Combination Treatment with TTX-030, a First-in-class Anti-CD39 Antibody, in Patients with Advanced Pancreatic Cancer

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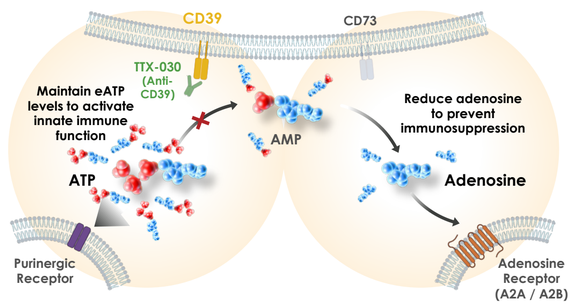
BACKGROUND

- TTX-030: fully-human IgG4 antibody targeting CD39
- Non-competitive allosteric inhibitor of CD39 ectoenzyme activity
- Inhibits CD39 at sub-nanomolar potencies

Phase 1 Safety Results

- No MTD identified as monotherapy
- Well-tolerated in combination with anti-PD1 and with chemotherapy

TTX-030, A First-in-Class CD39 Inhibitor with Two Mechanisms to Promote Anti-Tumor Immunity



STUDY DESIGN

Key Eligibility Criteria

- Locally advanced unresectable or metastatic pancreatic adenocarcinoma
- No prior systemic treatment for incurable/ metastatic disease
- Age >18 years
- ECOG 0-1

Expansion Cohorts

TTX-030 40mg/kg IV once then 20mg/kg Q2W
Gemcitabine 1000mg/m2 **+ nab-Paclitaxel** 125 mg/m2 d1,18,15 of 28-day cycles

TTX-030 40mg/kg IV once then 20mg/kg Q2W
Budigalimab (anti-PD1 mAb) 500mg IV Q4W
Gemcitabine 1000mg/m2 **+ nab-Paclitaxel** 125 mg/m2 d1,18,15 of 28-day cycles

METHODS

Key Outcomes & Endpoints

- Primary: Safety (incidence of adverse events)
- Secondary: Efficacy (overall response rate, progression-free survival per RECIST v1.1, overall survival), PK, ADA

Enrollment

- 59 patients enrolled in Phase 1 expansion cohorts between May 2020 and February 2022 at 28 sites in USA and South Korea
  - TTX-030+G/nP (n=31)
  - TTX-030+budigalimab+G/nP (n=28)
- Phase 1 complete in March 2024 (median follow-up of 10 months)

Biomarker Analysis

- Pre- and on-treatment tumor biopsies were analyzed retrospectively using a customized NanoString PanCancer Immune Profiling Panel

RESULTS

Patient Demographics and Baseline Disease Characteristics

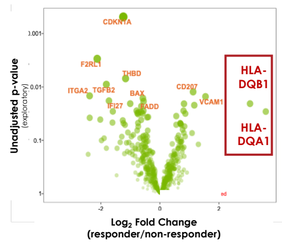
Demographics & Disease Characteristics	TTX-030+G/nP (N=31)	TTX-030+budigalimab +G/nP (N = 28)	Total (N = 59)
Age, yrs			
Median [range]	67 [46–86]	67 [52–79]	67 [46–86]
Sex, n (%)			
Female	16 (52)	13 (46)	29 (49)
Male	15 (48)	15 (54)	30 (51)
Race, n (%)			
White	22 (71)	16 (57)	38 (64)
Black or African American	4 (13)	2 (7)	6 (10)
Asian	3 (10)	9 (32)	12 (20)
Other/Unknown	2 (7)	1 (4)	3 (5)
ECOG Performance Status, n (%)			
0	13 (42)	13 (46)	26 (44)
1	18 (58)	15 (54)	33 (56)
Time from diagnosis, mos (median [range])			
Initial diagnosis	1.1 [1–52]	1.1 [0-58]	1.1 [0-58]
Metastatic disease at screening, n (%)	27 (87)	27 (96)	54 (92)
Prior chemotherapy			
Number of patients with any, n (%)	7 (23)	6 (21)	13 (22)
Number of prior regimen, n (median [range])	2 [1–3]	1 [1–2]	1 [1-3]
Liver metastases, n (%)	23 (74)	22 (79)	45 (76)

