Model Name
Xenograft, Lymphoma, U-937

Item Number
581000

Introduction
The U-937 human histiocytic lymphoma xenograft model is used to evaluate therapeutic efficacy of investigational antineoplastic agent(s) in immune compromised mice.

Procedure Summary
Groups of eight (8), specific-pathogen-free (SPF) female nu/nu mice bred in an animal isolator (IVC racks) under SPF conditions at 22 ± 2°C are used. Viable human histiocytic lymphoma U-937 (ATCC CRL-1593) cells are injected subcutaneously into the right flank of experimental mice. Dose administrations are initiated when tumor volumes reach 100-150 mm³ (Day 1). Tumor volumes and body weights are measured and recorded twice weekly over the course of the study period. Study will continue for “n” days. Therapeutic efficacy may be evaluated for Tumor Growth Inhibition (TGI), Tumor Growth Delay (TGD), or both TGI and TGD.

Suggested Testing
Tumor Growth Inhibition (%TGI) is determined twice weekly by the formula: %TGI = (1 −[(Tn)/(Cn)]) × 100 where Tn = mean tumor volume of treated group on day “n”, and Cn = mean tumor volume of control group on day “n”. Tumor Growth Delay (%TGD) is expressed as the percentage by which the treated group median tumor volume is delayed in reaching the established tumor volume endpoint compared to the controls using the formula ((T-C)/C)) x 100 where T and C are median times (days) to reach the established tumor volume endpoint for the treated and control group, respectively.

Endpoint Parameters
Recommended tumor volume endpoint: 2000 mm³

Study Parameters
Tumor volume (mm³) is estimated according to the prolate ellipsoid formula: Length (mm) x [Width (mm)]² x 0.5.

Reference Compound(s)
Mitomycin, 2 mg/kg, IP, q4d x 4

Optional Services
- In Vitro cell proliferation
- MTD determination
- PK and bio-analysis for plasma and tumor
- Clinical chemistries and CBC data collection
- Continuous infusion dose administration (osmotic pump)
- Tumor and organ sampling

Literature
Biological Characterization of 3-(2-amino-ethyl)-5-[3-(4-butoxyl-phenyl)-propyldene]-thiazolidine-2,4-dione (K145) as a Selective Sphingosine Kinase-2 Inhibitor and Anticancer Agent. Kai Liu et al. PLOS One, Vol. 8, Issue 2, e56471, February 2013

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Modified Protocols
We will readily accommodate client-specified alterations.

Laboratory
These assays are performed at our AAALAC accredited laboratory in Taipei.

Animal Welfare
All aspects of this work is performed in general accordance with the Guide for the Care and Use of laboratory animals (National Academy Press, Washington, DC, 2011). The study protocol was approved by the Pharmacology Discovery Services IACUC and is performed with the oversight of veterinarians to assure the humane treatment of laboratory animals.

Therapeutic Response Data

Data shown are in male CB.17 SCID mice inoculated with $1 \times 10^7$ U-937 cells.

Two-way ANOVA followed by Bonferroni post-tests were applied for comparison between the vehicle and test substance-treated groups (**p<0.001).

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