Open Label, Phase I/II Study of the Safety, Tolerability and Efficacy of Intravenous Alpha-1 Antitrypsin (AAT) [Glassia®] in Type 1 Diabetes

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Introduction

Alpha-1-Antitrypsin (AAT) has been shown to reduce pro-inflammatory markers and protect pancreatic islets from autoimmune responses in pre-clinical studies.

Study Design

Phase I/II, open-label study to evaluate the safety and efficacy of AAT (Glassia®; Kamada Ltd) on beta cells preservation and glycemic control in Type 1 Diabetes (T1D) (clinicaltrials.gov NCT01304537).

Methods

24 patients (12 male; age 9-17 years) with recently diagnosed T1D (mean 65±44.3 days) were allocated to receive 40, 60, or 80 mg of AAT/kg bw in 18 infusions. Patients were followed for additional 8 weeks with no treatment. Patients were assessed for adverse events (AEs), beta-cell function (MMTT), insulin intake and HbA1c%.

Results

All subjects completed the study. No Serious AEs occurred. AEs were mild and mostly infusion-related (fatigue, headache). End-of-study slope analysis of C-peptide [max] and C-peptide [AUC] revealed no significant changes from baseline. After 12-15 months from diagnosis, mean C-peptide [max] was 0.51±0.40 pmol/mL vs. 0.69±0.42 pmol/mL at baseline; AUC% decreased 23% from baseline vs. ~40-50% expected decrease after 12-15M from diagnosis. Mean HbA1c levels decreased significantly from baseline (7.16±0.82% vs. 8.82±1.78%, p< 0.001) (Figure 1). At end-of-study, 48% of patients decreased insulin dose and anti-GAD and anti-islet antibodies level decreased in the entire cohort (Figure 2).

Figure 1 - HbA1c levels during the study

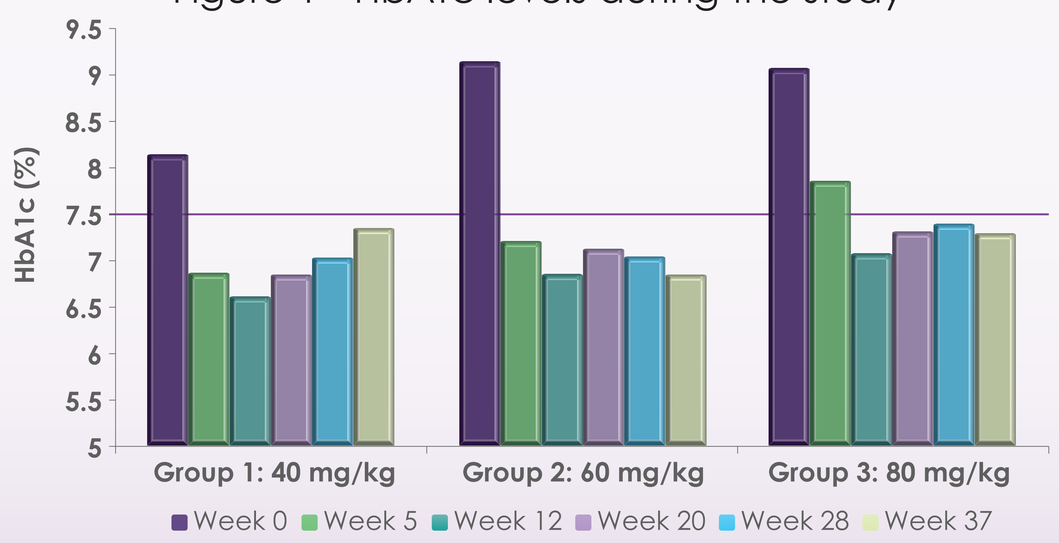
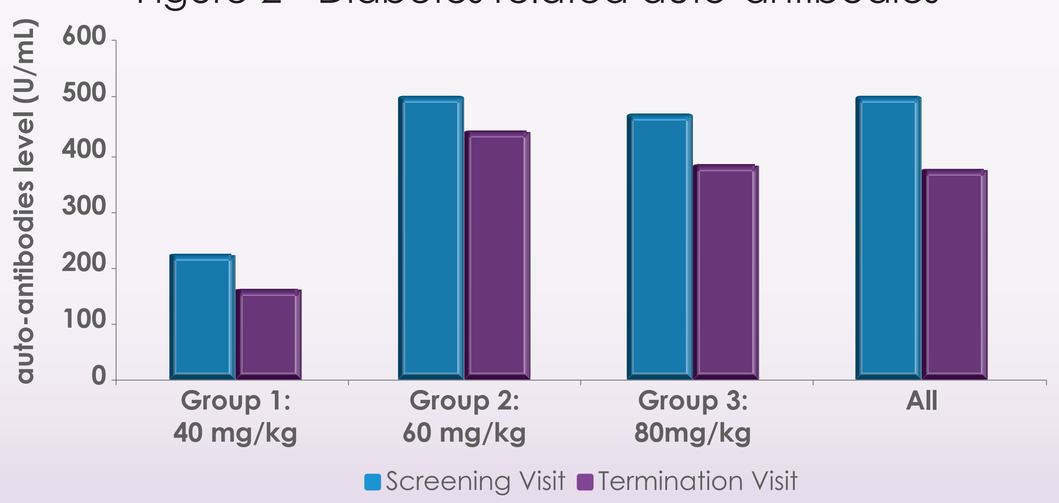
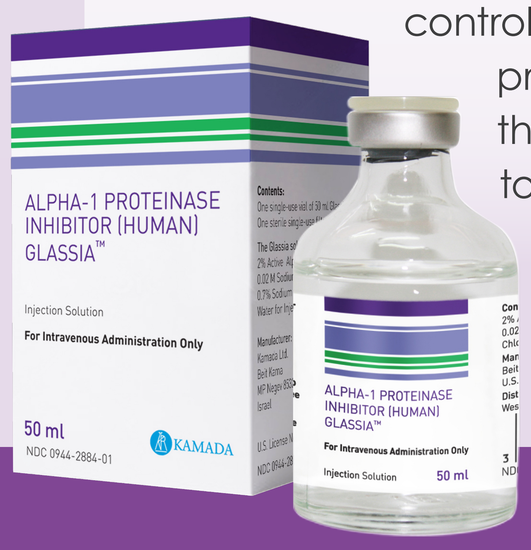


Figure 2 - Diabetes related auto-antibodies



Conclusion

Glassia has a high safety and tolerability profile in pediatrics T1D patients. The improved metabolic control and beta-cell function after 12-15 months from diagnosis may indicate that AAT exerts a protective effect on beta-cells, leading to a halt in disease progression and re-modulation of the autoimmune attack. Long-term placebo-controlled studies with larger cohorts are needed to confirm this effect.



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