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POSTER

**Results of chemotherapy with etoposide, methotrexate, cyclophosphamide, actinomycin D and cisplatin (EMCAP) chemotherapy for high risk gestational trophoblastic neoplasia, a retrospective study by the Dutch Working Party on Trophoblastic Tumors**

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**Background:** In 1982 a schedule with etoposide (100 mg/m<sup>2</sup> day 1-5), methotrexate (300 mg/m<sup>2</sup> day 1), cyclophosphamide (600 mg/m<sup>2</sup> day 1), actinomycin D (0.6 mg/m<sup>2</sup> day 2), cisplatin (60 mg/m<sup>2</sup> day 4 (EMCAP), q 21 days, was developed for the treatment of high risk Gestational Trophoblastic Neoplasia (GTN) in the Netherlands.

**Methods:** To assess the efficiency and toxicity of this combination chemotherapy, a retrospective study was conducted on high risk GTN patients registered between 1982 and 2009 by the Dutch Working Party on Trophoblastic Tumors (DWTT).

**Results:** Fifty-seven patients received 236 treatment cycles. Sixteen primarily high risk patients (28.1%, group 1) were treated primarily with EMCAP, 41 (71.9%, group 2) were treated secondarily after failure of single agent or combination chemotherapy. Adjuvant surgery was used in 5 patients. The median observation time was 35 months (range 3 to 284 months). The overall 3-year survival rate was 94.7%; 87.5% for group 1, and 97.6% for group 2. Eight patients progressed after chemotherapy, of whom 2 died, 3 patients progressed during chemotherapy (1 died), and 2 patients, despite a sufficiently decreasing serum hCG + hCGβ, chose surgery instead of continuing EMCAP. The median time period between the first treatment cycle of EMCAP and progression was 7 months. Seven patients underwent salvage surgery, 1 underwent high dose chemotherapy with bone marrow transplantation, and 5 underwent both chemotherapy and surgery after EMCAP treatment. In 236 treatment cycles dose reduction occurred in 23 cycles, treatment delay in 28 cycles, and both occurred in 7 cycles. The most common reason for dose reduction and treatment delay was leucocytopenia in 53.3% (16/30) and 54.3% (19/35), respectively. Nausea grade 3 or 4 was reported in 12 of 57 patients. Neuropathy more than grade 2 was not reported. Regarding long term toxicity, 3 patients developed a secondary Acute Myeloid Leukemia (AML), of which 2 were cured and 1 died.

**Conclusion:** EMCAP combination chemotherapy is considered an effective treatment for high-risk GTN. However, it should be noted that there is a relatively high risk of developing secondary malignancy which is most likely brought about by etoposide.

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**How relevant is the CA-125 monitoring for patients with ovarian cancer in the follow-up? - Results from a multicenter survey in 1060 patients with ovarian cancer**

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**Background:** The potential benefit of CA-125 controls in the absence clinical symptoms in the follow-up periode are still unclear, CA-125 monitoring is frequently applied in the clinical routine of ovarian cancer patients (OC). To evaluate the expectations and preferences of patients with OC we initiated the present multi-institutional survey.

**Methods:** A semi-structured consisting 15 questions was developed in a pilot-study of 20 patients. After this validation all gynecological departments and gynecological-oncological practices were invited to participate in this trial using an anonymous print version of the questionnaire.

**Results:** Between 12/2006 and 12/2007 a total of 1060 patients were enrolled. The median age of the patients was 58 years (range, 16-87). 60% of the patients had primary ovarian cancer, 40% had relapsed ovarian cancer. Patients were informed about the procedures and goals of follow up care predominantly after primary surgery (62.5%), 15.7% after last cycle of first-line chemotherapy, 7.7% were informed only at the first follow-up visit in the after care unit and 9.2% stated that they had never received any information about their cancer care management. The visits were mostly performed by gynaecologists in a gynaecological practice (56.9%) and in hospitals (49.5%). In more than 90% of OC CA 125 measurements were done. These were the procedure with highest anxiety but also the most important procedure in the patient's opinion.

**Discussion and Conclusions:** The present study underlines the high clinical need for a detailed discussion between patients and their physicians about the primary goals of the cancer care procedures to avoid misunderstanding and unsatisfaction.

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**Serous papillary peritoneal carcinoma: unknown primary tumour, ovarian cancer counterpart or a distinct entity? A systematic review**

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**Introduction:** Serous peritoneal papillary carcinoma (SPPC), though managed according to ovarian cancer therapeutic principles, has been variably considered as an ovarian cancer counterpart, a peritoneal malignancy with distinct characteristics or a cancer of unknown primary (CUP).

**Patients and Methods:** We systematically reviewed all publications studying molecular pathophysiology, clinical presentation, management and outcome of at least ten patients with SPPC from 1980 to 2008 in anglophone medical journals and critically analyzed the data.

