

7168

POSTER

# Health Related Quality of Life (QOL) Assessment in Stage 1 Seminomatous Germ Cell Tumour Patients Treated With Either Adjuvant Carboplatin Chemotherapy, Adjuvant Radiotherapy or High Intensity Chemotherapy

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**Background:** Treatment options for patients (pts) with stage 1 seminoma post orchidectomy include adjuvant chemotherapy (carboplatin), adjuvant radiotherapy (RT) or observation and, if relapse, high intensity chemotherapy (BEP). Cure rates are similar across the 3 options and hence morbidity and QOL concerns are major factors in determining treatment.

**Methods:** A retrospective questionnaire was sent to stage 1 seminoma patients who completed adjuvant carboplatin treatment (1 or 2 cycles) or adjuvant RT between the years 2003–2010. A surveillance arm and subsequent relapse was replicated via selecting patients receiving high intensity chemotherapy from non-seminomatous tumours (BEP regimen). QOL questionnaires were completed via mail (based on EORTC QLQ-C30). QOL was assessed by comparing symptoms at time of initial adjuvant treatment with current symptoms. Further domains were assessed including time off work, hospital admissions, medical appointments and time to return to 'normal' self.

**Results:** 164 pts were identified over 3 hospitals (2 public, 1 private). Preliminary data shows significantly fewer days off work in the carboplatin and RT arm compared to BEP (13.50 vs 14 vs 150). Pts receiving BEP had the highest amount of hospital admission rates, medical appointments in the first year of treatment and days in bed post-treatment. Pts receiving carboplatin had the least. Pts subjective experience of returning to 'normal' self occurred earlier in the carboplatin arm (4½ months) compared with BEP (11 months) and RT (17 months). QOL was similar in carboplatin and RT arm but RT was associated with higher gastrointestinal complaints at time of treatment (poor appetite, vomiting, diarrhoea). Pts treated with either carboplatin or RT had superior QOL compared to pts treated with BEP, although this returned to normal once treatment was completed. We will present completed data at the meeting.

**Conclusion:** Preliminary analysis reveals a large subjective improvement in returning to 'normal' self in the carboplatin arm. Patients receiving carboplatin also had less days off work, fewer hospital admissions and the least amount of medical appointments in the first year compared to RT and BEP. QOL is similar whether receiving carboplatin or RT, but superior to receiving BEP.

7169

POSTER

# Study of Dynamic Contrast-enhanced Ultrasound (DCE-US) for the Early Evaluation in Patients Included in Phase II Treated With TKI 258 in Renal Cell Carcinoma

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**Background:** To determine the best timing for the early assessment of a functional parameter calculated with DCE-US in order to rapidly distinguish poor responders from good responders among patients treated with TKI 258 in phase II.

**Materials and Methods:** All patients had an examination just before the start of TKI 258 (D-1) and at D7, D14, D 30, D 60 and D 120. Each examination included a bolus injection of 4.8 ml of Sonovue (Bracco®) and raw linear data were recorded over 3 minutes with an Aplio (Toshiba). The raw linear data were analyzed with a mathematical model (patent PCT/IB2006/003742) to evaluate one parameter (the area under the curve (AUC) correlated with the blood volume) characterizing the tumour perfusion curve. Response to treatment was evaluated with RECIST criteria with scanographic evaluations. Complete or partial responses and stabilization were classified as successes and progression as treatment failure.

**Results:** A total of 7 patients were included for the DCE-US evaluation. According to RECIST criteria, the median time to event of 3 poor responders was 4 months and the time to event of the 4 good responders was always more than 12 months. 36 DCE-US examinations were performed. Among good responders: The median variation in the AUC between baseline and D7, 14, 30, 60 and D 120 was -85%, -55%, -77%, -59% and -81% respectively.

**Conclusions:** Our results confirm the interest of DCE-US for monitoring TKI 258 in metastatic RCC. The dramatic decrease in the AUC started from D7 after the beginning of treatment.

7170

POSTER

# Modifiable Obstacles to Early Treatment of Testicular Germ Cell Tumours

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**Background:** Early diagnosis of TGCTs could potentially limit the exposure of patients (pts) to chemotherapy and/or radiotherapy with their long-term complications. We have retrospectively studied the impact of delayed diagnosis of TGCT on the initial stage of the disease and the outcome of first-line therapy.

