in detecting local relapse after radical prostatectomy for prostate cancer by analysis of post-prostatectomy fossa appearance in pre- and post salvage radiotherapy DCE-MRI.
Methods and Materials: 33 patients undergoing DCE-MRI without endorectal coil before salvage radiotherapy (RT) without evidence for metastases were selected retrospectively and evaluated using information of post treatment DCE-MRI with an interval $\geqslant$ 12 months and response of Prostate-specific antigen (PSA) after RT, median <0.01 ng/mL (mean 0.02 ng/mL, range, <0.01–0.08 ng/mL). The median PSA at diagnosis of biochemical recurrence before salvage RT was 0.34 ng/mL (mean 0.57 ng/mL, range 0.08- 2.38 ng/mL). Pre-RT DCE-MRI scans were compared with post-RT-DCE-MRI-scans to assess behaviour of any suspicious lesions.
Results: 22/33 patients had 24 enhancing nodules in the post-prostatectomy fossa in pre-RT-DCE-MRI at a median PSA of 0.51 ng/ml (mean 0.74 ng/mL, range 0.11 to 2.38 ng/mL). These pre RT enhancing nodules disappeared in post treatment DCE-MRI while PSA showed biochemical remission after RT. Therefore these nodules were considered as highly specific for macroscopic local prostate cancer recurrence. 11/33 patients had normal post-prostatectomy MRI findings at median PSA of 0.22 ng/mL (mean 0.24 ng/mL, range 0.08 and 0.53 ng/mL) without changes after salvage RT. Calculated sensitivity for the MRI identification of the location of the source of the PSA recurrence within the prostatic bed was 72% per lesion for all cases and reached 100% at PSA-levels >0.53 ng/mL. Specificity was 100%.
Conclusions: Enhancing nodules in the DCE-MRI of the post-prostatectomy fossa can be detected depending on the PSA-level with high sensitivity and specifitiy. Thus DCE-MRI without endorectal coil, which can simultaneously be used for RT planning, may be a valuable tool to detect local recurrence even at low PSA-levels (>0.11 ng/mL), and may be used for dose escalation on macroscopic sites of local recurrence.

7010 POSTER DISCUSSION

The Impact of Rectal Distension Present on Planning Scans on Localized Prostate Cancer Outcomes in the Era of Image-guided Radiotherapy

G. Mok[1], S. Baxi[2], T. Craig[1], J. Pertili[1], A. Lau[3], T. Panzarella[3], C. Catton[1].
[1]Princess Margaret Hospital, Radiation Medicine Program, Toronto Ontario, Canada; [2]Alan Walker Cancer Centre, Radiation Oncology, Tiwi, Australia; [3]Princess Margaret Hospital, Biostatistics, Toronto, Canada

Background: Rectal distension (RD) at time of radiation planning has been associated with lower rates of biochemical progression free survival (bPFS). Use of daily image-guided radiotherapy (IGRT) on prostate may overcome prostatic displacement from RD. We review the impact of RD on prostate cancer outcomes in patients treated with daily IGRT.
Methods and Materials: 189 localized prostate cancer patients were treated with daily IGRT on implanted fiducials from 2001–2003. Patients treated with neoadjuvant/adjuvant hormone therapy were excluded. All patients received 79.8 Gy in 42 fractions delivered via 3D conformal radiotherapy (88.9%) or intensity modulated radiotherapy (11.1%). Clinical target volume (CTV) was prostate +/- seminal vesicles. The planning target volume was a 10 mm expansion on the CTV in all directions except for posteriorly where a 7 mm margin was used. Six RD parameters were measured on CT simulation scans: rectal length (RL); rectal volume (RV); average cross sectional area (CSA); superior rectal diameter (SRD); inferior rectal diameter (IRD); and average rectal diameter (ARD). The primary end-point was the impact of the RD on bPFS using the PSA nadir + 2 definition. After adjusting for T-stage (T1 vs T2+) and risk-category (low vs intermediate vs high), associations between bPFS and RD were determined through multivariate analysis using a Cox-proportional hazard model. Secondary end-points were physician scored RTOG acute/late gastrointestinal (GI) and genitourinary (GU) toxicity scores.

