1231 POSTER

Intravenous (IV) nedaplatin and intra-arterial (IA) cisplatin with transcatheter arterial embolization (TAE) for patients with locally advanced uterine cervical cancer

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Purpose: Nedaplatin is a platinum analogue with less renal toxicity and higher efficacy for cervical cancer than cisplatin. And IA cisplatin is more effective than IV cisplatin. In order to improve the prognosis of uterine cervical cancer, we studied combination chemotherapy of IV nedaplatin and IA cisplatin with TAE.

Method: Inclusion criteria were as follows: stages IB2-IV, 16-75 years of age, PS between 0 and 2, a Ccr > 40 ml/min, adequate bone marrow, adequate renal and hepatic function. Nedaplatin (30-70mg/m2) was administered intravenously on day 1, and cisplatin (70mg/m2) was administered IA via both uterine arteries on day 3 using the Seldinger method. This was then followed by TAE. This course of treatment was repeated every 3 weeks for 2 - 3 cycles. Written informed consent was obtained from all patients.

Results: A total of 32 patients were treated; age 29-72 (median: 55), stage 1B2: 7, 2: 11, 3: 8, 4A: 6 pts, SCC: 27, adeno and adeno-sq.: 5 pts.. The response to therapy was defined by MRI as follows: PR in 59% (19/32) and CR in 34% (11/32) of patients, and an overall response rate of 94% (30/32). Myelosuppression was manageable. Grade 2 neuro-toxicity was not observed in any patient. Median follow up period was 32 months (6-53), and overall survival of 1 year: 84%, and 2 year: 77%.

Conclusion: The combination chemotherapy of this regimen showed high response rate, but its influence on long term survival remains to be determined.

1232 POSTER

Complications of primary external radiation therapy followed by radical hysterectomy for bulky stage IB and II cervical cancer

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Purpose: Recent randomized published studies have demonstrated that concomitant chemotherapy and radiotherapy should be the gold standard for treatment of patients with bulky cervical cancer. The role of surgery following such treatment is questioned. The aim of this study was to evaluate complications of primary external pelvic radiotherapy (+/– chemotherapy) followed by radical hysterectomy as treatment for patients with bulky stage Ib and II tumor in order to precise the place and the type of radical surgery in these cases.

Materials: From 1985 to 1998, 233 patients with cervical cancer > 4 cm (stage Ib: n = 67 patients); stage II: n = 166 patients), were treated in two French anti-cancer Center (Institut Gustave Roussy and Centre Jean-Perrin), by primary external radiation therapy (20-35 Gy) +/– utero-vaginal brachytherapy followed by radical hysterectomy (type II: n = 30 or III: n = 203) with pelvic +/– para-aortic lymphadenectomy (in 155 patients).

Results: Ninety major complications were observed in 83 patients (35.6%). The most frequent complications were: lymphocysts (n = 33; 14.1%), urinary fistula (n = 16: 6.8%) and ureteral stenosis (n = 11: 4.7%). The rates and types of complications were not statistically different according to the center of treatment.

Conclusions: According to the high rate of complications observed in this series, place and interest of systematic radical surgery after external radiation therapy (+/– chemotherapy) for patients with bulky stage IB/II cervical cancer should be evaluated in prospective studies.

1233 POSTER

Results of a french survey assessing the role of post-operative high-dose-rate (HDR) brachytherapy (BT) in patients (PTS) with endometrial carcinoma (EC)

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Purpose: To analyze exclusive post-operative HDR BT in terms of technique, indications and results in EC in French centers.

Methods: A questionnaire was sent to the cancer centers, hospitals and private practice with HDR facilities in order to register all the cases of post-operative HDR in EC since their setting. Patient characteristics, BT indications, technical aspects, doses and results were registered.

Results: 655 pts were registered among 13 centers: 10 cancer centers, 2 private practices and 1 university hospital. The mean age was 64.5 years (+/–20.6). Surgery consisted of total hysterectomy in 99.5%, bilateral annexectomy in 93.6%, pelvic node dissection in 69.5%, and para-aortic node dissection in 2%. Stage distribution was IA in 11.3%, IB in 64.3%, IC in 16.2% and IIA in 5.5%, Post-operative BT was delivered with a median dose of 6 Gy per session (1 Gy–7 Gy) in a median number of 4 sessions (1–6). A cylindrical applicator (Nucletron) was used in 64%, while other types of applicators were used in 17% end mould applicator in 16%. The length of treated vagina was upper 1/3 in 16.6%, upper 1/2 in 57%, upper 2/3 in 1.8% and total vagina in 24.4%. Differences were observed according to centers. The dose was prescribed at 0.5 cm from the vaginal surface in 98.2%. With a median follow-up of 33 months, 37 carcinologic events occurred in 27 pts: metastasis: 10, centre-pelvic recurrence: 8, vaginal recurrence: 8, latero-pelvic recur: 4, para-aortic node: 2, unknown: 5. NED survival was 95% at three-years.

