#TPS2673

FIPO23 trial: First-in-human phase I/II study of XON7 in advanced solid tumors

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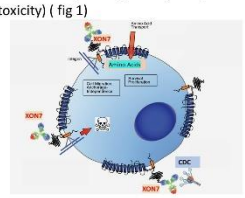
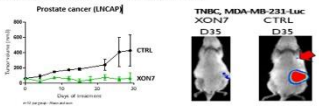
Background:

- XON7 is a first in class glyco-humanized polyclonal oncolytic IgG antibody (GH-pAb) produced by immunizing with human tumor antigens, a double Knock-Out swine lacking the two xeno-antigens: α-1-3 galactose (αGal) and N-glycolylneuraminic acid (Neu5Gc).
- XON7 targets selectively multiple epitopes on several tumor associated antigens that modulate tumor metabolism. It induces tumor cell apoptosis and promotes the elimination of tumor cells mainly through CDC (Complement Dependent Cytotoxicity) (fig 1)



- Notable antitumor and antimetastatic effects of XON7 have been demonstrated in mice and rat xenografted with human solid tumors such as colon, sarcoma, prostate, lung and triple negative breast cancers.



Methods:

- Phase I of a multicenter, non-randomized, phase I/II study in patients with relapsed refractory, locally advanced or metastatic solid tumor types (NCT06154291).
- Explore ascending doses of intravenous XON7 monotherapy given every 2 weeks, during 12 cycles, of 28 days, using a BOIN design, to characterize:
  - Safety, maximum tolerated dose MTD, and recommended dose for expansion (RDE)
  - PK, PD
  - Anti-drug antibody (ADA)
  - Preliminary anti-tumor activities

Eligible patients: adults, who had previously progressed after ≤ 4 lines of therapy, or for whom no other approved therapy exists. PS ≤2. Adequate organ functions. No known CNS involvement.

Dose escalation/de-escalation : based on the Bayesian Optimal Interval (BOIN) design, through pre-planned dose levels (1.5; 3; 6; 12; 16; 20 mg/kg)

The dose limiting toxicity (DLT) period was 4 weeks.

PK assessment included serial PK sampling during the first Cycle then pre- and post-first dose of Cycles 2, 3 and 7.

ADA assessment performed at Days 1, 5, 7 and 15 of Cycle 1 then at the first day of each subsequent cycle up to Cycle 12.

Response assessment performed by the investigator per RECIST at screening, the end of every 2 cycles, up to cycle 12. Then every 3 months up to 1 year.

The first in class glyco-humanized polyclonal antibody, XON7, administered Q2W, in patients with advanced refractory solid tumors is very well tolerated at doses up to 3mg/kg. Further doses escalation is ongoing.

Results:

- At the time of data cut-off, 3 dose levels have been tested
- Presented in this poster are data (as of May 20, 2024) from 6 relapsed / refractory solid tumor patients, enrolled to cohort 1.5 mg/kg and 3 mg/kg.

Baseline Characteristics	Total n=6
Median Age, years [min-max]	64 (61-78)
Male, n (%)	3 (50)
ECOG PS 0-1, n (%)	6 (100)
Primary Diagnosis, n (%)	
NSCLC	1 (17)
Choroidal Melanoma	1 (17)
Adenocarcinoma of Appendix	1 (17)
Colorectal Adeno-carcinoma	1 (17)
Endometrial Carcino-sarcoma	1 (17)
Stomach Adenocarcinoma	1 (17)
Overall Stage at Study Entry, n (%)	
Stage IV	6 (100)
Prior Therapy, n (%)	
Chemotherapy	6 (100)
ICI	5 (83)
TKI	1 (17)
ADC	1 (17)
mAb	5 (83)
Median Lines of Prior Therapy, [min-max]	3 (2-4)
Median Time between Last Treatment and Progression, days [min-max]	8 (0-150)
Median Number of Doses Received, [min-max]	5 (3-10)

Dose escalation

Safety:

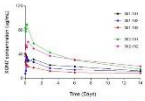
- XON7 at a dose 1.5 and 3 mg/kg was well tolerated
- No related SAEs or DLT to date
- No related Gr ≥ 3 anemia, thrombocytopenia, neutropenia observed to date
- No required dosing action due to AE