Rectal distension parameter	Median distension (range)	Hazard Ratio	95% Confidence Interval
Rectal length	7.9 cm (5.6–12.4)	0.98	0.74–1.31
Rectal volume	49.8 cm^3 (20.9–123.6)	1.00	0.99–1.02
Average cross-sectional area	6.4 cm^2 (3.1–13.4)	1.03	0.89–1.18
Superior rectal diameter	3.0 cm (1.3−6.4)	0.87	0.62–1.21
Inferior rectal diameter	2.6 cm (1.5−4.3)	1.14	0.61–2.10
Average rectal diameter	2.9 cm (2.0−4.3)	0.95	0.47–1.94

Results: Median follow-up was 7.7 years for patients alive at last visit. 84.1% of patients had a T-category of T1a-T2a (T2b/T2c 14.3%; >T2c or Tx 1.6%). Low or intermediate risk disease was 92.6% of patients, while 7.4% had high-risk disease. The 7-year bPFS rate was 78.7%. There were no significant associations between any of the RD parameters and bPFS (see table). Acute GI toxicity grade >2 was 0%. Acute GU toxicity grade >2 was 5.3%. There were 2 events of acute grade 4 urinary obstruction requiring catherization. Late GI toxicity grade >2 was 1.1%. Late GU toxicity >2 was 1.1%. No late GU or GI grade 4 toxicities were reported.
Conclusion: RD does not appear to impact bPFS when patients are treated with daily IGRT on prostate. Severe acute or late toxicity was uncommon and bPFS is consistent with other reports.

7011 POSTER DISCUSSION

Cellular and Humoral Immune System Activation by Sipuleucel-T − Preliminary Data From the OpenACT Phase 2 Trial

D. Petrylak[1], J. Corman[2], S. Hall[3], C. Nabhan[4], A. Ferrari[5], A. Armstrong[6], N. Dawson[7], R. Sims[8], F. Stewart[9], N. Sheikh[10].
[1]Columbia University Medical Center, Medicine, New York, USA; [2]Virginia Mason Medical Center, Urology, Seattle, USA; [3]Mount Sinai School of Medicine, Urology, New York, USA; [4]Advocate Lutheran General Hospital, Hematology and Oncology, Park Ridge, USA; [5]New York University Cancer Institute, Clinical Cancer Center, New York, USA; [6]Duke Comprehensive Cancer Center, Medicine and Surgery, Durham, USA; [7]Georgetown University Medical Center, Lombardi Cancer Center, Washington, USA; [8]Dendreon Corporation, Clinical Affairs, Seattle, USA; [9]Dendreon Corporation, Biometrics, Seattle, USA; [10]Dendreon Corporation, Preclinical Development, Seattle, USA

Background: Sipuleucel-T is an autologous cellular immunotherapy designed to stimulate an immune response against prostate cancer. It is made from peripheral blood mononuclear cells (PBMCs) cultured ex vivo with a recombinant fusion antigen, PA2024 comprising prostatic acid phosphatase [PAP] linked to granulocyte-macrophage colony-stimulating factor [GM-CSF]). Sipuleucel-T has demonstrated improved overall survival (OS) in men with asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer (mCRPC). OpenACT is a Dendreon-sponsored Phase 2 trial, designed to further evaluate the safety and immune responses in mCRPC patients (pts). Survival follow-up is ongoing.
Materials and Methods: Sipuleucel-T was administered every 2 weeks (wks) $\times$ 3 and antigen presenting cell (APC) activation (CD54 upregulation) was assessed by flow cytometry. In vivo responses to PA2024 and PAP antigens were assessed at baseline and 2 wks after the 3rd infusion by IFNγ ELISPOT, ^{3}H-thymidine T cell proliferation assays; humoral responses were measured by ELISA. Cytokines were profiled during manufacture of sipuleucel-T and in pt serum before and after treatment (multiplex MSD assay).
Results: 104 pts were enrolled. Following the manufacture of sipuleucel-T, CD54 upregulation was greater at the 2nd and 3rd infusions, suggesting a prime-boost phenomenon. Analysis of the culture supernatants showed an increase in T cell activation-associated cytokines (IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, IFNγ, and TNFα) after the 1st infusion. Cytokines associated with APCs (IL-8, IL-12p70, IL-1β, MCP-1, MIP-1β, TARC, and Eotaxin) were elevated. Compared to baseline, humoral responses against PAP and PA2024 after therapy were robust ($P < 0.001$ for both). Post-treatment IFNγ ELISPOT responses to PA2024 and PAP were increased from baseline ($P < 0.001$ and 0.073, respectively) as well as proliferative responses ($P < 0.001$ and 0.003, respectively). Serum cytokines associated with immune activation were increased from baseline (IL-6, TNFα, and IL-10 [$P < 0.05$]). Prior docetaxel exposure (28% of treated pts) did not adversely affect immune responses. Adverse events reported here were comparable to those reported in the pivotal Phase 3 IMPACT trial.
Conclusions: Sipuleucel-T generates a prime-boost immune response in pts with mCRPC by activating the immune system. The humoral response to PAP and newly reported serum cytokine profiles provide support for sipuleucel-T's mechanism of action.

