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TAMSULOSIN VERSUS FINASTERIDE: EFFECT ON BOTHER AND URINARY FLOW

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INTRODUCTION & OBJECTIVES: Several direct comparative trials have investigated the efficacy and tolerability of alpha1-adrenoceptor antagonists (AA) and finasteride. Although tamsulosin is the most frequently prescribed AA in the treatment of lower urinary tract symptoms suggestive of benign prostatic hyperplasia (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 and finasteride.

MATERIALS & METHODS: This was a 26-week multicentre, randomised, double-blind study in LUTS/BPH patients (I-PSS≥ 13; SPI≥ 7; Qmax 4-15 mL/s) receiving tamsulosin 0.4 mg once daily 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 63±7.1 years, mean prostate volume 39±18.9 mL) to finasteride (n=204) or tamsulosin (n=199). At 26 weeks tamsulosin induced a greater reduction in total SPI compared to finasteride (borderline significance in intention-to-treat population, significant (p=0.03) in per protocol population). At 1 and at 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.

Parameter: mean (SD)	Assessment	Finasteride	Tamsulosin	p-value
Primary parameter: total SPI (points)	Baseline	14.0 (4.2)	13.6 (4.4)	
	Change at endpoint	-4.5 (5.0)	-5.2 (5.0)	0.061
	% Change at endpoint	31.9%	38.4%	
% of SPI responders*	Endpoint	35%	44%	0.088
Qmax (mL/s)	Baseline	10.8 (3.4)	10.7 (3.7)	
	Change at week 1	0.6 (4.4)	2.3 (5.2)	<0.001
	% Change at week 1	6%	21%	
	Change at endpoint	1.8 (4.7)	2.5 (6.1)	0.243
	% Change at endpoint	17.8%	23.8%	

SD: standard deviation; *≥ 50% decrease from baseline

CONCLUSION: 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. SOURCE OF FUNDING: Boehringer Ingelheim SpA.

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

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INTRODUCTION & OBJECTIVES: The optimal dose and schedule of IL2 and IFN-α in MRCC is not yet defined. In this study we employed very low doses of IL2 and IFN-α given for all the duration of the patients' life, 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% was 90-100, 42% was 60-80), entered into a prospective study. Metastatic sites were lung (54%), bone (24%), lymph nodes (34%), liver (16%), others (29%). 87% of the patients were nephrectomised. Treatment consisted of IL2 administered s.c. at a dose of 1 MUI/mq/12h on days 1 and 2, followed by 1 MUI/mq/24h on days 3-5 of each week for 4 consecutive weeks. Concomitantly IFN-α was given i.m. at a dose of 1.8 MUI/mq/die on days 3 and 5. No therapy was administered on days 6 and 7. The cycles were repeated at months 3, 5, 8, 11, 14, 17, 20 and successively at 4-month intervals

RESULTS: At present the median follow-up is 35 months (range 7-1114); 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 (SS) and 72 (72%) a progressive disease. Of 10 non-evaluable patients: 4 were lost to follow-up and 6 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 1 or 2 metastatic sites (15/87) (no response was observed in patients with ≥ 3 metastatic sites) and with PS 90-100 (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 arthralgias/myalgias were the most common toxicities observed: grade 3 (WHO criteria) of fatigue was observed in 4%, of fever in 14%, of arthralgias/myalgias in 4%; no grade 4 toxicity was observed. As compared to basal values the treatment resulted in a significant increase in CD56, CD3-CD56+, CD25+ and DR+ ($p < 0,05$).

CONCLUSIONS: In conclusion, low and chronically repeated doses of IL2 and IFN-? had a therapeutic effect similar to other published studies using higher IL2 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 IL2 and IFN-α is ongoing

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

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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 nephrectomy in this experimental setting remains controversial. We assessed the feasibility of interleukin-2 (IL-2) based immunotherapy prior to nephrectomy in a prospective cohort study 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 evaluated with regard to age, sex, sites of extrarenal disease, morbidity, response, nephrectomy rate, time to progression and survival. Immunotherapy consisted of 2 courses low dose IL-2 4 MIU/m^2, subcutaneous granulocyte-macrophage colony stimulating factor (GM CSF) 2.5 μg/kg and interferon-alpha (IFN-A) 5 MU flat on day 1-13 and 22-34. Patients with either partial remission (PR) or stable disease (SD) underwent nephrectomy followed by a 3rd and 4th course.

RESULTS: No response was seen in the primary tumours. With regard to extrarenal sites SD was noted in 9 cases, PR in 2 and progressive disease (PD) in 5. Eleven patients underwent nephrectomy. No surgical CR could be achieved. All patients with PD died after a median overall survival of 3 months versus 11.5 (4-22) months in those who underwent nephrectomy. Four patients are still alive at 10, 12, 18 and 19 months. Median duration of response was 6 (2-10) months. One patient with SD following nephrectomy developed CR 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.

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

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INTRODUCTION & OBJECTIVES: In 4 to 10% renal cell carcinomas (RCC) have an extension of tumourthrombi (TT) into the vena cava inferior. There is a controversial discussion concerning the prognostic importance and therapy of suprahepatic and intraatrial TT (stadium III and IV by STAEHLER). 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 Charité Medical School. Surgery included tumournephrectomy and thrombectomy. IT was performed using IL-2, IFN-alpha and 5-FU. 100 patients with RCC, median age 59 years (range 34 to 74 years) are 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 IT, 18 patients with metastatic RCC, no TT, no IT; 16 patients with nonmetastatic 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 probability of progression was not significantly ($p>0,05$) increased in TT patients. Suprahepatic and intraatrial TT's were no independent prognostic factors.

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