**Results:** Molecular profiling of CUP was performed in eight papers reporting on 211 patients with stage III/IV SPPC by means of immuno-histochemistry or PCR-based assays. Twenty-five clinical series, mostly retrospective, reported management and outcome of 579 patients with SPPC, in several cases matched to advanced ovarian cancer controls. Though we did not identify statistically significant differences in molecular biology, clinical presentation, management and outcome of SPPC and ovarian cancer cases, some subtle differences emerged: Patterns of loss of heterozygosity at several chromosomal loci differed from those seen in ovarian cancer, while the overexpression of the HER2 oncogene was encountered more often. Serous peritoneal tumours affected older patients and were more frequently multifocal or exhibited virulent clonal expansion in metastatic sites. Diffuse micronodular spread formed a high total load of malignancy in omental, peritoneal surfaces, difficult to debulk optimally. Despite effective chemotherapeutic cytoreduction and occasional long-term remissions, SPPC patients survived 2-6 months less than ovarian cancer patients.

**Conclusions:** Patients with SPPC should not be classified in the poor-risk CUP category, in view of the therapeutic and prognostic differences. Still, the assimilation of the SPPC entity by ovarian cancer hindered further research into its genotypic and phenotypic characteristics that may differ from ovarian cancer. Subgroup analyses of large ovarian cancer trials may shed light in this issue.

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**Multicenter survey of 323 gynaecological departments in Germany: current standards in the clinical management of borderline tumours of the ovary**

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**Background:** The aim of this survey was to analyze the current standards in diagnostic, surgery, chemotherapy and aftercare management of patients with borderline tumors of the ovary (BOT) in German gynecological departments.

**Methods:** Using a questionnaire comprising different clinical aspects of the treatment of BOT 323 gynecological departments were anonymously

interviewed. All data were statistically analyzed, where some questions enabled multiple statements.

**Results:** The overall response rate was 29.0%. The most gynecological departments were on secondary care (71.8%), tertiary care (23.2%) or university hospital (5.0%) level. The most clinicians performed not more than 5 BOT operations (89.2%) per year. 93.2% of the gynecological departments used additional preoperative diagnostic procedures to the classical bimanual examination and vaginal ultrasound in a case of unclear ovarian tumor: CA-125 or CEA detection (95%), CT-scan (76%), Doppler ultrasound (66%), MRI (36%) or PET-CT scan (1.7%) techniques. In the most university departments (87%), tertiary care (80%), secondary care (68%) and general practitioners' hospitals (64%) a regular fresh frozen section was performed. The surgical treatment of BOT based mostly on laparotomy (48%) and laparoscopy (15%), whereas 19% of the clinics used diagnostic laparoscopy, followed by laparotomy for completion in a second intervention or switch from laparoscopy to laparotomy in the primary surgical session (18%). In younger women clinicians performed much seldom unilateral salpingo-oophorectomy (92%) and only in 53% biopsies of the contra lateral ovary. Generally biopsies of the contra lateral ovary were performed in 4% to 53% of the patients. Chemotherapy was mostly favored in "high-risk" patients with postoperative tumor residual, micro invasion or invasive implants.

**Conclusions:** Thus high grade of insecurity in diagnostic and therapy of BOT exists in some gynecological departments and underlines the need of more educational and study activities.

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#### Ovarian germ cell tumours: cancer institute (wia), Chennai, experience over 10 years including quality of life data

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**Background:** Ovarian germ cell tumors are highly curable malignancies which affect young women of childbearing potential. They usually present in early stages and fertility-preserving surgery followed by adjuvant chemotherapy is considered standard of care. The quality of life issues of long-term survivorship are of great importance among the young survivors. The aims of our study were to 1) study the clinical profile and outcome of Malignant Ovarian germ Cell tumors (MOGCT), and 2) analyze the quality of life among long-term survivors.

**Materials and Methods:** Patients diagnosed as MOGCT during the period 1995–2005 was retrospectively analyzed for Clinico-pathological profile, outcome and in 50 Survivors of MOGCT Quality of analysis was conducted using two questionnaires, EORTC QLQ-C30 and EORTC OV 28.

