INTEGRATING IMMUNOTHERAPY INTO LYMPHOMA

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Disclosures

Ronald Levy, MD, has affiliations with Abpro, Apexigen, BeiGene, Checkmate, Corvus, Dragonfly, Five Prime, 47 Inc., Gigagen, Immune Design, Innate Pharma, Nohla, Nurix, Sutro, Teniobio, Viracta (*Consulting Fees*); BMS, Dynavax, Pfizer, Pharmacyclics (*Contracted Research*)

Note:

I will discuss as yet unapproved or off label uses of various immunotherapies

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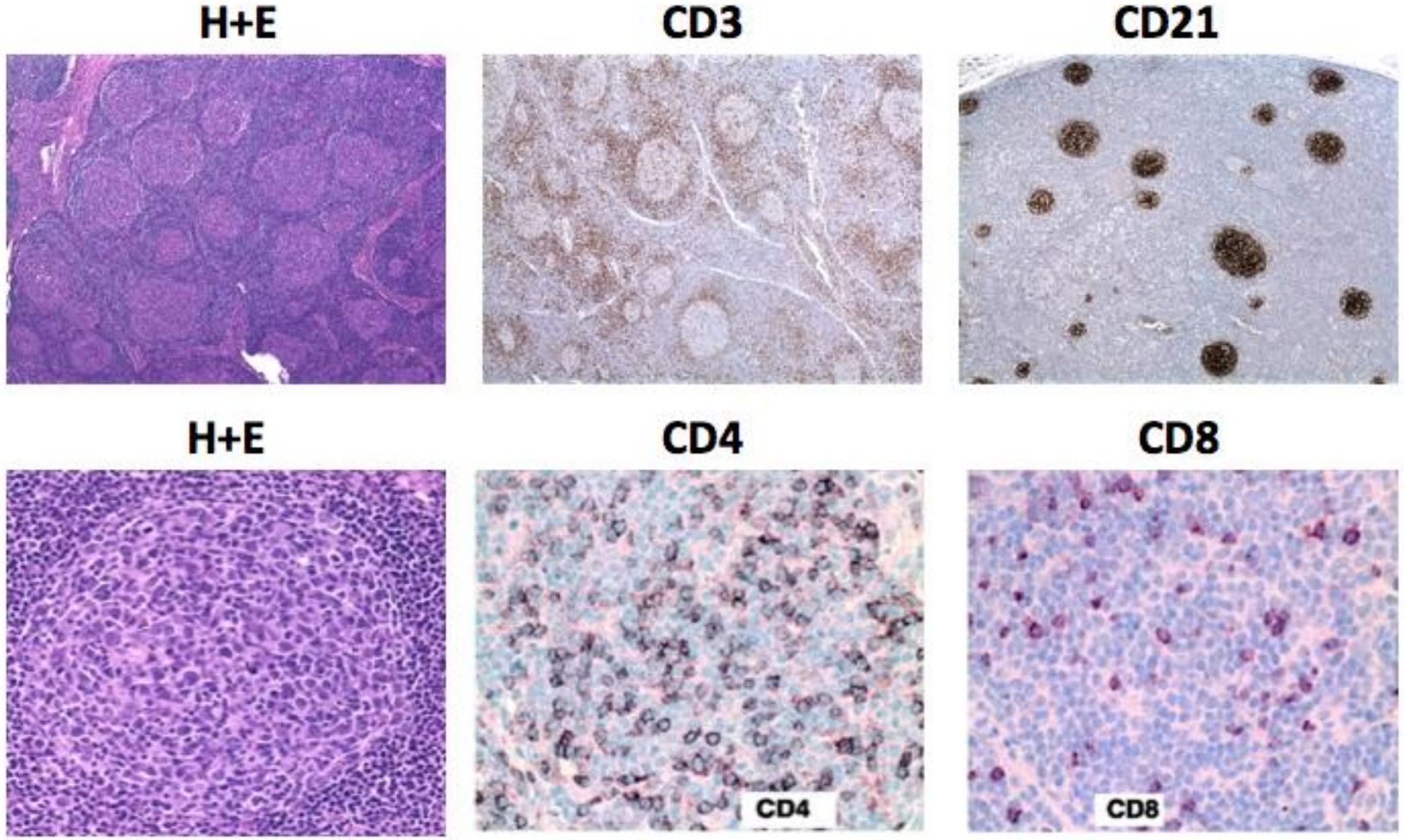
Immune Cells are Prevalent at Sites of Lymphoma but Do Not Eradicate It



