TAMSULOSIN VERSUS FINASTERIDE: EFFECT ON BOTH URINARY FLOW AND URINARY FLOW

Rigoni Patrizio1, Brunai Maurizio, Scarpa Roberta, Pero Danielle2, on behalf of the MICTUS Study Group

1Divisione di Urologia, Università Vita-Salute S. Raffaele, Milan, Italy, 2Divisione di Urologia, Ospedale Estate S. Agostino, Modena, Italy, 3Divisione di Urologia, Ospedale S. Luigi Gonzaga, Orbassano, Italy, 4Divisione di Urologia, Policlinico S. Matteo, Pavia, Italy, 5Divisione di Urologia, B. Rottura Hospital, Vicenza, Italy

INTRODUCTION & OBJECTIVES: Several direct comparative trials have investigated the efficacy and tolerability of alpha-adrenoceptor antagonists (AA) and finasteride. Although tamsulosin is the most frequently prescribed AA in the treatment of lower urinary tract symptoms (LUTS/BPH), it has never been directly compared with finasteride. The MICTUS (Multicentre Investigation to Characterise the Effect of Tamsulosin on Urinary Symptoms) study therefore compared tamsulosin with finasteride.

MATERIAL & METHODS: This was a 26 week multicentre, randomised, double-blind trial in LUTS/BPH patients (IPSS ≥ 10, SFU ≥ 7, Qmax 4 mL/s) receiving tamsulosin 0.4 mg or finasteride 5 mg once daily following a 2-week placebo run-in period. The primary parameter was the change in total Symptom Problem Index (SPI), a validated questionnaire, at endpoint. i.e. 26 weeks. Treatment was continued up to 1 year efficacy and safety parameters as secondary endpoints.

RESULTS: 50 centres in Italy randomised 403 patients (mean age 64±7.1 years, mean prostate volume 45.19±10.9 mL in finasteride arm or 44.9 mL in tamsulosin arm). At 26 weeks tamsulosin induced a greater reduction in total SPI compared to finasteride (borderline significance in intention-to-treat population; significant in per protocol population). At 1 and 6 weeks, tamsulosin improved Qmax maximally and significantly more than finasteride. At 6 months the effects of both treatments were comparable. Both treatments were well tolerated. The occurrence of acute urinary retention on finasteride or tamsulosin was also comparable.

CONCLUSIONS: Patients receiving tamsulosin have a more rapid increase in urinary flow than finasteride. Furthermore they experience a greater improvement in level of bother associated with LUTS. Hence tamsulosin offers the advantage of early onset efficacy.

THE ROLE OF INITIAL IMMUNOTHERAPY AS SELECTION FOR NEPHRECTOMY IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA AND THE PRIMARY IN SITU

Bex Axel1, Horenblas Simon1, Meinhardt Wim1, Verra Natasha2, de Gast Bert2

1Urology, The Netherlands Cancer Institute, Amsterdam, The Netherlands, 2Medical Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

INTRODUCTION & OBJECTIVES: Two recent randomised trials have shown nephrectomy and immunotherapy to be superior to immunotherapy alone in patients with metastatic renal cell carcinoma and the primary tumour in situ. However, the timing of the experimental setting remains controversial. We assessed the feasibility of interleukin-2 (IL-2) based immunotherapy prior to nephrectomy and evaluated the role of immunotherapy as selection for cytoreductive surgery.

MATERIAL & METHODS: 16 patients with metastatic renal cell carcinoma and an asymptomatic primary tumour in situ at the time of immunotherapy were included. All patients with PD died after a median overall survival of 3 months. The cycles were repeated at intervals of 3.5, 5, 8, 11, 14, 17, 20 and successively at 4-month intervals.

RESULTS: Of the 16 patients, 11, 12, 18 and 19 months. Median duration of response was 6 (2-10) months. One patient with SD following nephrectomy developed CA after 2 additional cycles, which is currently maintained for >10 months.

CONCLUSIONS: Absence of progression at metastatic sites following immunotherapy with the primary tumour in situ may be used as a selection for nephrectomy in this selected group. Non-responding patients can be spared from surgery. A randomised study is needed to assess the timing of nephrectomy in combination with immunotherapy with regard to morbidity, survival and quality of life.

A PHASE II STUDY OF CHRONIC LOW DOSE OF INTERLEUKIN-2 (IL-2) AND α-INTERFERON (IFN-α) IN METASTATIC RENAL CELL CARCINOMA (MCC)

Potenzoni Michele1, Benecchi Luigi2, Ulivano Nicoletta1, Canton Federico3, Dalla Chiesa Matteo1, Cengarle Rita2, Pavone Laura2, Potenzoni Domenico1

1Urology, University of Parma, Parma, Italy, 2Oncology, University of Parma, Parma, Italy, 3Nephrology, University of Parma, Parma, Italy, 4Oncology, Ospedale di Parma, Parma, Italy, 5Urology, Azienda UISL di Parma, Parma, Italy

INTRODUCTION & OBJECTIVES: The optimal dose and schedule of IL-2 and IFN-α in MCC is not yet defined. In this study we employed very low doses of IL-2 and IFN-α given over the whole duration of immunotherapy, with the aim of measuring its therapeutic effects (response rate, survival, toxicity) and immunological changes.

