

SUPPLEMENTARY MATERIAL**A Phase 1, Open-label Study of Trebananib Combined With Sorafenib or Sunitinib in Patients With Advanced Renal Cell Carcinoma**

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Appendix

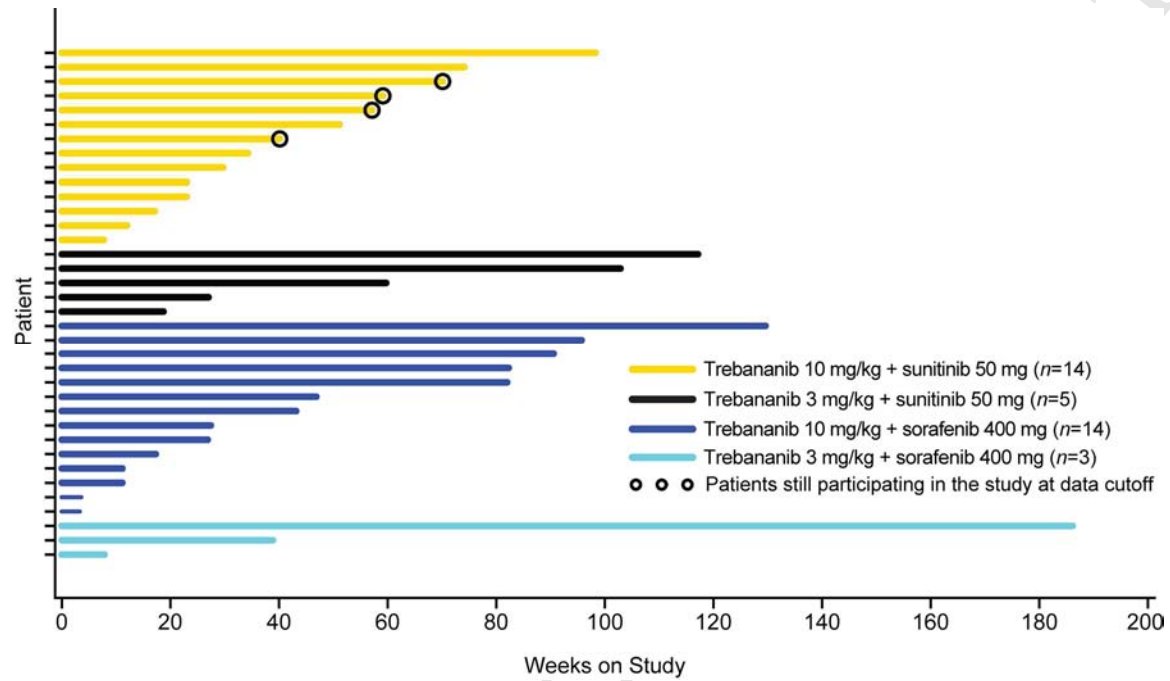
S1. Schedule of Pharmacokinetic Assessments

Pre-dose serum samples for measurement of trebananib concentrations were collected on day 1 of weeks 2, 3, 4, 5, 6, 8, and every 8 weeks thereafter until 4 weeks after treatment termination; post-dose samples were collected immediately and 6, 24, 48, and 96 hours after dosing on day 1 of weeks 4 and 5. Pre-dose plasma samples for the evaluation of sorafenib PK were collected on days 1 and 5 of week 1 and on day 1 of weeks 2, 3, 4, 5, 6, 8, and every 8 weeks thereafter; post-dose sampling was conducted 2, 3, 4, 6, and 12 hours following sorafenib administration on day 5 of week 1 and on day 1 of week 5. Plasma samples for PK evaluation of sunitinib and its active metabolite occurred pre-dose on days 1 and 5 of week 1 and on day 1 of weeks 2, 3, 4, 5, 6, and 10, and every 6 weeks thereafter. Additional samples were collected 2, 3, 4, 8, 12, and 24 hours after sunitinib dosing on day 5 of week 1 and on day 1 of week 4. The last sorafenib and sunitinib samples were collected 4 weeks after a patient's last dose of trebananib.

S2. Schedule of Biomarker Assessments

All serum samples were collected pre-dose during weeks 1, 2, 3, and 4, and every 8 weeks thereafter. Post-dose samples were collected 24 and 72 hours following dosing during weeks 1 and 2.

Supplementary Figure 1: Duration (Weeks) of Participation in the Study From Enrollment to Treatment Termination For Each Patient.



Supplementary Figure 2: Changes in Concentrations of Circulating Biomarkers During Treatment With Trebananib Plus Sorafenib or Sunitinib Relative to Baseline. Mean (\pm SE) Fold Change in PLGF (A), VEGFR-2 (B), VEGF (C), and sKit (D) From Baseline as a Function of Treatment Time Across all Treatment Cohorts.

^aIndicates significant change from baseline ($P < 0.01$). Abbreviations: PLGF = placental growth factor; SE = standard error; sKit = soluble c-Kit; VEGF = vascular endothelial growth factor; VEGFR-2 = vascular endothelial growth factor receptor 2.

