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: _____

Inclusion criteria	**Yes**	**No**
Histologycally / cytologically confirmed locally advanced or metastatic carcinoma of the breast	☐	☐
Primary tumor or metastasis HER2 IHC 3+ or FISH +	☐	☐
Expected lifetime more than 12 weeks	☐	☐
WHO PS ≤ 2	☐	☐
Informed consent, orally and in writing	☐	☐
Age ≥ 18 and ≤ 75 years	☐	☐
Patient compliance	☐	☐
All questions must be answered by Yes		

Exclusion criteria	**Yes**	**No**
Chemotherapy for metastatic disease	☐	☐
(Neo-) adjuvant chemotherapy ≤ 4 weeks before study entry. (Neo-)adjuvant treatment with taxanes, vinorelbine, trastuzumab ≤ 12 months ago.	☐	☐
Earlier treatment targeting components of the EGF-system	☐	☐
Dyspnoea at rest due to advanced malignancy or patients requiring oxygen	☐	☐
Pregnant or lactating woman. Negative pregnancy test is required during screening period	☐	☐
Fertile woman who does not use adequate anticonception	☐	☐
Clinical symptoms or signs suggesting CNS-metastasis or meningeal carcinomatosis	☐	☐
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.	☐	☐
Congestive heart failure despite adequate treatment (cardiomegalia, objective signs of insufficiency or left ventricular ejection fraction (LVEF) under normal limit for the institution)	☐	☐
WBC < 3.0×10^9/l , neutrophiles < 1.5×10^9/l or platelets ≤ 100×10^9/l.	☐	☐
Bilirubin > UNL and/or ASAT/ALAT > 2.5 × UNL (patients with liver metastasis 5 × UNL) and/or alkaline phosphatase > 5 × UNL ASAT/ALAT ≥ 1.5 × UNL and alkaline phosphatase > 2.5 × UNL	☐	☐
Se- creatinine ≥ 1.5 × UNL	☐	☐
Known allergy to any contents of study medication or murine proteins	☐	☐
Sensory neuropathy > grad 1	☐	☐
All questions must be answered by No		

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 Traztuzumab ☐
Patient number: ⌊_⌊_⌊_⌊_	Treatment arm 2: Vinorelbine and Trastuzumab ☐
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 Sweden

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

Investigator approval	
Date:	Signature:

Treatment arm 1: Docetaxel and Trastuzumab 2: Vinorelbine and Trastuzumab	☐

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

Disease information		**Date:**
Date of primary diagnosis		☐☐☐☐☐☐
Localisation of primary tumor 0: Right breast, 1: Left breast 2: Bilateral, 9: Unknown	☐	
Primarily disseminated disease 0: No, 1: Yes, 9: Unknown	☐	
ER-status 0: Negative, 1: Positive, 9: Unknown	☐	
PgR-status 0: Negative, 1: Positive, 9: Unknown	☐	
HER2-status: IHC 1: 3+, 2=2+, 9=Not done FISH 0: Negative, 1:Positive, 9=Not done	☐ ☐	

Treatment of primary cancer	
Surgery 0: None, 1: Mastectomy, 2: Tumorrectomy, 3: Biopsy (alone)	⌊_⌋
Date of surgery	⌊_⌊_⌊_⌊_⌊_⌊_⌋
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	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Adj. CMF 0: No, 1: Yes, 9: Unknown	⌊_⌋
Adj. CEF 0: No, 1: Yes, 9: Unknown	⌊_⌋
Adj. Docetaxel 0: No, 1: Yes, 9: Unknown	⌊_⌋
Adj. Paclitaxel 0: No, 1: Yes, 9: Unknown	⌊_⌋
Other adjuvant cytotoxic treatment 0: No, 1: Yes, 9: Unknown If yes, specify: _____	⌊_⌋
Epirubicin given alone or in combination 0: No, 1: Yes, 9: Unknown	⌊_⌋
If yes, indicate cumulative dose (mg)	⌊_⌊_⌊_⌊_⌋
Doxorubin given alone or in combination 0: No, 1: Yes, 9: Unknown	⌊_⌋
If yes, indicate cumulative dose (mg)	⌊_⌊_⌊_⌊_⌋
Date of last adj. Cytotoxic treatment	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Adj. Trastuzumab 0: No, 1: Yes, 9: Unknown	⌊_⌋
If yes, date of last adj. trastuzumab	⌊_⌊_⌊_⌊_⌊_⌊_⌋
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	⌊_⌊_⌊_⌊_⌊_⌊_⌋