**Patients and Methods:** We have analysed a cohort of 136 pts. The median age was 33 years (range 17–63 years), 59 pts (43%) had diagnosis of seminoma and 77 (57%) were diagnosed with nonseminomatous TGCT. Pts were subdivided according to TNM stage and current treatment recommendations as follows: disease limited to testis (TNM stage IA and IB; n = 71 [52%]), early metastatic disease (TNM stages IS, IIA and IIB; n = 35 [26%]), and advanced metastatic disease (TNM stages IIC or higher; n = 30 [22%]). Statistical analysis was carried out using nonparametric tests including Kruskal-Wallis ANOVA and the median test.

**Results:** Median time from the onset of symptoms to first urology appointment was 31 days (range 0–398 days). Median time from first urology appointment to diagnostic surgery (orchidectomy in most cases) was only 3.5 days (range 0–177 days) and the median time from surgery to chemotherapy/radiotherapy (when applicable) was 32 days (11–119 days). Delayed first urology appointment was associated with higher stage at presentation (p = 0.001), increased probability of regional lymph node involvement (p = 0.004) and metastatic disease (p = 0.005), but not with T or S stage at presentation. There was a trend to earlier presentation in patients with nonseminomas as compared to seminoma patients. No significant associations were found between delayed presentation and age or education of patients, year of diagnosis, and presenting signs/symptoms. The probability of achieving complete response to first-line treatment was lower in pts presenting later (p = 0.04) but the difference had only trending statistical significance if the analysis was limited to patients in stage II or higher.

**Conclusions:** Delayed presentation of patients with TGCTs is associated with higher stage at diagnosis and reduced probability of achieving complete response to first-line treatment. According to current guidelines, this upward shift of initial clinical stage translates into more aggressive treatment regimens.

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7171

POSTER

# Hypogonadism in Long-term Survivors After Testicular Cancer and Malignant Lymphoma

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**Background:** Chemotherapy and radiotherapy may lead to impaired gonadal function. The aim of this study was to compare gonadal function in male survivors after treatment for testicular cancer (TCSs) and lymphoma (LSs). The hypothesis was that hypogonadism would be more pronounced in TCSs compared to LSs due to inherent biological weakness of the remaining testicle.

**Patients and Methods:** The study included assessment of gonadal hormones (testosterone, SHBG [sex-hormone binding globulin], LH [Luteinizing hormone] and FSH [Follicle stimulating hormone]) and responses to questionnaires in TCSs (n = 1117) and male LSs (n = 259) diagnosed in 1980–1994 (TCSs) and 1980–2002 (LSs). Data collection with assessment of gonadal hormones were performed in 1998 (TCSs) and 2007 (LSs).

The patients' hormone levels were separated into two groups: 1) Normal (Testosterone: 9.0–31.0 nmol/L, LH <10.0 IU/L, FSH <12.0 IU/L), and 2) Hypogonadal (Testosterone <9.0 nmol/L, and/or LH >10.0 IU/L, and/or FSH >12.0 IU/L). Treatment was separated into three groups according to expected gonadotoxicity: low, medium and highly toxic treatments. Logistic regression analyses were used to explore variables associated with hypogonadism in uni- and multivariate analyses with p < 0.05 considered significant. Variables significantly associated with hypogonadism in univariate analyses were included in the multivariate model.

**Results:** Significant differences were observed between LSs and TCSs concerning age at survey and observation time [mean age at survey: LSs: 48.2 versus TCSs: 44.6 years, (p < 0.001), mean observation time: LSs: 15.1 versus TCSs: 11.0 years, (p < 0.001)]. Among LSs 133 (51.4%) and among TCSs 543 (48.6%) were hypogonadal (p = 0.43). Increasing age, increasing observation time, increasing treatment intensity, increasing total

fatigue score and low educational level were significantly associated with hypogonadism in univariate analyses.

