7107 ORAL

A randomized, prospective, Phase 2 study, with Sorafenib (So) and Interleukin-2 (IL-2) versus So alone as first line treatment in advanced Renal Cell Cancer (RCC): ROSORC Trial

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Background: So is an oral tyrosine kinase inhibitor that represents a significant improvement in the treatment of metastatic RCC, a malignancy arising from the proximal renal tubular epithelium in both a sporadic (nonhereditary) and a hereditary form. IL-2 is a pleiotropic cytokine with an antitumoral activity dependent on dose and schedule. The different mechanism of action and the possible therapeutic synergistic effects of So and IL-2 represented the rational for this study.
Material and Methods: In this multicenter, randomized, open label, Phase 2 study 128 patients (pts) with previously untreated metastatic RCC were randomized to receive So given orally at 400 mg twice daily continuously plus IL-2, 4.5 MIU beginning day 1 for 5 day/week, for 6 weeks every 8 weeks (arm A), or So alone (arm B) at the same dosage. Therapy continued until progression of disease or unacceptable toxicity. The primary end point was the progression free survival (PFS) and the secondary endpoints were the overall survival, response rate and safety profile in both arms. Eligible pts had cito-histological diagnosis of RCC, good performance status (ECOG PS 0–2), no brain metastases or previous systemic treatment for metastatic disease, measurable disease as per RECIST criteria and every MSKCC score. To ensure balance between arms with respect to center, MSKCC score and histology, the minimization method was applied for patient's assignment to either of the two arms.
Results: All the expected cases were enrolled from October 2006 to February 2008. Response rate (all partial responses, PR) was 23% and 10% in arm A and B respectively. Overall disease control rate (PR+ stable disease, SD) was 81 % versus 74% in favour of the combined treatment. Tumour shrinkage was reported in 52% and 34% in arm A and B respectively. Median and 1-year PFS was 38 weeks (interquartile range 18–70) and 35% for So+IL-2 and 30 weeks (range 15–65) and 30% for So alone (one-sided Log-rank test $p = 0.216$). The most common observed adverse events (AEs) were asthenia, hand foot syndrome, hypertension, fever, diarrhoea, mucositis, rash, nausea and vomiting. Usually the side effects were low or moderate in severity. Grade 3–4 AEs were reported in 30% and 20% in arm A and B respectively.
Conclusion: The safety and efficacy data suggest that the association So+IL-2 is safe and feasible and improves, disease control rate and PFS compared to So alone.

Poster discussion presentations
(Wed, 23 Sep, 11:15–12:15)
Genitourinary malignancies – Renal cancer

7108 POSTER DISCUSSION

Phase II study of IMC-1121B in patients with metastatic renal cell carcinoma (mRCC) following failure of VEGFR-2 tyrosine kinase inhibitor (TKI) therapy: interim results (IMCL CP12–0605/NCT00515697)

