TEMPEST

THERAPEUTICS

ASCO 2022 Investor Breakfast

June 5, 2022

Agenda

- Introductions and Brief Overview of Tempest
- TPST-1120

  Mark Yarchoan, M.D.
  Associate Professor of Oncology
  Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

- TPST-1495

  Susanna V. Ulahannan, M.D., MMEd
  Assist. Professor of Medicine, Stephenson Cancer Center, the Univ. of Oklahoma
  Associate Dir, Oklahoma TSET Phase 1 Program

- TREX1

  Jason J. Luke, M.D., FACP
  Associate Professor
  Director of the Cancer Immunotherapeutics Center, Univ. of Pittsburgh School of Medicine

- Q&A

  Drs. Yarchoan, Ulahannan and Luke to be joined by:

  Toni K. Choueiri, M.D.
  Director, Lank Center for Genitourinary Oncology, Dana Farber Cancer Institute
  Jerome and Nancy Kohlberg Chair and Professor of Medicine,
  Harvard Medical School

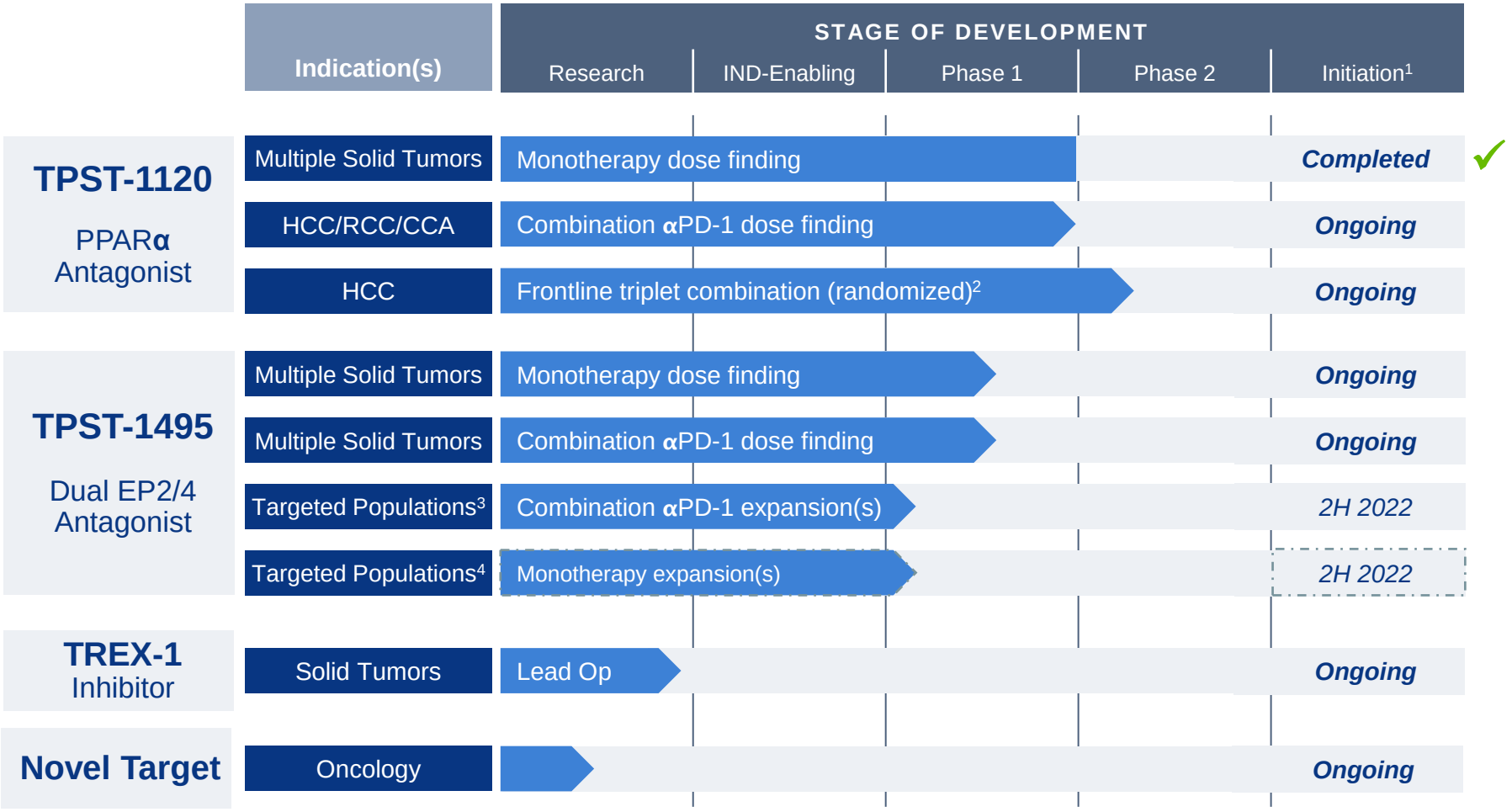
Information Regarding Disclosures

Forward-Looking Statements

This presentation contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (the "Securities Act")) concerning Tempest Therapeutics, Inc. ("Tempest Therapeutics"). These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Tempest Therapeutics, as well as assumptions made by, and information currently available to, management of Tempest Therapeutics. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "could", "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: our strategies, prospects, plans, expectations or objectives for future operations; the progress, scope or timing of the development of our product candidates; the benefits that may be derived from any future products or the commercial or market opportunity with respect to any of our future products; our ability to protect our intellectual property rights; our anticipated operations, financial position, ability to raise capital to fund operations, revenues, costs or expenses; statements regarding future economic conditions or performance; statements of belief and any statement of assumptions underlying any of the foregoing. Many of these risks are described in greater detail in the Form 10-Q filed by Tempest Therapeutics with the Securities and Exchange Commission on May 13, 2022.

Except as required by applicable law, Tempest Therapeutics undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

First-in-Class* Oncology Pipeline with Broad Potential



"HCC" hepatocellular carcinoma, "RCC" renal cell carcinoma, "CCA" cholangiocarcinoma

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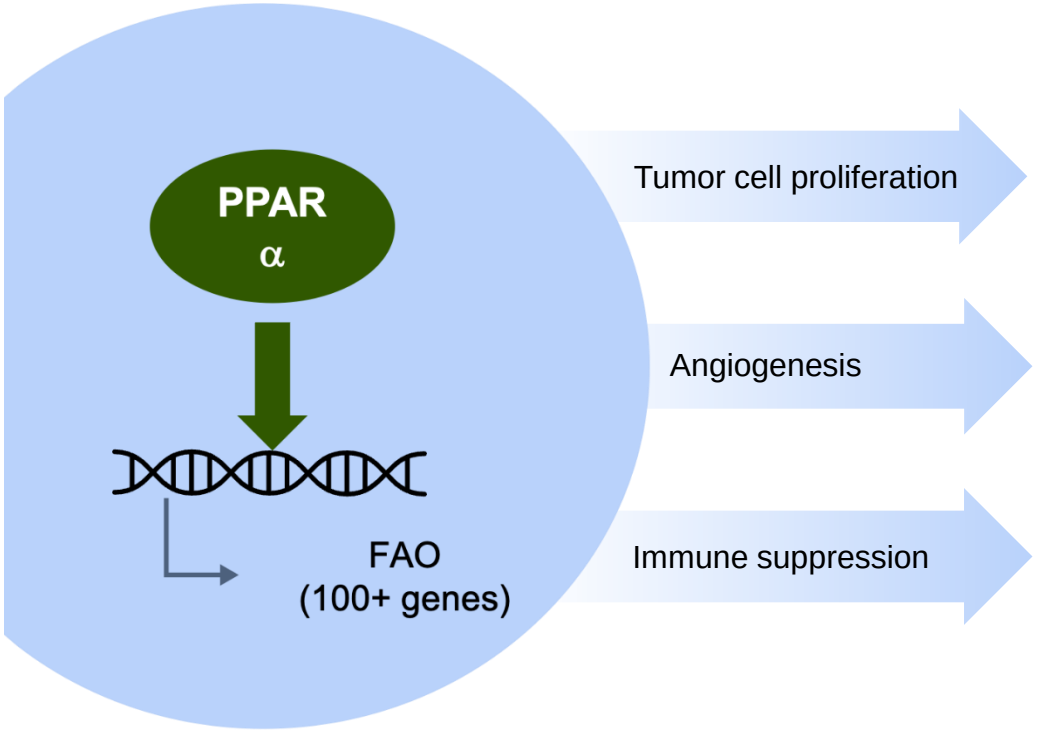
* If approved by FDA [1] Timing is an estimate based on current projections. [2]Pursuant to a collaboration with Roche; TPST retains all product rights. [3] Study could be either a single indication or biomarker-based basket [4] With additional funding, monotherapy expansion(s) would be in select indications based on target expression and/or a biomarker-positive basket cohort;

TPST-1120

PPARα Antagonist

Mark Yarchoan, M.D.
Associate Professor of Oncology
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center

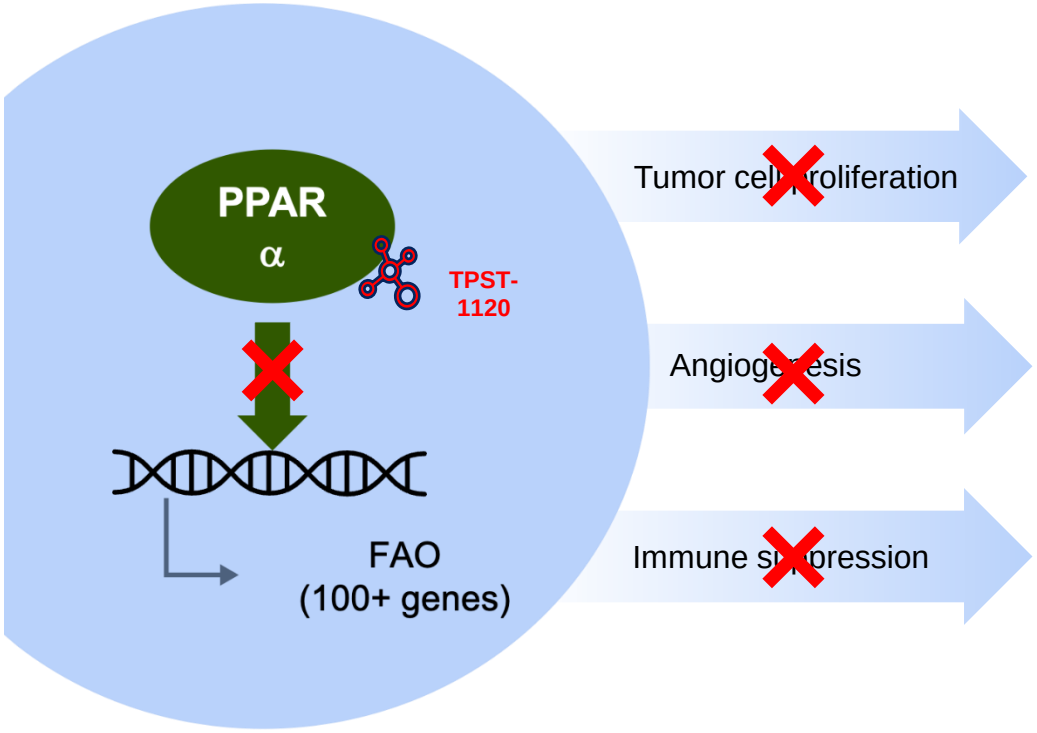
Fatty Acid Oxidation Supports Cancer Progression



- **FAO** is a key cancer metabolic adaptation that supports tumor growth and metastasis
- **FAO** is a principal metabolic pathway for immune suppressive cell types and FAO induces angiogenesis
- **PPARα** is a transcription factor and master regulator of FAO, controlling > 100 lipid metabolism genes
- **Inhibiting PPARα** to reduce FAO is a promising strategy to inhibit tumor growth and relieve immunosuppression.

TPST-1120: First-in-Class PPARα Antagonist

Targets both tumor cells and immune suppressive cells



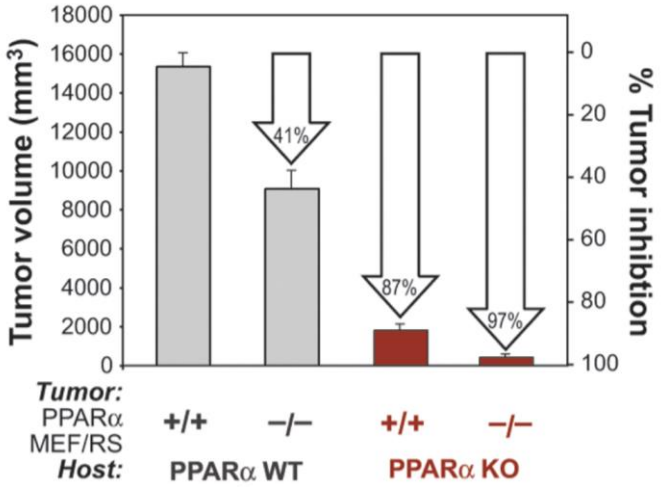
PPAR Inhibition* IC50 (μM)	Species	
Isoform	Human	Mouse
α	**0.052**	0.42
β/δ	13	29
γ	33	30

**Luciferase Reporter*

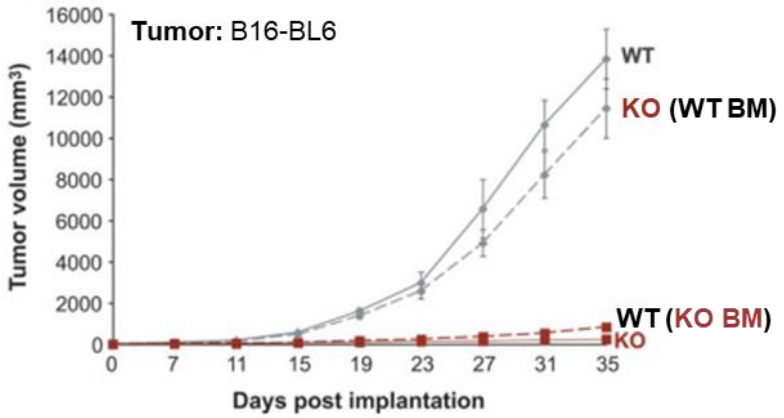
Genetic Validation for Targeting PPARα

PPARα and FAO are required to sustain tumor growth

PPARα KO Prevents Tumor Growth



PPARα Signaling in Immune Cells is Critical For Tumor Growth

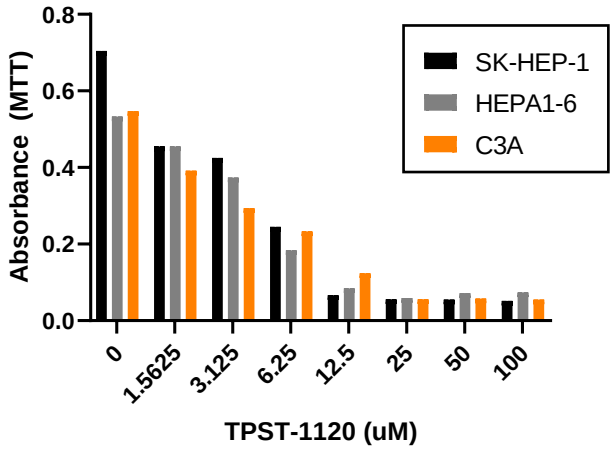


Bone Marrow Transplantation Confers Transplant Phenotype

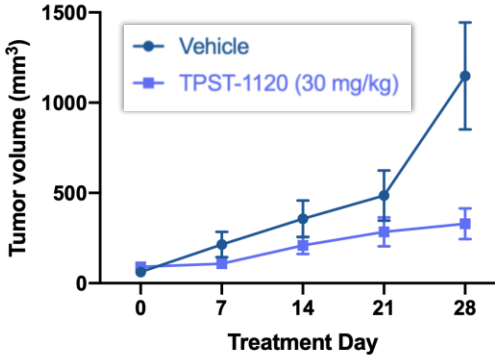
Kaipainen et al., PLoS ONE 2007, 2(2): e260

TPST-1120 Dual Mechanism of Action: Combined Tumor Cell Killing and Immune Activation

Direct Tumor Killing

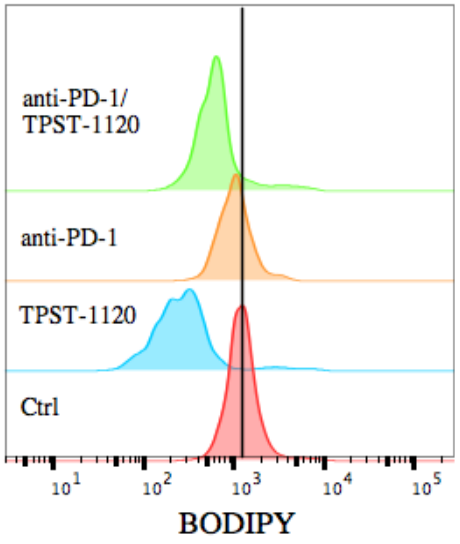


Caki-1 RCC Xenograft model



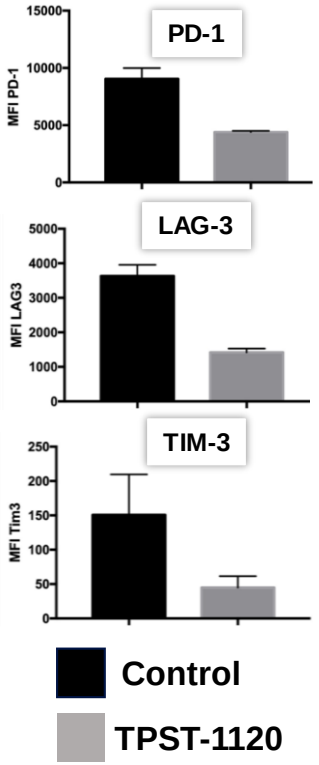
Immune Activation in the TME

Dendritic cells (CD45+CD11c+F4/80-)



