for adjuvant therapy was estimated as well as the cost-effectiveness of treatment according to the 1998 guidelines compared to the conventional policy (year 1994) and of treatment according to the 2001 guidelines compared to the 1998 guidelines.

Methods: Estimated percentages of patients eligible for adjuvant therapy in 1994, 1998 and 2001 were based on clinical data from 128 patients who were operated in 1994. 10-Years overall survival rates were used as a measure of effectiveness, based on two EBCTCG meta-analyses [Lancet, 1998]. For the costs of the treatment options, actual resource costs were calculated. With a decision analytic model, the incremental cost-effectiveness ratios (conventional (year 1994) *versus* 1998 and 1998 *versus* 2001) were calculated to estimate the incremental costs per life years gained resulting from implementing the novel guidelines.

Results: The introduction of the 1998 guidelines resulted in a relative increase of 96% in the total number of eligible patients compared to 1994 (from 36% to 70%), with minimal differences for the 2001 guidelines. With an estimated absolute increase of 2% 10-years overall survival the 1998 guidelines were found to have an expected incremental cost-effectiveness ratio of approximately 3400 euro per life-year gained compared to the conventional policy.

Conclusion: The implementation of these new guidelines considerably affected the workload of medical specialists, as a result from a substantial increase of the number of patients eligible for adjuvant systemic therapy. However, the incremental cost-effectiveness ratio is well within the range of values that are generally considered acceptable.

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Darbepoetin alfa given once every 3 weeks (Q3W) either synchronously or asynchronously with Q3W chemotherapy (ctx) improves anaemia in patients with breast cancer: results of a randomised, open-label study

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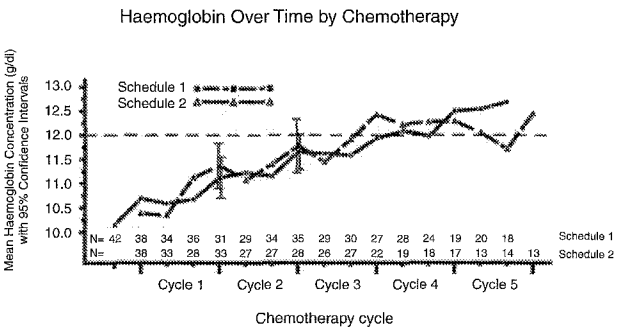
Background: The timing of administration of erythropoietic therapy relative to multicyclic ctx in anaemic patients (pts) with cancer may affect the response of the pt (Hartley et al., 2003; Glaspy, 2002). To evaluate the effect of timing and efficacy of Q3W administration, darbepoetin alfa (DA; Aranesp®) was given Q3W either synchronously or asynchronously with Q3W ctx treatment in pts with non-myeloid malignancies.

Materials and Methods: This was a randomised, multicentre, open-label study. Eligible pts were ⁎18 years old, diagnosed with a non-myeloid malignancy, anaemic (haemoglobin [Hb] ⁎9 and ⩽11 g/dL), and were receiving ctx on a Q3W schedule. Pts were randomised 1:1 to receive DA at 6.75 mcg/kg Q3W on schedule 1, asynchronous (day 15; ie, 7 days prior to the next ctx cycle) or schedule 2, synchronous (day 1 of ctx cycle) for up to 16 weeks. The primary endpoint was Hb assessment after 6 weeks to prevent confounding effects of delays to ctx, pt attrition, and differential dose escalation in the 2 treatment groups. An optional pharmacokinetic study was available to pts to assess concentrations of endogenous erythropoietin and of DA at prespecified time points within the first 3 weeks of the first administration of study drug. Pts were allowed to continue DA treatment if receiving Q3W ctx treatment.



