**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.

**7111** POSTER DISCUSSION

**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.

**7112** POSTER DISCUSSION

**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

with TEMSR developed pneumonitis compared with one treated with IFN (Bellmunt et al. Ann Oncol 19:1387). In a retrospective review of pts with endometrial carcinoma or neuroendocrine tumors treated with TEMSR, 36% (8/22) had radiographic abnormalities consistent with drug-induced pneumonitis (DIP) and 50% (4/8) of them were asymptomatic (Duran et al. Eur J Cancer 42:1875). Therefore, we performed a retrospective review of the phase 3 pts to examine the association between treatment and development of radiographic findings consistent with DIP.
**Materials and Methods:** Patients were required to have chest radiographic evaluations every 8 wk. To be evaluable for this analysis, pts had to have chest CT images at baseline, without radiographic evidence of pneumonitis, and at least one post-baseline examination. An independent, blinded radiographic review of sequential CT images was conducted. A pt was determined to have developed DIP if CT images showed changes consistent with pneumonitis and not pneumonia or disease progression, based on correlation with clinical data, including adverse events occurring between 8 wk prior to and 4 wk after the onset of radiographic changes.
**Results:** Of 178 evaluable pts in the TEMSR group, 52 (29%) developed DIP. Of 138 evaluable pts in the IFN group, 8 (6%) developed DIP (chi-square $p < 0.0001$ for the difference between treatments). Most TEMSR-treated pts who developed radiographic changes consistent with DIP did so within the first 8 wk of treatment (31/52, 60%), and 31% (16/52) had associated respiratory symptoms around onset of DIP. The most common were dyspnea (6 pts) and increased cough (8 pts). One pt who developed radiographic changes consistent with DIP discontinued TEMSR treatment.
**Conclusions:** DIP occurred in 29% (52/178) of poor-prognosis advRCC pts treated with TEMSR who were evaluable for this analysis; 9% (16/178) had associated respiratory symptoms. Pts with TEMSR-related DIP, based on radiographic findings, should be monitored closely and their clinical management should be altered only if clinical symptoms develop.
Study NCT00065468 was sponsored by Wyeth Pharmaceuticals.

**7114** POSTER DISCUSSION

**Interstitial pneumonitis during RAD-001 treatment: incidence by blinded radiological analysis**

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**Background:** Everolimus (RAD001) is an oral inhibitor of the mammalian target of rapamycin (mTOR), approved for metastatic renal cell carcinoma (mRCC). This targeted agent is currently under trial in a various range of cancers. Clinical pneumonitis have been previously reported with mTOR inhibitors.
**Objectives:** i) Determine the incidence and features of pulmonary radiological changes occurring on RAD001, and ii Determine the predictive value of this pneumonitis on progression free survival (PFS).
**Methods:** We performed a retrospective analysis of patients (pts) with advanced renal cell carcinoma (mRCC) included in the randomized, double-blind, RECORD 1 trial at Gustave Roussy Institute. Patients with mRCC were randomised (2/1) between RAD001 (10 mg per day) and placebo. Patient follow-up was performed by CT-scans at baseline and every 8 weeks. All patients had pulmonary function tests (PFT) and carbon monoxyde diffusing capacity (DLCO) measurements before inclusion. If progressive disease occurred, treatment was unblinded, and placebo pts could switch to RAD001. All CT-scans were retrospectively reviewed, in a blinded manner, by one independent thoracic senior radiologist (CC), in order to detect interstitial changes at first evaluation (8 weeks).
**Results:** Forty one pts were randomised in our site, 28 pts in the RAD001 arm vs 13 pts in the placebo arm. Interstitial changes were detected in 13 out of 28 patients (46 %) on first CT-scan vs 1 pt of 13 in the placebo arm ($p = 0.03$). All 13 pts in the placebo arm further received RAD001 and 11 were assessable by CT-scan after cross over: 5 pts developed interstitial changes at first evaluation under RAD001. Main radiological features were bilateral patchy ground-glass opacities and reticular interlobular pattern. Only 3 of the 18 pts with radiological changes had pulmonary symptoms, one of these 3 was documented with bacterial infection, the 2 others had no fever and were resolutive. No dose reduction was related to pneumonitis in the 18 pts. Eight (44%) of the pts who developed radiological interstitial pneumonitis had restrictive or obstructive patterns at baseline PFT vs 20% among the treated patients without interstitial pneumonitis (ns). DLCO evaluation at baseline was similar in the 2 groups. Metastatic pulmonary involvement at baseline was similar in patient with and without radiological changes. Median PFS was 7.3 vs 5.5 months in pts with radiological changes vs no change ($p = ns$).
**Conclusion:** RAD001 treatment is associated with interstitial radiological pneumonitis in about 45% of patients with mRCC at 8 weeks in this trial. This radiological pneumonitis did not interfere with treatment continuation. Whether the occurrence of pneumonitis is associated with improved efficacy should be considered in future studies.

