

PROTOCOL HERNATA
A randomized fase III study of
trastuzumab (Herceptin®) – docetaxel (Taxotere®)
VS
trastuzumab – vinorelbine
in 1st line treatment of patients with metastatic HER 2 positive
breast cancer

CRF

DBCG
Rigshospitalet afsnit 2501
2100 København Ø

**HERNATA
Randomization Worksheet**

Name: _____ Initials: _____ For Sweden, Norway Date of birth (ddmmyy): _____ For Denmark Cpr.no.: _____	Country / Department: _____ Phone number: _____ Fax number: _____ Center number: _____
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Inclusion criteria	Yes	No
Histologically / cytologically confirmed locally advanced or metastatic carcinoma of the breast	<input type="checkbox"/>	<input type="checkbox"/>
Primary tumor or metastasis HER2 IHC 3+ or FISH +	<input type="checkbox"/>	<input type="checkbox"/>
Expected lifetime more than 12 weeks	<input type="checkbox"/>	<input type="checkbox"/>
WHO PS \leq 2	<input type="checkbox"/>	<input type="checkbox"/>
Informed consent, orally and in writing	<input type="checkbox"/>	<input type="checkbox"/>
Age \geq 18 and \leq 75 years	<input type="checkbox"/>	<input type="checkbox"/>
Patient compliance	<input type="checkbox"/>	<input type="checkbox"/>
All questions must be answered by Yes	<input type="checkbox"/>	<input type="checkbox"/>

Exclusion criteria	Yes	No
Chemotherapy for metastatic disease	<input type="checkbox"/>	<input type="checkbox"/>
(Neo-) adjuvant chemotherapy \leq 4 weeks before study entry. (Neo-)adjuvant treatment with taxanes, vinorelbine, trastuzumab \leq 12 months ago.	<input type="checkbox"/>	<input type="checkbox"/>
Earlier treatment targeting components of the EGF-system	<input type="checkbox"/>	<input type="checkbox"/>
Dyspnoea at rest due to advanced malignancy or patients requiring oxygen	<input type="checkbox"/>	<input type="checkbox"/>
Pregnant or lactating woman. Negative pregnancy test is required during screening period	<input type="checkbox"/>	<input type="checkbox"/>
Fertile woman who does not use adequate contraception	<input type="checkbox"/>	<input type="checkbox"/>
Clinical symptoms or signs suggesting CNS-metastasis or meningeal carcinomatosis	<input type="checkbox"/>	<input type="checkbox"/>
Other existing or earlier malignancy except, ^{a)} adequately treated and cured carcinoma in situ cervicis uteri, ^{b)} planucellular carcinoma of skin or ^{c)} other cancer with minimal expected risk of recurrence.	<input type="checkbox"/>	<input type="checkbox"/>
Congestive heart failure despite adequate treatment (cardiomegalia, objective signs of insufficiency or left ventricular ejection fraction (LVEF) under normal limit for the institution)	<input type="checkbox"/>	<input type="checkbox"/>
WBC $<$ $3.0 \times 10^9/l$, neutrophiles $<$ $1.5 \times 10^9/l$ or platelets \leq $100 \times 10^9/l$.	<input type="checkbox"/>	<input type="checkbox"/>
Bilirubin $>$ UNL and/or ASAT/ALAT $>$ $2.5 \times$ UNL (patients with liver metastasis $5 \times$ UNL) and/or alkaline phosphatase $>$ $5 \times$ UNL	<input type="checkbox"/>	<input type="checkbox"/>
ASAT/ALAT \geq $1.5 \times$ UNL and alkaline phosphatase $>$ $2.5 \times$ UNL	<input type="checkbox"/>	<input type="checkbox"/>
Se- creatinine \geq $1.5 \times$ UNL	<input type="checkbox"/>	<input type="checkbox"/>
Known allergy to any contents of study medication or murine proteins	<input type="checkbox"/>	<input type="checkbox"/>
Sensory neuropathy $>$ grad 1	<input type="checkbox"/>	<input type="checkbox"/>
All questions must be answered by No	<input type="checkbox"/>	<input type="checkbox"/>

Investigator approval	
Date: _____	Signature: _____

**Fax this page to DBCG Center for randomization between 8 am and 4 pm. Fax no: +45 3526 3525
Phone-number +45 3538 6530**

