4105 TRPH-222, a Novel Anti-CD22 Antibody Drug Conjugate (ADC), Has Significant Anti-Tumor Activity in NHL Xenografts and is Well Tolerated in Non-Human Primates

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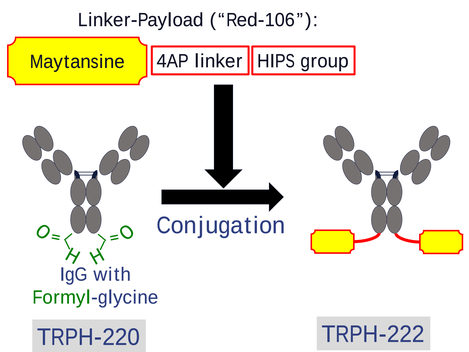
INTRODUCTION

- CD22 is a B-cell specific transmembrane protein and is overexpressed on a wide range of B cell malignancies including NHL (non-Hodgkin's lymphoma), FL (follicular lymphoma), DLBCL (diffuse large B-cell lymphoma), MCL (mantle cell lymphoma) and MZL (marginal zone lymphoma)
- The restricted lineage of CD22 and rapid internalization upon antibody binding make CD22 an appealing target for an antibody-drug conjugate (ADC) therapeutic for B-cell malignancies

TRPH-222 SMARTag™ ADC

- TRPH-222 is an anti-CD22 antibody site-specifically modified at one site in each heavy chain to express formylglycine (FG), allowing site-specific conjugation of a maytansinoid payload, a protease-insensitive spacer, and a functional group for coupling to an aldehyde on the antibody FG residues
- SMARTAG™ site specific non-cleavable conjugation enforces a maximum drug to antibody ratio (DAR) of 2 with high stability, enabling improved therapeutic index



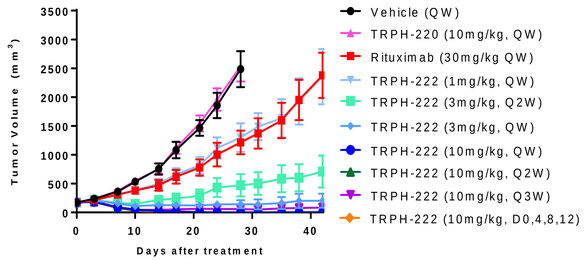
- *In vitro* evaluation of TRPH-222 demonstrates that it binds CD22, is rapidly internalized, and has pM potency against NHL cell lines (Drake, 2017, Mol. Canc. Ther.)

STUDY AIMS

- Characterize the anti-tumor activity of TRPH-222 in human NHL xenograft models
- Evaluate the PK and tolerability of TRPH-222 in cynomolgus monkeys

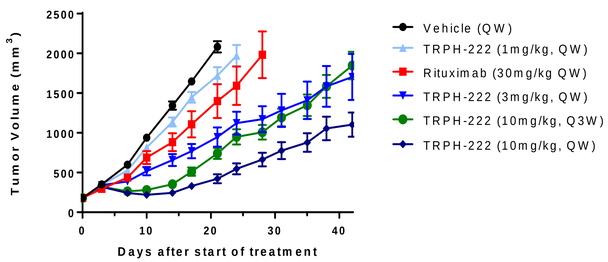
RESULTS

TRPH-222 Results in Tumor Stasis in WSU-DLCL2 DLBCL Xenografts

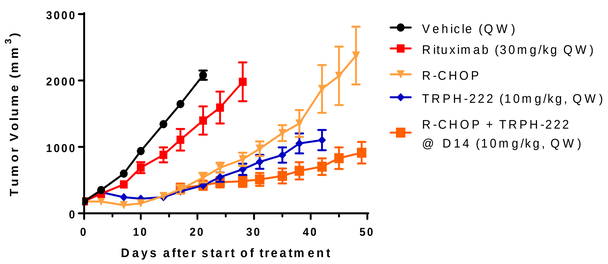


- TRPH-222 was well tolerated with no body weight loss
- Dose and schedule dependent TRPH-222 anti-tumor activity
- All tumors were eradicated in 10mg/kg QW & Q2W schedule and 5/8 tumors on Q3W schedule

TRPH-222 Inhibits Tumor Growth in Granta-519 MCL Xenografts following R-CHOP Escape



