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

L. Albiges[1], C. Caramella[2], C. Ferte[1], C. Massard[1], M. Gross-Goupil[1], B. Besse[1], P. Girard[3], J.C. Soria[1], B. Escudier[1]. *[1]Institut Gustave Roussy, Department of Medical Oncology, Villejuif, France; [2]Institut Gustave Roussy, Department of Diagnostic Radiology, Villejuif, France; [3]Institut Mutualiste Montsouris, Department of Pneumology, Paris, France*

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

N. Andreu[1], F. Meyer[2], G. Le Teuff[3], L. Lacombe[4], Y. Fradet[4], B. Tetu[5]. *[1]CHRU Hotel Dieu, Medical informatics, Angers, France; [2]Laval University Cancer Research Center, Epidemiology, Quebec, Canada; [3]Keyrus Biopharma, Biometrics, Levallois Perret, France; [4]Laval University Cancer Research Center, Urology, Quebec, Canada; [5]Laval University Cancer Research Center, Pathology, Quebec, Canada*

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)

I. Tsimafeyeu[1], L. Demidov[2], E. Stepanova[3], T. Hung[4]. *[1]Kidney Cancer Research Bureau, Russian Office, Moscow, Russian Federation; [2]N.N. Blokhin Russian Cancer Research Center, Department of Biotherapy, Moscow, Russian Federation; [3]N.N. Blokhin Russian Cancer Research Center, Institute for Experimental Diagnostic and Therapy of Cancers, Moscow, Russian Federation; [4]University of Toronto, Department of Medicine, Toronto, Canada*

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

extent of stained cells and intensity of corresponding immunostained cells; 0+ to 3+.
Results: Expression of FGFR1 was observed in 98% (98/100) of primary renal tumors and in 82.5% (33/40) of lymph node metastases. Intensity was 3+ in all cases. Nuclear expression of FGFR1 was found in 68% (95/140). FGFR2 staining was seen in 4% (4/100) of primary tumors and in 5% (2/40) of lymph node metastases. FGFR2 was expressed in RCC of non-clear cell histology. Expression of FGFR1 was significant lower in the normal tissue of kidney ($P < 0.01$) and was detected in 2.5% of cases (1/40); no FGFR2 expression was found.
Conclusions: In this study we have shown for the first time that FGFR1 is highly expressed in RCC patients. FGFR1 is an interesting alternative target as it can be targeted relatively easy. Human monoclonal antibodies IO-1/IO-2 for therapy and imaging in RCC patients were developed.

7117 POSTER DISCUSSION

Do circulating tumor cells (CTCs) correlate with response to first-line sunitinib in metastatic renal carcinoma?

U. Basso[1], E. Rossi[2], S. Indraccolo[2], C. Barile[3], T. Sava[4], M. Aieta[5], A. Brunello[1], A. Jirillo[1], A. Amadori[2], R. Zamarchi[2]. *[1]Istituto Oncologico Veneto IOV-IRCCS, Medical Oncology, Padova, Italy; [2]Istituto Oncologico Veneto IOV-IRCCS, Immunology and Molecular Diagnostics, Padova, Italy; [3]Santa Maria della Misericordia Hospital, Medical Oncology, Rovigo, Italy; [4]Ospedale Civile Maggiore, Medical Oncology, Verona, Italy; [5]Centro Riferimento Oncologico della Basilicata, Medical Oncology, Rionero in Vulture-Potenza, Italy*

Background: Circulating tumor cells (CTCs) are frequently present in pts with different types of epithelial cancer, and low values before and during cytotoxic chemotherapy are an independent predictor of longer progression-free and overall survival in pts with metastatic breast and colorectal carcinoma. First-line Sunitinib obtains radiological responses and improves survival in pts with metastatic renal cancer, but no predictive markers of activity are currently available. Recent data have provocatively shown that sunitinib may increase systemic diffusion of tumor cells in pre-clinical models [Paez-Ribes M. et al. Cancer Cell 2009].
Materials and Methods: Since the antiangiogenic properties of sunitinib would suggest interference with extravasation and circulation of tumor cells, we designed a pilot study to measure CTCs prospectively during treatment with sunitinib and to assess their correlation with tumor response in previously untreated pts with metastatic renal cell carcinoma. The automated analysis of CTCs was conducted by means of Cellsearch platform (Veridex). Peripheral blood samples were drawn on day 1 and 28 of cycles 1 and 2, on day 1 of cycles 3, 5 and 7, then at radiological progression. Sunitinib was administered by the 4 weeks on-2 weeks off regimen, at daily dosages ranging from 50 to 25 mg according to age and toxicity. Reduction of either tumor diameter or tumor density at CT scan was considered response.
Results: 20 pts have been accrued so far, median age 68 years (range, 34 to 87). Clear cell histology was predominant (85%), then papillary or rarer histologies (15%). Sixty percent of patients had 2 or more sites of disease. Most frequently involved organs were lungs (65% of total patients), lymph-nodes (35%), liver (20%), bone (30%). After a mean of 2.2 cycles (range, 1 to 8), there were 42.8% of responses in 14 evaluable pts. At baseline, 80% of pts had 1 or more CTCs/7.5 mL, while 50% had at least 2 CTCs (range, 0−10). Using an arbitrary cut-off of 4 CTCs, no correlation was found between baseline CTC count and age, number of metastatic sites, and response to sunitinib. Indeed, CTC count fluctuated in most pts during treatment, mean change was $\pm$6.8 cells (0−12). CTCs either disappeared in one responsive pt (3 CTCs found at baseline, then 0 after 2 cycles of sunitinib) or increased in three responsive pts (from 5 CTCs at baseline to 16 after sunitinib, from 0 to 3, from 1 to 8, respectively).
Conclusions: CTCs are often present in pts with metastatic renal cancer but baseline count does not appear to correlate with extension of disease and subsequent response to sunitinib. Moreover, radiological response of metastatic disease may be accompanied by either reduced or increased levels of CTCs.