Adverses Events (AE)	Total n=6 patients
Any AE, n	26
Grade 1 n (%)	26 (72)
Grade 2 n (%)	9 (25)
Grade ≥3	1 (3)
Any AE possibly related	11 (31)
Any Serious AE	0 (0)
Infusion reaction	0 (0)

Adverse Events Occurring in > 2 patients	ALL		Possibly Related		Total n=36
	Gr 1-2	Gr 3-4	Gr 1-2	Gr3-4	
Asthenia	5 (14)	0	2 (6)	0	5 (14)
Fever/Chills	5 (14)	0	2 (6)	0	5 (14)
Skin Dryness/Rash	2 (6)	0	1 (3)	0	2 (6)

Pharmacokinetics

- Preliminary data indicate dose-dependent increases in PK exposure and no accumulation



Dose (mg/kg)	Patient	C_{max} 1st inj (µg/ml)	C_{trough} (µg/ml)	AUC_{last} (µg/ml*h)	AUC_{inf} (µg/ml*h)	T_{half} (day)	C_{max} 3rd inj (µg/ml)	Ratio C_{max3}/C_{max1}
1.5	001-101	40.81	12.27	756.5	6584	10.5	60.75	1.49
	001-102	33.75	11.65	703.2	5949	12.8	38.81	1.11
	001-105	27.08	8.72	476.8	3745	11.0	47.81	1.71
3	002-101	89.34	15.26	1800.0	11194	7.0	91.74	1.03
	002-102	60.32	19.98	1307.0	10777	10.6	50.29	0.83

Immunogenicity

- No ADA was detected in patient serum treated with 1.5mg/kg after 5 infusions and 3mg/kg after 4 infusions.

Abstract

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Background: XON7 is a first-in-class glyco-humanized polyclonal antibody (GH-pAb) targeting selectively multiple tumor-associated antigens. XON7 induces tumor cell apoptosis and promotes the elimination of tumor cells by immune effector cells through CDC (Complement Dependent Cytotoxicity) and ADCP (Antibody-Dependent Cell Phagocytosis). XON7 demonstrated anti-tumor efficacy in mice xenograft models with human solid tumors such as colon, prostate, lung and triple negative breast cancers. Safety pharmacology and toxicology studies in

non-human primates demonstrated an acceptable safety profile for XON7. Taken together, these preclinical data support the initiation of human trials in patients with advanced solid tumors.
Methods: First-in-patient, multicenter, open-label, two phases (dose-escalation (ESC) followed by dose expansion (EXP)) study of XON7 single agent, in patients with relapsed refractory, locally advanced or metastatic solid tumors without standard available treatments (*NCT06154291*). Key eligibility criteria include disease progression after ≤ 4 lines of therapy; age > 18 years; ECOG performance status ≤2; adequate organ functions; no known CNS involvement. All advanced or metastatic tumor types except glioblastoma, can be included during ESC. Primary endpoints: safety, tolerability and determination of MTD/RP2D. Secondary endpoints: pharmacokinetics (PK), pharmacodynamics, immunogenicity and preliminary anti-tumor activity (RECIST 1.1). AEs graded according to CTCAE 5.0. In the ESC part, XON7 is administered as 60-min intravenous infusion every 2 weeks according to an escalating schedule of doses from 1.5 to 20 mg/kg for up to 12, 28-day cycles. Dose escalation/de-escalation is based on the Bayesian Optimal Interval (BOIN) design, up to 45 pts are planned. At the recommended dose, up to 7 EXP cohorts (30 pts each) defined according to the primary tumor site are planned. Bayesian sequential monitoring will be used. Patient recruitment is planned or ongoing at 25 sites worldwide.
Results: As of Feb 3rd, 2024, 3 pts are enrolled in the first dose cohort and have received XON7 at dose 1,5 mg/kg Q2W for the first 28-days cycle.
Conclusions Accrual is ongoing in this first-in-human trial of XON7.
Clinical trial information: NCT06154291.