Exclusion Criteria (selected):

Details see protocol pages 15 - 16

Pregnant or lactating women

Radiation of the target lesion within the last 4 weeks

Active bacterial, viral or fungal infection

Patients with clinically apparent brain metastases

Known positivity for HIV

Positivity for Hepatitis B or C

History of other malignancy; patients who have been disease-free for 5 years or patients with a history of completely resected non-melanoma skin cancer or successfully treated in situ carcinoma are eligible.

Concurrent cancer therapy (chemotherapy, immunotherapy, antihormonal or biologic therapy) or concurrent treatment with an investigational drug

Antihormonal therapy must have been discontinued prior to start of treatment (if possible at least 3 weeks before)

Known hypersensitivity to the study drugs capecitabine and bendamustine or their excipients

Pretreatment with capecitabine (pretreatment with infusional 5-FU in the adjuvant or neoadjuvant setting is allowed) or bendamustine

Treatment with sorivudine or derivates e.g. brivudin (Mevirc) within the last 4 weeks before and during study treatment with capecitabine

Inclusion Criteria (selected):

Details see protocol pages 15 - 16

Female patients, age ≥ 18 years (women of childbearing potential must have a negative pregnancy test at screening and must use effective contraception)

Advanced or metastatic Her2-negative breast cancer, histologically confirmed

At least one measurable lesion according to RECIST criteria (Version 1.1)

Documented disease progression

Patients with progression after anthracycline and/or taxane treatment (palliative or neoadjuvant or adjuvant)

Life expectancy of at least 12 weeks

Performance status 0-2

Adequate hematology, liver and renal function:

Hematologic:

ANC (absolute neutrophil count) ≥ 1.5 x 10^9/L
Hemoglobin ≥ 9 g/dL
Platelets ≥ 100 x 10^9/L

Liver Function:

Albumin ≥ 2.5 g/dL
Serum bilirubin ≤ 2 mg/dL
AST and ALT ≤ 3 x ULN without liver metastases
≤ 5 x ULN if documented liver metastases

Renal Function:

Serum Creatinine ≤ 1.5 mg/dL OR Calculated Creatinine Clearance ≥ 40 mL/min

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Capecitabine in combination with Bendamustine in women with pretreated locally advanced or metastatic Her2-negative breast cancer, a Phase II Trial

EudraCT Nummer: 2012-005593-64

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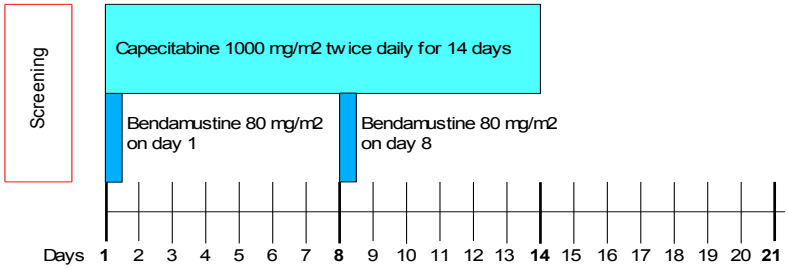
An academic trial by AGMT
Arbeitsgemeinschaft medikamentöse Tumortherapie
Univ. Prof. Dr. Richard Greil

Study Design:

THERAPY REGIMEN:

Capecitabine
1000 mg/m^2 twice daily p.o. for 14days q3w, until progression

Bendamustine
80 mg/m^2 i.v. day 1 and 8 q3w for a max. of 8 cycles



Repeat cycle for a maximum of 8 cycles, then capecitabine mono-therapy will be continued until progression

Study Procedures:

Assessments	Base-line	Assessment therapy start (day 1 of the first cycle)	Assessments therapy (every 3 weeks)	Additional assessments (every 9 weeks)	End of study treatment	Follow Up (every 3 months)
ICF	x					
Genetic ICF	x					
Tumor anamnesis (HER2 st.)	x		x		x	
Medical history	x		x		x	
CT (is preferred) or MRI	x			x	x	
Physical examination	x		x		x	
ECOG performance status	x		x		x	
ECG	x		x[1]		x[1]	
Vital signs[2]	x		x		x	
Complete blood cell count[3]	x	x	x		x	
Laboratory parameters[4]	x	x	x		x	
Blood samples for scientific research program (only if genetic ICF signed)35 ml whole blood	x	x **additionally** on day 8 of cycle 1		x	x	
Hepatitis B and C	x					
Questionnaires	x			x	x	
Pregnancy Test[5]	x		x			
History of last cycle			x			
Adverse Events			x			
Survival Status						x

1 Only if clinically indicated; 2 Vital signs (blood pressure, HR, weight); 3 Complete blood cell count (hemoglobin, platelets, leucocytes, lymphocytes, monocytes and neutrophils); 4 Laboratory parameters (ASAT, ALAT, GGT, AP, Albumin, total bilirubin, creatinine, creatinine-clearance, Na, Ca, K, Ca15-3, CEA); 5 Pregnancy Test every 4 weeks

Study Design:

Phase II study in pretreated patients with Her2-negative advanced breast cancer.

Following a two-stage design efficacy and safety of bendamustine and capecitabine will be evaluated following recruitment of the first 20 patients. Upon favorable results a further 20 patients will be recruited to reach the target population of 40 evaluable patients.

Primary Objective:

Primary Endpoint of this study is to determine the efficacy of a capecitabine plus bendamustine combination regimen in the treatment of Her2-negative advanced metastatic breast cancer, in terms of overall response rates

Secondary Objectives:

Progression free survival (PFS)

Clinical benefit (CR, PR or stable disease for at least 24 weeks)

Safety profile of a combination with capecitabine and bendamustine

Quality of Life

Predefined subgroup analysis of triple-negative patients vs hormone receptor positive patients in terms of overall response rates and clinical benefit rate