

chemotherapy. E. g. 70% of the children with acute lymphoblastic leukemia can be cured by conventional chemotherapy. This is also true, but to a lower degree, for acute myelogenous leukemia. The conventional results of the treatment of M. Hodgkin and NHL are even better than those in ALL. For most solid tumors good results can also be obtained with the combination of surgery, chemotherapy, and radiotherapy. This is why the indication for autologous BMT is limited to metastatic tumors. High-dose chemotherapy (HDC) with stem cell rescue can cure some of the children. In general, one can say that tumors which are not responding to conventional doses of chemotherapy do not benefit of HDC. BMT is an important factor of therapy in pediatric oncology. However, it is needed only in a limited number of children with cancer. Recently the use of parents as haploidentical donors has appeared to be a possibility even for those children who lack an identical sibling or an unrelated matched donor.

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### The role of prognostic factors in the management of epithelial ovarian carcinoma

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Prognostic factors predict outcome in many ways including survival, response to therapy, etc. Their role is continuously increasing in individualizing treatment, and thereby avoiding under- and over-treatment. Staging is actually the anatomical extension of the tumor and per se is a prognostic factor. The major concerns in the management of epithelial ovarian carcinoma include: 1. the need for adjuvant chemotherapy in early-stage ovarian carcinoma, 2. the place of lymphadenectomy, 3. the role of neoadjuvant chemotherapy in advanced-stage ovarian carcinoma, 4. surgical radicality, 5. selection of drugs, and 6. novel treatment modalities. Using molecular biology techniques in testing the underlying genetic mutations in the tumors of individual patients, i.e. applied genetic testing, we have been able to identify more and more new independent prognostic indicators in terms of outcome, therapeutic effectiveness, etc. In most instances, the role of these novel prognostic factors in the management of epithelial ovarian carcinoma has yet to be determined. Some of them, however, appear to have a place. Their possible therapeutic implications will be discussed.

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### Surgical dilemma in the management of epithelial ovarian carcinoma

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Surgical dilemmas in the management of epithelial ovarian cancer involve: 1) role of conservative treatment on the uterus and contralateral ovary in young women with very early stages; 2) role of lymphadenectomy as part of complete surgical debulking in advanced stages; 3) role, advantages and limits of primary surgery in grossly bulky late stage III and IV stages; 4) role of surgical reexploration in patients optimally debulked after completion of first line chemotherapy; 5) role of surgery in converting a partial response to chemotherapy in a complete response; 6) role of second surgical effort. Clinical trials are now on-going trying to clarify these problems. Unfortunately surgical clinical trials often suffer of difficulties related to different percentage of patients optimally debulked in any single Institutions, different attitude, towards maximal surgical effort in primary surgery, of the surgeons different opinions concerning second surgery in the general plan of treatment in patients with advanced stages.

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### The role of neoadjuvant chemotherapy in advanced ovarian carcinoma

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Recently, neoadjuvant chemotherapy (NCT) has been reported in patients with advanced ovarian carcinoma (8 studies; total n = 438). These studies suggest that the same survival with a lower operative morbidity can be obtained with NCT compared with primary debulking surgery (PDS).

In our own study on 338 patients with Stage III or IV ovarian carcinoma the actuarial crude survival was higher in the period in which we administered NCT in 44% of the patients than in an earlier period in which PDS was performed in all patients (3 year crude survival 37% and 26%, respectively;

p = 0.05). Selection of NCT or PDS was mainly based on the possibility to debulk the patient primarily to no residual tumor (no residual tumor in 90% of the group with PDS). The EORTC recently started a prospective randomised study in which patients with ovarian cancer Stage IIIc or IV are randomised between PDS followed by 6 courses of platin-taxoid based chemotherapy (Arm A) versus NCT (same as Arm A) with interval debulking surgery (IDS) after 3 courses. The results of this randomised study must be awaited before the role of NCT followed by IDS in advanced ovarian cancer can be established.

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### Current trends in the management of epithelial ovarian cancer

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The GOG conducted three prospective randomized trials of adjuvant therapy in patients with localized ovarian cancer (OC). In patients with stages Ia and Ib (G1-G2) OC there were no significant differences between the patients given no CT and those treated with melphalan. In stage I tumors (G3) or stage II treatment with either melphalan or a single intraperitoneal dose of 32P was similar with respect to 5-year disease-free survival and overall survival. In the third trial stage I and II patients received 3 cycles of CP compared with intraperitoneal 32P. The results of this trial will be presented shortly and it seems that CP is more effective than 32P. The EORTC is now closing a randomized trial for stages I and IIa OC patients comparing the adjuvant CT, with a regimen containing cisplatin or carboplatin, versus no adjuvant treatment. In advanced ovarian cancer (ADVOCA) cisplatin-based combination chemotherapy regimens have produced response rates of 60% to 80% and a median overall survival of approximately 20 months. Before taxol was used in the treatment of patients with ADVOCA, cisplatin was considered the best drug. Most prospective studies comparing a "standard" dose of cisplatin "versus" a dose intensification were not able to show any differences concerning survival in favor of cisplatin dose intensification. Clinical comparisons of carboplatin and cisplatin as single agents or in combination have yielded comparable results. The GOG has conducted a randomized clinical trial comparing paclitaxel and cisplatin (TP) with CP in suboptimally debulked stages III and IV patients. There was a statistically significant improvement in the clinical response rate in the TP arm and median survival was also significantly better in the TP arm. A confirmatory trial has been run in Europe and Canada and the data are similar to GOG trial. TP is now considered to be the preferred combination regimen. There is no consensus about the treatment of patients with OC in PCR after second-look surgery. The main options are: wait-and-see; maintenance therapy using three to six more cycles of the same induction CT; whole abdominal radiation therapy; high-dose CT followed by autologous bone marrow transplant; intraperitoneal CT. None of these modalities has proved a clear and definitive advantage in terms of disease free survival or survival.

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Abstract not received.

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### New approaches in the management of ovarian cancer

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Although the tests of treatment with conventional chemotherapy are gradually improving, the majority of women with epithelial ovarian cancer still die of the disease. A range of new approaches to treatment are therefore under active investigation. These are largely based on a rapidly expanding body of information on the molecular and genetic make-up of the ovarian cancer cell itself, its interaction with surrounding stroma, and the basis for resistance to chemotherapy. The approaches thus include:

- agents designed to circumvent drug resistance including novel cytotoxics.
- signal transduction inhibitors, and new forms of hormone therapy
- angiogenesis and matrix metalloproteinase inhibitors
- immunotherapy, immunotoxins and radioconjugates
- new forms of (intraperitoneal) gene therapy.

All of these approaches will need to be used in conjunction with conventional chemotherapy, which itself will be augmented by the addition of newer agents, e.g. topotecan, gemcitabine, preferably in imaginative (sequential) schedules.