# Kv9 a novel cancer immunotherapeutic for solid tumours in dogs

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## Background

Cancer is the number one cause of death in dogs, with 25% of all dogs getting cancer in their lifetime. We have extrapolated this to be that 25,000 dogs in New Zealand, six million dogs in the US, and 30 million dogs world-wide are diagnosed with cancer annually. Cancer immunotherapy is an emerging field of treatment for dogs, primarily due to issues with current treatment options (surgery, chemotherapy and radiation). Up to 60% of pet owners decline treatment due to concerns about the cost, quality of life and side effects associated with current treatment options. With the additional limitation that 70% of current treatments are only available to specialists, however 94% of pets with cancer never visit a specialist. This means a large portion of dogs with cancer are being left untreated.

An immune stimulating molecule, AGI-134, a Kode Technology construct (Henry *et al.* 2023) was identified for use in solid human cancers. In human phase 1/2a clinical trials it demonstrated an excellent safety profile and initial efficacy data (BiolineRx, 2022). Unfortunately, AGI-134 is unsuitable for use in animals as it targets α-Gal antigen which is found naturally in almost all animals except higher primates (Shaw *et al.* 2019). We therefore adapted these principals and identified two alternative compounds suitable for use in animals, which we have called Kv9.

## Pharmaco-kinetics

It has been extensively proven that Kv9 molecules incorporate into cell membranes, and therefore cells (primarily tumour cells) that are near the injection site will become labelled with Kv9. Existing antibodies in the circulation then attach to the Kv9 labelled cells, which activates the complement cascade, causing a localised immune response and destruction of the labelled cells. The resultant cell fragments highly decorated in immune compounds (antibody and complement) are processed by the immune system. If previously hidden tumour markers become recognised, then new antibodies and immune cells which recognise these cancers markers will circulate throughout the body, and attack both primary and secondary tumours. The process is essentially a vaccination, albeit personalised, and so immune memory should also develop, which may provide protection against further development of tumours.

## In-vitro research

Two versions of Kv9 have been tested with 45 canine and 13 equine serums. We assessed both the presence of pre-existing antibodies and their ability to activate the complement cascade. Both Kv9 constructs when tested at the concentration range for clinical use were able to activate complement and cause destruction of target cells.

## Clinical trial

Both versions of Kv9 will initially be trialled in New Zealand to determine the safety, dose and efficacy of these two molecules in canines. Kv9 compounds have an experimental drug approval Research Approval Certificate A012161 (expiry 17th day of May 2028) from MPI (Ministry for Primary Industries) according to ACVM

81(agricultural compounds, including veterinary medicines) Veterinary Medicine Trial Approval criteria. Ethical approval for experimental use is granted by AgResearch AEC # A012161-01.

The plan is to recruit 90 dogs presenting with a palpable cancer mass into the trial, initially from the Hawkes Bay area and once established expand nationwide. Participants will need to meet the following criteria:

- Suspected soft tissue sarcoma
- Not requiring surgery within the next 30 days
- Estimated to survive three months minimum
- Minimum tumour size of 1cm x 1cm (no maximum)
  - No minimum or maximum weight for the animal
- Not be receiving chemotherapy or immune modulatory drugs (prednisone etc)
- Not knowingly immunocompromised
- Not pregnant or lactating.

Each dog will receive three doses by intra-tumoural injections (multiple sites) every 10-14 days. At least 10 days after the third injection, surgery may be elected by the owner. All animals will be monitored by our study team at regular intervals for up to two years.

## Wider implications

Canines are increasingly recognised as a valuable model for studying human cancers. The progress made in developing cancer therapies for canines not only advances veterinary medicine but also supports human medical research. Positive developments from this canine trial are expected to support ongoing research with Kode Technology compounds in human medicine.

## References

**Henry SM, Tuzikov AB, Bovin NV.** *Kode Technology Illustrated Technical Manual (1st Ed.)*, 2023 (accessed 17-03-2025)

**Shaw SM, Middleton J, Wigglesworth K, Charlemagne A, Schulz O, Glossop MS, Whalen GF, Old R, Westby M, Pickford C, Tabakman R, Carmi-Levy I, Vainstein A, Sorani E, Zur AA, Kristian SA.** AGI-134: a fully synthetic α-Gal glycolipid that converts tumors into in situ autologous vaccines, induces anti-tumor immunity and is synergistic with an anti-PD-1 antibody in mouse melanoma models. *Cancer Cell Int.* 19(1): 346, 2019

**BiolineRx Ltd.** BioLineRx *Announces Results from Phase 1/2a Study of Investigational Anti-Tumor Vaccine AGI-134 in Metastatic Solid Tumors*. BiolineRx Ltd.: Waltham, United States; 2022