A PHASE II STUDY ON COMBINATION OF AXITINIB AND TRANSARTERIAL CHEMOEMBOLIZATION (TACE) FOR TREATMENT OF INOPERABLE HEPATOCELLULAR CARCINOMA (HCC)

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Aim: TACE is associated with an upregulation of VEGF leading to revascularization. Axitinib is a potent and selective inhibitor of VEGFR1, 2 and 3. We hypothesized that the addition of axitinib to TACE has synergistic activity by abolishing the VEGF driven signal after TACE. To prove this concept, we designed a phase II study to evaluate the efficacy and safety of the combination for treatment of inoperable HCC.

Methods: This is an investigator-initiated phase II single-arm study. The target sample size is 50. Key eligibility criteria include confirmed diagnosis of inoperable HCC, Child’s A liver function; ECOG PS 0-2; absence of prior systemic nor TACE treatment; the absence of main portal vein thrombosis or distant metastases. Treatment consists of 8 weekly cycle of axitinib 5mg twice daily. In each cycle, TACE is administered at 5th week when there is radiologically viable tumour and absence of ≥ grade 3 toxicity from axitinib. Axitinib is withheld 24h before each TACE, and resumed 24h after TACE when patients (pts) have preserved liver function. Reassessment imaging is done every 8 weeks. In the 1st year, each pt is treated with a maximum number of 6 cycles of TACE. Pt is put on maintenance axitinib alone if there is no PD after 1 year.

Results: Total 50 pts have been accrued. Baseline characteristics: BCLC stage B 38; C 12. Median age 62.1years. At the time of data cutoff on 17 Apr 2014, the median follow-up was 1.32 years. 27 pts have PD, and the median TTP is 10.4 months (95% CI = 5.43-13.72). The median OS is 15.9 months (95% CI = 12.9-not reached). Amongst 42 evaluable pts, the response rate (mRECIST) is 48.8% (7 CR; 14 PR) and the disease control rate is 88.4% (21 CR/PR and 16 SD). Amongst the responders, 3 pts underwent hepatectomy after shrinkage of tumour, and surgical specimen showed extensive tumour necrosis; 2 pts just had portal vein embolization to induce left lobe hypertrophy, and is currently wait-listed for hepatectomy. Total 5 pts could proceed to the axitinib maintenance phase. Common ≥ grade 3 toxicity events from axitinib include hypertension (20%), hand foot skin reaction (10%), fatigue (4%) and hyperbilirubinaemia (4%). The toxicity of TACE is not worsened by axitinib.

Conclusions: Combination of axitinib and TACE is associated with high tumour response rate and efficacy in unresectable HCC. Further evaluation with randomized study is indicated. (NCT01352728)

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