To be filled by DBCG:	
Date of randomization: _____	Treatment arm 1: Docetaxel and Trastuzumab <input type="checkbox"/>
Patient number: _____	Treatment arm 2: Vinorelbine and Trastuzumab <input type="checkbox"/>
Signature: _____	

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Institution Numbers (IN) and LAB-Ids (LAB) :**Denmark**

IN	LAB	
13	1301	: Rigshospitalet
15	1516	: Herlev
20	2001	: Hillerød
25	2501	: Roskilde
	2502	: Køge
35	3501	: Næstved
	3001	: Holbæk
	3002	: Slagelse
42	4202	: Odense
50	5001	: Sønderborg
55	5501	: Esbjerg
60	6008	: Vejle
65	6502	: Herning
70	7003	: Århus
76	7601	: Viborg
80	8001	: Ålborg

Sweden

IN	LAB	
01	0101	: Stockholm, Karolinska (Danderyd + Radiumhemmet)
02	0201	: Stockholm, SÖS
03	0301	: Malmö
04	0401	: Lund
05	0501	: Helsingborg
06	0601	: Göteborg
07	0701	: Linköping
08	0801	: Karlstad
09	0901	: Västerås
10	1001	: Uppsala
11	1101	: Sundsvall
12	1201	: Umeå

Norway

IN	LAB	
91	9101	: Ullevål Universitetsh.
92	9201	: Rogaland
93	9301	: Ålesund
94	9401	: Molde
95	9501	: Frederikstad

Instructions

1. Type or print **using only black ballpoint ink**.
2. The CRF must be completed in **English**.
3. Corrections should be made **only** as follows:
 - Draw a single line through the incorrect entry
 - Enter correct data in the box or alongside
 - Initials and date the correction
(Only investigator or the study nurse is allowed to do this)
 - **Do not erase, write over, (or use correction fluid)**
4. Patient number must be written in the box in the top of all pages.
5. Where information is not available, enter "ND" in the box. If the box has a precoded value indicating "Not done" USE THE CODE instead of typing ND. Overall response on page 20b is an example of such a box.
6. Cross out any box that has been considered, but obviously must be left empty
7. Dates are given as ddmmyy.
Complete dates should be entered whenever it is possible. If month or day is unknown, enter a dash (--) in the field. Year must be entered in all date fields.
8. All comments must be entered on the appropriate Comments Page. Whenever it is possible state which variable in the CRF remarks refer to.
9. Adverse events are graded according to NCI-CTC version 3.0.

Protocol HERNATA

Reference Units
Denmark

Institution Number (LAB ID)			
Valid from (date)			
	Lower limit	Upper limit	Unit
Haemoglobin			mmol/l
WBC			10 ⁹ /l
ANC			10 ⁹ /l
Platelets			10 ⁹ /l
ASAT			IU/l
ALAT			IU/l
Bilirubin			μmol/l
Serum creatinine			mmol/l
Alkaline phosphate			IU/l
LDH			IU/l
Ca ⁺⁺ (ionised or albumin corrected)			mmol/l
MUGA/ Echocardiography			%

Investigator approval	
Date:	Signature:

Patient no.	<input type="text"/>	Protocol HERNATA	On study Page 1 of 7
Initials	<input type="text"/>		

Treatment arm 1: Docetaxel and Trastuzumab 2: Vinorelbine and Trastuzumab	<input type="checkbox"/>
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Patient data at time of On-study		Date:
PS WHO (0 – 4)	<input type="checkbox"/>	<input type="text"/>
Height (cm)	<input type="text"/>	<input type="text"/>
Weight (kg)	<input type="text"/>	<input type="text"/>
MUGA /Echocardiography (%)	<input type="checkbox"/>	<input type="text"/>
Date of ECG		<input type="text"/>
CT/ X-ray chest 0: Not done, 1: Yes, date	<input type="checkbox"/>	<input type="text"/>
CT/ X-ray bones 0: Not done, 1: Yes, date	<input type="checkbox"/>	<input type="text"/>
CT/Ultrasound liver 0: Not done, 1: Yes, date	<input type="checkbox"/>	<input type="text"/>
MR-scan 0: Not done, 1: Yes, date. If yes, specify organ: _____	<input type="checkbox"/>	<input type="text"/>
Bone scintigraphy 0: Not done, 1: Yes, date	<input type="checkbox"/>	<input type="text"/>
Other 0: Not done, 1: Yes, date. If yes, specify: _____	<input type="checkbox"/>	<input type="text"/>
Other 0: Not done, 1: Yes, date. If yes, specify: _____	<input type="checkbox"/>	<input type="text"/>
Pregnancy test: 0: Not relevant, 1: Done, 2: Not done	<input type="checkbox"/>	<input type="text"/>
Please note that all investigations should have been made within 3 weeks prior to treatment start.		

