

TPS4159      General Poster Session (Board #33E), Sun, 8:00 AM-11:45 AM

**Metiv-HCC: A phase III clinical trial evaluating tivantinib (ARQ 197), a MET inhibitor, versus placebo as second-line in patients (pts) with MET-high inoperable hepatocellular carcinoma (HCC).**

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**Background:** Tivantinib is a selective, non-ATP competitive, oral inhibitor of MET, the tyrosine kinase receptor for hepatocyte growth factor (HGF). MET over-expression is associated with poor prognosis in HCC patients. A phase Ib study (Santoro et al, Br J Cancer, 2013) with tivantinib 360mg BID revealed no worsening of liver function in cirrhotic HCC pts. A randomized, placebo-controlled phase 2 study identified HCC patients with high tumor MET expression at immunohistochemistry (IHC) as the target population for tivantinib in second line (overall survival: 7.2 months on tivantinib, 3.8 months on placebo, HR: 0.38, p=0.01), and selected 240mg BID as the appropriate dose for HCC patients (Santoro et al, Lancet Oncol, 2013). **Methods:** Enrollment for this phase III clinical trial (ARQ 197-A-U303, NCT01755767) has begun. Eligible pts must present with Child Pugh A; ECOG performance score <1; inoperable RECIST 1.1 measurable disease; adequate bone marrow, liver and kidney functions; no prior liver transplant. Pts must have progressed after or not tolerated one prior line of systemic therapy including sorafenib and their tumor samples must be deemed MET-High by IHC at a central laboratory to be eligible. Approximately 303 pts are randomized 2:1 to receive tivantinib 240mg PO twice daily or placebo. Pts are stratified by vascular invasion, metastases, and alpha-fetoprotein level, and they are evaluated by CT or MRI scan at 8-week intervals. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival and safety. Treatment continues until confirmed disease progression or unacceptable toxicity. Pts discontinued from study treatment will be followed for survival. Participating centers are located in Europe, Australia, New Zealand, and the Americas. This trial is expected to complete enrollment by mid-2015, and an interim analysis is planned when approximately 60% of OS events are reached. Clinical trial information: NCT01755767.