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

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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

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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

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