study form 24 institutes (Kansai Clinical Oncology Group and the Study group of Japan Ministry of Health, Labor and Welfare on Uterine Sarcoma Treatment). One hundred and eighty-six of 191 patients (pts) diagnosed as uterine sarcoma during the last decade were eligible for retrospective analysis.

Results: The subtypes of uterine sarcoma were endometrial stromal sarcoma (ESS) in 27 pts, leiomyosarcomas (LMS) in 71 pts and carcinosarcoma (CS) in 85 pts. Seventy pts were treated by cytoreductive surgery alone and 86 pts were treated by cytoreductive surgery followed by adjuvant chemotherapy. Median progression free survival (mPFS) and median overall survival (mOS) were as follows. The mPFS of ESS, LMS, and CS were 18.4, 11.7 and 10.2 months, respectively (n.s.). The mOS were 23.6, 18.6 and 18.5 months, respectively (n.s.). Patients with LMS who had received adjuvant chemotherapy after surgery showed a trend for a longer PFS than patients who had received only surgical treatment (p=0.123, Wilcoxon test). In 30 types of chemotherapy regimens, CyVADIC (cyclophosphamide, vincristine, doxorubicin and DTIC) therapy was chosen for 28 pts and CAP (cyclophosphamide, doxorubicin and CDDP) therapy was administered for 31 pts. Platinum-based and non-platinum regimens were compared. Non-platinum regimens (39 pts) were superior to platinum based regimens (64 pts) in PFS of LMS patients with stage Ic or more advanced tumor (p=0.001; odds ratio 0.10, 95%CI: 0.015-0.664, Logrank test). New agent of irinotecan (CPT-11) weekly chemotherapy has been conducted as a pilot study in few cases and responders were identified.

Conclusion: Adjuvant chemotherapy of non-platinum regimen for LMS patients might be useful to prevent from recurrence of tumor. Considering to a few feasible results, phase II study of CPT-11 for patients with LMS and CS has been proposed.

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The impact of spontaneous apoptosis on DNA ploidy, proliferative activity, status of human papillomavirus(HPV) and treatment outcome in cervical carcinoma

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Background: To evaluate the effect of apoptosis on ploidy pattern, S-phase fraction (SPF), clinical stage, status of HPV16 & 18 and treatment outcome.

Material and Methods: Seventy five irradiated cervical cancer patients were collected for archival specimens. A minimum follow-up period of 5 years was required for all patients. Flow cytometry & polymerase chain reaction (PCR) were used to identify the status of DNA index, proliferative activity (SPF with a cut-off value of 10) and HPV 16 and 18. In situ quantification of apoptotic cells was performed by in situ Nick end labeling and Klenow DNA Fragmentation Detection Kit. The apoptotic index (AI) was calculated as percentage of apoptotic cells in the counted cells.

The semi-quantitative approach was used to identify the presence of mutant P53. The immunohistochemical staining reaction of formalin-fixed, paraffin-embedded specimen was evaluated by assessments of the overall staining intensity and by the fraction of stained cells in percentage categories.

Results: Mean (± SD) apoptotic index (AI) correlated inversely with DNA index (DI) which are 11.98 ±4.57, 8.77 ±4.49 and 7.43 ±4.96 respectively for DI value of 1, 1-1.5 and > 1.5 (P = 0.002) . A significantly high value of AI corresponded to patients with a low SPF: 15.30 ±2.35 (SPFd10) vs. 7.41 ±3.56 (SPF > 10) (P < 0.001). Status of HPV 16, 18 and mutant P53 beared no significant correlation to mean AI values (P = 0.898, 1.00 and 0.714) . Patients with clinical stage (CS) of d2b yield relatively high mean value of AI than CS of > 2b did (11.08 ±4.66 vs. 8.63 ±5.15, P = 0.038) . Increased spontaneous apoptosis induced increased treatment response, that is, AI value of 11.29 ±4.50 for 48 complete responders while only 8.36 ±5.22 in 28 patients with partial or no response to treatment (P = 0.012)

Conclusions: High proliferative activity (SPF > 10) and aneuploid pattern (DNA > 1) signified a relatively low AI value which beared no significant correlation to status of HPV 16, 18 or mutant P53. Increased spontaneous apoptosis occurred in patients with low clinical stage (f2b) and high treatment response. This, however, did not translate into a change of the status of relapse or 5-year overall survival.

