Results: Currently 1529 pts are valid for baseline characteristics; 91% were prescribed sorafenib 400 mg bid. The table shows baseline characteristics in PREDICT compared to TARGET. While the most frequently reported AEs were similar in the two sorafenib-treated populations, incidences were lower in PREDICT (valid for safety: N = 1606) vs TARGET (N = 451), ie, hand-foot skin reaction (22% vs 30%), diarrhea (18% vs 43%), rash (10% vs 40%), and alopecia (7% vs 27%).

	PREDICT	TARGET
Baseline characteristics, sorafenib-treated pts	1529	451
Male, n (%)	1104 (72)	315 (70)
Median age, y (range)	60.0 (18–88)	58.0 (19–86)
Only clear-cell histology, n (%)	1257 (82)	449 (99)
Prior nephrectomy, n (%)	1306 (85)	422 (94)
ECOG Performance Status, n (%)		
0	322 (21)	219 (49)
1	768 (50)	223 (49)
2	350 (23)	7 (2)
>2	85 (6)	0
Pts with metastases, n (%)	1466 (96)	451 (100)
Lung	1066 (70)	348 (77)
Bone	381 (25)	110 (24)
Liver	324 (21)	116 (26)
Memorial Sloan Kettering Cancer Center Prognostic Risk, n (%)		
Low	335 (22)	233 (52)
Intermediate	541 (35)	218 (48)
High	133 (9)	0
Missing/not assessed	520 (34)	0

Conclusions: These initial findings of PREDICT show that the safety profile of sorafenib is similar to that seen in the research setting of TARGET. However, pts in the real-world setting of PREDICT have a somewhat worse baseline tumor/disease condition and prognosis.

7129 POSTER

Long-term follow-up of metastatic renal cancer patients undergoing HLA-identical reduced-intensity allografting

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Background: Stem cell transplantation from a HLA-compatible sibling donor is an adoptive immunotherapy for cytokine-refractory, metastatic clear-cell renal cell cancer (RCC). However, the recent introduction of targeted therapy compounds has reduced the interest in this therapeutic strategy. We have reanalyzed our series with the aim to assess long-term benefit from allografting.
Materials and Methods: Twenty-five RCC patients received a reduced-intensity allograft from an HLA-identical sibling donor. All patients received a thiotepa, fludarabine, and cyclophosphamide conditioning regimen, and a cyclosporine-based GVHD prophylaxis.
Results: Best response to allograft was evaluable in 24 patients: 1 CR, 4 PR, 12 MR/SD, 7 PD. One-year survival was 48%, and 5-yr survival was 20%. At a median observation time of 65 months, 5 patients are alive, one in CR, one in PR, and three with stable disease. At multivariate analysis, CRP value before transplant, number of CD34+ infused cells and disease status at +90 significantly correlated with survival. Survival of patients at favourable/intermediate-risk according to the MSKCC score that underwent allografting was better in comparison to the survival predicted by historical controls.
Conclusions: We conclude that twenty percent of cytokine-refractory RCC patients are alive long-term after allografting. Transplantation is able to induce long-term disease control in a fraction of relapsed RCC patients. It is unknown if relapse or PD after targeted therapy will be susceptible to allograft-mediated graft-versus-tumor effect. The place of allografting in the treatment of metastatic RCC, alone or in combination with targeted therapies, needs reappraisal.

7130 POSTER

Efficacy and safety of sorafenib in patients with advanced clear-cell renal-cell carcinoma (RCC) with bone metastases: results from the phase III target study