7012 POSTER DISCUSSION

Patients Treated With Sipuleucel-T Who Had Prior Docetaxel Had Positive Immune Responses and Survival Benefit

N.A. Dawson[1], D.A. Pessis[2], D.G. McNeel[3], A.C. Stubbs[4], N.A. Sheikh[5], J.B. Whitmore[6]. *[1]Lombardi Comprehensive Cancer Center, Georgetown Unversity, Washington DC, USA; [2]Rush University Medical Center, Urology, Chicago, USA; [3]University of Wisconsin, School of Medicine and Public Health, Madison, USA; [4]Dendreon Corporation, Medical Affairs, Seattle, USA; [5]Dendreon Corporation, Preclinical Development, Seattle, USA; [6]Dendreon Corporation, Biometrics, Seattle, USA*

Background: Sipuleucel-T, an FDA-approved therapy for men with asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer, has been demonstrated to prolong

overall survival (OS). To explore the effect of prior treatment with docetaxel on immune response and OS, data for the subset of pts with prior docetaxel use from the IMPACT study (NCT00065442) were analyzed.
Materials and Methods: 512 pts were randomized 2:1 to sipuleucel-T or control. The trial was sponsored by Dendreon; enrollment and follow-up are complete. Pts treated with chemotherapy ⩾3m prior to registration were eligible provided they received ⩽2 chemotherapy regimens. Pts received 3 infusions of sipuleucel-T or control at approx. 2-wk intervals, and were followed for safety and clinical endpoints. Product parameters ($CD54^+$ count, CD54 upregulation, and total nucleated cell count) were evaluated by flow cytometry in the wk 0, 2, and 4 products. Immune response was measured by ELISA, IFNγ ELISPOT, and stimulation index, OS was analyzed using a Cox regression model.
Results: The majority of pts with prior chemotherapy received docetaxel: 15.5% of sipuleucel-T and 12.3% of control pts had prior docetaxel (last dose a median of 10.2m before randomization [10.6m for sipuleucel-T and 9.6m for control pts], range 2.8–73.0m). Pts with prior docetaxel had slightly less favorable prognostic features. Adverse events within 1 day of sipuleucel-T infusion were similar between groups (79.2% for pts with prior docetaxel and 79.6% for pts without prior docetaxel). 86.8% of prior docetaxel pts received the 3 planned infusions of sipuleucel-T vs 92.7% of pts without prior docetaxel. Sipuleucel-T product parameters and immune responses were similar for pts with and without prior docetaxel. The OS hazard ratio (HR) for sipuleucel-T was consistent (interaction P = 0.638) in pts with prior docetaxel (HR = 0.672 [95% CI: 0.364, 1.241]) and without prior docetaxel (HR = 0.788 [95% CI: 0.612, 1.014]).
Conclusions: Sipuleucel-T can be administered safely and successfully manufactured for pts previously treated with docetaxel. While the limited sample size of pts with prior docetaxel precludes definitive conclusions, the results of this study suggest that pts who received prior docetaxel appear to generate immune responses and experience a survival benefit.

