vs 46%. There were not differences between both groups in % of patients who received consolidation therapy or in the best response to salvage regimens.

Results: (NOTAX-P vs TAX-P): Clinical response rates were complete (CCR): 38.2% vs 50%, partial (CPR): 17.1% vs 26% and overall (OCR): 55.3% vs 76%. The 95% CI values for the difference in response were for CCR: -4 to 27% and for OCR: 6 - 35% in favour of TAX-P. In 68 p with CCR or CPR who underwent 2nd look laparotomy, pathologic complete response rates (PCR) were 48.8% vs 48.1% (p ns). With a median follow-up of 81 and 31 months, median survival are 26 vs 29 months respectively, and 3-y survival rates (95% CI) are 42.8% (32 - 53%) vs 41.3% (25.9 - 56.7%).

Conclusion: We have obtained a better OCR rate with TAX-P compared to NOTAX-P regimens, but, contrary to the results of some randomized clinical trials, PCR rates, median survival and 3-y overall survival remain basically unchanged in our series.

964 POSTER DISCUSSION

Clinical development of Ovarex MAb-B43.13 monoclonal antibody for treatment of ovarian cancer: impact of immune responses and circulating CA125 levels on clinical efficacy

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OvaRex Mab-B43.13 is a murine monoclonal antibody (MAb) targeting the tumor-associated antigen CA125. Intravenous administration was associated with prolonged survival in patients (pts) with relapsed ovarian cancer, correlated with nonspecific (HAMA) and specific (Ab2) immune responses (Bolle, Proc. ASCO 19:476a, 2000). Paradoxically, prolonged survivals were seen in poor-risk pts, assessed by elevated circulating CA125 levels relative to pts with lower levels of CA125 (Noujaim A.A., Cancer Biother Radiopharm, in press). A prospective, randomized, placebo-controlled, double blind study of 345 pts with stage III-IV ovarian cancer was designed to determine clinical efficacy, safety, and biologic activity of OvaRex MAb administered after attainment of CR from primary chemotherapy. Preserving integrity of the blind, independent review was conducted from an initial cohort of 252 pts. Clinically meaningful immune responses were observed in >50% of the MAb-treated pts, measured by serum HAMA >5000 ng/mL and Ab2 >100 ng/mL associated with improved time to relapse (TTR). Pts with specific immune response (Ab2 serum level >100 ng/mL) demonstrated two-fold improved TTR to 18.9 mos vs. 7.4 mos in pts with Ab2 < 100 ng/mL. Irrespective of immune response, baseline CA125 prior to protocol treatment was a strong predictor of TTR, similar to previous reports (Makar, Gyn Oncol 49:73, 1993) and was confirmed to be a valid covariate for analysis of efficacy outcomes. In a poor prognosis subgroup (CA125 >20 U/mL), the proportion of pts surviving 6 months without disease relapse improved two-fold with OvaRex MAb therapy (relapse-free survival 79% vs. 39% in placebo-treated controls, p <0.05). Taken together, the favorable clinical outcomes in the high-risk pts with elevated CA125 levels support the proposed mechanism to induce immune responses to MAb + CA125 immune complexes, generated after intravenous MAb administration. Results from prospective, controlled trials confirm that OvaRex Mab-B43.13 frequently induces immune responses relevant to clinical efficacy, and provide rational approaches to development as an adjunct to treatment of ovarian cancer and possibly to treatment of other types of cancer associated with circulating serum CA125 levels.

965 POSTER DISCUSSION

Phase II clinical study of BBR 3464, a novel, bifunctional platinum analogue, in patients with advanced ovarian cancer

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BBR 3464 is a trinucleate platinum compound, differing from cisplatin in its structure, nature of the adducts formed, and pre-clinical spectrum of anti-tumour activity. The Phase I study of a 1 hour infusion every 28 days identified diarrhoea and myelosuppression as the dose limiting toxicities and initially 1.1mg/m2 as the recommended Phase II dose. Activity was observed in three patients, with respectively melanoma, pancreatic and lung cancer.

Purpose: The objectives of this Phase II study are to determine the efficacy of BBR 3464 in patients with ovarian cancer failing platinum-taxane regimens and to further characterise the toxicity and pharmacokinetic profile of this compound.

