Overall survival results from a Phase III study of tivozanib hydrochloride vs sorafenib in patients with renal cell carcinoma

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Introduction

• Multiple vascular endothelial growth factor (VEGF) receptor inhibitors have been approved for treatment of renal cell carcinoma (RCC) based on prior randomized controlled trials (RCTs) showing improved progression-free survival (PFS) compared with earlier agents.

• Overall survival (OS) remains a critical endpoint of VEGF-targeted agents. • The benefit of sorafenib, the standard of care for advanced renal cell carcinoma (RCC), was confirmed in a randomized trial of 1068 patients comparing sorafenib (400 mg twice daily) to placebo. 

• Median OS was longer with sorafenib (10.8 months) compared to placebo (5.1 months) (HR: 0.65; 95% CI: 0.50–0.85).

• Median OS was 15.4 months in the phase II trial of sorafenib in patients with clear cell RCC (J Clin Oncol 2007;25:2248–2256).

• A recent meta-analysis confirmed sorafenib’s OS benefit (JAm CollSurg 2012;214:612–618).

• Prior nephrectomy

• Advanced RCC

Key Eligibility Criteria:

• Number of metastatic sites/organs

• Intermediate MSKCC prognostic group, 10%

• ECOG score, a%

• Patients randomized to the tivozanib arm had a higher percentage of patients who received next-line therapy in each setting.

• Patients remaining progression-free on tivozanib were more likely to receive next-line therapy as compared to the sorafenib arm (Figure 5).

• Significantly longer survival was observed for patients in the tivozanib arm versus the control arm (Figure 7A).

• Patients in the sorafenib arm were much more likely to receive next-line therapy, and a higher percentage of patients received anti-VEGF therapies in the control arm compared with the tivozanib arm

• Patients at risk:

- Still on therapy: 94%

- Discontinued initial treatment: 6%

- This subset was small and further study is needed to confirm differential use of next-line cancer therapies

• After discontinuation of initial therapy, 64% of patients in the tivozanib arm continued OS evaluation compared with 56% of patients in the sorafenib arm

• In North America/Western Europe, a trend toward longer OS was observed in the tivozanib arm compared with the sorafenib arm (Figure 8).

• Median OS in the tivozanib arm was 28.8 months, median OS in the sorafenib arm was 20.3 months

• The OS comparison between study arms was confounded by differences in next-line VEGF therapy options for RCC

• This result was consistent with the study’s well-calibrated co-variates compared to the experimental therapy after disease progression in the control arm

• Predominantly residing in Central and Eastern Europe may have also contributed to this result, as access to subsequent effective treatments may vary

• More patients in the tivozanib arm received progression-free, if not randomized treatment (73% vs 64% in the control arm)

• Following discontinuation of initial treatment, fewer tivozanib patients received next-line VEGF therapy (10%) than patients in the control arm (25%) 

• Patients who received tivozanib in the control arm

• In North America/Western Europe, a trend toward longer OS was observed in patients with metastatic renal cancer in comparison with patients from Eastern Europe (Figure 8). Median OS was not reached at the time of analysis in either arm

• Compared with the ITT population

A higher percentage of North America/Western Europe patients received next-line therapy in both arms and the difference in use of next-line therapy between the two arms was less pronounced

Reference

