Abstract

ICOS Agonist JTX-2011 Background

• JTX-2011 is a humanized IgG1x agonist monoclonal antibody that specifically binds to the inducible CD-39 Stimulator of T Cells (ICOS) and is designed to generate an anti-tumor immune response through stimulation of T effector cells and selective reduction of T regulatory cells within tumors.

• JTX-2011 has shown preclinical anti-tumor effects both as a single agent and in combination with anti-PD-1 antibodies. In preclinical models, single agent efficacy correlated with percent of ICOS expressing T cells in tumors. An ICOS IHC assay was used to identify human tumor types with the highest levels of ICOS expressing T cells.

• Phase 1/2 ICONIC: Phase 1/2 Trial of ICOS Agonist JTX-2011 Alone and in Combination with Nivolumab (nivo) Background: JTX-2011 is an agonist monoclonal antibody that targets ICOS, Inducible CD-39 Stimulator of T Cells. A dual mechanism of action is intended to induce proliferation and stimulation of CD4+ T effector cells and selectively deplete intratumoral regulatory cells. JTX-2011 has shown preclinical anti-tumor effects both as a single agent and in combination with anti-PD-1 antibodies, with single agent efficacy correlated with percent of ICOS expressing T cells in tumors. An ICOS IHC assay was used to identify human tumor types with the highest levels of ICOS expressing T cells.

• Major Exclusion Criteria:
  - Maximal tolerated dose (MTD) and recommended Phase 2 dose,
  - Evaluate preliminary efficacy.

• Methods: ICONIC is a first-in-human Phase I/II, open-label, adaptive clinical study of JTX-2011 alone or in combination with a fixed-dose nivo in subjects with advanced solid tumors. The study is designed to assess safety and tolerability, determine the recommended Phase 2 dose, and evaluate preliminary efficacy.

• Part A: 4+3 dose escalation of JTX-2011, with safety/PK/PD expansion cohorts at 2 or more dose levels.

• Part B: 4+3 dose escalation of JTX-2011 in combination with nivo, with Safety/PK/PD expansion cohorts at 2 or more dose levels.

• Part C: All JTX-2011 cohorts in tumors expected to have lower levels of ICOS expressing T cells (e.g., small cell lung cancer [SCLC], head and neck squamous cancer [HNSCC], and others), with ICOS-enrichment by IHC.

• Part D: JTX-2011 + nivo cohorts in tumors expected to have higher levels of ICOS expressing T cells (NSCLC, HNSCC, triple-negative breast cancer [TNBC], melanoma, gastric, and others), with ICOS-enrichment by IHC.

• Major Inclusion Criteria:
  - Confirmed cancer that is recurrent, metastatic, or persistent after at least one line of therapy and with no further standard treatment options.
  - Part A/B: available and consent to provide archival tumor tissue.
  - Part C/D: available and consent to provide archival tumor tissue, with a lesion that can be biopsied at acceptable clinical risk (as judged by the investigator), and agree to a fresh biopsy before starting study treatment.

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- JTX-2011 has shown preclinical anti-tumor effects both as a single agent and in combination with anti-PD-1 antibodies.

- In preclinical models, single agent efficacy correlated with percent of ICOS expressing T cells in tumors.

- JTX-2011 is being developed in patients with advanced solid tumors who have no standard therapeutic options.

- An ICOS IHC assay was used to identify human tumor types with the highest levels of ICOS expressing T cells.

- Digital Readout

Inclusion and Exclusion Criteria

General Inclusion Criteria:

- Willing and able to participate and comply with all trial requirements and provide informed consent
- Have confirmed cancer that is recurrent, metastatic or persistent after at least one line of therapy and with no further standard treatment options
- Male or female ≥ 18 years of age
- ECOG Performance Status: 0-1
- Predicted life expectancy of ≥ 3 months
- Archival tumor tissue required for all subjects

Part A/B Dose Escalation Criteria:

- Any advanced, non-hematological, extramedullary malignancy with disease progression after treatment with all available therapies known to confer clinical benefit
- May have evaluable but non-measurable disease

Parts A and B PK/PD Expansion Criteria:

- Must have a tumor lesion that can be biopsied at acceptable risk and must agree to both a fresh biopsy between screening and C1D1 and a second biopsy after completion of two cycles of study treatment

Part C and D Criteria:

- All subjects must have a tumor lesion that can be biopsied at acceptable risk and must agree to a fresh biopsy between screening and C1D1

Major Exclusion Criteria:

- Refusal standard therapy
- History of intolerance, hypersensitivity, or treatment discontinuation due to severe adverse events on prior immunotherapy
- Immunodeficiency
- Active or prior history of autoimmune disease
- Symptomatic or uncontrolled brain metastases, leptomeningeal disease, or spinal cord compression

Clinical Sites

1. Stanford University School of Medicine
2. Sarah Cannon Research Institute at HealthONE
3. Yale New Haven Hospital
4. The University of Chicago Medicine Comprehensive Cancer Center
5. Massachusetts General Hospital Cancer Center
6. Washington University School of Medicine
7. Georgetown Lombardi Comprehensive Cancer Center
8. University of Washington
9. Sarah Cannon Research Institute at TriStar Health
10. South Texas Accelerated Research Therapeutics, LLC
11. The University of Texas–MD Anderson Cancer Center
12. Memorial Sloan-Kettering Cancer Center
13. Massachusetts General Hospital - Boston, MA
14. Yale Cancer Center - New Haven, CT
15. MD Anderson Cancer Center - Houston, TX