**Results:** Of the 1125 case of Ovarian cancers diagnosed during the study period MOGCT constituted 103 patients (9.1%). The median age at diagnosis was 18 years (7–45). 14.5% of patients were in the premenarcheal age. Mean duration of symptoms were 2.2 months (1–8). Acute abdomen due to torsion was seen in (7.7%). Fertility preservation surgery was performed in 82 patients (79.6%). BEP was administered in 96.2% of the patients who received chemotherapy. Stage distribution for Stage I–IV was 43.8%, 9%, 33.7% and 13.5% respectively. Dysgerminoma was the commonest subtype and constituted 41%. The 5 years and 10 years disease free survival was 80.5% and 78.4% respectively and 5 and 10 years overall survival was 85%. 91.6% patients regained their menstrual cycles in the fertility preserved group. 11 successful deliveries were noted with 50% of the fertility preserved group remaining unmarried. Total QOL score was not statistically significant among fertility preserved and unpreserved group. Both had high scores with a mean of 90.47 and 77.65 respectively. Physical functioning, role functioning and emotional functioning were significantly better in the fertility preserved group. Hormonal symptoms were significantly more in advance stage survivors and the ovaries removed group. There were no statistically significant different scores among early and advance stage survivors.

**Conclusions:** Conservative surgery and BEP based chemotherapy can cure majority of patients with MOGCT. The general psychological health and total quality of life is quite good for survivors of ovarian germ cell tumor survivors.

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#### The new approach in early diagnosis and treatment planning of cervical cancer

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**Background:** According to statistical data in Russian Federation there is trend for increasing of incidence of invasive cervical cancer in reproductive age women. It can be explained by stopping of total cytological screening and short time of preinvasive to invasive carcinoma transformation in this age category. It is necessary to revise traditional approach in diagnosis and treatment disease with taking into account the data about role of human papillomavirus (HPV) oncogenic type for malignant progression.

**Materials and Methods:** There are retrospective and prospective clinical and morphological data of 875 patients with preinvasive and invasive cervical carcinoma. We used virusological methods, statistical methods and meta-analyses of literature data.

**Results:** It was found that squamous cell carcinoma prevails in reproductive age women. Endocervical adenocarcinoma often was found in postmenopausal women. Metastasis in lymphatic nodes often occurred in reproductive age women. In this age there were often occurred 16, 18 ? 56 HPV type and complex HPV infection. Episomal form of HPV 16, 18 DNA was found in CIN I and CIN II cases. Integrated form of HPV DNA was found in CIN III ? Ca in situ cases (HPV 16: 50%, HPV 18: 90%). Persistence of HPV 16 and 18, integrated form of HPV DNA and low viral load correlated with malignant progression and could be used as indication for loop excision or conization of cervix uteri in CIN I-II cases. Lymph-vascular space involvement and positive margins were poor factors of prognosis. HPV type and viral load correlated with lymph-vascular space involvement and morphological type and could predispose to metastasis in regional lymphatic nodes. HPV 16 type was independent prognosis factor and could evidence about poor prognosis. Low viral load or integrated form HPV DNA indicated the malignant progression and poor prognosis at I-IIa staging. These factors while choosing of more radical volume for fertility preserving treatment in patients with Ia1 stage of cervical cancer are indication for abdominal radical trachelectomy with lymphadenectomy. If integrated form of HPV 16, 18 types DNA had been found after treatment it could indicate the high risk of disease recurrence.

**Conclusion:** Application of modern high technological methods permits to show up patients with poor prognosis opportunely and plane the volume of treatment more precisely, which is important for reproductive age women.

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#### Intraperitoneal cancer cell spreading following diagnostic hysteroscopy for endometrial cancer - a systematic review and meta-analysis

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**Background:** Hysteroscopy is a diagnostic procedure with a high accuracy for the detection of endometrial cancer. Nonetheless, several observational studies underscored a risk associated with the increase in intrauterine pressure during the procedure, suggesting that hysteroscopy may result in seeding of cancer cells into the peritoneal cavity through the fallopian tubes, and eventually upgrade the stage of the disease when limited inside the uterus. In order to clarify whether hysteroscopy is associated with a risk of intraperitoneal endometrial cancer cell dissemination we performed a meta-analysis of available trials.

**Materials and Methods:** We searched the Cochrane Central Trials Registry and PubMed without year and language restriction through March 2009. We considered eligible all retrospective, prospective and randomized controlled studies in which patients were allocated to hysteroscopy (alone or following other diagnostic procedure e.g. D&C, biopsy) versus other diagnostic procedure than hysteroscopy or no procedure. In all eligible trials patients had histologically proven endometrial cancer and underwent hysterectomy with peritoneal washings in order to confirm the presence of endometrial cancer cells within peritoneal fluid. The main outcomes were the rate of positive peritoneal cytology and the rate of disease upstaging.

**Results:** Overall 9 trials were considered eligible; 1 randomized trial, 1 prospective and 7 retrospective cohorts. Five hundred and ninety patients were allocated to hysteroscopy and 1125 to no hysteroscopy. The rate of malignant cytology was significantly higher in the hysteroscopy group OR 1.77, 95% CI 1.13–2.77 p=0.013. The positive peritoneal cytology incidence was also higher when normal saline was used as distention