Weill Cornell Medicine

6-Ethylthioinosine for the Treatment of Cancers that Overexpress Adenosine Kinase (ADK)

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Background & Unmet Need

- The γ-herpesvirus KSHV, also called HHV-8, is the etiological agent of Kaposi's sarcoma (KS), multicentric Castleman's disease, and primary effusion lymphoma (PEL)
- KS, the most common malignancy in AIDS patients, is often treatable by antiviral therapy and radiation or chemotherapy
- PEL is a rare HIV-associated non-Hodgkin's lymphoma (NHL) that is largely a highly aggressive and intractable disease, with rapid progression to death
- **Unmet Need:** Specific and effective therapeutics for diseases caused by KSHV

Technology Overview

- **The Technology:** Identification of 6-ethylthioinosine (6-ETI) as a potent inhibitor of cancers that overexpress adenosine kinase (ADK)
- 6-ETI was identified through a high throughput screen of compounds that selectively inhibit NF-κB in a KSHV-infected PEL cell line (LC_{50}=50nM)
- The inventors then demonstrated that 6-ETI is converted into phosphor-6-ETI by ADK, which is commonly overexpressed in several cancers
- **PoC Data:** 6-ETI is highly effective in both PEL and disseminated multiple myeloma (MM) xenograft mouse models, with significant reduction in tumor burden and prolonged survival
- 6-ETI was also demonstrated to be effective against solid tumors that overexpress ADK, including those with resistance to 1L therapies
- 6-ETI is therefore a promising lead compound for targeted treatment of ADK positive cancers

Inventors:
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Patents:
US Application Filed

Publications:
Nayar et al. *J Clin Invest.* 2017.

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Technology Applications

- Treatment of plasma cell malignancies including PEL, PBL, and MM
- Treatment of solid tumors with ADK overexpression, such as NSCLC, colorectal, and pancreatic

Technology Advantages

- Precision medicine approach
- Applicable to multiple tumor types
- Demonstrated efficacy in PEL and MM xenograft models
- Overcomes treatment resistance to gemcitabine and erlotinib in pancreatic and NSCLC cancer

Supporting Data / Figures

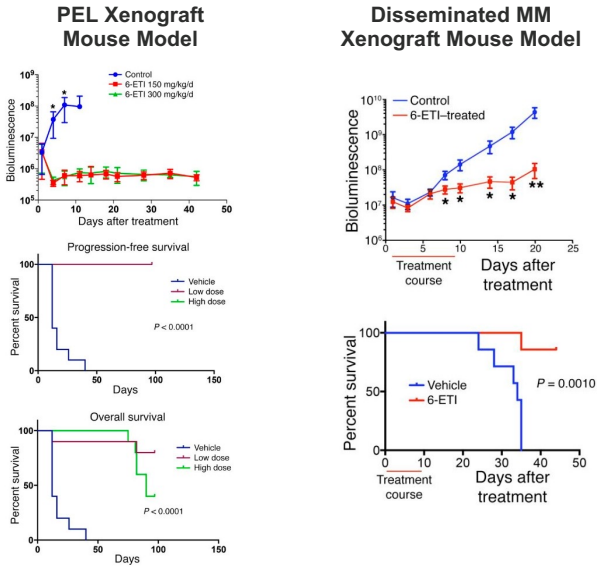

Figure 1: 6-ETI has demonstrated in vivo efficacy in both PEL and MM mouse models.

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