(CT). 40 consecutive patients (pts), bearing T2–T4, N0–1, M0 primary breast cancer received 3 cycles of either epirubicin 120 mg/sqm (38 pt) or CMF regimen (2 pts) as neoadjuvant chemotherapy before surgery. All pts were assessed, immediately before and after 3 cycles of CT, for several biological parameters (ER, PgR, Ki 67) using immunocytochemistry on fine-needle aspiration biopsy material. Clinical response to treatment was assessed after primary CT; the overall response rate was 24/40 pts (60%). The evolution of biomarkers was examined in 39 pts. Ki 67 changed in 11/31 pts (35.5%); ER changed in 16/38 pts (42.1%); PgR changed in 18/39 pts (46.1%) In responder pts ER changed in 27.2%, PgR in 39% and Ki 67 in 41% whereas non responders showed variations in hormone receptor status in 62% of pts and in Ki 67 in 28.6% of pts. Primary CT with antracycline produces significant tumor reduction (60%).

At present the study is ongoing; non responder pts seem to present greater variations in hormone receptor status than responder pts, while a decrease of Ki 67 has been observed in responder pts.

898 PUBLICATION

Tc-99m MIBI uptake in advanced breast cancer: Predictive value of response to chemotherapy

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Purpose: Multidrug resistance (MDR) is a major therapeutic problem limiting advanced breast cancer (BC) treatment. Tc-99m MIBI has been reported to be extruded from tumoral cells by the P-glycoprotein (Pgp), encoded by the MDRI gene. The aim of this study was to investigate the possible relationship between MIBI uptake and response to chemotherapy in advanced BC.

Methods: We studied 14 pts with biopsy proven BC; 8 with advanced locorregional disease, 3 with locorregional and metastatic disease and 3 with recurrent disease. MIBI scintigraphy was performed 2–8 days prior chemotherapy. Images were acquired 10 minutes and 1 hour post injection of 740 MRq of Tc-99m MIBI. Tumor-to-normal tissue uptake ratios (T/N) were calculated in each evaluable lesion. All pts received combination chemotherapy containing doxorubicin for at least 2 cycles.

Results: Twenty-two BC lesions were evaluable for response to chemotherapy. Early T/N were significantly higher in lesions that showed a complete or partial remission than in non responding lesions (1.85, 1.5–2.9 vs. 1.40, 1.3–1.6; median, range respectively; p = 0.0006). No lesion with a T/N < 1.5 responded to chemotherapy.

Conclusion: These preliminary results suggest that Tc-99m MIBI scintigraphy may be a valuable tool for guiding chemotherapy in BC pts.

Brain tumours in children and adults

899 ORAL

Radiation therapy of intracranial pure germinoma: Results of the German prospective trials MAKEI '83, '86, '89

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Purpose: The trials (MAKEI '83/'86/'89) were conducted to assess the therapeutic outcome in pure intracranial germinoma after radiotherapy of the neuroaxis alone at reduced radiation doses.

Methods: 64 pat. were enrolled. In the MAKEI '83/'86 study (n = 12) the total dose was 36 Gy (neuroaxis) and 14.0 Gy (tumour site). In the MAKEI '89 study (n = 51) the dose was reduced to 30 and 15 Gy, resp..

Results: The 5 year relapse-free survival rate was 87.5% +/− 4.8% at a median follow-up of 50 months. The 5 year overall survival rate was 93.0% +/− 3.9%. 6 to 33 months (mean 16.3 months) after diagnosis relapses occurred in 6 pat. (9.5%), in 1 pat. a spinal recurrence in 1 pat. cerebral and spinal metastases and in 4 pat. metastases outside the CNS. Salvage chemotherapy achieved a second complete remission in 5 pat.. 2 pat. died of disease (3.2%) and 1 pat. (1.6%) of septicemia.

