Genomics-based studies of gastric tumors identify ICOS as potential target for therapeutic intervention

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ABSTRACT & BACKGROUND

ICOS is a co-stimulatory molecule that is expressed on activated T cells and also by other immune cells such as regulatory T lymphocytes (Tregs). In the context of cancer, ICOS is being studied as a potential target for therapeutic intervention. Jounce Therapeutics has acquired preclinical data and clinical data that identified ICOS as a potentially key molecule in adenocarcinoma tumors with high prevalence in both EBV+ and MSI-H tumors as well as a dynamic range of ICOS expression across gastric cancers. This analysis shows that tumor reduction in animals occurs only when a certain percentage of ICOS-expressing immune cells is present, identifying ICOS as a key target for further investigation.

RESULTS

ICOS RNA expression is independent of gastric or esophageal cancer location. ICOS RNA expression was not associated with location in the digestive tract.

ABSTRACT #1

Response of esophageal tumors (beadlet) with an ICOS agonist, compared to ICOS expression in esophageal tumors from TCGA data. ICOS expression in esophageal tumors is more correlated with PD-L1 expression. Within gastric cancer, ICOS is still frequently expressed in PD-L1 low tumors, though the proportion of ICOS tumors in PD-L1 high tumors was lower in gastric cancer than in esophageal cancer. This suggests that the ICOS agonist may have a different effect in gastric cancer compared to esophageal cancer.

ABSTRACT #2

Exploratory biomarker assessment in ICONIC

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SUMMARY

ICOS is highly expressed in gastric and esophageal cancers. Supporting these findings are indications that ICOS expression positively correlates with the ICOS agonist antibody JTX-2011. ICOS expression is unrelated to tumor location within the digestive tract, but is related to tumor subtype and genomic alterations associated with gastric cancer and esophageal cancer.

REFERENCES


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JTX-2011 ICONIC Trial

Gastric cancer cohorts are included in the JTX-2011 ICONIC trial in level 1 exploratory biomarker assessment.

- Gastric cancer patients have been enrolled in level 1, as both single-agent and combination arms of the trial.

Figure 1: Monotherapy response is related to percentage of ICOS-expressing immune cells in syngeneic tumor models

Figure 2: Gastric cancer shows ICOS RNA expression, with a range of expression observed at the protein level

Figure 3: Protein levels of ICOS can be approximated by RNA expression in gastric and esophageal tumors from TCGA

Figure 4: ICOS RNA expression is independent of gastric or esophageal cancer location

Figure 5: Subtypes of gastric cancer are enriched for higher ICOS RNA expression

Figure 6: Co-expression of ICOS RNA with immunological, microenvironment, and tumor-intrinsic markers

Figure 7: Identification of PD-L1 low, ICOS high patients

Figure 8: Integrative analysis reveals genomic alterations associated with ICOS RNA expression

Figure 9: Kaplan-Meier survival analysis for gastric cancer patients receiving JTX-2011 in ICONIC trial

Figure 10: Assays for immune markers in ICONIC trial