A first-in-human, multicenter, open-label, phase 1 study in patients with advanced and/or refractory solid malignancies to evaluate the safety of intravenously administered ATOR-1015

Jeffrey Yachnin[1], Gustav J Ullenhag[2], Ana Carneiro[3], Dorte Nielsen[4], Kristoffer Staal Rohrberg[5], Anne Månsson Kvarnhammar[6], Anna Dahlman[6], Erika Bågeman[6], Camilla Wennersten[6], Charlotte Astrid Russell[6]*;

1) Karolinska University Hospital, Stockholm, Sweden; 2) Uppsala University Hospital, Uppsala, Sweden; 3) Skane University Hospital and Lund University, Lund, Sweden; 4) Herlev and Gentofte Hospital, Herlev, Denmark;
5) University Hospital of Copenhagen Rigshospitalet, Copenhagen, Denmark; 6) Alligator Bioscience AB, Lund, Sweden
*Presenting author crl@alligatorbioscience.com

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Background

ATOR-1015 is a human bispecific IgG1 antibody targeting CTLA-4 and OX40 (CD134).

ATOR-1015 induces activation of cytotoxic T cells and depletes regulatory T cells both *in vitro* and *in vivo* [1].

Treatment with ATOR-1015 reduces tumor growth and improves survival in several tumor models in human OX40 transgenic (hOX40tg) mice cross-reacting with both targets [1].

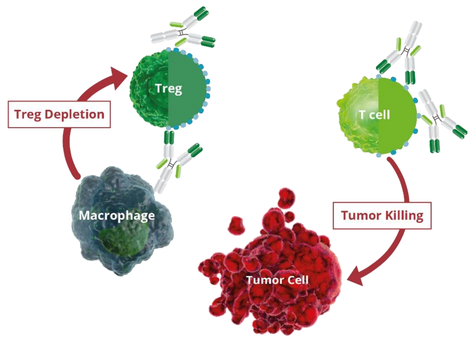
Further, the effects of ATOR-1015 are shown to be directed to the tumor area [1].

The non-clinical safety profile and the pharmacokinetics were established in cynomolgus monkeys and the data were used for the dosing schedule.

1: Månsson Kvarnhammar *et al*. Journal for ImmunoTherapy of Cancer 2019 Apr 11;7(1):103.

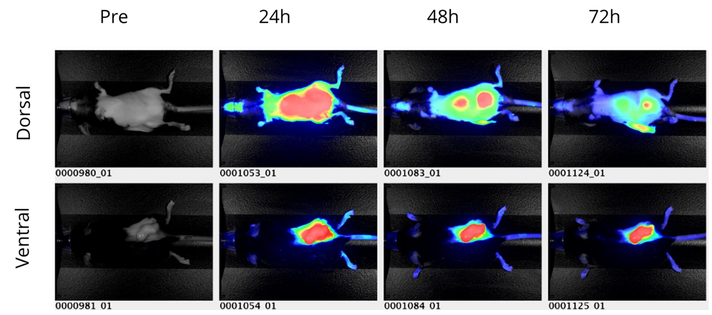
Mode of Action

- CTLA-4 and OX40 are highly expressed on regulatory T cells in the tumor area
- ATOR-1015 activates effector T cells and depletes regulatory T cells
- Dual targeting directs the effect to the tumor area



Tumor Localization

ATOR-1015 is demonstrated to localize to the tumor area in hOX40tg mice with MC38 colon carcinoma.



hOX40tg mice with MC38 tumors were treated intravenously with near infrared-labelled ATOR-1015 on day 17. Tumor targeting was investigated prior to and 24, 48 and 72 h post administration using *in vivo* imaging.

Study

This is a multicenter, open-label, dose escalation study enrolling patients with advanced and/or refractory solid malignancies (NCT03782467).

ATOR-1015 is administered intravenously biweekly as a single agent until confirmed progressive disease, unacceptable toxicity or withdrawal of consent.

The study will start with single patient cohorts until grade 2 toxicities are observed, thereafter the study follows a modified 3+3 design with up to 14 additional patients planned for safety and efficacy evaluation.

First patient was dosed in March 2019.

Up to 53 patients are planned to be enrolled in the study.

