Abstract # 3061: A first-in-human phase 1 study in patients with advanced and/or refractory solid malignancies to evaluate the safety of ATOR-1015, a CTLA-4 x OX40 bispecific antibody

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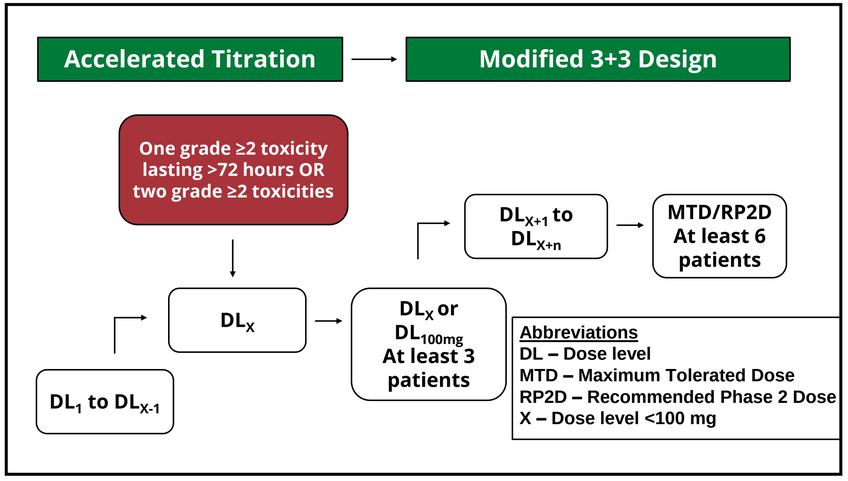
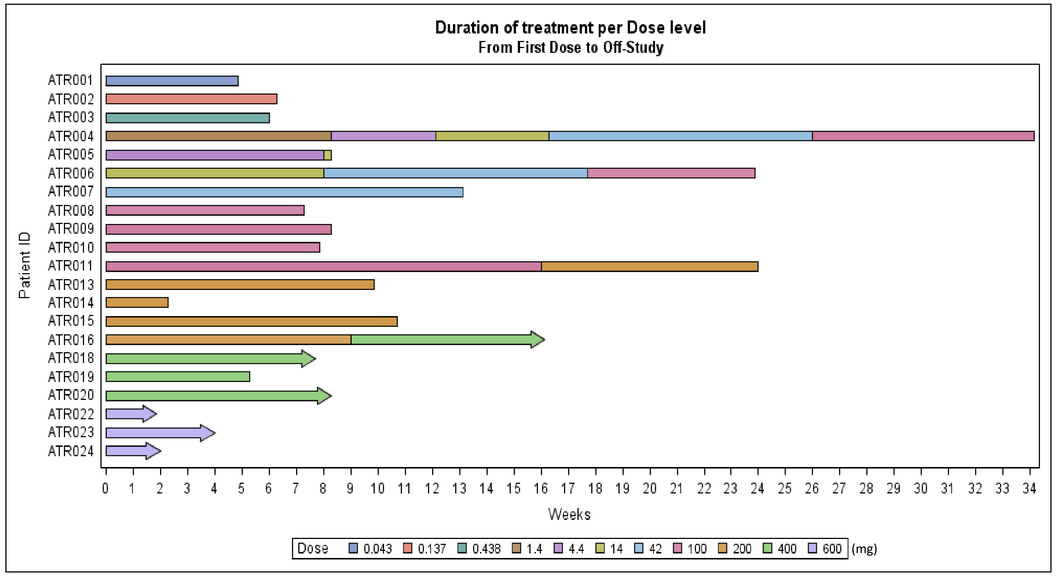
Background:

- ATOR-1015 is a first-in-class tumor localizing CTLA-4 x OX40 bispecific antibody, developed for improved efficacy and tolerability
- CTLA-4, a checkpoint receptor expressed on regulatory T cells and OX40, a co-stimulatory receptor on T cells, are highly upregulated in the tumor environment
- ATOR-1015 induces T-cell activation and depletes regulatory T cells *in vitro*
- ATOR-1015 reduces tumor growth and improves survival in *in vivo* tumor models

Study design:

- A first-in-human dose escalation study of ATOR-1015 dosed intravenously every 2 weeks until confirmed progression, unacceptable toxicity or withdrawal of consent
- Patients with advanced and/or refractory solid malignancies included
- Intra-patient dose escalation is allowed





Results:

- Twenty-one patients have been dosed with ATOR-1015 given as a flat dose from 0.043 mg to 600 mg
- Median age is 54 years (range 40-72)
- Median prior lines of therapy are 5 (1-16)
- Median time on study is 8.5 weeks (range 2-34)
- Adverse events have been reported in 20 of the 21 patients and 11 of the patients have had drug related adverse events
- Preliminary pharmacokinetics data show dose proportional kinetics
- Best response has been stable disease

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Drug related adverse events	Number of patient (%)
Infusion related reaction	7 (33)
Rash Eczema Vitiligo	3 (14.3) 1 (4.8) 1 (4.8)
Cortisol increased Thyroxine free increased	1 (4.8) 1 (4.8)
Chest discomfort Fatigue Pyrexia	1 (4.8) 1 (4.8) 1 (4.8)
Myalgia	1 (4.8)
Abdominal pain	1 (4.8)
Flushing	1 (4.8)

Conclusion:

- ATOR-1015 is well tolerated up to 600 mg as a flat dose
- No dose limiting toxicity has been observed
- No severe immune-related adverse events have been reported
- Dose escalation continues, currently 750 mg of ATOR-1015 is under evaluation
- When MTD or RP2D is established, further clinical development with ATOR-1015 is planned with malignant melanoma being the first indication