ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/23/2014

ClinicalTrials.gov ID: NCT01363986

Study Identification

Unique Protocol ID:	ML25432
Brief Title:	A Study of Herceptin (Trastuzumab) in Combination With Whole Brain Radiotherapy in Patients With HER-2 Positive Breast Cancer
Official Title:	A Multicenter, Open Label Study to Assess the Effect of Trastuzumab + Whole Brain Radiotherapy (WBRT) on Brain Metastases From HER-2 Positive Breast Cancer. (bHERt-2)
Secondary IDs:	

Study Status

Record Verification:	July 2014
Overall Status:	Terminated
Study Start:	September 2011
Primary Completion:	June 2012 [Actual]
Study Completion:	June 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? No Delayed Posting?
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 113/10 Board Name: COMITATO ETICO DELL'IRCCS ISTITUTI FISIOTERAPICI OSPITALIERI DI ROMA Board Affiliation: IRCCS ISTITUTO REGINA ELENA (IFO) - ROMA (RM) Phone: 0039 06 52662719 Email: dambrosio@ifo.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This single-arm, multicenter, open-label study will evaluate the efficacy and safety of Herceptin (trastuzumab) in combination with whole brain radiotherapy on brain metastases in patients with HER-2 positive breast cancer. The patients will receive Herceptin 4 mg/kg (loading dose) followed by 2 mg/kg for a maximum of 18 weekly cycles. The anticipated time on study treatment is 18 weeks.
Detailed Description:	

Conditions

Conditions:	Breast Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 3 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Trastuzumab Monotherapy Participants received an initial loading dose of 4 milligrams per kilogram (mg/kg) trastuzumab intravenous (i.v.), followed by weekly doses of 2 mg/kg i.v. for up to 18 weeks.	Drug: trastuzumab [Herceptin] Initial loading dose of 4 mg/kg i.v. infusion, followed by weekly doses of 2 mg/kg for up to 18 weeks.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Adult patients, >/=18 years of age
- Diagnosis of breast carcinoma with HER-2 overexpression
- At least one measurable brain metastasis
- Patients for whom, according to investigator assessment, whole brain radiotherapy is the best therapeutic option
- Performance status (WHO) </=2
- Life expectancy >/=3 months

Exclusion Criteria:

- Presence of neoplastic meningitis
- Any prior radiotherapy to the brain
- Patients for whom, according to investigator assessment, stereotactic radiotherapy is the best therapeutic option
- Previous neoplasms, other than breast carcinoma, within 5 years since enrolment

Contacts/Locations

Study Officials: Clinical Trials

Study Director
Hoffmann-La Roche

Locations: Italy

Meldola, Italy, 47014

San Giovanni Rotondo, Italy, 71013

Viterbo, Italy, 01100

Torino, Italy, 10126

Firenze, Italy, 50134

Candiolo, Italy, 10060

Ravenna, Italy, 48100

Latina, Italy, 04100

Saronno, Italy, 21047

Rozzano, Italy, 20089

Lecce, Italy, 73100

Ancona, Italy

Roma, Italy, 00168

Latina, Italy, 04100

Parma, Italy, 43100

Brindisi, Italy, 72100

Sassari, Italy, 07100

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 milligrams per kilogram (mg/kg) trastuzumab intravenously (i.v.) on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Overall Study

	Trastuzumab Monotherapy
Started	3
Completed	2
Not Completed	1
Disease progression	1

Baseline Characteristics

Analysis Population Description

Intent to treat (ITT) population included all consented participants who received study treatment.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Baseline Measures

	Trastuzumab Monotherapy
Number of Participants	3
Age, Continuous [units: years] Median (Full Range)	60 (37 to 74)

	Trastuzumab Monotherapy
Gender, Male/Female [units: participants]	
Female	3
Male	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Participants With Brain Objective Response According to Response Evaluation Criteria In Solid Tumors (RECIST) Criteria at Cycle 7
Measure Description	Brain objective response was defined as either a complete response (CR) or partial response (PR), provided that there was no increase in steroid requirements or worsening of neurological signs and symptoms. CR was defined as the disappearance of all central nervous system (CNS) lesions. PR was defined as a greater than or equal to (≥) 30 percent (%) reduction in the volumetric sum of all measurable CNS lesions.
Time Frame	Baseline and Cycle 7 (Week 7, approximately 5 weeks after completion of whole brain radiotherapy [WBRT])
Safety Issue?	No

Analysis Population Description

ITT population; 1 participant was not assessed at Cycle 7.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Measured Values

	Trastuzumab Monotherapy
Number of Participants Analyzed	2
Number of Participants With Brain Objective Response According to Response Evaluation Criteria In Solid Tumors (RECIST) Criteria at Cycle 7 [units: participants]	2

