the chemotherapy arm 90% completed three courses of chemotherapy. 30% showed complete or partial remission; 50% showed stable disease; 20% showed progression. Median dose intensity was 98% (85%–106%) (In both arms radical margins were obtained in 90%. Preoperative chemotherapy did not increase surgical or radiotherapeutic morbidity.

137 eligible patients could be analyzed, at a median follow up of 4.5 years, for overall and disease-free survival.

No significant statistical difference was found for either overall survival or disease-free survival between the two arms. (p = 0.35 and 0.37 resp.)

Conclusion: The chemotherapy-regimen was feasible; the accrual was too slow. No long term benefit was shown with this regimen. Adjuvant chemotherapy in soft tissue sarcoma should only be studied in trials.

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Achievements in the treatment of acute myelogenous leukemia (AML)

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The induction and post-remission treatment in AML has been progressively intensified, this intensification being made tolerable by progresses in supportive care. Thus, the complete remission (CR) rate has increased from 60 to 70–80% in patients aged less than 60 yrs, most CR being achieved after a single induction course. The 5 yrs disease-free survival (DFS) is now between 30 and 50%, according to prognostic factors and post-CR treatment protocol. The overall survival (OS) is around 30%, all cooperative groups having the same level of achievement. The main treatment options, intensive chemotherapy, autologous stem cell transplantation and allogeneic BMT are currently assessed by EORTC and other groups.

In the elderly, the prognosis is far worse, due to host and tumor-related factors, with a 5 yrs OS not higher than 5–10%. Specific clinical trials are designed by the EORTC group, exploring the value of more intensive treatments in the elderly along with hematopoietic growth factors, and of maintenance treatment.

The main objectives in the future will be to overcome multiple drug resistance, to target cytotoxic drugs, to reduce morbidity of transplantation, and to control the leukemic cell regrowth through the use of various cytokines.

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Genetic and cytogenetic alterations in ovarian cancer

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Purpose: Molecular genetic alterations on ovarian tumorigenesis have been identified recently. Approximately 90% of ovarian cancer are sporadic forms, 10% are estimated to be carriers of an ovarian/breast cancer susceptibility gene; these women are found primarily in families characterized by multiple cases of the early onset of ovarian cancer syndromes. Cancer susceptibility genes such as BRCA1 and BRCA2 have been recently identified and cloned.

Methods: Genetic and cytogenetic evaluation of ovarian cancer has utilized techniques including *in situ* hybridization, mutation and sequencing studies.

Results: Cytogenetic studies in sporadic ovarian cancer demonstrate in approximately 50% of cases chromosome abnormalities, 40% of those reveal clonal and 10% nonclonal changes. Disruption of chromosomes as numerical or structural changes involve most frequently chromosome X, 1, 2, 6, 7, 11, 12 and 19. However, detailed cytogenetic karyotype information is limited. Competitive *in-situ*-hybridization (comparative genome analysis [CGH]) demonstrates DNA gains of chromosomes 8q, 3 p, 20 q, 1 p, 19 p, 1 q, 12 p, 6 p, 2 q and losses on 18 q, 4, 13 q, 16 q as an indication for consistent chromosomal abnormalities and genetic instability. Germ line mutations of BRCA1 (80%) and BRCA2 (15%) are found in families that display heritable ovarian cancer syndroms. Over 111 unique BRCA1 mutations distributed throughout the gene have been described. DNA chip-based assay are now developed to scan large genes (as BRCA).

Conclusion: The general distribution of new technologies (DNA chip) for accurate and cost-efficient detection of genetic alterations is wanted. Further research is required for families with hereditary ovarian cancer syndrom to evaluate efficacy of counselling and prophylactic efforts. In sporadic ovarian cancer detection of gene mutations with phenotype modification (i.e. drug resistance) can be used to develop new therapeutic strategies.

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Primary cytoreductive surgery in advanced ovarian carcinoma: Is it necessary in all patients?

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"Optimal" cytoreductive surgery has been defined in different ways. We suggest that optimal cytoreductive surgery should be defined as no or less than 1 g of total residual tumor load after primary surgery. In some subgroups of patients the survival does not improve with optimal surgery. For instance, patients with Stage IV disease or a total metastatic tumor load of more than 1000 g prior to cytoreductive surgery have a poor survival despite cytoreduction. Patients who can not be optimally debulked primarily should be very carefully selected. We compared retrospectively 96 patients with Stage III or IV disease treated according to the above mentioned principles with 112 patients from the former time period. In the latter group 89% of the patients were debulked to less 1.5 cm largest residual tumor mass. No significant survival differences were observed between the 2 groups. The improvement in survival after interval debulking surgery reported in a prospective randomized EORTC trial is encouraging (NEJM, 1995, 332: 629). Based on the total metastatic tumor load, the presence of Stage IV disease or of uncountable peritoneal metastases, etc., it may be possible to select patients for whom upfront chemotherapy followed by interval debulking surgery is an option. This concept needs to be tested in a prospective randomized study.

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T cell retargeting for local and systemic control of disease

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Purpose: Bispecific antibodies (bsmAbs) with specificity for a tumor target antigen on one arm and a lympho/monocyte activation molecule on the other represent new reagents able to target cytotoxic immune cells to tumors and offer a promising means of killing minimal residual disease (mrd) without adverse reactions. This type of approach is being used in numerous phase I/II trials.

Methods: Ovarian carcinoma patients with: a) intraperitoneal (ip) disease after conventional treatments, b) mrd after I line treatment and previous history of retroperitoneal lymph node involvement, c) evident tumor infiltration in lymph nodes, entered studies aimed to evaluate: a) the efficacy of ip treatment, b) the feasibility of systemic treatment and c) the localization of bsmAb-coated radiolabeled lymphocytes.

Results: Treatment with autologous activated lymphocytes retargeted with the bsmAb OC/TR resulted in an overall ip response rate of 27% with only mild and transient toxicity. The activity was mainly local and a persistent HAMA response precluded repeated treatments. The combination of iv and ip administration of OC/TR retargeted lymphocytes, which might possibly lead to an extraperitoneal cure, was feasible and clinical follow up of treated patients is ongoing. A method for radiolabeling lymphocytes was developed and localization studies are now in progress.

Conclusions and Future Directions: We expect further improvement of the retargeted-lymphocyte technology through the selection of reagents from human antibody phage libraries which will enable to repeat courses of treatment.

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Ovarian cancer – Are we making progress?

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Histology-specific long-term trends in the incidence of ovarian cancer and borderline tumours in Norway were examined, based on data from the population-based Cancer Registry of Norway. A total of 14,352 cases of ovarian cancer were diagnosed between 1954 and 1993, of which 94% of the histologically verified ovarian cancer was epithelial tumours. The age-adjusted incidence rate rose from 10 per 100 000 persons-year in 1954–58 to a peak of 14 per 100 000 person-year in 1984–88. In women older than 50 years, there was an increasing trend in incidence rates during the entire study period From the cohort perspective, the largest increase