7013 POSTER DISCUSSION

A Phase 1 Study of DI17E6, an Antibody Targeting AV Integrins, in Progressive Castrate-resistant Prostate Cancer With Bone Metastases (mCRPC) After Chemotherapy

M. Wirth[1], A. Heidenreich[2], J.E. Gschwend[3], T. Gil[4], S. Zastrow[1], M. Laniado[1], L. Bernard[5], T. Vardar[5], W. Uhl[6], H. Lannert[6]. *[1]University Hospital Carl Gustav Carus Dresden, Department of Urology, Dresden, Germany; [2]RWTH Aachen University, Department of Urology, Aachen, Germany; [3]Technical University of Munich Klinikum Rechts der Isar, Department of Urology, Munich, Germany; [4]Université Libre de Bruxelles, Institut Jules Bordet, Brussels, Belgium; [5]Merck Serono, Geneva, Switzerland; [6]Merck KGaA, Darmstadt, Germany*

Background: The αv integrin subfamily is composed of at least five members, including αvb1, αvb3, αvb5, αvb6, and αvb8. These integrins exhibit classical integrin functions such as regulation of cell adhesion to extra-cellular matrices, cell spreading, and cell migration. Over-expression of αv integrins has been demonstrated in a number of human cancers including melanoma and breast, renal, cervical, gastric, lung, and prostate tumours. DI17E6 (EMD 525797) is a de-immunized monoclonal IgG2 antibody specifically targeting αv integrins involved in tumour progression.
Methods: This study assessed the safety, tolerability, pharmacokinetics and effect of DI17E6 on e.g. PSA and tumour size (by RECIST 1.0 criteria) in mCRPC patients (pts) progressing after chemotherapy in salvage setting (clinicaltrials.gov identifier NCT00958477). 26 pts were treated with iv infusions of 250, 500, 1000 or 1500 mg DI17E6 given over 1 hour. 24 pts (43−80 years) received 3 doses (weeks 1, 3 and 5) prior to response assessment at the end of week 6. Pts without progressive disease could receive further doses every 2 weeks. Dose-limiting toxicities (DLTs) were assessed over the first 6 weeks and pts were followed for safety until 4 weeks after the last administration of DI17E6.

Table 1: Treatment days per cohort

Pt	250 mg	500 mg	1000 mg	1500 mg
1	42	297	113	91
2	42	380+	121	84+
3	42	85	198+	72+
4	42	142	41	64+
5	56	140	56	77+
6	98	56	43	57+
7	14*			
8	28*			

+ = ongoing treatment; * dropped out pts (1 and 2 infusions only).

Results: At cut-off for analysis, the mean duration on treatment was 95.4 days (26 pts). 4 out of 6 pts in cohort 2 (500 mg) and 3 out of 6 pts in cohort 3 had >16 weeks on treatment (Table 1). No DLTs occurred. Pt 1 and 2 of cohort 2 (500 mg) had a marked decrease in PSA and stabilization. Pt 2 also had primary tumour shrinkage and normalisation of lymph node size. These pts had long term anti-integrin treatment (21 infusions and 27 infusions, respectively). Both subjects additionally showed signs of clinical benefit in term of quality of life and pain reduction.
Conclusions: Clinical single agent activity of DI17E6 in salvage therapy was observed in dose cohort 2 and higher. This supports further investigations in mCRPC. DI17E6 is well tolerated without premedication and did not show clinically relevant dose-related changes in safety parameters assessed.

