Abstract 3067: A first-in-human (FIH) study of ATX-101, a drug targeting proliferating cell nuclear antigen (PCNA), shows a favorable safety profile and disease stabilization in late stage, heavily pre-treated, solid tumor patients

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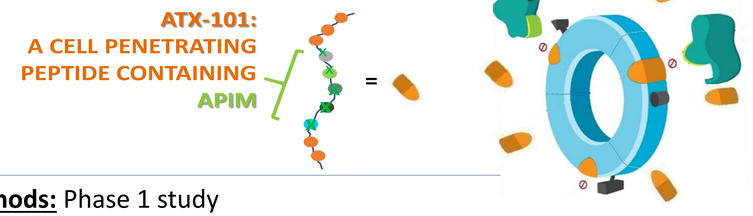
Background: *(Colors in text refer to Figure 1)*

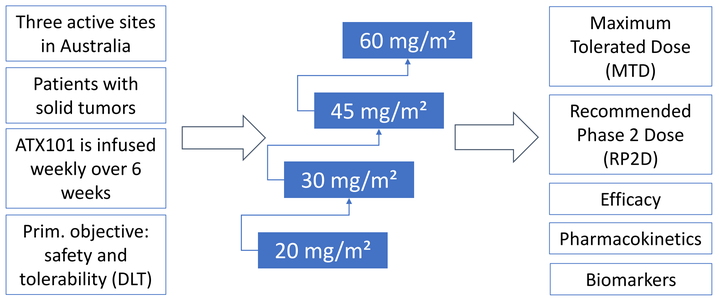
- Proliferating Cell Nuclear Antigen (**PCNA**) is essential for DNA replication and repair and is shown to have cytosolic roles in regulation of cellular signaling, metabolism and immune responses
- **APIM*: a PCNA binding motif** with **high binding strength** (affinity) only during **cellular stress** is found mainly in proteins involved in cellular stress defense mechanisms.
- Cancer and anti-cancer treatments cause cellular stress
- **ATX-101** blocks protein - PCNA interactions in stressed cells (indicated by ⊘ in Figure 1)
- **ATX-101 inhibits** cellular stress responses

Fig. 1: ATX-101 – mode of action



Methods: Phase 1 study

Study ATX101-01: Open label, safety & tolerability study using a common 3+3 design



Study ATX101-02: Long-Term-Follow-Up for patients not progressing after 6 weeks treatment in study -01: continue with same weekly regimen

- 22 patients treated; safety/PK cut-off on 31 Oct 2020 (n=21):
  - Median age 57 [31-73]; 48% female; solid tumors (see Figure 3)
  - Heavily pretreated: median of 3.8 prior systemic treatments [1-9]
  - 95% of patients with progressive disease at study entry
  - 76% of patients refractory to the most recent treatment
  - Standard anti-tumor treatment has been exhausted

- ATX-101 has a *favorable safety profile*
- Mild to moderate *infusion related reactions*, observed in 71% of patients, are not dose dependent
- The *short half-life* in plasma confirms *in vivo* data demonstrating a quick uptake of ATX-101 by cells of all organs
- *Long disease stabilization* in progressive tumors has been observed at all doses levels and may be attributed to ATX-101 activity

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*AlkB homologue 2 PCNA Interacting Motif; ** Infusion related reactions; ***Infusion site reactions

Results: No DLT, no related SAE, no related Grade 3/4/5 AE

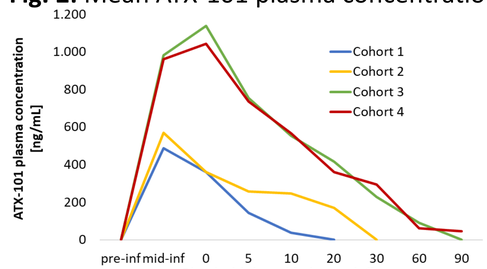
Number of patients with at least one treatment related adverse event:

Severity (CTCAE)	20 mg/m² (n=8)	30 mg/m² (n=3)	45 mg/m² (n=4)	60 mg/m² (n=6)
Grade 1	4 (50%)	3 (100%)	4 (100%)	4 (66.7%)
Grade 2	2 (25%)	1 (33.3%)	3 (75%)	5 (83.3%)
Grade 3	0	0	0	0
Grade 4	0	0	0	0

Treatment related adverse events observed ≥2 times:

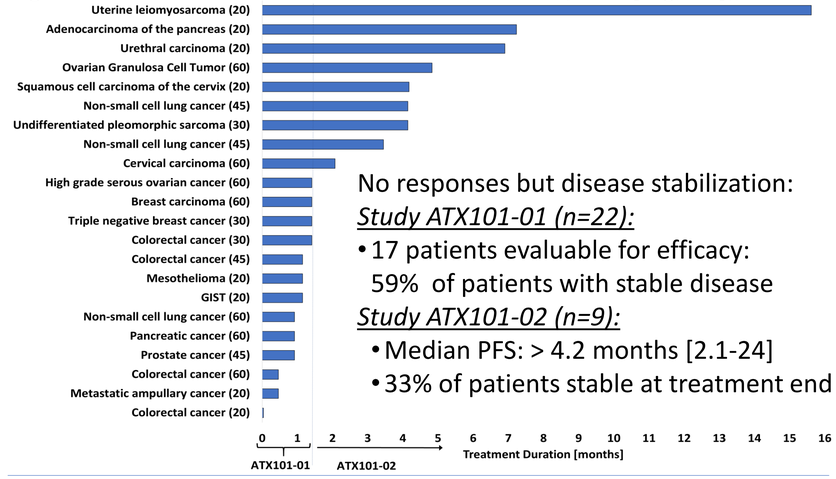
Preferred Term	Grade 1	Grade 2
IRR**	13	14
Fatigue	4	2
ISR***	3	2
Dysgeusia	3	0
Diarrhea	2	0

Fig. 2: Mean ATX-101 plasma concentration per cohort on Day 1



- Dose dependent exposure
- Different infusion times (115-345 min) affected PK profile (c_{max})
- Short half-life
- No signs of accumulation or changes in elimination

Fig. 3: Treatment duration for individual patients (dose [mg/m²]); n=22



No responses but disease stabilization:

Study ATX101-01 (n=22):

- 17 patients evaluable for efficacy: 59% of patients with stable disease

Study ATX101-02 (n=9):

- Median PFS: > 4.2 months [2.1-24]
- 33% of patients stable at treatment end

Future Directions for Research:

- A phase 1b/2a study with ATX-101 plus platinum based therapy in ovarian carcinoma is ready to start (NCT04814875)
- An IST with ATX-101 monotherapy in sarcoma will be supported