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.
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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