Relapse prior to HERNATA	
Date of 1. relapse	☐☐☐☐☐☐
Did the patient receive treatments for relapse 0: No, 1: Yes, 9: Unknown	☐
Surgery 0: No, 1: Yes, 9: Unknown	☐
RT 0: No, 1: Yes, 9: Unknown If yes, was RT administered to Residual Breast/Chestwall 0: No, 1: Yes, 9: Unknown	☐ ☐
1. line endocrine treatment for relapse *	☐
2. line endocrine treatment for relapse *	☐
Further lines of 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

Metastasis at baseline	
Ipsilateral breast 0: No, 1: Yes, 9: Unknown	☐
Contra lateral breast 0: No, 1: Yes, 9: Unknown	☐
Lymph nodes 0: No, 1: Yes, 9: Unknown	☐
Skin 0: No, 1: Yes, 9: Unknown	☐
Bones 0: No, 1: Yes, 9: Unknown	☐
Bone marrow 0: No, 1: Yes, 9: Unknown	☐
Pleura 0: No, 1: Yes, 9: Unknown	☐
Lung 0: No, 1: Yes, 9: Unknown	☐
Liver 0: No, 1: Yes, 9: Unknown	☐
Other 0: No, 1: Yes, 9: Unknown If other metastases, specify location: _____	☐

Has the present recurrence been verified histologically/cytologically: 0: No, 1: Yes, 9: Unknown	☐

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.	⌊_⌋

Tumor Assessment at baseline				
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
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)				

Non-target lesions, non measurable disease	
Non- target lesions present 0: No, 1: Yes, 9: Unknown If yes, specify below	⌊_⌋

Assessment at baseline		
	Lesion 0: Absent 1: Present 9: Unknown	Date of assessment
Ascites	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Pleural effusion	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Bone metastasis	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Lymfangitic carcinoma of the skin	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Lymfangitic carcinoma of the lung	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋

Remarks regarding Non-target lesions

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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	☐	
Vomiting	☐	
Alopecia	☐	
Infection	☐	
Diarrhoea	☐	
Stomatitis	☐	
Neuropathy, motor	☐	
Neuropathy, sensor	☐	
Hypersensitivity	☐	
Oedema	☐	
Pain	☐	
Loss of appetite	☐	
Nail changes	☐	
Fatigue	☐	
Febrile neutropenia	☐	
Fever	☐	
Dyspnoea	☐	
Constipation	☐	

Adverse event type	**CTC-grade**	
	☐	
	☐	
	☐	
	☐	
	☐	
	☐	
	☐	
Please use CTC codes for AEs		

Remarks regarding On-study

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Investigator approval	
Date:	Signature:

Treatment arm 1 (Docetaxel and Trastuzumab)

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: ____________________	└┘ └┴┘ └┘

Treatment arm 2 (Vinorelbine and Trastuzumab)

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

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

Treatment arm 2 (Vinorelbine and Trastuzumab) Continued

Treatment delay	
Has day 1 been delayed: 0: No, 1: Yes	⌊_⌋
If yes, number of days	⌊_⌊_⌋
If yes, reason for delay 1: Delay due to haematological toxicity, 2: Delay due to other toxicity, 3: Other, 9: Unknown If 2 or 3, specify: _____	⌊_⌋
Has day 8 been delayed: 0: No, 1: Yes	⌊_⌋
If yes, number of days	⌊_⌊_⌋
If yes, reason for delay 1: Delay due to haematological toxicity, 2: Delay due to other toxicity, 3: Other, 9: Unknown If 2 or 3, specify: _____	⌊_⌋