Stephen Ansell

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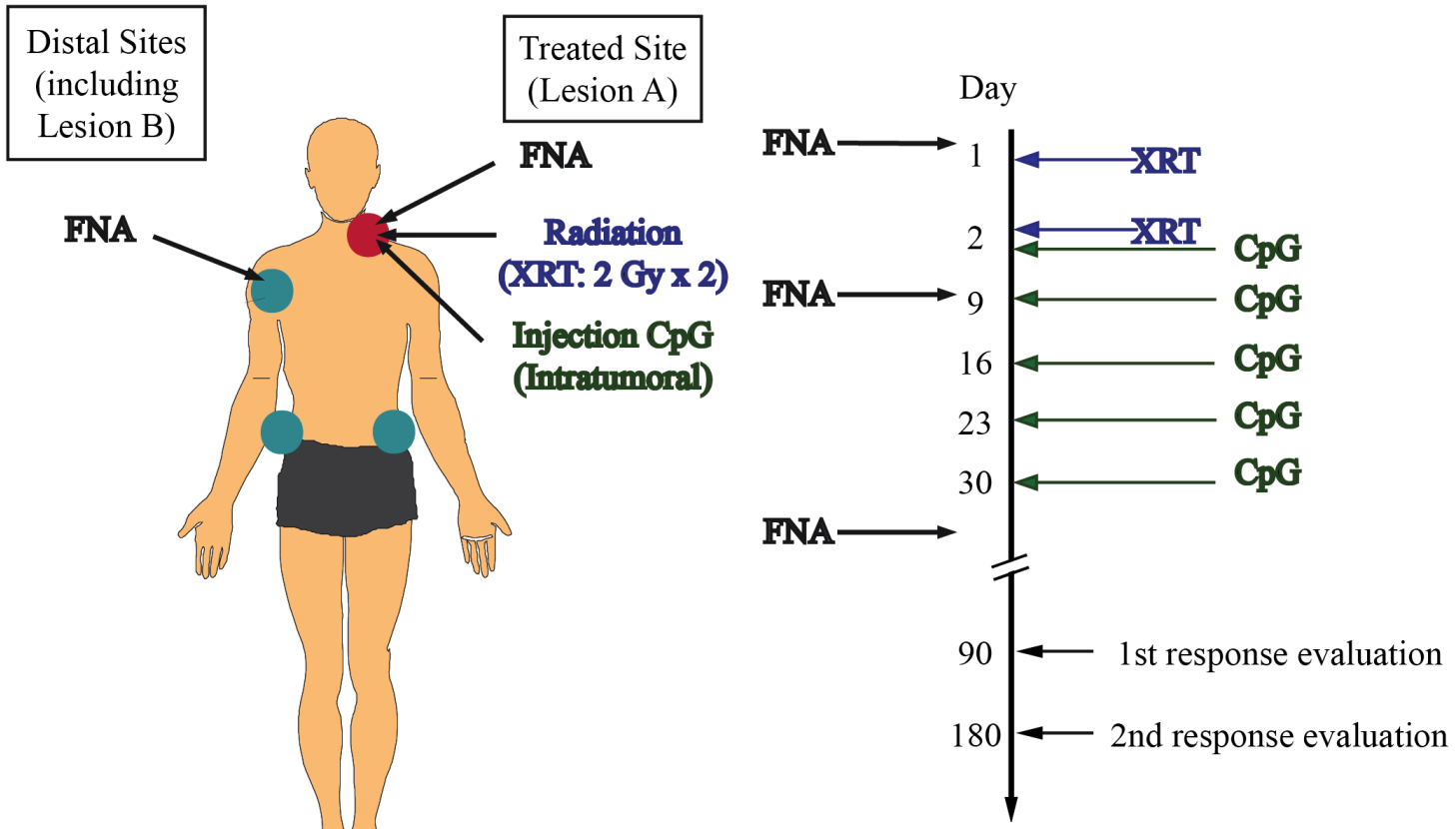
Trial Schema: Patients with Untreated Indolent Lymphoma



Frank MJ, et al. *Cancer Discov*. 2018;8(10):1258-1269.

