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

anorexia and elevation of AST and ALT levels. Some AEs, including hand-foot skin reaction, hypertension, and elevation of lipase or amylase levels, emerged specifically in the early stage of treatment, while others, such as flu-like syndrome and elevation of AST and ALT arose throughout the treatment period. Eleven pts died within 30 days of receiving sorafenib, but no deaths were considered drug-related. Ten pts were on treatment at the end of the extension study; these pts were transferred to treatment with commercially available sorafenib.
Conclusions: In this study of Japanese pts, sorafenib 400 mg BID was found to be a safe and effective long-term treatment in pts with unresectable/metastatic RCC.

Median treatment duration, wk (range)	33.6 (0.6−168)
PFS, wk (95% CI)	34.4 (27.9, 47.1)
OS, wk (95% CI)	110.1 (82.6, 139.3)
Tumor response, no. (%)	
Partial response	25 (19.4)
Stable disease	87 (67.4)
Progressive disease	13 (10.1)
Disease control rate, % (95% CI)	73.6 (65.2, 81.0)

7148 POSTER

Prognostic value of tumor cell proliferative activity in disseminated kidney cancer

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Background: To study prognostic value of the nuclear antigen Ki-67 expression in disseminated kidney cancer.
Material and Methods: There were studied 34 patients with primary generalizes kidney cancer. Of 34 patients there were males 22 and females 12. The age of patients fluctuated from 35 to 73 years. The mean age was 55.4 years. The primary tumor was localized in the right kidney in 17 patients, and in the left kidney in 17 patients. All patients had primary-generalized form of kidney cancer. The symptoms of disease depended on localization of metastases except primary tumor. The degree of tumor process dissemination was evaluated as T2−4Nl-2Ml. Of 34 patients 15 (44%) had metastases in the lungs, 1(3%) patient has them in the liver, 2(6%) in the bones of the skeleton, one (3%) in the pleura, 1(3%) in the adrenal gland, one (3%) in the brain and one (3%) in the bed of kidney removed. In 12 (35%) patients there was noted lesion in two and more organs (lungs, liver, bones of skeleton, juxtaregional lymph nodes, soft tissues). The involvement of retroperitoneal lymph nodes was noted in 11 cases (32%). Of 34 patients 30 (88%) underwent palliative nephrectomy, 3 (9%) expanded nephrectomy and one (3%) nephrureterectomy. The operative samples were studied with use of immunohistochemical method (by technique of firm “DAKO”) with measurement of proliferative activity marker, that is nuclear antigen Ki-67. On the basis of Ki-67 indices of 34 patients 13 (38%) had negative results and 9 (26%) had weak-positive results and 12 (36%) had moderate-positive findings.
Results: The patients underwent long-term observation during the period from 2 months to 8 years. Of 34 patients 26 (76%) dead and 8 (24%) are under control. We studied effect of Ki-67 parameters on life durability. In cases of negative indices of Ki-67 the life durability was 27 months, in weak positive and moderate positive results – 20 and 8 months respectively.
Conclusion: The high level of expression of the nuclear antigen Ki-67, marker of proliferative activity, is an unfavorable factor for prognosis of patient survival and it may be used as molecular biological factor for prognosis of kidney cancer.

7149 POSTER

Prognostic significance of gene-suppressor p53 and Bcl-2 in disseminated kidney cancer

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Background: To study prognostic value of gene-suppressor p53 and Bcl-2 in disseminated kidney cancer.
Material and Methods: We have study 34 patients with primary generalized kidney cancer. Of 34 patients males were 22, and females 12. The age of patients was from 35 to 73 years, mean age was 55.4 years. In 17 patients the primary tumor was located in the right kidney and in 17 patients in the left one. All patients had primary generalized form of the kidney cancer. The symptoms of disease except primary tumor depended on localization of distance metastases too. The degree of tumor process extension was evaluated as T2−4N1−2M1. Of 34 patients 15 (44%) had metastases located in the lungs, and one (3%) patients had in the liver, and in 2 (6%) in the skeleton bones, and in 1 (3%) in the pleura, 1 (3%) in the adrenal gland, in 1 (3%) in the brain and in 1 (3%) in the bed of kidney removed. In 12 (35%) cases there were noted lesions in the two and more organs. Of 34 patients, 30 (88%) underwent palliative nephrectomy, 3 (9%) enlarged nephrectomy and 1 (3%) nephruterectomy. The intraoperative samples were investigated with use of immunehistochemical method with measurement of gene-suppressor p53 and bcl-2. In this case by parameters of p53 of 34 patients 15 (44%) had negative, 6 (18%) had mild, 6(18%) had moderately positive and 7(20%) had marked positive values. According to bcl-2 of 34 patients 15 (44%) had negative, 11 (32%) gas weak positive and 8(23%) had moderately positive results.
Results: The patients were observed during follow up period from 2 months to 8 years. Of 34 patients 26 (76%) died and 8 (24%) are under regularly control. We studied effect of the parameters p53 and bcl-2 on the life duration. In cases with negative parameters p53 the life durability was 27 months, in moderate and weak positive parameters 12 and 19 months, respectively and in marked positive results 5 months. In negative parameters bcl-2 the average life durability was 14 months and weak and moderate positive results life durability was 24 and 20 months, respectively.
Conclusion: The measurement of parameters p53 and bcl-2 has prognostic value and they should be used as molecular-biological prognostic factors in kidney cancer.

7150 POSTER

Response of renal lesions in patients with metastatic renal cell carcinoma (mRCC) treated with sunitinib − a single center retrospective analysis

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Backround: Multi-target tyrosin kinase inhibitors (MTKI), such as sunitinib has to be considered as standard treatment of patients with mRCC. Treatment with sunitinib may achieve partial remissions (PR) in 39% of patients with metastatic disease. During the era of immunotherapy objective responses remain scarce and renal lesions have not been reported to respond to such therapies after all. Palliative nephrectomy prior to immunotherapy improves overall survival and is considered a prerequisite for such therapies. Response of the primary renal lesion has been reported with sunitinib and fostered the debate whether or not palliative nephrectomy is necessary in these patients. We report on nine patients with mRCC and renal lesions who received sunitinib.
Materials and Methods: Nine patients with stage IV clear cell RCC with renal lesions treated with sunitinib 50 mg (4/2 scheme) were evaluated. The average age at the beginning of treatment was 58 years (range 49−72), the MSKCC-Score was 0 (n = 1), 1 (n = 5) and 2 (n = 3), while the ECOG performance status was predominantly 0 (n = 8) with the exception of one patient with ECOG performance status 1. The tumour grading on histopathology was G2 (n = 6) and G3 (n = 3). Tumour assessment was according to local practice, which included CT scans every 2 cycles. Early assessment was additionally performed in 4 patients after cycle 1.
Results: Altogether 50 target lesions were analysed for RECIST. During treatment in two cases dose reduction from 50 mg to 37.5 mg was necessary to reduce side effects, while in one case dose reduction to 25 mg was essential. The median progression free survival (PFS) was 347 days after a median number of 6 applied cycles. Tumour response of target lesions according to RECIST consisted of 44% (n = 4) PR, 44% SD (n = 4) and 11% (n = 1) PD. Response of renal lesions was similar and achieved a $\geqslant$30% reduction of tumour size in 44% (n = 4), 20−30% reduction of tumour size in 33% (n = 3) and lack of response in 22% (n = 2). 2 of 9 patients are still ongoing and receive sunitinib. One patient received nephrectomy after 2 courses of treatment.
Conclusion: Sunitinib is effective in patients with renal lesions with mRCC. Our data support the use of sunitinib in these patients.