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Background: VEGF inhibitors represent an effective front-line treatment option for patients (pts) with clear cell mRCC. Despite of their encouraging activity, their use is limited by adverse events (AEs) and development of refractory disease. IMC-1121B is a fully human IgG_1 monoclonal antibody to the VEGF receptor-2 (VEGFR-2) that blocks VEGF ligand binding and confers potent anti-cancer activity in multiple preclinical models. The target specificity, potency and phase 1 tolerability of IMC-1121B provided a rationale for this phase 2 multi-institutional study in pts with TKI-refractory mRCC.
Methods: Pts with disease progression (PD) or intolerance to either sorafenib, sunitinib or both, predominant clear cell histology, ECOG PS 0–1, prior nephrectomy and preserved organ and bone marrow function were eligible. The primary endpoint was overall response rate (ORR), based on the alternate hypothesis that ORR is >15% vs. <3%. Secondary endpoints included progression-free survival (PFS), pharmacokinetics and safety. Pts received IMC-1121B, 8 mg/kg IV every 2 weeks; tumor assessments were performed every 6 weeks.
Results: Forty pts have enrolled (median age 60); 28 (70%) received one prior TKI; 12 (30%) received multiple TKIs. Thirty-nine pts received IMC-1121B. This preliminary analysis includes data from 27 pts treated as of January 1, 2009 (11 of whom remain on study). To date, at least 2 confirmed PRs have been observed. Seventeen pts (63%) had stable disease lasting $\geqslant$4 months (m). The median time-to-progression (TTP) is 5 m. To date, three pts have received therapy without PD for $\geqslant$ 12m. The most common observed adverse events (AEs) for the entire cohort of 40 pts were of mild-to-moderate intensity and included headache, fatigue, rhinitis, cough, dyspnea, and edema; none of these occurred in >25% pts. Two pts experienced grade (G) 2 proteinuria in conjunction with an unrelated G3 UTI and a G2 hemoptysis in a pt with known endobronchial metastases. Five G3 AEs were noted in 4 pts. One (fatigue) was considered drug related and the remaining 4 (motor neuropathy, fatigue, dyspnea and back pain) were considered unlikely related or unrelated. No G4 AEs have been reported to date.
Conclusions: Preliminary results suggest that second-line treatment with IMC-1121B is well tolerated and has clinical activity in TKI-refractory mRCC patients. The safety and clinical activity observed with IMC-1121B in mRCC is promising and warrants further investigation.

7109 POSTER DISCUSSION

Phase 2 results of ABT-869 treatment in patients with advanced renal cell cancer (RCC) after sunitinib failure

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Background: ABT-869 is a novel, orally active and potent inhibitor of all VEGF and PDGF receptor tyrosine kinases. Phase 1 study results suggested antitumor activity in advanced solid tumors including RCC. Phase 2 recommended dose was 0.25 mg/kg (maximum 25 mg) daily.
Materials and Methods: We conducted an open-label, multicenter phase 2 trial of oral ABT-869 in advanced RCC. Patient eligibility criteria included progressive disease (PD) within 100 days of enrollment after at least 2 cycles of sunitinib, prior nephrectomy, and adequate organ function. The primary endpoint was ORR per RECIST by central imaging. Secondary endpoints were progression free survival (PFS), overall survival (OS), and time to disease progression (TTP). Safety was assessed by NCI-CTCAE, v3.0. Trial abbreviation: *ABT-869 in Subjects With Advanced RCC, Previously Treated With Sunitinib*. Trial registry: NCT00486538. Trial status: ongoing; not recruiting; sponsored by Abbott Laboratories. ABT-869 is being developed in collaboration with Genentech.
Results: Of the 53 patients, enrolled from 8/07 to 10/08, all were previously treated with sunitinib. Additional prior treatments included cytokine (23%), sorafenib (19%), temsirolimus (4%), and bevacizumab (17%). Median age was 61 y [range, 40–80]; 43 (81%) patients had clear-cell histology; and median number of prior therapies was 2 [range, 1–4]). Best response to prior sunitinib was 13.2%. For 53 patients with baseline CT data per central imaging, ORR was 9.4% and median [95% CI] PFS was 5.4 mos [3.6, 6.3]. Median [95% CI] TTP was 5.4 mos [3.6, 6.3], and OS 11.6 mos [10.1, NR]. The most common adverse events (AEs) were diarrhea (72%), fatigue (72%), hypertension (57%), nausea (53%) and anorexia (40%). Grade 3/4 AEs included hypertension (28%), fatigue (19%), diarrhea (17%) and hand-foot syndrome (17%). Dose reductions were required for 31 patients. The most common reasons for dose reduction were hypertension (13%), fatigue (13%), and hand-foot syndrome (11%), which were reversible. 15 patients remained on study at the time of the analysis. 30 patients had discontinued due to PD (clinical, radiographic or AE related to PD), 7 due to AEs not related to PD, and 1 for other reasons. There were no deaths due to treatment-related AEs.
Conclusions: ABT-869 demonstrated antitumor activity in RCC after sunitinib failure. The dose will be optimized for future studies.