UK vs 5% in UK centres [Fisher's: p<0.0001]. In FIGO stage 3 aggressive debulking procedures were more likely to be performed in non-UK centres. 'TAH/BSO & Omentectomy'was performed in 62% of cases from non-UK centres vs 49% in UK centres [p=0.0002]. These differences corresponded to a greater likelihood of optimal debulking of tumour [non-UK centres 71% vs 58%: p<0.0001]. This increased surgical activity was associated with a longer operating time. [Non-UK centres, median=136 minutes; UK centres, median=95 minutes: Mann Whitney: p<0.0001].

Conclusion: This study demonstrates clear differences in surgical practice among gynaecologists referring patients for entry into this clinical trial, comparing the UK with non-UK centres. These differences in surgical practice are particularly relevant to the management of stage 3 tumours where there appears to be a greater likelihood of residual disease >2cm following UK procedures. As this is known to be a key prognostic factor, these are potentially large enough to impact significantly on treatment outcome, and might explain some of the variability in survival outcome seen in the EUROCARE studies. Survival data are awaited.

1017 ORAL

Conservative treatment of ovarian borderline tumor

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Purpose: The aim of this study is to assess the clinical outcome and fertility of patients treated conservatively for a low malignant potential ovarian tumor (LMPOT).

Methods: Forty-four followed-up patients treated with conservative management for a stage I (n = 32) or II and III (n = 12) LMPOT were followed-up. 33 patients underwent a unilateral adnexectomy and 11 had a cystectomy (bilateral in 1 patient; with contralateral adnexectomy in 5 patients).

Results: The recurrence rates following radical surgery, adnexectomy and cystectomy were respectively: 5.7%, 15.1% and 36.3% (p < 0.01). None of the recurrences in the patients who were initially treated conservatively were under the form of ovarian carcinoma. Five patients who had recurrence underwent again a conservative management of these recurrences. All patients treated conservatively are alive and disease-free. Seventeen pregnancies (15 spontaneous) were obtained in 14 patients. Thirteen pregnancies were obtained in patients with stage I disease and 4 in patients with stage III.

Conclusion: The conservative management of LMPOT increases significantly the risk of recurrence but without affecting the overall survival. Such a management offered a chance of having spontaneous pregnancies even in patients with advanced stage of the disease (noninvasive peritoneal implants). Conservative management could be proposed in young patients wishing to preserve their fertility. But careful follow-up will be required to detect any recurrence in the ovaries.

1018 ORAL

Epirubicin/paclitaxel/carboplatin (TEC) vs paclitaxel/carboplatin in first line treatment of ovarian carcinoma figo stage II b-IV. Preliminary results. A GINECO randomized trial

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Purpose: The objective of this randomized trial was to demonstrate whether the three drug chemotherapy regimen (TEC) increases overall survival over two drug (TC).

Methods: Between 11/1997 and 02/2000, 1281 patients were randomized to receive 6 cycles of paclitaxel (175 mg/m2, 3 h iv) followed by carboplatin (AUC 5, Calvert formula) with (TEC) or without (TC) epirubicin (60 mg/m2 iv prior to Paclitaxel) on a 3 weekly schedule. Patients (pts) were stratified for stage and residual tumor (rT) (II-III + residual T ≤ 1 cm = Strate 1/IV and II-III + residual rT > 1 cm = Strate 2).

Results: Patient characteristics are well balanced between two arms (1190 pts). NCI-CTC toxicity of 3-4 grade was observed in 54% of the cycles of TEC and 30% of TC. Hematologic toxicity was grade 3-4 in 68% of the patients in TEC arm, versus 30% TC arm. Non hematologic toxicity was not significantly different between TEC and TC except for nausea and vomiting. Adjonction of epirubicin did not increase cardiac toxicity. There is no significant difference in progression free survival between TEC and TC (1190 pts). But there is a trend in favour of TEC in strate 1, 323 events/605 pts, med 18 (16/21) vs TC 333/585, med 17 (15-19). There is no difference between TEC and TC for overall survival. Follow up and analysis will be updated in autumn 2001.

Conclusion: this is the first trial evaluation of standard chemotherapy versus three drug regimen. Both regimens are feasible. TEC induces more hematologic and vomiting toxicities than TEC. Until today there is no advantage in terms of overall survival of TEC over TC.

1019 ORAL

ACTION + ICON1: two parallel randomised phase III trials comparing adjuvant chemotherapy to no adjuvant chemotherapy following surgery in women with high risk early ovarian cancer

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Background: Despite a number of small randomised trials it is not clear whether adjuvant chemotherapy improves survival in women with early stage epithelial ovarian cancer.

Method: We carried out two parallel international, multicentre, randomised trials ICON1 (International Collaborative Ovarian Neoplasm studies) and ACTION (EORTC: Adjuvant Clinical Trial In Ovarian Neoplasm) to compare adjuvant platinum-based chemotherapy against chemotherapy delayed until indicated, in women with surgically resected early ovarian cancer. The primary outcome was length of survival.