Disease information		Date:
Date of primary diagnosis		<input type="text"/>
Localisation of primary tumor 0: Right breast, 1: Left breast 2: Bilateral, 9: Unknown	<input type="checkbox"/>	
Primarily disseminated disease 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>	
ER-status 0: Negative, 1: Positive, 9: Unknown	<input type="checkbox"/>	
PgR-status 0: Negative, 1: Positive, 9: Unknown	<input type="checkbox"/>	
HER2-status: IHC 1: 3+, 2=2+, 9=Not done	<input type="checkbox"/>	
FISH 0: Negative, 1:Positive, 9=Not done	<input type="checkbox"/>	

Patient no.	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Protocol HERNATA	On study Page 2 of 7
Initials	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		

Treatment of primary cancer	
Surgery 0: None, 1: Mastectomy, 2: Tumorectomy, 3: Biopsy (alone) Date of surgery	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Adj. radiotherapy (RT) 0: No, 1: Yes, 9: Unknown If yes: Localisation of RT : 1: Breast, 2: Chest wall, 9: Unknown Side: 1: Right, 2: Left, 3: Both End date of RT	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Adj. CMF 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Adj. CEF 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Adj. Docetaxel 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Adj. Paclitaxel 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Other adjuvant cytotoxic treatment 0: No, 1: Yes, 9: Unknown If yes, specify: _____	<input type="checkbox"/>
Epirubicin given alone or in combination 0: No, 1: Yes, 9: Unknown If yes, indicate cumulative dose (mg)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Doxorubicin given alone or in combination 0: No, 1: Yes, 9: Unknown If yes, indicate cumulative dose (mg)	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Date of last adj. Cytotoxic treatment	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Adj. Trastuzumab 0: No, 1: Yes, 9: Unknown If yes, date of last adj. trastuzumab	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Adj. endocrine treatment 0: None, 1: Tamoxifen, 2: Aromataseinhibitor (e.g. letrozole/anastrozole), 3: Aromataseinactivator (e.g. exemestan), 4: Progestin (e.g. Megestrolacetat), 5: Ovarian suppression (e.g. surgical, LH/RH-analogs), 6: Fulvestrant 7: Other (e.g. combinations), 8: NA, 9: Unknown If other, specify: _____ End date of endocrine treatment	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

Patient no.	<input type="text"/>	Protocol HERNATA	On study Page 3 of 7
Initials	<input type="text"/>		

Relapse prior to HERNATA	
Date of 1. relapse	<input type="text"/>
Did the patient receive treatments for relapse 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Surgery 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
RT 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
If yes, was RT administered to Residual Breast/Chestwall 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
1. line endocrine treatment for relapse *	<input type="checkbox"/>
2. line endocrine treatment for relapse *	<input type="checkbox"/>
Further lines of endocrine treatment *	<input type="checkbox"/>
* 0: None, 1: Tamoxifen, 2: Aromataseinhibitor(e.g. letrozole/anastrozole), 3: Aromataseinactivator (e.g. exemestan), 4: Progestin(e.g. Megestrolacetat), 5: Ovarian suppression (e.g. surgical, LH/RH-analogs), 6: Fulvestrant, 7:Other (e.g. combinations),8: NA, 9: Unknown	

Metastasis at baseline	
Ipsilateral breast 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Contra lateral breast 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Lymph nodes 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Skin 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Bones 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Bone marrow 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Pleura 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Lung 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Liver 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
Other 0: No, 1: Yes, 9: Unknown If other metastases, specify location: _____	<input type="checkbox"/>

Has the present recurrence been verified histologically/cytologically: 0: No, 1: Yes, 9: Unknown	<input type="checkbox"/>
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Patient no.	<input type="text"/>	Protocol HERNATA	On study Page 4 of 7
Initials	<input type="text"/>		

Target lesions, measurable disease	
Measurable disease lesions present? 0: No, 1: Yes, 9: Unknown If yes: Select up to 10 measurable target lesions, and code them as M1, M2 and M3 etc.	<input type="checkbox"/>