Dendritic cells isolated from treated syngeneic $BRAF^{V600E}$ $PTEN^{-/-}$ mice

CD8+ T cells

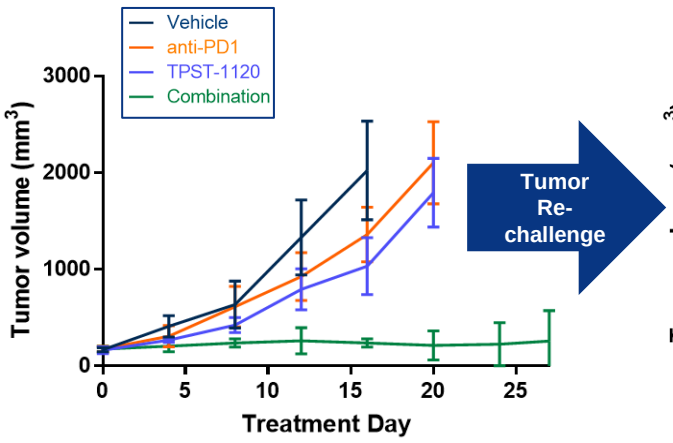


CD8+ T cells isolated from treated C57BL/6 mice bearing MC38 tumors

TPST-1120 + α-PD-1 Synergize and Confer Durable Immunity

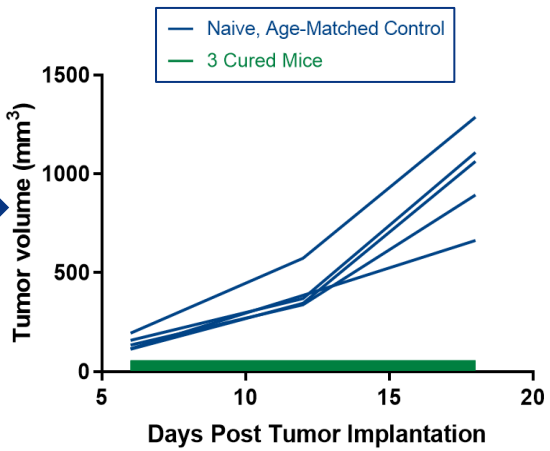
MC38 colorectal cancer tumor model, C57BL/6 immunocompetent mice

TPST-1120 + anti-PD1 treatment

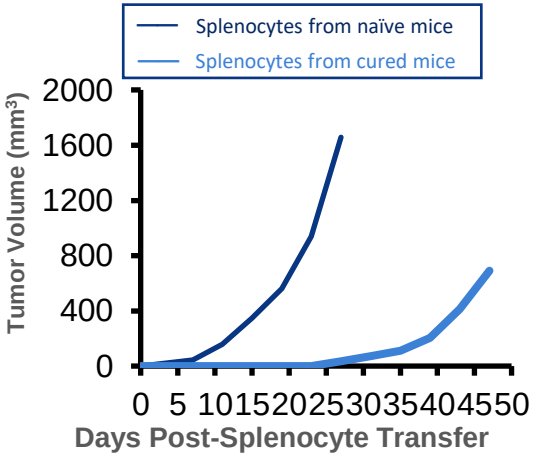


Tumor Re-challenge

Tumor re-challenge



Adoptive transfer of splenocytes into naïve C57BL/6 mice, MC38 tumor cell challenge



C57BL/6 mice bearing 150 mm^3 MC38 flank tumors treated with TPST-1120 30 mg/kg BID and 200 µg α-PD-1 Q3D

Adoptive transfer of splenocytes from naïve C57BL/6 mice or MC38 tumor-bearing mice cured with TPST + αPD-1 into naïve C57BL/6 mice, followed by challenge with 1 x 10^6 MC38 tumor cells

TPST-1120 Phase 1 Study Design

Study nearly complete; ASCO 2022 oral presentation

Key Eligibility Criteria

Inclusion:

- Advanced/metastatic solid tumor
- ECOG PS 0-1
- Adequate renal, hepatic and hematologic function
- No standard therapy available
- Archived or fresh tumor Bx, paired Bx optional

Exclusion:

- Immunosuppressive meds
- Autoimmune disease
- Fibrates within 28 days of enrollment

Part 1: Monotherapy Dose Escalation

Solid Tumors
3+3 Design
TPST-1120 up to 600 mg BID

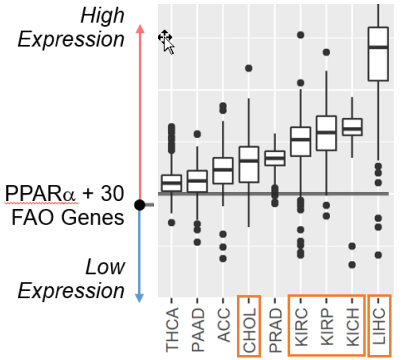
Part 2: Combo with αPD-1 (nivo) Dose Escalation

HCC, RCC, Cholangiocarcinoma
3+3 Design
TPST-1120 up to 600 mg BID
Full-dose nivolumab

Endpoints

- Safety
- MTD and/or OBD of TPST-1120
- PK
- Preliminary efficacy

TCGA gene expression profile



ECOG PS - Eastern Cooperative Oncology Group Performance Status; Bx biopsy; BID twice daily; RCC renal cell carcinoma; HCC hepatocellular carcinoma; RP2D recommended phase 2 dose; MTD maximal tolerated dose; OBD optimal biologic dose; DLT dose limiting toxicity

Demographics and Patient Characteristics

Baseline Characteristics		TPST-1120 Monotherapy (N=20)	TPST-1120 + Nivolumab (N=18)
Age [median (range)]		65 (41-78)	64 (43-84)
Female [n (%)]		10 (50)	9 (50)
TPST-1120 Dose [n (%)]	100 mg BID	3 (15)	-
	200 mg BID	4 (20)	3 (17)
	300 mg BID	3 (15)	3 (17)
	400 mg BID	4 (20)	3 (17)
	600 mg BID	6 (30)	9 (50)
Primary Cancer Type [n (%)]	Castration Resistant Prostate Cancer	1 (5.0)	-
	Cholangiocarcinoma	5 (25)	9 (50)
	Colorectal Cancer	4 (20)	-
	Hepatocellular Carcinoma	1 (5.0)	4 (22)
	Non-small-cell Lung Cancer	1 (5.0)	-
	Pancreatic Cancer	8 (40)	-
	Renal Cell Carcinoma		5 (28)
Prior systemic regimens	Median (range)	3 (2-9)	3 (1-6)
	Prior α-PD-1/α-PD-L1* [n (%)]	6 (30)	10 (56)
ECOG PS [n (%)]	0	5 (25)	8 (44)
	1	15 (75)	10 (56)

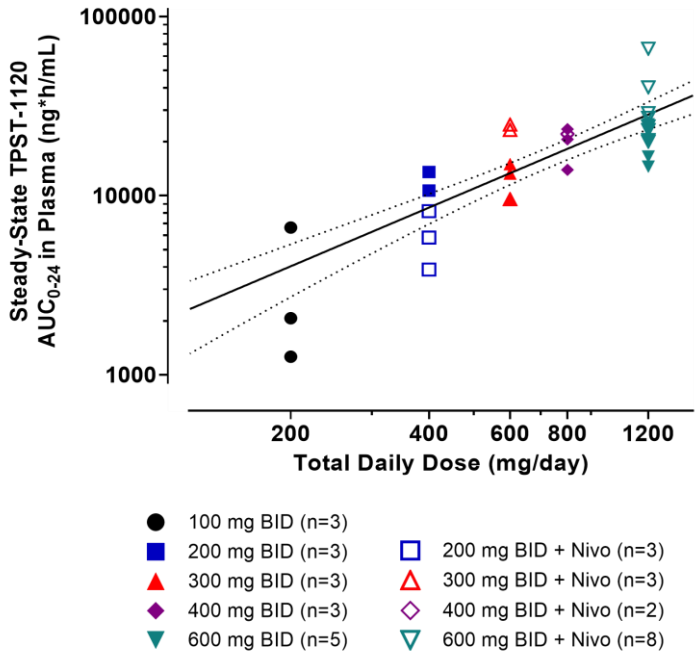
*All enrolled NSCLC, HCC, and RCC patients had prior treatment with at least one approved α-PD-1 or α-PD-L1

N is safety population, Data cut: April 15, 2022

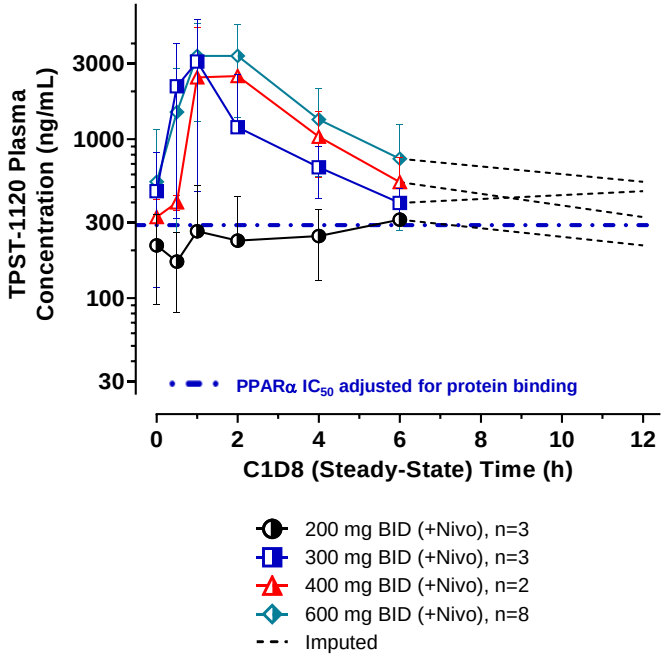
TPST-1120 Exposure Increases Linearly with Dose

Pharmacokinetics

Dose-Exposure Relationship



Steady-State Profile (Combination)



TPST-1120 Has A Tolerable Safety Profile

Treatment-related adverse events occurring in ≥ 2 Patients

AE, n (%)	TPST-1120 Monotherapy (N=20)	
	Any Grade	Grade 3
Any AE	10 (50.0)	1 (5.0)†
Nausea	4 (20.0)	0
Fatigue	3 (15.0)	0
Diarrhoea	2 (10.0)	0

†Hypertension

AE, n (%)	TPST-1120 + Nivolumab (N=18)	
	Any Grade	Grade 3
Any AE*	15 (83.3)	3 (16.7)^
Fatigue	6 (33.3)	0
Diarrhoea	4 (22.2)	0
Nausea	3 (16.7)	0
Abdominal pain	2 (11.1)	0

^Arthralgia, Hepatic enzymes increased, Muscle spasms

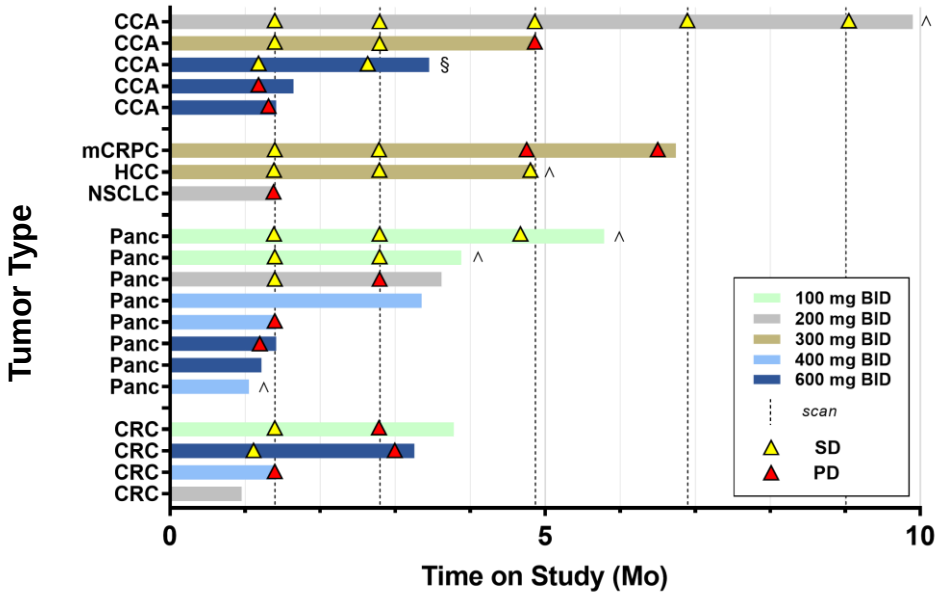
*Related to either TPST-1120 or nivolumab

- TPST-1120 showed tolerable safety profile as monotherapy and in combination with nivolumab
- Most common treatment related AEs were nausea, fatigue and diarrhea
- No DLTs during dose escalation
- RP2D 600 mg PO BID for monotherapy and combination

TPST-1120 Monotherapy

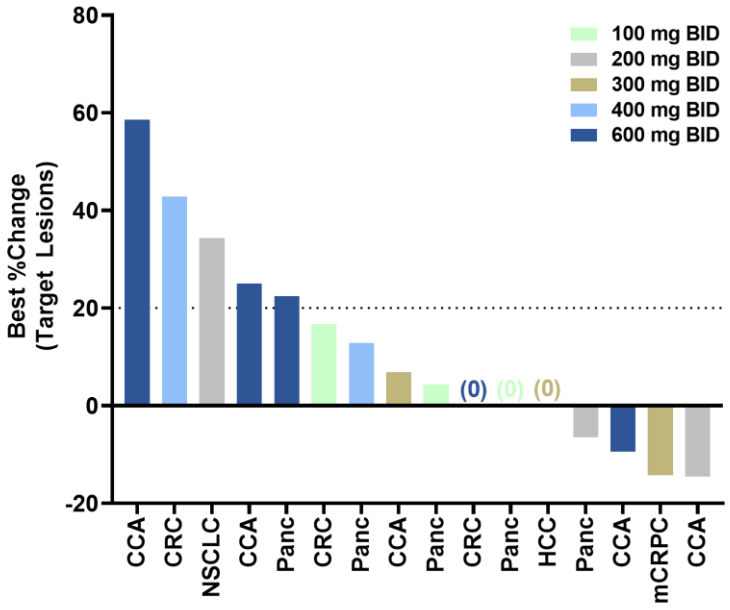
Prolonged disease control and tumor shrinkage in late line patients

20 Enrolled



Discontinuation for other than disease progression: ^Clinical Deterioration, §Consent withdrawn

TPST-1120 Monotherapy (N=19[a]): 53% DCR



[A] Response evaluable patients include pts with a postbaseline scan or discontinued treatment due to disease progression. DCR, disease control rate = complete response + partial response + stable disease

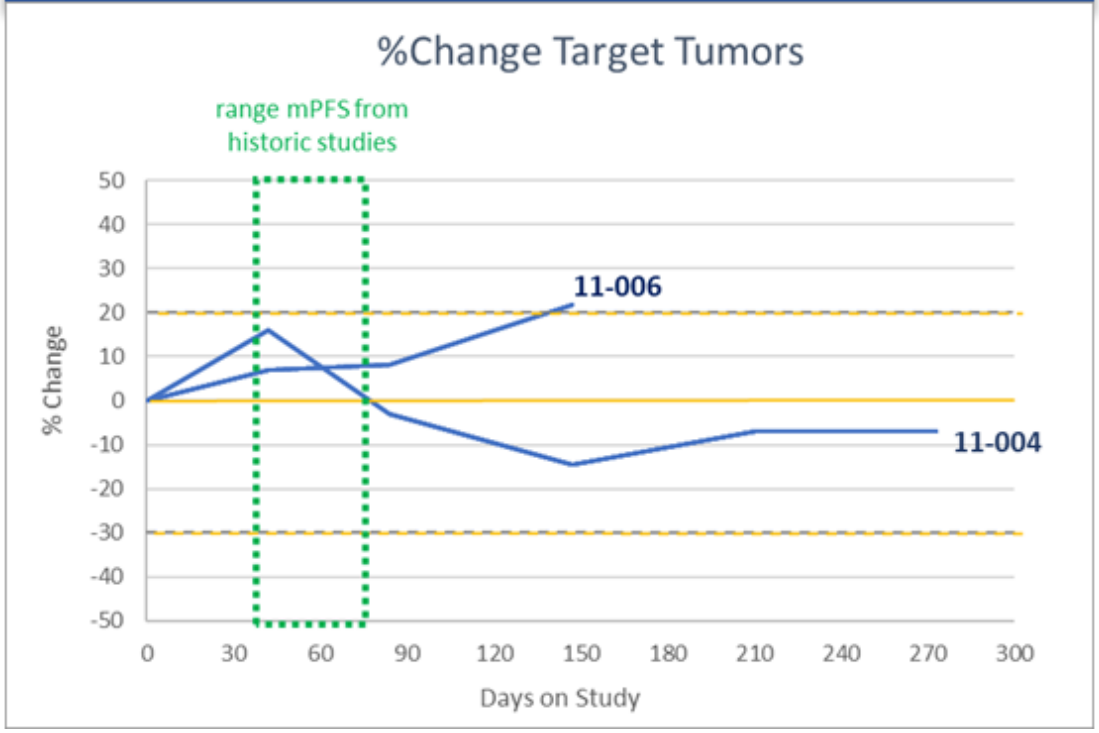
April 15, 2022 data cut

Monotherapy Tumor Control in Late-Line Cholangiocarcinoma

11-004
- 4 prior systemic therapies
  - Carboplatin/taxol
  - Gemcitabine
  - Oxaliplatin/5-FU
  - IDOi/investigational anti-PD-1
    discontinued due to progression
- IDH1 mutation

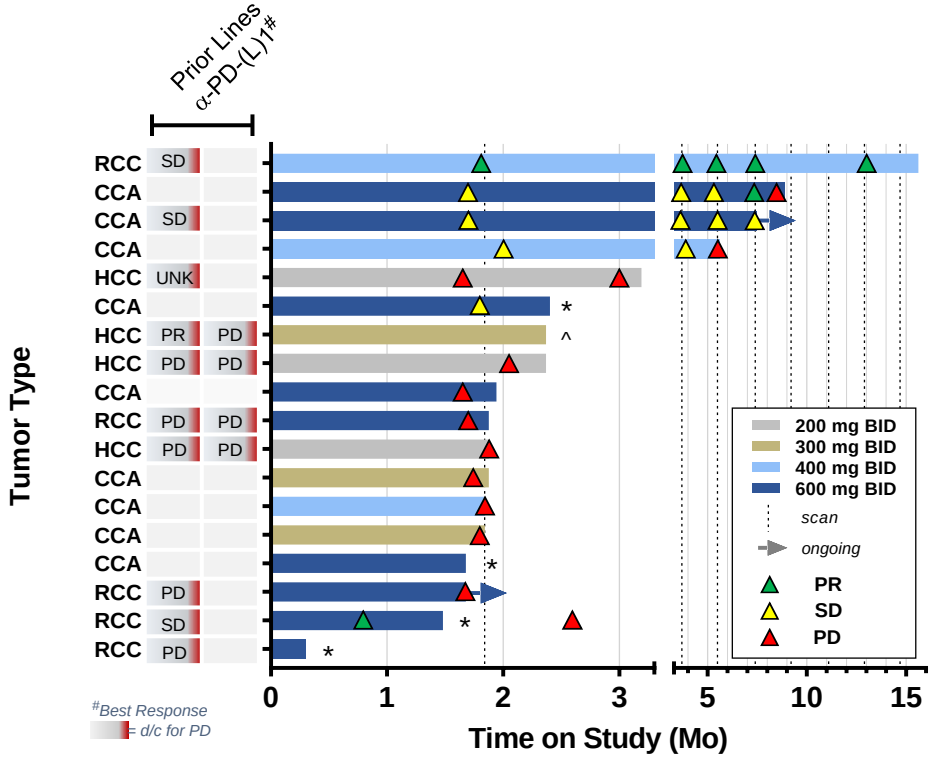
11-006
- 3 prior systemic therapies
  - Cisplatin/gemcitabine
  - Investigational TKI
  - Investigational anti-PD-1
    discontinued due to progression
- IDH1 mutation

Long-term stable disease in two patients with advanced CCA*

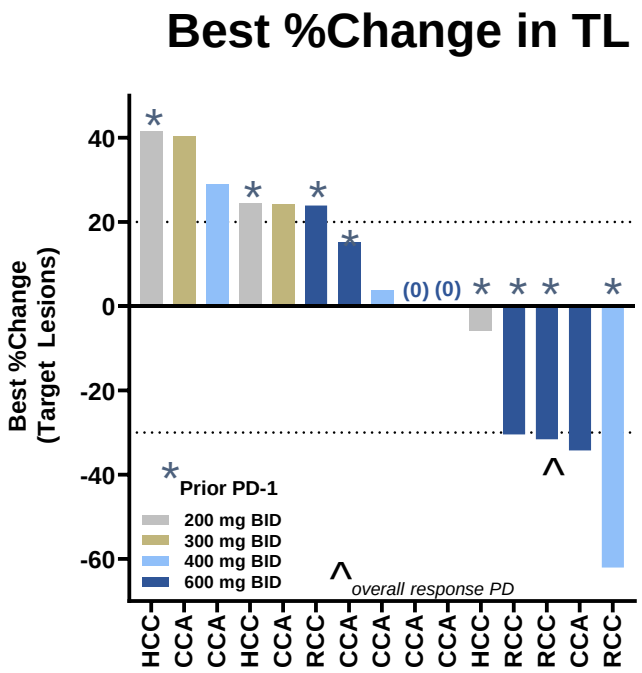


TPST-1120 + Nivo: RECIST Responses in RCC and CCA

Subjects with IO refractory (HCC and RCC) or IO non-responsive (CCA) indications



*Discontinuation for other than disease progression: *Adverse Event, ^Clinical Deterioration*



15 response evaluable patients include pts with a postbaseline scan or discontinued treatment due to disease progression

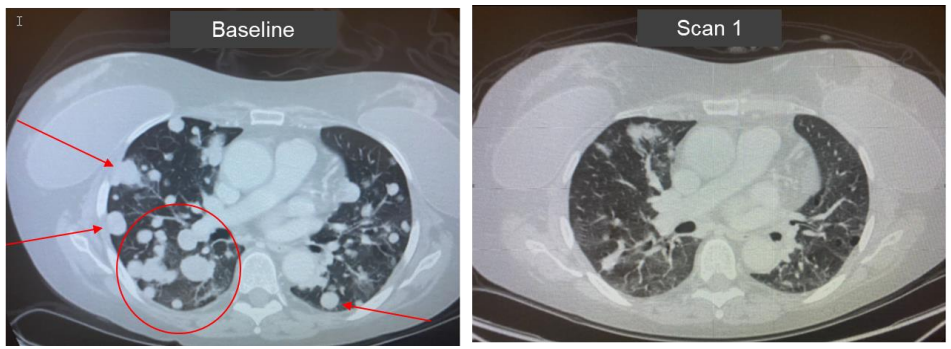
RCC Responses with TPST-1120 + Nivolumab

Two of two patients with IO-refractory, late-line, RCC experienced rapid RECIST responses

Subject 14-008

- 1st scan -54% RECIST response with 12+ month ongoing duration (current response -62%)
- Prior therapy (best response, reason for discontinuation)
  - 1L: ipilimumab + nivolumab (SD, PD)
  - 2L: cabozantinib (SD, PD)
  - 3L: everolimus (SD, PD)
- Sites of metastatic disease: pulmonary; multiple soft tissue (chest, peri-renal, peri-vaginal); bone

-54% at 1st Scan



Subject 22-008

- Extensive lymphadenopathy in chest and abdomen, nephrectomy bed recurrence, malignant pericardial effusion
- LDH 2X ULN
- Prior therapy (best response, reason for discontinuation)
  - 1L: pembrolizumab + axitinib (SD, PD)
  - 2L: cabozantinib (SD, PD)
- Rapid -30% RECIST response on study, but came off treatment for unrelated AE[1]

Consistent with preclinical data showing that TPST-1120 reverses T cell exhaustion

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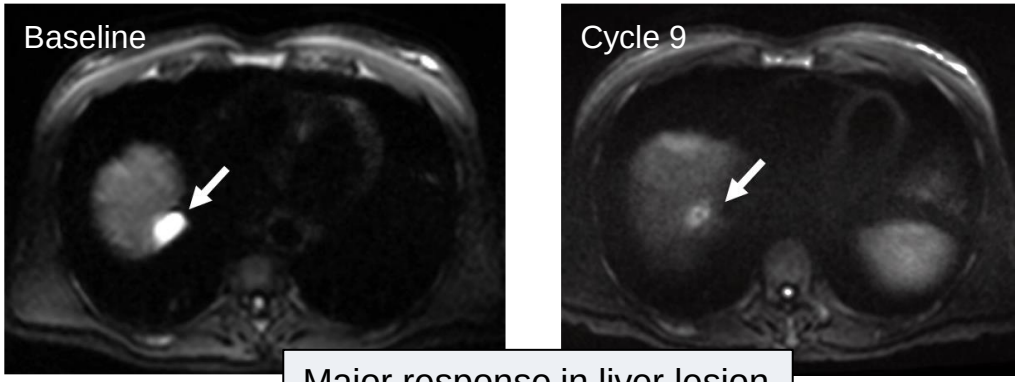
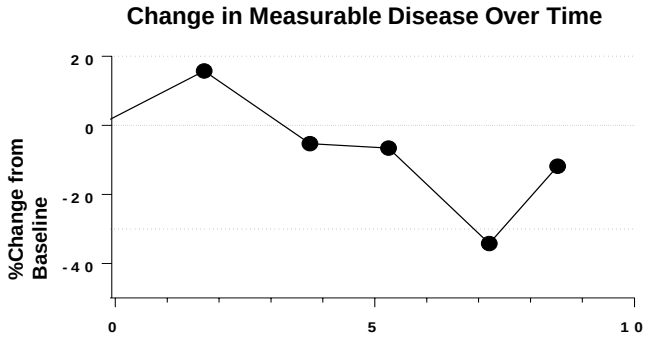
[1] Was unable to restart treatment; disease progressed while off treatment

Cholangiocarcinoma Response with TPST-1120 + Nivolumab

84yo M with late line PD-L1 negative and MSS metastatic cholangiocarcinoma



Major response in liver lesion

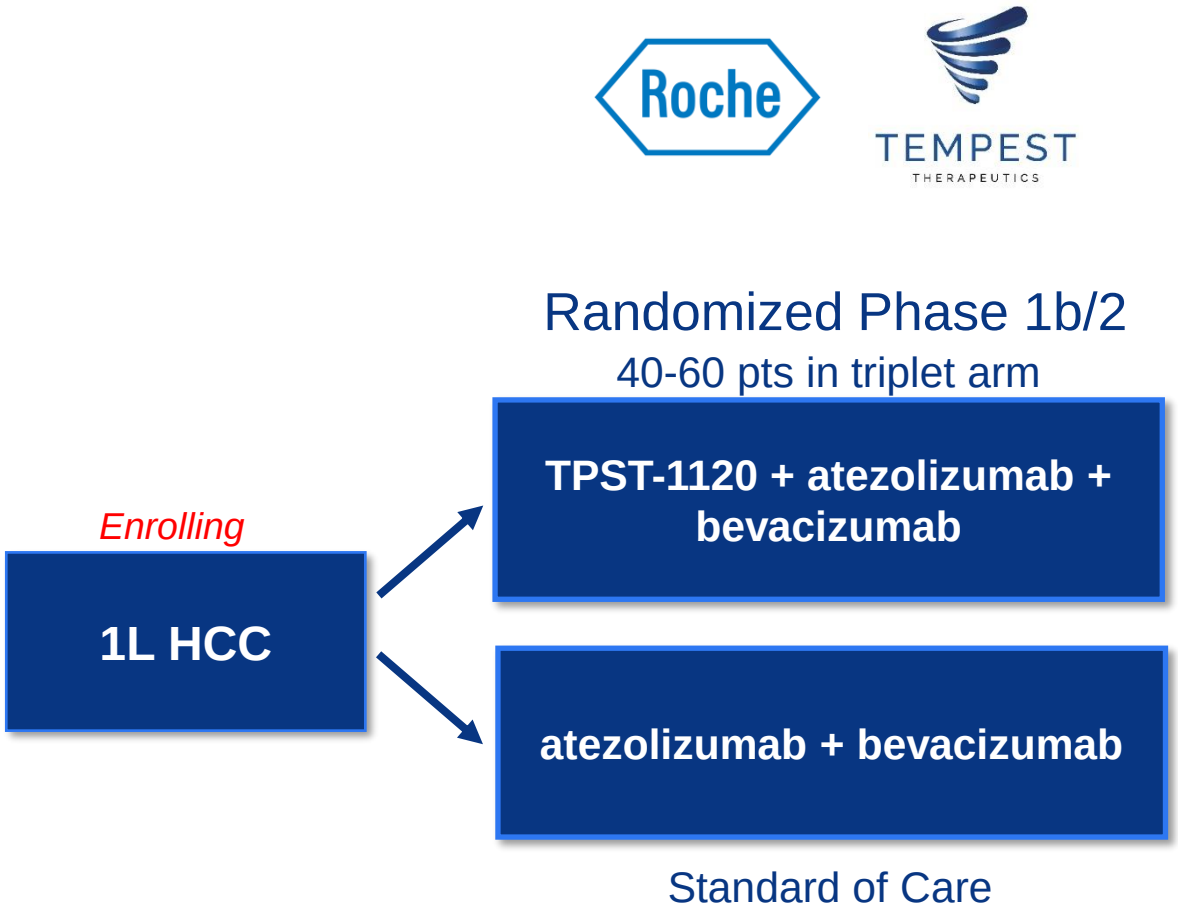


Baseline SLD: ***76 mm***
Target lesion sites: ***liver, lymph node, peritoneum***

Treatment History

	Prior Regimen	Reason for DC
1	Gemcitabine	Adjuvant therapy
2	Gem + Cisplatin + Herception	Completed
3	Capectabine + RT	Completed
4	Herceptin	Progressive Disease
5	Gem + Herceptin	Progressive Disease
6	FOLFOX	Progressive Disease

TPST-1120 Accelerating to Frontline HCC Randomized Study



- Standard of care 1L regimen +/- TPST-1120
- Ongoing multi-arm global study[1]
  - US, Asia, Europe
- Roche operationalizing

[1] Morpheus HCC study allows for rapid implementation. Other investigational agents being evaluated include: tiragolumab, tocilizumab, RO7247669 (NCT04524871)

Conclusions

- TPST-1120 is a first-in-class antagonist of the FAO regulator PPARα
- TPST-1120 demonstrated a tolerable safety profile in patients as monotherapy and in combination with nivolumab
- TPST-1120 demonstrated disease control as monotherapy and promising responses in combination with nivolumab
- Responses in patients previously refractory to anti-PD-(L)1 are consistent with PPARα mechanism targeting T-cell exhaustion and immune suppressive cells
- TPST-1120 in combination with atezolizumab and bevacizumab randomized against atezolizumab and bevacizumab is now enrolling in 1L HCC

TPST-1495

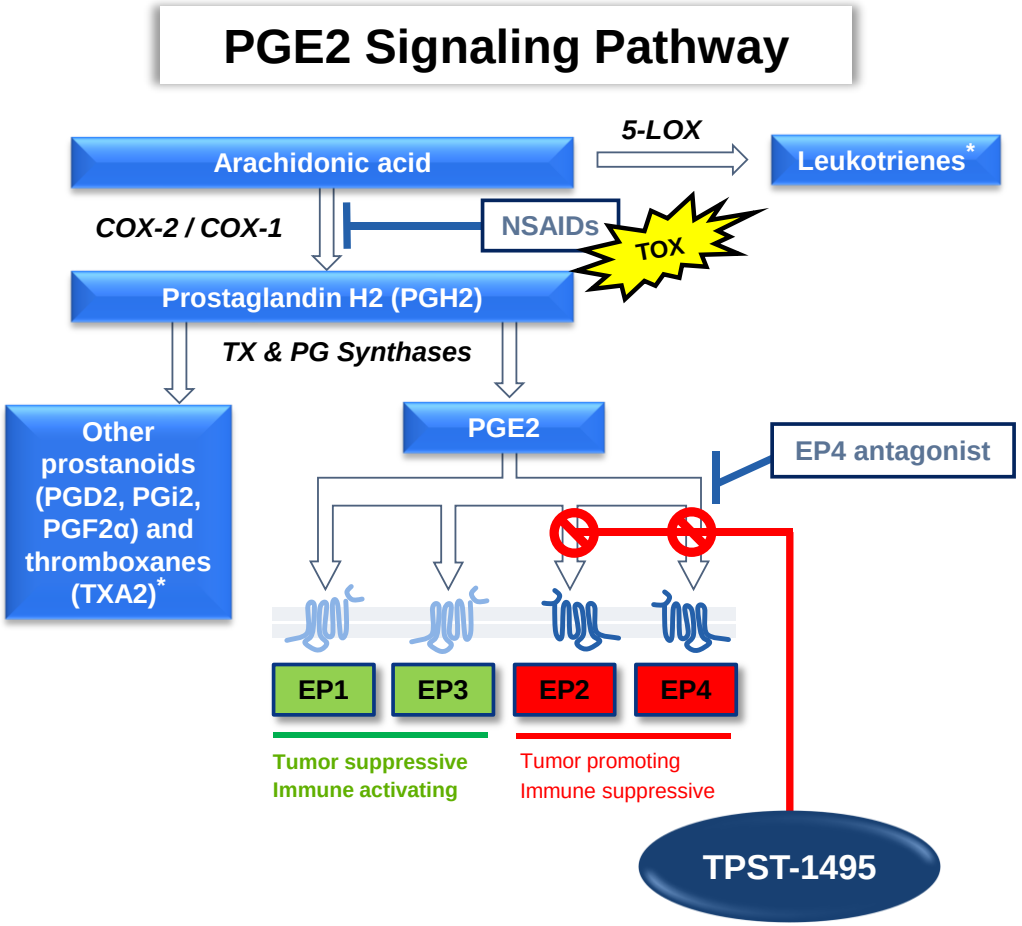
Dual EP2/4 Antagonist

Susanna V. Ulahannan, M.D., MMEd
Assistant Professor of Medicine
Associate Director, Oklahoma TSET Phase 1 Program
Stephenson Cancer Center at the University of Oklahoma

TPST-1495 is a First-in-Class[1] Dual EP2/EP4 PGE2 Receptor Antagonist

Rationally designed, based on an understanding of PGE2 signaling in cancer progression

- Prostaglandin E_2 (PGE2) has both tumor *promoting* and tumor *suppressing* activity through its 4 receptors (EP 1-4)
  - NSAIDs prevent signaling through beneficial EP receptors and have toxicity
- TPST-1495 features
  - First in class, highly specific antagonist inhibits *only* the tumor promoting EP2 and EP4 receptors
  - Oral therapy
  - Nanomolar potency[2]
  - Targets *both* tumor cells and immune suppressive cells



*Alterations in thromboxanes, prostacyclins and leukotrienes are associated with cardiovascular toxicity of NSAIDs

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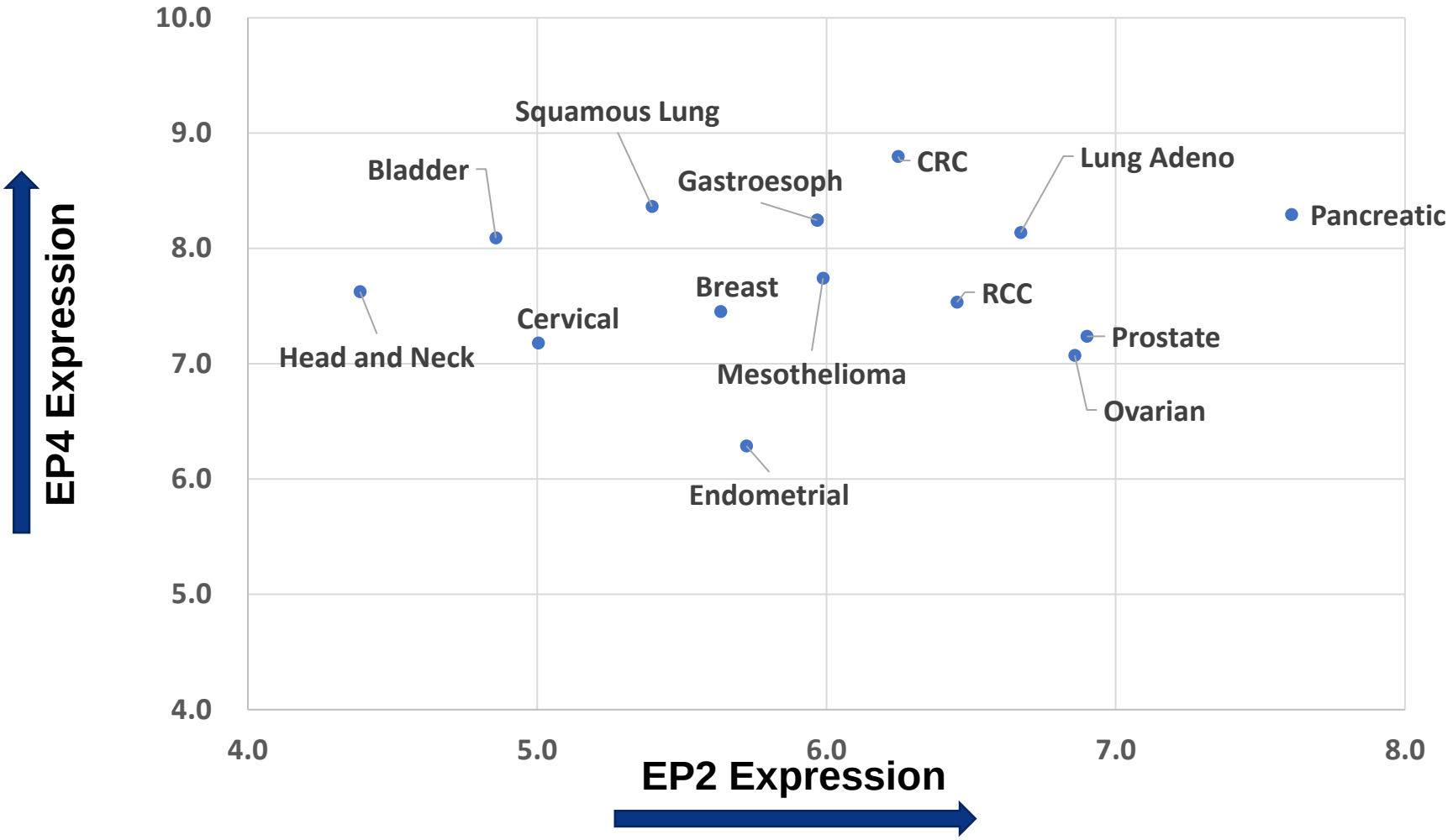
[1] If approved by FDA
[2] IC50s: 17 nM for EP2, 3 nM for EP4, and 51 nM in human whole blood assay

EP2 & EP4 Are Overexpressed in Multiple High-Need Cancers

Dual blockade needed to block PGE2 signaling for cancer therapy

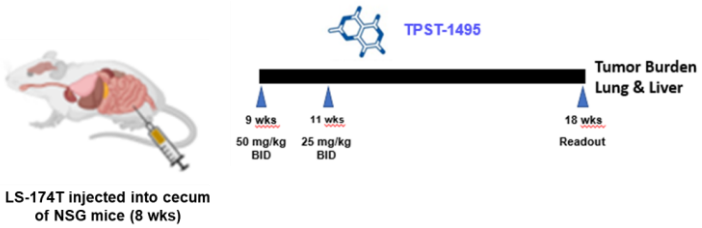


*Ratio of malignant vs normal tissue expression – medians from TCGA database

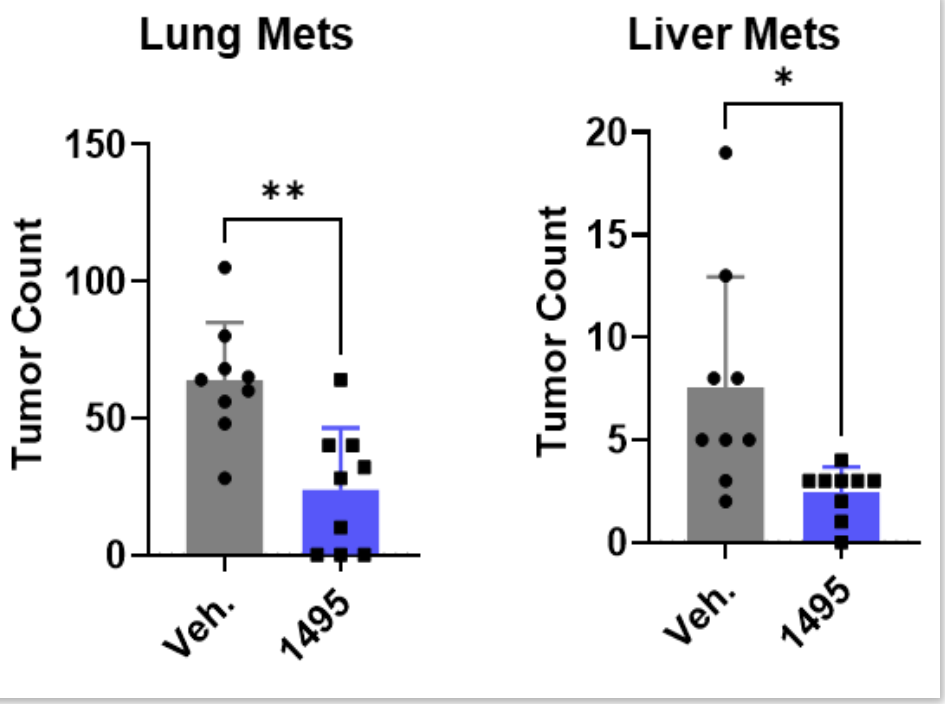
TPST-1495 Directly Inhibits Tumor Growth

Anti-tumor activity in immune-deficient models

Patient-derived orthotopic colon cancer model

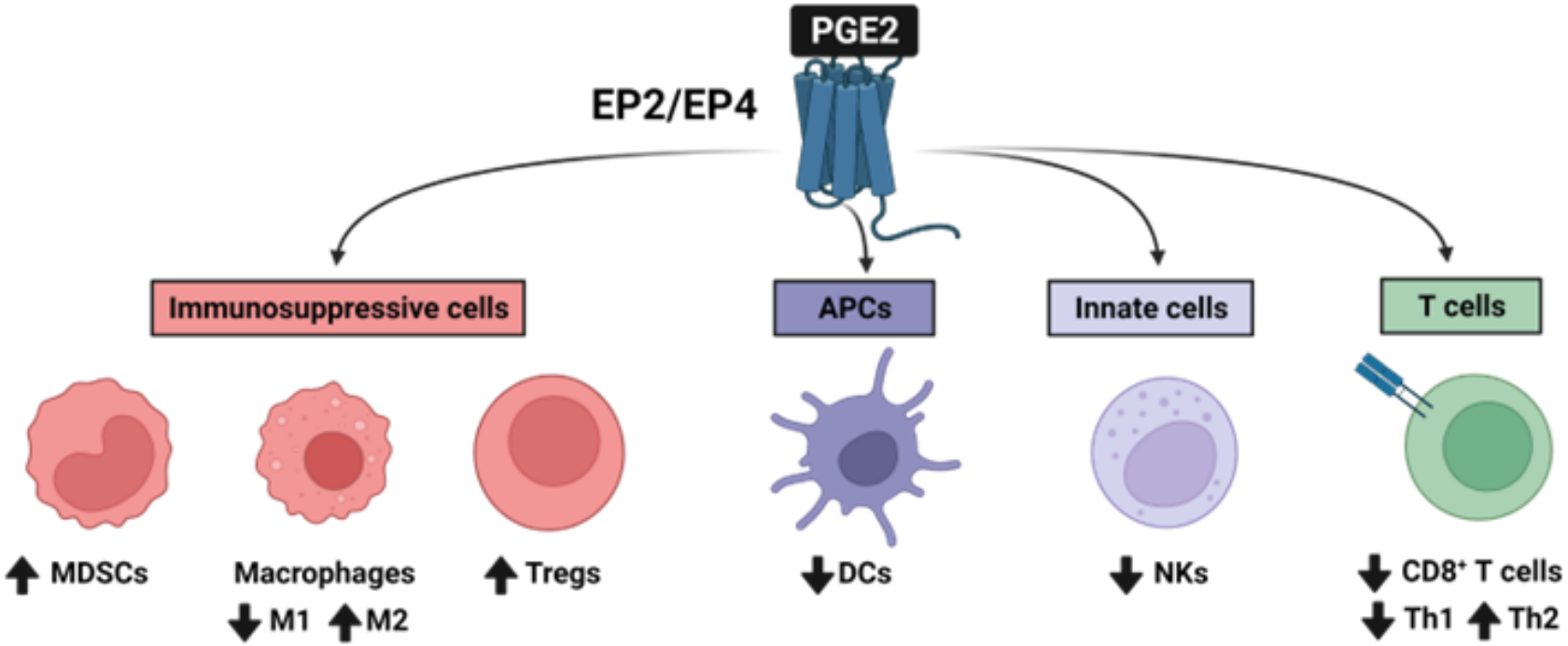


Immune-deficient NSG mouse



LS-174T tumor cells isolated from Duke's type B human colorectal adenocarcinoma; ATCC CL-188

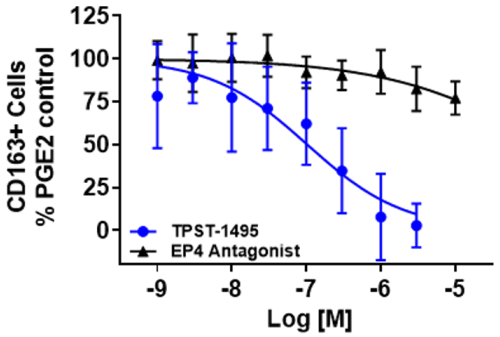
PGE2 EP2/EP4 Signaling Inhibits Immune Activity



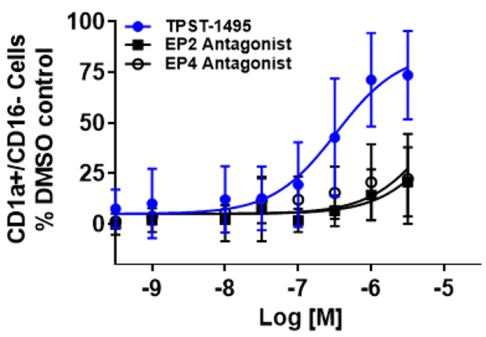
Adapted from: Wang and DuBois, J Clin Invest. 2018;128(7):2732–2742

TPST-1495 Reverses PGE2-mediated Immune Suppression

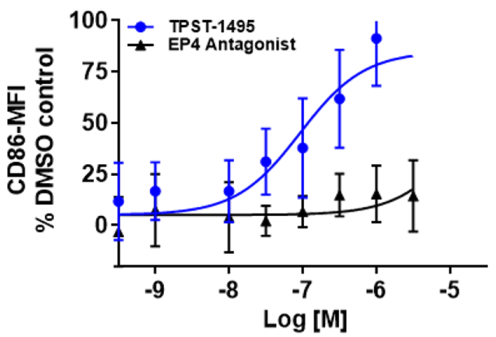
M2-Macrophages



DC Differentiation

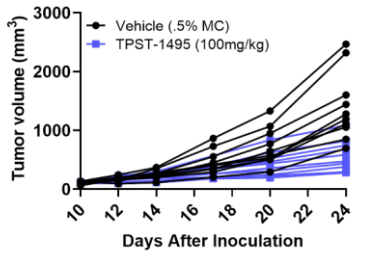


DC Maturation

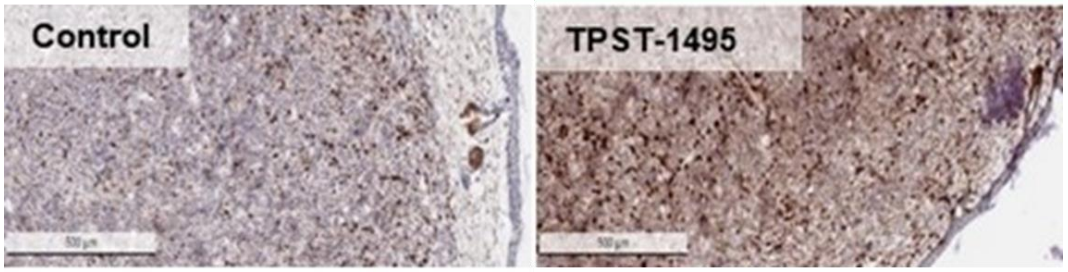


Human monocytes cultured with GMCSF + IL4 + PGE2 + EP receptor antagonist

Anti-tumor Efficacy



CD8+ T cell TME Infiltration



CT26 tumors in BALB/c mice

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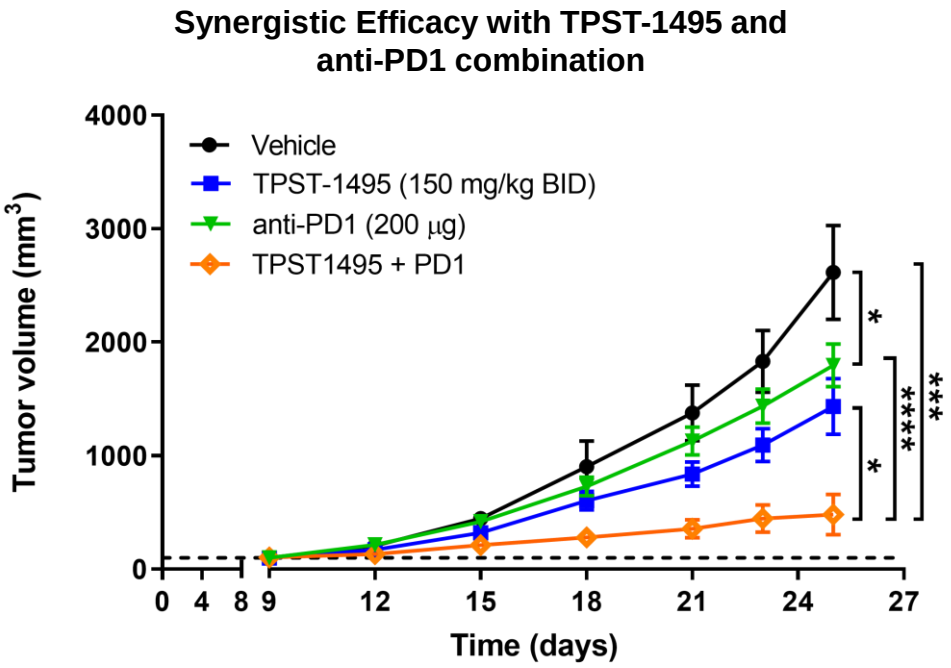
Head-to head comparison of DC differentiation and activation in human monocytes cultured with PGE2 and treated with TPST-1495 or single EP4 or EP2 antagonists

Rationale for Combination with Checkpoint Inhibitor

Combination designed to overcome “adaptive immune resistance”

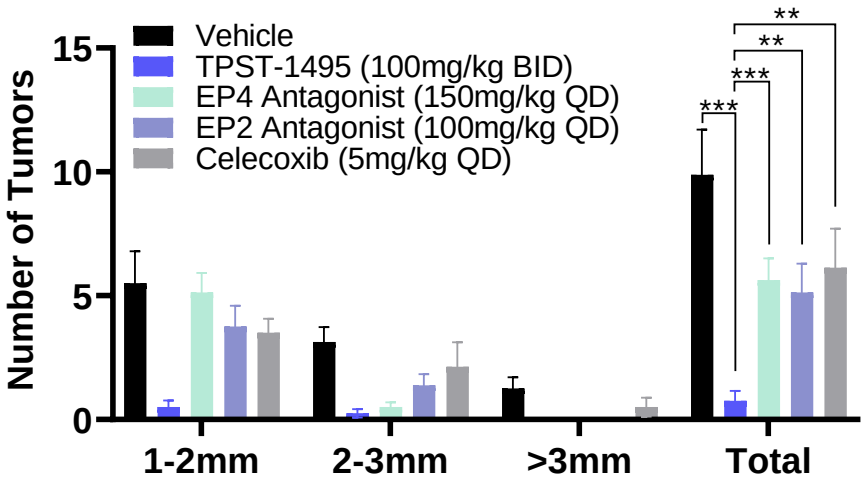


- PGE2 is a potent suppressor of immune function in the TME
- COX-2 upregulation is associated with both primary and secondary (adaptive) resistance to immune checkpoint inhibitor therapy
- TPST-1495 blocks the immunosuppressive signaling of PGE2 and stimulates anti-cancer immune function
- COX-2 and PD-L1 are induced by non-redundant signals and represent independent and potentially complimentary therapeutic targets

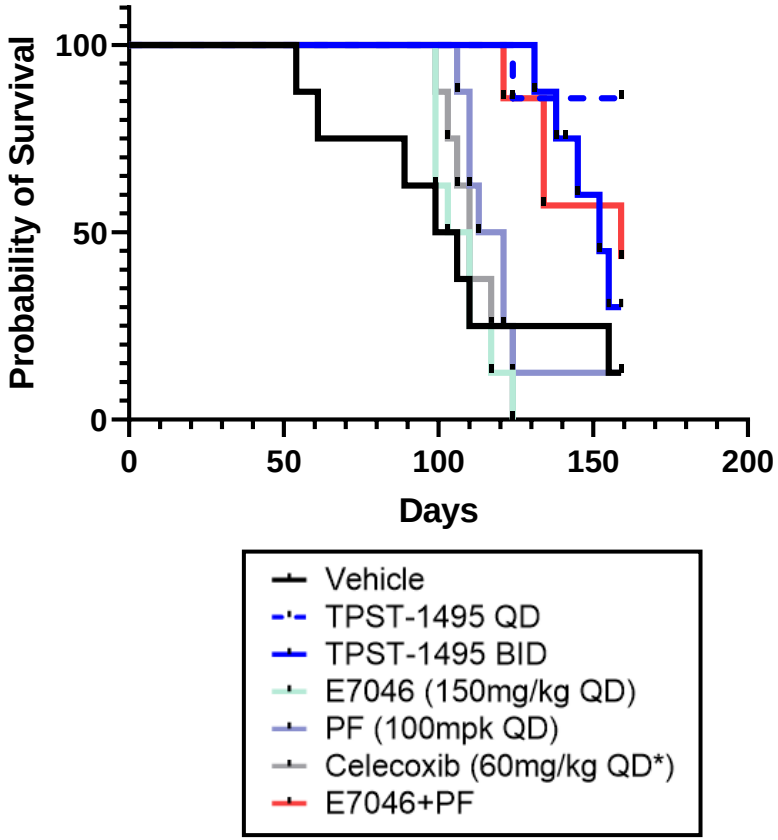
TPST-1495 Therapy Confers a Significant Survival Advantage Compared to Other Prostaglandin Pathway Inhibitors

TPST-1495 therapeutic efficacy comparison in $Apc^{Min/+}$ mouse model of CRC

Tumor burden after 3 weeks of therapy*



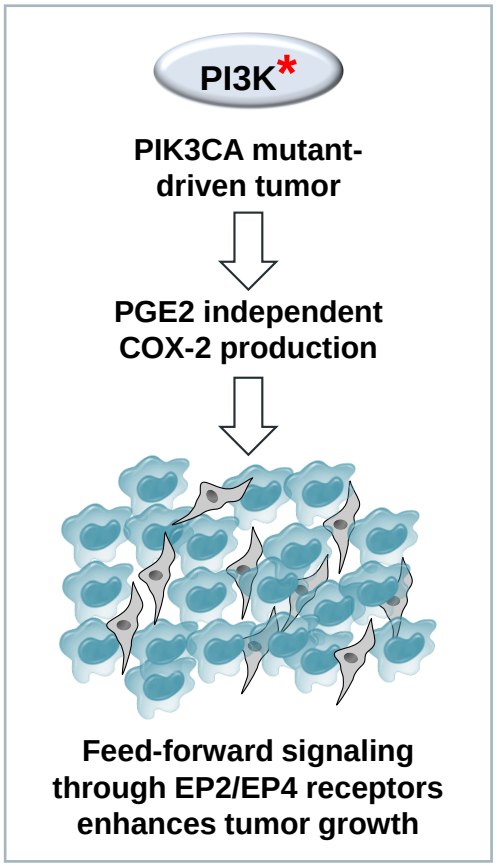
Survival

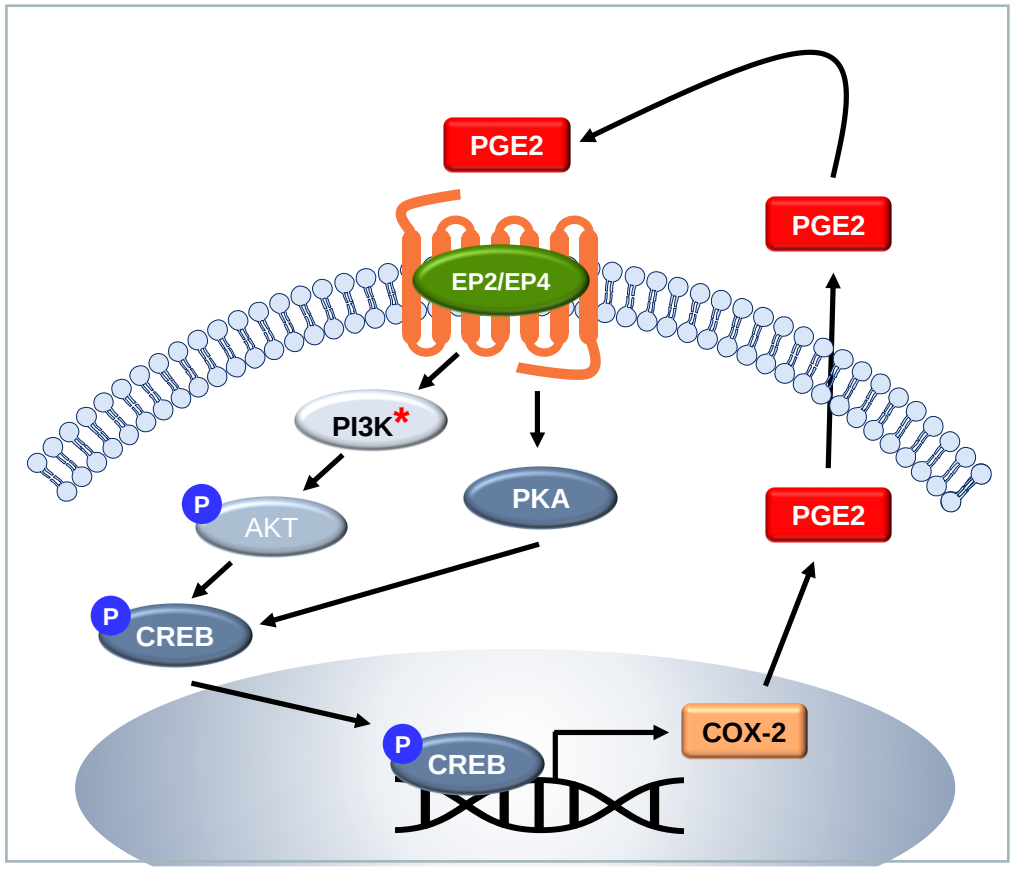


*Treatment initiated in 13 week old mice.

PIK3CA Mutation Promotes Tumor Growth & PGE2 Production

Driver mutation predictive of NSAID benefit in CRC and SCCHN





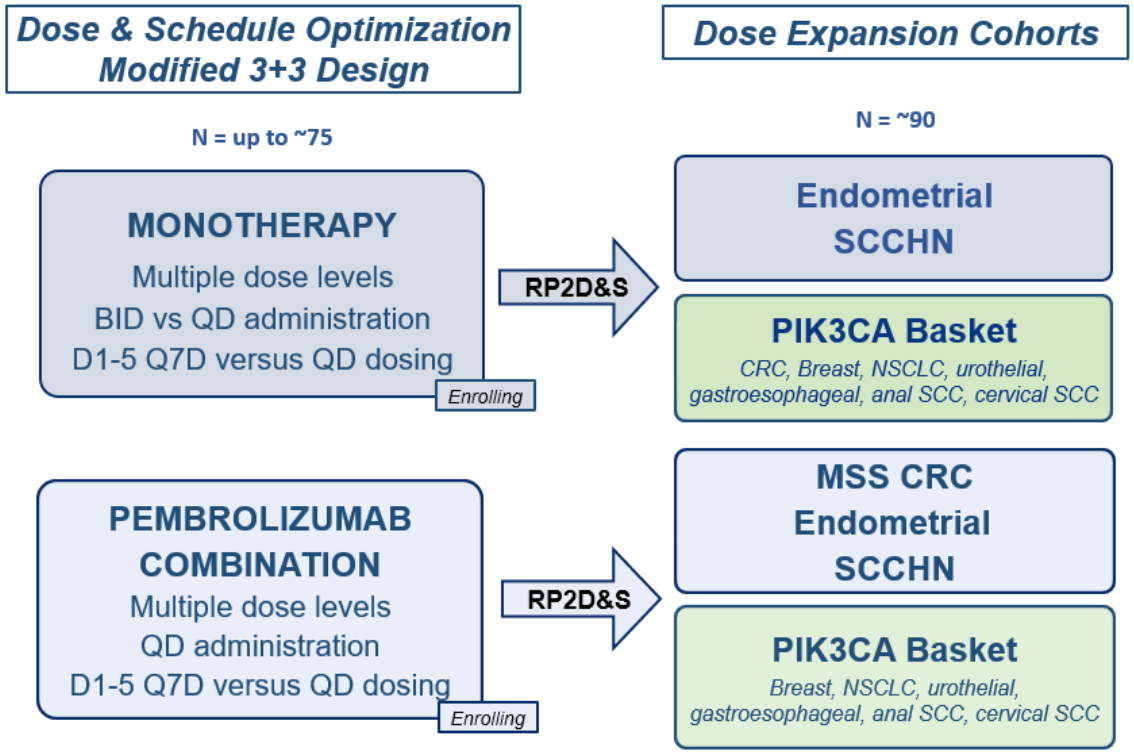
- PIK3CA tumor driver mutation constitutively activates cell proliferation and production of PGE2 and may be a biomarker for TPST-1495 responsive tumors

TPST-1495-001 Phase 1 Trial Design (NCT04344795)

Inclusion
- ECOG PS 0 or 1
- Measurable disease
- Met/adv cancer with no remaining standard therapy

Exclusion
- Intolerance to NSAIDs (including bleeding/ulcer)
- On anticoagulation therapy or at increased risk of bleeding
- Intolerance to prior checkpoint inhibitor therapy (CPI)

Objectives:
1°: Safety, tolerability, determine MTD and/or RP2D and schedule
2°: Evaluate anti-tumor activity, PK
Exploratory: PD, Immunomodulatory effects in blood, tumor



PIK3CA: 100% of basket cohort and 40% of each disease specific expansion with documented pathogenic PIK3CA mutation

PAIRED BIOPSIES: 30% of each expansion cohort will have paired biopsy for PD evaluation

Combination dose expansion to occur first, with potential to expand as a monotherapy

Summary

- Prostaglandin E2 stimulates tumor cell growth and suppresses anti-cancer immunity through the EP2 and EP4 receptors
- TPST-1495 is a first-in-class, potent and selective, dual antagonist of EP2 and EP4 that does not inhibit the immune-stimulating EP1 and EP3 receptors
- TPST-1495 has immune-independent and immune-dependent anti-tumor activity in preclinical models and overcomes PGE2-mediated immune suppression more effectively than single antagonists of either EP2 or EP4, or the COX-2 inhibitor celecoxib
- Enrollment is ongoing in the first-in-human TPST-1495 Phase 1 clinical study to determine the optimal dose and schedule of administration, safety profile, pharmacokinetics, pharmacodynamic and immunomodulatory activity, and to evaluate anti-tumor activity of TPST-1495 as monotherapy and in combination with pembrolizumab
- Potential expansion cohorts at the RP2D include key tumor indications and a biomarker-selected cohort supported by PGE2 biology and medical literature, including MSS CRC, SCCHN, endometrial cancer, and PIK3CA-mutated tumors

TREX-1 Targeting to Fulfill the Therapeutic Potential of STING Agonism for Cancer

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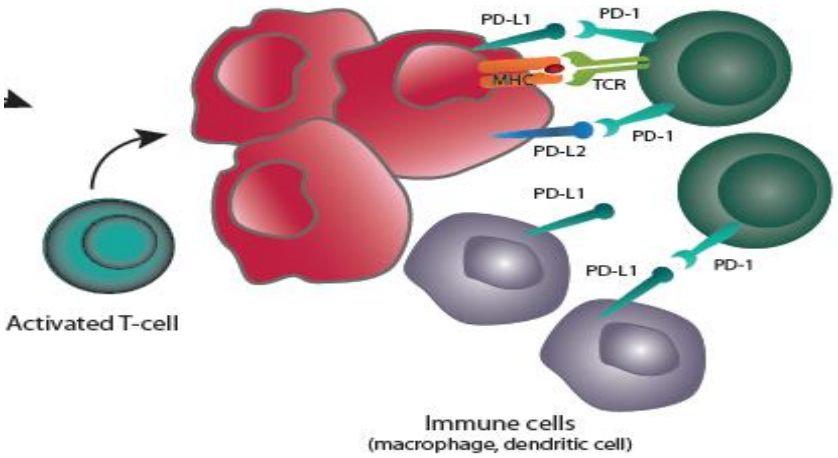
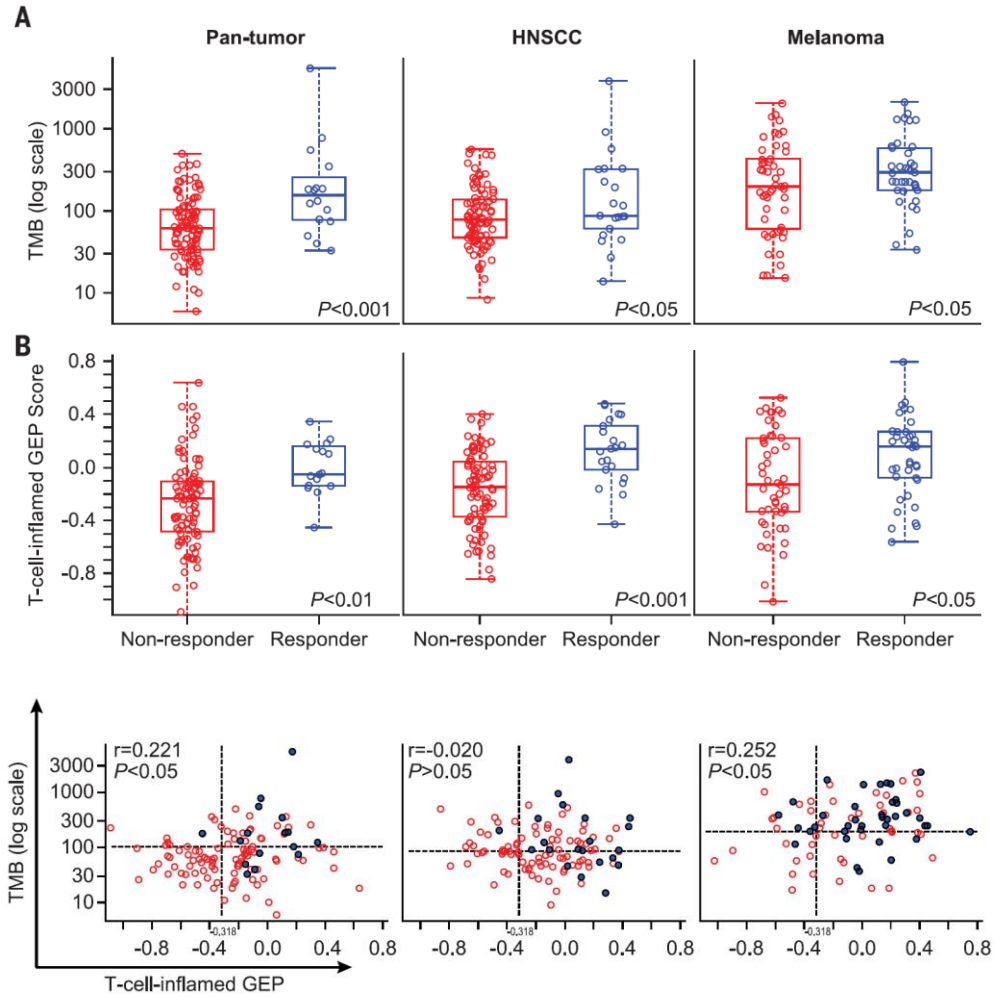
Associate Professor
Director of the Cancer Immunotherapeutics Center
University of Pittsburgh School of Medicine

Disclosures

- Updated disclosures available at: https://www.linkedin.com/in/jason-luke-11a38910/
- DSMB: Abbvie, Immutep, Evaxion
- Scientific Advisory Board: (no stock) 7 Hills, Bright Peak, Exo, **Fstar**, **Inzen**, RefleXion, Xilio (stock) **Actym**, Alphamab Oncology, Arch Oncology, Kanaph, **Mavu**, NeoTx, Onc.AI, **OncoNano**, Pyxis, **STipe**, **Tempest**
- Consultancy with compensation: **Abbvie**, Bayer, Bristol-Myers Squibb, Castle, Checkmate, **Codiak**, Crown, Day One, Duke St, EMD Serono, Endeavor, Flame, Genentech, Gilead, Glenmark, HotSpot, Kadmon, Janssen, Ikena, Immunocore, Incyte, IO Biotech, Macrogenics, Merck, Nektar, Novartis, Partner, Pfizer, Regeneron, Roivant, Servier, **STINGthera**, **Synlogic**, Synthekine
- Research Support: (all to institution for clinical trials unless noted) AbbVie, Astellas, Astrazeneca, **Bristol-Myers Squibb**, Corvus, Day One, EMD Serono, **Fstar**, Genmab, Ikena, Immatics, Incyte, Kadmon, KAHR, Macrogenics, Merck, Moderna, Nektar, Next Cure, Numab, Palleon, Pfizer, Replimmune, Rubius, Servier, Scholar Rock, **Synlogic**, Takeda, Trishula, Tizona, Xencor
- Patents: (both provisional) Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomarkers for Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses

T cell-inflamed gene expression and tumor mutational burden/tumor neoantigenicity predict immunotherapy treatment outcomes





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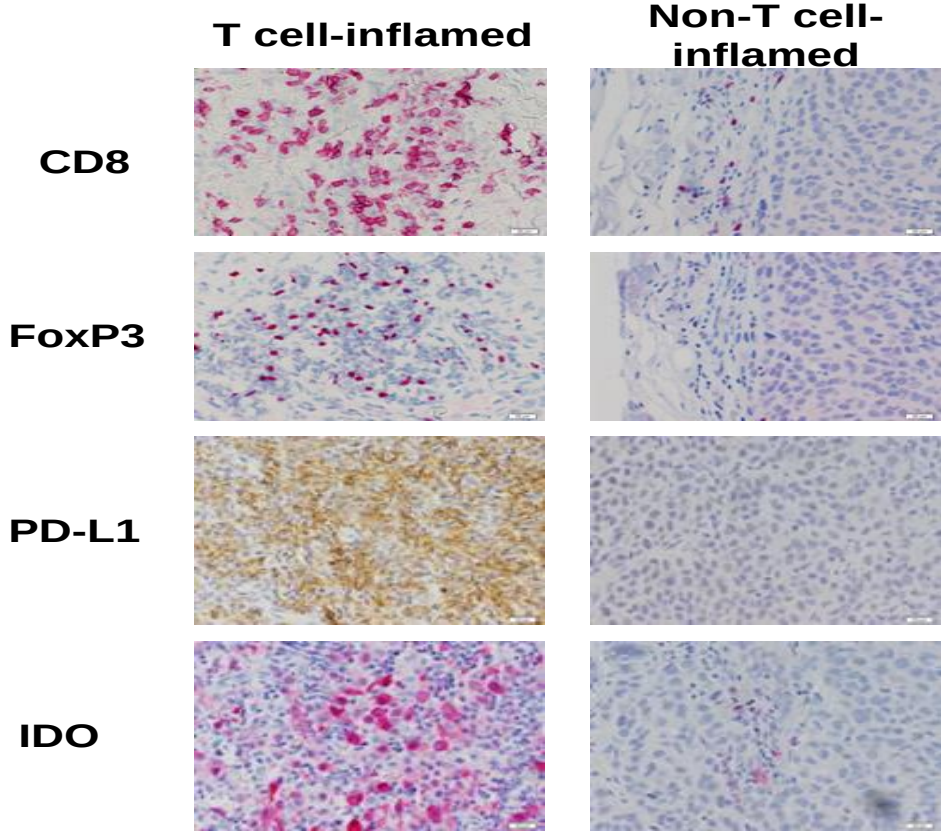
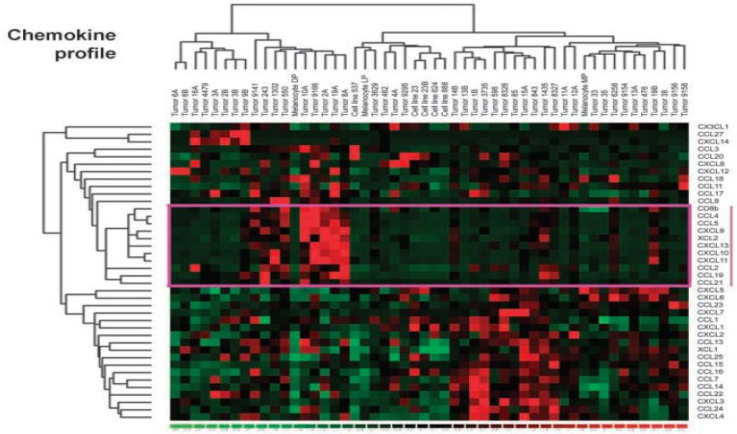
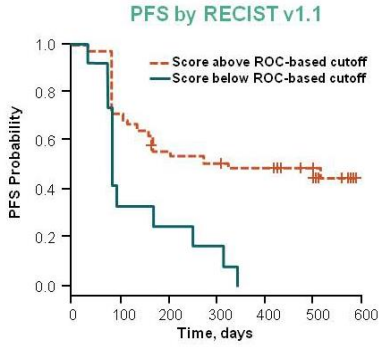
Luke and Ott. *Oncotarget*. 2015; Cristescu *et al*. *Science* 2018

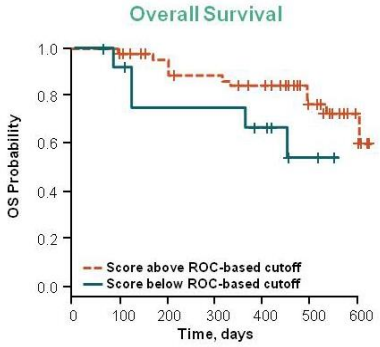
Immunobiology of T cell-inflamed & non-T cell-inflamed tumor microenvironment





PFS and OS in Patients With Melanoma and IFNγ Signature Score Above and Below the Cutoff





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Gajewski et al. Nature Immunol. 2013
Spranger et al., Science Trans. Med. 2013
Harlin et al. Clin Can Res. 2009
Ribas et al. J Clin Oncol 33, 2015 (suppl; abstr 3001)

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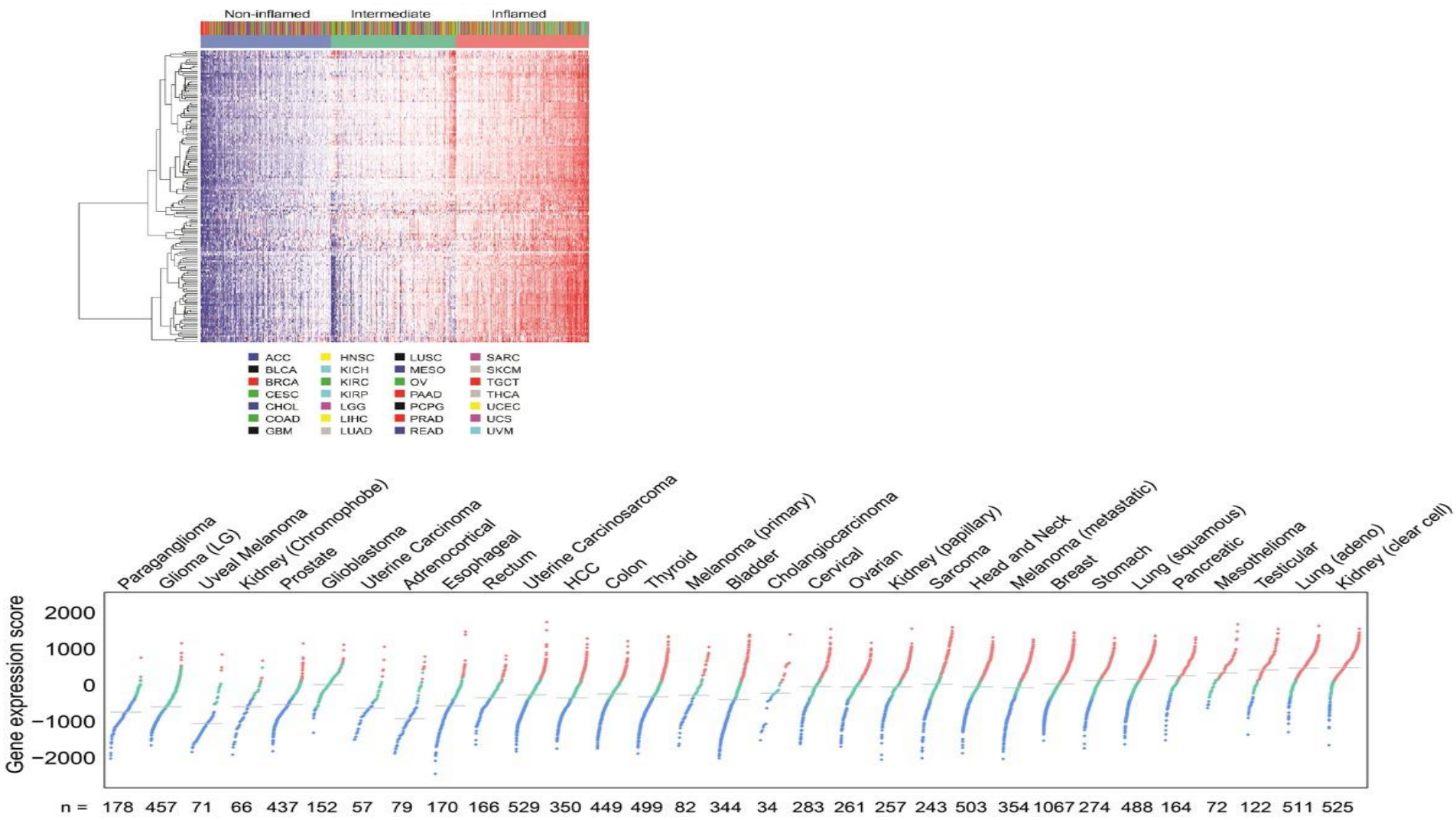
Spectrum of T cell-inflamed tumor microenvironment by increasing frequency across tumor types



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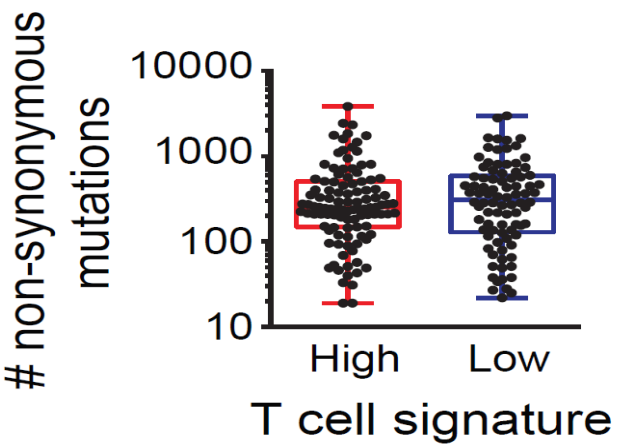
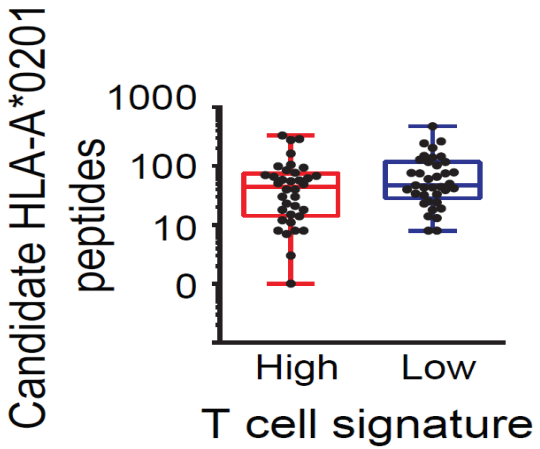
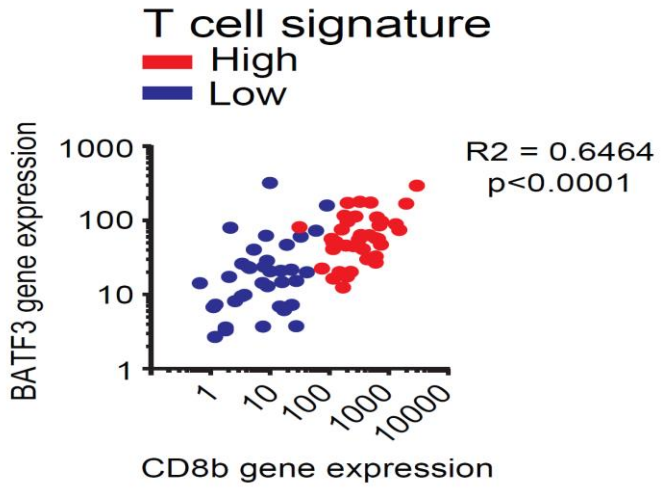
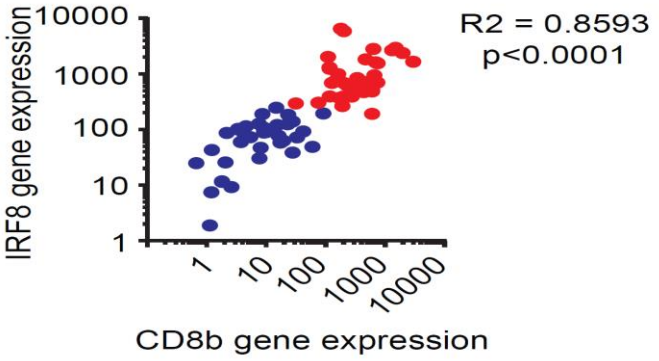
Antigen is NOT rate-limiting in non-T cell-inflamed tumors, rather Batf3 dendritic cells appear to be









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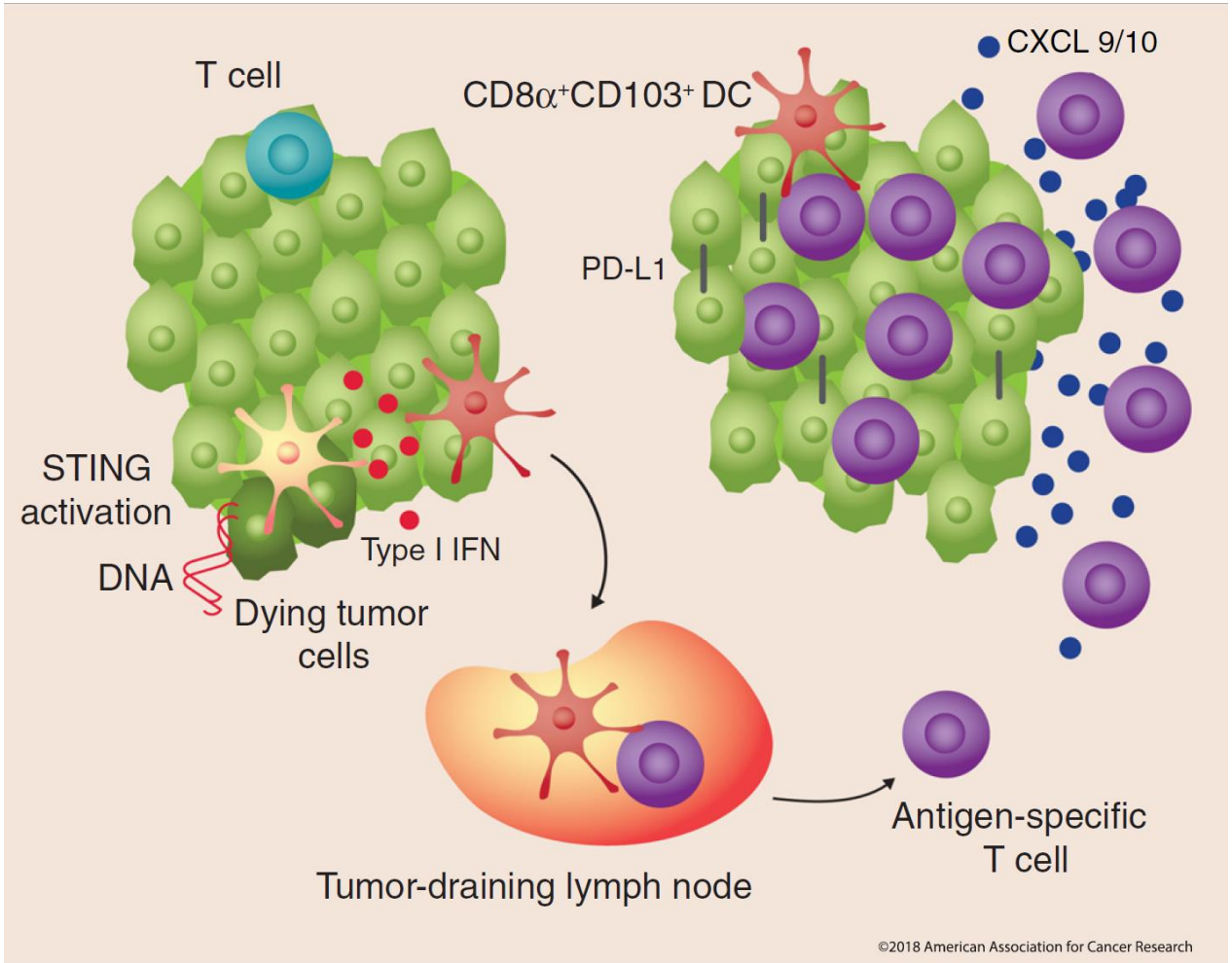
Development of the T cell-inflamed tumor microenvironment



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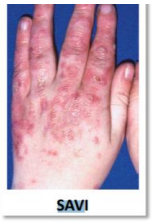
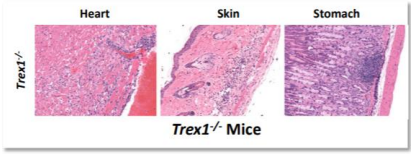
Complexity of STING as a therapeutic target

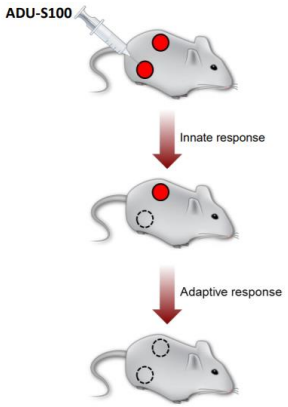
Is STING a validated innate immune target?

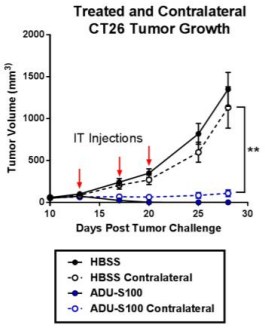
- Genetic validation—interferonopathies due to dysregulation of STING pathway
  - **Humans**:
    - STING-associated vasculopathy with onset in infancy (SAVI) (ligand-independent activated STING)
    - Aicardi–Goutieres syndrome (AGS), chilblain lupus (TREX-1 mutation)
    - Epigenetic silencing of STING in tumor cells
    - DNA tumor virus inactivation of STING
  - **Mice**:
    - STING (*TMEM173*)$^{-/-}$: HSV-1 virus infection sensitivity
    - TREX-1$^{-/-}$: recapitulates human AGS

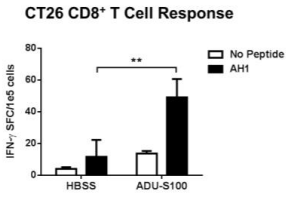




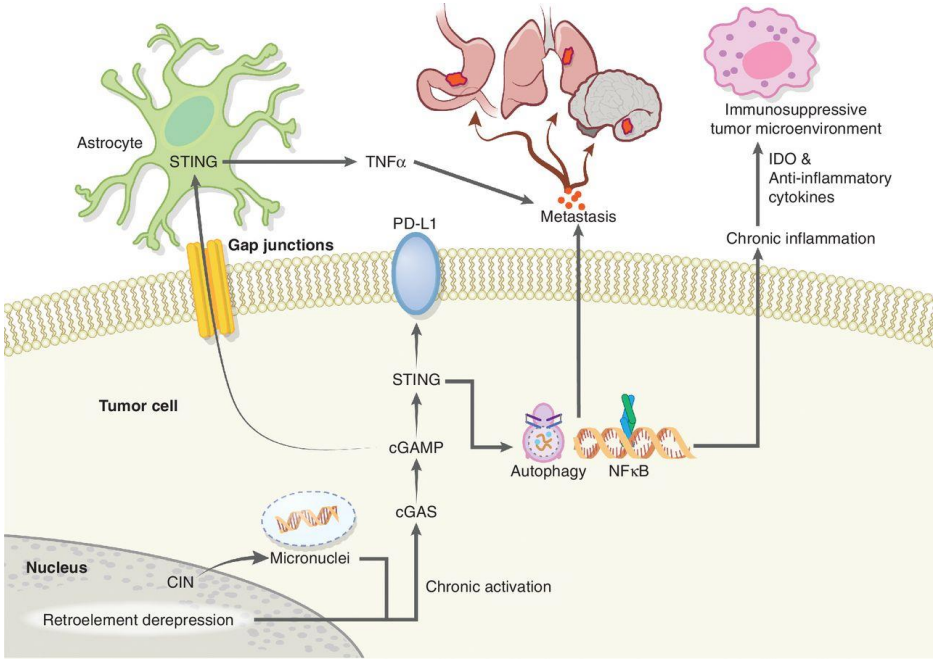
Gray et al., J. Immunol (2015); Ishikawa et al., Nature (2009); Lau et al. Science (2015); Liu et al., NEJM (2014); Stetson et al., Cell (2008); Xia et al., Cell Reports (2016)







Corrales and Hix Glickman et al, Cell Reports (2015)



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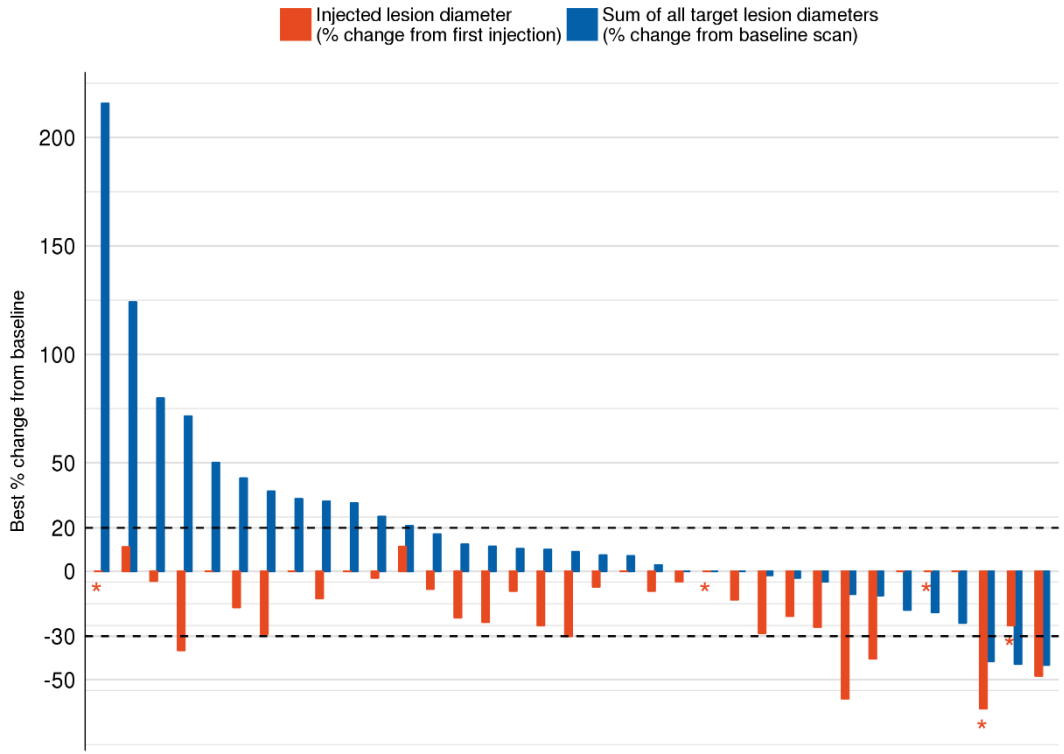
Dubensky SITC 2019

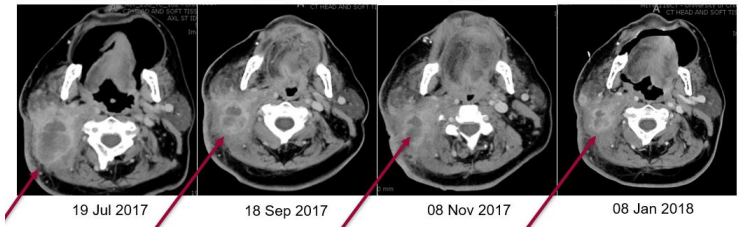
Kwon and Bakhoum *Cancer Discovery*. 2020

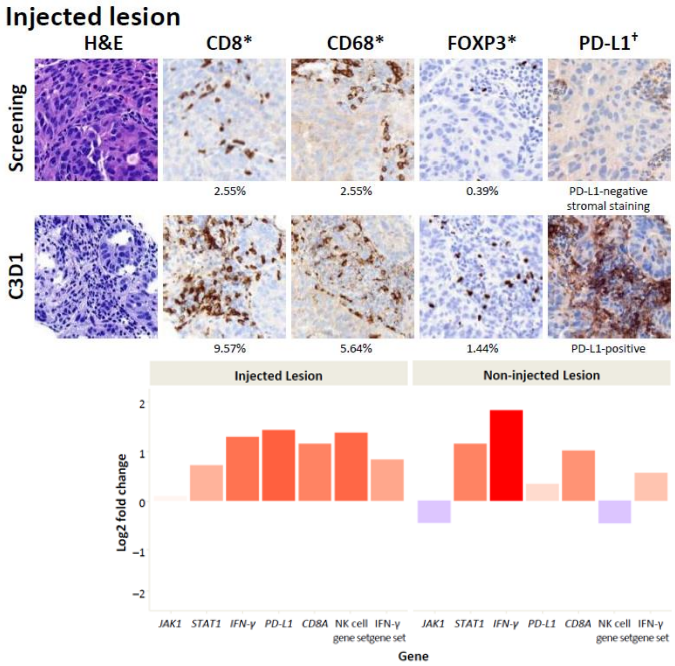
Phase I study of MIW815 (ADUS100)



Clinical Case Vignette

Patient with parotid adenocarcinoma (800 ug) – Partial response x 7 months
- Progressed on pembrolizumab prior to study entry





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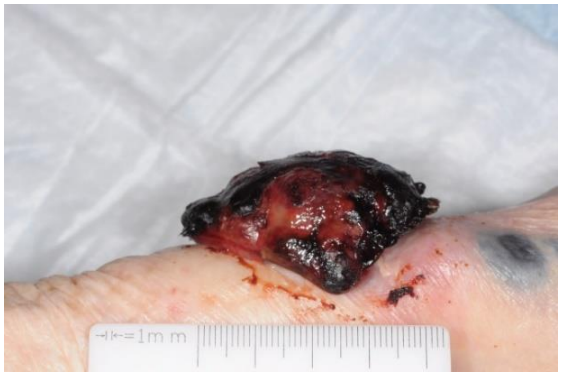
Meric-Bernstam…Luke *et al*. *Clin Can Res*. 2021

Pictures: Jason Luke, MD

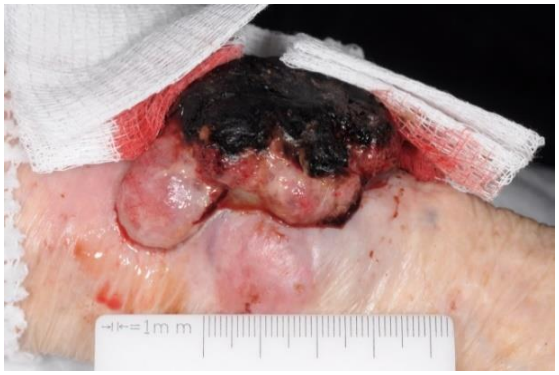
Clinical Case Vignette

93 year old with locally advanced PD1 naïve melanoma – biopsy proven complete response after MIW815 + spartazliumab

Screening



C1D1



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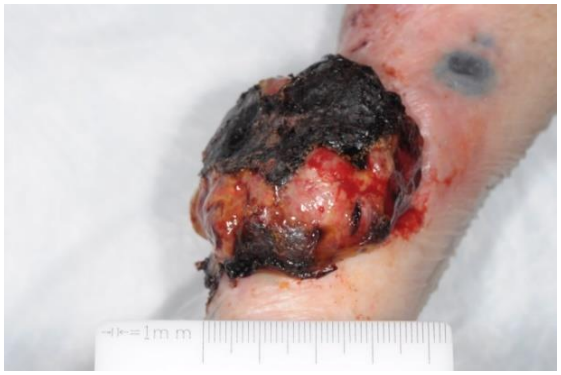
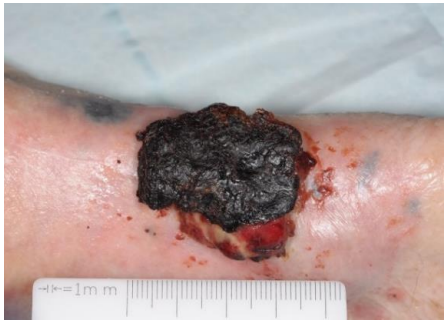


C2D1



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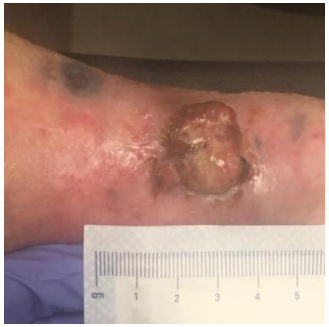

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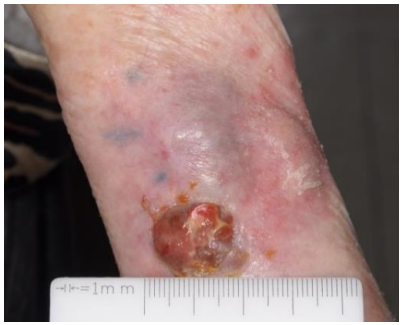
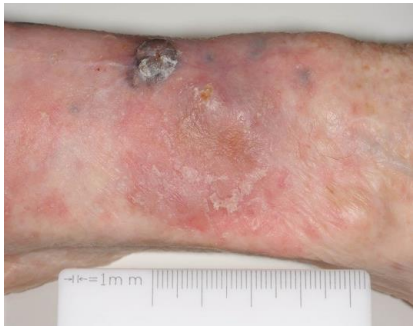


C4D1



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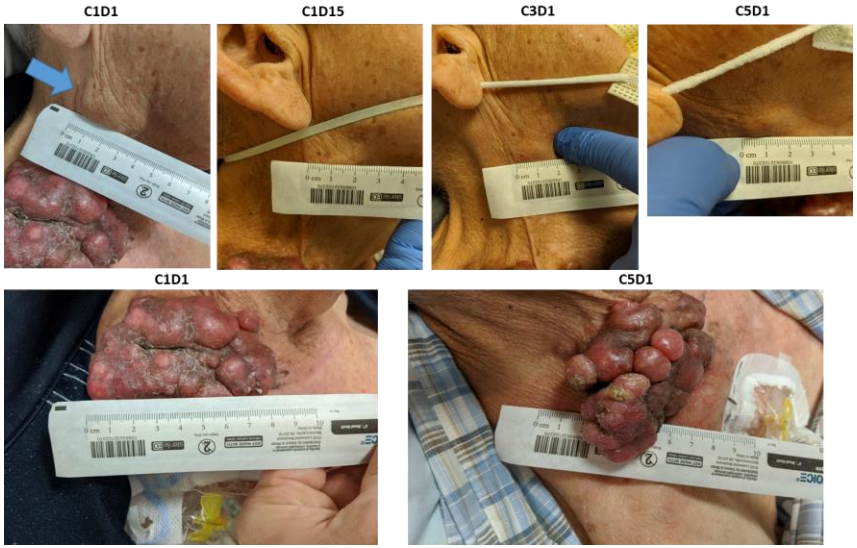
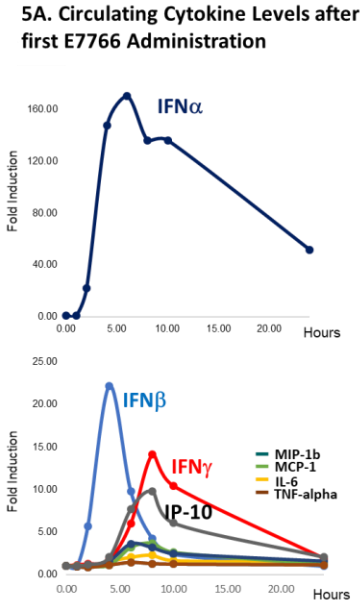
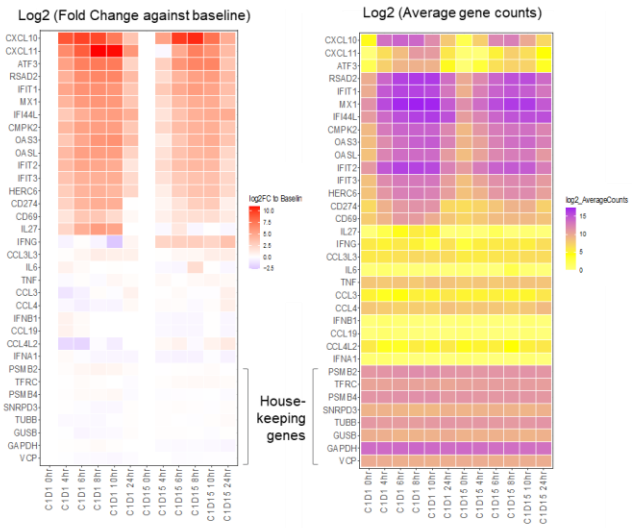
STING agonism can drive systemic responses in some patients







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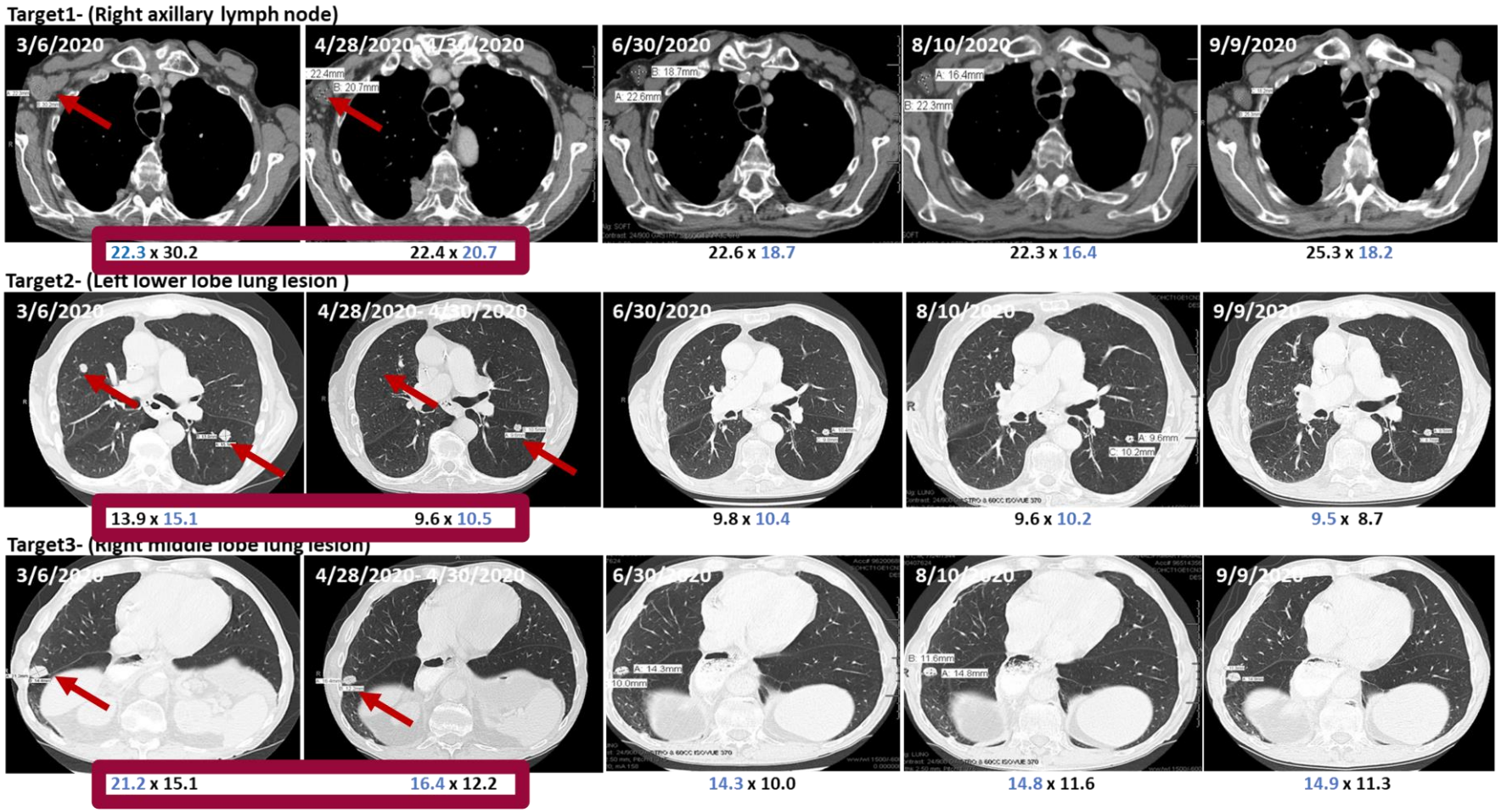
IT injection of low dose E7766 induced IFNs, IP-10, and durable anti-tumor activity in a patient with esophageal carcinoma



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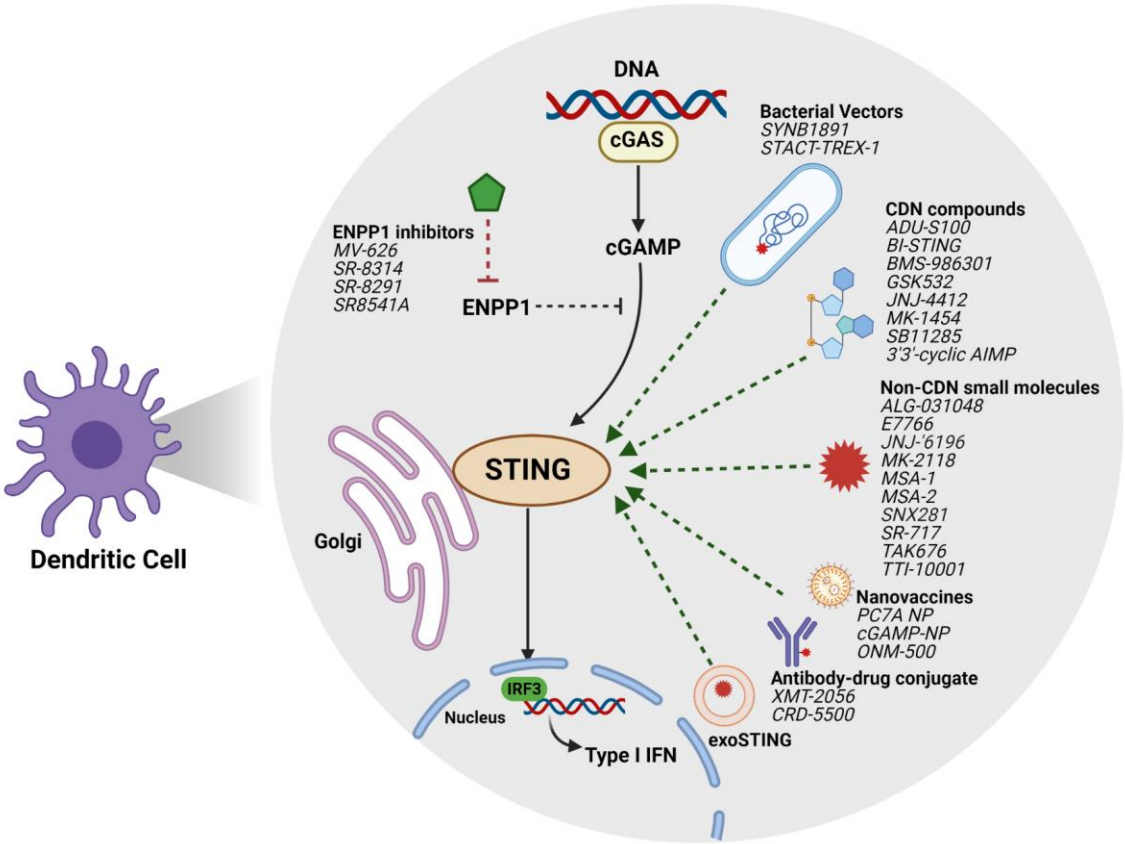
STING agonism in development



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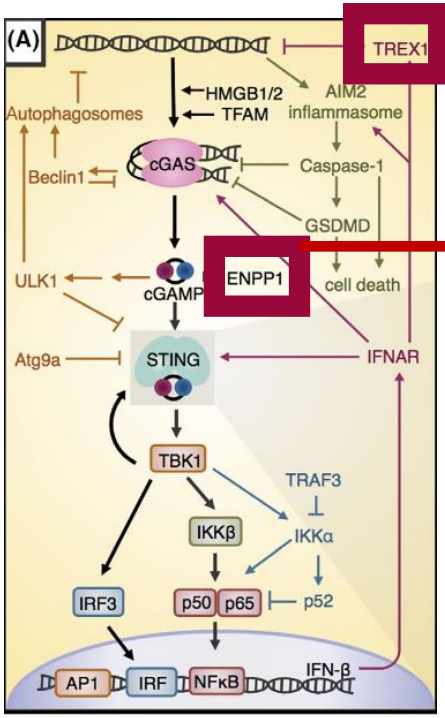
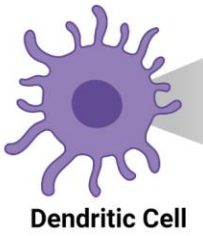
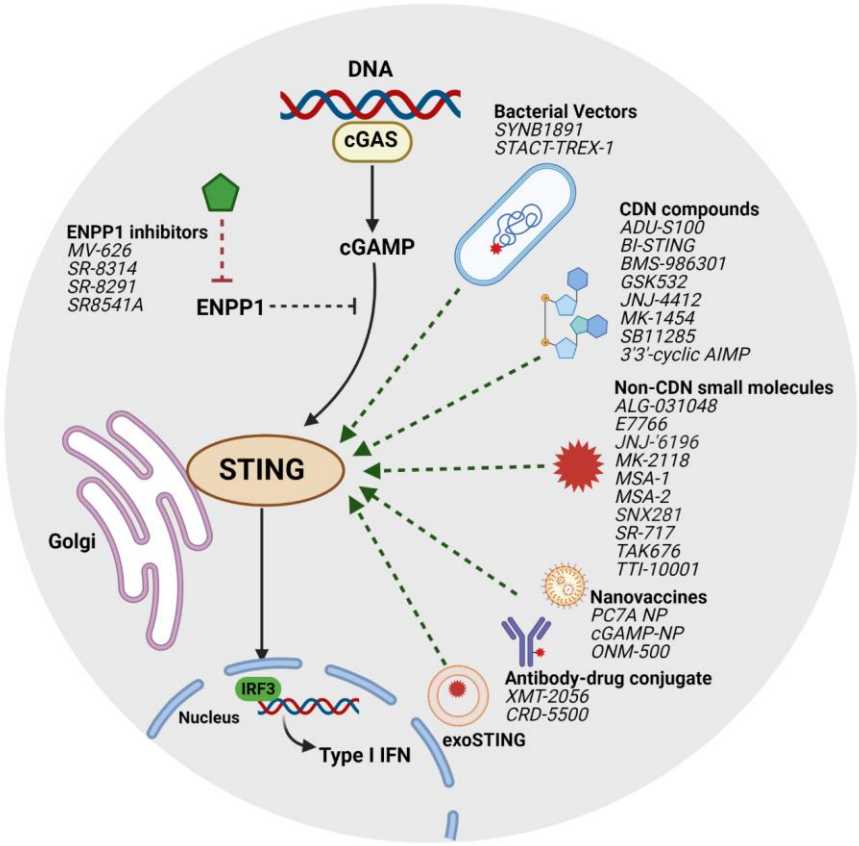
Amouzegar *et al*. *Cancers (Basel)*. 2021
Flood *et al*. *Immunol Rev*. 2019

