



Fondation du Centre
Pluridisciplinaire d'Oncologie

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ZOOM SAKK 24/09

Indication	Sein Métastatique
Title	Safety and tolerability of bevacizumab plus paclitaxel vs. bevacizumab plus metronomic cyclophosphamide and capecitabine as first-line therapy in patients with HER2-negative metastatic or locally recurrent breast cancer. A multicenter, randomized phase III trial.
Protocol ID	SAKK 24/09
Phase	Phase III
Sponsor	SAKK (Swiss Group for Clinical Cancer Research)
Local Principal Investigator	Dr K. Zaman
Primary Objective	The main aim of this trial is to demonstrate that a combination of bevacizumab + “metronomic chemotherapy” with cyclophosphamide and capecitabine causes less medication related adverse events compared to paclitaxel + bevacizumab.
Inclusion/exclusion criteria	<p>Inclusion Criteria include the following :</p> <ul style="list-style-type: none"> • Patient must give written informed consent before randomization. • Female patient at the age of 18 years and who is legally competent. • Patient compliance and geographic proximity allow proper staging and follow-up • Women are not breastfeeding. Women with child bearing potential are using effective contraception, are not pregnant and agree not to become pregnant during participation in the trial and during the 12 month thereafter. A negative pregnancy test before inclusion into the trial is required for all women with child-bearing potential. • Patient is a candidate for taxane-based chemotherapy. • WHO performance status of 0, 1, or 2. • Histologically or cytologically confirmed diagnosis of HER2-negative adenocarcinoma of the breast with measurable or evaluable locally advanced/recurrent or metastatic disease. • Radiological evaluations performed within 4 weeks before randomization. • Adequate hematological, hepatic and renal function • Baseline Quality of Life questionnaire has been completed. • Baseline Health Economics (BL-HEA, baseline EQ-5D)

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Exclusion Criteria include the following:

- Presence or history of CNS metastasis; any clinical suspicion of CNS metastasis must be confirmed by CT or MRI.
- Previous malignancy within 5 years with the exception of adequately treated cervical carcinoma in situ or localized non-melanoma skin cancer.
- Previous chemotherapy for metastatic or locally recurrent breast cancer. Prior hormone therapy for metastatic disease is allowed. Hormonal therapy must be completed at least 10 days before expected trial treatment starts.
- Previous radiotherapy for the treatment of metastatic disease. Radiotherapy administered for the relief of metastatic bone pain is allowed prior to trial entry, as long as no more than 30% of marrow-bearing bone was irradiated.
- Treatment with other experimental drugs or other anti-cancer therapy, treatment in a clinical trial within 30 days prior to expected trial entry. Treatment with bevacizumab or other anti-VEGF drug 12 months prior to expected first treatment administration.
- Major surgical procedure (including open biopsy) within 28 days and minor surgical procedures 24 hours prior to expected first trial treatment, or anticipation of the need for major surgery during the course of this trial.
- Treatment with capecitabine or with continuous (>24 hours) 5-FU infusion or other oral fluoropyrimidine such as eniluracil/5-FU, uracil/tegafur, S1, or emitefur 12 months prior to expected treatment administration.
- Treatment with any other (neo)adjuvant chemotherapy within 6 months prior to first trial treatment administration; treatment with taxane-based chemotherapy within 12 months prior to expected first trial treatment administration.
- Any continuous daily treatment with corticosteroids with the exception of inhaled steroids.
- Chronic daily treatment with aspirin (> 325 mg/day) or clopidogrel (> 75 mg/day).
- Any concomitant drug(s) contraindicated for use with the trial drug(s) according to the Swissmedic approved product information.
- Known hypersensitivity to trial drug(s) or its active compound (e.g. fluoropyrimidine) or hypersensitivity to any other components of the trial drugs or drugs formulated with cremophor EL including hypersensitivity to Chinese hamster ovary cell products or any other humanized recombinant antibodies.
- Patients not receiving anticoagulant medication who have an International Normalized Rate (INR) > 1.5 (or Quick ≤ 70%)

	<p>or an activated partial thromboplastin time (aPTT) >1.5x ULN within 7 days prior to expected first trial treatment.</p> <ul style="list-style-type: none">• Pre-existing peripheral motor and sensory neuropathy > NCI CTCAE grade 2 (moderate symptoms; limiting instrumental ADL).• History or evidence of inherited bleeding diathesis or coagulopathy with the risk of bleeding or serious non-healing wound, active peptic ulcer, non-healing bone fracture or bleeding metastases.• History of abdominal fistula, grade 4 bowel obstruction or gastrointestinal perforation or intra-abdominal abscess with 6 months prior to randomization.• Evidence of other medical conditions which would impair the ability of the patient to participate in the trial or might preclude therapy with trial drugs (e.g. DPD deficiency, severe respiratory, cardiac, hepatic, or renal disease, active infection, uncontrolled diabetes mellitus, uncontrolled hypertension > 140/100 mmHg, history of myocardial infarction in the last 12 months prior to first trial treatment, cerebrovascular accident (CVA)/stroke within 6 months prior to the first trial treatment, history of haemorrhagic disorders, non healing wound, ulcer, or bone fracture).• Psychiatric disorder precluding understanding of information on trial related topics, giving informed consent, filling out QoL forms, or interfering with compliance for oral drug intake.
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