gastrointestinal tumours, non-colorectal

A PH 1B STUDY OF THE ANTI-CANCER STEM CELL AGENT DEMCIZUMAB (DEM) & GEMCITABINE (GEM) +/- PACLITAXEL PROTEIN BOUND PARTICLES (NAB-PACLITAXEL) IN PTS WITH PANCREATIC CANCER

M. Hidalgo1, M. Jameson2, A. Carrato3, P. Cooray4, P. Parnis5, P. Grimson6, G.M. Jeffery7, R. Stagg8, J. Dupont9, N. Tebbutt10

1CIOCC, Hospital Madrid Norte San Chinarro Centro Integral Oncologico Clara Campo, Madrid, SPAIN
2Medical Oncology, Waikato Hospital, Hamilton, NEW ZEALAND
3Medical Oncology, Hospital Ramon y Cajal, Madrid, SPAIN
4Medical Oncology, Box Hill Hospital, Box Hill, AUSTRALIA
5Medical Oncology, Royal Adelaide Hospital RAH Cancer Centre, Adelaide, AUSTRALIA
6Medical Oncology, Sydney Cancer Centre, Sydney, ACT, AUSTRALIA
7Oncology Service, Christchurch Hospital, Christchurch, NEW ZEALAND
8Clinical Research, OncoMed Pharmaceuticals, Redwood City, CA, USA
9Clinical Research, OncoMed Pharmaceuticals, Redwood City, CA, USA
10Medical Oncology, Austin Hospital, Heidelberg, AUSTRALIA

Aim: Delta-like ligand 4 (DLL4) is a ligand that activates the Notch pathway. DEM is a humanized IgG2 anti-DLL4 antibody that inhibits tumor growth & decreases cancer stem cell frequency in minimally passaged human xenograft models. In addition, DEM has an antiangiogenic effect & synergistic activity when combined with GEM & nab-paclitaxel in human pancreatic tumor-derived xenograft models.

Methods: Pts with 1st line pancreatic cancer were enrolled. Pts in cohorts 1-3 received DEM (2.5 every 2 or 4 wks or 5 mg/kg every 4 wks including 3 truncated pts) & GEM 1000 mg/m² 7 of 8 wks, then 3 of 4 wks. Pts in cohorts 4 & 5 received truncated DEM (2.5 or 5 mg/kg every 2 wks through Day 70) & nab-paclitaxel 125 mg/m² + gemcitabine 1000 mg/m² 3 of 4 weeks. The primary objective was to determine the MTD. Other objectives were safety, efficacy, immunogenicity, PK & biomarkers.

Results: Thirty-eight pts were enrolled; 8, 8, 6 & 8 pts received 2.5 mg/kg every 2 wks, 2.5 mg/kg every 4 wks, 5 mg/kg every 4 wks, 2.5 mg/kg every 2 weeks (truncated) & 5 mg/kg every 2 weeks (truncated), respectively. Related AEs in > 20% of pts were nausea (37%), fatigue (34%), nausea, vomiting (32%), decreased appetite (24%) & hypertension (21%). Hypertension was managed with anti-hypertensives. Increased BNP is an early indicator of the cardiac effects of DEM & mildly elevated values are used to initiate cardioprotective therapy with an ACE inhibitor or carvedilol. One pt who received 5 mg/kg continuously developed reversible pulmonary hypertension & heart failure on day 143. As a result, DEM was limited to 70 days in cohorts 4 & 5. In cohorts 1-3, 4 of 16 (25%) pts had a partial response (PR) & 7 had stable disease (SD). In cohorts 4 & 5, 6 of 14 (43%) pts had a PR & 6 had SD. The median PFS for 2.5 & 5 mg/kg every 4 wks and 2.5 mg/kg (truncated) & 5 mg/kg (truncated) every 2 wks were 1.7, 7, 3.4, not reached and 3.5 mos., respectively. The 3 truncated pts in cohort 3 had PFS of 5.4, 7 and 9.1 mos.

Conclusions: This therapy was generally well tolerated with fatigue, nausea & vomiting being the most common related AEs. Encouraging early clinical activity was observed. Additional data with truncated DEM will be presented.

Disclosure: R. Stagg and J. Dupont: I am an employee of OncoMed and own stock in the company. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology 2014. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.