

updated and are presenting now the long-term clinical outcome of the 16 patients involved in the dose-finding trial, together with that of the 9 pts enrolled in the phase II study.

**Materials and Methods:** from June 1999 to December 2004, we have treated in our institution a consecutive series of 25 T2–4 N0 ITBC pts (median age 67 yrs, range 51–80). After macroscopically radical TUR, all pts received XRT (54 Gy in 30 fractions over 6 weeks) and concurrent C (100 mg/sqm on days 1, 22). In dose finding study G was given weekly from 200 to 500 mg/sqm: since unacceptable toxicity was observed in two cases (one death for toxicity), at the dose of 500 mg/sqm/week, and considering the treatment toxicity profile, the recommended G dose for phase II trial was 400 mg/sqm on day 1.8 q 21 for 2 courses together C and XRT. At the trial closure, 9 pts have received such treatment.

**Results:** Except the pt who died for toxicity before the end of treatment, all the remaining 24 pts were microscopically disease free at the cystoscopic re-evaluation performed within 8 weeks after the treatment. Seven local and 2 distant relapses have been observed so far, at a median follow-up of 66 mos. Presently, 67% of pts is alive and disease-free, with one patient died for lung cancer. All pts alive have retained their bladder, with a normal organ function, in absence of any relevant long-term toxicity. The median survival has not been reached yet, while the OS at 7 years is 66%. The 5-year DFS, local DFS and survival without cystectomy, were 62%, 70%, and 95% respectively.

**Conclusions:** in our experience G + C with concurrent XRT in ITBC pts, appears encouraging, even at long-term follow-up. Considering the 100% of complete response observed after the treatment, this combination may be of interest in enhancing the disease control of C plus XRT that is today the treatment of choice in the conservative therapy of ITBC.

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POSTER

#### Feelings of loss and shame after having lost a testicle: a population-based long-term follow-up of testicular-cancer survivors

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**Background:** Knowledge about the reactions and feelings among men who have lost a testicle due to testicular cancer is rather limited.

**Materials and Methods:** We identified 1173 eligible men diagnosed with non-seminomatous testicular cancer treated according to the national cancer-care programs SWENOTECA I-IV between 1981 and 2004. During an 18-month qualitative phase we constructed a study-specific questionnaire, primarily on cognitive functioning in every-day life. In addition, we also asked the men about their feelings after having lost one testicle.

**Results:** We obtained information from 960/1173 (82 percent) testicular-cancer survivors 3 to 26 years after diagnosis. We found that 32 percent of these men miss or have missed their ablated testicle and that 26 percent have or have had feelings of shame related to their body because of the ablated testicle. These feelings were more common among younger men (20–34 years old) than among older (44–74 years old) men. Relative risk for younger men of having or having had feelings of loss was 1.5 (95% confidence interval, CI 1.2 to 1.9) and of shame 1.8 (95% CI 1.3 to 2.3). Furthermore, we found that a greater percentage of singles missed the testicle (RR 1.7; 95% CI 1.3 to 2.3) and had feelings of shame related to their body (RR 1.9; 95% CI 1.3 to 2.7) than did non-singles. We did not find that feelings of loss and shame were less common among those who had, compared to those who did not have, a prosthesis. However, we found it was more common for men who had never been offered a prosthesis to report feelings of loss (RR 1.7; 95% CI 1.3 to 2.2) and shame (RR 1.3; 95% CI 1.0 to 1.8) than for men who had been offered but rejected one.

**Conclusion:** A substantial amount of Swedish testicular-cancer survivors treated between 1981 and 2004 have or have had feelings of loss and shame due to having lost one testicle due to testicular cancer. These feelings are more common among younger men and single men. Feelings of loss and shame are not less common among men who have a prosthesis than among those without a prosthesis. However, these feelings are more common among men who never were offered a prosthesis than among men who were offered but rejected a prosthesis.

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POSTER

#### Combination ifosfamide, bleomycin, etoposide and cisplatin (IBEP) as first line chemotherapy in patients with intermediate and poor prognosis advanced cancer of the testis

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**Background:** Patients with intermediate and poor prognosis advanced testis cancer according to the International Germ Cell Consensus Classification (IGCCC) have a rather dismal long-term outcome (five-year survival roughly 80% and 50% respectively) when treated with the standard initial chemotherapeutic combination of Bleomycin, Etoposide and Cisplatin (BEP). Therefore, the use of more aggressive approaches in the context of clinical studies is recommended.

**Aim:** The estimate of effectiveness and toxicity of combination IBEP as first line chemotherapy in patients with advanced cancer of the testis of intermediate and poor prognosis.

**Patients and Methods:** Patients are treated with IBEP chemotherapy with Ifosfamide 1.2 g/m<sup>2</sup> for 3 days, Bleomycin 15 mg for 3 days, Etoposide 80 mg/m<sup>2</sup> for 5 days and Cisplatin 20 mg for 5 days with support with hydration and mesna. Primary endpoints are overall survival (OS) and the Disease-free survival (DFS).