MATERIAL & METHODS: One hundred and ten immunotherapy naive patients, 80 males and 30 females, median age 62 years (range 27-81), Karnofsky PS 60-100 (58% were 90-100, 42% were 80-90), entered into a prospective study. Metastatic sites were lung (54%), bone (20%), lymph node (13%), liver (6%), others (9%), 87% of the patients were neoprotected. Treatment consisted of IL-2 administered s.c. at a dose of 1 MU/m^2/12h on days 1 and 2, followed by 1 MU/m^2/24h on days 3.6 of each week for 4 consecutive weeks. Concomitantly IFN was given i.m. at a dose of 18 MIU/m^2 on days 3 and 7. No therapy was administered on days 6 and 7. The cycles were repeated at intervals of 3 months.

RESULTS: At present the median follow-up is 35 months (range 7-114); median survival is 16 months (range 1-106). Of 110 enrolled patients, 100 were evaluable for response: 6 (6%) obtained a complete response (CR), 9 (9%) a partial response (PR), 13 (13%) a stable disease (SD), 7 (7%) a progressive disease (PD). Of 100 evaluable patients 4 were excluded from follow-up and were without evaluable parameters. At 36 months 35% of patients are alive; 2 patients had a PR after an initial progression. Responses were observed in patients with non metastatic sites (15%) and in 4% of patients with metastatic sites and with PS 60-100 (21% of patients with good PS responded versus 7% of patients with PS 60-80). The toxicity of this scheme was acceptable. Fatigue, fever, chills and arthralgia/myalgias were the most common side effects observed in 3 (6%) of patients. Fatigue was observed in 4%, of fever in 14%, of arthralgia/myalgias in 4%. grade 4 toxicity was observed. As compared to basal values the treatment resulted in a significant increase in CD56, CD3-CD56+, CD25+ and CRTH2 (p < 0.05).

CONCLUSIONS: In conclusion, low and chronically repeated doses of IL-2 and IFN-α had a therapeutic effect similar to other published studies using higher IL-2 doses. This schedule determines significant immunological change. Treatment-related toxicity is mild. A multicenter randomised study in order to confirm the utility of chronic immunotherapy with IFN-α and IFN-α is ongoing.

PROGNOSTIC IMPORTANCE OF SUPRAHEPATIC AND INTRAATRIAL TUMOURTHROMBI IN RENAL CELL CARCINOMA: A RETROSPECTIVE ANALYSIS INCLUDING IMMUNOTHERAPY AS THERAPEUTIC OPTION IN ADVANCED DISEASE

Winter Klaus, Roupas Jan, Wille Andreas, Deger Serdar, Schnorr Dietmar

Urology, Charité Hospital, Berlin, Germany

INTRODUCTION & OBJECTIVES: In 4 to 10% renal cell carcinoma (RCC) patients an extension of tumourthrombi (TT) into the vena cava inferior. There is a controversy discussion concerning the prognostic importance and therapy of suprarecphatic and intraatral TT (stadium III and IV by STAHELER). Due to the use of cardiosurgical techniques the mortality of the operation could be decreased and with the use of subsequent immunotherapy (IT) the survival of patients can be prolonged.

MATERIAL & METHODS: In a retrospective analysis we have investigated our patients treated at the Charite Medical School. Surgery included tumournephrectomy and thrombectomy. IT was performed using IL-2, IFN-alph and IFU. 100 patients with RCC, median age 59 years (range 34 to 74 years) were included. Patients were subdivided into 4 groups: 24 with TT (13 stadium III, 11 stadium IV); 42 patients with metastatic RCC, no TT, treated with FT, 18 patients with metastatic RCC, no TT; 10 TT; 16 patients with non metastatic RCC, no TT, no IT. Statistics were performed using Kaplan-Meier and Log-Rank for follow-up and Cox-regression for multivariate analysis.

RESULTS: Tumournephrectomy and thrombectomy were completed successfully in all 24 patients with RCC and TT. The perioperative mortality was at 0%. There was no significant (p>0.05) difference between the survival of the nonmetastatic RCC’s with or without TT. With IT a benefit and a significant increase of survival could be achieved in metastatic patients. In a multivariate analysis metastases and IT proved to be prognostically independent factors. The proportion of progression was significantly (p<0.05) increased in TT patients. Suprahepatic and intraatral IT’s were no independent prognostic factors.

CONCLUSIONS: Tumournephrectomy with extirpation of tumourthrombi is the only curative therapeutic option for patients with RCC and vena cava extension. The occurrence of TT has no prognostic significance. In metastatic disease, also in patients with TT, immunotherapy offers the chance of advanced survival.