Conclusions: Pts treated with both SU and SOR experienced high rates of tx modifications due to AEs. Further analysis is needed to understand the impact of these tx modifications on clinical outcomes. Results from this real-world clinical practice study suggest a need for more tolerable treatments for advanced RCC.

7134 POSTER

Updated Safety and Efficacy Results for Sunitinib From a Global, Expanded-Access Trial in Metastatic Renal Cell Carcinoma (mRCC)

M. Gore[1], C. Porta[2], S. Bracarda[3], L. Crinò[4], R. Hawkins[5], G. Bjarnason[6], S. Oudard[7], S.H. Lee[8], T.M. Kim[8], C. Szczylik[9]. [1]*The Royal Marsden Hospital NHS Trust, Cancer Medicine, London, United Kingdom;* [2]*IRCCS San Matteo University Hospital Foundation, Medical Oncology, Pavia, Italy;* [3]*Ospedale San Donato, Medical Oncology, Arezzo, Italy;* [4]*Azienda Ospedaliera di Perugia, Medical Division, Perugia, Italy;* [5]*Christie Hospital NHS Trust, Medical Oncology, Manchester, United Kingdom;* [6]*Sunnybrook Odette Cancer Centre, Medical Oncology, Toronto, Canada;* [7]*Hôpital Européen Georges Pompidou, Medical Oncology, Paris, France;* [8]*Seoul National University Hospital, Internal Medicine, Seoul, Korea;* [9]*Military Medical Institute, Oncology, Warsaw, Poland*

Background: Sunitinib demonstrated a manageable safety profile and encouraging efficacy in an expanded-access trial (ClinicalTrials.gov, NCT00130897; Pfizer) in which it was provided to trial-ineligible patients (pts) with mRCC in countries where regulatory approval had not yet been granted (Gore et al, 2009). We sought to evaluate whether the demonstrated efficacy and safety was consistent with extended follow-up.
Methods: Pts aged ⩾18 years with treatment-naïve or previously treated mRCC received oral sunitinib on the approved 50 mg/day 4-week-on/2-week-off schedule. Eligibility criteria were minimized to broaden the trial population. Safety was assessed regularly and tumour measurements were done as per local standard practice using RECIST-defined response. Analyses included all pts who received ⩾1 dose of sunitinib.
Results: As of March 2011, 4,572 pts were enrolled of whom 4,533 had received treatment, including 7% with brain metastases, 14% Eastern Co-operative Oncology Group performance status (ECOG PS) ⩾2, 12% non-clear cell RCC, and 33% aged ⩾65 years; traditionally poorer prognosis pts. Median treatment duration was 7.6 months; treatment was ongoing in 169 pts (4%). 4,084 pts (90%) had discontinued, reasons for which included lack of efficacy (34%), death (24%) and adverse events (13%). The most common treatment-related adverse events of any grade were diarrhea (47%), fatigue (40%), nausea (36%), decreased appetite (31%), mucosal inflammation (29%), stomatitis (28%), hand–foot syndrome and vomiting (both 27%), dysgeusia (25%), hypertension (24%), thrombocytopenia (23%) and asthenia (22%). The most common treatment-related grade 3/4 adverse events were fatigue (9%), thrombocytopenia (8%), hand–foot syndrome and asthenia (both 7%), hypertension and neutropenia (both 6%), and diarrhea (5%). In 3,361 evaluable pts, the overall objective response rate (ORR) was 19% (n = 651) with subgroup ORR as follows: baseline brain metastases (30 of 218 [14%]), ECOG PS ⩾2 (33 of 309 [11%]), non-clear cell RCC (41 of 374 [11%]), and age ⩾65 years (188 of 1,031 [18%]). Overall median progression-free survival was 9.7 months (95% CI: 9.1, 10.4) and overall survival was 18.4 months (95% CI: 17.4, 19.4).
Conclusions: The results from this large expanded-access trial in mRCC in a real-world setting confirm the safety and efficacy of sunitinib in a broad population. The sunitinib adverse event profile was manageable and consistent with that previously reported.

7135 POSTER

Treatment of Metastatic Renal Cancer With High-dose Interleukin-2 After Targeted Therapy Can Be Given Safely and Can Produce High Rates of Response Including Complete Remissions

R. Hawkins[1], K. Sikand[2], J. Shanks[2]. [1]*Christie Hospital NHS Trust, Medical Oncology, Manchester, United Kingdom;* [2]*Christie Hospital NHS Trust, Pathology, Manchester, United Kingdom*