Tumor Assessment at baseline				
Site	Diagnostic Method <small>1: CT-scan, 2: MR- scan, 3: X-ray, 4: Ultrasound, 5: Clinical examination, 6: Photo, 7: Other</small>	Date of measurement	Size (longest diameter) cm	Comment
M1 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M2 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M3 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M4 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M5 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M6 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M7 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M8 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M9 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
M10 _____	<input type="checkbox"/>	<input type="text"/>	<input type="text"/> , <input type="text"/>	
Sum of longest diameters (cm) :			<input type="text"/> , <input type="text"/>	
Remember the codes MUST be maintained throughout the entire CRF. Osteolytic bone lesions should be regarded as measurable lesions (See protocol 5.2.1)				

Patient no.	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Protocol HERNATA	On study Page 5 of 7
Initials	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>		

Non-target lesions, non measurable disease	
Non- target lesions present 0: No, 1: Yes, 9: Unknown If yes, specify below	<input type="checkbox"/>

Assessment at baseline		
	Lesion 0: Absent 1: Present 9: Unknown	Date of assessment
Ascites	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Pleural effusion	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Bone metastasis	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Lymfangitic carcinoma of the skin	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Lymfangitic carcinoma of the lung	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Other, specify _____	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Other, specify _____	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Other, specify _____	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

<p>Remarks regarding Non-target lesions</p> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/> <hr style="border: 0; border-top: 1px solid black; margin-bottom: 10px;"/>
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Patient no.

Initials

Protocol HERNATA

On study
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Ongoing signs and symptoms

Signs and symptoms at treatment start

0: No, 1: Yes, 9: Unknown

If yes, specify below

Adverse event type	CTC-grade	
Nausea	<input type="checkbox"/>	
Vomiting	<input type="checkbox"/>	
Alopecia	<input type="checkbox"/>	
Infection	<input type="checkbox"/>	
Diarrhoea	<input type="checkbox"/>	
Stomatitis	<input type="checkbox"/>	
Neuropathy, motor	<input type="checkbox"/>	
Neuropathy, sensor	<input type="checkbox"/>	
Hypersensitivity	<input type="checkbox"/>	
Oedema	<input type="checkbox"/>	
Pain	<input type="checkbox"/>	
Loss of appetite	<input type="checkbox"/>	
Nail changes	<input type="checkbox"/>	
Fatigue	<input type="checkbox"/>	
Febrile neutropenia	<input type="checkbox"/>	
Fever	<input type="checkbox"/>	
Dyspnoea	<input type="checkbox"/>	
Constipation	<input type="checkbox"/>	

Patient no.

Initials

Protocol HERNATA

On study
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Adverse event type	CTC-grade	
	<input type="checkbox"/>	
	<input type="checkbox"/>	
	<input type="checkbox"/>	
	<input type="checkbox"/>	
	<input type="checkbox"/>	
	<input type="checkbox"/>	
	<input type="checkbox"/>	

Please use CTC codes for AEs

Remarks regarding On-study

Investigator approval

Date:

Signature:

Patient no.	□□□□	Protocol HERNATA	Course no.	□□
Initials	□□□□			Page 1 of 6

Treatment arm 1 (Docetaxel and Trastuzumab)
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Trastuzumab	□□□□□□
Date	
Actual dose given (mg)	□□□□
Dose reduction 0: No, 1: Yes	□
If yes, specify reason: _____	
Docetaxel	□□□□□□□□
Date	
100% dose as per protocol (mg)	□□□□
Actual dose given (mg)	□□□□
Dose reduction 0: No, 1: Yes	□
If yes, reason for dose reduction: 1: Febrile neutropenia, 2: GI 3: Neuropathy, 4:Oedema, 6: Liver function, 7:Other	□
If other reason for dose reduction, specify: _____	

Treatment delay	
Has day 1 been delayed 0: No, 1: Yes	□
If yes, number of days	□□
If yes, reason for delay: 1: Haematological toxicity, 2: Other toxicity, 3: Other, 9: Unknown	□
If 2 or 3, specify: _____	

Patient no.	<input type="text"/>	Protocol HERNATA	Course no.	<input type="text"/>
Initials	<input type="text"/>			Page 2 of 6

