



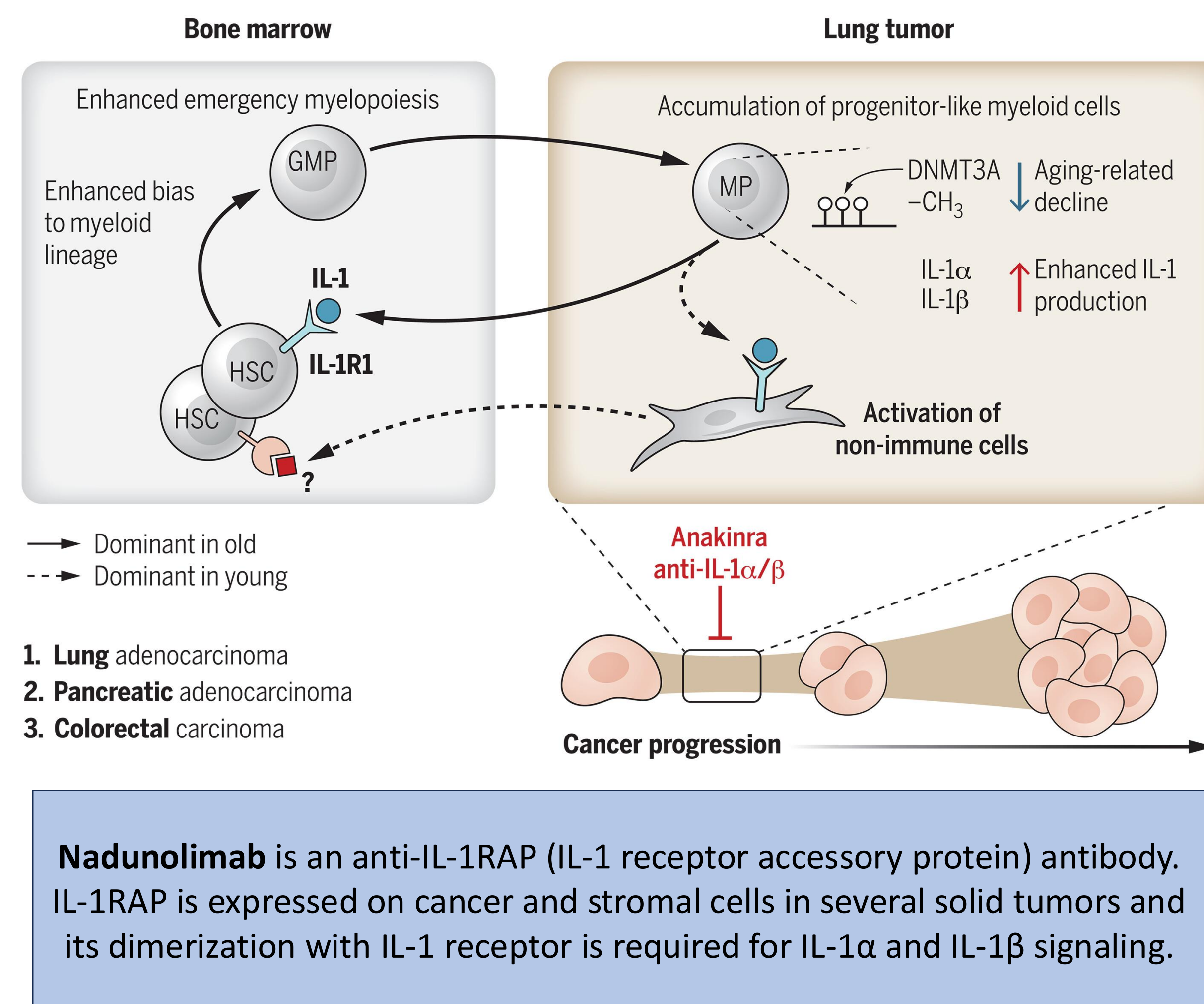
A non-randomized Phase 2 trial of nadunolimab in patients with a smoking history and high-risk lung nodules

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BACKGROUND

- No intervention currently exists to prevent progression of screen-identified high-risk pulmonary nodules to lung cancer.
- Pre-clinical models have shown that IL-1 α and IL-1 β drive emergency myelopoiesis, generating an immunosuppressive, myeloid-predominant microenvironment that permits early lung tumor growth.
- Early antagonism of IL-1 α and IL-1 β in preclinical models delayed progression to invasive lung cancer.
- Secondary analysis of the CANTOS trial demonstrated reduced lung cancer incidence among patients treated with the IL-1 β inhibitor canakinumab.
- Preliminary results from the Can-Prevent-Lung Trial observed shrinkage or slower growth trajectory of high-risk nodules in most patients treated with canakinumab.



METHODS

Study Design

- Phase 2, open-label, single-arm trial of nadunolimab in patients with high-risk lung nodules
- Simon's optimal two-stage design (Stage 1: 20 patients)

Eligibility

- Current smokers or ≥ 20 pack-year smoking history
- Multifocal part-solid nodules (≥ 2 lesions; ≥ 1 with a solid component < 9 mm)
- Documented progression on ≥ 1 follow-up CT
- Not eligible for surgical intervention at enrollment

Intervention

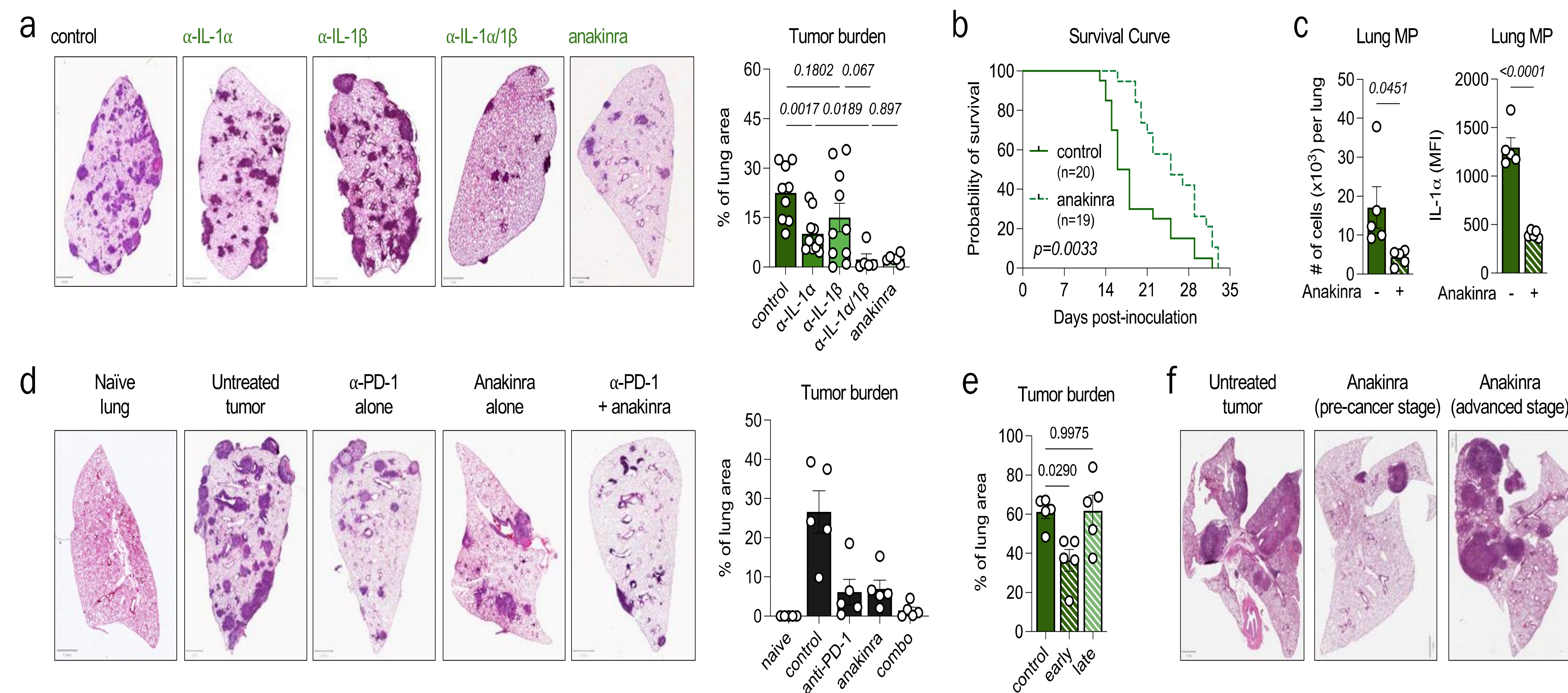
- Nadunolimab 10 mg/kg IV every 3 weeks $\times$ 4 doses

Endpoints

- Primary:** Response rate ($> 20\%$ radiologic regression in ≥ 1 nodule at 3 months)
- Secondary:** progression-free survival; incidence of grade ≥ 2 treatment-related AEs (CTCAE v5)

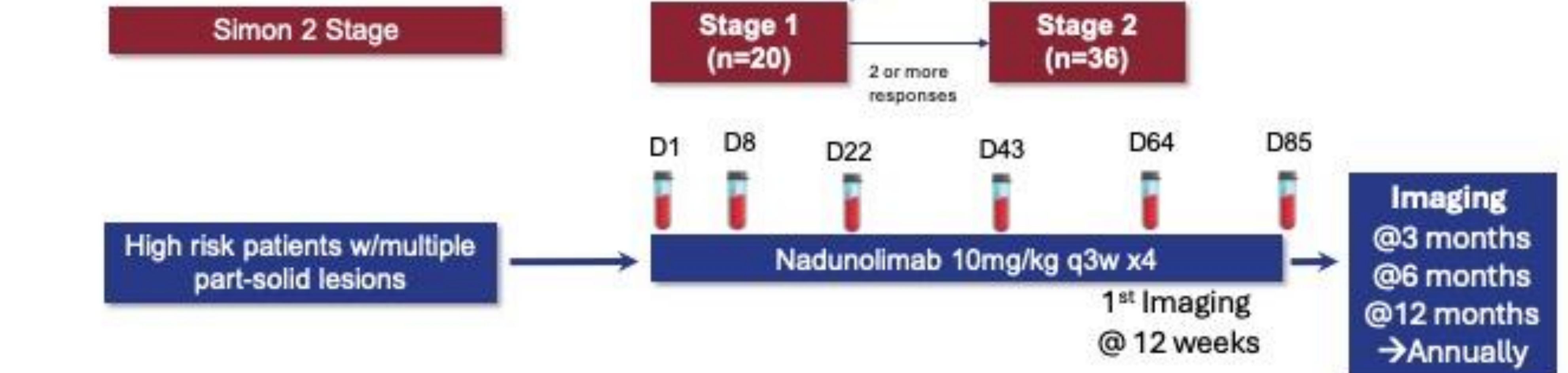
Assessments

- Serial blood draws for immunodynamic profiling (cytokines, proteomics, transcriptomics)



Early anakinra during tumor initiation deters progression.

- Tumor burden in mice either treated with neutralizing antibodies against IL-1 α , IL-1 β , both, or anakinra.
- Kaplan-Meier survival curve of control and anakinra-treated mice.
- Abundance of lung MPs (left) and their production of IL-1 α in control and anakinra-treated mice.
- Tumor burden in naïve mice or mice either treated with anakinra, PD-1 blocking antibody, or both.
- /(f) Tumor burden in mice either treated with anakinra early during tumor initiation or during late-stage progression in (e) the orthotopic and (f) GEMM settings.



ACKNOWLEDGMENTS/ REFERENCES

Park et al, Science 2024, LaMerche et al, Nature 2024, Zhang et al JTO, 2023.

