Gynaecological cancers I

525 ORAL

Response and early progression according to CA 125 to assess activity of topotecan vs paclitaxel in relapsed ovarian carcinoma

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Purpose: We have shown that response of ovarian cancer can be defined by a serial fall of CA 125 *[J. Clin Oncol 1996,* **14:** *1545–51].* To help rank the activity of drugs we have now compared both response and progression rate according to CA 125 in the SmithKline Beecham trial of paclitaxel (P) versus topotecan (T) for first relapse. Because CA 125 may over estimate response to taxanes, we tested both CA 125 response and progression definitions.

Methods: 112 patients (pts) received T 1.5 mg/m^2 d x 5 and 114 received P 175 mg/m^2 as a 3 hr infusion, both q 21d. Response was assessed by EORTC criteria (EC) in 204 pts, by CA 125 in 165, and CA 125 progression was assessed in 180. CA 125 progression was based on a 25% increase over 4 samples or 50% increase over 3 samples or persistence of >100 U/ml for >2 months (m) calculated by a computer programme *[Ann Oncol 1994,* **4:***S71–77].*

Results:

	Clinical response	CA 125 response	Clinical progression	CA 125 progression
Topotecan	24%	20%	53%	21.9% (CI 13.6–32.5)
Paclitaxel	14%	21%	63%	35.7% (CI 26.3–46.0)

Both drugs were active according to CA 125 response. However there was a higher early progression rate by 4 months in those receiving P versus T by both clinical (p = 0.12) and CA 125 criteria (p = 0.04).

Conclusion: In trials of new drugs for ovarian carcinoma the use of CA 125 response and progression criteria may be helpful in deciding whether further development of a drug is justified.

526 ORAL

Outome of advanced epithelial ovarian cancer in women under 40 years

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Purpose: We have studied the outcome of treatment of epithelial ovarian cancer (EOC) in women under 40 years treated in three randomised phase III studies of platinum-based chemotherapy between 1984 and 1994.

Methods: 652 patients (pts) were entered into trials of carboplatin versus carboplatin plus radiotherapy, carboplatin v. iproplatin, and carbo- or cisplatin (5 v. 8 cycles). 28 were excluded on histological review with non invasive EOC.

Results: Median age of 624 pts was 60 yr (17–79). 29 (4.6%) were under 40 yr. FIGO stage, grade and residual disease were significantly worse in pts >40 yr. but histology and performance status (ECOG) were not different. Response was assessed by second look laparotomy in 229 patients (9 under 40 yr) and by CT scans and/or serum CA125 in the others. The median follow up is 5.2 yr. Survival and time to progression were significantly better in women under 40 yr. At 5 yrs, for those under and over 40 yr the RFS is 58.6% and 16% (95% CI: 24.3–60.8%) p < 0.0001 and the OS is 65.2% and 20.1% (95% CI: 27.2–63%) p < 0.001. No pts <40 yr relapsed after 1.5 yr. A Cox proportional hazards model identifed age <40 yr as a good prognostic variable for serious histology (hazard ratio (hr): 2.1). Other prognostic factors were ECOG (hr: 1.3), residual disease (hr: 1.3), and stage (hr: 1.4).

Conclusions: The biology of serous carcinomas of the ovary in young women appears to be different from older women and is associated with a more favourable outcome.

527 ORAL

Immunotherapy of advanced ovarian cancer with the anti-idiotypic antibody MAb ACA 125 – Results of a clinical phase IB study

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Purpose: The idiotypic network offers a method for immunotherapy by presentation of tumor antigens as an idiotypic determinant in a different environment. Therefore, we have generated an IgG1 murine monoclonal anti-idiotype antibody (Ab2) designated ACA 125, which mimics a specific epitope on the tumor-associated antigen CA 125. We used ACA 125 as a surrogate for the tumor-associated antigen CA 125 for vaccine therapy.

Methods: 18 patients with advanced epithelial ovarian cancer (n = 5) or recurrences (n = 13) received a minimum of three injections up to nineteen injections of the complete anti-idiotype MAb ACA125 at a dosage of 2 mg per injection.

Results: 11 of 18 patients developed anti-anti-idiotypic (Ab3) responses to the ACA 125. 9 of 18 patients developed a CA 125 specific cellular immune response by their PBL. The median progression free survival in those patients, who showed a specific immune response to the tumor-associated antigen CA 125, was 10.3 months without any other therapy, in contrast to 7.1 months in the anti-anti-idiotype negative group.

Conclusion: This is the first clinical trial of the induction of a specific active immunity to the tumor-associated antigen CA 125 in patients with advanced ovarian cancer treated with an anti-idiotype antibody that "mimics" CA 125. Patients showed the development of a specific humoral and cellular immune response to an otherwise non-immunogenic tumor antigen. (supported by DFC, Wa 740/1–3).

528 ORAL

A phase II study with GI147211 in ovarian cancer

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GI147211 is a water soluble analog of camptothecin with preclinical antitumor activity in a broad range of tumor xenografts. Main toxicities reported in Phase I studies were hematologic and gastrointestinal.

The ECSG has performed a Phase II study in ovarian cancer at the recommended dose of 1.2 mg/m^2/dx5 q3wks. Patients (pts) were stratified for "response to prior treatment". O_1 were pts relapsing/progressing during or <4 months after last platinum (Pt)-containing treatment; O_2 were pts relapsing between 4–12 months after the last Pt-containing regimen. Pts could have had 2 prior Pt regimens. A total of 55 eligible pts were entered (27 O_1, 28 O_2) of whom currently 23 O_1 and 23 O_2 are evaluable for response. 208 (median 4, range 1–12) cycles (c) were administered, with dose reductions to 0.9 mg/m^2/d in 51 c and to 0.6 mg/m^2/d in 2 c, mostly due to hematologic toxicity. Dose escalation to 1.5 mg/m^2/d was possible in 11 c. Main hematologic toxicities were neutropenia (grade 3/4 in 21%) and anemia (grade 3 in 9%). Asthenia, nausea, and alopecia were the main non-hematologic toxicities, but rarely exceeded grade 2. 1/23 O_2 pts developed a CR and 7 pts (3/23 O_1, 4/23 O_2) had a PR.

We conclude that GI147211 has moderate activity in Pt-pretreated ovarian cancer.

529 ORAL

Weekly high dose cisplatin (P) and daily oral vepesid (VP): A highly active salvage regimen for progressive or recurrent ovarian cancer after platinum therapy

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Purpose: To increase the efficacy of P in ovarian cancer by weekly administration.

Methods: 92 Patients (pts) were treated with 2 cycles of weekly P day 1, 8, 15 and daily oral VP 50 mg, day 1–15 q. day 29, followed by VP 50 mg/m^2/day, day 1–21 q day 29, times 9. The P dose for pts with a P free interval (PFI) of <1 year was 70 mg/m^2 and for a PFI of >1 year 50 mg/m^2.