Safety Summary

Events, n (%)	TTX-030 + G/nP (n=31)	TTX-030 + budigalimab +G/nP (n=28)	Total (n=59)
Any TEAE	30 (96.8)	28 (100)	58 (98.3)
TEAE with Grade >= 3	25 (80.6)	27 (96.4)	52 (88.1)
TEAE Related to TTX-030	23 (74.2)	16 (57.1)	39 (66.1)
TEAE with Grade >= 3 Related to TTX-030	9 (29.0)	7 (25.0)	16 (27.1)
Any Serious TEAE	12 (38.7)	17 (60.7)	29 (49.2)
Serious TEAE Related to TTX-030	2 (6.5)	2 (7.1)	4 (6.8)
TEAE Leading to Discontinuation of TTX-030	3 (9.7)	3 (10.7)	6 (10.2)
TEAE Leading to Death	1 (3.2)	1 (3.6)	2 (3.4)

BASELINE TUMOR HLA-DQ EXPRESSION ASSOCIATED WITH CLINICAL BENEFIT WITH AND WITHOUT ANTI-PD1

Gene Expression in Tumor at Baseline



ORR by Group (%)	Efficacy-Evaluable	Biomarker Set*	HLA-DQ^{high}	HLA-DQ^{low}
TTX-030 +G/nP	27% (8/30)	32% (7/22)	**43%** (6/14)	**13%** (1/8)
TTX-030 +budi +G/nP	33% (9/27)	39% (7/18)	**50%** (7/14)	**0%** (0/4)
Overall	30% (17/57)	35% (14/40)	**47%** (13/28)	**8%** (1/12)

*NanoString results available from 40 patients

Median PFS, Months (95% CI)

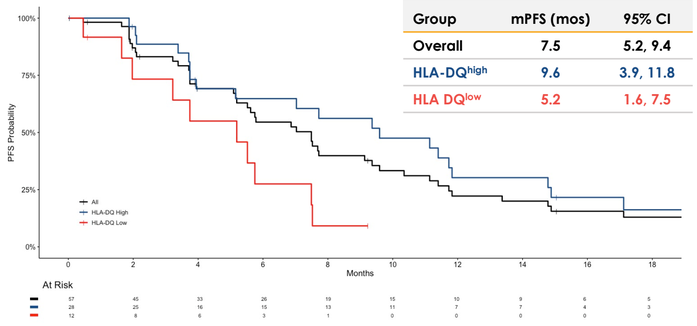
Treatment	HLA-DQ^{high}	HLA-DQ^{low}
TTX-030 +G/nP	[N=14] **9.4** (3.7, 11.7)	[N=8] **3.7** (1.6, 7.5)
TTX-030+budigalimab +G/nP	[N=14] **9.6** (3.9, 17.1)	[N=4] **5.4** (0.5, NR)

TREATMENT-EMERGENT ADVERSE EVENTS (>20%; All-Cause)

	TTX-030+G/nP (N = 31)		TTX-030+budigalimab+G/nP (N = 28)		Total (N = 59)	
Preferred Term	**All Grades**	**≥ Grade 3**	**All Grades**	**≥ Grade 3**	**All Grades**	**≥ Grade 3**
Fatigue	21 (67.7)	4 (12.9)	18 (64.3)	3 (10.7)	39 (66.1)	7 (11.9)
Nausea	16 (51.6)	0 (0.0)	16 (57.1)	0 (0.0)	32 (54.2)	0 (0.0)
Neutrophil count decreased	15 (48.4)	12 (38.7)	12 (42.9)	12 (42.9)	27 (45.8)	24 (40.7)
Anaemia	11 (35.5)	4 (12.9)	15 (53.6)	8 (28.6)	26 (44.1)	12 (20.3)
Alopecia	12 (38.7)	0 (0.0)	12 (42.9)	0 (0.0)	24 (40.7)	0 (0.0)
Decreased appetite	12 (38.7)	0 (0.0)	10 (35.7)	1 (3.6)	22 (37.3)	1 (1.7)
Diarrhoea	11 (35.5)	1 (3.2)	10 (35.7)	2 (7.1)	21 (35.6)	3 (5.1)
Vomiting	8 (25.8)	1 (3.2)	12 (42.9)	0 (0.0)	20 (33.9)	1 (1.7)
Constipation	11 (35.5)	0 (0.0)	6 (21.4)	0 (0.0)	17 (28.8)	0 (0.0)
Oedema peripheral	8 (25.8)	1 (3.2)	8 (28.6)	1 (3.6)	16 (27.1)	2 (3.4)
Platelet count decreased	8 (25.8)	4 (12.9)	8 (28.6)	1 (3.6)	16 (27.1)	5 (8.5)
Aspartate amino-transferase increased	6 (19.4)	1 (3.2)	9 (32.1)	3 (10.7)	15 (25.4)	4 (6.8)
Neuropathy peripheral	6 (19.4)	0 (0.0)	9 (32.1)	0 (0.0)	15 (25.4)	0 (0.0)
Neutropenia	8 (25.8)	8 (25.8)	6 (21.4)	5 (17.9)	14 (23.7)	13 (22.0)
Pyrexia	4 (12.9)	0 (0.0)	10 (35.7)	0 (0.0)	14 (23.7)	0 (0.0)
Alanine amino-transferase increased	6 (19.4)	2 (6.5)	7 (25.0)	4 (14.3)	13 (22.0)	6 (10.2)
Rash maculo-papular	7 (22.6)	0 (0.0)	5 (17.9)	1 (3.6)	12 (20.3)	1 (1.7)

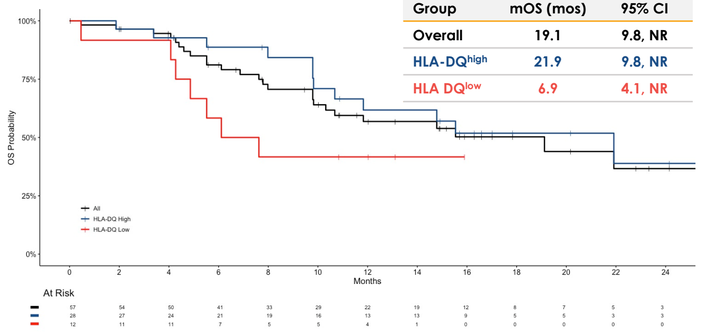
- Incidence and severity of most frequent adverse events (irrespective of attribution) was qualitatively similar to what has been seen with gemcitabine + nab-paclitaxel
- No clear signal of increase in frequency or severity of immune-related adverse events when combined with budigalimab (anti-PD1)

PROGRESSION-FREE SURVIVAL



Group	mPFS (mos)	95% CI
Overall	7.5	5.2, 9.4
HLA-DQ^{high}	9.6	3.9, 11.8
HLA DQ^{low}	5.2	1.6, 7.5

OVERALL SURVIVAL



Group	mOS (mos)	95% CI
Overall	19.1	9.8, NR
HLA-DQ^{high}	21.9	9.8, NR
HLA DQ^{low}	6.9	4.1, NR

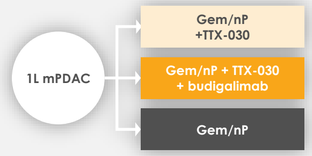
CONCLUSIONS

TTX-030 with and without budigalimab was well-tolerated in combination with gemcitabine and nab-paclitaxel

TTX-030 combinations showed promising progression-free survival and overall survival in 1L patients with advanced pancreatic adenocarcinoma

Retrospective analysis identified a relationship between high tumor expression of HLA-DQ at baseline and clinical benefit from TTX-030 combinations

The randomized, 3-arm phase 2 ELTIVATE study is currently enrolling (NCT06119217) to further evaluate the activity of these TTX-030 combinations



https://www.trishulatx.com/

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