Anti-CCR8 Antibody CHS-114 (SRF114) Depletes Tumor-Infiltrating Regulatory T Cells in Dissected Tumor Infiltrates from Patients with Head and Neck Squamous Cell Carcinoma


Therapy Oncology (invited by Coherus Biosciences, Cambridge, MA, USA; Coherus Biosciences, Redwood City, CA, USA)

Background

- Dose-dependent activation of myeloid cells in response to CHS-114 (SRF114) treatment leads to increased expression of mPD-L1 in the tumor microenvironment.
- Anti-CCR8 and anti-PD-1 combination treatment improves overall survival in a checkpoint inhibitor-resistant HNSCC mouse model.
- In dissected HNSCC tumors, CHS-114 (SRF114) activates NK cells and specifically induces cytotoxicity against tumor-infiltrating Tregs.
- The mechanism of action is demonstrated in humanized mice: CHS-114 (SRF114) depletes human CRCB Tregs in vivo, resulting in the expansion of CD8+ T cells and activation of murine myeloid cells.

Conclusions

- CCRB expression is highly enriched within the TME and predominantly expressed on intratumoral Treg cells.
- CCRB+ Tregs are abundant in HNSCC tumors, which exhibit an activated phenotype, and their frequency correlates with PD-L1 expression in CRCB.
- In dissected HNSCC tumors, CHS-114 (SRF114) activates NK cells and specifically induces cytotoxicity against tumor-infiltrating Tregs.
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Anti-CCR8 and Anti-PD-1 Combination Treatment Enhances Overall Survival and Promotes Expansion of Effective T Cells in CRCB Tumor Cell Lines

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Representative images of mPD-L1 IHC at 10x.

Levels of CCRB- Treg cells are more abundant in HNSCC samples that express PD-L1, but do not appear to correlate with disease stage, disease-free status or disease severity. Anti-CCR8 and anti-PD-1 combination treatment leads to increased expression of mPD-L1 in the tumor microenvironment.

Dose-Dependent Deposition of CCRB Tregs by CHS-114 (SRF114) Treg cells, decreased detectable CCRB expression, and increased CD8+ Tconv frequencies, and decreased PD-L1 expression in CRCB Tregs. CHS-114 (SRF114) treatment leads to increased expression of mPD-L1 in the tumor microenvironment.

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