A FIRST-IN-HUMAN STUDY OF PEGYLATED RECOMBINANT HUMAN IL-10 (AM0010), DAILY ADMINISTERED FOR FOUR MONTHS IN SELECTED ADVANCED SOLID TUMORS.

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AM0010 - BACKGROUND

- Recent developments in cancer immunity have sparked the interest of scientists and clinicians, yielding novel and exciting immunotherapeutics.
- AM0010 is a pegylated recombinant form of human IL-10 (PEG-rHuIL-10) that is being developed for the treatment of cancer.
- PEG-IL-10 increases and activates intra-tumoral CD8+ T cells (Fig. 2).
- Intra-tumoral memory T cells correlate with survival in cancer patients.
- In preclinical studies, PEG-IL-10 induces the rejection of large tumors and the development of immunologic memory against the tumor cells (Fig. 4).

AM0010 / PEG-IL-10 Mechanism of Action

- Induces CD8+ T cell expansion via increased STAT3 phosphorylation (Fig. 2a,c).
- Activates CD8+ T cell via STAT1 phosphorylation (Fig. 2c).
- T cell activation increases Signal 2 via reduction of PD-1 expression.
- Induces IFN-γ in CD8+ T cells (Fig. 2b).
- IFN-γ induces MHC in tumor cells and dendritic cells (Signal 1) and induces co-stimulatory molecules on dendritic cells (Signal 2).
- Induces Granzymes in CD8+ T cells to kill tumor cells (Fig. 2b).

STUDY OBJECTIVES

Primary

- To assess the safety, tolerability, maximum tolerated dose (MTD), and pharmacokinetics (PK) of AM0010.

Secondary

- To assess the tumor response.
- To evaluate anti-AM0010 antibodies.

Exploratory Biomarkers

- Serum cytokines.
- T and B cell responses to tumor associated antigens.
- Immuno-profiling.
- Immuno-score.

ENDPOINTS

- Tumor Response will be assessed using the immune related response criteria (irRC) or the Prostate Cancer Working Group Criteria (PCWG2) for progression in bone.
- Adverse Events will be graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE v 4.02).

TRIAL DESIGN

- First-in-human, open-label, dose escalation study to evaluate the safety and tolerability of AM0010 in patients with advanced solid tumors dosed daily subcutaneously (SC) (clinicaltrials.gov identifier NCT02009445).

TRIAL STATUS

- This study is open for enrollment at 4 sites in the United States.
- As of May 22, 2014 22 patients have been enrolled in the Dose Escalation phase.
- Enrollment in Cohort 4 (10 µg/kg) has been completed without the MTD being reached.
- Cohort 5 (20 µg/kg) opened to enrollment in May 2014.

ACKNOWLEDGMENTS

The authors would like to acknowledge the contribution of patients and their families in participating in this clinical trial.

SPONSORS

AM0010 is being developed by ARMO Biosciences.

REFERENCES

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3. Munn, Emmerich et al. 2011

CONTACT INFORMATION

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