Clinical activity and safety of PEGylated human IL-10 (AM0010) in combination with anti-PD-1

Aung Naing1,4, Kyriacos P. Papadopoulos1,6, Jeffrey R. Infante3, Deborah J. Wong2, Karen A. Autio2, Patrick A. Ott4, Gerald S. Falchook2, Manish Patel2, Shubham Pant3, Amita Patnaik2, Melinda Whiteside10, John B. Mumm11, Ivan H. Chan12, Johanna C. Bendell2, Todd M. Bauer3, Filip Janku5, Milind Javle5, Rivka Colen5, Nizar Tannir5, Peter Van Vlaetelaere7 and Martin Oft10

1 MD Anderson Cancer Center; 2 Sarah Cannon Research Institute/ Tenascine Oncology, PLLC; 3 Memorial Sloan-Kettering Cancer Center, New York, NY; 4 Dana-Farber Cancer Institute, Boston, MA; 5 University of California Los Angeles (UCLA), Los Angeles, CA; 6 Sarah Cannon Research Institute at NorthShore, Deerfield, IL; 7 Amgen Inc.; 8 ARMO BioSciences; 9 Beth Israel Deaconess Medical Center; 10 Memorial Sloan-Kettering Cancer Center, New York, NY; 11 University of Texas MD Anderson Cancer Center; 12 Dana-Farber Cancer Institute, Boston, MA

**Background and Methods**

**ARMO-0010** is a novel, PEGylated form of recombinant human IL-10 (rHuIL-10) that combines the anti-cancer activity and immune stimulation of IL-10 with a long blood half-life to allow continuous daily subcutaneous (SC) injection. AM0010 has been evaluated alone and in combination with several anti-cancer drugs. Here we report on the use of AM0010 in combination with pembrolizumab, a humanized antibody that targets PD-1.

**Study Design and Blinding**

- **Randomized, open-label, multi-center, multi-first phase trial**
- **Dose escalation and expansion phases**
- **Patients**: RCC, NSCLC and Melanoma patients
- **Combination**: Continuous Daily Subcutaneous Injection

**Immune Activation by PEGylated IL-10**

- **Key proteins in PEGylation**:
  - Tumor antigen recognition
  - T cell receptor
  - MHC restriction, cytokine production
  - IL-12p70, IFN-γ, TGF-β

**Key proteins in Tumor rejection with Pembrolizumab**

- **Tumor antigens
  - MHC restriction, cytokine production
  - IL-12p70, IFN-γ, TGF-β**

**Immunotherapy: PD-1/PD-L1 blockade**

- **Blockade slows tumor growth and increases pre-existing immune cell infiltration**
- **Tumors respond to pre-existing immune cell infiltration**
- **Tumor rejection**

**Immune Activation by PEGylated IL-10**

- **IL-10 induces CD8+ T cells and increases pre-existing immune cell infiltration**
- **Tumor rejection**

**Combination with Pembrolizumab**

- **CD8+ T cells and tumor rejection**
- **Increased pre-existing immune cell infiltration**
- **Tumor rejection**

**Results**

- **AM0010 monotherapy**
  - **Clinical activity and safety**
  - **PD-L1 blockade**

- **AM0010 + pembrolizumab**
  - **Induced sustained suppression of PD-1**
  - **Effector cells**

**Conclusion and Outlook**

- **Summary**
  - **10 patients with immune checkpoint inhibitor intolerance**
  - **Clinical activity and safety**
  - **Pretreatment with AM0010 + pembrolizumab**

**Mechanism of Action**

- **PEGylation**
  - **IL-10 half-life increased from 10 min to 2.5 days**
  - **Continuous SC injection**
  - **Decreased immune toxicity**

**Safety**

- **10 patients with immune checkpoint inhibitor intolerance**
- **Clinical activity and safety**
- **Pretreatment with AM0010 + pembrolizumab**