2. Secondary Outcome Measure:

Measure Title	Number of Participants With Brain Objective Response According to RECIST Criteria at Cycle 15
Measure Description	Brain objective response was defined as either a CR or PR, provided that there was no increase in steroid requirements or worsening of neurological signs and symptoms. CR was defined as the disappearance of all CNS lesions. PR was defined as ≥30% reduction in the volumetric sum of all measurable CNS lesions.
Time Frame	Baseline and Cycle 15 (Week 15, approximately 13 weeks after completion of WBRT)
Safety Issue?	No

Analysis Population Description

ITT population; 2 participants were not assessed at Cycle 15.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Measured Values

	Trastuzumab Monotherapy
Number of Participants Analyzed	1
Number of Participants With Brain Objective Response According to RECIST Criteria at Cycle 15 [units: participants]	0

3. Secondary Outcome Measure:

Measure Title	Number of Participants With Brain Objective Response Defined According to RECIST Criteria at the Final Visit
Measure Description	Brain objective response was defined as either a CR or PR), provided that there was no increase in steroid requirements, or worsening of neurological signs and symptoms. CR was defined as the disappearance of all CNS lesions. PR was defined as ≥30% reduction in the volumetric sum of all measurable CNS lesions.
Time Frame	BL and 4 weeks after Cycle 15 (Week 15, approximately 13 weeks after completion of WBRT) or the last dose of study treatment
Safety Issue?	No

Analysis Population Description

ITT population; 1 participant was not assessed at the final visit.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Measured Values

	Trastuzumab Monotherapy
Number of Participants Analyzed	2
Number of Participants With Brain Objective Response Defined According to RECIST Criteria at the Final Visit [units: participant]	1

4. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	The number of participants surviving at the final visit.
Time Frame	Baseline, weekly for 3 weeks (pre-WBRT phase), Cycles 1 through 15 (treatment phase Weeks 1 through 15), and 4 weeks after Cycle 15 (Week 15) or the last dose of study treatment
Safety Issue?	No

Analysis Population Description

ITT population; survival status of 1 participant was unknown at the final visit.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Measured Values

	Trastuzumab Monotherapy
Number of Participants Analyzed	2
Overall Survival [units: participant]	1

5. Secondary Outcome Measure:

Measure Title	Brain Progression-Free Survival (B-PFS)
Measure Description	B-PFS was defined as the time from the date of first study drug assumption and the date of documented evidence of brain progression (defined as appearance of new brain metastases or progression of pre-existing lesions) or death for brain progression, whichever came first. Progression in other metastatic sites, deaths not due to brain-progression and withdrawals due to adverse events were to be considered as competing risk.
Time Frame	Baseline, weekly for 3 weeks (pre-WBRT phase), Cycles 1 through 15 (treatment phase Weeks 1 through 15), and 4 weeks after Cycle 15 (Week 15) or the last dose of study treatment
Safety Issue?	No

Analysis Population Description

Due to the premature interruption of the study and the small number of enrolled participants (3 nerolled), all participant data were listed only, without any descriptive statistics or data analysis. The endpoint of B-PFS was thus not analyzed.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Measured Values

	Trastuzumab Monotherapy
Number of Participants Analyzed	0

No data displayed because Outcome Measure has zero total participants analyzed.

Reported Adverse Events

Time Frame	Adverse events were reported from randomization up through 28 days after the final study drug treatment.
Additional Description	Safety was assessed in all consented participants who received study treatment.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by doses of 2 mg/kg trastuzumab i.v. once weekly for up to 18 weeks.

Serious Adverse Events

	Trastuzumab Monotherapy
	Affected/At Risk (%)
Total	0/3 (0%)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Trastuzumab Monotherapy
	Affected/At Risk (%)
Total	3/3 (100%)
Gastrointestinal disorders	
Diarrhoea [A] *	1/3 (33.33%)
Nausea [B] *	1/3 (33.33%)
General disorders	
Asthenia [A] *	3/3 (100%)
Headache [A] *	2/3 (66.67%)
Pyrexia [A] *	1/3 (33.33%)
Speech disorder [A] *	1/3 (33.33%)
Infections and infestations	
Device-related infection [A] *	1/3 (33.33%)
Metabolism and nutrition disorders	
Hyperglycaemia [A] *	1/3 (33.33%)
Musculoskeletal and connective tissue disorders	
Gait disturbance [A] *	1/3 (33.33%)

	Trastuzumab Monotherapy
	Affected/At Risk (%)
Musculoskeletal pain [A] *	1/3 (33.33%)
Nervous system disorders	
Epilepsy [A] *	1/3 (33.33%)
Respiratory, thoracic and mediastinal disorders	
Dyspnoea [A] *	1/3 (33.33%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 14.1
B Term from vocabulary, NCI-CTC AE 4.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

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