Findings: 925 (477 in ICON1, 448 in ACTION) patients were randomised from 124 centres in 13 countries; 465 to adjuvant chemotherapy and 460 to no adjuvant chemotherapy. The median age was 55 years with over 90% patients being FIGO stage 1. The major histological cell types were serous (34%), mucinous (20%), endometrioid (25%) and clear cell (14%). Differentiation of disease was classified as poor in 31% of patients, intermediate in 46%, and well in 22% of patients. The patient characteristics were similar in both treatment groups. With over 3 years median follow-up for survivors, the hazard ratio for recurrence-free survival is 0.64 (95% confidence interval 0.50 to 0.83), p = 0.001, in favour of adjuvant chemotherapy. For overall survival the hazard ratio is 0.68 (95% confidence interval 0.51 to 0.92), p = 0.01, in favour of adjuvant chemotherapy. These results translate into an absolute difference of 7% in overall survival at 5-year from 75% in the no adjuvant chemotherapy to 82% in the adjuvant chemotherapy.

Preliminary Conclusion: Adjuvant chemotherapy improves both recurrence-free survival and overall survival. The clinical interpretation of these results will be discussed.

1020 ORAL

CA125 response and disease stabilisation are associated with estrogen receptor expression in a phase II trial of letrozole in ovarian cancer

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Purpose: We are exploring the therapeutic potential for estrogen receptor (ER) targeted approaches in ovarian cancer. In a phase II trial of the aromatase inhibitor letrozole (Femara) in relapsed ovarian cancer, we have investigated the relationship between antitumor response to letrozole and several markers relating to estrogen regulation predicted by our experimental ovarian cancer models.

Methods: 60 patients were treated with letrozole (2.5 mg daily) at CA125 relapse. To date, 45 patients are evaluable for response by CT scan and 48 by CA125 criteria. ER and progesterone receptor (PR) expression were measured in primary tumors by immunohistochemistry (IHC) using a scoring system ranging from 0 to 300 (product of % cells positive and intensity). EGF receptor and erbB2 were also measured by IHC.

Results: After 3 months treatment, using UICC criteria, letrozole produced no complete or partial responses, 8 patients had stable disease and 37 progressed. Using CA125 criteria, 5 patients had a partial response (> 50% fall), 13 had a stable value at 3 months (<50% rise) and 30 had a clearly progressing value. The UICC stable disease group had a significantly higher ER (p=0.032) and PR value (p=0.0096) than the progressive disease group and a combination of these ER > 150, PR > 70 was associated very strongly with stable disease (p < 0.0001). Using CA125 criteria, comparison of the CA125 stable/responding disease with progressive disease again indicated

that higher ER (p = 0.019), lower erbB2 (p = 0.046) and higher EGF receptor (p = 0.033) were associated with CA125 stable/responsive disease.

Conclusion: These results imply that letrozole treatment can produce disease stabilisation and CA125 responses which in turn are linked to higher levels of ER expression. These data suggest the presence of an "endocrine-sensitive" group which could be targeted in future studies.

1021 ORAL

Ovarian cancer: comparison of F-18-FDG-PET imaging technique versus computed tomography scan and serum CA-125 level for diagnosis of recurrent disease

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Purpose: To evaluate the sensitivity of whole body FDG-Positron Emission Tomography study in detecting recurrence of ovarian cancer.

Methods: 18 consecutive stage III and IV ovarian cancer patients (pts) previously treated with surgery and chemotherapy with suspicion of relapse, were evaluated with FDG-PET imaging scan. Recurrence disease was suspected by abnormal CA 125 levels and/or by CT scan. The images corrected by attenuation of thoracic, abdominal and pelvic regions were obtained 45 minutes after the iv injection of 370 MBq of F-18-FDG with an ECAT EXACT HR+ scanner. Ovarian cancer recurrence was confirmed by histopathologic analysis (9 pts) or follow up (9 pts).The sensitivity value of the functional imaging technique has been compared with the CA 125 levels and the CT scans.

Results: The sensitivity for CT scan, CA 125 and F-18-FDG-PET were 44%(8/18 pts), 83%(15/18 pts) and 100%(18/18 pts) respectively. PET has successfully detected recurrent disease in 3 pts with normal CA 125 levels and in 10 pts with non suspicious CT scan. There was significant difference between PET and CT in regard to sensitivity (The p value for the McNemar test was < 0,01).

Conclusion: In this small series of 18 pts with suspicion of relapsed ovarian cancer, PET has proven to have more sensitivity than CT scan in detecting recurrent disease. Updated results with more pts will be presented.

