36%)	4 / 67 (5.97%)	
occurrences (all)	3	4	
Abdominal pain upper			
subjects affected / exposed	3 / 127 (2.36%)	2 / 67 (2.99%)	
occurrences (all)	3	2	
Constipation			
subjects affected / exposed	3 / 127 (2.36%)	2 / 67 (2.99%)	
occurrences (all)	3	2	

Diarrhea			
subjects affected / exposed	16 / 127 (12.60%)	12 / 67 (17.91%)	
occurrences (all)	16	12	
Dyspepsia			
subjects affected / exposed	4 / 127 (3.15%)	0 / 67 (0.00%)	
occurrences (all)	4	0	
Nausea			
subjects affected / exposed	34 / 127 (26.77%)	13 / 67 (19.40%)	
occurrences (all)	37	25	
Stomatitis			
subjects affected / exposed	11 / 127 (8.66%)	2 / 67 (2.99%)	
occurrences (all)	11	2	
Vomiting			
subjects affected / exposed	12 / 127 (9.45%)	7 / 67 (10.45%)	
occurrences (all)	12	7	
Reproductive system and breast disorders			
Menstruation irregular			
subjects affected / exposed	3 / 127 (2.36%)	1 / 67 (1.49%)	
occurrences (all)	3	1	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	4 / 127 (3.15%)	1 / 67 (1.49%)	
occurrences (all)	4	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	34 / 127 (26.77%)	13 / 67 (19.40%)	
occurrences (all)	76	36	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 127 (1.57%)	2 / 67 (2.99%)	
occurrences (all)	2	2	
Bone pain			
subjects affected / exposed	34 / 127 (26.77%)	13 / 67 (19.40%)	
occurrences (all)	51	24	
Myalgia			

subjects affected / exposed	5 / 127 (3.94%)	1 / 67 (1.49%)	
occurrences (all)	5	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 127 (6.30%)	0 / 67 (0.00%)	
occurrences (all)	8	0	
Hypocalcaemia			
subjects affected / exposed	3 / 127 (2.36%)	2 / 67 (2.99%)	
occurrences (all)	3	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported