Efficacy and Safety of PEGylated Human IL-10 (AM0010) in Combination with an anti-PD1 in Renal Cell Cancer

Aung Naing1, Jeffrey R. Infante2, Deborah J. Wong3, W. Michael Korn4, Raid Aljumaily5, Kyriakos P. Papadopoulos6, Karen A. Autio7, Shubham Pant3,8, Todd M. Bauer2, Alexandra Drakaki3, Naval G. Daver1, Navneet Ratti8, Annie Hung8, Peter Van Vlasselaer8, Gail L. Brown8, Martin OFF and Nizar Tannir9

Background

At therapeutic concentrations, AM0010 (PEGIL-10) stimulates the cytotoxic, survival and proliferation of CD8+ T cells. IL-10 receptors are expressed on activated and exhausted CD8+ T cells, providing a rationale for combining AM0010 and an anti-PD1. Partial tumor responses (PR) were observed in 4 of 16 patients with poor to intermediate risk RCC (G1-2) treated with AM0010 monotherapy. In dose escalation, 4 of 8 RCC patients receiving AM0010 plus pembrolizumab in 3rd line of therapy, had a PR. The mPFS was 16.7 months.

Study Design and Eligibility

Patients in the AM0010 + Pembrolizumab cohort received 10 or 20 mg/kg AM0010 daily and 2mg/kg Pembrolizumab. AM0010 doubled every 2 weeks until progression, severe toxicity or unacceptable toxicity. Pembrolizumab was administered for a maximum of 2 years. In both arms, pembrolizumab was discontinued if tumor progress. Pembrolizumab treatment was reinstated if confirmed CR/PR or stable disease. Tumors were evaluated every 2 cycles. Excluded prior Guillain-Barré syndrome and neuro-inflammatory diseases.

Mechanisms of Action

IL-10 protects activated, Granzyme + T cells and continuous activation leads to the activation and proliferation of CD8+ T cells.

Results - AM0010 + Nivolublimab in Pembrolizumab

ARMS0010 Monotherapy in RCC Patients

AM0010 + anti-PD1 - RCC Patient Characteristics

Table: Efficacy of AM0010 or AM0010 + anti-PD-1 in RCC Patients

Summary of Results

AM0010 + anti-PD-1 is well tolerated in RCC (Recommended Phase 2d) dose is 10 µg/kg in combination with an anti-PD1.

No exacerbation of autoimmune TAEs observed in combination with anti-PD1 antibodies.

AM0010 + anti-PD1 induces infiltration of CD8+ T cells and clonal expansion of novel T cells within analysis of the pretreatment immune microenvironment may correlate with tumor response.

Further subpopulation analysis is in progress.

The preliminary clinical responses and the observed immune activation are encouraging and warrants further exploration of this combination in Phase 2 and 3 studies in RCC.

Information

SPONSOR

Analysis is being developed by AM0010 Holdings Inc.

REFERENCES

Naing et al., JCO, 2016; Mumm et al., Cancer Cell, 2011; Emmerich et al., Cancer Research, 2012

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Naing et al., JCO 2016; Mumm et al., Cancer Cell 2011; Emmerich et al., Cancer Research, 2012

For more information on the trial, go to clinicaltrials.gov (NTCT number: NCT02913642).