First-in-human, open-label, multicenter, phase 1 clinical study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of anti-Siglec-15 PYX-106 in subjects with advanced solid tumors

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PYXIS ONCOLOGY

Abstract #: 756

BACKGROUND

Anti-programmed cell death-1 (PD-1) / PD ligand 1 (PD-L1) checkpoint blockade has not been effective for all patients and alternative therapies are needed for those who do not respond to currently approved checkpoint inhibitors. Sialic acid-binding immunoglobulin-like lectin-15 (Siglec-15) is an immunomodulatory pathway independent of PD-1/PD-L1. Siglec-15 is expressed on tumor cells and macrophages and has been shown to play a role in the inhibition of T cells (2). Blocking Siglec-15 overcomes T cell inhibition and limits tumor growth.

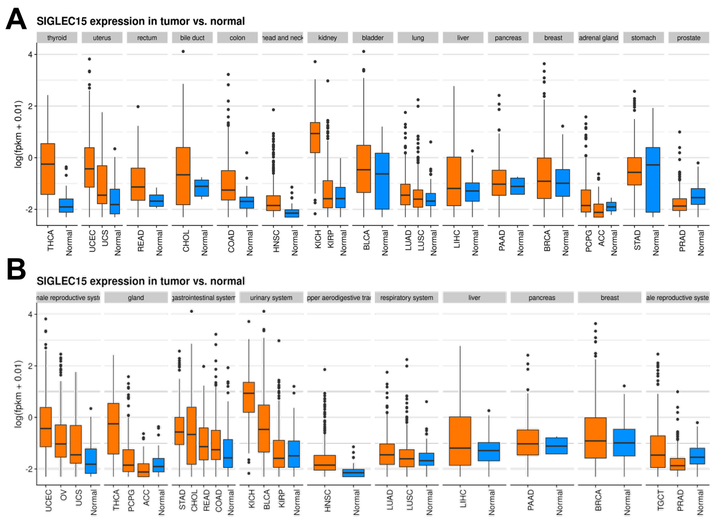


Figure 1: Siglec-15 RNA is highly expressed in tumor tissue (orange bars) compared to normal tissue (blue bars). Comparison of tumor vs. normal expression by A) tissue and B) tissue category. In particular, thyroid and kidney cancers have higher expression of Siglec-15 RNA compared to normal tissues.

RATIONALE

PYX-106 is an investigational, fully human, anti-Siglec-15 immunoglobulin G1 kappa (IgG1k) monoclonal antibody that binds to human Siglec-15 with high affinity and cross-reacts to cynomolgus monkey, rat, and mouse Siglec-15. PYX-106 potently reverses Siglec-15-mediated suppression of CD4+ and CD8+ proliferation and induces IFN-gamma secretion in an ex vivo model. The PYX-106-101 clinical trial is in progress in participants with advanced cancers (NCT05718557).

