Preliminary Results of an Exploratory Phase I Clinical Trial of Anchored Canine Interleukin-12 (cANK-101) in Dogs with Advanced Oral Malignant Melanoma

Matheus Moreno Passos Barbosa1, Angel J. Lopez1, Rachel Uyehara1, Rebecca L. Kamerrer1, Michael Schmidt2, Sallaija Battula2, Howard L. Kaufman2, Timothy M. Fan1
1University of Illinois Urbana-Champaign, Urbana, IL, 2Ankyra Therapeutics, Boston, MA

ABSTRACT

Malignant melanoma is the most common form of skin cancer with a median survival of 6 months by stage with stage IV or IVb disease. Currently, there are limited effective systemic treatment options for these patients with advanced disease. We have developed an engineered cytokine delivery approach in which canine cIL-12 is covalently linked to autologous human Alhydrogel® to form the complex cANK-101. The anchored cIL-12 form is stable, functional, and capable of inducing positive clinical responses in a phase I clinical trial. We report here the preliminary results of the exploratory Phase I trial of cANK-101 in dogs with oral melanoma.

The clinical study was approved by the University of Illinois, College of Veterinary Medicine, Institutional Animal Care and Use Committee, and all procedures adhered to the principles described in the Guide for the Care and Use of Laboratory Animals. Clinical trial participants were provided with oral melanoma diagnosis, staging and progression data, as well as medical history.

CANCINE MALIGNANT MELANOMA

Study Design

Figure 1. Schematic of “Anchored Immunotherapy” platform. A. A lymphocyte or cell line of interest bearing peptide (ABP) co-expressed with the Fc domain of human IgG2 is coupled to the terminus of an injected or implanted peptide (ABP). B. The resulting complex is injected or implanted to engage antigen expressing cells in vivo. cIL-12-ABP displays efficacy in both lethally irradiated and intact mice at both 100 µg/kg and 200 µg/kg with corresponding increase in efficacy.

CANINE ANK-101

Table 1. Baseline Characteristics and Demographics (n=8/20)

Table 2. Summary of treatment-emergent adverse events (TEAEs) per patient

Figure 2. Tumor biopsies were collected as per the clinical protocol and analyzed for IL12p35 and IL12p40 expression. The treatment groups were determined as patient #005 (20 µg/kg cohort) and patient #007 (10 µg/kg cohort).

Figure 3. Tumor-bearing mice were subcutaneously injected with cANK-101 peptide (ABP) solution. A. Tumor growth following treatment (125 µg/kg) was observed in a murine melanoma model in vivo. B. Tumors were imaged at 129 days post-treatment with cANK-101 peptide. C. Significant tumor growth inhibition was observed in a murine melanoma model in vivo.

CONCLUSIONS & FUTURE DIRECTIONS

- Ankyra’s proprietary Anchored Immunotherapy platform utilizes the FDA-approved vaccine adjuvant Alhydrogel® (aluminum hydroxide) as a scaffold to locally retain antigen-cytokine drugs and is designed to improve the therapeutic window of patient immunotherapies.
- The canine melanoma cell line (cIL-12-ABP) is stable and has shown efficacy in multiple animal platforms in vivo and in vitro.
- The results from this ongoing clinical trial suggest that cANK-101 is safe and well-tolerated in dogs with advanced melanomas.
- cANK-101 treatment is associated with increases in serum IL-10, IFN-γ, and IL-12, increases in tumor infiltration of CD8a+ T-cells and regulatory T (Treg) cells, and decreases in MyD88 expression.
- Based on the emerging safety profile, the study will expand cANK-101 to an additional cohort at 20 µg/kg.
- Data from this study will help us to remove new thresholds and may represent a new treatment paradigm for dogs with advanced melanoma and possibly other solid tumors.

ACKNOWLEDGMENTS

The authors would like to thank the canine participants for their participation in the study. We also thank Dr. Braden for his expertise in veterinary drug development and Melissa Wiley for her support with biomedical and electronic data management. We thank the Cancer Engineering and Pharmacology (CEP) shared resource at the Cancer Center of Illinois for scientific support and Cancer Care Clinics at the University of Illinois Veterinary Teaching Hospital for patient care.

REFERENCES