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# Role of surgery in patients with liver metastases from nonseminomatous germ cell tumors

J.T. Hartmann<sup>1</sup>, O. Rick<sup>2</sup>, K. Oechsle<sup>1</sup>, T. Gauler<sup>3</sup>, P. Schoeffski<sup>4</sup>, J.-Schleicher<sup>5</sup>, M. Kuczyk<sup>6</sup>, L. Kanz<sup>1</sup>, C. Bokemeyer<sup>1</sup>.

<sup>1</sup>Eberhard-Karls-University, Hem/Onc, Tuebingen, Germany; <sup>2</sup>Charité Campus Berlin, Hem/Onc, Berlin, Germany; <sup>3</sup>West German Cancer Center, Hem/Onc, Essen, Germany; <sup>4</sup>MH Hannover, Hem/Onc, Hannover, Germany; <sup>5</sup>KH Stuttgart, Hem/Onc, Stuttgart, Germany; <sup>6</sup>Eberhard-Karls-University, Urol, Tuebingen, Germany

**Background:** The presence of liver metastases (LM) represents an independent poor prognosticator for patients (pts) with germ cell cancer (GCT).

**Material and methods:** The charts of 43 male pts with metastatic GCT and who have undergone liver resection between 1990 and 1999 were reviewed.

**Results:** Thirty-three pts (77%) were initially diagnosed with LM and advanced GCT. Ten pts (23%) had metachronous LM occurring after a median interval of 16 months (range, 6-103). Median age was 29 years (range, 18-54). All pts had received platinum based chemotherapy prior to the resection of LM, 81% of the pts as first-line and 19% as second-line treatment. Sixty-five percent of the pts achieved a marker negative partial response (PRm-). PR m+ was observed in 23% and PD in 12% of the pts. Twelve pts (28%) had isolated LM after chemotherapy while 31 pts (72%) had residual extrahepatic tumor masses including the retroperitoneum (48%), lungs (42%), mediastinal lymph nodes (5%) (other sites; 5%). Liver surgery included enucleation or single segment resection in 32 pts (74%) and hemihepatectomy or \* 3 segments in 11 pts (26%). Resection of LM yielded necrosis in 67% (n=29), teratoma in 21% (n=9) and vital carcinoma in 12% (n=5). Additional resections have been performed in 31 pts revealing necrosis in 61% (n=19), teratoma in 32% (n=10) and vital carcinoma in 7% (n=2). In 12 of 31 pts (39%) histological results differed between the findings in LM and in resections at other locations. After a median follow up of 37 mos (range, 16-216) the calculated 5-yr survival was 76% (CI95%, 58-93%). Univariate analysis identified mediastinal LN involvement, elevated AFP and refractoriness to chemotherapy as negative prognostic factors.

**Conclusion:** Surgery of residual hepatic lesions either following induction or second-line chemotherapy is a feasible approach. The high rate of vital carcinoma and teratoma found in liver specimens, different histological results at residual tumor locations and the high survival rate achieved, support a multidisciplinary approach including resection of masses at all locations.

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# A phase II study testing intravenous (iv) vinflunine (VFL) as second line therapy in patients with advanced transitional cell cancer (TCC) of the bladder.

S. Culine<sup>1</sup>, C. Théodore<sup>2</sup>, M. De Santis<sup>3</sup>, B. Bui<sup>4</sup>, T. Demkow<sup>5</sup>, J. Lorenz<sup>6</sup>, F. Rolland<sup>7</sup>, F. Fabry<sup>8</sup>, B. Longerey<sup>9</sup>, N. James.<sup>1</sup> CRLCC Val d'Aurelle, Department of Medical Oncology, Montpellier, France; <sup>2</sup>Institut Gustave Roussy, Department of Oncology, Villejuif, France; <sup>3</sup>LBI-ACR and CESAR, Department of Oncology, Wien, Austria; <sup>4</sup>Institut Bergonie, Bordeaux, France; <sup>5</sup>Im Marii Skłodowskiej-Curie, Centrum Onkologii, Warsaw, Poland; <sup>6</sup>Klinika Urologii Akademia Medyczna, Wrocław, Poland; <sup>7</sup>Institut de Recherche Pierre Fabre, Clinical Research, Boulogne, France; <sup>8</sup>Institut de Recherche Pierre Fabre, Biometrics, Boulogne, France; <sup>9</sup>Institute for Cancer Studies, Birmingham, United Kingdom

**Introduction:** VFL (Javlor®) is a novel vinca alkaloid selectively fluorinated by superacidic chemistry at the 20'position of vinorelbine. VFL was selected for clinical development on account of its markedly superior in vivo antitumour efficacy, with respect to other vincas, and of its promising phase I results. The aim of this trial was to determine the efficacy and safety of VFL in pre-treated patients (pts) with advanced TCC of the bladder. Pts must have progressed after one line of platinum-containing chemotherapy, given for metastatic or locally advanced disease. Patients and methods: fifty-seven pts (46 males, 11 females) have been analysed by intention to treat (ITT) and 52 are evaluable for response. Median age was 63 (range 42-81) years and median Karnofsky Performance Status 90%. At study start, VFL 350 mg/m2 was given every 21 days. Due to 1 episode of fatal neutropenic sepsis in 1 of the first 6 pts, VFL dose was reduced to 320 mg/m2 for subsequent pts.

**Results:** a total of 211 cycles, with a median of 4 cycles per patient (range 1-12), were administered. Further treatment related dose reductions were only required in 19 (9%) cycles and dose delays occurred in 11

(7%) cycles. There were 2 further fatal episodes of neutropenic sepsis at VFL 320 mg/m2. Grade(G) 3-4 neutropenia occurred in 32% and 39% of patients, respectively. Other G 3-4 toxicities were: fatigue (16% pts), constipation (12% pts), myalgia (3.5% pts), vomiting (7% pts). G2 alopecia was experienced only in 17.5% of patients. Efficacy data were: 9 PR (17%; 95% confidence interval 8-30%, and 16% by ITT), confirmed by an independent panel, 27 NC (52%), including 5 (10%) non-confirmed PR and 3 MR (6%), 16 PD (31%). Estimated median progression-free and overall survival were 3 months (95% confidence interval 2.4-3.8) and 6.4 months (95% confidence interval 4.6-7.6) respectively, with a median follow-up of 4.6 months (range: 0.3 to 15).

**Conclusions:** VFL has shown substantial activity at the dose of 320 mg/m2, comparable to the most active agents, in the second line treatment of TCC of the bladder, with manageable toxicity. A phase III trial is ongoing to further evaluate VFL in this setting. Final time-related parameters will be presented at the meeting.

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# Long-term colorectal, bladder and sexual dysfunction in patients treated with radical radiotherapy for urinary bladder cancer.

L.U. Fokdal, M. Høyer, P. Meldgaard, H. von der Maase. Department of Oncology, Aarhus University Hospital, Aarhus, Denmark

**Background:** There are only few studies on functional long-term normal tissue morbidity due to radical radiotherapy (RT) for bladder cancer. The aim of this study is to investigate functional long-term bladder-, intestinal- and sexual dysfunction after RT in patients (pts) treated for bladder cancer T1-T4aNx-N1M0.

**Material and Methods:** In the period 1/1994-6/2001, 270 pts received RT for bladder cancer at the Department of Oncology, Aarhus University hospital, Aarhus, Denmark. All pts were treated with a CT-based three-field technique and individual blocks with a total dose of 60 Gy to the tumour and bladder and a mean of 46 Gy (range: 0-60 Gy) to the internal and external iliac lymph nodes. Sixty-two (23%) pts were still alive and were candidates to participate in a structured telephone interview based on the LENT/SOMA scoring system.

**Results:** Fifty-three (85%) pts agreed to participate in the study. Mean follow-up was 34 month (range: 18-80 month). Twenty-nine (55%) pts reported changes in bowel function, 15 (28%) with moderate or severe impact on daily activities. Twelve (23%) pts had loose/liquid stools, 6 (11%) pts had more than 5 motions each day and 7 (13%) pts used anti-diarrhoeal medication on a weekly basis or more often to control stool consistency and frequency. Twenty-eight (53%) pts had fecal urgency, 10 (19%) pts had regular episodes of fecal leakage and 4 (8%) pts were using incontinence pads. Twenty-five (47%) pts reported changes in bladder function, 8 (15%) with moderate or severe impact on daily activities. Eleven (21%) pts had frequent urination with less than 2 hours interval. Thirteen (25%) pts had regular episodes with urinary incontinence and 11 (21%) pts were using incontinence pads. Thirty-two (60%) pts had no sexual activity, however, 24 (75%) of these reported that this was not associated with RT.

**Conclusion:** The present study shows that RT of urinary bladder cancer is associated with considerable long-term side effects. Persistent major dysfunctions are related with diarrhoea, fecal urgency, frequent urination as well as fecal and urinary incontinence.

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# Long term toxicity following definitive radiotherapy of prostate cancer: analysis of EORTC study 22863

F. Ataman<sup>1</sup>, A. Zurlo<sup>2</sup>, X. Artignan<sup>3</sup>, G. van Tienhoven<sup>4</sup>, L.E. Blank<sup>4</sup>, P. Warde<sup>5</sup>, J.B. Dubois<sup>6</sup>, W. Jeanneret<sup>7</sup>, F. Keuppens<sup>8</sup>, M. Bolla<sup>3</sup>.

<sup>1</sup>EORTC, Radiotherapy Group, Brussels, Belgium and Akdeniz University, School of Medicine, Dept. of Radiation Oncology, Antalya, Turkey; <sup>2</sup>EORTC, Radiotherapy Group, Brussels, Belgium; <sup>3</sup>CHR de Grenoble - La Tronche, Radiation Oncology, Grenoble, France; <sup>4</sup>Academisch Medisch Centrum, Radiation Oncology, Amsterdam, The Netherlands; <sup>5</sup>University Health Network - OC/Princess Margaret Hospital, Radiation Oncology, Toronto, Canada; <sup>6</sup>CRLC Val d'Aurelle, Radiation Oncology, Montpellier, France; <sup>7</sup>Centre hospitalier universitaire Vaudois, Radiation Oncology, Lausanne, Switzerland; <sup>8</sup>Academisch Ziekenhuis VUB, Urology, Brussels, Belgium

**Purpose:** Late treatment toxicity is analyzed in the multi-centre EORTC trial 22863 evaluating the value of adjuvant endocrine treatment for patients with locally advanced prostate cancer.