endocrine therapy (tamoxifen). Prior palliative chemotherapy had been given to six patients (42.9%) and prior palliative endocrine therapy to 13 patients (92.9%) (goserelin+anastrozole and/or exemestane). Three patients (21.4%) had clinically apparent non-visceral metastases only, one patient (7.1%) had clinically apparent visceral metastases only and 10 patients (71.4%) had both. Eleven patients are currently evaluable for response: one patient had a partial response (PR) and four patients (36.4%) had stable disease (SD) $\geqslant$ 6 months, resulting in a clinical benefit rate of 45.5%. Also one patient had SD > 3 months but < 6 months. Both patients with HER2-positive disease experienced SD $\geqslant$ 6 months. Median time to progression was 5 months (range 2–12+ months). No local or systemic adverse events were reported.
Conclusions: Goserelin+fulvestrant appears to be an effective and well-tolerated treatment for premenopausal women with ABC including those with asymptomatic visceral metastases and HER2-positive disease. These data compare very favourably with similar data reported with fulvestrant treatment in naturally postmenopausal women with ABC. Further evaluation of fulvestrant in premenopausal women with iatrogenic menopause is supported in controlled clinical trials.

456 PUBLICATION

Phase II study of vinorelbine (VRL) alternating i.v. and oral in combination with docetaxel (DTX) as 1st line chemotherapy (CT) of metastatic breast cancer (MBC)

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Background: VRL and DTX are targeting tubulin-microtubule system, either inhibiting tubulin polymerisation (VRL) or microtubule depolymerisation (DTX). Both agents have proven activity in MBC.
Material and methods: This study was designed to evaluate the efficacy and the tolerance of the combination of i.v. VRL 20 mg/m^2 with DTX 60 mg/m^2 on day 1 and oral VRL 60 mg/m^2 on day 15 of a three-week cycle in first line treatment MBC for a maximum of 6 cycles (recommended dose established in Phase I study, abstract no. 684, ASCO 2004). Prior adjuvant CT was allowed if completed at least 12 months before study entry. At least one bidimensionnally measurable lesion (WHO criteria) was required.
Results: 49 patients (pts) were treated: with a median age of 53 years; 31 pts (63.3%) had received prior adjuvant chemotherapy; 44 pts (89.9%) had a KPS *80%; and 22 pts (44.9%) had *3 sites involved. A total of 261 cycles were given (median 6). Median relative dose intensities (RDI) of i.v. VRL and DTX were over 99% and median RDI of oral VRL was 76.4%. Neutropenia was the major side effect: grade (G) 4 in 51% of pts and 22.1% of cycles but only complicated in 5 pts: 4 febrile neutropenia (8.2%) and one neutropenic infection (2%). In terms of non-haematological related toxicity (all grades), the most frequent events reported were alopecia (61.2%), fatigue (22.4%), weight loss (18.4%), stomatitis (16.3%) and constipation, diarrhoea and nausea (14.3% each). Only one patient experienced G4 dehydratation. G3 events were stomatitis, vomiting and amenorrhea (4.1% each) and fatigue, constipation, diarrhoea, nausea, infection, syncope and abdominal pain (2% each). The combination was highly effective with 24 responses documented and validated by an independent panel review, yielding a response rate of 49% [95%CI: 34–64] in the 49 enrolled pts. Median duration of progression-free survival was 5.5 months [95%CI: 4.2–7.2]. Median duration of overall survival has not been reached with a median duration of follow-up of 9.7 months.
Conclusions: This combination with oral VRL on day 15 avoiding hospitalisation is highly efficient and manageable in contrast with previous Phase II studies having used higher doses and different schedules. VRL i.v./oral D1/D15-DTX D1 every 3 weeks is an attractive option to combine DTX and VRL at doses which are convenient for every day practice in MBC.

