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## FIPO23: A First-in-Human Trial of XON7, a Glyco-Humanized Polyclonal Antibody (GHpA)Targeting Multiple Tumor Antigens in Advanced Solid Tumors

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**Background:**
Despite the success of monoclonal antibodies , tumor heterogeneity and acquired resistance remain major therapeutic limitations. XON7 is a first-in-class GH-pAb targeting simultaneously multiple tumor antigens, among which SLC3A2 (tumor metabolism and ferroptosis), Annexin A2 (β-catenin signaling), and CKAP4 (DKK1 receptor). In vivo XON7 monotherapy outperformed combinations of monosepcific antibodies against these targets.

XON7 induces tumor apoptosis and clearance via complement-dependent cytotoxicity and antibody-dependent cellular phagocytosis , while enhancing antitumor immunity through CD8+ T cell activation and macrophage polarization.

**Methods:**
FIPO23 (NCT06154291) is an ongoing multicenter, open-label, phase I/II study including dose-escalation (ESC) and expansion (EXP) cohorts. Eligible patients have advanced/metastatic solid tumors (excluding glioblastoma) refractory to standard therapies (≤4 prior lines), ECOG PS ≤2, and adequate organ function. XON7 is administered IV every 2 weeks for up to 12, 28-day cycles. Dose escalation (1.5, 3, 6, 12, 16, 20 mg/kg) follows a BOIN design. Phase I primary endpoints: safety,(CTCAE V5); 1st cycle DLTs, main secondary endpoints : PK/PD, immunogenicity; ORR (RECIST 1.1)

**Results:**18 DLT evaluable patients (median age: 61 years; 66% male) were treated across all planned doses. Tumor types included colorectal (n=4), NSCLC (n=4), pancreatic carcinoma (n=3) and others (n=6).

No DLT was observed.

A single moderate and transient infusion reaction was observed among a total of 106 infusions administered

A total of 139 AE was observed : 12% of grade ≥ 3 and 5% of SAE

XON7 showed a linear PK response, and no accumulation with repeated doses

Preliminary efficacy showed one partial response (colorectal cancer) and four cases of stable disease. Efficacy data from patients at the 20 mg/kg level are not yet available.

**Conclusions:**
XON7 demonstrates a favorable safety profile and early signs of antitumor activity in heavily pretreated patients with advanced solid tumors.

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## Background:

XON7 is a first in class glyco-humanized polyclonal IgG antibody (GH-pAb) , it induces tumor cell apoptosis, promotes the elimination of tumor cells mainly through CDC (Complement Dependent Cytotoxicity) and modulates the TME by targeting selectively and simultaneously multiple epitopes **on 3 major tumor associated antigens** :

**SLC3A2 (CD98)**: an amino acid transporter that: promotes tumor cell metabolism, activate c-Myc, which promotes cell growth, proliferation, and survival. It also creates a hostile TME that makes it difficult for the cytotoxic immune cells to infiltrate the tumors

**Annexin A2**: a Ca2+-dependent phospholipid-binding protein that is important for cytoskeletal rearrangement, cell proliferation, and motility . Increased expression of annexin A2 in cancer cells promotes the degradation of the extracellular matrix-increased angiogenesis, and the invasion

**CKAP4**: a DKK1 surface receptor, DKK1/CKAP4 signaling promotes cancer cell proliferation through the PI3K/AKT pathway

## Methods:

FIPO23 (NCT06154291) is an ongoing multicenter, open-label, phase I/II study including dose-escalation (ESC) and expansion (EXP) cohorts.

**Eligible patients**: adults with advanced / metastatic solid tumors (excluding glioblastoma) refractory to standard therapies (≤4 prior lines), ECOG PS ≤2, and adequate organ function. No known CNS involvement.

