Trial 2 – MPA Study Description

Prepared by Replica Analytics using the study sponsor's trial description

Background

Pancreatic cancer has an estimated annual incidence of 45,000 in the United States, with 38,000 of those diagnosed dying from the disease[1]. Most patients have advanced inoperable disease and potentially metastases (i.e., metastatic pancreatic adenocarcinoma or MPA). At the time of this trial the first line therapy for patients with inoperable disease was gemcitabine monotherapy, although this treatment does not benefit all patients. One transporter (hENT1: human equilibrative nucleoside transporter-1) has been identified as a potential predictor of successful treatment via gemcitabine. In a study by Giovannetti and colleagues, patients with low expression of hENT1 had the poorest survival when receiving gemcitabine-based therapy[2].

This trial compares standard gemcitabine therapy to a novel fatty acid derivative of gemcitabine, called CO-1.01. CO-1.01 is hypothesized to be superior to gemcitabine in MPA patients with low hENT1 activity as it exhibits anticancer activity independent of nucleoside transporters like hENT1 while gemcitabine seems to require nucleoside transporters for anticancer activity.

Study Design

The study conducted was a phase II open label randomized two-armed trial, comparing gemcitabine to CO-1.01. Patients were randomized, stratified on the basis of performance status and region to receive either CO-1.01 weekly for 3 weeks out of every 4 weeks or gemcitabine weekly for 7 weeks. Recruitment for this study sought patients with histologically confirmed (MPA who were generally healthy (high performance status, estimated life expectancy ≥ 12 weeks, with sufficient bone marrow and liver function as diagnosed by lab measures). Patients were excluded from the study if there was reason to believe they could not participate fully (e.g., allergy to the study drug, other commitments to another ongoing trial, or presence of a serious or unstable concomitant systemic disorder that could influence their participation), if they were pregnant or breastfeeding or if they had received recent surgery.

This study was designed to detect an expected increase in overall survival from 4 months in gemcitabine treated patients to 7.7 months in CO-1.01 treated hENT1-low patients with 90% power. This assumes that randomizing 180 patients over 20 months with 8 months follow-up will yield 144 death events during the study period. Secondary outcomes of interest included comparing the treatments for all levels of hENT1 expression, as well as assessing the tolerability and toxicity of CO-1.01.

Main Findings

This trial failed to show an increase in overall survival for patients with MPA and low hENT1 as the median survival for CO-1.01 treated participants was 5.7 months (95% confidence interval: 4.7-7.6) while participants who received gemcitabine had a median survival of 6.1 months (95% confidence interval: 5.2-7.7).

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013 Jan;63(1):11-30. doi: 10.3322/caac.21166. Epub 2013 Jan 17.
2. Giovannetti E, Del Tacca M, Mey V, Funel N, Nannizzi S, et al. Transcription analysis of human equilibrative nucleoside transporter-1 predicts survival in pancreas cancer patients treated with gemcitabine. Cancer Res, 2006;66:3928–3935.