Adverse events 0: No, 1: Yes, 9: Unknown ☐
If yes, specify below

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	☐	☐	☐	☐
Vomiting	☐	☐	☐	☐
Alopecia	☐	☐	☐	☐
Infection	☐	☐	☐	☐
Diarrhoea	☐	☐	☐	☐
Stomatitis	☐	☐	☐	☐
Neuropathy, motor	☐	☐	☐	☐
Neuropathy, sensor	☐	☐	☐	☐
Hypersensitivity	☐	☐	☐	☐
Oedema	☐	☐	☐	☐
Pain	☐	☐	☐	☐
Loss of appetite	☐	☐	☐	☐
Nail changes	☐	☐	☐	☐
Fatigue	☐	☐	☐	☐
Febrile Neutropenia	☐	☐	☐	☐
Fever	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐
Constipation	☐	☐	☐	☐

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: Hospitatisation 2: Other 9: Unknown
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Remarks regarding this course

_____

_____

_____

Investigator approval	
Date:	Signature:

Institution Number (LAB ID)	⌊_⌊_⌊_⌊_⌋

Blood samples			
	Sample date	Value	Units
Haemoglobin	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌊_⌋	g/l
WBC	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌊_⌋	10^9/l
ANC	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌊_⌋	10^9/l
Platelets	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌊_⌊_⌋	10^9/l
ASAT	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌊_⌋	µkat/l
ALAT	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌊_⌋	µkat/l
Bilirubin	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌊_⌋	µmol/l
Serum creatinine	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌊_⌋	µmol/l
Alkaline phosphate	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌋	µkat/l
LDH	⌊_⌊_⌊_⌊_⌊_⌊_⌋	⌊_⌊_⌋ , ⌊_⌋	µkat/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.			

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

Tumor Evaluation

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
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)

Non-target lesions, non measurable disease	
Non-target lesions present? 0: No, 1: Yes, 9: Unknown If yes, specify below	⌊_⌋

Tumor Evaluation		
	Lesion 0: Absent 1: Present 9: Unknown	Date of evaluation
Ascites	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Pleural effusion	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Bone metastasis	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Lymfangitic carcinoma of the skin	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Lymfangitic carcinoma of the lung	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋
Other, specify _____	⌊_⌋	⌊_⌊_⌊_⌊_⌊_⌊_⌋

Remarks regarding Non-target lesions

_____

_____

Physical examination	
Date	⌊_⌊_⌊_⌊_⌊_⌊_⌋
PS (WHO)	⌊_⌋

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:

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: _____	☐☐☐☐☐☐	☐☐☐☐☐☐

Treatment discontinuation

Date of treatment discontinuation ⌊_⌊_⌊_⌊_⌊_⌊_⌋

Primary reason ⌊_⌋

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: ⌊_⌋

1. CR
2. PR
3. SD
4. PD
5. NE
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. ☐☐☐☐ Initials ☐☐☐	**Protocol HERNATA**	Follow-up no. ☐☐ After PD or other treatment

Patient status

Is the patient: alive ☐ dead ☐ complete death report form

Date of last contact ☐☐☐☐☐☐

Are there changes since previous assessment? 0: No, 1: Yes, specify below ☐

☐ Progression of disease, specify date ☐☐☐☐☐☐

☐ Second primary malignancy, specify ______________________________

☐ Significant cardiac disease, specify ______________________________

☐ Lost to follow up (specify date) ☐☐☐☐☐☐

☐ Patients voluntary withdrawal

☐ 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 ☐	If 8, specify: ______	☐☐☐☐☐☐	☐	☐☐☐☐☐☐
Type ☐	If 8, specify: ______	☐☐☐☐☐☐	☐	☐☐☐☐☐☐
Type ☐	If 8, specify: ______	☐☐☐☐☐☐	☐	☐☐☐☐☐☐

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 ☐	If 7, specify: ______	☐☐☐☐☐☐	☐	☐☐☐☐☐☐
Type ☐	If 7, specify: ______	☐☐☐☐☐☐	☐	☐☐☐☐☐☐

Remarks:

Investigator approval	
Date:	Signature:

Death report form

Date of death ⌊_⌊_⌊_⌊_⌊_⌊_⌋

Cause of death (the most probable cause) ⌊_⌋

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 ?
0: No
1: Yes
9: Unknown

Investigator approval	
Date:	Signature: