ASP8374/PTZ 201
NON-CONFIDENTIAL SUMMARY

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ASP 8374/PTZ 201 SUMMARY

Project Code	A8374/PTZ201
Project Name	ASP8374/PTZ201
Mechanism of Action	Blocking binding of TIGIT [1)] to its ligands PVR [2)] (CD155) and PVRL2 [3)] (CD112) which functions as immune checkpoint
Target Indication(s)	Solid tumors and potential hematologic malignancies
Dosing and Administration	700mg/3weeks, iv infusion, until PD
Latest Phase Development	P1

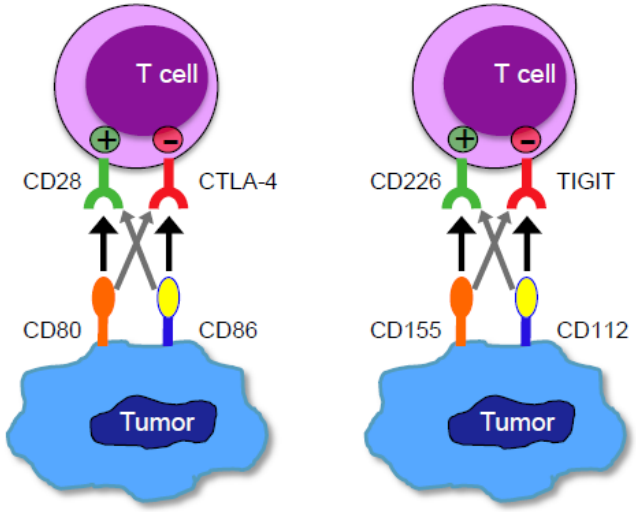
1) TIGIT: T Cell Immunoreceptor With Ig And ITIM Domains
2) PVR: PVR cell adhesion molecule
3) PVRL2: Poliovirus receptor-related 2
4) PD-1: Programmed cell death 1

TIGIT AS A TARGET

- TIGIT (T cell immunoreceptor with Ig and ITIM domains) is a well validated immune checkpoint expressed on memory CD4+ & CD8+ T cells, Tregs, and NK cells
- CD226/TIGIT is an immune checkpoint analogous to CD28/CTLA-4
  - CD226 provides a costimulatory signal to T cells
  - TIGIT provides a coinhibitory signal to T cells
- TIGIT ligands CD155 (PVR) and CD112 (PVRL2) are overexpressed in tumors, providing an immune suppressive environment
- Anti-TIGIT blocking antibodies
  - Enhance T cell proliferation and IFN-γ secretion
  - Increase cytotoxic activity of NK cells

Competitors

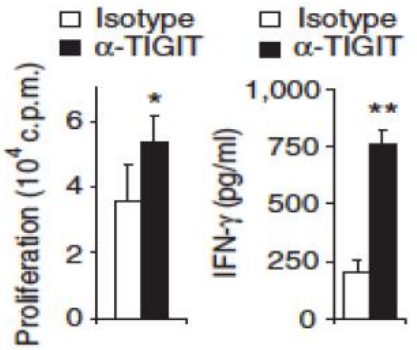
- Roche/Genentech (Johnston RJ. Cancer Cell 2014);
  - FIH started in May 2016
- BMS (Chauvin J-M. JCI 2015)



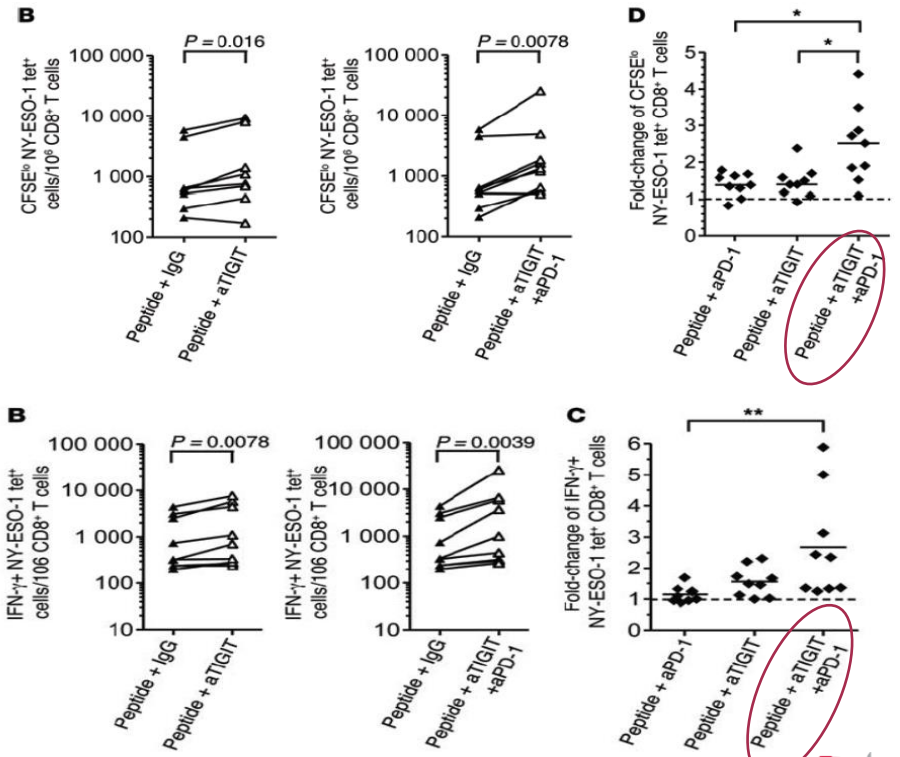
TIGIT AS A TARGET

- TIGIT inhibition increases immune cell activity
- TIGIT is co-expressed with PD-1 in tumor infiltrating lymphocytes
  - Co-blockade of PD-1 and TIGIT ⇑ proliferation & cytokine production in NY-ESO-1 specific CD8+ T cells

Inhibition of TIGIT on human T cells



Yu et al., Nat Imm 2009 10:48

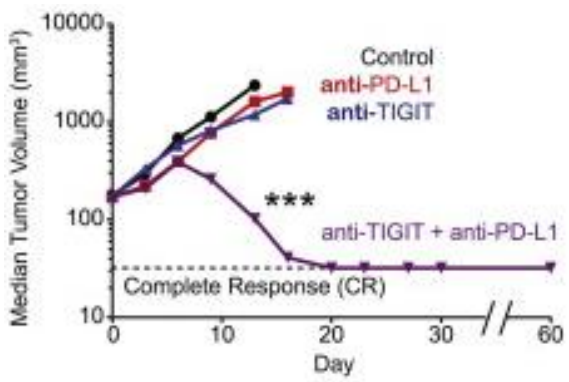


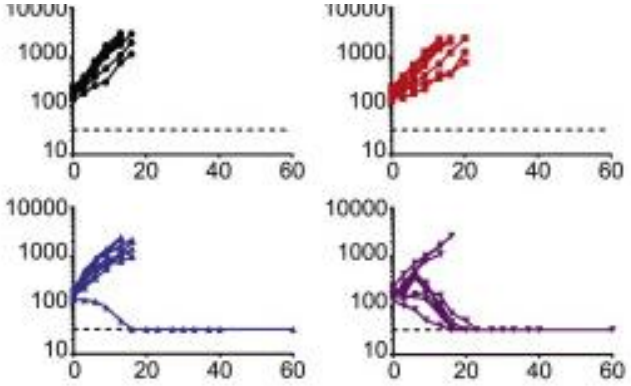
Chauvin et al., JCI 2015

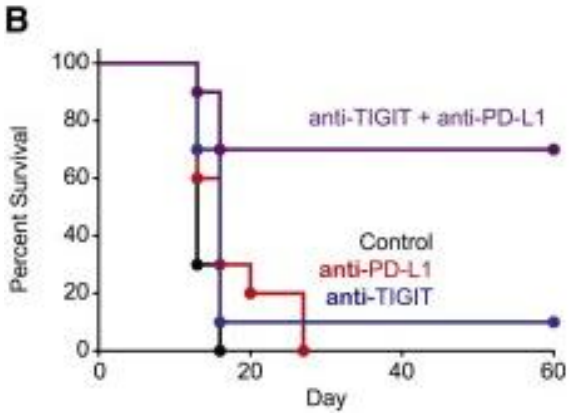
BMS antibody: Published Data

TIGIT AS A TARGET

- Combination of anti-PD1 and anti-TIGIT Abs demonstrated superior efficacy in tumor models







- CT26 syngeneic mouse models were treated with isotype control (black), anti-PD-L1 + control (red), anti-TIGIT + control (blue), or anti-PD-L1 + anti-TIGIT (purple) antibodies for 3 weeks.
- Minimal activity observed with single agent anti-TIGIT or anti-PD-L1.
- Combination of anti-PD-L1 and anti-TIGIT demonstrated potent anti-tumor activity.

Johnson et al., Cancer Cell, 2014

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Genentech Antibody: Published Data

ASP8374 CHARACTERIZATION IN NONCLINICAL MODELS

Characterization of ASP8374, a fully-human, antagonistic anti-TIGIT monoclonal antibody

- ASP8374 stimulated cytokine production in cultured human primary cells
- ASP8374 in combination with pembrolizumab induced higher T-cell activation in vitro than either treatment alone
- An anti-mouse TIGIT antibody surrogate of ASP8374 elicited anti-tumor activity as monotherapy or in combination with anti-PD1 in syngeneic tumor models
- *See reference and link below for full details*

Shirasuna et al. (2021) **Characterization of ASP8374, a fully-human, antagonistic anti-TIGIT monoclonal antibody.** *Cancer Treat Res Commun.* 2021 Jul 11;28:100433. https://doi.org/10.1016/j.ctarc.2021.100433

ASP8374/PTZ-201: HISTORY/STATUS

- MOA: Fully humanized IgG4 anti-TIGIT mAb that blocks binding of TIGIT to its ligands PVR and PVRL2
- Target Indications: Solid Tumors
- Pre-IND Meeting Request: Submitted to FDA on 13Jul2016
- IND Submission in 1Q2017
- Phase I –FSI 3Q2017

CLINICAL STUDIES THUS FAR

ASP8374-CL-0101: Active study, Not enrolling
A Phase 1b Study of **ASP8374**, an Immune Checkpoint Inhibitor, as a Single Agent and in Combination With Pembrolizumab in Subjects With Advanced Solid Tumors

8374-CL-0102: Completed
A Phase 1, Open Label Study of **ASP8374**, an Immune Checkpoint Inhibitor, in Japanese Patients with Advanced Solid Tumors
https://astellasclinicalstudyresults.com/hcp/findresult.aspx?RID=;;;8374-CL-0102;;;

IIT: Active, Not enrolling yet.
Phase Ib Trial of ASP8374 and Cemiplimab in Recurrent Malignant Glioma Patients.

INTELLECTUAL PROPERTY

Patents covering ASP8374

- **Substance Patent Family: WO/2017/059095 (filed on Sep. 29, 2016)**
  - Granted: Indonesia, Russia, South Africa, US
  - Pending: Argentina, Australia, Brazil, Canada, China, Colombia, Europe, Gulf Coast, Hong Kong, Israel, India, Indonesia, Japan, Malaysia, Mexico, Philippines, Russia, Singapore, South Africa, South Korea, Thailand, Taiwan, Ukraine, US, Vietnam
- **Use Patent Family: WO/2018/183889 (filed on Mar. 30, 2018)**
  - Pending: Australia, Brazil, Canada, China, Colombia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Jordan, Malaysia, Mexico, Philippines, Russia, Singapore, South Africa, South Korea, Thailand, Ukraine, US, Vietnam