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Background: Results of the phase III TARGET trial, a randomized, double-blind, placebo-controlled study of sorafenib (SOR) treatment in patients with clear-cell RCC in whom 1 prior systemic therapy had failed, indicated that SOR is effective and safe for patients with advanced RCC (Escudier et al. *N Engl J Med*. 2007), leading to global approval of SOR for the treatment of advanced RCC. Bone metastases in patients with RCC are frequent and are associated with increased morbidity. An exploratory subset analysis was performed to evaluate the efficacy and safety of SOR in patients enrolled in TARGET with/without bone metastases at baseline.
Methods: Patients (N = 903) with advanced clear-cell RCC, ECOG PS 0–2, and low- or intermediate-risk MSKCC score were randomized 1:1 to SOR 400 mg BID or PBO. The primary end point was OS; secondary end points included PFS and safety. A planned independently-assessed formal analysis of PFS showed significant benefit for SOR over PBO; consequently, patients originally assigned to PBO were able to cross over to SOR. Thus, final OS results are confounded by crossover.
Results: Precrossover efficacy data by subset are shown in the table. The incidence of drug-related adverse events (AEs) across subgroups was consistent with that reported for the overall population. The most common grade 3/4 AEs in SOR populations were hand-foot skin reaction, fatigue, and diarrhea.
Conclusions: SOR benefitted patients with advanced RCC, whether or not bone metastases were present at baseline. SOR was well tolerated and AEs were manageable.

	n		1º endpoint: OS (SOR/PBO)		2º endpoint: PFS (SOR/PBO)*	
Population	SOR	PBO	Median (mo)	HR (95% CI)	Median (mo)	HR (95% CI)
Overall	451	452	NA†/14.7	0.71 (0.54–0.94)	5.5/2.8	0.44 (0.35–0.55)
Bone metastases	110	109	NA†/14.0	0.54 (0.31, 0.97)	5.2/2.5	0.48 (0.34, 0.70)
No bone metastases	341	343	NA†/15.9	0.80 (0.57, 1.11)	5.7/2.8	0.51 (0.41, 0.62)

*Final PFS of overall study population based on independent review from Jan 2005; all other data from May 2005 database; †Value cannot be estimated due to censored data

7131 POSTER

Overall survival among metastatic renal cell carcinoma patients corrected for crossover using inverse probability of censoring weights: analyses from the everolimus phase III trial

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Background: Intent-to-treat (ITT) analyses of trial data with crossover provisions included for ethical reasons often results in underestimation of treatment effects. RECORD-1 (NCT00410124, funded by Novartis Oncology), which examined the impact of everolimus on progression free survival (PFS) and overall survival (OS) in metastatic renal cell carcinoma (mRCC) patients following failure on a VEGF-TKI therapy, allowed for crossover following progression on placebo. The previously published ITT analysis indicated a positive effect of everolimus on OS (HR = 0.83, 95% CI: 0.50–1.37, p = 0.23). Because the ITT effect estimate does not account for crossover, it is likely biased towards null hypothesis of no effect.
Materials and Methods: To estimate the effect of everolimus on OS corrected for crossover in the RECORD-1 trial data from the cutoff of February 28, 2008, the following post hoc analysis was implemented. Patients randomized to placebo who crossed over were artificially censored at the time of initiation of active treatment. Pooled logistic regressions were used to estimate the probability of remaining not censored due to crossover to be used to weight the patients in the Cox model, i.e. inverse probability of censoring weights (IPCW) were used to correct the potential selection bias induced by censoring. Clinical parameters, such as monthly time-varying progression status and adverse event occurrence (prior to crossover), in addition to baseline characteristics were used in the estimation of stabilized weights. A Cox proportional hazards model for the effect of treatment in the absence of crossover was fit using the estimated IPCWs. The dichotomous treatment indicator as well as baseline covariates were included as predictors in the Cox model to adjust for selection bias related to the baseline covariates.
Results: Based on the IPCW Cox model, treatment with everolimus reduced the risk of mortality by 45% (HR: 0.55; 95% CI 0.31–0.97).
Conclusions: The trend in overall survival benefit of everolimus among VEGF-TKI refractory mRCC patients suggested by the ITT analysis was confirmed by the IPCW Cox model. Specifically, the weighted Cox model provides a treatment effect estimate corrected for crossover corresponding to 45% mortality risk reduction for patients treated with everolimus compared to patients treated with best supportive care alone.