FDA Grants ODD Status to TTI-101 for Hepatocellular Carcinoma

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The FDA has granted orphan drug designation to the STA3 inhibitor, TTI-101, for the treatment of hepatocellular carcinoma. The agent is currently being investigated in a phase 1 clinical trial.

The FDA has granted orphan drug designation to the STA3 inhibitor, TTI-101, for the treatment of hepatocellular carcinoma (HCC), according to a press release by Tvardi Therapeutics, Inc.1
TTI-101 is an orally delivered, small molecule, and as a STAT3 inhibitor, it plays an important role in the pathogenesis of HCC by starting tumorigenesis as well as promoting an immunosuppressive tumor microenvironment.

“We are pleased to receive orphan drug designation for TTI-101 in HCC from the FDA,” said Imran Alibhai, PhD, chief executive officer of Tvardi Therapeutics, Inc, in a statement. “This designation builds on the compelling safety and efficacy we have seen in last-line HCC patients in our ongoing phase 1 trial. We look forward to the impending initiation of our phase 2 trial in HCC to test TTI-101 as monotherapy as well as in combination.”

In the phase I study of TTI-101 as a treatment for advanced cancers (NCT03195699), about 60 patients will be enrolled. Investigators of the study will execute a 3 + 3 design in which 3 patients will be initially enrolled into a given dose cohort, and more patients will be enrolled if no dose-limiting toxicities are identified with TTI-101.2

The study aims to evaluate tolerability, pharmacokinetics, and preliminary efficacy. The coprimary end points of the study include the determination of the maximum-tolerated dose (MTD) of TTI-101, and pharmacokinetics defined by Cmax, Tmax, and area under the curve. The secondary endpoints include pharmacokinetics defined by levels of pY-STAT3 measured before and before and after receiving TTI-101, and efficacy determined by complete response rate, partial response rate, and stable disease rate in targeted lesions, CR rate in non-target lesion, non-CR and progressive disease in non-target lesions, PD in non-target lesion, and best overall response.

Exploratory outcomes being investigated in the ongoing study include the association between biomarkers and antitumor efficacy and survival outcome based on RECIST 1.1 for patients with unresectable HCC, as well as the effect of food on bioavailability of TTI-101 in the dose expansion phase of the study.

To be eligible for inclusion in the study, patients are required to be at least 18 years of age with histologically confirmed diagnosis of a locally-advanced, inoperable, metastatic and/or treatment-refractory solid tumor. Patients with HCC specifically are required to with histologically confirmed diagnosis of locally advanced, inoperable, unresectable disease and have failed the first and second lines of therapy. The HCC population must also have Child-Pugh is A disease or be beyond the second line if the performance status is preserved and Child-Pugh is A. All patients are required to have an ECOG performance status of 0 or 1, have a hemoglobin of≥ 9.0 g/dL, neutrophil count ≥ 1.0 x 109/l, platelets ≥100 x 109/L at baseline, as well as adequate liver and renal function, and measurable disease.

Orphan drug designations are granted by the FDA to any drug or biological product that demonstrate promise for treating rare disease. TTI-101 may eventually improve outcomes for patients with HCC, which are currently poor with a 5-year survival rate of just 18%.1

Source: **Targeted Oncology by Nichole Tucker**

REFERENCES:

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2. Oral STAT3 inhibitor, TTI-101, in patients with advanced cancers. Clinicaltrials.gov. Updated March 16, 2022. Accessed April 25, 2022. https://bit.ly/3LdzD4V