METHODS

ABSTRACT: ITK is a non-receptor tyrosine kinase that plays a key role in T cell receptor (TCR) signaling in malignant T cells and may be a therapeutic target for the treatment of T cell lymphoma. In a previous pilot study, we observed that treatment with CPI-818, an irreversible small molecule inhibitor of ITK, resulted in clinical response and stabilization of disease in dogs with T cell lymphoma. In this study, we aimed to determine the degree of selectivity for ITK over other kinases with a similar structure (RLK or Non-hematopoietic Tyrosine Kinase, NHTK), explore the pharmacodynamic effect of CPI-818, and determine the potential of CPI-818 to act as an alternate signaling pathway, to induce antitumor activity in dogs with T cell lymphoma.

Methods and Materials: To assess the potential of CPI-818 to treat T cell lymphoproliferative disorders, the safety and tolerability of CPI-818 was investigated in dogs with spontaneous T cell lymphoma. The study was granted CSU IACUC/Clinical Review Board approval; written, informed consent from owner. A dose of 20 mg/kg CPI-818 BID was used, with plasma exposure predicted to be associated with full occupancy of ITK. Although CPI-818 is predominantly a T cell agent, dogs with cutaneous T cell lymphoma (CTCL). Full ITK occupancy in peripheral blood was pharmacodynamic evaluation of CPI-818 was performed in dogs with spontaneous T cell lymphoma.

Pharmacokinetic and Pharmacodynamic Analysis: To assess the potential of CPI-818 to treat T cell lymphoproliferative disorders, the safety and tolerability of CPI-818 was investigated in dogs with spontaneous T cell lymphoma. The study was granted CSU IACUC/Clinical Review Board approval; written, informed consent from owner. A dose of 20 mg/kg CPI-818 BID was used, with plasma exposure predicted to be associated with full occupancy of ITK. Although CPI-818 is predominantly a T cell agent, dogs with cutaneous T cell lymphoma (CTCL). Full ITK occupancy in peripheral blood was pharmacodynamic evaluation of CPI-818 was performed in dogs with spontaneous T cell lymphoma.

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