increased in 74% patients. In 3 patients, an increase of preexisting anti-PSA antibody levels was measured. NK-cells showed a tendency for increased activation (CD25 and CD69). Individual patients had prolonged stabilization of PSA-levels after initial rises. One patient had a greater than 85% drop in his PSA-level.
Conclusions: CV9103 was safe and well-tolerated and displayed an unexpectedly high level of cellular immunogenicity.

7047 POSTER

A Phase I Pharmacodynamic Dose Escalation Study of Steroid Sulphatase Inhibitor Irosustat in Patients With Prostate Cancer

S. Denmeade[1], D. George[2], G. Liu[3], C. Peraire[4], A. Geniaux[4], F. Baton[4], T. Ali[4], E. Chetaille[4]. *[1]Johns Hopkins University, Oncology, Baltimore MD, USA; [2]Duke University, Oncology, Durham NC, USA; [3]University of Wisconsin, Oncology, Madison WI, USA; [4]Ipsen Innovation, Oncology, Les Ulis, France*

Background: The reservoir of inactive steroid hormones like DHEA-sulphate which are present at plasma concentrations up to 500 times higher than testosterone could potentially play an important role in intracrine androgen synthesis, by serving as a precursor source. Irosustat is an irreversible steroid sulphatase (STS) inhibitor blocking the hydrolysis of sulphated steroids to their biologically active forms.
Methods: A phase I dose escalation study was conducted in castration-resistant prostate cancer (CRPC), chemo-naïve patients with evidence of disease progression. The aim of the study was to evaluate the safety, tolerability and pharmacokinetic (PK) and pharmacodynamic (PD) profiles of irosustat (STS inhibition in peripheral blood mononuclear cells (PBMC), inhibition of Adiol, Adione, Testosterone (T) and ratio of DHEA: DHEAS in the plasma) after 28 days of daily oral administration. The steady-state PKs of irosustat were assessed in all patients. Plasma concentrations of androgens were determined pre-dose, and D28 by HPLC-MS/MS analysis. Six patients were recruited in each of 3 sequential cohorts (20, 40 and 60 mg).
Results: 17 patients were evaluable for safety, PK and PD assessment. Irosustat was well tolerated at all doses and there were no reports of drug related $\geqslant$ grade 3 adverse events. The most common toxicity was grade 1, 2 dry skin and itching observed in all 3 cohorts. Other toxicities included grade 1, 2 pain, headache, cramps and nausea. Irosustat exposure (AUC_{0-24}) increased with dose but proportionality was not seen at the highest concentration. Nearly complete STS enzyme inhibition was observed in the 3 patient cohorts from the first dose. Effect on hormone was similar between 40 and 60 mg cohorts but slightly better as compared to 20 mg. At 40 mg, mean Adiol reduction was −67.4% (range −84.5 to −51.0); T was −30.5% (range −75.5 to +18), DHEA was −52.5% (range −89.0 to +13.3) and DHEA: DHEAS ratio was decreased by 338% (range 4.3 to 472.7%).
Conclusion: Irosustat was well tolerated with dry skin as most common related adverse event and PD proof of concept was demonstrated with a full inhibition of STS enzyme leading to an increase of DHEAS and notable suppression of non sulphated androgens (DHEA, Adiol and testosterone) in CRPC patients with on-going androgen deprivation therapy.

7048 POSTER

Chemotherapy Use in Metastatic Castration Resistant Prostate Cancer (mCRPC) in the UK

R. Jones[1], S. Harland[2], D. Mazhar[3], N. James[4], M. Mason[5], K. Peperell[6]. *[1]Beatson West of Scotland Cancer Centre, Medical Oncology, Glasgow, United Kingdom; [2]University College Hospital, Medical Oncology, London, United Kingdom; [3]Addenbrookes Hospital, Medical Oncology, Cambridge, United Kingdom; [4]Queen Elizabeth Hospital, Medical Oncology, Birmingham, United Kingdom; [5]Velindre Cancer Centre, Medical Oncology, Cardiff, United Kingdom; [6]PH Associates, Independent Consultant, Marlow, United Kingdom*

Background: In the UK, NICE guidance (TA101, June 2006) endorsed the use of docetaxel in patients with prostate cancer who progress and become unresponsive to hormone treatment. There has been an increasing acceptance of the role of 2nd and subsequent line chemotherapy following docetaxel failure however until recently there has been a lack of evidence to guide choice of regimen. This evaluation aimed to describe current chemotherapy practice across a number of specialist cancer centres.
Material and Methods: A series of local service evaluations were undertaken in 5 UK NHS cancer centres. Appropriate approvals to conduct the evaluation in each centre were obtained. Data were sourced retrospectively from patients medical records and electronic hospital systems, from the start of chemotherapy for CRPC to the present time or death. Data were analysed and reported for each centre individually. There was no change to the management of patients for the purposes of any part of this review.
Results: A total of 111 patients with a mean age at diagnosis of between 67−72 yrs between centres were included. Patients were initiated on 1st line docetaxel between Nov 2006-Jan 2010.

