there was a significant association between tx interruption and OS and any tx change and OS. In the sensitivity analysis, increased risk for OS remained statistically significant for these tx changes.
Conclusions: For SU and SOR pts, tx changes due to AEs may have a detrimental impact on OS. Limitations of the study include retrospective data collection.

7137 POSTER

Safety and Efficacy of Everolimus in Patients With Non-clear Cell Renal Cell Carcinoma Refractory to VEGF-targeted Therapy – a Subgroup Analysis of the REACT Expanded-access Program

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Background: Approximately 25% of all renal cell carcinomas (RCCs) have non-clear cell histology. Metastatic non-clear cell RCC (mncRCC) is characterized by resistance to treatment and poor overall survival. While the recent advent of targeted therapies has provided improved treatment options for patients with metastatic clear cell RCC, effective therapies for patients with mncRCC remain limited. The REACT (RAD001 Expanded Access Clinical Trial in RCC) study was initiated to provide patients with mRCC of any histology refractory to VEGF-targeted therapy access to everolimus in advance of regulatory approval.
Material and Methods: The open-label, international, expanded-access program REACT (Clinicaltrials.gov: NCT00655252; Trial sponsor: Novartis Pharmaceuticals) enrolled patients with measurable or nonmeasurable mRCC of any histology who were intolerant of, or progressed while on, VEGFR-TKI therapy. Patients received 10 mg everolimus daily. The primary study objective was to evaluate the long-term safety of everolimus, as determined by overall incidence of grade 3/4 and serious adverse events (AEs). Tumour response to everolimus was assessed by local investigator according to RECIST. A subgroup analysis of safety and efficacy in patients with mncRCC was performed.
Results: A total of 1367 patients were enrolled from July 2008 to June 2010; of these, 75 patients (5.5%) had mncRCC. Median everolimus treatment duration in the mncRCC subgroup was 12.14 weeks (range, 0.9–49.0 weeks), as compared with 14.0 weeks (range, 0.1–83.7 weeks) for the overall REACT population. Most commonly reported grade 3/4 AEs in the mncRCC subgroup included: anemia (17.3%), dyspnea (10.7%), pleural effusion (9.3%), fatigue (8.0%), and hyperglycemia (6.6%). Best overall response for the mncRCC subgroup was 1.3% partial response and 49.3% stable disease, as compared with 1.7% and 51.6% for the overall population.
Conclusions: The duration of everolimus treatment in patients with mncRCC was slightly lower than that of the overall REACT population, and nearly 50% of these patients achieved disease control on treatment. Everolimus was well tolerated in this patient subgroup, with no new safety issues identified and a comparable AE profile to that of the overall study population. Our results represent the first data reported on the safety and efficacy of everolimus in patients with mncRCC, and support further evaluation of everolimus in these patients.

7138 POSTER

High Rate of Complete Remission (CR) Using Two Sequential, Dose-dense Regimens of Cisplatin, Gemcitabine, and Paclitaxel (CGP) Followed by HD-MVAC in Patients With Metastatic Bladder Cancer (mBC)