Objectives

Primary objective

To assess the safety and tolerability of increasing doses of ATOR-1015 and to determine the dose-limiting toxicities, the maximum tolerated dose, and/or the recommended phase 2 dose.

Secondary objectives

To determine the:

- Pharmacokinetics of ATOR-1015
- Immunogenicity
- Clinical efficacy assessed by response evaluation criteria in solid tumors (iRECIST)

Exploratory objective

To investigate the pharmacodynamic effect of ATOR-1015 on the immune system.

Key Eligibility Criteria

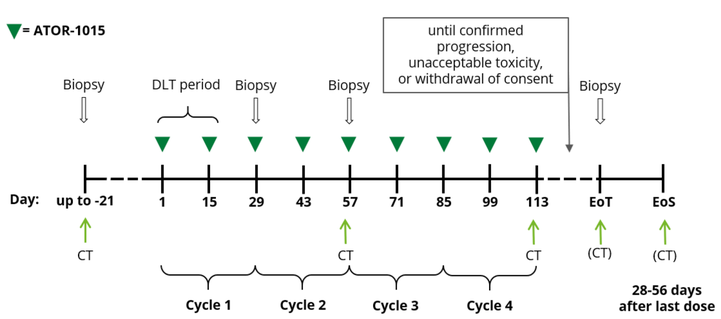
Inclusion

- Diagnosis of advanced and/or refractory solid malignancy
- ECOG performance status of 0 or 1
- Minimum of one measurable tumor lesion (≥10 mm in diameter (≥15 mm for nodal lesions)) per iRECIST
- Acceptable hematological and clinical chemistry laboratory values
- Life expectancy of at least 3 months

Exclusion

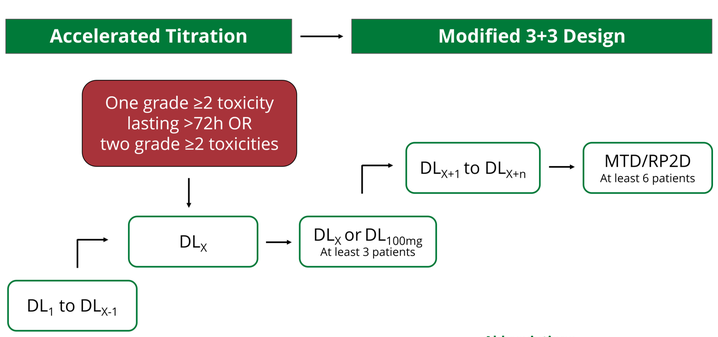
- Organ transplant recipient
- Active autoimmune disorder
- Symptomatic, steroid-dependent or progressive brain metastasis/ metastases within 4 weeks prior to signing the informed consent
- Receiving treatment with systemic immunosuppressant medication
- Other malignancy

Dosage Schedule and Key Assessments



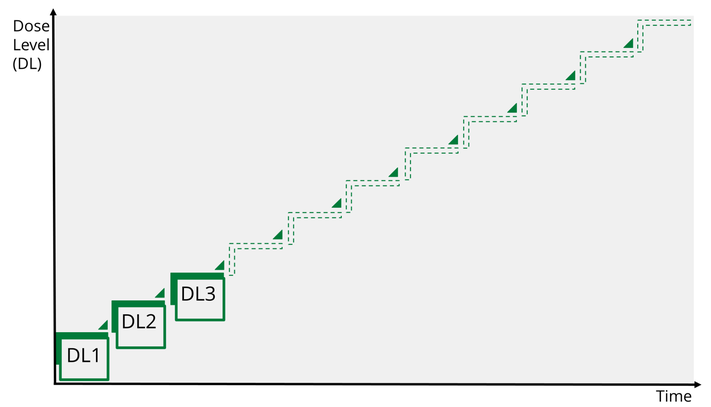
Abbreviations
CT Computed Tomography
DLT Dose - Limiting Toxicity
EoT End of Treatment Visit
EoS End of Study Visit

Dose Escalation Design



Abbreviations
DL Dose Level
H Hours
MTD Maximum Tolerated Dose
RP2D Recommended Phase 2 Dose
X Dose Level <100 mg

Dose Escalation Steps



Enrollment is ongoing, and dose levels 1, 2 and 3 have been evaluated.

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