Fourteen of the 28 (50%) evaluable patients who received DLL4 in combination with GEM/Nab-Pac showed a Benefit Rate of 89%. This result was observed in a small cohort of patients (n = 15).

Summary

This was a Phase I/II dose-exploration study of demcizumab, a cancer stem cell targeting monoclonal antibody (targeting the DLL4 ligand in the Notch pathway) plus gemcitabine with or without nab-paclitaxel in 1st line pancreatic cancer patients.

Demcizumab and gemcitabine with or without nab-paclitaxel were generally well tolerated with fatigue, nausea and vomiting being the most common dose related toxicities. The hypotension was managed with antihypertensives. Grade 1-2 related pulmonary hypertension occurred in 3 patients and Grade 2 related heart failure occurred in one patient receiving demcizumab for greater than 100 days, but none of the patients treated with truncated demcizumab developed pulmonary hypertension or heart failure.

Patients are being followed with cardiac monitoring using B-type natriuretic peptide (BNP) and echocardiography. BNP appears to be an early indicator of cardiotoxicity. In addition, a carvedilol-torsemide (i.e. an angiotensin converting enzyme inhibitor or carvedilol) was administered to patients with high BNP levels and this strategy is being repeated cardiologically.

Truncated demcizumab therapy (i.e. 70-90 days of therapy) appears to prevent the onset of late cardiotoxicity toxicity, as none of the 32 patients treated in this manner developed heart failure or pulmonary hypertension.

Fourteen of the 28 (50%) evaluable patients who received DEM/GEM/nab-Pac had a RECIST partial response and 17 had stable disease. In the 21 patients who received DEM/GEM/nab-Pac, the median progression free survival was 7.1 months (4.3-13.5) and the Kaplan Meier estimate of overall survival was 12.7 months (8.7, 11.4) for the patients who received DEM/GEM/nab-Pac.

A predictive biomarker was not identified, although potential biomarkers will continue to be assessed in the Phase 2 study.

A randomized Phase 2 trial (FOSEMT) in 1st line pancreatic cancer is ongoing. The truncated dose of demcizumab for the Phase 2 study is 3.5 mg/kg once every 2 weeks.