**ESC part**, (up to 45pts): explore 6 dose levels (1.5, 3, 6,12, 16, 20 mg/kg) of intravenous XON7 monotherapy, Q 2 weeks, during 12 cycles, of 28 days, using a BOIN design, to characterize:

- Primarily: Safety,(CTCAE V5), 1st cycle DLTs, and determine maximum tolerated dose MTD, or recommended dose for expansion
- Secondarily: PK ; Immunogenicity;
- Anti-tumor activities( RECIST 1.1):
  Objective Response Rate : PR+CR
  Disease Control Rate : CR+PR+SD
- **EXP part** (up to 210 pts): evaluate primarily ORR in prespecified several tumor types :
  Colorectal, Sarcoma, TNBC, Pancreatic, NSCLC, Gastro-esophageal and Ovarian cancers.

## Patients:

Presented in this poster are data (cut-off on 23 sept 2025) from 22 patients enrolled to dose cohorts 1,5 to 20 mg/kg ( table 1).

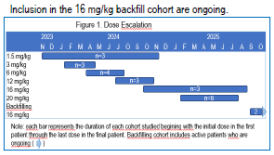
Data from the ongoing backfilling cohort are not presented.

| Table 1: Demographic and Baseline disease Characteristics | n=22 patients |
|---|---|
| Median Age, years (min-max) | 63 (29-79) |
| Male, n (%) | 14 (64) |
| ECOG PS 0-1, n (%) | 22 (100) |
| Primary Diagnosis, n (%) | |
| Colorectal Adenocarcinoma | 5 (23) |
| NSCLC | 4 (18) |
| Pancreatic Adenocarcinoma | 3 (14) |
| Choroidal Melanoma | 1 (4,5) |
| Adenocarcinoma of Appendix | 1 (4,5) |
| Endometrial Carcinosarcoma | 1 (4,5) |
| Adenoid Cystic Carcinoma | 1 (4,5) |
| Dedifferentiated Liposarcoma | 1 (4,5) |
| Rete Testis Adenocarcinoma | 1 (4,5) |
| Esophageal Adenocarcinoma | 1 (4,5) |
| Triple negative breast cancer | 1 (4,5) |
| Kidney carcinoma | 1 (4,5) |
| Urachal Adenocarcinoma | 1 (4,5) |
| Overall Stage at Study Entry, n (%) | |
| Stage IV | 21 (95) |
| Stage III | 1 (5) |
| Prior Therapy, n (%) | |
| Chemotherapy | 19 (86) |
| IO | 8 (36) |
| mAb | 6 (27) |
| TKI | 3 (14) |
| Other therapies | 5 (23) |
| ADC | 1 (5) |
| Endocrine therapy | 1 (5) |
| BsAb | 1 (5) |
| Median Lines of Prior Treatment, med (min-max) | 3 (1-4) |
| Median Time between Last Treatment and Progression, days (min-max) | 9 (28-1143) |

## Dose Escalation: (Figure1)

At the time of data cut-off, 6 dose levels ranging from 1,5 to 20 mg/kg were tested in 22 patients and determined safe.

Inclusion in the 16 mg/kg backfill cohort are ongoing.




## Infusions administration:

Median number of doses received 4 (range 2- 29).

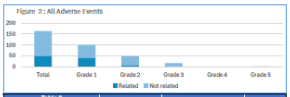
A single moderate and transient infusion reaction was observed among a total of 147 infusions administered

No required dosing action due to AE.

No premedication was administered.

## Safety:

- XON7 at a dose 1.5 to 20 mg/kg was well tolerated.
- NO DLT was observed
- 90% of AEs were grade 1-2 ( Figure 2)
- Most common AEs were pain, asthenia, fever ( Table 2)
- No related Gr ≥ 3 anemia, thrombocytopenia or neutropenia
- No related renal, cardiac or hepatic toxicity.