7014 POSTER DISCUSSION

Evaluation of Circulating Tumour Cells (CTCs) in Chemotherapy-naïve Patients With Metastatic Castration-resistant Prostate Cancer (mCRPC) Receiving TAK-700, an Investigational 17,20-lyase Inhibitor

M. Gross[1], D. Shevrin[2], R. Dreicer[3], W.L. Trepicchio[4], D. MacLean[5], I. Webb[5], J. Wang[6], D.B. Agus[7]. *[1]USC Westside Cancer Center, Clinical Medicine, Beverly Hills, USA; [2]NorthShore University Health System, Medicine, Evanston, USA; [3]Cleveland Clinic, Solid Tumour Oncology, Cleveland, USA; [4]Millennium Pharmaceuticals Inc., Molecular Medicine, Cambridge, USA; [5]Millennium Pharmaceuticals Inc., Oncology Clinical Research, Cambridge, USA; [6]Millennium Pharmaceuticals Inc., Biostatistics, Cambridge, USA; [7]USC Keck School of Medicine, Medicine, Beverly Hills, USA*

Background: CTC enumeration provides prognostic information in patients with metastatic prostate cancer. In particular, the categorical shift from ⩾5 to <5 cells per 7.5 mL of whole blood may represent a better predictor of overall survival than changes in prostate-specific antigen (PSA) levels. In a phase 1/2 study in chemotherapy-naïve patients with mCRPC (TAK-700_201, NCT00569153), the investigational 17,20-lyase inhibitor TAK-700 was well tolerated (the most common AE was fatigue) and resulted in profound reductions in circulating concentrations of testosterone and the adrenal androgen DHEA-S. PSA response rate (⩾50% decrease) at 12 weeks was observed in 52% of patients receiving TAK-700 at 400 mg BID plus prednisone. Here we report preliminary data on candidate biomarkers of response from this study.
Materials and Methods: Patients received oral TAK-700 at 100–600 mg BID, 400 or 600 mg BID plus prednisone 5 mg BID, or 600 mg QD. Blood samples were collected on a 28-day cycle (at baseline and on Day 1 of cycles 2, 4, and every 3 cycles thereafter) for evaluation of biomarkers of response to TAK-700. CTCs were enumerated using the CellSearch methodology.
Results: As of November 2010, CTCs could be enumerated in 99 (90%) of 110 patients enrolled in the study. CTC at baseline was ⩾5 in 43 (43%) patients and <5 in 56 (57%) patients. Of those with CTC ⩾5 at baseline, 21 (49%) achieved CTC <5 at follow-up. Overall, 31 (72%) patients with baseline CTC ⩾5 had a ⩾50% reduction in CTCs at follow-up. Of patients with CTC <5 at baseline, the majority (51, 91%) maintained CTC <5 at follow-up.
Conclusions: TAK-700 treatment resulted in CTC reductions in the majority of patients. Notably, approximately half of patients with CTC ⩾5 at baseline converted to CTC <5 with TAK-700 treatment. Correlation with other biomarkers of clinical outcome, including PSA response, will be presented. Patient follow-up is ongoing.
Funding: Millennium Pharmaceuticals, Inc.

7015 POSTER DISCUSSION

Fatigue Improvement/Reduction With Abiraterone Acetate in Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC) Post-docetaxel − Results From the COU-AA-301 Phase 3 Study

C.N. Sternberg[1], H.I. Scher[2], A. Molina[3], S. North[4], P. Mainwaring[5], Y. Hao[6], D. Gagnon[7], T. Kheoh[3], C.M. Haqq[3], J. de Bono[8]. *[1]San Camillo and Forlanini Hospitals, Department of Medical Oncology, Rome, Italy; [2]Memorial Sloan Kettering Cancer Center, Genitourinary Oncology Service, New York NY, USA; [3]OrthoBiotech Oncology Research & Development (A Unit of Cougar Biotechnology), Los Angeles CA, USA; [4]Cross Cancer Institute, Medical Oncology, Edmonton AB, Canada; [5]Haematology and Oncology Clinics of Australasia, Medical Oncology, Milton, Australia; [6]Johnson & Johnson Pharmaceutical Services, Global Strategic Marketing & Market Access, Raritan NJ, USA; [7]Thomson Reuters, Strategic Consulting Healthcare, Santa Barbara CA, USA; [8]The Institute for Cancer Research and Royal Marsden Hospital, Section of Medicine, Sutton, United Kingdom*

Background: Fatigue is a common, debilitating side effect of prostate cancer and its treatment, particularly androgen deprivation therapy.