Background: High-Dose Interelukin-2 (HD IL2) remains a good option for treatment of metastatic renal cancer. As a first-line treatment, in carefully selected patients, it can produce high rates of response (response rate 50%) with around 50% of these being complete remissions (Shablak A et al., J Immunotherapy 2011, 34(1): 107–122). Its use after targeted therapies is controversial and there are reports of increased toxicity, particularly an increased incidence of cardiovascular toxicity (and possibly a reduced response rate (Cho DC et al., J Immunotherapy 2009, 32(2): 181–520).
Methods: Here we present the outcomes of six patients treated with first-line immunotherapy with HD-IL2 after targeted therapy. Four had been treated with sunitinib alone and two had been treated with the sequence sunitinib followed by sorafenib and then everolimus. The histological characteristics of the tumours all fitted into the "favourable" group as defined previously by us and all had high levels of expression of CAIX (>80%). All had a satisfactory baseline stress echo and all had an interval of at least 8 weeks from last dose on TKI to start of HD-IL2. The patients ranged from 42 to 65, all had only one or two organ sites of disease and all were ECOG PS 0/1.
Results: Toxicity is indistinguishable from that of patients without prior treatment and no patient needed inotropic support or admission to intensive care. The number of doses given per cycle was also similar to that in unpretreated patients. Overall the response rates are excellent − 4/6 have had RECIST defined response. Three of these are complete remissions and the fourth is in complete remission after surgical resection of residual disease. The current duration of follow-up is relatively short but to date no responding patient has progressed with follow up of 15+, 12+, 12+, 10+ months. The responses have been particularly striking following treatment with multiple drugs with both patients being in complete remission.
Conclusions: Overall, HD IL2 is a viable and effective salvage treatment in carefully selected renal cancer patients who have previously failed treatment with targeted therapy. Updated results will be presented.

7136 POSTER

The Association Between Treatment (tx) Modifications Due to Adverse Events (AEs) and Overall Survival (OS) in Patients (pts) With Advanced Renal Cell Carcinoma (RCC) Treated With Sunitinib and Sorafenib: Results From a Multi-country Study in Europe

S. Oudard[1], C. Porta[2], D. Castellano[3], R. McDermott[4], P. Nathan[5], J. McCaffrey[6], M.P. Neary[7], C. Korves[8], E. Dial Suthoff[8], M.S. Duh[8]. [1]*Hôpital Européen Georges Pompidou, Medical Oncology, Paris, France;* [2]*IRCCS San Matteo University Hospital Foundation, Internal Medicine and Medical Oncology, Pavia, Italy;* [3]*Hospital 12 de Octubre, Medical Oncology, Madrid, Spain;* [4]*Adelaide & Meath Hospital, Medical Oncology, Dublin, Ireland;* [5]*Mount Vernon Cancer Centre, Medical Oncology, Middlesex, United Kingdom;* [6]*Mater Misericordiae Hospital, Medical Oncology, Dublin, Ireland;* [7]*GlaxoSmithKline, Global Health Outcomes Oncology, Collegeville, USA;* [8]*Analysis Group Inc., Healthcare, Boston, USA*

Background: Tx modifications due to AEs are frequent among advanced RCC pts treated with angiogenesis inhibitors. This study evaluates the association of these changes with OS among advanced RCC pts in European clinical practice.
Materials and Methods: Medical records, not part of a disease-based registry, from 542 adult pts with advanced RCC who received sunitinib [SU] (N = 409) or sorafenib [SOR] (N = 133) as first anti-angiogenesis tx from 1/1/2005 to 9/15/2010 were reviewed at 11 large oncology centers in France, Ireland, Italy, UK and Spain. Tx changes were defined as pts having experienced SU or SOR tx discontinuation, interruption or dose reduction due to an AE. Cox proportional hazards (PH) model and a landmark analysis (at 24 weeks; 30 weeks in a sensitivity analysis) were used to evaluate survival differences between pts with and without tx change due to AE. Landmark analysis was corrected for the "guarantee time" bias, a false-positive association between tx changes and longer survival. Each model was adjusted for age, gender, number metastatic sites, country, prior immunotherapy, AE during landmark period, time from RCC diagnosis to tx initiation; each model was adjusted to meet the PH assumption. Adjusted hazard ratio (HR) of death for pts with vs without tx change due to AEs were determined.

SU (n = 309)		SOR (n = 113)	
Tx change due to AE	$HR_{adjusted}$ (95% CI)	Tx change due to AE	$HR_{adjusted}$ (95% CI)
Discontinuation yes(y) = 15, no(n) = 294	3.44 (1.42–8.34)	Discontinuation y = 4, n = 109	Not estimable
Reduction y = 78, n = 231	0.96 (0.60–1.55)	Reduction y = 14, n = 99	2.13 (0.80–5.62)
Interruption y = 58, n = 251	1.42 (0.90–2.23)	Interruption y = 21, n = 92	2.56 (1.07–6.12)
Any change y = 112, n = 197	1.31 (0.86–2.00)	Any change y = 31, n = 82	2.94 (1.39–6.24)

Results: 309 SU and 113 SOR pts who did not have death/censor before the landmark period were eligible for analysis; of them, 112 and 31, respectively, had a tx change due to AE during the landmark period. For the more common AEs such as fatigue, diarrhea, nausea, hand foot syndrome, mucositis/stomatitis and skin rash, the majority were reported as possibly/probably treatment-related. In general, tx changes due to AE had negative impact on OS. For SU (Table), there was a strong and statistically significant association between tx discontinuation and OS. Analysis of discontinuation was not conducted for SOR due to limited data. For SOR,