Model Name
Syngeneic, Breast, 4T1 (orthotopic)

Item Number
578591

Introduction
The 4T1 orthotopic murine breast carcinoma model is used to evaluate therapeutic efficacy of investigational antineoplastic agent(s) in immune competent mice of the same background.

Procedure Summary
Groups of eight (8), specific-pathogen-free (SPF) female BALB/c mice bred in an animal isolator (IVC racks) under SPF conditions at 22 ± 2°C are used. Viable murine breast carcinoma 4T1 (ATCC CRL-2539) cells are injected into the mammary fat pad of experimental mice. Dose administrations are initiated when tumor volumes reach 40-80 mm$^3$ (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: \( \%TGI = (1 - ([Tn]/[Cn])) \times 100 \) 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 \( \frac{(T-C)}{C} \times 100 \) 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: 1000 mm$^3$

Study Parameters
Tumor volume (mm$^3$) is estimated according to the prolate ellipsoid formula: Length (mm) x [Width (mm)]$^2$ x 0.5.

Reference Compound(s)
Paclitaxel, 25 mg/kg, IV, qod x 5; anti-CTLA-4, 20 mg/kg, IP, q4d x 3; anti-PD-L1, 20 mg/kg, q4d x 3; anti-PD-1, 20 mg/kg, IP, q4d x 3

Supplemental Data
Baseline immune cell data generated from naïve tumor bearing mice: Lymphoid cell populations (CD4+, CD8+, T-reg) and Myeloid cell populations (Dendritic cells, MDSC, Neutrophils) within the tumor, liver, lung, and spleen.

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
- Ex vivo sample analyses using flow cytometry

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Literature
Reduction of Established Spontaneous Mammary Carcinoma Mastases following Immunotherapy with Major Histocompatibility Complex Class II and B7.1 Cell-based Tumor Vaccines. Beth A. Pulanski et al. Cancer Research, 58, 1486-1493, April 1, 1998

Related Assay(s) (Item # - Assay Name)
578590 - Syngeneic, Breast, 4T1

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

Two-way ANOVA followed by Bonferroni post-tests were applied for comparison between the vehicle and test substance-treated groups (*p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001).

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Baseline Immune Cell Data

Baseline Immune Cell Data: 4T1 Orthotopic Tumor

Baseline Immune Cell Data: 4T1 Orthotopic Liver

Baseline Immune Cell Data: 4T1 Orthotopic Lung

Baseline Immune Cell Data: 4T1 Orthotopic Spleen

Last modified July 17, 2018