Rosnilimab binds to a membrane-proximal epitope of PD-L1, distinct from the binding epitope of PD-L1 and the membrane-distal binding epitope of reference 1.

**BACKGROUND/PURPOSE**

- Programmed cell death protein 1 (PD-1), a T cell checkpoint receptor, functions to down regulate activated T cells by inducing a negative signaling pathway when engaged with its ligand PD-L1.
- PD-1 expressing T cells are elevated in the synovium and in the periphery, and PD-L1+ T cells. Reference antibody 1 reduced PD-L1+ T cells by 68.5%. Isotype control did not mediate any depletion.

**METHODS**

- Rosnilimab, a PD-1 agonist, IgG1 isotype monoclonal antibody, mimics the function of PD-L1 by inducing negative signaling on activated T cells resulting in reduction of T cell proliferation and reduction in inflammatory T cell activation (Figure 1).
- Binding to a membrane-proximal region of suppressive receptors such as PD-L1, together with FC receptor engagement on an opposing cell, can contribute to tight immune synapse formation between an immune cell and an antigen presenting cell. This has been proposed to improve potency.
- Activation of agonistic signaling by excluding activating phosphatases from the immune synapse and promoting receptor clustering.
- Optimized activation: induces negative signaling on activated T cells resulting in reduction of T cell proliferation.
- Membrane proximal regions of suppressive receptors, together with Fc interactions with receptors on opposing cells, can contribute to PD-L1 agonist activity.

**REFERENCE**

- 1. Luu, et al. ACR2023 poster 0455

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**REFERENCES**