PF and 32 docetaxel-PF. Grade $\geqslant$ 3 hematologic toxicity was observed in 4 pts, grade $\geqslant$ 3 renal and neurotoxicity occurred in 1 pt each.
Median PFS and OS in the whole series were 6 (1−73) and 9.5 mos (1−73) respectively. Positive p53 staining significantly associated with better OS and PFS at univariate analysis (Log-Rank test p = 0.0421 and p = 0.0483, respectively).
Adjuvant setting: 17 pts (4 bilateral pN+ and 11 pelvic pN+) underwent adjuvant TPF. Median PFS and OS were 10 mos (1−73) and 13 mos (1−73). 10 pts (59%) were alive with 17 mos (1−73) of median follow-up (f-u).
Neoadjuvant setting: 16 pts with cN2/3 SCC (9 cN3) were treated, either at diagnosis (11) or following recurrence after prior lymphadenectomy (5). Median PFS was 4 mos (1−46). 3 pts achieved a complete response (CR) and 6 pts achieved a partial response (PR, RR = 62%). OS was 5 mos (3−46). 11/16 pts underwent surgery that was radical in 9 (82%). 3 pathologic-CR (27%) have been achieved. 8 pts (50%) were alive with a median f-u of 9 mos (3−46).
Metastatic setting: 7 pts were treated. 2 pts had a PR and 1 a SD that lasted a median of 5 mos (3−8), and all died of disease. Median PFS and OS were 2 mos (1−8) and 5 mos (2−12).
Conclusion: Perioperative TPF was effective in advanced penile SCC, either in A or NA setting. It deserves further investigation including earlier stages (probably all cN+), combined with surgery. Neoadjuvant TPF allowed to obtain a significant number of responses in very advanced pts and to perform radical surgery even in nodal relapses after prior intervention. Mature results on the predictive role of biomarkers will be available in Sept 2011.

7147 POSTER

The REACT Expanded-access Program of Everolimus in Patients With Metastatic Renal Cell Carcinoma Refractory to VEGF-targeted Therapy: Subgroup Analyses by Prior Therapy

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Background: Everolimus has demonstrated clinical efficacy in metastatic renal cell carcinoma (mRCC) refractory to vascular endothelial growth factor receptor-tyrosine kinase inhibitor (VEGFR-TKI) therapy, and is approved for use in this indication in 65 countries. The REACT (RAD001 Expanded Access Clinical Trial in RCC) study was initiated to provide patients with VEGFR-TKI-refractory mRCC access to everolimus in advance of regulatory approval.
Materials and Methods: REACT was an open-label, international, expanded-access clinical trial (Clinicaltrials.gov: NCT00655252; Trial sponsor: Novartis Pharmaceuticals) that enrolled patients with measurable or nonmeasurable mRCC of any histology who were intolerant of, or progressed while on, VEGFR-TKI therapy. Everolimus 10 mg/day was administered orally. The long-term safety of everolimus in patients with mRCC, as determined by the overall incidence of grade 3/4 and serious adverse events (AEs), was the primary study objective. RECIST-defined tumour response was also assessed by local investigator. Several subgroup analyses were performed to evaluate the effect of prior treatment on safety and efficacy of everolimus.
Results: From July 2008 to June 2010, 1367 patients were enrolled. Most patients (92.7%) had progressed on prior VEGFR-TKI therapy, and some (24.4%) were VEGFR-TKI intolerant (some patients experienced both VEGFR-TKI intolerance and disease progression). Median everolimus treatment duration was similar across patient subgroups by prior VEGFR-TKI treatment, including VEGFR-TKI intolerant patients (Table). Best overall response rates in the VEGFR-TKI-intolerant subgroup were 1.8% partial response (PR) and 53.5% stable disease (SD), as compared with 1.7% PR and 51.6% SD for the overall population. The incidence of grade 3/4 AEs across all prior treatment subgroups were similar to those of the overall population.

Table: Everolimus treatment duration in REACT by prior therapy

	All	Progression on prior VEGFR-TKI	Intolerant to prior VEGFR-TKI	Treated with only 1 prior VEGFR-TKI	Treated with only prior sunitinib
n	1367	1267	333	895	742
Treatment duration, median (range), weeks	14.0 (0.1–83.7)	14.1 (0.1–83.7)	13.1 (0.6–71.7)	13.7 (0.1–83.7)	13.1 (0.1–83.7)

Conclusions: Patients enrolled in REACT derived benefit from everolimus irrespective of prior VEGFR-TKI therapy, including those who were VEGFR-TKI intolerant. Everolimus is well-tolerated and affords disease stabilization in the majority of patients with VEGFR-TKI-refractory mRCC, and is the standard-of-care in this patient population.

7148 POSTER

Hyperglycemia and Hypercholesterolemia and Associated Outcomes of Patients With Metastatic Renal Cell Carcinoma Treated With Everolimus in the Expanded-access Program REACT

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Background: The occurrence of specific adverse events (AEs) has been shown to correlate with clinical efficacy of targeted therapies in the treatment of patients with metastatic renal cell carcinoma (mRCC). Subanalyses of REACT (RAD001 Expanded Access Clinical Trial in RCC) evaluated the potential association of hyperglycemia and hypercholesterolemia with outcomes in mRCC patients treated with everolimus.
Materials and Methods: REACT was an open-label, international, expanded-access clinical trial (Clinicaltrials.gov: NCT00655252; Trial sponsor: Novartis Pharmaceuticals) that evaluated the long-term safety and efficacy of everolimus (10 mg/day) in patients with mRCC who were intolerant of, or progressed while on, VEGFR-TKI therapy. All grade 3/4 AEs and any grade 1/2 AEs resulting in study drug modification were collected. Subgroup analyses of patients who developed hyperglycemia or hypercholesterolemia of any grade were performed.
Results: REACT enrolled 1367 patients from 34 countries. The median everolimus treatment duration was longer for patients who developed hyperglycemia (n = 78) or hypercholesterolemia (n = 14) than for the overall population (19.14, 19.71 vs 14.0 weeks, respectively; Table). Overall, 30.3% of REACT patients remained on therapy for $\geqslant$6 months, as compared with 42.3% and 35.7% of patients with hyperglycemia and hypercholesterolemia, respectively. Best overall response was stable disease in 51.6% of the overall study population, as compared with 65.4% of patients with hyperglycemia and 71.4% of patients with hypercholesterolemia.

Table. Everolimus treatment duration and best overall response in patients with hyperglycemia and hypercholesterolemia

	All n = 1364	Pts with hyperglycemia n = 78	Pts with hypercholesterolemia n = 14
Duration of treatment, median, weeks	14.0	19.14	19.71
Duration of treatment, weeks, %			
$\leqslant$4	8.6	1.3	7.1
>4 to $\leqslant$8	13.8	10.3	14.3
>8 to $\leqslant$16	32.8	35.9	14.3
>16 to $\leqslant$24	14.6	10.3	28.6
>24 to $\leqslant$32	11.7	17.9	14.3
>32 to $\leqslant$52	14.6	14.1	21.4
>2	4.0	10.3	0
Best overall response			
Partial response, n (%)	23 (1.7)	2 (4.6)	0
Stable disease, n (%)	705 (51.6)	51 (65.4)	10 (71.4)

Conclusions: Our results suggest that hyperglycemia and hypercholesterolemia do not lead to permanent everolimus treatment discontinuations, as most patients with these AEs remained on therapy longer than the overall REACT population. Hyperglycemia and especially hypercholesterolemia were observed in low numbers of patients, but they may be associated with improved response to everolimus treatment and should be further explored as putative biomarkers for mTOR inhibition.