

# Regulating dendritic cells to promote mature tertiary lymphoid structures and enhance anti-tumor immunity

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## Abstract

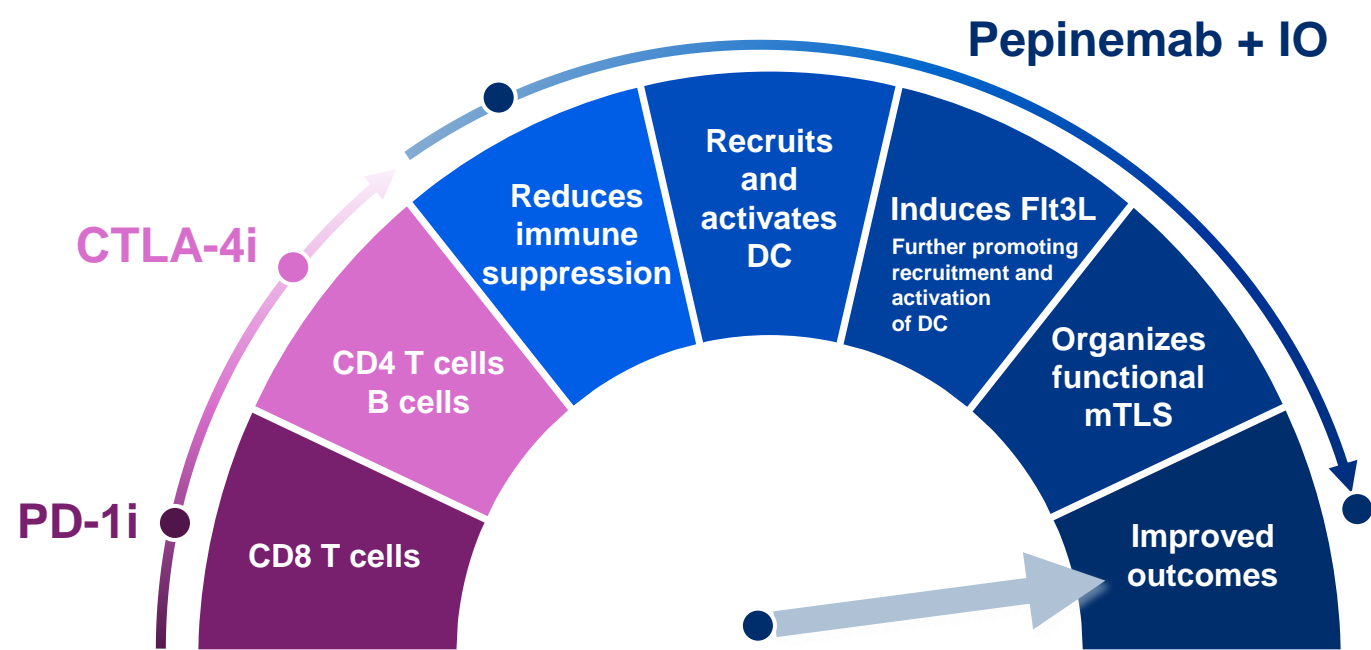
Mature tertiary lymphoid structures (TLS) characterized by the presence of germinal centers are strong predictors of response to immunotherapy. DCs play critical and decisive roles in determining the outcome of the immune responses in the TME and within TLS. Therefore, strategies to recruit and activate DC have the potential to induce TLS and enhance response to immunotherapy.

Pepinemab represents a novel strategy to boost dendritic cell infiltration, activation, and organization of functional TLS to overcome limitations of immune checkpoint therapies. When combined with ICI, pepinemab induced de novo formation of TLS that correlated with clinical benefit, even in poorly immunogenic tumors that do not respond well to ICI, including HPV-negative and PD-L1 low HNSCC. When combined with modalities to further expand DC, SEMA4D blocking antibodies inhibited tumor growth in preclinical models, including in ICI-resistant models.

## Objectives

Based on clinical biomarker data highlighting the contribution of DC to clinical benefit, we hypothesize that the therapeutic effects of pepinemab could be further enhanced by increasing the population of DC available in the TME.

## Conclusions



The combination of pepinemab with immune checkpoint inhibitors (IO) has shown promising results in improving treatment outcomes in certain cancers, particularly in overcoming resistance mechanisms associated with immune-oncology therapies.

