Blockade of the PPARα metabolic checkpoint with TPST-1120 suppresses tumor growth and stimulates anti-tumor immunity

Chen C. Whiting1, Nick Stock1, Davorka Messmer2, Austin Chen3, Lisa Rahbaek4, Derek Metzger2, Amanda Enstrom1, Michael Stundiv5, Nicholas DeVito1, David Sanner1, Peppe Prisanti4, Brent Hankes1, Dipak Panigrahy4, Girna Laport1

1Tempest Therapeutics, Inc., San Francisco, CA; 2Inception Sciences, San Diego, CA; 3Sunnybrook, Toronto, Canada; 4Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; 5Duke Cancer Institute, Duke University Medical Center, Durham, NC

ABSTRACT

TPST-1120 in vitro killing was conducted on primary CLL tumor cells. Flow cytometry was used to evaluate immune cell infiltrate in the tumor microenvironment (TME). TPST-1120 is a first-in-class, orally administered, potent, small molecule selective PPARα antagonist. TPST-1120 is a first-in-class, orally administered, potent, small molecule selective PPARα antagonist (Figures 1-5). TPST-1120 is a first-in-class, orally administered, potent, small molecule selective PPARα antagonist (Figures 1-5). TPST-1120 is a first-in-class, orally administered, potent, small molecule selective PPARα antagonist (Figures 1-5). TPST-1120 is a first-in-class, orally administered, potent, small molecule selective PPARα antagonist (Figures 1-5).

INTRODUCTION

TPST-1120 is a first-in-class, orally administered, potent, small molecule selective antagonist of the human peroxisome proliferator-activated receptor alpha (PPARα) (Figures 1-5).

TPRα is a transcription factor which induces fatty acid oxidation (FAO) and inflammation (Figure 1).

PPARα is an important regulator of metabolic processes and anti-tumor immunity.

TPST-1120 has significant anti-tumor activity as a monotherapy and in combination with chemotherapeutic or anti-PD1 agents.

Anti-tumor activity of TPST-1120 is mediated through: 1) direct killing of tumor cells dependent on FAO; 2) inhibition of PI3K-AKT-mTOR pathway suppressing immune effector cells and inhibiting suppressor cells; and 3) restoration of TSP1 to homostatic levels.

METHODS

TPST-1120 + anti-PD1 therapy induces significant anti-tumor efficacy in PancOH7 model (n=6) and PancOH7 model (n=6) and PancOH7 model (n=6). TPST-1120 + anti-PD1 therapy induces significant anti-tumor efficacy in PancOH7 model (n=6) and PancOH7 model (n=6)

RESULTS

TPST-1120 blocks PPARα metabolic checkpoint First-class oral PPARα antagonist

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REFERENCES