Poster presentations (Mon, 21 Sep, 14:00−17:00)
Genitourinary malignancies − Renal cancer

7118 POSTER

An Asian subpopulation analysis of the safety and efficacy of sunitinib in metastatic renal cell carcinoma

S. Lee[1], H.C. Chung[2], P. Mainwaring[3], C. Ng[4], J.W.C. Chang[5], P. Kwong[6], R.K. Li[7], V. Sriuranpong[8], C.K. Toh[9], S. Pitman Lowenthal[10]. *[1]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea; [2]Yonsei University College of Medicine, Yonsei Cancer Center, Seoul, Korea; [3]Mater Adult Hospital, Medical Oncology, South Brisbane, Australia; [4]University Malaya Medical Centre, Department of Medicine Medical Oncology, Kuala Lumpur, Malaysia; [5]Chang Gung Memorial Hospital, Department of Internal Medicine Division of Hematology-Oncology, Taoyuan, Taiwan; [6]Queen Mary Hospital, Department of Clinical Oncology, Hong Kong, China; [7]St. Luke's Medical Center, Cancer Institute, Quezon City, Philippines; [8]Chulalongkorn University, Department of Medicine Medical Oncology Unit, Bongkok, Thailand; [9]National Cancer Centre, Department of Medical Oncology, Singapore, Singapore; [10]Pfizer Oncology, Pfizer Medical Affairs, New York City, USA*

Background: Sunitinib (SU) is an oral, multitargeted receptor tyrosine kinase (RTK) inhibitor of VEGFRs, PDGFRs, and other RTKs. It is approved multinationally for the treatment of metastatic renal cell carcinoma (mRCC). In order to evaluate SU among ethnic populations, safety and efficacy of SU treatment was assessed in Asian and non-Asian patients (pts).
Materials and Methods: This ongoing, expanded-access, phase 3B prospective open-label clinical trial (A6181037; ClinicalTrials.gov number NCT00531544) was performed at 246 sites in 52 countries. Pts: had histologically confirmed mRCC; were both previously-treated and treatment-naïve; had not received prior SU; an ECOG performance status ranging from 0−2. SU was self-administered at a starting dose of 50 mg/day orally in 6-wk cycles (4 wks of SU followed by 2 wks off). Dose interruptions or reductions to 37.5 mg or 25 mg were allowed to manage AEs. AEs and hematology parameters were assessed on days 1, 14, and 28 of cycle 1, days 1 and 28 of cycle 2, and day 1 on cycles $\geqslant$3. Efficacy (ORR, PFS and OS) was evaluated according to schedules determined by local institutional standards of care.
Results: Data from 325 Asians pts (7%) and 4046 non-Asian pts (93%) was available at the time of analysis. Baseline characteristics were similar for both groups. Among Asian pts, 35% were treated at non-Asian sites. Common non-hematologic AEs in Asians and non-Asians, respectively, were diarrhea (42% and 45%), fatigue (40% and 37%), stomatitis (39% and 26%), and hand-foot syndrome (39% and 23%); the frequency of diarrhea was lower in Asians at non-Asian sites (29%) compared to Asian sites (49%). Grade 3−4 non-hematologic AEs in Asians and non-Asians, respectively, included hand-foot syndrome (13% and 6%), fatigue (8% for both), and diarrhea (7% and 5%). Grade 3−4 hematologic AE's in Asians at Asian sites, Asians at non-Asian sites, and non-Asians, respectively, included leukopenia (29%, 9%, and 12%) and thrombocytopenia (30%, 17%, and 13%). ORR was 18% (95% CI: 13.8−22.5) for Asian and 14% (95% CI: 12.5−14.6) for non-Asians. Median PFS was 8.7 months (95% CI: 8.1−11.1) for Asians and 10.9 months (95% CI: 10.5−11.3) for non-Asians. OS was 18.9 months (95% CI: 15.5−23.5) for Asians and 18.4 (95% CI: 17.4−19.2) months for non-Asians.
Conclusions: The results of this study demonstrate that the safety profile of SU treatment is similar for Asian and non-Asian pts for most AEs. SU is similarly effective and well-tolerated in Asian and non-Asian pts.

7119 POSTER

Genitourinary malignancies - Renal cancer Quality of life (QOL) in treatment-naïve and cytokine-pretreated patients with advanced renal cell carcinoma (RCC) treated with pazopanib: results from a phase III double-blind, placebo-controlled trial

R. Hawkins[1], R. Hodge[2], M. Chen[3], M. Neary[3], A.S. Pickard[4], C. Sternberg[5]. *[1]University of Manchester, School of Cancer and Imaging Sciences, Manchester, United Kingdom; [2]GlaxoSmithKline, Global Health Outcomes - Oncology, Uxbridge Middx, United Kingdom; [3]GlaxoSmithKline, Global Health Outcomes - Oncology, Collegeville PA, USA; [4]University of Illinois, College of Pharmacy, Chicago IL, USA; [5]San Camillo and Forlanini Hospitals, Department of Medical Oncology, Rome, Italy*

Background: Anti-cancer agents for the treatment of RCC may have toxicities that can cause considerable decrements for QOL. This study reports on QOL assessments from a double-blind, placebo-controlled Phase III trial of pazopanib 800 mg QD in advanced RCC pts, which showed