Multivariate analysis showed that TCSs had more than doubled risk for hypogonadism compared to LSs (OR=2.29, 95% CI: 1.56–3.38). With low gonadotoxic group as reference, treatment with medium gonadotoxicity showed OR=2.55 (95% CI: 1.97–3.31), and treatment with highly gonadotoxic treatment OR=23.78 (95% CI: 12.72–44.48). In addition, increasing age at survey ( $p < 0.001$ ) and increasing total fatigue score ( $p = 0.04$ ) were significantly associated with hypogonadism in multivariate analyses.

**Conclusions:** Approximately 50% of both TCSs and LSs included in this study were hypogonadal at a mean of 11.7 years after primary treatment emphasizing the importance of awareness to this late effect after treatment. The TCSs had more than doubled risk for hypogonadism compared to LSs, and one might speculate if this is related to impaired testicular function at diagnosis and/or reduced testicular volume after orchiectomy.

7172

POSTER

### The Prognosis of Patients With Non-Muscle Invasive Bladder Tumour Less Than 40 Years

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**Background:** Bladder tumour tend to increase morbidity, generally peak incidence was in 60–70 generation but, recently gradually increasing morbidity demonstrate in young age. We investigate characteristics and prognosis of patient less than 40 years with non-muscle invasive bladder tumour.

**Materials and Methods:** We retrospectively analyzed 42 patients (group 1) less than 40 years with bladder tumour, and they were followed up for more than 6 months after transurethral resection of bladder tumour (TUR-BT) under the impression of bladder tumour from October 1998 to February 2010. As controlled group, we analyzed 44 patients (group 2) more than 60 years with bladder tumour, and they were followed up for more than 6 months after TUR-BT from January 2009 to December 2009. We investigated pathologic result that confirmed to biopsy after operation and assessed recurrence, progression.

**Results:** Average age was  $33.6 \pm 10.3$  years in group 1,  $71.6 \pm 7.4$  years in group 2. Group 1 and 2 were not significant different in sexual distribution (30:12 vs 33:11). In stage of group 1, 33 patients were Ta (78.6%), 4 patients were T1 (9.5%), 5 patients were T2 and more (11.9%). In stage of group 2, 23 patients were Ta (52.3%), 16 patients were T1 (36.4%), 5 patients were T2 and more (11.4%). The proportion of muscle invasive type was not different in both group, non-muscle invasive type in group 1 were lower stage than that of group 2 ( $p = 0.01$ ). The differentiation of non-muscle invasive tumour in group 1, low grade was 31 patients (73.8%), in group 2, high grade was 23 patients (52.3%). Relatively low grade was more found in group 1 ( $p = 0.013$ ). The patients of recurrence were 2 patients (4.8%) in group 1, 17 patients (38.6%) in group 2, so recurrence rate was lower in group 1 ( $p = 0.001$ ). When recurrence was found, stage elevation was none in group 1, was 1 patient in group 2.

**Conclusions:** In young patients less than 40 years, non-muscle invasive bladder tumour happen to equivalent rate comparing that of older patients, but stage, differentiation and recurrence rate was low, so we can expect better prognosis.

## Oral Presentations (Mon, 26 Sep, 09:00–11:05) Gynaecological Cancer

8000

ORAL

### Results of the GYNECO 02 Study, a FNCLCC Phase III Trial Comparing Hysterectomy Versus No Hysterectomy in Patients With a (Clinical and Radiological) Complete Response After Chemoradiation Therapy in IB2/II Stage Cervical Cancer

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**Background:** Concomitant chemotherapy and radiation (including brachytherapy) (CRT) is considered as the standard treatment for IB2/II

stage cervical cancer in many countries but the benefit from the surgery (hysterectomy: HT) following CRT needs to be defined.

**Methods:** A randomized trial was opened in France in 2003 to evaluate the benefit of HT after CRT. The main inclusion criteria were: 1. stage IB2/II cervical cancer; 2. no extrapelvic disease on conventional imaging; 3. pelvic external radiation therapy (45–50 Gy +/- a parametrial or nodal boost) with concomitant cisplatin chemotherapy (40 mg/m<sup>2</sup>/week) followed by uterovaginal brachytherapy (15 Gy); 4. no residual macroscopic disease (clinical and radiological response) 6 to 8 weeks after brachytherapy. The main criteria was the 3 year event-free survival. Patients were randomized between HT (arm A) versus no HT (arm B). Unfortunately, in total 61 patients out of 320 (160/arm) were enrolled (poor accrual) and are described in this study.

