ABSTRACT

ICOS is a co-stimulatory molecule upregulated on activated T cells. JTX-2011 (vopratelimab) is an ICOS agonist antibody intended to stimulate primed CD4 T effector cells. Vopratelimab was assessed in pts with advanced solid tumors as monotherapy (mon) and combined (combo) with nivolumab (nv) in the Phase 1/2 ICOS oncologic (NCT02994282). Peripheral T cell phenotyping in ICORS documented emergence of an ICOS hi (high) subset of CD4 T cells associated with tumor reductions in mon and combo pts. Emergence of this peripheral ICOS hi CD4 T cell population is associated with frequent changes in target lesion. PD-1/L1 inhibitor monotherapy does not induce the T cell population.

Background: ICOS is a co-stimulatory molecule upregulated on activated T cells. JTX-2011 (vopratelimab) is an ICOS agonist antibody intended to stimulate primed CD4 T effector cells. Vopratelimab was assessed in pts with advanced solid tumors as monotherapy (mon) and combined (combo) with nivolumab (nv) in the Phase 1/2 ICOS oncologic (NCT02994282). Peripheral T cell phenotyping in ICORS documented emergence of an ICOS high (hi) subset of CD4 T cells associated with tumor reductions in mon and combo pts. Emergence of this peripheral ICOS hi CD4 T cell population is associated with frequent changes in target lesion. PD-1/L1 inhibitor monotherapy does not induce the T cell population.

Methods: Ad hoc flow cytometry phenotyping on PBMCs from a subset of pts with evaluable samples (n=5) was performed retrospectively in early 2018 in ongoing pts, then prospectively on newly enrolled pts. Clinical characteristics, demographics, and outcomes were included in exploratory statistical analyses. Phenotyping was also done on samples from pts treated with PD-1/L1 inhibitor (PD-1/L1 inhibitor) in a subset outside of ICRS, consisting of 30% patients with metastatic melanoma (MM), and 70% in metastatic renal cell carcinoma (mRCC).

Results: Available samples from 55 subjects were analyzed longitudinally for the presence of a treatment emergent ICOS hi T cell population. Clinical characteristics and outcomes of the patients who were assessed are presented in Table 1. Emergence of ICOS hi CD4 T effector cells (cell Pop) subject to KEGWe was observed in all pts with >30% target lesion reduction by investigator assessment (mon and combo therapy; n=40). Emergence was seen in pts with mRCC (9/34, 26%) and MM (4/10, 40%). The median number of cycles was 3 (range 1-14) for mRCC and 7 (range 2-23) for MM. Patients with stable disease progression ICOS hi CD4 T cells were not seen in ICORS oncologic pts with target lesion reduction by investigator assessment (n=6).

Emergence of ICOS hi CD4 T cells appears to correlate with improved PFS and OS.

CONCLUSION

Emergence of a distinct and persistent population of ICOS hi peripheral CD4 T cells is associated with improved survival with vopratelimab monotherapy and combination therapy, with improved PFS (median 6.2 mo for patients with ICOS hi CD4 T cells vs 0.8 mo for patients with only CD4 T cells and patients on study, respectively) and improved survival for patients with ICOS hi CD4 T cells and alive for all ICORS patients. The emergence and persistence of ICOS hi CD4 T cells is associated with tumor reductions in subjects treated with the ICOS agonist antibody JTX-2011.

Additional analyses are needed to confirm these findings and to understand the mechanisms underlying these responses.

REFERENCES


Figure 1: Emergence and Persistence of ICOS hi CD4 T Cells Correlates with Clinical Response in Subjects Treated with Vopratelimab.

Figure 2: ICOS hi CD4 T Cells Emerge Due to JTX-2011, not an Anti-PD-1/L1.

Figure 3: Gastric Cancer Patient, 24 months later.

Figure 4: Six Month Median PFS for Patients with ICOS hi T Cell Emergence.

Figure 5: Median OS for Patients with ICOS hi T Cell Emergence Not Yet Reached.

Figure 6: Target Lesion Response Association with Emergence of an ICOS hi CD4 T Cell Population in the Peripheral Blood: No Apparent Trend with Common Predictive Markers.

Table 1: Baseline Characteristics in ICORS Patients with Emergence of ICOS hi vs Persistent ICOS hi CD4 T Cells

See Abstract #4053: Genetic and molecular profiling of ICOS hi CD4 T cells demonstrates clonal expansion of TH1 effector cells following vopratelimab (JTX-2011) treatment in subjects with solid tumors.