Efficacy, Safety and Immune Activation with PEGylated Human IL-10 (AM0010) plus FOLFOX in Metastatic Pancreatic Adenocarcinoma (PDAC)

J. Randolph Hecht1, Gerald S. Falchook2, Manish Patel2, Raid Alijmovich3, Jeffrey R. Infante4, Aung Naing5, Deborah J. Wong6, Karen A. Auto7, Nav Ratsi7, Zev A. Wainberg7, Johanna C. Bendell7, Shubham Pant8, Annie Hung9, Peter Van Vlasselaer9, Galil L. Brown9, Martin O'He9, and Kyriakos P. Papadopoulos9

1. David Geffen School of Medicine at UCLA, Santa Monica, CA; 2. Sarah Cannon Research Institute at HealthONE, Denver, CO; 3. Houston University; 4. Oncology Research Institute/Neovasc Biology, Houston, TX; 5. Albert Einstein Medical Center, New York, NY; 6. Massachusetts General Hospital, Cincinnati, OH; 7. Memorial Sloan-Kettering Cancer Center, New York, NY; 8. ARMO BioSciences, Redwood City, CA; 9. START Center for Cancer Care, San Antonio, TX

Background

Overall survival on oral therapy of PDAC with g-IL10 plus oral fluoropyrimidine is 1.4 months. PDAC is refractory to many therapies, the descriptive burdens of PDAC tumors is relatively low and tumor infiltrating CD8+ T cells are rare. AM0010 stimulates survival, expansion and cytotoxicity of intratumoral CD8+ T cells, while reducing cytokine production. Available water soluble and long-acting IL-10 analogues have limited clinical utility. AM0010 (Pegilodecakin) plus oxaliplatin or nal-irinotecan is 5-6 months. PDAC is refractory to most other inflammatory cytokines were analyzed. AM0010 - Mechanism of Action

• IL-10 induces the IL-10 receptor on CD8+ T cells
• IL-10 regulates expression of FasL
• IL-10 activates TGF-α, IL-18, TNF-α
• IL-10 also activates other autoimmune diseases incl. RA, Crohn’s disease, psoriasis

AM0010 + FOLFOX
• Of those, a cohort of 21 pts. were treated in a phase 1b study
• Tumor responses were measured according to irRC criteria.
• 19 pts. were evaluable for tumor response and 21 were analyzed

Results

No prior platinum containing regimen,
• Allowed all other autoimmune diseases incl. RA, Crohn’s disease, psoriasis
• Median (range) OS 12.4+ months for PDAC on AM0010

Overall Survival of PDAC on AM0010 and AM0010 + FOLFOX

• Tumor correlates with OS
• Encouraging response rates, PFS and OS seen with combination therapy
• Of note, incidence of G4/A4 anemia and thrombocytopenia were mitigated by 5 days on/2 days off dosing schedule

Information

Phase 3 study of AM0010 + FOLFOX vs FOLFOX as Second-line Therapy in Patients with Metastatic Pancreatic Cancer that has Failed Progressed During or Following a First-Line Gemcitabine Containing Regimen (NCT02709251)

IHC and evaluation by Navneet Ratti of AM0010 and AM0010 + FOLFOX

References

1. Study in progress. Numbers as of August 11, 2017. Median follow-up 17.6 months (range 11.3, 21.3)

Sponsors

For more information on this trial, go to clinicaltrials.gov (NCT02009449) or contact info@armobio.com

Phase 1 Enrolling

AM0010 + FOLFOX was well tolerated
• Tolerated on continuous dosing without autoimmune AEs
• G4/A4 anemia (6%) and thrombocytopenia (12%)
• AM0010 + FOLFOX: 2-months PFS (N=20) vs FOLFOX: 1-months PFS (N=19)

Survival

• Median OS (months) 15.0 vs 12.4
• 12-month OS % (AM0010 + FOLFOX: 54% vs FOLFOX: 45%)

AM0010 + FOLFOX - Median OS 15.0 vs FOLFOX - Median OS 12.4

• Median OS (months) 15.0 vs 12.4
• 12-month OS % (AM0010 + FOLFOX: 54% vs FOLFOX: 45%)

Overall Survival with AM0010 and AM0010 + FOLFOX