(moab) 17/1A to reduce residual tumor cells remaining after high dose chemotherapy (cth.).

Patients and Methods: High risk BrCa pts. involving >/= 10 axillary lymph nodes (N = 7) and stage IV (N = 3) breast cancer pts. were treated with two cycles of induction cth. (VIP-E) followed by high dose cth. VIC with transplantation of tumor cell purged PBSC grafts. PBSC were mobilized with 5 μg/kg G-CSF and collected after I. VIP-E and II. VIP-E. Grafts collected after II. VIP-E were subjected to immunomagnetic selection of BrCa cells using three anti-breast cancer antibodies (HID9184, HID 9187, HID9189, Baxter). Grafts collected after I. VIP-E were used as back-up. After completion of cth. all pts. were treated with moab 17/1A (IgG2a, Glaxo-Wellcome) directed against 37 kD epithelial membrane adhesion molecule. Pts. received 500 mg moab 17/1A followed by 4 cycles with 100 mg each 4 weeks. Immunocytochemical staining (ICC) of 4 × 10 (6) MNC of bone marrow (BM) and PBSC grafts using anti-pancytokeratin F(ab)2 fragment A45B/B3 (Micromet, Munich) was performed to evaluate residual tumor cells ICC of grafts were performed before and after tumor cell selection. BM aspirates of both posterior iliac crests were performed before I. and II. VIP-E, before VIC and after VIC and after each cycle of antibody treatment.

Resultes: It was shown that cytokeratin positive (CK+) cells occur less frequent in PBSC grafts than in correspondent BM. Compared with grafts collected after I. VIP-E risk of malignant contamination was decreased in grafts collected after II. VIP-E. Prior to tumor cell selection CK+ cells were detected in 5/10 grafts after I.VIP and in 2/9 patients after II.VIP-E. After completion of TuCe purging 1 CK+ cell/4 × 10 (6) was revealed in 1/10 grafts. CK+ cells were detected in 3/10 patients BM before (no. CK+ cells: 10 to 4892) application of cth. Despite significant reduction of number of TuCe (no. CK+ cells: 1 to 120) CK+ cells persisted in BM of all 3 pts. after completion of high dose chemotherapy Infusion of moab 17/1A revealed further tumor cell reduction in BM to a minimum level of 0–20 CK+ cells per 4 × 10 (6) MNC.

Conclusion: Our data show that immunomagnetic in vitro TuCe purging can reduce tumor cell load of PBSC grafts. Immunotherapy with moab 17/1A might use as consolidation of high risk breast cancer pts. after completion of high dose chemotherapy.

675 POSTER

Analysis of failures and survival following local treatment of isolated local-regional recurrence (LR) of breast cancer

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Purpose: To assess prognostic factors for local control, dissemination, and survival of patients (pts) with LR treated with surgery and/or radiotherapy.

Methods: From 1983–85, 99 pts with LR after mastectomy for breast cancer were treated with radical excision and/or radiotherapy. No pts had distant metastases at study entry. Time to local failure, dissemination and survival according to potential prognostic factors were analyzed using multivariate analyses. Median follow-up was 123 months

Results: 45 pts had local and 44 pts had regional recurrence. Type of therapy (surgery *vs.* radiotherapy) and local *vs.* regional recurrence was not related to survival. The 10 year survival rate was 38% and median survival time was 89 months. Independent prognostic factors were node status and hemoglobin level. The 10 year failure rate was 66% – primary tumor size and node status were independent prognostic factors. Distant metastases were observed in 56 pts after median 55 months; level of hemoglobin level was the only significant prognostic factor for dissemination.