Conclusion: Radiotherapy alone is highly effective. Decreased dose levels were successful in local tumor control and prevention of spinal seeding. We advocate the irradiation of the neuroaxix and to continue to reduce the dose prescription to avoid major adverse effects of irradiation. The results were introduced in the current European prosp. study SIOP-CNS-GCT 96 with a further dose reduction to 24 Gy and 16 Gy, resp. to reduce acute and long term side effects.

900 ORAL

Treatment of carcinomatous meningitis (CM) with intra-CFS sustained-release encapsulated cytarabine (DEPOCYT™) vs. methotrexate (MTX)

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Neoplastic infiltration of the leptomeninges is a serious complication of cancer, and current intra-CSF (I-CSF) chemotherapy must be administered by frequent bolus injections. DepoCyt has an increased half-life in the CSF compared to MTX leading to reduced peak exposure with sustained cytotoxic CSF levels of ara-C, which allows for markedly decreased frequency of dosing. A randomized, Phase III, open-label, multicenter trial of DepoCyt vs. MTX was conducted in patients (pts) with CM. 61 pts were randomized to DepoCyt (31) or MTX (30). Primary neoplasms included breast (22), central nervous system (14), non small cell lung cancer (6), small cell lung cancer (4), melanoma (5), and other (10). Pts received either I-CSF DepoCyt (50 mg q14d x 2. [Induction]; 50 mg q28d x 4 [Consolidation]) or I-CSF MTX (10 mg 2×/wk × 8 [Induction]; 10 mg 1×/wk × 8 [Consolidation]). Cytological responses were noted in 9 of 23 (39%) DepoCyt and 7 of 24 (29%) MTX pts evaluable for response (p = 0.34). A Kaplan-Meier estimate of survival between treatment groups (log rank, p = 0. 12) showed median survival of 105 (DepoCyt) vs. 87 days (MTX); mean survival of 195 (DepoCyt) vs. 128 days (MTX). At 6 months, the number of surviving pts was 11 (35%) DepoCyt and 5 (17%) MTX pts. I-CSF DepoCyt provides a more convenient dosing schedule than MTX, results in a cytological response rate that is at least comparable to MTX, and may offer a survival advantage over conventional I-CSF chemotherapy.

901 ORAL

Phase II study of intravenous RMP-7 and carboplatin for chemotherapy naïve recurrent malignant glioma

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RMP-7, a selective bradykinin analogue, transiently increases the permeability of the blood brain barrier and the delivery of hydrophilic agents into brain tumours.

Aim: To assess clinical and 3-D MRI response to and toxicity of RMP-7 (300 ng/kg) + carboplatin (AUC 7) in treatment of recurrent glioma, WHO histology III + IV.

Methods: 45 patients (median age 42, Karnofsky 80%) were treated q 28 days. Neurological impairment, performance status and steroid use were measured over 4 cycles, plus tumour volume by 3-D MRI at the end of cycles 2 & 4.

Clinical response = stable or improved compared to baseline, and steroids stable or reduced, for ≥2 cycles. Primary evaluation of first 4 cycles.

Results:

Responding by Assessment Tool: Intent to Treat Analysis

Assessment	All	Grade III	Grade IV
EFIT[1]. improved/stable (n = 41)	39/22	47/20	35/23
Karnofsky: stable + improved (n = 45)	74	80	70
MRI volume· CR/PR/SD[2] (n = 43)	7/21/51	12/35/30	4/12/65
CR+PR+SD	79	77	81

[1] an objective, validated measure of neurological impairment. [2] CR ≥ 95% volume reduction + off steroids; PR > 50% reduction + stable or reduced steroids; PD > 50% increase, SD all other situations; all maintained ≥2 cycles.

Toxicity: no toxic deaths, 1 thrombocytopaenic withdrawal. Thrombocytopaenia and/or neutropaenia CTC grades 3/4: 2% at baseline; 27% at cycle 1; 29% at cycle 2; 45% at cycle 3; 35% at cycle 4. 3 patients had treatment-associated transient focal seizures.

Conclusions: Clinical and MRI response to RMP-7 and carboplatin combination is promising and toxicity is mild.