7152 POSTER

Interim Analysis of a Non-interventional Study of Everolimus After Failure of the First Anti-VEGF Therapy

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Background: To date, six targeted agents have been approved for the treatment of metastatic renal cell carcinoma (mRCC). Their role and place as part of a sequential treatment concept is subject to an ongoing debate and data beyond clinical trials is limited. Everolimus (EVE) is approved and recommended for the treatment of mRCC after failure of the first anti-VEGF therapy. Here, we report for the first time prospective non-interventional second-line data on EVE in routine use after failure of anti-VEGF therapy.
Material and Methods: A prospective, single arm, open label, multi center non-interventional study for patients with mRCC was initiated in Germany in 08/2009 to determine efficacy defined as time between first EVE intake until disease progression due to any cause (TTP) and patient related quality of life as measured by EORTC-QLQ-C30. Accrual is still ongoing. After 100 patients had been enrolled, a pre-planned interim analysis was conducted.
Results: Included were the first 113 patients enrolled at 59 German sites. The safety population consisted of 99 patients with documented EVE treatment. Median time since diagnosis of RCC was 3.5 years and median time since diagnosis of mRCC was 1.9 years. 88% of patients had prior nephrectomy. Before receiving EVE, most patients had received sunitinib (78%). The main reason for switching to EVE was progression on previous treatment (86%). Median time to progression (TTP) was 9.7 months (95% CI: 6 months; n.d.). A total of 230 AEs occurred in 61% of patients including 18 serious adverse drug reactions in 12 patients (12%). The nature of the AEs corroborated the safety profile of EVE. Median Karnofsky performance status (KPS) across all visits was $\geqslant$80% and median time to deterioration of KPS by 10% was 9.1 months. 44% of patients received third-line treatment after EVE (75% TKI). 80% of treating physicians attested EVE favorable tolerability, coinciding with high therapy compliance of patients as assessed by physicians and patients' diaries (>80%).
Conclusions: This non-interventional study on EVE in the treatment of RCC after prior failure of anti-VEGF therapy confirms its safety and efficacy in an early treatment setting. With this ongoing study, promising data on EVE treatment after failure of anti-VEGF therapy in the routine setting were obtained. Final results are eagerly awaited.

7153 POSTER

Treatment (trx) Modalities After a Front Line Targeted Therapies in Patients (pts) With Metastatic Renal Cell Carcinoma (mRCC)

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Background: New targeted therapies (TT) have been approved for metastatic renal cell carcinoma (mRCC) in the past 5 years, based on large multicenter randomized phases III trials. Median overall survival (OS) in these studies ranged from 19 to 26.4 months (mths). Whether this OS is also observed in routine practice has not been reported. We report here the experience of Institut Gustave Roussy (IGR) in France.
Methods: Data from all mRCC patients (pts) who were treated at IGR from 2005 to 2009 with first line TT (sunitinib (SU), sorafenib (SO), bevacizumab (B), temsirolimus or everolimus pooled together as mTOR) were analyzed. Only pts with subsequent follow up have been kept for this study. Pts were considered as eligible for 2nd line analysis if not progressive or still on first line treatment. Outcome of pts in terms of overall survival (OS), number of subsequent therapies have been analyzed.
Results: 264 pts, median age 62 y, median follow-up 37 months (mths) were treated with TT with a median OS of 25.5 mths. Median OS with SU (131), SO (59) or B (66) containing regimen are respectively 26.3, 16.3 and 29.5 mths. Only 8 pts received mTOR as first line. Among 199 pts eligible for 2nd line, 55% for SU (51/93), 51% for SO (26/51) and 73% for B (35/48) respectively received a 2nd line. A 3rd line was given to 53%, 31% and 46%, respectively for SU, SO and B. In those pts who received more than one line, median OS is respectively 16, 16.4 and 19.3 mths. Interestingly, when we split pts in 2 periods (2005–2006 and 2007–2009), there is no difference in OS ($p = 0.86$) or in % of 2nd and 3rd lines.
Conclusions: Median OS in pts treated with targeted therapies for mRCC exceeds 2 years. More pts treated with B could receive 2nd line therapy, with a trend to better OS. Update and characteristics of pts and treatments will be presented at the meeting.