Treatment arm 2 (Vinorelbine and Trastuzumab)
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Day 1	
Trastuzumab	<input type="text"/>
Date	<input type="text"/>
Actual dose given (mg)	<input type="text"/>
Dose reduction 0: No, 1: Yes	<input type="text"/>
If yes, specify reason: _____	
Vinorelbine	
Date	<input type="text"/>
Vinorelbine dose level: 1: 30 mg/m ² 2: 35 mg/m ²	<input type="text"/>
100% dose as per protocol (mg)	<input type="text"/>
Actual dose given (mg)	<input type="text"/>
Dose reduction: 0: No, 1: Yes	<input type="text"/>
If yes, reason for dose reduction: 1: Thrombocytopenia, 2: Leucopenia, 3:Neuropathy, 4:Liver function, 5: Other, 9: Unknown	<input type="text"/>
If other reason for dose reduction, specify: _____	

Day 8	
Vinorelbine	<input type="text"/>
Date	<input type="text"/>
Vinorelbine dose level: 1: 30 mg/m ² 2: 35 mg/m ²	<input type="text"/>
100% dose as per protocol (mg)	<input type="text"/>
Actual dose given (mg)	<input type="text"/>
Dose reduction: 0: No, 1: Yes	<input type="text"/>
If yes, reason for dose reduction: 1: Thrombocytopenia, 2: Leucopenia, 3:Neuropathy, 4:Liver function, 5: Other, 9: Unknown	<input type="text"/>
If other reason for dose reduction, specify: _____	

Patient no.	□□□□	Protocol HERNATA	Course no.	□□
Initials	□□□□			Page 3 of 6

Treatment arm 2 (Vinorelbine and Trastuzumab) Continued
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Treatment delay	
<p>Has day 1 been delayed: 0: No, 1: Yes</p> <p>If yes, number of days</p> <p>If yes, reason for delay 1: Delay due to haematological toxicity, 2: Delay due to other toxicity, 3: Other, 9: Unknown</p> <p>If 2 or 3, specify: _____</p>	<p style="font-size: 2em;">□</p> <p style="font-size: 2em;">□□</p> <p style="font-size: 2em;">□</p>
<p>Has day 8 been delayed: 0: No, 1: Yes</p> <p>If yes, number of days</p> <p>If yes, reason for delay 1: Delay due to haematological toxicity, 2: Delay due to other toxicity, 3: Other, 9: Unknown</p> <p>If 2 or 3, specify: _____</p>	<p style="font-size: 2em;">□</p> <p style="font-size: 2em;">□□</p> <p style="font-size: 2em;">□</p>

Patient no.	<input type="text"/>	Protocol HERNATA	Course no.	<input type="text"/>
Initials	<input type="text"/>			Page 4 of 6

Adverse events 0: No, 1: Yes, 9: Unknown If yes, specify below	<input type="text"/>
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Adverse event type	CTC-grade	Relation	Outcome	Action taken
	If present	0: Unrelated 1: Possibly rel. 2: Probably rel. 3: Related 9: Unknown	0: Resolved 1: Ongoing 9: Unknown	0: None 1: Hospitalisation 2: Other 9: Unknown
Nausea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vomiting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Alopecia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Infection	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diarrhoea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stomatitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Neuropathy, motor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Neuropathy, sensor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Hypersensitivity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oedema	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Loss of appetite	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nail changes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fatigue	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Febrile Neutropenia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fever	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dyspnoea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Constipation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Patient no. <input type="text"/>	Protocol HERNATA	Course no. <input type="text"/>
Initials <input type="text"/>		Page 5 of 6

Adverse event type	CTC-grade	Relation	Outcome	Action taken
	If present	0: Unrelated 1: Possibly rel. 2: Probably rel. 3: Related 9: Unknown	0: Resolved 1: Ongoing 9: Unknown	0: None 1: Hospitalisation 2: Other 9: Unknown
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Remarks regarding this course

Investigator approval	
Date:	Signature:

Patient no.	□□□□	Protocol HERNATA	Course no.	□□
Initials	□□□□		Page 6 of 6 (Denmark)	

Institution Number (LAB ID)	□□□□
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Blood samples			
	Sample date	Value	Units
Haemoglobin	□□□□□□□□	□□□□ , □	mmol/l
WBC	□□□□□□□□	□□□ , □□□	$10^9/l$
ANC	□□□□□□□□	□□□ , □□□	$10^9/l$
Platelets	□□□□□□□□	□□□□□	$10^9/l$
ASAT	□□□□□□□□	□□□□□	IU/l
ALAT	□□□□□□□□	□□□□□	IU/l
Bilirubin	□□□□□□□□	□□□□□	$\mu\text{mol/l}$
Serum creatinine	□□□□□□□□	□ , □□□□	mmol/l
Alkaline phosphate	□□□□□□□□	□□□□□	IU/l
LDH	□□□□□□□□	□□□□□	IU/l
Ca ⁺⁺ (ionised or albumin corrected)	□□□□□□□□	□□□ , □□□	mmol/l
MUGA/Echocardiography	□□□□□□□□	□□□	%
If further blood samples are necessary, please fill in new pages and enumerate them 6b, 6c, etc.			