STING agonism in development



ENPP1 and TREX1 are regulators of the STING pathway and potential therapeutic targets





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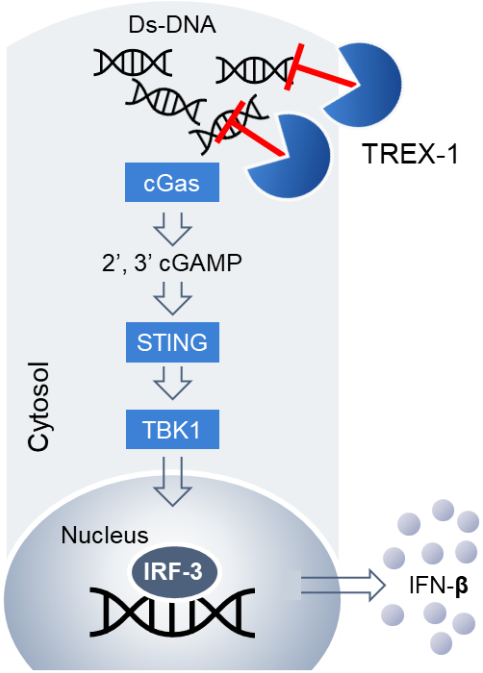
TEMPEST THERAPEUTICS

Amouzegar *et al*. *Cancers (Basel)*. 2021
Flood *et al*. *Immunol Rev*. 2019

In Vivo TREX1 Inhibition May Target Two Distinct MOA

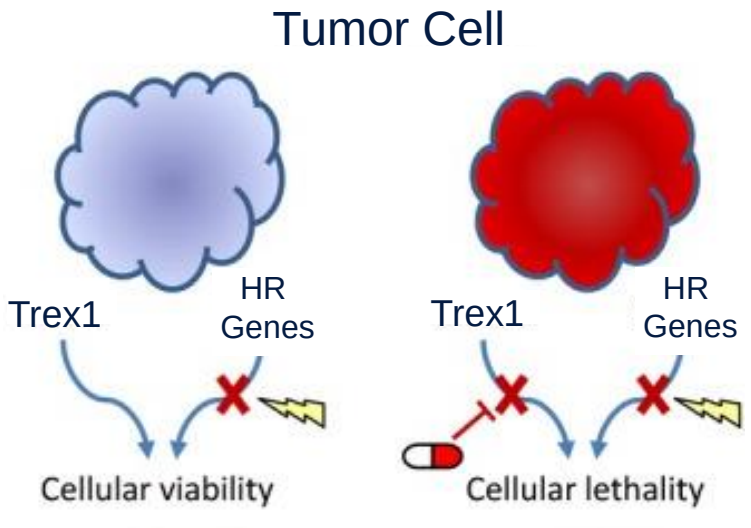
TREX1 not only prevents STING activation, but also DNA repair

Immune Activation Via STING Pathway



TREX1 inhibition activates innate immunity by increasing dsDNA concentrations that can be sensed by STING pathway

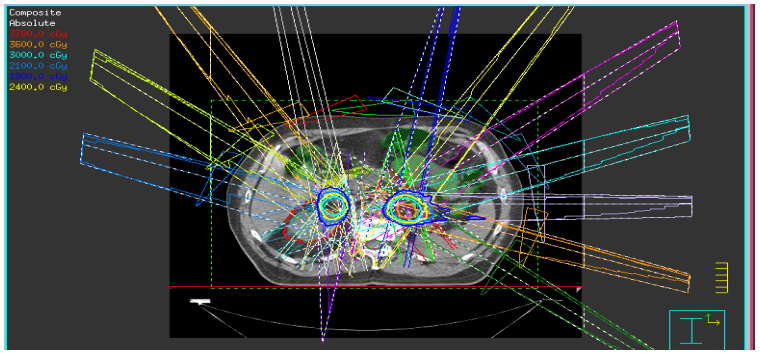
Tumor Cell Viability

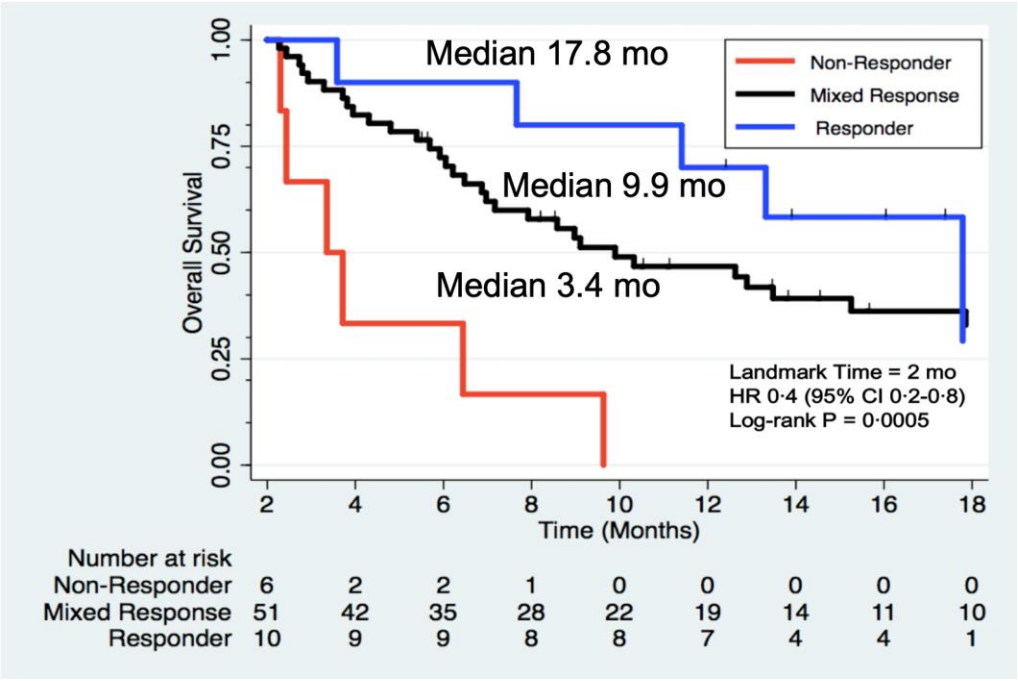


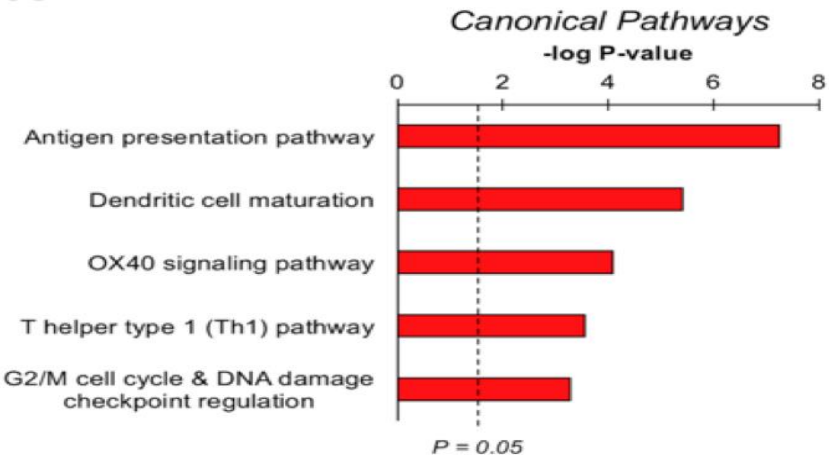
Homologous recombination (HR) deficient tumors may be susceptible to TREX inhibition due to TREX1's role in DNA repair

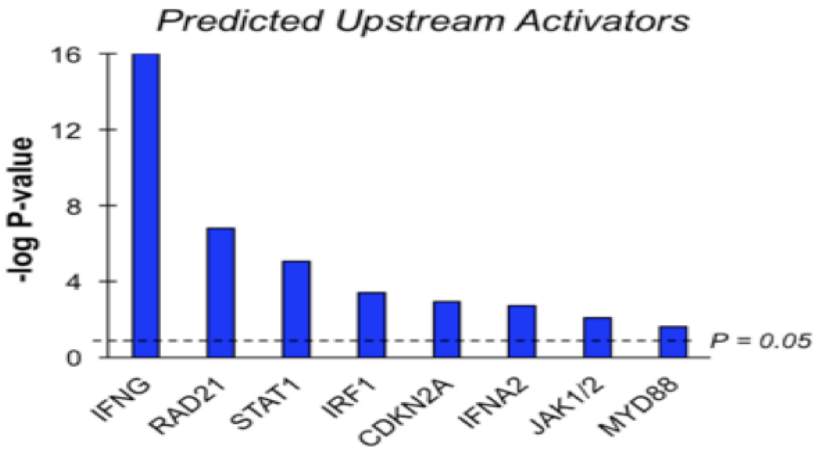
Adopted from Thompson et. Al. Pig Cell Mel Res, 2017

Response of irradiated lesion dictates overall survival to SBRT + pembrolizumab









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TEMPEST THERAPEUTICS

Luke *et al. J Clin Oncol*. 2018
Luke *et al. Clin Cancer Res*. 2020

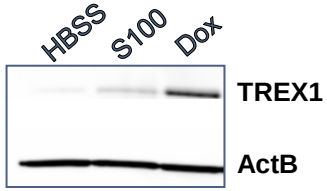
In Vivo Activity with Proprietary TREX1 Inhibitor

TREX1 inhibitor-dependent reduction of tumor volume

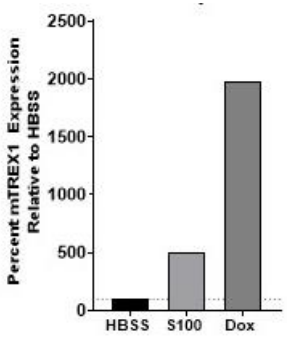
Experimental Rationale:

Doxorubicin (Dox) induces DNA strand breaks in tumor cells and induces TREX1 expression. Inhibition of TREX1 with TPST-994 leads to activation of the cGAS/STING pathway and anti-tumor efficacy

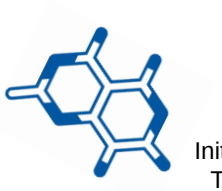
Doxorubicin induces TREX1 in CT26 tumors

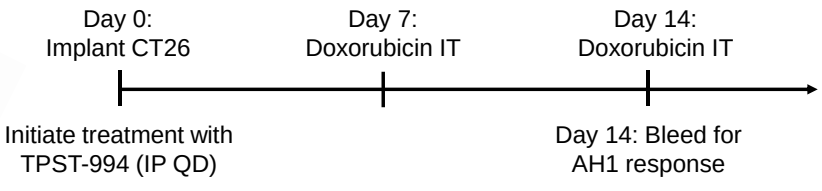


TREX1 Relative Protein Expression

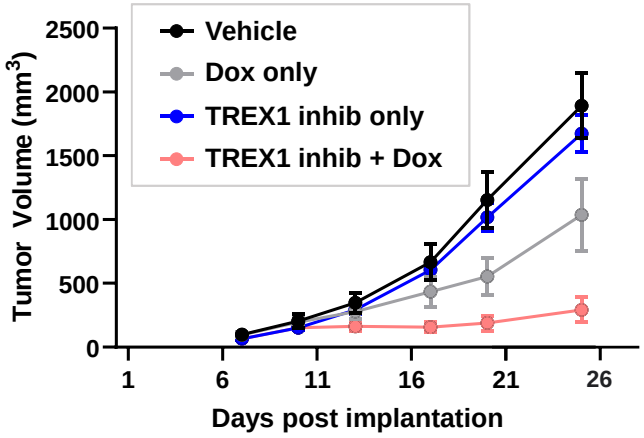


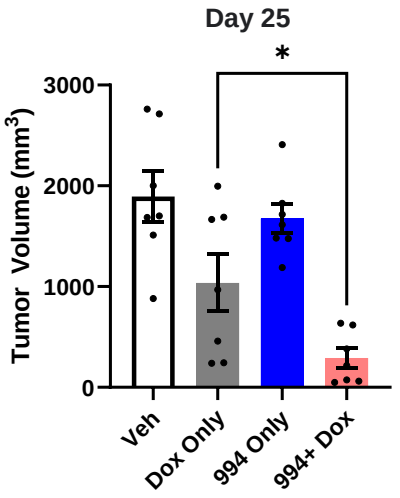
*S100 is a direct STING agonist





CT26 tumor volume





TREX1 is a high priority therapeutic target

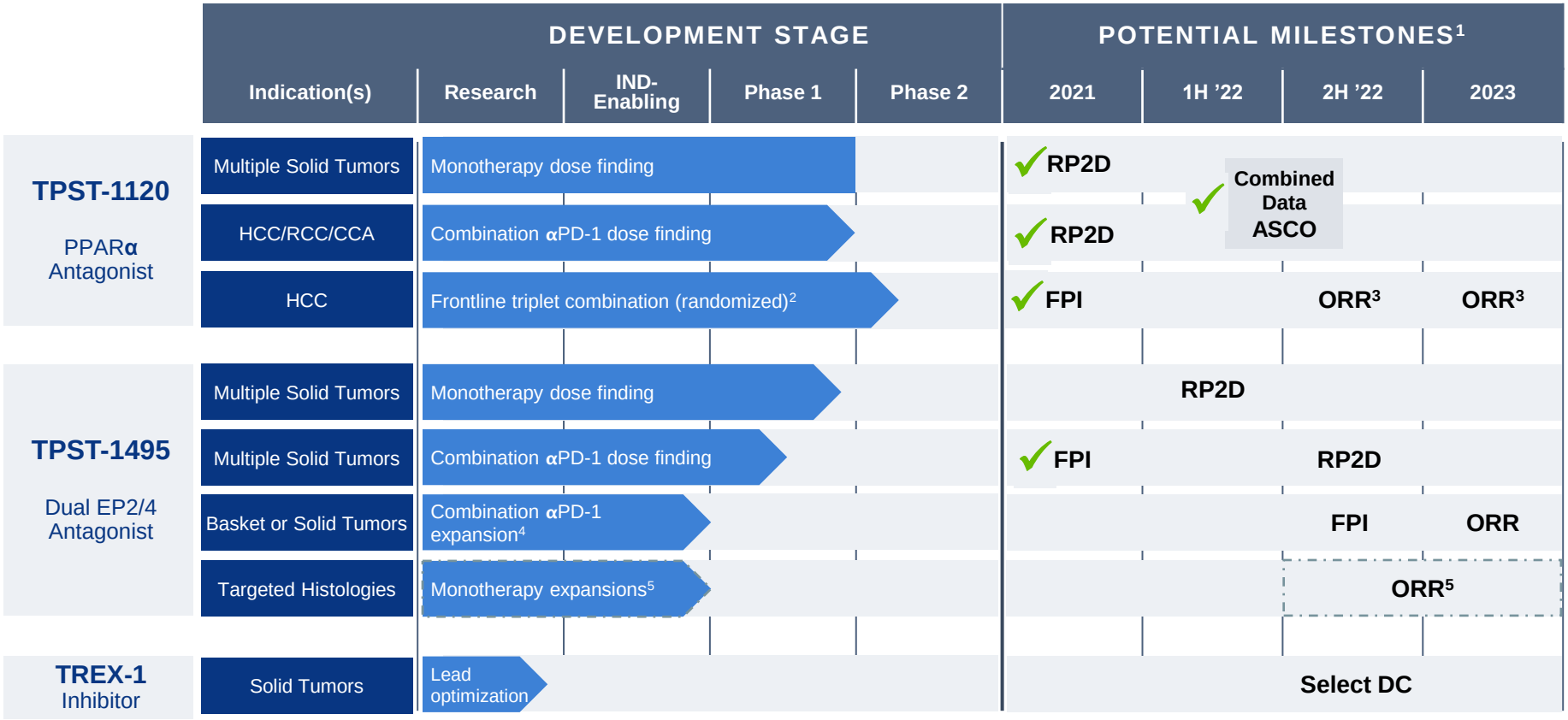
- STING **agonists may provide means to deliberately initiate innate immune inflammation to promote an endogenous T cell response in non-T cell-inflamed tumors** xx
  - First STING agonists have not moved the needle and novel approaches are needed to find success
  - **Intratumoral delivery is a major barrier**

- TREX1 **targeting represents a novel systemic approach to optimize STING agonism, exploit synthetic lethality and combine with other therapies**

Q&A

Significant Potential Newsflow Through 2022-2023

Diversified clinical and pre-clinical portfolio engenders a broad opportunity



"RCC" renal cancer; "HCC" hepatocellular carcinoma; "CCA" cholangiocarcinoma "FPI" first patient in; "RP2D" recommended Ph2 dose

[1] Timing is an estimate based on current projections. [2] Pursuant to a collaboration with Roche; TPST retains all product rights [3] Based on partner projections, ORR on 40 pts in triplet arm expected by YE/early 2023, with additional data in 2023 (including on additional patients, if study expanded) [4] Expansion study could be either a single indication or biomarker-based basket [5] With additional funding, monotherapy expansion would be in select indications based on target expression and/or a biomarker-positive basket cohort; ORR data expected from monotherapy expansion arms within 12-18 months of study commencement, depending on the histology