Clinical trial results:
Randomised phase II study of paclitaxel alone versus paclitaxel plus sorafenib in second- or third-line treatment of patients with metastatic breast cancer

Summary

EudraCT number	2009-018025-73
Trial protocol	DE
Global end of trial date	19 July 2014

Results information

Result version number	v1 (current)
This version publication date	04 June 2022
First version publication date	04 June 2022

Trial information

Trial identification

Sponsor protocol code	GMIHO-008/2008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01320111
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	CRO, iOMEDICO AG, 0049 761152420, info@iomedico.com
Scientific contact	CRO, iOMEDICO AG, 0049 761152420, info@iomedico.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	18 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2014
Global end of trial reached?	Yes
Global end of trial date	19 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This Study will assess the potential prolongation in progression free survival in patients with metastatic breast cancer in combination with standard chemotherapy paclitaxel compared with the paclitaxel monotherapy.

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailes in the Declaration of Helsinki. The study waas also carried out in keeping with applicable local law(s) and regulation(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2010
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was initiated in July 2010 and recruitment were stopped in November 2012 for an interim analysis. Based on the results, recruitment was terminated. A total of 60 (Arm A: 30, Arm B: 30) patients were enrolled at 21 sites in Germany.

Pre-assignment

Screening details:

The patients were randomised between the study groups and stratified according to line of treatment (2nd or 3rd) and pretreatment with bevacizumab.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (Standard treatment)

Arm description:

Paclitaxel monotherapy with 80 mg/m² as one-hour i.v. infusion on day 1, 8, 15 every 28 days (one cycle). Dosing levels for dose reduction: 61.6 mg/m² and 45.6 mg/m².

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m² as one-hour i.v. infusion on day 1, 8, 15 every 28 days (one cycle)

Arm title	Arm B (Test treatment)

Arm description:

Combination therapy with paclitaxel 80 mg/m2 as one-hour i.v. infusion on day 1, 8, 15 and sorafenib 400 mg orally twice daily (bid), i.e. 2x200 mg tablets in the morning and 2x200 mg tablets in the evening, taken continuously throughout 28-day cycles. Sorafenib levels for dose escalation and dose reductions: 200 mg in the morning, 200 mg in the evening (200 mg bid) and 200 mg in the morning, 400 mg in the evening. Paclitaxel levels for dose reductions: 61.6 mg/m² and 45.6 mg/m².

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

paclitaxel 80 mg/m2 as one-hour i.v. infusion on day 1, 8, 15

Investigational medicinal product name	Sorafenib
Investigational medicinal product code	
Other name	Nexavar®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
400 mg orally twice daily (bid) taken continuously throughout 28-day cycles

Number of subjects in period 1	Arm A (Standard treatment)	Arm B (Test treatment)
Started	30	30
Completed	28	28
Not completed	2	2
Consent withdrawn by subject	-	1
non-eligible	1	1
non-evaluable	1	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	Arm A (Standard treatment)
Reporting group description:	
Paclitaxel monotherapy with 80 mg/m² as one-hour i.v. infusion on day 1, 8, 15 every 28 days (one cycle). Dosing levels for dose reduction: 61.6 mg/m² and 45.6 mg/m².	
Reporting group title	Arm B (Test treatment)
Reporting group description:	
Combination therapy with paclitaxel 80 mg/m2 as one-hour i.v. infusion on day 1, 8, 15 and sorafenib 400 mg orally twice daily (bid), i.e. 2x200 mg tablets in the morning and 2x200 mg tablets in the evening, taken continuously throughout 28-day cycles. Sorafenib levels for dose escalation and dose reductions: 200 mg in the morning, 200 mg in the evening (200 mg bid) and 200 mg in the morning, 400 mg in the evening. Paclitaxel levels for dose reductions: 61.6 mg/m² and 45.6 mg/m².	

Primary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
End point description:	
End point type	Primary
End point timeframe:	
from randomisation to disease progression or death	

End point values	Arm A (Standard treatment)	Arm B (Test treatment)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: month				
median (confidence interval 95%)	6.6 (5.1 to 9.0)	5.6 (3.8 to 6.5)		

Statistical analyses

Statistical analysis title	Primary efficacy
Comparison groups	Arm A (Standard treatment) v Arm B (Test treatment)
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0409
Method	Logrank

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: from randomisation until disease progression or death	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

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

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: Apart from 1 patient in Arm A, all patients experienced at least 1 adverse event. The most common adverse events of any toxicity grade in Arm A were peripheral neuropathy (55% of patients), fatigue (45%), diarrhoea (41%) and alopecia (41%). In Arm B, the most common adverse events were diarrhoea (57%), fatigue (50%), mucositis oral (39%) and peripheral neuropathy (36%).

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2010	Study protocol (3.0, 02 Nov 2010): Clarification of wording of inclusion/exclusion criteria; formal corrections/changes; subsequent submission of study sites;
05 April 2013	Study protocol (4.0, 15 Feb 2013): Formal implementation of temporary halt of recruitment after recruitment of the 60. patient (measure not caused by safety issue); implementation of a prospective efficacy interim analysis (including enhancement of required total patient number (128 to 148); prolongation of recruitment phase); formal corrections/changes

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 December 2012	Temporary halt of recruitment after recruitment of the 60. patient (measure not caused by safety issue); announcement of implementation of a prospective efficacy interim analysis and related protocol amendment.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Premature study termination due to futility (decision based on results of prospective efficacy interim analysis July/2013); recruitment was not resumed; study continued regular follow-up phase as per protocol.

Notes: