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Feasibility of assessment and management of internal organ motion of cervix during radiotherapy by means of megavoltage computed tomography

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Background: Assessment of interfractional organ motion of cervix by megavoltage computed tomography (MVCT) during intensity-modulated radiotherapy (IMRT). Evaluation of impact of cervix soft tissue matching for management of cervix motion.
Methods and Materials: Ten patients with stage IIB-IVA cervical cancer underwent daily MVCT imaging. Interfractional organ motion was evaluated on 150 pre-treatment MVCT images by measuring shifts in their boundaries between the MVCT and planning kV CT scan in the anteroposterior (AP), laterolateral (LL) and superoinferior (SI) directions. Intrafractional patient movement was evaluated on 50 post-treatment MVCT images. Additional cervix soft tissue matching was performed for cervix alignment and impact of image-guidance on CTV-PTV margin was evaluated.
Results: Measured cervical motion (mean $\pm$ SD) was 0.4 ± 10.1 mm in anterior, -3.0 ± 6.9 mm in posterior direction, -3.5 ± 6.9 mm in left and 0.2 ± 4.5 mm in right lateral direction, 2.2 ± 8.0 mm in superior and 0.5 ± 5.0 mm in inferior direction. Compared to the cervix, larger uterine motion was observed. Patient movement during treatment was limited to 1.1 ± 1.25 mm, -0.26 ± 1.56 mm, and 0.22 ± 2.26 mm in AP, LL and SI direction respectively. Cervical alignment asked mean additional manual adaptation of 1.1 ± 9.5 mm in anterior, 0.8 ± 6.5 mm in posterior and 0.9 ± 5.9 mm in lateral direction. Cervix soft tissue matching can allow for a reduction of CTV-PTV margin of 10 mm in anteroposterior direction.
Conclusions: MVCT imaging can be used to study patient setup accuracy and internal cervical motion during IMRT. MVCT image guidance could be a valuable tool for management of cervical motion during IMRT.

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Preliminary results of the ENDORAD trial: RAD001 (everolimus) monotherapy as second-line or third-line treatment of endometrial carcinoma: a phase II trial of GINECO group

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Background: The PTEN mutation was find in 40−60% of endometrial carcinoma, the loss of PTEN will activate the PI3K/AKT/mTOR pathway. RAD001 (everolimus) is an oral inhibitor of mTOR, an intracellular kinase that regulates cell proliferation and angiogenesis. Antitumor activity has been shown in a single-arm Phase-II trial in patients with recurrent endometrial carcinoma (Slomovitz and al, ASCO 2008).
Materials and Methods: A multicenter phase II study was conducted to assess efficacy and safety of mTOR inhibitor (RAD001) in patients (pts) with recurrent endometrial carcinoma refractory to chemotherapy. Inclusion criteria were disease not amenable to cure with surgery and/or radiation, a measurable progressive lesion(s) according to RECIST criteria, pretreatment with at least one line of chemotherapy with platinum salts, ECOG performance status <2, age $\geqslant$18 years. RAD001 was given at the dose of 10 mg/day until progression or intolerance. Primary endpoint was the rate of non progression at 3 months. A two step Simon design was used to include 44 patients. The first 22 included patients were evaluated for non progression at 3 months and for toxicity.
Results: Between 04/08 and 08/08, 22 patients were enrolled in 13 centers. Median age was 64 years (range 53−77). Histological subtypes were endometrioïd (64%), serous (23%) and other (13%). Histological grading was well, intermediate and poorly differentiated for 27%, 37%, and 18% respectively. Metastatic sites were pelvic 18%, peritoneal 27%, lymph nodes 59%, lung 55%, and bone 18%. Pts had received 1 (68%) or 2 (32%) lines of CT before inclusion. Median treatment duration was 72 days (range 4−119). Reported toxicity (G1−4) included fatigue (88%), diarrhea (50%), nausea vomiting (50%), dyspnea (43%), cutaneous rash (40%), anorexia (46%) and haematological (60%). G3−4 toxicities were dyspnea (4%), fatigue (36%), anorexia (13%), nausea (4%), diarrhea (4%), anaemia (11%), pneumonitis (4%), and infection (4%). There was no drug related death. 6 dose reductions have been reported, and treatment had to be temporarily interrupted in 23% of the patients due to toxicity (dyspnea 2, fatigue 1, and thrombopenia 2). There was one partial response and eight stabilized disease reported at 3 months (41%). Only 2/9 pts in the poorly differentiated group were not progressive at 3 months compared to 7/13 pts in other subgroups.
Conclusion: RAD001 shows a clinical benefit in pre-treated patients with recurrent endometrial carcinoma refractory to chemotherapy (first stage). According to the protocol, the study will continue to enroll 44 patients. Due to the results for pts with poorly or non-differentiated tumor, patients with this histological type will be excluded in the next step of the trial. Biological molecular analyses on tumor samples are on-going.

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Feasibility of a modified outpatient regimen of intravenous/ intraperitoneal chemotherapy (IV/IP) in optimally debulked stage III ovarian cancer patients: A GEICO Study

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Background: The high rates of toxicities reported with I.P. chemotherapy appear to be a serious obstacle to widespread implementation of this approach in spite of the results of meta-analysis performed by National Cancer Institute that showed improved survival compared with IV therapy. The purpose of this study was to evaluate the toxicity of a modified outpatient IV/IP regimen in a routine clinical setting.
Methods: 51 women from Institutions of the Spanish Ovarian Cancer Group (GEICO) who were treated with the regimen: Day 1, IV Paclitaxel 175 mg/m^2, over 3h; Day 2, IP Cisplatin 100 mg/m^2 (option for 75 mg/m^2); and Day 8, IP Paclitaxel 60 mg/m^2 every 21 days, between February 2006 and November 2008, were included in this study. The planned treatment was six cycles of IP. CTCAE v 3.0 was used to grade toxicity.
Results: Median age 49 (range 36−75). The median time from surgery to first cycle of IP chemotherapy was 40 days (range 30 to 53). In 34 (67%) patients the IP catheter port was placed at initial surgery. Venous access devices were utilized in 50 (98%) patients. Five patients never initiated IP chemotherapy due to fluid leak from vagina (2), wound infection (1), catheter blockage (1) and patient refusal (1). Cisplatin was initiated at a dose of 75 mg/m^2 in 10 (21.7%) out of 46 women. Dose reduction occurred in 5.6% and 7.8% of the IP Cisplatin and IP Paclitaxel cycles respectively. Twenty-eight women (61%) completed all six IP cycles with 39 (85%) completing four or more IP cycles. Twenty-three patients were switched to IV chemotherapy. All patients received six courses of chemotherapy. Reasons for discontinuing IP therapy per patient were: catheter related 3 (6.5%), gastrointestinal 5 (11%), neuropathy 2 (4.4%), metabolic 1 (2.2%); abdominal pain 1 (2.2%), febrile neutropenia 1 (2.2%), patient refusal 3 (6.5%) and unknown 1 (2.2%). There were 14 cases (30.4%) of grade 3/4 neutropenia and 2 cases (4.3%) of febrile neutropenia. Grade 3/4 non-hematologic toxicities were nausea/vomiting (21.8%), renal/metabolic (11%), fatigue (10.9%), abdominal pain (4.3%) and neuropathy (4.3%). The median follow-up is 12 months [3.17−31.7]. Progression free survival at 12 months is 94% [95% CI: 86.0−100%].
Conclusions: The rate of completed planned treatment (61%) and the favourable toxicity profile reported support (IV/ IP) in routine practice. The optimal IP/IV regimen and duration of therapy have yet to be determined.

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Weekly cisplatin or gemcitabine concomitant with radiation in management of locally advanced carcinoma cervix

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Introduction: Carcinoma cervix is the most common malignancy amongst females in India. With current evidence, concomitant chemoradiation with cisplatin is recommended for treatment of locally advanced carcinoma cervix. The use of non-platinum drugs in concurrent setting has not been well explored and hence two arm study was planned to compare the outcome of concomitant cisplatin or gemcitabine in locally advanced carcinoma cervix.
Material and Methods: Thirty six (36) patients of locally advanced cervical malignancy were evaluated in this study in term of response rate and complications. These patients were divided into two arms, sixteen (16) patients in cisplatin arm and twenty (20) patients in gemcitabine arm. Cisplatin and gemcitabine was given as i.v. infusion at dose of 40 mg/m^2