represents an exciting improvement to serially investigate and accurately quantify these rare cells. At present, CTC count is indicated in the follow-up of metastatic breast cancer, colon rectal cancer and prostate cancer, so that cut-off values are now defined, predicting high risk of recurrence in metastatic disease. Moreover, variation in CTC can indicate a significant change in prognosis as early as the first treatment cycle and throughout the continuum of care. Preliminary reports indicate that CTC are present in patients with various metastatic carcinomas of epithelial origin with a wide range of incidences and frequencies but lack at presents extensively analysis of renal cell carcinoma (RCC) patients, both in sporadic and in VHL disease.

**Materials and Methods:** To investigate if RCC patients present CTC, we have designed a pilot study enrolling metastatic or advanced sporadic RCC patients and VHL patients, at diagnosis and naive for treatment. The first clinical objective of the study is to correlate CTC count with major prognostic factors determined at diagnosis. To gain further information on the biologic significance of CTC in patients with RCC both sporadic and VHL, we will also characterize the phenotypic profile of these cells, firstly regarding their metastatic potential. CTC and M30+ were measured in 12 consecutive patients affected by RCC and in 9 patients with VHL disease and renal cancer. CTC were measured in a group of healthy donors too. The study started at October, 2008 and is ongoing.

**Results and Conclusions:** Preliminary data obtained indicate that:

– Over 80% and over 70% of RCC samples, sporadic and VHL respectively, present CTC; no CTC were detected in healthy donors;
– The quote of live versus apoptotic CTC extensively differ between the two cohorts of patients (sporadic RCC and VHL);
– 50% of sporadic RCC patients presented 100% of apoptotic CTC, whereas in VHL patients the same percentage of apoptotic CTC was found in 66% of the cases.

**7145** POSTER

**Evaluation of safety, tolerability and activity: a registry for Temsirolimus-treated patients with advanced or metastatic renal cell carcinoma (aRCC) in the usual health care setting**

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**Background:** In Nov 2007, the mTOR-inhibitor Temsirolimus (TEMS) was approved in the EU for the first-line treatment of patients with aRCC who have at least 3 of 6 prognostic risk factors. A pivotal study had demonstrated significantly increased overall survival with TEMS in poor risk aRCC compared to the former standard Interferon (10.9 mo vs 7.3 mo). A pre-registration compassionate use program (CUP) for patients with aRCC confirmed the known safety profile of TEMS. However, the low incidence of reported serious adverse events (SAE) even in the CUP (8 SAE during about 2200 applications) reflects the low level of spontaneous SAE reporting in oncology in general. To better identify the true safety profile of newly approved drugs, collection of data on pharmacovigilance in the post-approval period is essential. Hence a non-interventional trial appears to be adequate.

**Methods:** To prospectively evaluate TEMS in the usual health care setting we started a registry for TEMS-treated patients with aRCC. Primary objective is the evaluation of TEMS's safety profile. Secondary objectives include the tolerability and activity of TEMS as well as the profile, comorbidity and characteristics of patients and sequence of systemic therapies in aRCC. Inclusion criteria are a histologically confirmed aRCC treated with TEMS and written informed consent by the patient.

**Results:** With regulatory and ethic committee's notification the registry started in Germany in Feb 2008. The registry is set up and managed by Wyeth's medical department in collaboration with a scientific advisory board. Up to the end of March 2009 73 active centers have recruited 176 patients. Preliminary documentation is available for 106 patients (79 male, 26 female), median age 66.9 yrs (40.4–86.7), median Karnofsky index 80% (40–100%). 56 patients experienced 191 AE, including 23 pts with 51 SAE (13 of them considered related, 38 not related by the treating physician). Clear cell carcinomas represent the predominant histological subtyp (74.5%) in the study-population.

**Conclusions:** To further evaluate the safety, tolerability and efficacy of TEMS in the treatment of aRCC in the post-approval period and also due to the low level of spontaneously reported SAE in oncology Wyeth started a registry for TEMS-treated patients in aRCC. Thus far, patient population represents the expected pattern regarding distribution of age, sex and histology. Updated results will be presented in September.

**7146** POSTER

**Metastatic renal cell carcinoma: a comparative effectiveness assessment of first-line bevacizumab + Interferon alpha-2a vs sunitinib**

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**Background:** Bevacizumab (BEV) + Interferon alpha-2a (IFN-α) [1] and sunitinib (SUN) [2] have shown significant increase in progression free survival (PFS) compared to IFN-α in first-line metastatic renal cell carcinoma (mRCC) therapy. There is no head-to-head evidence available comparing both regimens, however there is an increasing need to assess and compare the relative efficacy in order to offer a transparent basis for reimbursement purposes.

**Material and Methods:** On the basis of the pivotal phase III trials, widely accepted indirect comparison methods [3–5] were applied focusing on PFS. The unadjusted investigator-assessed PFS hazard ratio (HR) for BEV + IFN-α vs IFN-α (0.63) and for SUN vs IFN-α (0.52) have been used as the basis of the analysis. To enable valid indirect comparison, the IFN-α control arms of both trials have been standardised. Taking into account published evidence, sensitivity analyses on the effects of down-dosing and patient compliance have also been applied in order to re-evaluate PFS outcome.

**Results:** The base case unadjusted indirect comparison resulted in a non-significant PFS difference of SUN vs BEV + IFN-α (HR: 0.82; 95% CI: 0.64, 1.06; p = 0.13). Standardising the IFN arms and simulating SUN down-dosing and patient compliance fortifies the base case findings of non-significant PFS difference: the adjusted indirect PFS comparison HR of SUN vs BEV + IFN-α varied from 0.98 to 1.17, which may suggest a tendency in favour of BV + IFN-α. Results were most influenced by IFN-α control arm adjustment, followed by patient compliance and down-dosing.

**Conclusion:** BEV + IFN-α is similarly efficacious to SUN in terms of PFS based on a comparative effectiveness evaluation in first-line mRCC therapy. These findings imply that other treatment decision criteria such as tolerability need to be considered.

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**7147** POSTER

**Efficacy and safety of long-term use of sorafenib: final report of a phase II trial of sorafenib in Japanese patients with unresectable/metastatic renal cell carcinoma**

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**Background:** Results of the landmark TARGET study indicated that sorafenib, an oral multi-kinase inhibitor, is a safe and effective treatment for advanced renal cell carcinoma (RCC). By blocking cell growth and angiogenesis pathways, sorafenib significantly improves progression-free survival (PFS) and overall survival (OS) in patients (pts) with advanced RCC. Few analyses, however, have evaluated the long-term effects of sorafenib. Here we present efficacy and safety data from a phase II trial and extension study of pts with unresectable/metastatic RCC.

**Materials and Methods:** 131 pts with unresectable/metastatic RCC in Japan were treated with sorafenib 400 mg BID in a single-arm, phase II trial and extension study conducted from Nov 2004 through Jul 2008. All pts had undergone nephrectomy and cytokine therapy prior to study enrollment.

**Results:** Efficacy data is shown in the data table. In the 25 pts with a partial response (PR), the median time to response and duration of response were 12.0 weeks and 59.9 weeks, respectively. Notably, 6 of these pts achieved PR ⩽40 weeks after the start of sorafenib treatment. Drug-related adverse events (AEs) were observed in 127 pts (96.9%). However, most AEs were CTCAE grade 1–3. Drug-related grade 4 AEs were observed in 20 pts (15.3%), including high levels of lipase in 9 pts (6.9%), hyperuricemia in 4 pts (3.1%), and high levels of ALT in 3 pts (2.3%). Sorafenib was discontinued in 29 pts (22.1%) due to AEs, including