Table: Outcome data by centre

Centre	No. pts	Mean no. cycles 1st line docetaxel	% (n) pts receiving 2nd line treatment	Median time (months)				
				Diagnosis of CRPC to initiation of 1st line docetaxel	Initiation of docetaxel to progression	Completion of 1st line to initiation of 2nd line	Initiation of docetaxel to death or end of observation period	% complete pathway (patient deceased)
1	22	7.91	41% (9)	3.33	7.67	4.11	12.88	95%
2	24	6.83	25% (6)	2.97	8.03	6.41	14.46	71%
3	22	4.91	9% (2)	2.33	6.57	6.55	21.86	64%
4	22	6.77	73% (16)	3.48	5.57	4.60	19.94	68%
5	21	6.52	52% (11)	2.78	7.16	8.51	22.51	86%

Overall 34% (n = 38) received 2nd line cytotoxic chemotherapy using a number of regimens including mitoxantrone, docetaxel, ECarboF (epirubicin, carboplatin, fluorouracil) and Carboplatin + etoposide. 13 patients (11.7%) received further chemotherapy following 2nd line. The median time from initiation of docetaxel to either death or date of data collection was 17.81 (in 77% of patients complete pathway was available at time of data capture).
Conclusions: There is agreement between healthcare professionals regarding management of patients up to the completion of 1st line docetaxel, but a disparity of clinical opinion regarding care beyond this. A viable percentage of patients are amenable to 2nd line cytotoxic chemotherapy. It will be important to understand how currently available chemotherapy agents are used in practice and their effectiveness to formulate future treatment paradigms as novel therapies become available. The advent of licensed and approved 2nd line therapies will provide an evidence base for future therapeutic decisions.

7049 POSTER

Management of Metastatic Castration-resistant Prostate Cancer (mCRPC) After an Initial Good Response to First-line Docetaxel (D) − a Retrospective Study on 270 Patients (pts)

S. Oudard[1], G. Kramer[2], L. Creppy[3], Y. Loriot[4], H. Steinbjoern[5], M. Holmberg[5], F. Rolland[6], J.P. Machiels[7], M. Krainer[2]. *[1]HEGP, Service Oncologie, Paris Cedex 15, France; [2]AKH University Hospital, Departement of Urology, Vienna, Austria; [3]CHU de Bordeaux, Departement of Oncology, Bordeaux, France; [4]Institut Gustave Roussy, Departement of Oncology, Villejuif, France; [5]Odense University Hospital, Departement of Oncology, Odense, Denmark; [6]Centre René Gauducheau, Departement of Oncology, St Herblain, France; [7]Cliniques Universitaires St Luc, Departement Oncology, Brussels, Belgium*

Background: To evaluate the potential benefit of reintroducing a docetaxel-based (D) chemotherapy versus a non-taxane based (NT) regimen in mCRPC pts who were good responders to a first-line treatment with D and subsequently progressed.
Material & Methods: Records of 270 consecutive mCRPC pts with good response to first-line D (PSA decrease $\geqslant$50% and/or objective clinical response) were retrospectively collected in 7 European countries (17 centers). Management at progression and outcomes (PSA response, clinical response and overall survival) were analyzed. Impact of selected variables on PSA response to D rechallenge was analyzed by multivariate logistic regression analysis with stepwise procedure.
Results: Median time from last D dose to progression was 6 months. At progression, 47 received NT (mainly mitoxantrone, 40%) and 223 were rechallenged with D [median 6 cycles (range 1−24)], either in monotherapy (82.5%) or combined with estramustine (15.2%) or other drugs (2.3%). Median overall survival was 18.2 months [95% CI: 16.1–22.0] with D and 16.8 months [95% CI 13.4–21.5] with NT (p=ns). PSA decrease $\geqslant$50% was more frequent with D (40.4%) than with NT (10.6%, $p < 0.001$). Clinical improvement (i.e. improved performance status and/or pain relief and/or reduced analgesic consumption) and stable disease were more frequently reported with D than with NT. However, efficacy of D and progression-free interval since last D dose decreased with subsequent rechallenges (table). In multivariate analysis, combination with estramustine (OR 3.8; 95% CI 2.1−6.8) and a progression-free interval >6 months (OR 2.89; 95% CI 1.3−6.3) predicted PSA response to D rechallenge.
Conclusion: This retrospective study suggests that a first D rechallenge in mCRPC pts well responding to first-line D therapy is associated with a greater biochemical and clinical response compared to a non-taxane regimen. However, D efficacy is decreasing with subsequent rechallenges.