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A phase II second line study of liposomal doxorubicin and carboplatin in patients with recurrent ovarian cancer with a disease free interval equal or greater than 6 months

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Liposomal doxorubicin (Caelyx) trials in relapsed/refractory ovarian cancer patients have shown to induce a clinical benefit with a reduction in several toxicities attributed to anthracyclines. A recent phase I study of the combination of carboplatin and Caelyx conducted by the above investigators has shown that carboplatin at an area under the curve (AUC) 5 and Caelyx 50mg/m2 given every 4 weeks, could be combined with acceptable toxicity. The aim of this phase II second line study is to determine the feasibility, efficacy and toxicity of Caelyx at a dose of 50mg/m2 in combination with carboplatin AUC of 5 in patients with recurrent ovarian cancer with a disease free interval equal or greater than 6 months. All patients were previously treated with platinum and taxane based regimens. Cycles are repeated every 28 days. Eighteen patients (pts) have been entered on this study to date. The median ECOG performance status (PS) is 1 (range 0-1). The median age is 58 years (range 47-75). A total of 66 cycles have been administered, with a median of 4 cycles (range1-7). Ten pts had measurable and 8 pts had evaluable disease. At this stage 10 of the 18 pts are evaluable for response. Two pts withdrew consent and 6 pts are too early for evaluation. Documented responses include 6 complete and 2 partial responses. Two pts had stable disease. Haematological toxicities include anaemia (grade I: 3 pts; grade II: 1 pt), leucopenia (grade I: 3 pts; grade II: 4 pts; grade III: 3 pts), neutropenia (grade I: 2 pts; grade II: 3 pts; grade III: 3 pts; grade IV: 3 pts) and thrombocytopenia (grade I: 1 pt; grade III: 5 pts). Febrile neutropenia or active clinical bleeding has not been documented. Non haematological toxicities include PPE (grade I: 2 pts; grade II: 5 pts; grade III: 3 pts). Nausea and vomiting (grade I- III in 11 pts), stomatitis (grade I- II in 9 pts) and aesthenia (grade I-III: 12 pts). No renal toxicity has been observed. The combination of Caelyx at a dose of 50mg/m2 with carboplatin at an AUC of 5 appears to be a active and safe second line chemotherapy regime for advanced ovarian cancer. The study is still ongoing.

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Combined radiotherapy with irinotecan (CPT-11), interferon a2b (IFNa2b) and amifostine in patients with locally advanced cervical carcinoma (LACC)

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Background: Radiotherapy (RT) constitutes a standard treatment for LACC. CPT-11 is an active chemotherapeutic agent and presents a remarkable radiosensitizing action, while IFNa2b potentiates the antiproliferative action of CPT-11 and has also been shown to be a radiosensitizing agent. Amifostine has been shown to protect against radiotherapy and chemotherapy toxicities in various indications and settings. The purpose of this study is the evaluation of the efficacy and safety of the combination CPT-11, IFNa2b and RT in LACC under the cytoprotective action of Amifostine.

Materials and Methods: Twenty-five patients with LACC stage IIB (17), IIIA (1) and IIIB (7) have been entered in the study. Median age was 57 years (range 36-75 years). The patients received standard fractionated RT (1.8 Gy/fraction, 5 days/week) for 6 weeks with a median dose of 54.7 Gy, CPT-11 30 mg/m2/ week, IV, on day 1 and IFNa2b 3 MU, SC, TIW, prior to RT. All 21 patients completed the scheduled RT. A 20 Gy additional intracavitary treatment with Cs was administered. Amifostine was administered IV at a flat dose of 500 mg prior to each RT fraction.

Results: Until now 21 patients have been evaluated with a median follow-up of 6 months (range 3-21 months). CPT-11 was administered at 90% of the scheduled dose, IFNa2b at 91% and RT at 97.5%. Amifostine was administered as scheduled, except for 2 patients to whom administration was interrupted due to emesis (1) and hypotension (1). Response to treatment was as follows: 11 patients (52.4%) achieved a clinical complete response (cCR), 9 (43%) a clinical partial response (cPR) and one showed stabilization of the disease. No relapses have been observed so far.