7110 POSTER DISCUSSION

Efficacy and safety of AMG 102 in patients with advanced renal cell carcinoma (RCC)

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Background: AMG 102 is an investigational, fully human monoclonal antibody to hepatocyte growth factor (HGF) that prevents HGF from binding to the c-Met receptor thus inhibiting downstream signaling. This Amgen-sponsored, open-label, 2-stage, phase 2 study (ClinicalTrials.gov ID: NCT00422019) evaluated AMG 102 monotherapy in patients (pts) with advanced RCC. The primary endpoint was overall response rate (ORR); secondary endpoints included progression-free survival (PFS), safety, and biomarkers.
Patients and Methods: Eligible pts were ⩾18, ECOG 0−2, had measurable disease, no CNS metastases, and were unable to receive or failed prior therapy with anti-VEGF(R) agents. AMG 102 was administered at 10 or 20 mg/kg IV every 2 weeks (Q2W). Up to 20 pts were to receive 10 mg/kg AMG 102; if ⩾1 had a confirmed ⩾25% reduction from baseline in sum of longest diameter of all measurable lesions (minor response) after 8 weeks (wk) of treatment, up to 20 additional pts would receive 10 mg/kg AMG 102. If there were <5 responses in these 40 pts, up to 20 additional pts would receive 20 mg/kg with an additional 20 pts at this dose if ⩾1 pt had a minor response after 8 wk; in the absence of ⩾1 minor response, accrual was to be discontinued. CT or MRI for RECIST-based response assessment was performed every 8 wk. Tumor c-Met and levels of circulating total HGF and soluble (s)c-Met were assessed in pt samples.
Results: As of Dec08, 61 pts received ⩾1 dose of AMG 102 (10 mg/kg = 40; 20 mg/kg = 21). Pt characteristics: men, 70%; median (range) age, 59 (39−84) years; ECOG, 0 = 48%, 1 = 38%, 2 = 15%; histology, 74% clear cell, 11% papillary, 15% other; prior anti-cancer therapy, 92% (anti-angiogenic, 88%); mean (range) prior anti-cancer therapies, 2.4 (0−5). Forty-nine pts ended treatment (30 progressive disease, 8 adverse events, 11 other reasons). One of 61 pts had a partial response (clear cell RCC at 10 mg/kg); ORR=1.6% (95% CI, 0−9%). Fifteen of 61 patients had stable disease ⩾32 wk (range 32−79+ wk). There was no minor response in the first 20 mg/kg cohort, thus accrual was halted (per protocol-defined criteria). Median PFS (all pts) was 3.4 months (95% CI: 1.9−5.8). Forty pts (66%) had AMG 102-related adverse events; the most common were edema (26%, 5 with grade 3), fatigue (23%), nausea (18%), anorexia (11%), and rash (10%). Total HGF and sc-Met increased after AMG 102 dosing; tumor c-Met will be presented.
Conclusions: AMG 102 appeared to be well tolerated in RCC. Although the study did not achieve the target ORR, the long-term disease stability in 15/61 pts suggests disease-stabilizing activity of AMG102 in a subset of RCC pts.

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Evaluation of 18FDG PET/CT in the detection of recurrence of renal carcinoma

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Aim: To assess the diagnostic validity of ^{18}FDG PET/CT in the detection of recurrence of renal carcinoma.
Patients and Methods: This is a retrospective study concerning 36 patients (pts) – 30 male and 6 female – with renal carcinoma aged 38−83 (mean age: 63.9 years) referred to our hospital with the indication of possible relapse from February 2007 to February 2009. All patients underwent surgery for resection of the primary tumor and the diagnosis had been histological confirmed by surgical specimen. 30 pts had equivocal CT findings indicating relapse, 5 pts had equivocal MRI findings while 1 pt had both MRI and CT suspicious for relapse findings. ^{18}FDG PET/CT was done at least 30 days after chemotherapy and 12 weeks after radiotherapy. All scans were reviewed by two expert physician's one nuclear medicine physician and one radiologist.
Results: PET/CT examination was positive in 24/36 (66.7%) cases. In 16 (44.4%) patients PET/CT examination revealed more advanced disease than that of conventional imaging methods, leading to therapeutic change. In 8 (22.2%) patients PET/CT results were the same than that of conventional imaging modalities. The results were in concordance with MRI findings in 2 cases and CT findings in 6 cases. PET/CT examination was negative in 12/36 (33.3%) patients excluding recurrence despite the suspicious findings of CT or MRI. 2 (5.5%) patients had adrenal adenoma, 3 (8.3%) patients had benign pulmonary nodules, 4 (11.1%) patients loco regional fibrosis and 3 (8.3%) patients had equivocal CT.
Conclusions: ^{18}FDG PET/CT seems to be a reliable imaging modality for the detection of recurrence of renal carcinoma diagnosing accurately tumor extension, lymph nodes involvement and distant metastases. PET/CT provides further information for the extent of disease compare to CT and MRI, having a crucial influence on therapy management.

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CT response assessment combining reduction in size and arterial enhancement correlates with time to progression in metastatic renal cancer patients treated with TKIs

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Background: Objective assessment of treatment response is critical in evaluating the effectiveness of any therapy. Targeted therapy is now the standard of care in advanced Renal Carcinoma (RCC). Response assessment by RECIST criteria is insensitive as treated tumours often have only a modest change in size despite the induction of significant necrosis and size change does not correlate with time to progression (TTP). The Choi criteria, (10% size reduction or 15% contrast enhancement reduction) is routinely used in the assessment of GIST tumours treated with targeted agents. Here we report the use of combined size and density assessment in RCC metastases using arterial phase contrast CT scans in patients treated with either sunitinib or cediranib.
Materials and Methods Scans from 20 evaluable patients at baseline and 12 weeks on treatment were assessed using RECIST, Choi, and modified criteria in which both a 10% decrease in size and 15% decrease in enhancement in the arterial phase were required to define a response (PR). Response assessment was performed using each of the three methods. Patients were allocated into PR or SD groups and correlated with time to disease progression (itself RECIST defined). Median TTP with 95% confidence interval was estimated with Kaplan-Meier analysis and the significance of the difference obtained in TTP between different response groups was calculated with the log rank p test.
Results: Responses defined by modified criteria successfully identified patients who had long or short clinical benefit (TTP medians: PR 448 and SD 85 days, log rank p value 0.027).
The differences in median TTP between Partial Response (PR) and Stable Disease (SD) groups defined by RECIST (168 and 428 days respectively) and Choi criteria (399 and 260 days respectively) were not significant (log rank p test 0.316 and 0.273 for RECIST and Choi criteria respectively).
Conclusion: A combined reduction in both size and arterial phase enhancement of RCC metastases treated with TKIs significantly correlated with time to progression. RECIST and standard Choi criteria were inferior. Modified response assessment potentially enables the identification of patients with advanced RCC who will and will not derive significant clinical benefit from treatment with TKIs.

7113 POSTER DISCUSSION

Radiographic findings of drug-induced pneumonitis and clinical correlation in patients with advanced renal cell carcinoma treated with temsirolimus

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Background: Temsirolimus (TEMSR) is approved in Europe for the first-line treatment of patients (pts) with advanced renal cell carcinoma (advRCC) who have at least 3 of 6 poor-prognostic risk factors. In a phase 3 study, pts with previously untreated, poor-prognosis advRCC who received TEMSR had longer overall survival than those who received interferon-alfa (IFN, p = 0.008, Hudes et al. N Engl J Med 356:2271). Four pts treated