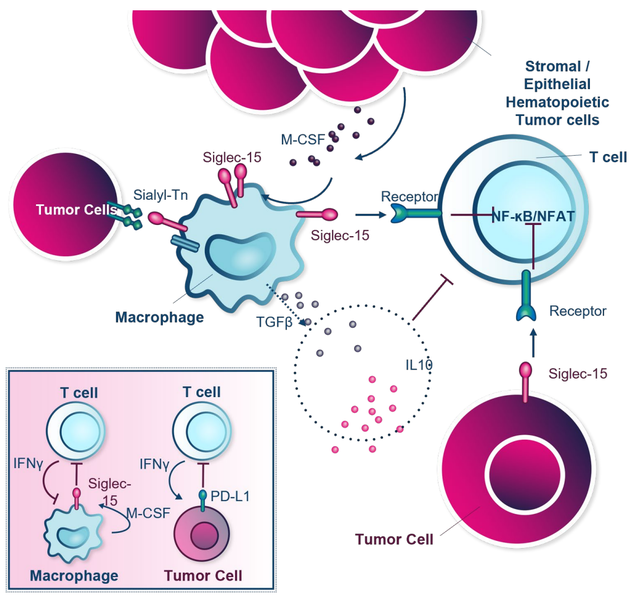


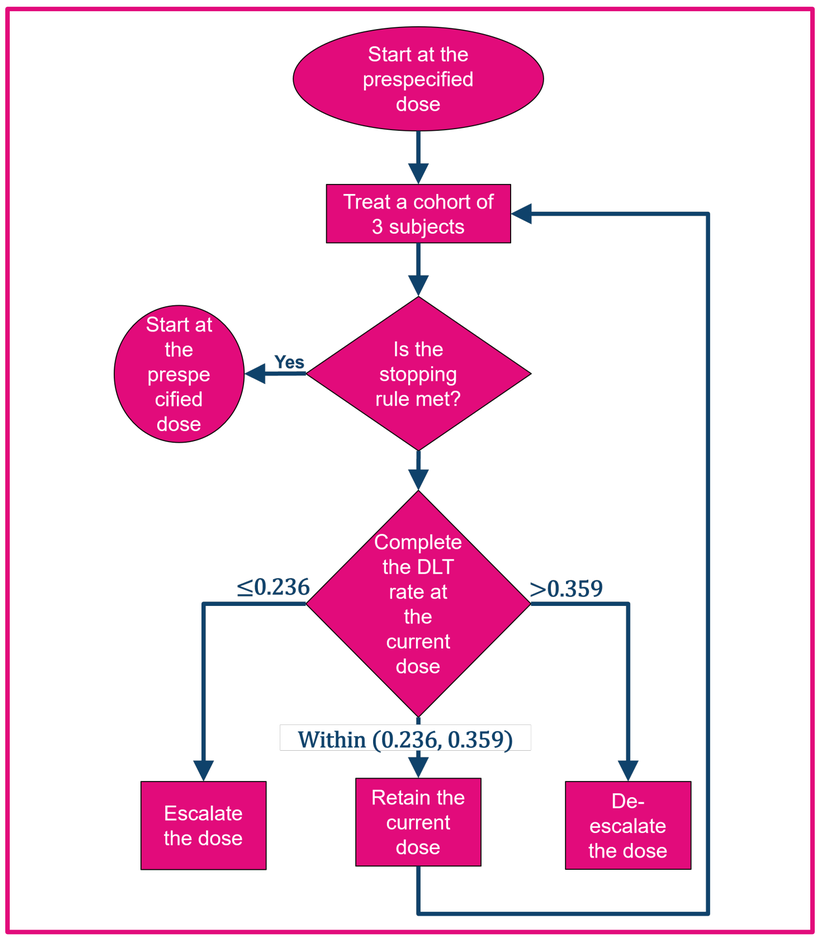
Figure 2: Siglec-15 is expressed on tumor cells and macrophages. PYX-106 blocks the interaction between Siglec-15 and an unknown receptor on T cells relieving suppression of T cell activation and induces tumor cell death [adapted from (3)].

STUDY DESIGN

Design: Phase 1, first-in-human, open-label, multicenter, non-randomized, dose-escalation study

Target Population: Participants with advanced solid tumors who have relapsed, been non-responsive, or have progressed with all available therapies, with a focus on those tumor types known to have expression of sialic acid-binding immunoglobulin-like lectin-15 (Siglec-15)

Sample Size: Up to 45 subjects (including backfill enrollment) will be enrolled into the dose escalation cohorts



INDICATIONS

Non-small cell lung cancer without driver mutations/ translocations	Breast cancer
Cholangiocarcinoma	Endometrial cancer
Bladder cancer	Thyroid cancer
Colorectal cancer	Kidney cancer
Head and Neck Squamous Cell cancer	

OBJECTIVES

Primary Objective:

- To determine the recommended dose(s) of PYX-106 in subjects with relapsed/refractory solid tumors

Secondary Objectives:

- To characterize the PK profile of PYX-106 as a single agent
- To evaluate the preliminary anti-tumor activity of treatment with PYX-106 at the recommended dose(s) of PYX-106

Exploratory Objectives:

- To explore predictive and pharmacodynamic biomarkers of response to PYX-106

ENDPOINTS

Primary Endpoints:

- Dose Limiting Toxicity rate
- Incidence of adverse events characterized overall and by type, seriousness, relationship to study treatment, timing, and severity graded according to the NCI-CTCAE Version 5.0
- Change in clinical laboratory parameters, vital signs, and ECG parameters

Secondary Endpoints:

- Single-dose and multiple-dose PK parameters (such as C_{max}, t_{max}, AUC_{0-t}, AUC_T, $AUC_{0-\infty}$, and $t_{½}$) for antibody and/or relevant metabolites
- Overall Response Rate
- Duration of Response
- Progression Free Survival
- Disease Control Rate (defined as Complete Response, Partial Response, or stable disease)
- Time to response (defined as the time from the first dose of PYX-106 to the time of response [CR/PR] first observed)
- Overall Survival

Exploratory endpoints:

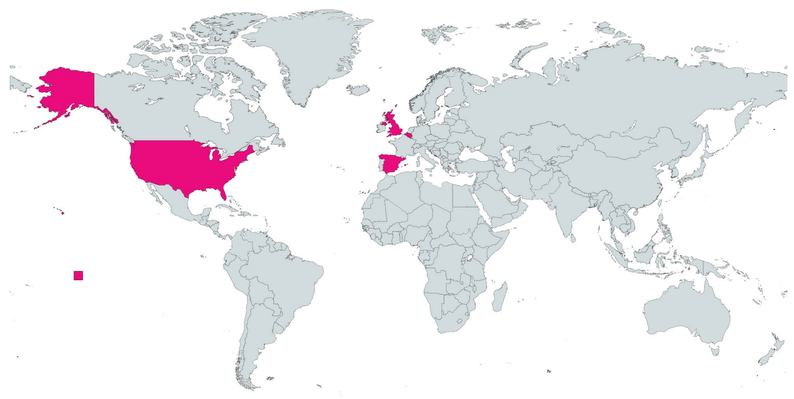
- Evaluate predictive and pharmacodynamic biomarkers of response to PYX-106

STUDY PROGRESS

Enrollment opened:

- February 2023

Up to 19 sites planned to be activated in the Unites States, Spain, Belgium and the United Kingdom



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