Expansion to the first Efficacy Stage has commenced and Pilot Phase safety data will soon be known.

4028 POSTER

Current outcomes of clinical trials in carbon ion radiotherapy for prostate cancer

H. Tsuji, H. Kato, T. Nomiya, T. Kamada, J. Mizoe, J. Shimazaki, H. Tsujii. *National Institute of Radiological Sciences, Research Center for charged particle therapy, Chiba, Japan*

Background: Carbon ion radiotherapy (C-ion RT) is characterized with better dose concentration and higher biological effect than photons. Three prospective clinical trials of hypofractionated C-ion RT for prostate cancer were performed at our institute since June 1995. The recommended dose-fractionation and treatment methods were established through two dose-escalation trials and validated by the following phase II trial.
Methods: Patient with previously untreated, biopsy proven adenocarcinoma of the prostate without metastasis was eligible for the trials and a total of 461 patients were treated until August 2006. Of those, 96 patients received the C-ion RT in the two consecutive phase I/II trials until March 2000. Radiation dose was escalated from 54.0 GyE up to 72.0 GyE in 20 fractions and the recommended dose of 66.0 GyE was obtained from the result of these dose-escalation trials. The following 365 patients received the C-ion RT with the recommended dose in the phase II trial and were analyzed in this study. Androgen deprivation was applied to the intermediate and high-risk patients combined with C-ion RT and low-risk patients received only C-ion RT. Primary endpoint of this study was biochemical relapse free rate (BRF) and the secondary endpoints were late radiation toxicity and disease specific survival (DSS). Biochemical failure was defined as 2.0 ng/ml increase from the nadir according to the new criteria of the American Society of Therapeutic Radiation and Oncology (ASTRO).
Results: No patient was lost to follow up and median follow up period of 365 analyzed patients was 38.3 months. Twenty-nine patients developed biochemical failure and 5-year BRF of entire group was 89.6%. Only four patients have died of prostate cancer so far and the 5-year DSS of the entire group was 98.2%. Clinical stage and centrally reviewed Gleason score were significant prognostic factors for both BRF and DSS. No grade 3 radiation toxicity was observed and the incidences of grade 2 rectal and genitourinary (GU) toxicities were 1.4% and 3.6%, respectively.
Conclusions: Sufficiently safe and effective treatment option using hypofractionated C-ion RT could be established.

4029 POSTER

Phase II clinical trial of metronomic cyclophosphamide (CTX) plus celecoxib (C) and dexamethasone (DEX) in advanced hormone refractory prostate cancer (HRPC): preliminary clinical and pharmacodynamic results

A. Fontana[1], G. Bocci[2], L. Galli[1], E. Fontana[1], C. Galli[1], L. Landi[1], A. Fioravanti[2], R. Di Marsico[1], M. Del Tacca[2], A. Falcone[3]. [1]*Civil Hospital, Division of Medical Oncology, Livorno, Italy;* [2]*University of Pisa, Division of Chemotherapy and Pharmacology, Pisa, Italy;* [3]*Civil Hospital and University of Pisa, Division of Medical Oncology, Livorno, Italy*

Background: Low-dose metronomic CTX and C have demonstrated a significant antiangiogenic activity in preclinical studies. Moreover, a single infusion of maximum tolerated dose chemotherapy, given before metronomic treatment, can increase its antiangiogenic activity.
Methods: A total of 27 patients (pts) with advanced HRPC received CTX 500 mg/sqm iv day 1 and CTX 50 mg po daily, DEX 1 mg po daily and C 200 mg po BID continuously, starting from day 2. Primary end point was activity (PSA reduction >50%); secondary were: objective responses, toxicities (NCI-CTC criteria), PFS, OS, evaluation of plasma levels of thrombospondin-1 (TSP-1), VEGF, sVEGFR-2, VE-cadherin mRNA; expression and synthesis of TSP-1 and VEGF in peripheral blood mononuclear cells. Pts characteristics: median age 74.5 years (54−91), median PS 1 (0−2), median baseline PSA 73 ng/ml (9.69–>5000); main sites of disease: bone 22 pts (81.5%), lymphnodes 10 pts (37%); previous chemotherapy 20 pts (74.1%).
Results: 27 pts are evaluable for toxicity and response. Overall PSA decrease $\geqslant$50% was found in 9 pts (33.3%). Median time to PSA progression was 3.2 months (95% CI 2.7−3.7 months) and median OS was 20.9 months (95% CI 14.5−27.3 months). No G3−4 hematologic or non-hematologic toxicities have been observed. Preliminary pharmacodynamic data indicate that a significant difference was observed in TSP-1 and VEGF levels between responders and non responders pts at day 84 of treatment. Indeed, the responders showed a significant increase of TSP-1 plasma concentrations (163.7$\pm$22.3% at day 84 vs. 100% at day 0; $P < 0.05$) and a concomitant significant decrease of plasma VEGF levels (29.8$\pm$11.7% at day 84 vs. 100% at day 0, $P < 0.05$), whereas the non responders showed a marked increase of both plasma TSP-1 and VEGF levels.
Conclusions: Metronomic chemotherapy with CTX plus DEX and C in pts with HRPC showed promising activity without relevant toxicity; interestingly, patients who responded to this metronomic schedule showed a concomitant increase of the endogenous inhibitor of angiogenesis and a decrease of a pro-angiogenic factor.

4031 POSTER

Pretreatment international prostate symptom score correlates with postbrachytherapy erectile dysfunction

A. Addesa[1], H. Saleh[1], V. Ramakrishnan[2], M. Anscher[1]. [1]*Virginia Commonwealth University, Radiation Oncology, Richmond VA, USA;* [2]*Virginia Commonwealth University, Biostatistics, Richmond VA, USA*

Background: To determine the factors that may predict for erectile dysfunction (ED) following prostate brachytherapy based on use and reported effectiveness of phosphodiesterase-5 inhibitors (PDE-5I)
Materials and Methods: 95 patients with T1c-T2c prostate cancer who underwent low-dose rate TRUS-guided brachytherapy +/− external beam radiation therapy (EBXRT) were retrospectively analyzed. Minimum follow-up = 12 months. Post-implant CT scans were performed 4−6 weeks following implant for dosimetry. Patients were asked about the use and effectiveness of any PDE-5I both prior to initiation of any therapy (brachytherapy or EBXRT) and on follow-up. Each patient was given an erectile function (EF) score (between 0 and 5) based on the scale in Table 1.

EF Score Definition

Score	Description
5	Normal EF; No PDE-5I use
4	EF sufficient for intercourse (IC) +/− PDE-5I
3	EF sufficient for IC only with PDE-5I, 100% efficacy
2	EF sufficient for IC with PDE-5I, but <100% efficacy
1	EF insufficient for IC even with PDE-5I
0	No EF or spontaneous erections (e.g., penile implant)

Results: The patients had a median follow-up of 27.4 months after brachytherapy. Median age was 66.5 years. There were 43 Caucasians and 52 African-Americans. Eighteen patients received adjuvant androgen ablation (AA) for a minimum of 4 months; 39 received supplemental EBXRT. Sixty-two had a history of smoking, 26 had diabetes mellitus (DM), and 71 had hypertension (HTN). The International Prostate Symptom Score (IPSS) prior to therapy ranged from 3 to 17 (median = 7). The median EF score before any therapy (EFpre) was 4 and after treatment (EFpost) was 3. A significant association was found between the decrease in EF score and AA ($p = 0.0002$) or DM ($p = 0.009$). In a multivariate analysis, there was a significant association between EFpost (adjusting for EFpre) and smoking history ($p = 0.003$), EBXRT ($p = 0.002$), prostate D90 ($p = 0.035$), prostate V100 ($p = 0.014$), and IPSS ($p = 0.001$); there was no correlation between EF and age, race, T-stage, initial PSA, Gleason Score, AA, DM, prostate volume, # seeds, or isotope. A multivariate logistic regression model of EF was obtained by dichotomizing EF groups into EF = 1 (EF scores 3, 4, 5) and EF = 0 (EF scores 0, 1, 2). We found that prostate D90 > 110% (adjusting for EBXRT, smoking, prostate V100 and IPSS) significantly increased the risk of ED (odds ratio = 8.7, confidence interval = 1.4−52.2); similarly, IPSS > 7 significantly increased the risk of ED (odds ratio = 6.7, confidence interval = 2.3−18.9). A bivariate analysis of EFpost by IPSS determined the following correlation: $EFpost = 4.85 - 0.25 \times IPSS$.
Conclusions: Patients with high IPSS on presentation have a significantly higher risk of reduced PDE-5I effectiveness, and hence ED following brachytherapy. Prostate D90 and V100 may be surrogate predictors of potential normal tissue injury to structures (e.g., neurovascular bundles) in the periphery of the prostate gland.

4032 POSTER

Hypofractionated conformal radiotherapy for good prognosis carcinoma of the prostate: seven year outcome analysis

D.M. Mitchell[1], R.A. Cowan[1], I.C. Bottomley[2], J.P. Wylie[1], J.E. Livsey[1], T. Elliott[1], J.P. Logue[1]. [1]*Christie Hospital, Clinical Oncology, Manchester, United Kingdom;* [2]*The University of Manchester Christie Hospital, Medical statistics, Manchester, United Kingdom*

Background: The optimal external beam radiotherapy dose and fractionation in the radical treatment of localised prostate cancer continues to be investigated. This includes not only dose escalation using conventional