GAIN Study

German Adjuvant Intergroup Node-positive Study

A phase III trial to compare ETC vs. EC-TX and Ibandronate vs. observation in patients with node-positive primary breast cancer

A German Intergroup Study of the
Arbeitsgemeinschaft Gynäkologische Onkologie (AGO)
German Breast Group (GBG)
Nordostdeutsche Gesellschaft für Gynäkologische Onkologie (NOGGO)

GBG 33
English Synopsis
Subprotocol 1
Protocol Amendment 3, Version 9
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1 Subprotocol Pegfilgrastim on day 2 vs day 4

Title	**Pegfilgrastim on day 2 vs day 4 to reduce the rate of leucopenia in patients with node positive primary breast cancer treated with ETC in the GAIN study.**
Confidentiality	Information and data included in this protocol contain trade secrets and privileged or confidential information which will be protected by GBG Forschungs GmbH. No person is authorized to make it public without written permission of GBG Forschungs GmbH. These restrictions on disclosure will apply equally to all future information supplied to you which is indicated as privileged or confidential. This material may be disclosed to and used by your staff and associates as may be necessary to conduct the clinical study.
Trial design	Prospective, multi-center, controlled, non blinded, randomized study to compare pegfilgrastim given on day 2 vs day 4 in each ETC cycle
Study Rationale	Currently pegfilgrastim as primary prophylaxis is been given on day 2 of the chemotherapy cycle. However, preliminary data suggest that pegfilgrastim given on day 4 instead of day 2 might reduce the rate of grade 4 leucopenia by 50% in patients treated with CHOP (Hartmann et al. ASCO 2007; #19511)
Objectives	Primary objective: To compare the rate of grade 4 leucopenia per patient in ETC of pegfilgrastim day 2 vs day 4 Secondary objectives: To compare the rate of grade 4 leucopenia per cycle and per treatment agent To compare the rate of neutropenia grade 3 and 4 per patient, per cycle and per treatment agent To evaluate the rate of febrile neutropenia per patient, per cycle and per treatment agent To compare the dose delays and dose reductions in ETC with pegfilgrastim day 2 vs day 4 To compare the incidence of infections during treatment per patient, per cycle and per treatment agent
Selection of patients	participant of the GAIN study and randomized to ETC
Treatment	ETC according to the protocol : **Pts will thereafter be randomized to receive primary prophylaxis with pegfilgrastim on day 2 or day 4** ESF (Epoetin beta oder darbepoetin alpha) will be distributed alternating as outlined in the main protocol during C mandatory, prophylactic oral administration of Ciprofloxacin 500 mg 2x 1 Tablet/Day 5-12 in both groups of pegfilgrastim according to the protocol will be given
Efficacy evaluation	An intention to treat (ITT) analysis will be conducted for all patients who have been randomized into that subprotocol and have received at least one dose of pegfilgrastim. In addition, a per protocol analysis will be conducted among the eligible patients who have completed the chemotherapy.

Statistical considerations	The following assumptions are made: • The rate of leucopenia grade 4 with ETC is around 50% with pegfilgrastim given on day 2. • It is estimated that there will be a risk reduction of 1.98 with pegfigrastim given on day 4 (1:1 randomization) • The error rate for a false positive outcome (α) is set to 5%, using two-sided significance test. The error rate for a false negative outcome (ß) is set to 20%, i.e. the power of the trial is set to 80% for the difference of clinical interest. A drop out rate of 10% will be assumed. • The estimated patients per arm will be n=68. Therefore 152 (136 plus 10% drop out rate) patients treated with ETC will be needed to be randomized to peg day 2 vs day 4 (76 patients in each arm)
Time lines	First patient in: October 2007 Last patient in: January 2007 Last patient EOBT: June 2008 Final analysis: October 2008