**7115** POSTER DISCUSSION

**Prognostic value of cyclooxygenase-1 and cyclooxygenase-2 expressions in human renal cell carcinoma**

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**Background:** The two isoforms of cyclooxygenase (COX), COX-1 and COX-2, play an important role in tumor cell proliferation, resistance to apoptosis, angiogenesis, and metastasis in various malignant tumors. However, the clinical significance of COX-1 and COX-2 expressions in kidney cancer remain controversial. We investigated the impact of COX-1 and COX-2 expressions on cancer-specific survival and cancer-free survival as well as their relationships with other clinicopathological features in patients with renal cell carcinoma (RCC).
**Material and Methods:** We analyzed using immunohistochemistry (IHC) COX-1, COX-2, Ki-67, p53, p27, p21, and Bcl-2 expressions on paraffin-embedded tumor tissues from 422 patients who underwent nephrectomy for RCC at the university hospitals of Quebec.
**Results:** COX-1 IHC positive expression was detected in 65% of the tumors whereas COX-2 was overexpressed in 62% of the tumors. COX-2 overexpression correlated with an older age (odds ratio (OR) = 1.02, $p = 0.01$), an increased TNM pathological stage (OR=1.57, $p < 0.0001$), as well as a higher nuclear grade. COX-2 overexpression was significantly more common in papillary and chromophobe carcinomas than in conventional clear cell RCC (OR = 2.54, $p = 0.003$; and OR = 6.48, $p = 0.002$ respectively). COX-2 overexpression also correlated with the Ki-67 (OR = 1.55, $p = 0.0002$), p53 (OR = 1.11, $p = 0.0012$) and Bcl-2 (OR = 0.89, $p = 0.01$) IHC expressions. On the contrary, COX-1 positive IHC expression inversely correlated with the Ki-67 proliferating index (OR = 0.85, $p = 0.03$). None of the clinicopathological variables and other biomarker expressions studied were associated with COX-1 expression. Univariate cancer-specific survival analyses showed that while COX-1 positive expression was associated with a protective effect on death rate (Hazard ratio (HR) = 0.42, $p = 0.007$), COX-2 IHC expression exhibited a worse prognostic effect (HR=3.49, $p \leqslant 0.0001$, respectively). COX-1 positive expression tended to show a protective effect in cancer-free survival though not statistically significant (HR = 0.71, $p = 0.13$) unlike for COX-2 overexpression (HR = 2.10, $p = 0.007$). Multivariate cancer-specific survival analyses showed that only COX-1 IHC expression was an independent prognostic factor after adjustment on age, TNM stage, Furhman nuclear grade, and the histological tumor types (HR = 0.48, $p = 0.025$).
**Conclusions:** Whereas new drugs targeting the COX-2 isoform are being developed for cancer therapy, our study suggests that the specific role of COX-1 in RCC should be further investigated.

**7116** POSTER DISCUSSION

**Expression of fibroblast growth factor receptors 1 and 2 in renal cell carcinoma (RCC)**

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**Background:** FGF/FGFR pathway could be an independent compensatory mechanism driving angiogenesis in the setting of VEGFR blockade in metastatic RCC patients. Membrane antigens like FGFR expressed in RCC are attractive targets for new therapeutic and diagnostic applications. Present study was performed to evaluate expression of FGFR1 and 2 in RCC.
**Materials and Methods:** Formalin-fixed, paraffin-embedded specimens of removed 100 primary tumors and 40 metastatic lymph nodes from untreated 140 RCC patients were evaluated by immunohistochemistry with anti-FGFR1 and anti-FGFR2 antibodies. Extent of FGFR expression was compared with 40 specimens of normal human tissue of kidney (selected from the surgical diagnostic files). Significant difference in immunoexpression of FGFR among these groups was assessed by Chi Square Fisher's Exact test utilizing semi-quantitative scoring system on