A total of 146 complications were registered. Distribution of complication site was: pelvic: 2, rectal: 4, intestinal: 6, bladder: 20 and vaginal: 114. 61% were grade 1, 31% grade 2 and 4 grade 3: 1 urinary and 3 vaginal. Differences were observed according to centers.

Conclusion: Exclusive HDR postoperative BT in 655 pts with limited stage EC evidenced a good local control with n low incidence of complications. Results were similar to those observed with low-dose-rate BT. Differences were observed between centers in terms of technique, treated volume, dose and complication assessment. As large treated volumes were not associated with better prevention of vaginal recurrences, a prophylactic treatment of the upper third of the vagina is recommended.

1234 POSTER

External radiotherapy and high dose rate brachytherapy concomitant to cisplatinum in cervical cancer - preliminary results - phase II study

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Objective: To study feasibility and acute toxicity of cisplatinum (CDDP) chemotherapy concomitant with external beam radiotherapy (RT) and high dose rate brachytherapy (HDR) in patients with cervical cancer.

Material and Methods: From Oct/99 to Sep/00, 22 patients with histological diagnosis of cervical carcinoma were submitted to a therapeutic protocol of radio-chemotherapy as follow: RT (45Gy - 25 fractions) + HDR (6Gy - four insertions - point A - weekly) + complementary boost to involved parametrium (9Gy -5 fractions) and chemotherapy (CDDP 40mg/m2 - weekly) concomitant - d1, d8, d15, d22, d30. Surgery: Total hysterectomy with salpingo-ooforectomy and pelvic lymphadenectomy (Piver II) for patients with surgical conditions after 2 HDR insertions (in this case, the treatment was interrupted after 45 Gy pelvic dose).Twenty two patients were admitted, with a median age of 45 years. The FIGO distribution was: Ib2 (1), IIa (3), IIb (6), IIIb (11) and IVa (1).

Results: Two patients did not complete the protocol program by nefrotoxicity. The median number of chemotherapy cycles was 4. The acute reactions observed were: fever (1 patient), diarrhea (1) and neutropenia (2). Thirteen patients received surgery and seven, definitive radiotherapy. Patients who underwent surgery, 5/12 (41,6%) did not present residual tumor on pathological specimen. In one patient the hysterectomy was not possible by adherences. Post-surgical complications occurred in six patients: abnormal bleeding (1), vaginal fistula (1), ureteral obstruction (2), cistitis and rectitis (2). Of patients treated by radical radiotherapy, two presented ureteral obstruction and one, a severe enteritis, requiring surgical repair.

The total time of radiotherapy was 77 days (11 weeks), three weeks longer than usual.

Conclusions: The protocol program showed high toxicity, mainly with associated surgery. Cisplatinum dose was adequate, but the combination with high dose rate brachytherapy must be avoided. This original program was modified excluding surgery approach and leaving brachytherapy after external beam radiotherapy. CDDP dose was reduced to 30 mg/m2 and administered only during RT.

Paediatric oncology

1235 POSTER

The Italian hospital-based registry of pediatric cancer: 11 years' experience

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Purpose: Since 1989, all centers belonging to AIEOP adopted a common centralized system for registration of all cases in age 0-14 affected by cancer. This system, known as 'Registry Mod.1.01', has allowed to create an hospital-based national registry of pediatric cancer, which leads to monitor activities (such as protocols accrual) and to plan future strategies in research of mechanisms of disease (such as incidence by cancer type and observed-to-expected ratios).

Methods: The physician in charge at each center provide to enter demographic, diagnostic and treatment data for each new eligible patient directly over a secure Internet connection at a centralized electronic data base, set up at CINECA and managed by AIEOP Operation Office in Bologna. The exhaustivity of this survey system has been estimated by comparing, the numbers of observed cases (O), with those expected (E) by applying to Italian population age-specific incidence rates for 1990-1992 produced by the Childhood Cancer Registry of the Piedmont, which covers about 10% of the Italian population.

Results: From January 1st 1989 to December 31st 1999, 11928 cases affected by malignancies, younger than 15 years and resident in Italy, were collected from 51 out of 53 AIEOP centers. M/F ratio resulted of 1.3 and the distribution of cases according to class of age was as follows: 5654 cases 0-4yrs, 3308 cases 5-9yrs and 2966 cases 10-14yrs. The median number of cases observed yearly was 1084, for an O/E ratio of 0.80. The O/E ratio according to disease showed an optimal recruitment for acute leukemias and lymphomas, in contrast with the lower O/E ratio of solid tumors, especially for Central Nervous System (CNS) tumors (0.44). At the same time, nevertheless the overall agreement with AIEOP protocols by centers was more than acceptable with a value of about 70%, only one third of CNS tumors entered a multicenter clinical trial.