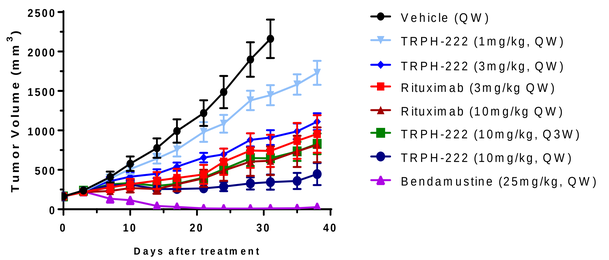
- Dose and schedule dependent anti-tumor activity
- 87% TGI at 10mg/kg QW schedule TRPH-222



- Transient tumor growth inhibition with R-CHOP
- TRPH-222 significantly inhibits tumor growth following R-CHOP escape

R-CHOP: Rituximab 30mg/kg D0, Cyclophosphamide 30mg/kg D0, Doxorubicin 2.475mg/kg D0, Vincristine 0.365mg/kg D0, Prednisone 0.15mg/kg QDx5

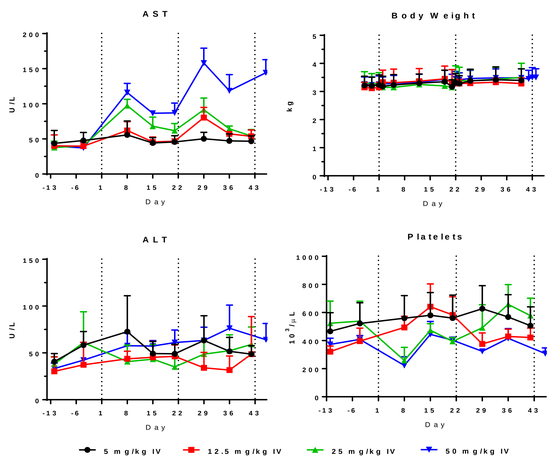
TRPH-222 Inhibits Tumor Growth in SU-DHL-2 DLBCL Xenografts



- 91% TGI at 10mg/kg QW TRPH-222
- Dose and schedule dependent TRPH-222 anti-tumor activity observed

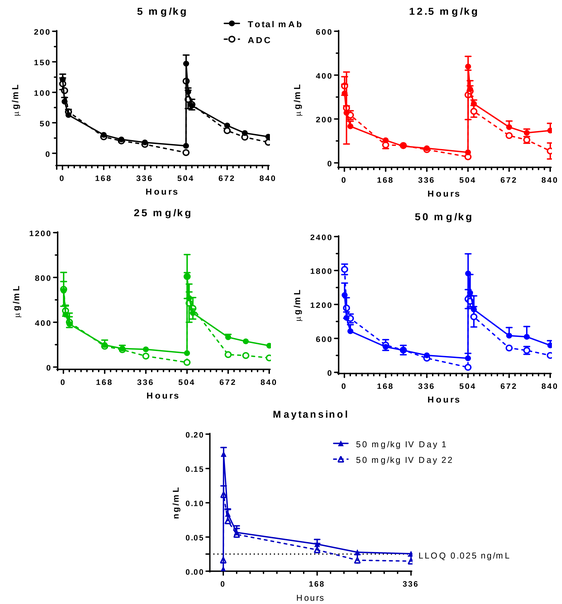
TRPH-222 Was Well Tolerated with Repeat Dosing in Cynomolgus Monkeys

- TRPH-222 was dosed IV once every 3 weeks
- 2 (5, 12,5 and 25mg/kg) or 3 (50mg/kg) doses



- No TRPH-222 related clinical findings up to 50mg/kg
- Minimal to mild platelet decreases that resolved 2 weeks post-dose
- Mildly increase AST activity ≥ 12.5mg/kg
  - Associated with minimal hypertrophy/ hyperplasia of Kuppfer cells in 50mg/kg group
  - Findings not considered adverse
- TRPH-222 was well tolerated with repeat dosing up to 50mg/kg with no test article related adverse findings

TRPH-222 Has Human IgG-like PK Properties



- TRPH-222 displayed PK properties predicted for a human IgG with $T_{1/2}$ slightly longer for mAb than ADC
- Maytansinol was the only maytansine containing species detected in monkey plasma
  - Maytansinol detected at very low levels (25-170pg/ml), ≤ LLOQ at 7 day
  - No intact free linker-payload detected

CONCLUSIONS

- TRPH-222 has significant anti-tumor activity
- Very high doses of TRPH-222 were well tolerated in monkeys supporting an improved therapeutic index. Doses described herein correspond to human equivalent doses significantly higher than for most ADCs approved or currently in development
- This may represent the highest dose of a maytansine containing ADC that has been tolerated in monkeys suggesting potential for best in class therapy in NHL
- IND-enabling toxicology studies are ongoing to support clinical evaluation of TRPH-222 in NHL in 2018