

Sunitinib for Unselected Korean Patients with Advanced Renal Cell Carcinoma : A Comparable Efficacy with Different Toxicity Profiles

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Background: As a standard first line treatment of advanced renal cell carcinoma (RCC), sunitinib demonstrated favorable efficacy with manageable toxicities, both for selected patients in clinical trials and unselected patients in compassionate-use studies. However, because most of the studies were done for western population, there is little experience for sunitinib in Asian population. Therefore, we performed this study to describe the efficacy and safety of sunitinib treatment in unselected Korean advanced RCC patients.

Methods: From November 2005 to August 2008, 132 patients with histologically confirmed advanced RCC (100 in global expanded-access programme and 32 in general oncology practice) were enrolled. Sunitinib was administered orally 50 mg once daily (4 weeks on treatment, 2 weeks off), and continuous 37.5 mg per day was allowed in some cases. Response and toxicity evaluation were assessed regularly according to the protocol.

Results: This population includes 82.6% of clear cell histology, 87.9% of Eastern Cooperative Oncology Group performance status 0-1, and 28.8% of treatment naive patients. The progression free survival (PFS) and overall survival were 8.2 months and 23.1 months, respectively. Patients received a median 5 cycles of sunitinib (range 1-30, 11.4% received continuous 37.5 mg treatment). With the 130 evaluable patients, the objective response rate was 34.1% (n=45), and 44.7% (n=59) exhibited stable disease. Reasons for discontinuation were disease progression (n=99 [75.0%]) and treatment related toxicity (n=10 [7.6%]). The mean and median relative dose intensity (RDI) were 82.0% (SD±14.20) and 84.1% (range 48.0-100), respectively. The most frequent adverse events were thrombocytopenia (75.0%), neutropenia (70.5%), anemia (69.7%), and stomatitis/mucositis (66.7%). Grade 3-4 adverse events were also very high, being thrombocytopenia (37.8%), neutropenia (29.5%), anemia (21.9%), and hand-foot syndrome (15.2%). Patients with grade 3-4 thrombocytopenia was peaked during week 1 through 4 (about 15-23.1%), and gradually reduced in accordance with the decreasing RDI. Proportion of patients experienced all grade thrombocytopenia were also decreased gradually with the RDI adjustment. Low body surface area (Odd ratio [OR] 4.2, 95% CI 1.2-13.8, P=0.02), and previously treated status (OR=3.1, 95% CI 1.3-7.4, P=0.01) were highly predictable for grade 3-4 toxicities. Based on these results, a nomogram predicting 12 month-PFS probability was constructed with the 0.675 of concordance index.

Conclusions: For unselected Korean advanced RCC patients, this study demonstrates favorable efficacy and manageable toxicities of sunitinib. Though more frequent and somewhat different toxicity profiles, adequate dose modification and careful follow up enables comparable treatment outcomes. Based on these different toxicity profiles, further studies to optimize the dose/schedule of sunitinib are warranted with the reliable pharmacokinetic/pharmacodynamic markers.