7154 POSTER

Hypothyroidism and Macrocytosis as Surrogate Markers for Response and Survival in Patients With Advanced Renal Cell Carcinoma Treated With Sunitinib as First-line Therapy

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Background: Sunitinib, a multi-target tyrosine kinase inhibitor, is considered as a standard first-line treatment for advanced renal cell carcinoma. Some analytical abnormalities, such as thyroid dysfunction or macrocytosis, could be surrogate markers for sunitinib efficacy, as reported in previous studies.
Material and Methods: From January-2006 to January-2010 we collected consecutive patients with advanced renal cell carcinoma who received sunitinib as first-line therapy for advanced renal cell carcinoma for at least three cycles. Patients with thyroid function abnormalities or macrocytosis before initiation of sunitinib were excluded. For every patient we reviewed data about appearance of thyroid disfunction, new-onset macrocytosis, best response achieved with sunitinib, relapse-free survival (RFS) and overall survival (OS).
Results: A total of 34 patients were included. Patients with hypothyroidism showed a clear trend to better PFS, although not statistically significant (66 vs 30 weeks, $p = 0.190$); in the same way, the benefit observed in OS was also non-statistically significant (140 vs 90 weeks, $p = 0.192$). There was also a trend for correlation of hypothyroidism and a higher probability of achieving a complete or partial response ($\chi^2 = 0.097$).
Patients with new-onset macrocytosis showed a marked advantage for better progression-free survival, statistically significant (68 vs 30 weeks, $p = 0.02$). There was also a clear benefit in overall survival in patients who developed macrocytosis during treatment with sunitinib (170 vs 69 weeks, $p = 0.001$). Patients with new-onset macrocytosis had a greater probability of showing a complete or partial response with sunitinib therapy ($\chi^2 = 0.007$).
Conclusions: Although limited by the small size of this study, new-onset macrocytosis can be a surrogate marker for response and survival in metastatic renal cell carcinoma treated with sunitinib as first-line therapy. Data regarding hypothyroidism seem to point in the same way, but this study did not reach statistical significance for this issue. These findings will be re-analyzed with longer follow-up and including new patients from other collaborating centres to confirm these data.

7155 POSTER

Is Epidermal Growth Factor Receptor R497K Polymorphism in Renal Cell Carcinoma a Molecular Marker of Advanced Disease?

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Background: Renal cell carcinoma (RCC) is the most common cancer in the adult kidney, accounting for 5% of all malignancies and is considered the most lethal urological cancer. Epidermal growth factor receptor (EGFR) is a member of HER/ErbB family of receptors tyrosine kinases affecting cell proliferation, differentiation, tumour growth, inhibition of apoptosis, migration and angiogenesis. EGFR is a major transducer of mitogenic signals involved in cancer pathogenesis and progression. Its activity is mainly elevated in most human solid tumours leading to progression. A functional polymorphism (*R497K*) was described in *EGFR* gene responsible for a G-to-A leading to an Arg-Lys substitution in codon 497 in the extracellular domain within subdomain IV of the EGFR. This transition has been associated with an attenuated receptor function. Genetic functional variants, which influence EGFR function, may have impact in RCC development/prognosis. Our purpose was to investigate the association between *EGFR R497K* functional polymorphism and RCC clinicopathologic features.
Material and Methods: DNA was extracted from peripheral blood cells of 170 patients histopathologically diagnosed with RCC. Genotyping of *R497K* polymorphism was performed by PCR-RFLP. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measure of the association between *EGFR R497K* genotypes and clinicopathologic features.