934 POSTER

Treatment of recurrent and/or metastatic adeno-carcinoma of the endometrium with cisplatinum and vinorel-bine: A phase II study

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Purpose: Treatment of advanced endometrial adenocarcinoma (AEC) is still largely unsatisfactory. Since the new semisynthetic vinca alkaloid vinorelbine (VNR) has been shown to be very active against several neoplasms, a phase II trial of VNR in combination with cisplatinum (CDDP) has been carried out.

Methods: Thirty pts received CDDP 80 mg/m2 i.v. with a standard hydration protocol on day 1 plus VNR 25 mg/m2 i.v. bolus on day 1 + 8 every 21 days. Median age of enrolled pts was 62 years, while mean PS (KI) was 85. Most pts had previous surgery, 12 had RT, but none had received chemotherapy. After 3 cycles pts were restaged for assessment of objective response according to the WHO criteria.

Results: No patient was excluded from result analysis. Two patients achieved CR (7%) with a median duration of 11+ mos. A PR was seen in 16 cases (53%) with a median duration of 8.2 mos, for an overall response rate of 62%. SD was observed in 5 pts (17%) with a median duration of 5.0+ mos, while PD was seen in the remaining 7 cases.

Conclusion: The combination of CDDP and VNR is quite effective in AEC in terms of objective response rate, with acceptable toxicity.

935 POSTER

The Vienna experience with primary and adjuvant irradiation of sarcoma of the corpus uteri

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The value of radiotherapy in the treatment of sarcoma of the corpus uteri is still not clear. Most reports in literature are based on small patient groups treated over a long time period with changing treatment techniques. Between 1981 and 1993 87 patients (34 with leiomyosarcoma, 13 with endometrial stromal sarcoma, 36 with mixed mullerian tumors and 4 with different histologies) were treated with radiotherapy at the University of Vienna. Age distribution ranged from 32 until 88 years, mean age was 63 years. There were 44 patients in stage I, 10 in stage II, 24 in stage III and 9 in stage IV. 15 patients with advanced tumors received radiotherapy alone, 72 were irradiated postoperatively. 18 patients were treated with brachytherapy alone, 21 with external beam therapy alone and 48 with a combination of both modalities.

After a mean follow-up of 47 months the actuarial 5-year disease specific survival for all patients was 57.7%, with leiomyosarcomas 54.8%, with endometrial stromal sarcomas 80.7% and with mixed mullerian tumors 49.1%. Disease-specific-survival in stage I was 75.9%, in stage II 60.0%, in stage III 41.8% and in stage IV 11.1%. Ten patients showed progressive disease, of the other 77 patients 19 developed a recurrence (local recurrence only with 3 patients, distant metastases only with 9 patients, locoregional and distant recurrences with 7 patients) after 4–65 months (median 12 months). The actuarial recurrence free survival at 5 years was 72.5%, actuarial local control was 83.1%.

In our experience with patients with sarcoma of the corpus uteri treated with a curative intent by surgery and adjuvant radiotherapy excellent local control rates can be achieved. The poor overall and disease specific survival rates are caused by a high proportion of advanced tumors and by frequent development of distant metastases even in earlier stages.

936 POSTER

HDR-brachytherapy is an effective treatment modality in primary treatment of inoperable patients with endometrial carcinoma

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In order to evaluate the efficacy of HDR brachytherapy in the primary treatment of endometrial carcinoma the results of 12 years of experience (1981–1992) covering 280 patients with a mean follow-up of 55 months (median 40 months) will be reported.

Age distribution ranged from 46 until 95 years, mean age was 72 year (median: 73 years). Staging was based on clinical examination and fractionated currettage. There were 116 patients in clinical stage Ia. 199 in stage Ib. 37 in stage II and 8 in stage II. brachytherapy was performed 4 to 5 times (8.5 Gy at 2 cm lateral the tip of the applicator) with a one-channel intracavitary applicator and 1 to 2 times (7 Gy at 7.5 mm lateral from the applicator surface) with an intravaginal cylinder-applicator.

At five years overall-survival, disease specific survival and local control was 52.7%/76.6%/75.4%, in stage Ia 63.9%/84.9%/86.0%, in stage Ib 47 3%/73.3%/68.6%/69.5%, according to histopathologic grade 1:65, 1%/83.5%/77.7%, grade 2: 44.7%/75.4%/75.8% and grade 3: 37.7%/63.9%/74.1%. Eight patients showed progressive disease, 64 patients developed a recurrence after a median of 13 months, 45 of those a local recurrence only, 6 a local recurrence with distant metastases, 6 a lymph node recurrence only and 7 patients distant metastases only. There were 3.2% late side effects at the bladder (2.1%mild, 0.7% moderate, 0.4%severe), 12.1% at the rectum (7.9%mild, 3.8% moderate, 0.4% severe), 5.4% at the small bowel (1.9%mild, 1.4% moderate, 0.7% severe).

At stages Ia, Ib, and II in endometrial carcinoma HDR-brachytherapy is a very effective treatment modality with acceptable local control rates and disease specific survival for those patients who are not fit for surgery. During the time frame of 12 years and on 280 patients the method has proven to have a low risk of acute complications and an acceptable risk of long term side

937 POSTER

RBC flux of the portio uteri & cervical carcinoma – The in vivo use of colposcopy directed laser doppler fluxmetry (LDF)

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Purpose: It is well established that tumor microcirculation play a important role in tumor growth & metastasis but also in cancer radio/chemotherapy or hyperthermia. The objective of this study was to apply LDF, which allows the direct and noninvasive measurement of RBC (Red Blood Cells) flux on patients with normal cervix (NC), carcinoma in situ (CIS) and cancer (CC)

Methods: Measurement of cervix blood flux were performed using the 2-channel LDF-Monitor DRT4 (2 mW, wavelenght 780nm, solid state laser diode) & a Leisegang colposcopy. 13 patients with histological verified squamous cell CC (Staging: 6 FIGO IA2–IB, 5 FIGO IIA–IIB, 3 FIGO IIIA–IIIB, 1 FIGO IVB), 10 with CIS and 15 patients NC were entered in this study.

Results: The mean RBC flux of patients with normal portio uteri was 228.3 AU (AU, arbitrary units, SD 55.1 AU), in CIS 259.5 (SD 87.3 AU) and in CC 280.5 AU (SD 79.4 AU). Analysis of cervix flux motion revealed three main frequency components: low frequency oscillations, high frequency waves and pulsatile waves (PW).

Conclusions: The present study shows differences in colposcopy directed noninvasive RBC flux monitoring of the cytologic/colposcopic normal portio uteri and dysplasia or cervical cancer.

938 POSTER

Results of the combined external- and Ir^{192} HDR-afterloading radiotherapy of cervical and endometrial cancer using an individual middle-block technique

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Between 1991 and 1994 81 patients (pts.) have been treated with inoperable cervical or endometrial cancer stage I–IV by combined tele- and brachytherapy at the Kiel University. The treatment schedule started with 6 brachytherapy (BT) fractions, 7 Gy each, in weekly interval. The external beam radiation (EBRT) was integrated after the third BT fraction conventional fractionated. After completing the BT, at 25 Gy EBRT an individual satellite was constructed according to the cumulated BT reference isodose line. Treatment outcome and complication rates were analysed.

In this retrospective analysis files of pts. with T 1b-4 N 0–3 M 0 cancer, without treatment modifications were considered. We could obtain data for 45 out of 81 cases, 4 pts. were lost for follow-up. 34 out of 41 pts. had squamous cell carcinoma of the cervix with the stages 12 × IIIb, 3 × IIIa, 15 × IIb, 1 × IIa and 3 × IV. 7 out of 41 pts. had adenocarcinoma of the endometrium with stages 2 × Ib, 1 × IIa, 2 × IIb and 2 × IIIb respectively. Follow-up ranged from 1 to 59 month (median 26 month) for cervical carcinoma and from 15 to 56 month (median 40 month) for

endometrial carcinoma. 11 out of 34 pts. with cervical cancer and 4 out of 7 pts. with endometrial cancer died on disease. 4 pts. (2 cervix carcinoma and 2 endometrial carcinoma) died on intercurrent disease. 9 pts (4 × stage II, 3 × stage III and 2 × stage IV disease) with cervical and 2 pts. with endometrial carcinoma (1 × IIb, 1 × IIIb) died of recurrent disease or progress. In the majority of treatments, rectum and bladder doses measured by in vivo-dosimetry were less than 65% of reference isodose.

As the only major side effect one patient with cervix carcinoma stage IIIb developed a recto-vaginal fistula (EORTC, RTOG-score grade 4). No severe late proctitis and cystitis have been observed.

We conclude that the individual blocking of the brachytherapy treatment region in the combined external beam and HDR- brachytherapy for inoperable cervical and endometrial cancer allows an aggressive and tumoradapted individual therapy without an increase of severe side effects.

939 POSTER

Treatment of advanced stages of cervical cancer: Interferon alpha-2α plus Isotretinoin versus radiotherapy

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Methods: Sixty two (62) women of mean age 59.6 ± 11.26 with cervical cancer (stages IIb–IVa) were evaluated (17.33% drope out) after treatment (Group A, n = 46) with Interferon alpha-2α (Roferon-A, Roche) plus Isotretinoin (Roaccutane, Roche) (9 MIU sc 3 times weekly + 60 mg daily for 3 months, respectively) or (Group B, n = 16) radiotherapy (external irradiation 18 MV photon beam 54 Gy + 20 Gy brachytherapy).

Results: Complete response (CR) was observed in 18 (39.13%) patients and partial response (PR) in 10 (21.73%) patients of Group A; also in 10 (62.5%) CR and in 5 (31.25%) PR of Group B was observed but this difference was not statistically significant. It was not observed any difference neither concerning the disease free survival (20.27 ± 6.9 vs 18.90 ± 8.49 months, t = 0.94, p = 0.266) nor the down staging rate (60.86% vs 62.5%, p = 0.50890). Twenty eight (60.86%) patients of Group A were submitted to Werthaim operation and histological remission rate was 26.08% It was not observed any difference between the two groups concerning the recurrence rate (11.11% vs 30%, p = 0.72561) nor the 2 years survival rate (95.65% vs 100%, p = 0.35840). All women were followed-up for a mean 40.5 ± 9.24 months (range 24–57 months). It was not observed any difference in response rate according the Stage of the Disease in Group A (x^2 = 6.79, p = 0.29340) but there were observed statistically significant more CR in Stage IIb in Group B (x^2 = 10.66, p = 0.03058).

Conclusions: The treatment of choice for stages IIb–IVa of cervical cancer should be the radiotherapy while for the stages IIIb–IVa could be also considered the combination of Interferon-alpha-2α plus Isotretinoin. It is interesting to note that the combination of Interferon-alpha-2α plus Isotretinoin could be considered as an alternative treatment at least in younger patients but under close (monthly) surveillance.

940 POSTER

Pretreatment with retinoic acid plus interferon improves tumor tissue oxygenation in cervical cancers

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Purpose: We have evaluated the tumor tissue pO_2 in cervical cancers in patients treated with radiotherapy plus 13-cis-retinoic acid/interferon-α-2a.

Materials and Methods: From June 1995 through April 1996, fourteen irradiated patients with cervical cancers FIGO IIB/III received additional treatment with 13-cis-retinoic acid (cRA) plus interferon-α-2a (IFN-α-2a) starting 14 days prior to radiotherapy (1 mg per kilogram body weight cRA orally daily plus 6 × 10^6 I.U. IFN-α-2a subcutaneously daily). After this induction period, standard radiotherapy was administered (external irradiation with 45Gy in 25 fractions of 1.8Gy plus HDR-brachytherapy with 5 × 7Gy). During radiotherapy, cRA/IFN-α-2a-treatment was continued with 50% of the daily doses. Tumor tissue pO_2-measurements were performed prior to radiotherapy, at 20Gy, and at the end of radiotherapy with an Eppendorf-pO_2-histograph.

Results: The 14 patients with cRA/IFN-α-2a-pretreatment prior to radiotherapy had significant higher median pO_2-values in their tumors at the beginning of irradiation than 14 comparable patients without cytokine-retinoid-pretreatment (median pO_2, 26.2 vs. 16.5 mmHg, p < 0.01). The higher pO_2 was maintained during the course of radiotherapy. Eight patients had pO_2-measurements prior to the cRA/IFN-α-2a-treatment and after the 2-week induction period. In six of them, the pO_2-values increased during the 2-week induction period.

Conclusions: Treatment with cRA/IFN-α-2a improves oxygenation of cervical cancers and requires further investigation.

941 POSTER

Cell cycling related nuclear antigen expression and detection of hyperplasia in routine endometrial biopsy

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Purpose: Endometrial biopsy architecture features extensive architectural changes related to the ovulatory cycle. Complex and simple hyperplasia are usually focal lesions. Recently monoclonal antibodies directed against nuclear antigens expressed in S-phase of cell cycle have become available for use in routine paraffin embedded tissue. We aimed to assess whether detection of hyperplastic lesions was facilitated by detection of proliferation activity.

Method: 143 consecutive unselected, routinely fixed and processed endometrial curettage biopsies from pre-menopausal women with metrorrhagia were studied. 5 micron paraffin sections were subjected to routine immunocytochemistry with commercially available monoclonal antibodies against PCNA (PC10, DAKO, USA) and cDNA defined segment of the Ki-67 antigen (MM1, NovaCastra, UK). In cases with hyperplasia, proliferative activity of hyperplastic glands was compared with that of adjacent normally cycling endometrium and classified for activity of cycling as absent, equal, increased or reduced, by two independent observers.

Results: Of 28 samples insufficient material was received for dependable assay. Of the remaining 115 samples, hyperplasia was detected in 13 samples (complex 7, simple 6). In the lesions, absence of proliferative activity was noted in 4 cases. In 2 of these proliferative activity in both normal and hyperplastic glands was undetectable. In all other (7/9) glands (segments), proliferation was lower than that of adjacent normally proliferating glands.

Conclusions: Hyperplastic lesions in endometrium biopsies of women with metrorrhagia may have consistently lower proliferation rates in comparison to adjacent cycling gland lining. The relationship of this proliferative rate limitation to neoplastic transformation warrants further study.

942 POSTER

148 cases of vulvar cancer – Results of radical surgical treatment

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Purpose: The aim of the present prospective study was to evaluate the value of radical surgery in vulvar carcinoma on the background of morphologic prognostic parameters (LN-involvement, depth of infiltration, tumor size and localization)

Methods: 148 patients with primary squamous cell carcinoma of the vulva were treated at the CRI St. Petersburg. 28 patients had FIGO I lesion, 58 FIGO II, and 62 patients had FIGO III tumor. Radical vulvectomy with inguinal lymphonodectomy was performed in 115 cases, a simple vulvectomy in 33 cases (Nx). 53 patients were nodalpositiv, 62 were nodal negative. In 41 cases the depth of infiltration was 1–5 mm, in 83 cases 6–10 mm, and in 24 cases it was greater than 11 mm.

Results: The stage dependent 5-year-survival rate was 96.4% (FIGO I), 87.7% (FIGO II), 62% (FIGO III), and 79.2% (overall). The 5-year-survival rate of lesions of the labium minus was 94.6%, of the labium majus was 83.1%, of the clitoris – 82.2%. In nodalpositive cases the prognosis was significantly better than in nodalnegative patients (61.6% vs. 86%). The prognosis of patients with a solitary LN metastase was significantly better than in patients with two or more LN metastasis (79.6% vs. 51.6%).

Conclusions: Tumor localization, tumor size, lymphnode status and especially the depth of invasion are the important prognostic factors in vulvar cancer.