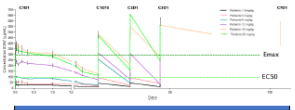

| Table 2 Adverse Events occurring ≥ 2 pat. N (%) | All Gr 1-2 | All Gr 3-4 | Related Gr 1-2 | Related Gr 3-4 | Patients n=22 |
|---|---|---|---|---|---|
| Pain | 22 (13) | 2 (1) | 6 (4) | 0 (0) | 24 (15) |
| Asthenia | 14 (9) | 1 (1) | 8 (5) | 0 (0) | 15 (9) |
| Fever | 8 (5) | 0 (0) | 3 (2) | 0 (0) | 8 (5) |
| Dyspnea | 8 (5) | 1 (1) | 0 (0) | 0 (0) | 8 (4) |
| Anemia | 4 (2) | 1 (1) | 1 (1) | 0 (0) | 5 (3) |
| Cough | 5 (3) | 0 (0) | 0 (0) | 0 (0) | 5 (3) |
| Headache | 5 (3) | 0 (0) | 4 (2) | 0 (0) | 5 (3) |
| Nausea | 5 (3) | 0 (0) | 5 (3) | 0 (0) | 5 (3) |
| Anorexia | 4 (2) | 0 (0) | 1 (1) | 0(0) | 4 (2) |
| Constipation | 3 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (2) |
| Oedema | 3 (2) | 0 (0) | 1 (1) | 0 (0) | 3 (2) |
| Anxiety | 2 (1) | 0 (0) | 0 (0) | 0 (0) | 2 (1) |
| ASAT increased | 2 (1) | 0 (0) | 0 (0) | 0 (0) | 2 (1) |
| Chills | 2 (1) | 0 (0) | 1(1) | 0 (0) | 2 (1) |
| Dry skin | 2 (1) | 0 (0) | 2 (1) | 0 (0) | 2 (1) |
| Pruritus | 2 (1) | 0 (0) | 2 (1) | 0 (0) | 2 (1) |

## Immunogenicity:

No ADA was detected.

## Pharmacokinetics:

Dose-dependent increases in PK exposure from 1.5mg/kg to16mg/kg.
Slight accumulation after repeated doses.
Similar PK profile after 16mg/kg and 20mg/kg.




| Dose | AUC Mean (SD) µg/ml.h-1 | Cmax Mean (SD) µg/ml | Half-life Mean (SD) days |
|---|---|---|---|
| 1.5 mg/kg | 5226 (1423) | 97.0 (7) | 12.5 (2) |
| 3 mg/kg | 10950 (344) | 74.7 (20) | 8.4 (3) |
| 6 mg/kg | 17688 (4355) | 120.8 (23) | 7.6 (3) |
| 12 mg/kg | 39559 (3797) | 249.0 (33) | 9.3 (1) |
| 16 mg/kg | 66466 (11924) | 364.3 (71) | 12.7 (5) |
| 20 mg/kg | 67635 (16877) | 419.1 (88) | 12.1 (2) |

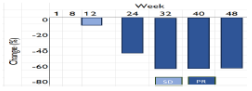
## Anti-tumor activities:

- Preliminary efficacy showed one partial response (colorectal) and five cases of stable disease (colorectal, appendix, pancreatic and adenoid cystic carcinoma)
- Duration of PR : 363 days
- Mean duration of stable disease : 152 days ( ± 108)

### Preliminary Efficacy in Colorectal adenocarcinoma (n=5 patients)

- 1 patient out of 5 had Partial response.

Subject 102-001: 73 y/o male, stage IV, 2 prior lines of therapy, refractory to latest line. RAF/RAS wild type, MSS .1.5 mg/kg




- 2 patients out of 5 had stable disease :

Subject 103-005: 59 y/o female, stage IV, 3 prior lines of therapy, KRAS G12A, BRAF neg, MSS,16mg/kg.

Subject 103-001: 61 y/o male, stage IV, 4 prior lines of therapy KRAS G12D, BRAF neg, MSS, 1.5 mg/kg.

## Conclusions:

- XON7 administered Q2W IV is well tolerated at dose up to 20 mg/ kg
- Preliminary data indicate dose-dependent increases in PK exposure up to 16 mg/kg, and similar PK profile between 16 and 20 mg/kg
- No dose limiting toxicity was observed at doses ranging from 1.5 to 20 mg/kg.
- Early signs of antitumor activity were observed in heavily pretreated patients with metastatic solid tumors. Notably an Objective response rate of 20% and a disease control rate of 60 % in colorectal adenocarcinoma

Trial sponsor : XENOTHERA.

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