Conclusion: Local therapy may be curative in a subset of pts with LR. Differences in prognostic factors for local-regional control and distant metastases suggest that LR is a heterogeneous disease that requires *different treatment strategies.*

676 POSTER

Bispecific antibody MDX210 (FcγRI × HER-2/neu) in combination with G-CSF: Results of a phase I trial in patients with metastatic breast cancer

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FcγRI (CD64), the high affinity receptor for IgG, is a promising trigger molecule on myeloid cells for immunotherapy, because it is selectively expressed on effector cells like monocytes/macrophages, and G-CSF primed neutrophils. In vitro, a bispecific antibody (MDXH210, constructed by chemically cross-linking F(ab') fragments of MoAb 520C9 to HER-2/neu, and F(ab') fragments of humanized MoAb 22 to FcγRI) mediated effective lysis of HER-2/neu overexpressing breast cancer cell lines. HER-2/neu (c-erbB2) is overexpressed in approx. 30% of breast carcinomas, and is a target for immunotherapy in clinical trials. In vitro assays showed that FcγRI positive neutrophils constitute a major effector cell population during G-CSF therapy. Based on these preclinical data, a phase I trial with escalating single doses of MDXH210 in combination with G-CSF was started with patients with stage IV breast cancer. So far, this therapy was generally well tolerated up to 30 mg/m². Side effects consisted mainly of fever and short periods of chills, which were timely related to elevated plasma levels of IL-6 and TNF-α. Changes in soluble Her-2/neu, signs of effector cell activation, and inflammatory reactions in skin metastasis indicate a potential role for G-CSF and bispecific antibodies in immunotherapy.

677 POSTER

TAXOL® (paclitaxel) 1-hour infusion plus doxorubicin as first line treatment for metastatic breast cancer (MBC) patients

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Introduction: The high activity rates previously reported for doxorubicin + paclitaxel in MBC suggest a synergistic effect and warrant the development of clinical trials fully exploiting the therapeutic advantage of this combination TAXOL® 1-hour infusion represents a convenient outpatient schedule with safety & activity profiles still to be confirmed.

Purpose: To assess the response rate and toxicity of TAXOL® 1-hour infusion plus doxorubicin as first line treatment for MBC patients.

Materials and Methods: Between July 1995 and January 1997, 51 patients with untreated MBC were recruited. All of them had measurable disease and were evaluable for toxicity. One patient presenting liver MBC refused treatment and response could not be assessed. Age average was 53.3 years (range 30–70).

Estrogenic receptors (RE):	RE+ 13/51 (25.5%) RE− 14/51 (27.5%) RE? 24/51 (47%)
Premenopausal 14/51 (27.5%)	Chemotherapy naive 38/51 (74.5%)
Postmenopausal 37/51 (72.5%)	Adjuvant treatment (CMF) 13/51 (25 5%)

All of them received doxorubicin 50 mg/m² as a short infusion immediately followed by paclitaxel 200 mg/m² 1-hour iv infusion with standard premedication plus 5 HT_3 antagonists.

Results: 281 cycles (median = 6) were administered without hypersensitivity reactions.

CR (%)	PR (%)	CR+PR (%)	NC (%)	Prog (%)
8/50 (16)	27/50 (54)	**35/50 (70)**	11/50 (22)	4/50 (8)

Toxicity: While only 7 patients used CSF, neutropenia ≥ G3 (most of them of short duration) was present in 28/51 patients (54.9%), with febrile neutropenia accounting for 3/28. Anemia ≥ G3 in 4/51 (7.8%).

Alopecia was universal. One G3 and 28/51 (54.9%) ≤ G2 myalgias & arthralgias were reported. Gastrointestinal toxicity was mild to moderate. Peripheral neuropathy ≤G2 was observed in 21/51 (41.1%).

None patient developed clinical congestive heart failure after a median of 300 mg/m² of cumulative doxorubicin. Furthermore, only one patient went off study due to decrease of the LVEF. Two patients died during treatment: one died with sepsis and pancytopenia after 5 cycles; another died due to lung thromboembolism.

Conclusions: (1) The overall response rate was 70% (95% CI, 57.3% to 82.7%).

(2) No clinical congestive heart failure was assessed and only one patient went off study due to LVEF decrease.

(3) Although doxorubicin 50 mg/m² followed by TAXOL® 200 mg/m² in 1-hour iv infusion presents a toxicity profile which demands a close follow-up, it represents a convenient outpatient schedule with a similar activity rate compared to standard longer infusions.