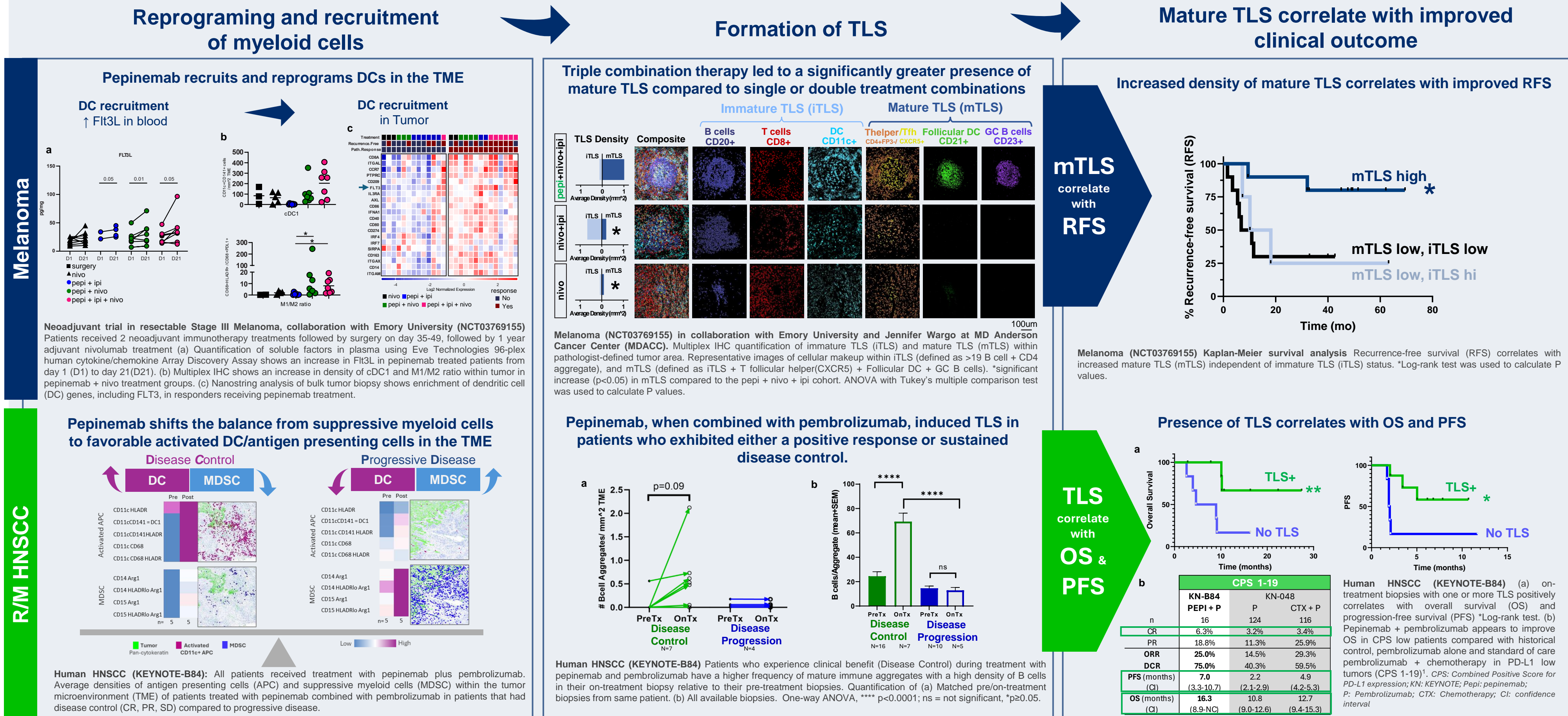
Immune Checkpoint Inhibitors (ICI) increase infiltration of B and T lymphocytes in TME.

Pepinemab induces Flt3L and further promotes recruitment and activation of DC, B cells and T cells.

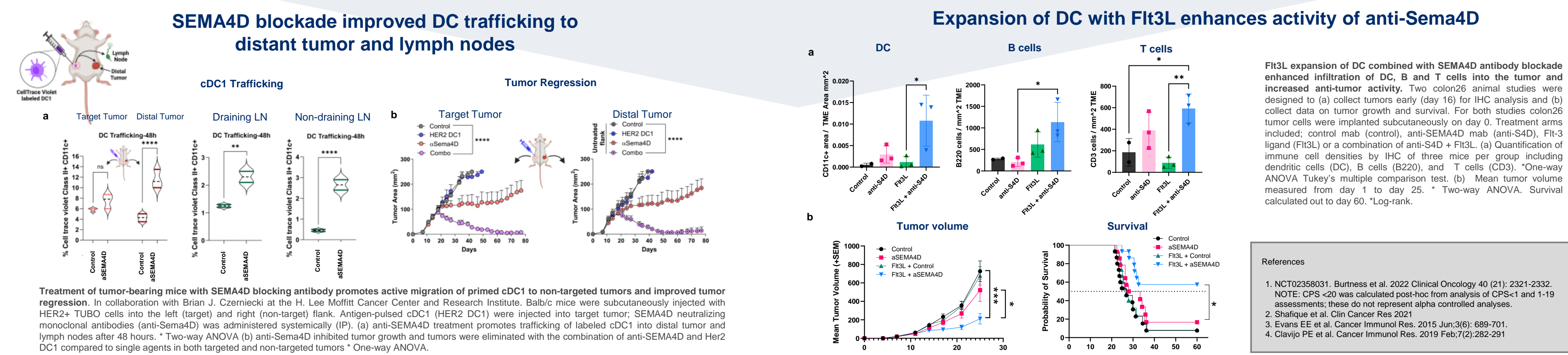
Pepinemab promotes the development of mature TLS by enhancing the infiltration and organization of CD21+ Follicular DC, CD23+ Germinal Center (GC) B cells, and CXCR5+ T follicular Helper Cells (Tfh).

The presence of mature TLS correlates with extended Recurrence Free Survival (RFS) in the neoadjuvant melanoma setting and with Overall Survival (OS) in Recurrent/Metastatic HNSCC. Study of HNSCC in the neoadjuvant setting is in progress.

## Clinical Experience: pepinemab promotes activated DC to infiltrate tumor and organize TLS



## Pre-clinical animal studies: DC expansion to complement pepinemab mechanism of action



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References

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