Patient no.	□□□□	Protocol HERNATA	Tumor evaluation
Initials	□□□		after Course no. □□
			Page 1 of 3

Target lesions, measurable disease	
Measurable disease lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below	□

Tumor Evaluation				
Site	Diagnostic Method <small>1: CT-scan, 2: MR- scan, 3: X-ray, 4: Ultrasound, 5: Clinical examination, 6: Photo, 7: Other</small>	Date of measurement	Size (longest diameter) cm	Comment
M1 _____	□	□□□□□□□□	□□□ , □□	
M2 _____	□	□□□□□□□□	□□□ , □□	
M3 _____	□	□□□□□□□□	□□□ , □□	
M4 _____	□	□□□□□□□□	□□□ , □□	
M5 _____	□	□□□□□□□□	□□□ , □□	
M6 _____	□	□□□□□□□□	□□□ , □□	
M7 _____	□	□□□□□□□□	□□□ , □□	
M8 _____	□	□□□□□□□□	□□□ , □□	
M9 _____	□	□□□□□□□□	□□□ , □□	
M10 _____	□	□□□□□□□□	□□□ , □□	
Sum of longest diameters (cm) :			□□□ , □□	

Remember the codes MUST be maintained throughout the entire CRF.
Osteolytic bone lesions should be regarded as measurable lesions (See protocol 5.2.1)

Patient no.	<input type="text"/>	Protocol HERNATA	Tumor evaluation
Initials	<input type="text"/>		after Course no. <input type="text"/>
			Page 2 of 3

Non-target lesions, non measurable disease	
Non-target lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below	<input type="text"/>

Tumor Evaluation		
	Lesion 0: Absent 1: Present 9: Unknown	Date of evaluation
Ascites	<input type="text"/>	<input type="text"/>
Pleural effusion	<input type="text"/>	<input type="text"/>
Bone metastasis	<input type="text"/>	<input type="text"/>
Lymfangitic carcinoma of the skin	<input type="text"/>	<input type="text"/>
Lymfangitic carcinoma of the lung	<input type="text"/>	<input type="text"/>
Other, specify _____	<input type="text"/>	<input type="text"/>
Other, specify _____	<input type="text"/>	<input type="text"/>
Other, specify _____	<input type="text"/>	<input type="text"/>

Remarks regarding Non-target lesions _____ _____

Physical examination	
Date	<input type="text"/>
PS (WHO)	<input type="text"/>

Patient no.	□□□□	Protocol HERNATA	Tumor evaluation
Initials	□□□		after Course no. □□
			Page 3 of 3

New lesions				
New lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below			□	
New measurable lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below			□	
Site	Diagnostic Method 1: CT-scan, 2: MR-scan, 3: X-ray, 4: Ultrasound, 5: Clinical examination, 6: Photo, 7: Other	Date of measurement	Size (longest diameter) cm	Comment
_____	□	□□□□□□□□	□□□ , □□	
_____	□	□□□□□□□□	□□□ , □□	
_____	□	□□□□□□□□	□□□ , □□	
New non-measurable lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below			□	
		Lesion 0: Absent 1: Present 9: Unknown	Date of evaluation	
_____		□	□□□□□□□□	
_____		□	□□□□□□□□	
_____		□	□□□□□□□□	

Response	
Overall response 1: CR, 2: PR, 3:SD, 4: PD, 5:NE, 6: Not done	□

Investigator approval	
Date:	Signature:

Patient no.	□□□□	Protocol HERNATA	Hospitalisation form Page 1 of 1
Initials	□□□		

HOSPITALISATIONS		
Fill in one form for each admission to hospital		
Always check if SAE's are mandatory!		
Reason for admission	Date of admission	Date of discharge
Surgery	□□□□□□	□□□□□□
Central venous catheter	□□□□□□	□□□□□□
Blood transfusion	□□□□□□	□□□□□□
Febrile neutropenia	□□□□□□	□□□□□□
Treatment of disease complications	□□□□□□	□□□□□□
Hospice admission	□□□□□□	□□□□□□
Other	□□□□□□	□□□□□□
If other, specify: _____		

