

## A Phase II Study of Axitinib in Advanced Carcinoid Tumors

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**Background:** Neuroendocrine tumors (NETs) are highly vascularized neoplasms overexpressing VEGF as well as VEGFR. Axitinib is an inhibitor of receptor tyrosine kinase with selective picomolar potency against VEGFR-1, -2 and -3 and nanomolar potency against PDGFR- $\beta$ .

**Methods:** We performed a phase II trial of axitinib 5 mg BID in patients with unresectable or metastatic low to intermediate grade carcinoid tumors. Prior antiangiogenic therapy with a dedicated VEGF pathway inhibitor was not permitted. The primary endpoints were PFS and 1-year PFS rate. H<sub>0</sub>=12 mo PFS rate of 36% (corresponding to median PFS of 8.1 months); H<sub>a</sub>= 12 mo PFS rate of 56.5% (corresponding to median PFS of 14.6 months). Preliminary findings are reported.

**Results:** 30 patients were enrolled and assessable for toxicity; 22 were assessable for response. Primary sites included small intestine (19 patients), lung (3), unknown (3), colon (2), rectum (2), and thymus (1). 21 patients had low-grade and 9 patients had intermediate-grade tumors. Median TTF was - 8.99 months (SD  $\pm$ 7.18 ) and the 12-month PFS rate was 65% (SD  $\pm$ 13%). The 1-year OS rate was 93% (SD $\pm$ 4.9%). Median PFS not yet determined due to small number of events. Best radiographic response was PR in 1/30 (3.3%) and stable disease in 21/30 (70%); 8/30 patients (27%) unevaluable. Among 25 patients with baseline elevated CgA levels, only 4 experienced major reductions (>50%) of the tumor marker. Axitinib treatment was associated with a 90% rate of hypertension. Grade 3 and 4 hypertension were seen in 18 (60%) and 2 (7%) patients respectively and led to treatment discontinuation in two cases. However, axitinib interruption prompted a fast recovery without sequelae.

**Conclusions:** The 12 mo PFS rate associated with axitinib in advanced carcinoid tumors is promising when compared to results observed in phase II studies of other antiangiogenic TKIs such as sunitinib or pazopanib. Although rates of hypertension were high, axitinib treatment was overall well tolerated.