457 PUBLICATION

Low value of serum Ca 15–3 and CEA in monitoring trastuzumab-based therapy of advanced breast cancer

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Background: Trastuzumab therapy has recently become standard management of HER-2 positive patients with advanced breast cancer. There are particularly few data on the usefulness of serum Ca 15–3 and CEA in monitoring of this management. We present here the relationship between serum levels of both markers and the outcomes of trastuzumab-based therapy assessed in a single-institutional retrospective study.
Material and methods: Study group included 43 patients (median age 50 years; range 31–71 years) with recurrent or advanced HER2/neu overexpressing breast cancer who were administered trastuzumab with or without additional systemic therapies. Serum levels of CEA and Ca 15–3 were measured prior to initiation of therapy and every 3 months during treatment. Samples were tested using ELISA assays. Ca 15–3 and CEA values below 30 U/ml and 5 ng/ml, respectively were considered normal. 36 patients were evaluable for this analysis, of whom 22 (61%) responded to treatment. The median follow-up in the entire group was 9 months (range 3 to 24 months). Correlation between serum levels of both markers and clinical outcomes was computed using linear regression analysis.
Results: Baseline Ca 15–3 and CEA levels were elevated in 62% and 48% patients, respectively. Changes in serum levels of both markers during therapy did not predict for relapse. Elevation of Ca 15–3 and CEA levels occurred in 7 (35%) and 6 (30%) of patients with progression, respectively, and the correlation factor for both markers was 0.34 and 0.30, respectively. Combined analysis of CEA and CA 15–3 did not increase their predictive value.
Conclusion: Monitoring trastuzumab therapy of advanced breast cancer patients with serum Ca 15–3 and CEA, considered as single tests or in combination is of limited clinical value.

458 PUBLICATION

Cellular immunotherapy with reactivated autologous Memory T-Cells from bone marrow in late stage breast cancer patients

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Tumorspecific Memory T-cells (MTC) can be found in the bone marrow (BM) in the majority of primary and metastatic breast cancer (BC) patients by using ELISpot-analysis. Upon specific restimulation with tumourantigen-pulsed dendritic cells (DC) those autologous T-cells exert specific effector functions like IFN-gamma or perforin production and specific cytotoxicity. Furthermore we have shown in NOD/Scid-mice that reactivated MTC are able to infiltrate autologous and heterologous tumor tissue, proliferate and kill tumor cells by induction of apoptosis, leading to a marked or complete tumor rejection within 21 days after transfer (Nature Med, 2001). Endocrine and cytostatic cancer therapies only have a limited influence on the frequency of tumorspecific MTC in BM of BC patients.
In a phase-I trial 11 patients with metastatic BC (inclusion criteria) were treated with autologous reactivated MTC of BM. Primary objective were feasbility, and toxicity, secondary were clinical response, and immunomonitoring. After testing patient's BM for presence of tumorspecific MTC those cells were reactivated by incubating them in vitro with autologous DC pulsed MCF-7 lysate for 12 days. Reactivated T-cells and pulsed DCs were injected once intravenously. Follow Ups were done after 7, 14, 21, 28, and 120 days. Study design was feasible in every way.
There were no side effects found during and after T-cell injection. There was a partial response in 3 of 5 measurable patients. In 5 Patients – who received a maximum of reactivated T-cells – we were still able to find these cells 7 days after vaccination.
We conclude that cellular immunotherapy with autologous reactivated MTC is an innovative way of BC treatment. We thus prepare a phase-II trial in metastatic and primary BC patients.

459 PUBLICATION

Risk factors for brain metastasis in patients with advanced breast cancer (abc)

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Background: Incidence of brain metastasis is apparently rising in pts with ABC, possibly due to better therapeutic approach and longer survival. Occurrence of brain relapse severely affects quality of life and is associated with extremely poor prognosis.
Patients and Methods: A retrospective analysis of 84 consecutive pts with brain metastasis and ABC was performed (March 1999-December 2004). Evaluated variables were: age at diagnosis, staging and nodal status, oestrogen and progesterone receptor status, c-erbB2 over-espression, site of first relapse, previous chemotherapy.
Results: Thirty-three percent of pts aged less than 45 years (13% less than 35 years). Thirty-nine percent had T1 tumour, 28% T2 tumour, 41% had N0 disease and 46% N1 at diagnosis, therefore stage seems not a risk factor for developing subsequent cerebral metastases. Twenty-one percent of pts were metastatic at diagnosis. Brain metastases occurred more frequently in pts with lung (24%), bone (27%) and liver (20%) metastasis