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Background: Currently, CGP and HD-MVAC are the most active regimens against bladder cancer. According to Norton and Simon, we tested the hypothesis that the administration of two sequential non cross-resistant dose-dense chemotherapy regimens, may target different cancer cells, avoid drug resistance, improve response rate and complete response.
Materials and Methods: This is a single institution phase II trial. Eligibility included histological diagnosis of mBC, PS 0−2 (ECOG), adequate organ function and no previous systemic regimens. Patients were treated with 4 cycles of CGP dose-dense (Gemcitabine 1000 mg/m^2 d 1, Paclitaxel 140 mg/m^2 d 1, Cisplatin 70 mg/m^2 d 2 plus PegFilgrastim 6 mg on day 3, every 2 weeks) followed by 4 cycles of M-VAC (Methotrexate 30 mg/m^2 d 1,Vinblastine 3 mg/m^2 d 2, Doxorubicin 30 mg/m^2 d 2, Cisplatin 70 mg/m^2 d 2 plus Pegfilgrastim 6 mg on day 3 every 2 weeks). All were evaluated with CT scan at the baseline, after 4 cycles, at the end of chemotherapy and then every 3 months for two years and 6 months thereafter. The primary end point was the response rate. The trial was designed to detect a 100% improvement of CR rate from 15% with traditional CGP to 30% with our approach.
Results: 21 consecutive pts were included, 19 were evaluable. Male were 80%; median age 66 years; median PS was 90 (60–100). Metastatic sites included retroperitoneal nodes, lung, liver and bone. Bajorin risk factors was 0 in 33%, 1 in 40%, 2 in 27%. All pts were hospitalized for three days and received chemotherapy with generous hydration and supportive therapy. After the first 4 cycles of CGP we observed 11.1% CR, 55.5% PR, 16.6% SD and 16.6% PD. With the 4 sequential cycles of HD- MVAC the response was enhanced in 33% of the patients with a global 32% CR, 31% PR, 11% SD and 26% PD. Main grade 3−4 toxicity included asthenia (33%), neutropenia (26%), febrile (6.6%), thrombocytopenia (6.6%), mucositis (13.3%), electrolite disorders (15%). All patients with RP recurred whereas 5/6 patients with CR maintained the NED status after 2+, 9, 10+, 15+,16+, 28+.
Conclusions: The sequential use of CGP and HD- MVAC demonstrates significant clinical activity in the first line treatment of mBC.Toxicity was accetable. Approximately one out of three patients gets a durable RC. A longer follow-up is needed in order to see if some patients are cured.

7139 POSTER

Sunitinib for RCC in a Public Brasilian Institution: Predictive Factors of Major Toxicity

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Sunitinib is an oral drug with inhibitory activity over VEGF TK, as well as other TKs associated with the platelet-derived growth factor receptor and c-kit oncogene. Molecular pathways appear to be critical for RCC growth, metastatic progression and angiogenesis. Based on data derived from a large prospective randomized trial, sunitinib has emerged as a front line standard of care for the majority of patients with metastatic renal-cell carcinoma (RCC) deemed not suitable for high-dose IL-2. This trailblazing activity has been balanced though with some rather morbid and burdensome toxicities seen in real daily practice. These patients usually have clinical features which may interact and aggravate these adverse events.
Material and Methods: The aim of our study was to look for those clinical features which could predict undue toxicities responsible for dose reduction or interruption of treatment. We retrospectively reviewed the records of patients with advanced RCC treated with sunitinib from September of 2008 to march of 2011 at the Instituto do Câncer do Estado de São Paulo.
Results: From the initial seventy-four patients, 10 were excluded because of upfront dose-reduction, leaving 64 patients treated with conventional sunitinib dose and schedule (50 mg once daily for 4 weeks, every 6 weeks). The majority of patients had clear-cell histology (only 3 non-clear cell) with median age of 55 years; 77% had an ECOG of 0 to 2; 46 of 64 had an debulkying nephrectomy; median OS was 16.5 m; response rate by RECIST 1.1 was 26.5% in evaluable patients. Seventy-one percent of patients required dose reduction due to non-manageable toxicity (grade 3 or 4). Clinical factors that were associated with dose reduction by univariate analysis by student's t-test were weight <65 kg ($p = 0.026$), body surface area ($p = 0.031$), low IMC ($p = 0.019$) and estimated creatinine clearance less than 60 ml/min ($p = 0.047$ analysis by coefficient $\chi 2$). By multivariate analysis, only weight <65 kg remained statistically significant ($p = 0.021$).
Conclusion: Sunitinib's clinical activity in our daily practice emulates the one seen in clinical trials but most of our patients required dose reduction during treatment due to major toxicities. Except for body weight, there were no demographic factors or clinical variates independently associated with possible increased drug exposure and dose-limiting toxicities. Identification of clinical, genetic and demographic factors associated with increased adverse events is of interest and should be addressed in future studies.