Results: An expression of HER2 was detected in 25% of the tumours. Immunhistochemical Scores of e2 were observed in 9% (7% Score 2, 2% Score 3) of the tumours. The results of immunhistochemical analysis and the FISH method were identical. Statistical analyses show that these 361 patients are representative for the whole group of 798 patients from the Ovar-3 trial. No correlation could be observed for the classical clinical factors, or for response rate. Also no different (HER2 overexpression vs no overexpression) in disease-free, as well for overall survival was observed.

Conclusion: HER2 overexpression in advanced ovarian cancer is rare. No prognostic or predictive importance could be shown.

42 ORAL

Phase I study for treatment of ovarian cancer patients with symptomatic ascites using the trifunctional bispecific antibody removab® (anti-CD3 X anti-EpCAM).

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Background: A new class of trifunctional bispecific antibodies has been developed for targeted therapy of epithelial tumors. Due to binding sites specific for tumor cells (EpCAM), T lymphocytes (CD3) and accessory cells (FcgRI/III) the antibody induces tumor specific cell mediated cytotoxicity in the peritoneal cavity.

Patients and methods: In the currently ongoing phase I study removab® was administered 4 times over 10 days in escalating doses by 6h intraperitoneal infusions, respectively. Pts had undergone 4 prior chemotherapies in median.

Results: To date, preliminary results of the first 16 pts are available. Patients were treated with total doses of 35 μg (3 pts), 60μg (2 pts), 80μg (1 pt), 130 μg (3 pts), 160 (1 pt), 180 μg (3 pts) and 280 μg (3 pts). So far, no dose limiting toxicity has been observed. Drug related adverse events (ADR) noted in more than 1 patient were fever (n=12), abdominal pain (n=11), vomiting (n=8), nausea (n=6), fatigue (n=4), exanthema (n=2), hypotension (n=3), hypertension (n=2), abdominal cramps (n=2). All ADR seen were mild to moderate (grade 1 to 2), except fever with grade (gr) 3 in 1 pt and hypertension with gr 3 in 1 pt. The following laboratory abnormalities (> gr 1) have been observed: elevation of liver enzymes (n=4; 2 gr 3), alkaline phosphatase (n=5; 2 gr 3) and bilirubine (n=3; 2 gr 3). Almost all patients showed a transient, clinically non-significant lymphocytopenia. Leukocytosis was also common. All pts responded to therapy. Immunocytochemical examination of ascites fluid showed a reduction of tumor cells by 4 logs at least, in most cases by more than 5 logs. In 5/16 pts no tumor cells were detectable after therapy. The disappearance of tumor cells correlated significantly with a reduced ascites production. Remarkably, only 1/16 pts required further paracentesis within 28 days after last dose (end of study).

Conclusion: Our preliminary results show a good tolerability of removab® in general without major toxicities and significant treatment effects on malignant ascites in ovarian cancer. Thus, the new concept of trifunctional antibodies offers promising perspectives in tumor therapy.

43 ORAL

Serendipitous findings of occult fallopian tube carcinoma in BRCA 1/2 germ line mutation carriers at prophylactic surgery

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Background: Carriers of a BRCA-1 or 2 mutation are at increased risk of developing breast and ovarian cancer. Prophylactic surgery has proven to reduce the risk of coelomic epithelial and ovarian cancer by 96 percent. The purpose of this study is to assess the risk of occult fallopian tube or ovarian cancer at prophylactic (salpingo)- oophorectomy specimen at the Antoni van Leeuwenhoek Hospital in a series of high risk women.

Patients and methods: The medical files and histological slides of patients, who had undergone prophylactic surgery, were reviewed. The patients were carrier of a BRCA-1 or 2 mutation or were member of a hereditary breast / ovarian cancer (HBOC) family.They were not suspected of having any tumor before surgery, determined by patient history, pelvic examination, transvaginal examination or serum CA-125 determination.

Results: From January 1990 to November 2001, 141 women underwent prophylactic surgery. Forty of whom had a bilateral oophorectomy and 101 women a bilateral salpingo-oophorectomy. Ninety-four were tested positive for a BRCA-1 or 2 mutation. Five occult carcinomas were found (3,5%). Three of these five were fallopian tube carcinomas and the pathology reports of the other two showed an ovarian carcinoma. All of these five patients had a BRCA mutation. In the follow-up, three patients (2,1%) developed a peritoneal papillary serous carcinoma; 27, 33 and 72 months after oophorectomy.

Conclusion: HBOC patients are not only at risk for ovarian cancer but also for fallopian tube carcinoma. We recommend prophylactic salpingo-oophorectomy and not only oophorectomy in women at high risk of developing fallopian tube carcinoma or ovarian cancer.

Gastro-intestinal tumours

44 ORAL

Phase III trial comparing Epirubicin, Cisplatin and 5-FU (ECF) versus 5FU, Etoposide and Leucovorin (FELV) in previously untreated patients with advanced biliary cancer.

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FELV has demonstrated an overall response rate (ORR) of 8% and a survival benefit compared to best supportive care in advanced biliary cancer but with significant toxicity (41% grade 3/4 toxicity). ECF has demonstrated an ORR of 40% with minimal grade 3/4 toxicity in this setting. Thus this multicentre randomised phase III trial was designed to compare the safety and efficacy of ECF versus FELV in patients with previously untreated locally advanced and metastatic biliary cancer.

Methods: Eligible patients had WHO performance status (PS) 0-2, adequate liver, renal and hepatic function, written consent and received no prior chemotherapy or radiotherapy. Patients were randomised to treatment with stratification for centre and histology. ECF treatment consisted of Epirubicin 60 mg/m2, Cisplatin 60 mg/m2 and 5FU 200mg/m2 daily by continuous infusion every 3 weeks for a maximum of 8 cycles. FELV consisted of 5FU 600 mg/m2 IV bolus days 1-3, Etoposide 120 mg/m2 IV infusion days 1-3 and Leucovorin 60mg/m2 IV bolus days 1-3 every 3 weeks. Response assessment by CT scan according to WHO criteria took place at 12 and 24 weeks.

Results: 50 patients were accrued between June 1997 and January 2002. 45 and 47 are evaluable for response and toxicity. Baseline characteristics were comparable in the two treatment groups with a median age 57 (range 39-73) years, WHO PS were 0,1,2 in 10%, 72% and 18% respectively, metastatic disease in 60%, adenocarcinoma 100%. No statistically significant differences in ORR or survival parameters were observed. The ORR for FELV was 15.8% versus 19.2% for ECF. The median overall survival (OS) for FELV was 367 days [95% CI: 251- 483] and 275 days for ECF [95% CI: 189-361]. One serious adverse event resulting in death occurred on the FELV treatment arm. Grade 4 neutropenia was observed in 19% of patients treated with ECF versus 46% in the FELV arm. Grade 3 infection was reported in 17% of patients receiving ECF versus 30% in the FELV group. The incidence of other non-haematological adverse events was similar in the two groups.

Conclusion: ECF has demonstrated similar efficacy with significantly less acute toxicity compared to FELV in untreated advanced biliary cancer.