Conclusion: These results confirms the leadership of AIEOP, which represent the reference point for Italian Institutions involved in childhood cancer care. On the contrary for CNS tumors, patients' accrual was not all satisfactory and this fact most likely reflects the tendency to treat children with brain cancer in non-pediatric institutions. For the future we plan to extend this system to other Institutions, not exclusively of pediatrics area, to improve the exhaustivity of our registry.

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1236 POSTER

The aetiology of second soft tissue sarcomas occurring after childhood cancer in Britain

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The risk of a second malignant neoplasm (SMN), of which second soft tissue sarcomas (SSTS) are one of the most frequent, is perhaps the greatest challenge to longevity faced by the increasing population of survivors of childhood cancer. We report the first case-control study to investigate the aetiology of SSTS, in an almost entirely population-based series of SSTS diagnosed in Britain since 1940.

Fifty-three cases of SSTS and 179 controls were identified; the controls were matched for gender, primary diagnosis, and age and calendar year of diagnosis. Excluding those with no treatment record, there was a significant excess of SSTS in those patients exposed to both radiotherapy (RT) and chemotherapy (CT) which was 5 times that observed amongst those exposed to neither RT nor CT ($p = 0.02$). The majority of individuals in the study were treated with RT either alone or in combination with CT, and there was a relative risk of 1.6 observed in those exposed to RT compared with those not exposed. Individual record-based radiation dosimetry is in progress to allow investigation of the dose-response relationship between radiation and SSTS risk. A 3-fold increased risk of SSTS was observed with exposure to CT. This effect was due mainly to exposure to alkylating agents, predominantly cyclophosphamide, the risk increasing substantially with increasing cumulative dose ($p = 0.04$). The greatest risk was observed in those exposed to doses of over 12g/m2 and was 5 times the risk amongst those not exposed to alkylating agents. There was no association with exposure to anthracyclines, antibiotics, vinca alkaloids or epipodophyllotoxins, although the numbers exposed were sometimes small.

In this study, the first reported case-control study of SSTS, we demonstrate a significant association with exposure to anti-cancer therapy during childhood. This finding should help clinicians identify the risks associated with particular aspects of treatment, plan modifications to treatment protocols and direct long-term surveillance to those at greatest risk.

1237 POSTER

Follow-up of long-term survivors of childhood cancer; results of a specialized screening program in over 800 patients

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Purpose: To evaluate in longitudinal setting late effects of childhood cancer treatment, and to provide adequate patient care, including secondary preventive measures.

Methods: Long-term survivors (LTS) of childhood cancer are regularly seen at a specialised outpatient clinic. The results of history taking and physical examination are recorded on case-report forms allowing for registration in a database, PLEKsys. Additional investigations are performed according to protocols based on the treatment modalities used in the patients, and results are also registered in PLEKsys. Medical and psychosocial 'serious' problems are registered in the database irrespective of an established relation with previous multimodality cancer treatment.

Results: As off April 2001, over 800 adults and children were seen at the LTS outpatient clinic. An average of 2.5 serious problems per LTS has been registered. As an elaborate update on all patient records is currently in progress, this number is still subject to change. Survivors of lymphoreticular malignancies have less serious problems than survivors of solid tumours. The average number found in, respectively, childhood ALL, Hodgkin's disease, nephroblastoma and brain tumour survivors were: 1,7; 1.9; 3.2 and 4.2.

In 3:3% of the visitors of our outpatient clinic a second benign or malignant tumour has been registered. The percentages per diagnostic group vary between 1.2% in ALL survivors and 17% in patients that survived their retinoblastoma. Even though the last group of retinoblastoma survivors is very small, the numbers almost certainly reflect the combination of genetic susceptibility and treatment related factors.

Conclusions: Following multimodality treatment, the majority of childhood cancer survivors suffer from serious medical and/or psychosocial problems. To evaluate the full impact of childhood cancer treatment on lifelong health status, cohorts of childhood cancer survivors must be followed lifelong. Our outpatient clinic and specialised database allow both for lifelong follow-up and adequate registration of all medical and psychosocial problems. Besides providing comprehensive care for the LTS it can therefore serve as a basis for further research in the field of late treatment effects. Adequate registration is a prerequisite for patient care as well as research. Much energy and effort will be needed in the future to ensure adequate and timely registration.