PEGylated IL-10 (AM0010) for advanced solid tumors - a Phase 1 study

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Abstract

Background: PEGylated IL-10 (AM0010) induces local infiltration and survival of immunotherapy-naive tumors in a phase 1/2 study. The presence of IL-10 and the expression of the tumor suppressor TSG-6 in the tumor microenvironment provide a rationale for the clinical activity observed in the phase 1/2 study. The aim of the current study was to further evaluate the antitumor activity of AM0010 in patients with advanced solid tumors.

Results: AM0010 was well tolerated in the dose range tested. The most common adverse events (AEs) were fatigue, rash, and increased transaminases. The drug had a favorable safety profile and was generally well tolerated. The tumor-infiltrating CD8+ T cells increased in patients treated with AM0010. The combination of AM0010 and immunotherapies is being evaluated in clinical trials.

Conclusion and Outlook: AM0010 has a favorable safety profile and is well tolerated in the dose range tested. The drug is being further evaluated in combination with immunotherapies in clinical trials.

Immune Activation by PEG-IL-10 in Patients

AM0010 Monotherapy Dose Escalation

- 5 patients (45%) treated at 20-40 µg/kg had disease control for at least 2 months.
- 5 patients had mixed responses indicating anti-tumor activity.
- 2 patients (18%) treated at 25-40 µg/kg had objective response (PR) and had minimal disease (Table 1).
- 2 patients continue treatment at 6 weeks (documented complete response and stable disease). Ten patients (91%) had IL-10 increases and cytokine expression were observed to be increased in patients treated with AM0010.

AM0010 Monotherapy Pancreatic Cancer

- 10 patients with pancreatic cancer patients treated at 25-40 µg/kg had at least stable disease for at least 2 weeks. (Fig. 10). Patients treated with AM0010 had a higher degree of activation (Fig. 10).

AM0010 Monotherapy Pancreatic Cancer (250µg/kg) (mOS=10 weeks)

- 35% of patients with pancreatic cancer patients treated at 25-40 µg/kg had at least stable disease for at least 2 weeks. (Fig. 10).

Method & Results

- In patients with immune suppressive tumor types (Melanoma, RCC, NSCLC) AM0010 was administered for 3 days a week (250µg/kg) and the combination with anti-PD-1 was administered for 3 days a week (250µg/kg + PD-1 inhibitor).

Conclusion

- Combination of AM0010 with anti-PD-1 is well tolerated.

Study Design - Part A: Monotherapy AM0010

- This is a phase 1, open-label, dose escalation study evaluating the preliminary clinical activity, tolerability and safety of AM0010 in patients with advanced solid tumor, dose-escalation was conducted in a 3+3 dose-escalation scheme.

Study Design - Part B: Combination therapy with Chemotherapy or Immuno-therapy

- Preliminary research and the clinical outcome of the mechanism of action supports synergies between AM0010 and other checkpoint inhibitors (Conclusion and outlook).

- The maximal tolerated dose (MTD) is defined as the dose that is safely administered in combination with a number of tumor therapies, including immune checkpoint inhibition inhibitors.