**Results:** 75 patients were treated in 9 centres. The median age of patients was 27 (16–54) years, while in the 83% of patients had non-seminomatous tumours. Apart alopecia, the main toxicities were nausea - vomiting, anaemia, leucopenia-neutropenia, thrombocytopenia and neurotoxicity. With a median follow-up of 56 months, in the initial analysis, the three-year survival is 84% and three-year DFS 72%. Detailed analysis, including 5-year outcome separately for each category of patients is under way in order to be presented during the congress.

**Conclusion:** Combination IBEP as first line chemotherapy in the advanced cancer of the testis of intermediate and poor prognosis is safe and relatively well tolerated, while the initial long-term results expressed as overall and Disease-free survival appear encouraging.

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POSTER

#### Bleomycin-induced pulmonary toxicity in patients with advanced germ-cell tumours: comparison of bolus administration vs 72-hour continuous infusion

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**Background:** The standard chemotherapy regimen for advanced germ-cell tumours (aGCT) consists of bleomycin as a bolus, etoposide and cisplatin (BEP). Retrospective evidence suggests that bleomycin-induced pulmonary toxicity (BIPT) may be decreased by the administration of bleomycin as a continuous infusion (CI). The aim of the study was to compare BIPT between bolus administration and CI in patients with aGCT treated with BEP.

**Materials and Methods:** male patients with testicular germ-cell tumors considered for BEP for 3 or 4 cycles were randomized to receive bleomycin as a bolus or as a 72-hour CI. High resolution CT (HRCT) scans of the lungs were obtained at baseline at every 2 cycles. BIPT was defined using Kazerooni scale, which assigns independent scores (0–5) for alveolar damage (ground-glass opacities) and interstitial damage (fibrosis) in patients with idiopathic pulmonary fibrosis. BIPT was defined as an score  $\geq 2$  for alveolar damage and/or  $>1$  for interstitial damage. Expected incidence of BIPT was 40% with bolus bleomycin. We hypothesized that bleomycin administered as a CI could decrease BIPT to 20%. To detect this difference with 80% power and 5%  $\alpha$  error, 127 patients were needed. The study was approved by the institutional ethics committee of the two institutions where patients were recruited.

**Results:** Between 03/2005 and 10/2006, 44 patients signed informed consent. Forty-one patients had at least one HRCT and were evaluable. Median age was 23 (17–41). According to the International Germ Cell Consensus Classification, 11 patients had good prognosis, 10 had

intermediate prognosis and 19 had poor prognosis. Creatinine clearance was normal in 95% of patients. Nineteen patients were randomized to bolus bleomycin and 22 patients were randomized to 72 hour CI. Recruitment was stopped due to slow accrual.

Eleven patients developed BIPT (27%) as defined by HRCT: in the bolus group, 5/19: in the CI group 6/22 (26.31% vs 27.27% respectively,  $p = 1$ ). Among 11 patients with BIPT, alveolar damage was observed in 4 patients (36%), interstitial damage in 5 patients (45%) and both in 2 patients (18%). No significant differences were observed in terms of response rate and survival.

Type of toxicity	Bolus (n = 19)	Infusion (n = 22)	p-value	Global (n = 41)	%
Alveolar damage	2	2	0.89	4	36
Interstitial damage	2	3		5	45
Both	1	1		2	18

**Conclusions:** among patients with aGCT treated with BEP, bleomycin administered as a 72-hour CI did not decrease the incidence of BIPT when compared to bolus administration.

## 7175

## POSTER

### Bilateral testicular germ cell tumors – a single hospital experience

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**Background:** Testicular germ cell tumour (TGCT) is the most common solid tumour in young adults (15–35 years) accounting for only 1% of all neoplasm. Incidence TGCT is increasing and the improvement in survival may lead to an increased incidence of bilateral tumours. It is also known that previous TGCT is the main factor for developing contralateral germ cell testicular tumour with a RR of 500 to 1000. We examined the incidence, prognosis, clinical and histological characteristics, treatment and outcome of patients with bilateral testicular germ cell tumours based on a 15-years long experience from a single institution.

**Material and Methods:** We reviewed the charts from all patients treated for a testicular tumour germ cell at Hospital Vall d'Hebron in Barcelona, Spain. The information was retrospectively obtained from the patients' hospital. All the patients were evaluated with clinical history, physical exam, serum markers (aFP, LDH and  $\beta$ hCG), ultrasonographic evaluation of the testicles, computed tomography (CT) scans of the chest, abdomen and pelvis, surgery, location and histology of first and second tumour, treatment after of the surgery and followup.

**Results:** From 151 patients with testicular germ cell tumours, 8 (5.3%) developed bilateral tumours, seven (4.6%) were metachronous and one (0.7%) synchronous tumours. Median age at presentation of the first tumour was 26 years. Second tumours 100% were diagnosed through scrotal ultrasound. Two patients underwent testis sparing surgery for the second tumour. When comparing histologies, most of the cases (85%) had the same histology pattern (seminoma) than the initial tumour. With a median follow-up of 73 months after the first testicular tumour and 40 months from the second tumour all patients are alive without evidence relapse. All the patients are alive without evidence of disease.

**Conclusions:** Survival in patients with bilateral germ cell testicular tumours (BGCTT) is similar to the patients with unilateral germ cell testicular tumour. There is not standard therapy to treat BGCTT and each patient requires a tailored therapeutic treatment.

## 7176

## POSTER

### DNA repair genes transcripts quantification in low and high grade bladder tumours

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**Background:** Bladder cancer is the second most frequent urogenital neoplasia in men and is the eighth most prevalent malignancy in women. Smoking and exposure to aromatic amines are the most important causes. The prolonged exposure of bladder cells to various substances can result in accumulation of lesions in the genome. DNA repair systems

play a significant role in protecting the integrity of the genome against cytotoxic and mutagenic agents and their normal expression must be tightly regulated to avoid cancer development. In this context, our goal is to quantify the transcripts of human DNA repair genes *APE1*, *XRCC1*, *POLB* and *POLK* by Real-Time PCR by comparing low- and high-grade bladder tumors samples.

**Material and Methods:** We analyzed bladder tumor samples from 33 patients, with mean age of 68 years, being 26 men and 7 women. The samples were divided in low-grade tumors (n = 17) and high-grade tumors (n = 16). After surgical resection, the molecular procedure included total RNA isolation by TRIZOL method followed by RNase-free DNase treatment. The cDNA synthesis was conducted (1  $\mu$ g) by using random primers. The uniplex reactions of Real Time PCR employed the SyBr Green methodology. *GAPDH* was chosen as a calibrator gene (constitutive expression). The gene expression analyses were compared with an inflammation case (cystitis).

**Results:** Low- and high-grade bladder tumors exhibited differences in the profile of expression for transcripts analyzed. The *APE1* and *XRCC1* expression were about two-fold greater in high-grade tumors samples. Of particular note, *POLB* was overexpressed (greater than three-fold) in high-grade tumors. The overexpression of the DNA polymerase beta can lead to an increased mutation rate because of its very low replicative fidelity. In contrast, *POLK* was found to be underexpressed in high-grade tumors compared with low-grade tumors samples. DNA polymerase kappa has an important role in translesion synthesis and its replicative fidelity may be accurate according to the substrate.

**Conclusions:** Bladder cells become susceptible to many lesions that, if not repaired correctly, could lead to bladder cancer. DNA repair mechanisms are essential to keep genetic stability. We compared low- and high-grade bladder tumors samples and we found differences in the profile of expression for human DNA repair genes. This differential expression may differentially contribute to the stability or progression of bladder tumors.

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## POSTER

### Weekly paclitaxel and paraplatin as first line treatment in patients with recurrent or metastatic bladder carcinoma

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**Background:** Paclitaxel is one of the most active drugs in several solid tumors as breast, lung, ovary, and bladder. Weekly paclitaxel seems less toxic and more efficient compared with paclitaxel every three weeks (possibly because of the proapoptotic and antiangiogenic activity), the dose intensity is quiet higher with less toxicity. The purpose of this study is to evaluate the efficacy of weekly paclitaxel and paraplatin as a first line treatment in patients with recurrent or metastatic bladder cancer.

**Patients and Methods:** Thirty patients with recurrent or metastatic bladder carcinoma were enrolled; between April 2002 to August 2004. All patients had measurable disease, ECOG PS 0–2, adequate renal, liver, and bone marrow functions. Patients received no prior chemotherapy for recurrence or metastasis. Patients were treated with 6–8 cycles of weekly paclitaxel 90 mg/m<sup>2</sup> (one hour IV infusion) and paraplatin AUC 2 (IV infusion over half an hour) for three weeks followed by one week rest, response was assessed every 2 cycles, patients showed an objective response (CR, PR or SD) had continued to 8 cycles.

**Results:** All patients were evaluable for response, toxicity, and survival. The median age was 52 years (range 48–65), Male/Female 22/8. Twenty patients were transitional cell carcinoma and ten patients were squamous cell carcinoma. The main location of disease was local recurrence in 7 patients (23.3%), liver metastasis in 8 patients (26.7%), lung metastasis in 6 patients (20%), bone metastasis in 4 patients (13.3%), and nodes in 9 patients (30%). A total of 227 cycles were administered with a median of seven cycles per patient, with no dose reduction. The overall response rate was 66.7% (CR 20%, PR 46.7%), 6 patients had stable disease (20%) and 4 patients had PD. Median time to progression and median survival were 10.1  $\pm$  1.2 months and 14.5  $\pm$  1.1 months respectively.

**Conclusion:** Weekly paclitaxel and paraplatin is an active, feasible, and well tolerated regimen as first line chemotherapy for patients with recurrent or metastatic cancer bladder with overall response rate 66.7%.

## 7178

## POSTER

### Clinical effectiveness of neoadjuvant chemotherapy for invasive bladder cancer

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**Background:** Neoadjuvant chemotherapy (CT) improves survival in patients (pts) with invasive bladder cancer. Our purpose was to assess the