Phase 1/2 trial of CF102, a selective A3 adenosine receptor (A3AR) agonist, in patients with hepatocellular carcinoma (HCC)

SM Stemmer¹, MH Silverman², WD Kerns², S Bar-Yehuda³, S Furman³, Z Harpaz³, M Farbstein³, O Binyaminov¹, G Medalia¹, P Fishman²

¹Institute of Oncology, Davidoff Center, Rabin Medical Center, Sackler School of Medicine, Tel Aviv University, Petach-Tikva, Israel
²Can-Fite BioPharma Ltd, Petach Tikva, Israel

Background: CF102, a novel, orally-active, A3AR agonist which induces tumor cell apoptosis in HCC experimental animal models, is under evaluation in this trial for the treatment of HCC patients with incurable disease.

Methods: The objectives of this trial are to evaluate the safety and pharmacokinetic (PK) behavior of CF102 in HCC patients. Utilizing a “3+3” design, successive cohorts of patients with advanced HCC were enrolled at CF 102 doses of 1, 5, or 25 mg twice daily, given orally in continuous cycles of 28 days each. Progression to a higher-dose cohort was based on first cycle toxicity. Standard safety and PK assessments were performed; α-fetoprotein (AFP) levels were obtained each cycle, and tumor imaging was obtained every other cycle.

Results: 9 patients (5 males), median age 75 (63-90) years, Child-Pugh Class A or B, have been administered CF102 across 3 cohorts, 3 at each dose level. No dose-limiting toxicities specifically attributed to CF102 have been observed at any dose level. Through 3 cohorts, with a maximum exposure of 8 cycles, adverse events reported in at least 2 subjects were: anorexia (5 subjects); abdominal pain, asthenia (4 each); diarrhea (3); and leg edema/swelling, fatigue, fever, nausea, back pain, chest pain, leg pain (2 each). All events classified as drug-related were either grade 1 or 2. No drug-related abnormalities of hematologic, renal, or hepatic function have been observed on laboratory testing. CF102 has shown good oral bioavailability and linear PK behavior after single doses and at steady state. To date, one patient, at the lowest dose level, has shown stable disease for 6 cycles accompanied by complete clinical regression of biopsy-proven skin metastases and a sustained fall in AFP. Furthermore, another patient infected with hepatitis C virus experienced a 1.4 log₈ drop in viral titer during dosing with CF102.

Conclusions: Daily oral CF102 is safe and well tolerated at doses up to 25 mg twice daily, and shows linear PK in patients with HCC. CF102 has shown preliminary evidence of clinical activity in HCC patients based on clinical observations of stable disease and AFP reduction. The observation of a decrease in hepatitis C viral load is consistent with CF102’s known preclinical anti-viral activity. A3AR agonist treatment appears to hold promise as a novel therapeutic strategy in the treatment of advanced HCC and related liver diseases, and enrollment in the dose-confirmation phase of this trial continues.