**Results:** Thirty-one and 30 patients were enrolled respectively in arms A and B. Twelve patients relapsed (5 of them died): respectively 8 and 4 in arms A & B. Three-year EFS rates were 72% (SE=9%) and 89% (SE=6%)(NS) in arms A & B respectively. Three-year overall survival rates were 86% (SE=6%) and 97% (SE=3%)(NS) in the A & B arms respectively.

**Conclusions:** The results of this trial seem to suggest that hysterectomy had no therapeutic impact on patients with a clinical and radiological complete response after CRT (but this conclusion is limited by the lack of power).

8001

ORAL

### Clinical and Dosimetric Outcomes for 3D Image Guided Adaptive Pulsed-dose-rate Brachytherapy in Locally Advanced Cervical Cancer

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**Background:** Integration of 3D images in brachytherapy planning allows dosimetric optimization and dose escalation in locally advanced cervical cancer patients. The objective was to evaluate the outcomes in a large series of patients, treated with 3D image guided brachytherapy (BT) after external beam radiotherapy (EBRT).

**Methods and Materials:** On behalf of the retro-EMBRACE study group, patient data was reviewed, for those with curable locally advanced cervical cancer treated with 3D image guided pulsed dose rate (PDR) BT after EBRT from March 2004 to July 2009. Patients lost to follow up or not followed in our institute, for whom follow-up data were not reliable were excluded. Patients received concomitant pelvic or pelvic plus para-aortic chemoradiation (45–50.4 Gy) followed by MRI or CT guided PDR BT (15 Gy to the IR-CTV). Brachytherapy was performed according to GEC-ESTRO guidelines. HR-CTV, IR-CTV, rectum, sigmoid colon and bladder were delineated. Additional nodal or parametrial EBRT boosts were performed when indicated.

**Results:** 130 patients fulfilled the inclusion criteria. At diagnosis, the estimated median tumour volume was 43 cm<sup>3</sup> (4–269). The stage distribution was: 1B 27%, IIA 6%, IIB 46%, IIIA 3%, IIIB 10%, IVA 3% and IVB 5%. Squamous cell carcinoma was the commonest histological subtype (85%). 38% had nodal involvement. 120 patients received concomitant chemotherapy, weekly cisplatin when not contra indicated. 18% of the patients received pelvic plus para-aortic EBRT. BT was based on MRI for 114 patients and on CT for the remaining 16. The doses delivered (EBRT + BT, in 2 Gy equivalent) were 66.7 Gy (51.7–86.9,  $\alpha/\beta=10$ ) to 90% of the IR-CTV, 77.4 Gy (51.9–104,  $\alpha/\beta=10$ ) to 90% of the HR-CTV. The D2cc for the bladder, rectum and sigmoid were 68.6 Gy (51.5–87,  $\alpha/\beta=3$ ), 58.8 Gy (46.7–73,  $\alpha/\beta=3$ ) and 58.3 Gy (46.5–77.1,  $\alpha/\beta=3$ ) respectively. Afterwards, 48 patients proceeded to radical hysterectomy.

After a median follow-up of 27 months (5–79), 32 patients had relapsed. Only 5 local relapses were reported (4 central and 1 lateral), of which only one was isolated. There were 17 nodal failures (8 pelvic and 9 para-aortic) and 22 metastatic relapses. The 2 year OS was 85% and the DFS was 75%. Local control was 96.5% and pelvic control (adding pelvic nodal control to local control) was 90.5%.

65% of the patients had grade 1–2 toxicities and 8.5% grade 3–4, according to the Common Toxicity Criteria 3.0. Regarding the long term grade 3–4 events, 5 of the 7 with bowel toxicity and 2 of the 3 with urinary toxicity had undergone post radiation radical surgery.

**Conclusion:** This is one of the first large series of patients treated with image guided adaptive PDR brachytherapy after chemoradiation. It provides excellent loco-regional control rates with a low level of late side effects. The rate of distant metastasis as first site of relapse raises the question of more aggressive systemic treatment.