of these, thrombocytopenia and neutropenia occurred in fourteen patients (77.8%).
Conclusions: Japanese patients with mRCC treated with sunitinib (50 mg/day in 6-week cycles) frequently experienced severe levels of thrombocytopenia and neutropenia. Most patients were unable to tolerate the present dose and subsequently failed to complete the four-week because of drug-related adverse events. Dose modification of sunitinib may be required for tolerable treatment.

Adverse events	All grades	Grade 3 and 4 (%)
Neutropenia	81.5	33.3
Thrombocytopenia	70.4	44.4
Hypertension	59.3	18.5
Fatigue	59.3	11.1
Anemia	55.6	3.7
Diarrhea	51.9	3.7
Hypothyroidism	48.1	7.4
Hand-foot syndrome	48.1	7.4
Rash	40.7	

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What is the impact of subsequent antineoplastic therapy on overall survival (OS) following first-line bevacizumab (BEV)/interferon-alpha2a (IFN) in metastatic renal cell carcinoma (mRCC)? – Experience from AVOREN

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Background: BEV (Avastin®) directly inhibits VEGF, the key mediator of angiogenesis. The phase III AVOREN trial (BO17705F) compared 1st-line BEV + IFN with IFN + placebo in patients (pts) with mRCC. The duration of OS, the primary endpoint, was increased in pts receiving 1st-line BEV + IFN compared with IFN + placebo (Escudier et al ASCO 2009). Given the recent availability of four new agents, sequencing of therapy in mRCC is of interest. We analysed OS data in subgroups of pts who received $\geqslant$1 dose of subsequent therapy following initial study medication.
Methods: Nephrectomised pts with clear cell mRCC, KPS of $\geqslant$70%, no CNS metastases and adequate organ function received IFN ($\times$3/week at a recommended dose of 9 MIU for up to 1 year) plus BEV (10 mg/kg q2w) or placebo until PD. Use of subsequent therapies was recorded and OS calculated in these subgroups.
Results: Between 06/04 and 10/05, 649 pts (641 treated) were randomised to BEV + IFN (n = 327) or IFN + placebo (n = 322). Post-protocol therapy was received by 180 (55%) pts in the BEV + IFN and 202 (63%) in the IFN + placebo arm; the majority (148 and 171) received 1 or 2 subsequent therapies. Pt characteristics, including MSKCC score, were similar in pts who received subsequent therapy and the overall population. The results of sequencing with different post-protocol therapies are shown below.

Median OS

	IFN + placebo (n)	BEV + IFN (n)	IFN + placebo (months)	Bev + IFN (months)	HR (95% CI)
All pts	322	327	21.3	23.3	0.86 (0.72–1.04)
TKI*	120	113	33.6	38.6	0.80 (0.56–1.13)
Sunitinib*	92	83	39.7	43.6	0.88 (0.58–1.35)
Sorafenib*	50	60	30.7	38.6	0.73 (0.44–1.20)
2nd-line TKI**	81	96	33.2	38.6	0.77 (0.51–1.15)

*Subsequent therapy defined as more than one treatment given as post-protocol therapy, any line; **2nd-line TKI therapy given for one-line only immediately after study therapy

Conclusions: Although the AVOREN trial was not designed to examine the effect of 2nd-line therapy on OS, this retrospective exploratory analysis suggests a potential improvement in OS (greater than 30 months) in pts who receive BEV + IFN followed by subsequent therapies such as TKIs. The overall sequence of therapies should be considered when selecting 1st-line therapy for pts with mRCC, but prospective studies are required to confirm these findings.
Trial sponsored by F. Hoffmann-La Roche, Ltd.

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Results from additional analyses of patient reported outcomes in RECORD-1 – a randomized trial of everolimus with metastatic renal cell carcinoma patients

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Background: Phase III trial of everolimus in metastatic renal cell carcinoma (mRCC) patients demonstrated reduced risk of disease progression or death compared to placebo (hazard ratio [HR] = 0.33, 95% confidence interval [CI] = 0.25−0.43, p < 0.001). Patient-reported outcomes (PRO) were also assessed in this trial. Main results, in terms of time to deterioration compared between groups of patients defined by best overall response, were analyzed and presented previously.
Materials and Methods: Patients with mRCC were randomized (n = 416) to receive everolimus or placebo plus best supportive care. Patients completed the FACT-Kidney Symptom Index-Disease Related Symptoms (FKSI-DRS) and EORTC-QLQ C30 at baseline and monthly during treatment. Deterioration was defined as a decrease from baseline of at least 3 points for FKSI-DRS and at least 10% for EORTC Physical Function (PF) and Global Quality of Life (QL) scales. This analysis considered as deterioration events a composite end-point including tumor progressions or deaths occurring prior to deterioration or censoring date. The impact of baseline and early changes in PRO scores on progression-free survival (PFS) was evaluated. Comparisons were made using stratified log-rank tests and Cox proportional hazard models.
Results: Regardless of treatment arm, patients whose tumors did not progress on study experienced delayed time to deterioration, compared to patients whose tumors did progress, in FKSI-DRS (HR = 0.41, 95% CI = [0.27, 0.63]; p < 0.001) and QL (HR = 0.68, 95% CI = [0.47, 0.97]; p = 0.033) scores. This comparison was not statistically significant for PF scores (HR = 0.69, 95% CI = [0.47, 1.01]; p = 0.053). For the composite endpoint a 55% risk reduction for progression or deterioration in FKSI-DRS was observed for the everolimus arm compared to placebo (HR = 0.45, 95% CI = [0.33, 0.61]; p < 0.001). A similar benefit was observed for PF (HR = 0.54, 95% CI = [0.40, 0.73]; p < 0.001) and QL (HR = 0.57, 95% CI = [0.42, 0.77]; p < 0.001). Baseline PRO scores were not predictive of PFS. However, patients whose FKSI-DRS scores worsened by at least 3 points during the first month had significantly shortened PFS compared to patients whose scores improved or remained stable (p = 0.021). Early changes in PF or QL were not predictive of PFS.
Conclusions: Compared to placebo, everolimus delayed progression of disease-related symptoms. The PFS benefit demonstrated for everolimus is associated with a corresponding delay in the worsening of symptoms.

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PREDICT (Patient characteristics in Renal cell carcinoma and Daily practice Treatment with Nexavar) global non-interventional study: first interim results

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Background: Sorafenib was shown to be effective for the treatment of metastatic renal cell carcinoma (mRCC) in randomized controlled trials (RCT). Because pts treated under daily-practice conditions have heterogeneous characteristics that may differ from RCT populations, the PREDICT (Patient characteristics in RENal cell carcinoma and Daily practICe Treatment with Nexavar) non-interventional study was undertaken to record baseline characteristics of mRCC pts and their potential influence on the efficacy and safety of sorafenib in community practice settings. PREDICT is ongoing in 14 countries throughout Europe, Latin America, and Asia, and thus encompasses a broad multi-ethnic population. Results of the first analysis (cutoff: Feb 25, 2009) categorizing the baseline characteristics and adverse events (AEs) of this population are compared to those in the pivotal Phase 3 TARGET study (Escudier, *N Engl J Med* 2007).
Methods: Clinicians follow mRCC pts, for whom they have prescribed sorafenib, for the length of therapy, up to 12 months. Baseline characteristics are recorded and at pts' normally scheduled follow-up visits, tumor status, pt status, and adverse events (AEs) are noted.