Patient no.	□□□□	Protocol HERNATA	Trial conclusion Page 1 of 1
Initials	□□□□		

Treatment discontinuation	
Date of treatment discontinuation	□□□□□□
Primary reason	□
<ol style="list-style-type: none"> 1. Patient dead (complete death report) 2. Progression of disease 3. Study drug toxicity (specify on AE form) 4. Patient request 5. Physicians decision 6. Lost to follow up 7. Other reason specify _____ 8. Change of chemotherapy (+/- continuing with trastuzumab) 	
Date of last Contact	□□□□□□

Clinical status	
Best clinical response:	□
<ol style="list-style-type: none"> <li style="width: 50%;">1. CR <li style="width: 50%;">4. PD <li style="width: 50%;">2. PR <li style="width: 50%;">5. NE <li style="width: 50%;">3. SD <li style="width: 50%;">6. ND 	
Date of best clinical response:	□□□□□□
If CR or PR please specify date of response verification:	□□□□□□
Date of Progression	□□□□□□

Patients without progression of disease who have stopped trial medication and who have not started other antineoplastic systemic treatment should be followed with same evaluations as **on** treatment every 9 weeks to PD.

Patients without progression of disease who have started other antineoplastic systemic treatment and patients with progression of disease should be followed using the form : "Patient status" every 3 months.

Remarks regarding trial conclusion:

Investigator approval	
Date:	Signature:

Patient no.	<input type="text"/>	Protocol HERNATA	Follow-up no.	<input type="text"/>
Initials	<input type="text"/>		After PD or other treatment	

Patient status

Is the patient: alive dead complete death report form

Date of last contact	<input type="text"/>
Are there changes since previous assessment? 0: No, 1: Yes, specify below	<input type="text"/>
<input type="checkbox"/> Progression of disease, specify date	<input type="text"/>
<input type="checkbox"/> Second primary malignancy, specify _____	
<input type="checkbox"/> Significant cardiac disease, specify _____	
<input type="checkbox"/> Lost to follow up (specify date)	<input type="text"/>
<input type="checkbox"/> Patients voluntary withdrawal	
<input type="checkbox"/> Other, specify _____	

This section should be completed if any anticancer therapy other than study drugs according to randomisation treatment has been given for breast cancer after treatment discontinuation or for occurrence of a second primary malignancy.

Continuing Trastuzumab 0: No, 1: Yes, 9: Unknown If no, specify stop date

Chemotherapy 0: No, 1: Yes, 9: Unknown If yes, specify type of chemotherapy

1: Epirubicin 2: Adriamycin 3: Docetaxel 4: Paclitaxel 5: Vinorelbine 6: Gemcitabine 7: Capecitabine 8: Other

	Start date	ongoing	Stop date
Type <input type="checkbox"/> If 8, specify: _____	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
Type <input type="checkbox"/> If 8, specify: _____	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
Type <input type="checkbox"/> If 8, specify: _____	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>

Hormone therapy 0: No, 1: Yes, 9: Unknown If yes, specify type of hormone therapy

1. Tamoxifen 2: Letrozol/ anastrozole 3: Exemestan 4: Progestin 5: Ovarian suppression (e.g. surgical, LH/RH-analogs)
6: Fulvestrant 7: Other (e.g. combinations) 9: Unknown

	Start date	ongoing	Stop date
Type <input type="checkbox"/> If 7, specify: _____	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>
Type <input type="checkbox"/> If 7, specify: _____	<input type="text"/>	<input type="checkbox"/>	<input type="text"/>

Remarks:

Investigator approval

Date:	Signature:
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Patient no.	<input type="text"/>	Protocol HERNATA	Death report
Initials	<input type="text"/>		Page 1 of 1

Death report form	
Date of death	<input type="text"/>
Cause of death (the most probable cause)	<input type="checkbox"/>
1. Toxicity due to chemotherapy (specify on AE form)	
2. Breast cancer	
3. Malignant disease, other than breast cancer	
4. Other, specify _____	
5. Unknown	
Was an autopsy performed ?	<input type="checkbox"/>
0: No	
1: Yes	
9: Unknown	

Investigator approval	
Date:	Signature: