The addition of nivolumab, an anti–programmed cell death protein 1 (anti–PD-1) antibody, to Tivozanib and Nivolumab Combination Therapy

On March 10, 2021, tivozanib was granted US Food and Drug Administration approval and is indicated for the treatment of adult patients with relapsed or refractory advanced RCC following ≥2 prior systemic therapies

Rationale for Tivozanib and Nivolumab Combination Therapy

The VEGFR Pathway and Tivozanib

In the past decade, treatment options have been transformed with the advent of antiangiogenic small-molecule vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitors (TKIs) in combination with immune checkpoint inhibitors (ICIs). Inhibitors of the VEGF pathway have demonstrated antitumor efficacy and a tolerable adverse event (AE) profile when combined with ICIs. Tivozanib inhibits all 3 VEGFRs (VEGFR-1, -2, and -3) and mediates antitumor activity by inhibiting endothelial cell proliferation, migration, and survival in cancer. Tivozanib is a potent, highly selective VEGFR TKI that inhibits all 3 VEGFRs (VEGFR-1, -2, and -3) in combination with immune checkpoint inhibitors (ICIs)

The addition of nivolumab, an anti-programmed cell death protein 1 (anti-PD-1) antibody, to tivozanib is a strategy to intensify immune checkpoint inhibition. Nivolumab blocks the immune checkpoint protein PD-1 from interacting with programmed death ligand 1 (PD-L1), and median progression-free survival (PFS) was 16.9 months (95% CI, 13.4 to 19.6 months) in a phase 1/2 trial. In a subanalysis of patients who received prior treatment for RCC, the ORR with tivozanib and nivolumab combination therapy was 62% (Figure 1A), and median PFS was not reached (Figure 1B). Approximately 326 patients will be randomized 1:1 to receive tivozanib in combination with nivolumab or tivozanib monotherapy in an international, 2-arm, phase 3 study (Figure 3). The study is actively enrolling and expected to be conducted in approximately 200 sites across Argentina, Australia, Belgium, Brazil, Canada, Chile, Croatia, Republic of France, Germany, Italy, Mexico, Poland, Portugal, the United Kingdom, and the United States (Figure 3)