Note: Available Data analysis: Error bars represent 95% Confidence intervals at end of chemotherapy cycle 1 and 2

Results: A total of 81 pts were randomised (43 to schedule 1; 38 to schedule 2). The breast cancer pts comprised 40% of the study population (20 on schedule 1; 12 on schedule 2) and represented the most common tumor type in the study. Of all pts, most were women (74%). For all pts, the mean (95% CL) change in Hb from baseline at week 7 (ie, primary endpoint) was 0.95 (0.56, 1.33) g/dL for schedule 1 and 1.03 (0.58, 1.47) g/dL for schedule 2. Hematopoietic response (Hb ⁎ 12 g/dL or Hb rise from baseline ⁎ 2 g/dL; Kaplan-Meier proportion) was similar between the schedules, at 74% (95% CL: 61, 87) for both groups combined. For all pts, the median (95% CL) time to a hematopoietic response was 49 (36, 5) days. Safety data will also be presented.

Conclusion: DA Q3W for the treatment of chemotherapy-induced anemia is effective regardless of the timing of administration relative to ctx. Less frequent administration of DA is possible due to the approximate 3-fold longer half-life compared with epoetin alfa. In pts with breast cancer, Q3W administration of DA allows for once-per-cycle dosing, as many breast cancer ctx regimens are given Q3W.

69 POSTER

NNBC-3 Europe Study: A trial to improve risk estimation and risk adapted adjuvant chemotherapy in node negative breast cancer patients by using new uPA and PAI-1 and to analise the efficacy of a sequential FEC–taxane chemotherapy versus a standard FEC–chemotherapy regimen

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Introduction: Recent results demonstrated strong evidence for the routine use of the invasion markers uPA and PAI-1 as prognostic factors in node-negative breast cancer patients. In contrast to risk estimation by St Gallen criteria, the use of these tumour-biological factors can spare approximately 50% of all node-negative breast cancer patients from adjuvant chemotherapy. Node-negative patients with elevated tumour tissue levels of uPA and PAI-1 had a similar risk recurrence as node-positive patients. Using adjuvant CMF therapy, a remarkable reduction of recurrences in high risk patients has been achieved. However, in these patients anthracycline and taxane combinations might be even more efficient.

Study Design: In order to evaluate these questions, we initiated a trial with the following design: Centres who participate have to decide whether they would perform risk estimation by traditional clinico-pathological factors or by tumour-biological factors uPA and PAI-1. After risk estimation by one of these methods low risk patients will be observed without adjuvant chemotherapy. High risk patients will be randomised to adjuvant chemotherapy using six courses FEC-100 versus three courses FEC-100 followed by three courses Docetaxel. All patients who had steroid receptor positive tumours will receive adequate endocrine therapy. Patients with HER-2/neu overexpressing tumours can be included into the adjuvant Herceptin® trial "HERA".

The study is planned to recruit 2392 patients in the high risk group. The study is performed in association with the EORTC Receptor and Biomarker Group and the German AGO Breast Group.

Questions: Two questions have to be answered:

- Does tumour biological risk estimation provide a more precise identification of patients who will benefit from adjuvant chemotherapy than traditional clinicopathological selection?
- Is an anthracycline and taxane containing sequence (FEC-Docetaxel) more efficient?

70 POSTER

The influence of classical prognostic factors and adjuvant chemotherapy on disease outcome in early grade 3 node-negative, and 1–3 node-positive breast cancer patients treated with adjuvant cyclophosphamide, methotrexate and fluorouracil (CMF), or untreated patients

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We evaluated a group of early breast cancer patients, diagnosed from 1986 to 1994, who were treated either with adjuvant CMF chemotherapy, or received no further therapy.

Sixty-six women with node-negative disease and grade 3 invasive breast carcinomas, and 95 women with 1–3 involved lymph nodes regardless of tumor grade received cyclophosphamide 500 mg i.v. D1–D4, methotrexate 35 mg i.v. D1 and D4, and fluorouracil 500 mg i.v. D1–D4 every 4 weeks. Untreated group consists of 25 node-negative women with grade 3 breast cancers and 49 patients with 1–3 involved nodes not treated with adjuvant systemic therapy, which were diagnosed and operated at the same time as were the women in CMF group. Log rank test was used to assess