1022 ORAL

In vivo induction of HPV 16 specific cytotoxic ctl and T-helper immunity in patients with advanced cervical cancer using autologous dendritic cells (dc) pulsed with tumour lysate as a potential anti-cancer vaccine

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The feasibility, and safety of inducing specific class 1 and 2 specific CTL response to HPV E6 and E7 antigens using autologous dendritic cells primed with HPV +ve tumour lysate as an anti cancer vaccine has been tested in a phase 1B clinical trial.

Patients and Methods: 9 patients with advanced cervical cancer (8 recurrent with distant metastases) have been vaccinated. Monocyte derived DCs were cultured from 10 9 PBMC obtained at leucophoresis using GMCSF and IL 4 for 7 days. CD1 a + CD14 - immature DC were pulsed with sonicated HPV +ve tumour lysate (5 autologous and 4 allogeneic lysate) and the frozen in aliquots for 6 weekly subcutaneous vaccinations of 107 DC. Immunological endpoints were DTH skin reactions to recall antigens and lysate, tetramer CTL response and ELISPOT CTL and T-helper response in 5 evaluable patients. Tumour response was assessed clinically and radiologically.

Results: Toxicity was mild with occasional fever and malaise but one patient developed a capillary leak syndrome which was successfully treated with steroids. Only 2/9 patients reacted to recall antigens on skin testing. Specific HPV specific CTL response was demonstrated in peripheral blood in 2/3 evaluable (HPV16 + HLA 002*) patients after vaccination. In these patients the frequency of HPV16E7 [11-20] rose to 2.2% as detected by class1 tetramers and the IFN gamma ELISPOT assay -revealed a specific - response to 4 HPV 16 E6 and 7 derived CTL epitopes, 1 week and 2 months respectively after vaccination. In 1/4 evaluable HPV 16 + patients a specific T-helper response was also observed. T cell immunity as detected by ELISPOT correlated with the DTH response to tumour lysate and these patients followed a favourable clinical outcome (NED of disease 18mo + after resection of lung metastasis, stable disease for 3+ mo after progression.

Conclusion It is feasible to induce in vivo HPV specific class 1 and 2 T cell specific response in cervical cancer patients even with advanced disease using autologous DC primed with tumour lysate. However the optimum strategy may require IL 12 producing mature DC which is being currently investigated.

1023 ORAL

Survival after relapse in patients with endometrial cancer: results from a randomized trial

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Purpose: To determine the rates of local control and survival after relapse in patients with stage I endometrial cancer treated in the multicenter randomized PORTEC-trial with surgery and pelvic radiotherapy (RT) or surgery alone.

Materials & Methods: The PORTEC trial included patients with FIGO stages IC grade 1 or 2 and IB grade 2 or 3 endometrial cancer. In all cases an abdominal hysterectomy was performed, without lymphadenectomy. After surgery, patients were randomized to receive pelvic RT (46 Gy), or no further treatment. 715 patients were randomized.

Results: The analysis was done by intention-to-treat. 714 patients could be evaluated. At a median follow-up duration of 60 months, 5-year actuarial locoregional recurrence rates were 4% in the RT group, and 14% in the control group (p<0.001). The 5-year overall survival rates were 81% (RT group) and 85% (control group, p=0.31). The majority of the locoregional relapses were located in the vagina, mostly in the vaginal vault. At 5 years, 7 vaginal and 5 pelvic recurrences were recorded in the RT group, and 32 vaginal and 13 pelvic recurrences in the control group. Five-year rates of vaginal, pelvic and distant failures as first failure were 2%, 1.4% and 6.3% in the RT group, and 9%, 4% and 3.2% in the control group. Five-year rates of distant metastases were 8.4% in the RT group and 6.1% in the control group. Most patients with an isolated locoregional relapse could be treated with curative intent, usually with external RT and brachytherapy, and/or surgery in some. A complete remission was obtained in 85%. At the time of the analysis, only 8 out of the 52 patients with a locoregional relapse had died due to the relapse, while 39 of the 48 patients with distant metastases had died from the metastases. Patients with a vaginal recurrence had 2- and 3-year post-relapse survival rates of 79% and 71%, in contrast to 22% and 9% 2- and 3-year survival rates after pelvic relapse and/or distant metastases (p<0.001). The 3-year survival after first relapse was significantly better for patients in the control group (51%) than for patients in the RT group (19%, p=0.02).

Conclusion: Pelvic RT in stage I endometrial cancer reduces the risk of locoregional relapse, but without a survival benefit. Treatment for vaginal relapse is often successful in patients not previously irradiated, leading to a significantly better post-relapse survival for patients in the control group. Updated results will be presented.

Cell biology/Genetics II

1024 ORAL

A microcell hybrid based approach identifies human chromosome 3p genes that are silenced following tumor growth, at four distinct regions

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Purpose: We had previously shown (Imreh et al., 1994; 1997) that inoculation of human chr3/A9 mouse fibrosarcoma microcell hybrids (MCHs) into SCID mice was followed by the regular elimination of some 3p regions. Using this approach, referred to as the elimination test (Et), we have defined a