Methods: This is a multi-centre, open label, Gehan design study. Patients are stratified into two categories: those who relapsed following a response after 6 months from the discontinuation of chemotherapy and those who have not responded or have relapsed within 6 months.

Results: 28 relapsed and 18 refractory patients have been recruited to date and have received in total 164 infusions of BBR 3464. Five partial responses, confirmed by independent peer review, have been reported and in three of them a repeat scan for confirmation was obtained. In responding patients, the average interval between previous treatment and the first BBR 3464 treatment was 18 months. Toxicity data is available on 44 patients. The main toxicity seen so far is neutropenia (G3 n=7 (16%), G4 n=5 (11%)) which led to a dose reduction to 0.9mg/m2 in 6 patients. In addition, anaemia (G2 n=8, G3 n=1), thrombocytopenia (G2 n=1), nausea (G2 n=11, G3 n=8) and vomiting (G2 n=11, G3 n=5) were reported. Diarrhoea was observed (G2 n=14, G3 n=3) but was kept manageable by a policy of active intervention with loperamide. No clear signs of drug-related neurotoxicity were seen. One patient with pre-existing hypomagnesaemia and paraesthesiae experienced grade 2 paraesthesiae associated with course 3 of treatment. Since the haematological toxicities were reversible within 3 weeks and there was no evidence of cumulative renal or lung toxicity, a schedule of 0.9mg/m2 every 21 days, which in the ongoing Phase I trial was shown to be better tolerated and of a similar dose intensity, has now been introduced. Recruitment into the refractory category continues using this amended schedule. Efficacy and toxicity analysis is ongoing.

Conclusion: BBR 3464 is showing provisional evidence of activity in relapsed ovarian cancer.

966 POSTER DISCUSSION

Weekly paclitaxel and carboplatin followed by topotecan (TC-TP), as first-line therapy for patients with advanced epithelial ovarian cancer (AOC) suboptimally debulked. Updated preliminary results

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Objective: To evaluate clinical response (overall, complete and partial: cOR, cCR and cPR respectively), pathological CR rate (pCR), and toxicity, of the schedule TC-Tp, administered as first-line therapy in patients (pt) with AOC suboptimally debulked, defined as FIGO III-IV with residual disease (RD)> 1 cm.

Patients and Methods: Phase II design. TC-Tp consisted of 2 courses of TC (weekly Paclitaxel 60 mg/m2 + Carboplatin AUC 2, x 6 doses each course) separated by a 14-day rest period, and followed by 4 courses of Tp (Topotecan 1.5 mg/m2/d x 5d every 3 weeks). All pt received Tp after TC even if they had no response to TC. Prophylactic filgrastim was allowed after an episode of neutropenia grade 3-4, and Tp doses were reduced after other G3-4 toxicities. Second-look laparotomy was planned at least for pt with cCR after TC-Tp. In those pt with pCR or microscopic residual disease, consolidation with TCx1 + Tp x2 was recommended.

Results: Since March '99, 65 pt have been included and 50 pt have already completed TC-Tp. Preliminary results from the first 37 pt were presented in ASCO'01. Results from the first 50 pt are presented here. Mean age was 58 y (34-77). There were 78% stages III and 22% IV. Debulking surgery was performed in 86% of pt, but 88% had RD >2 cm.

Grade 3-4 toxicities with TC were anemia 2%, neutropenia 23%, thrombocytopenia 4%, alopecia 37% and nephrotoxicity 2%. Toxicity after Tp was anemia 13%, neutropenia 40%, thrombocytopenia 11% and alopecia 70%. Astenia was present in some pt but it was not properly registered. There were no toxic deaths. Other toxicities were G1-2 or absent.

Response rate after TC (and 95% CI) were: cOR: 82% (69 - 91%), cCR: 36% (23 - 50%) and cPR: 46%. After TCTp we found cOR: 78% (64 - 88%), cCR: 48% (34 - 63%) and 30% cPR.

The difference in cCR between TCTp and TC is 12% (95% CI: -0.85 to 16%). Five pt have achieved pCR until now (11.6%, 95% CI: 4 - 25%), but results of 2nd look are pending for another 5 pt with cCR. Fourteen pt received consolidation therapy and 19 pt other 2nd line therapies. With a