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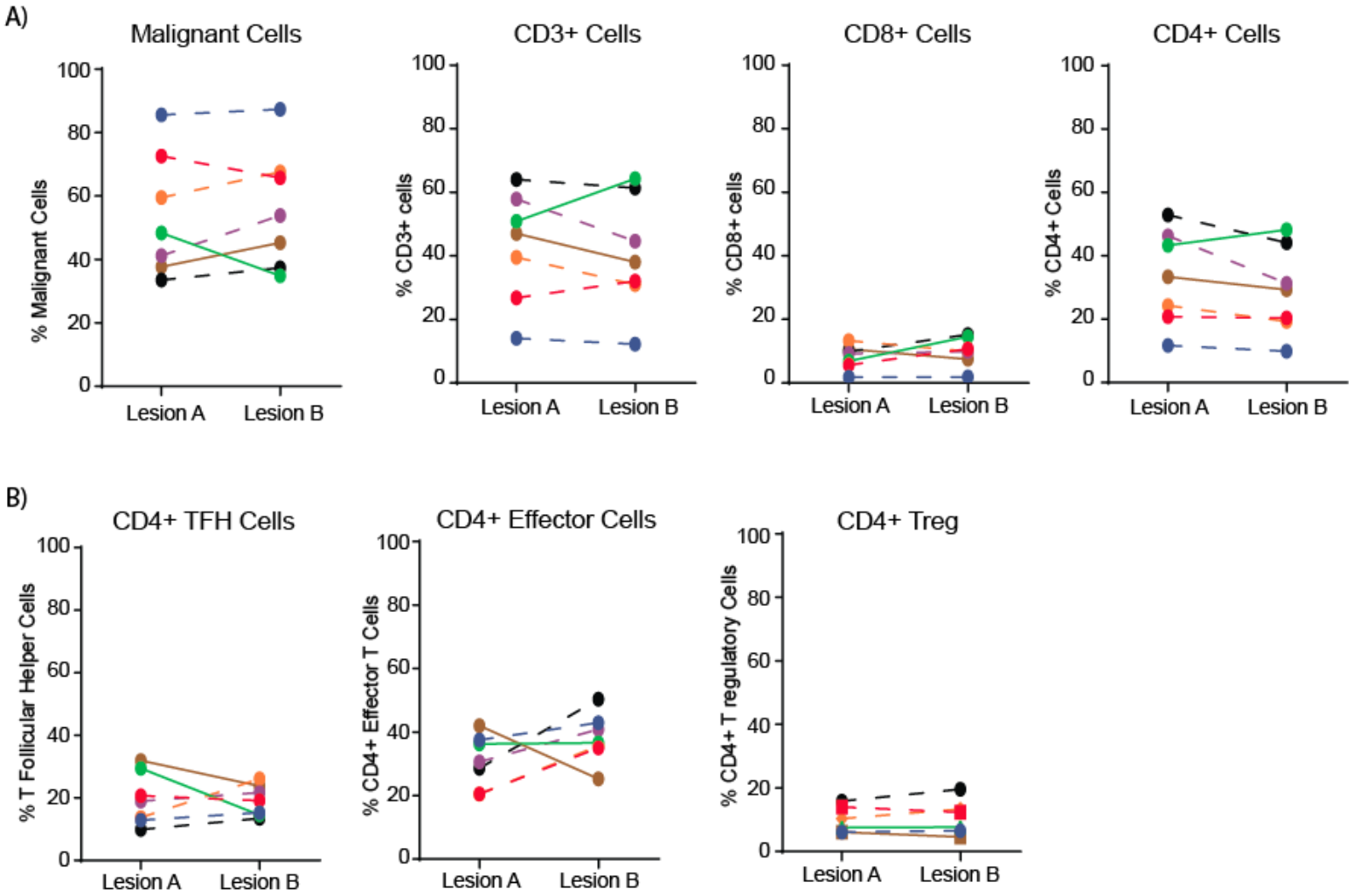
Lesion A to Lesion B Comparison Before Treatment



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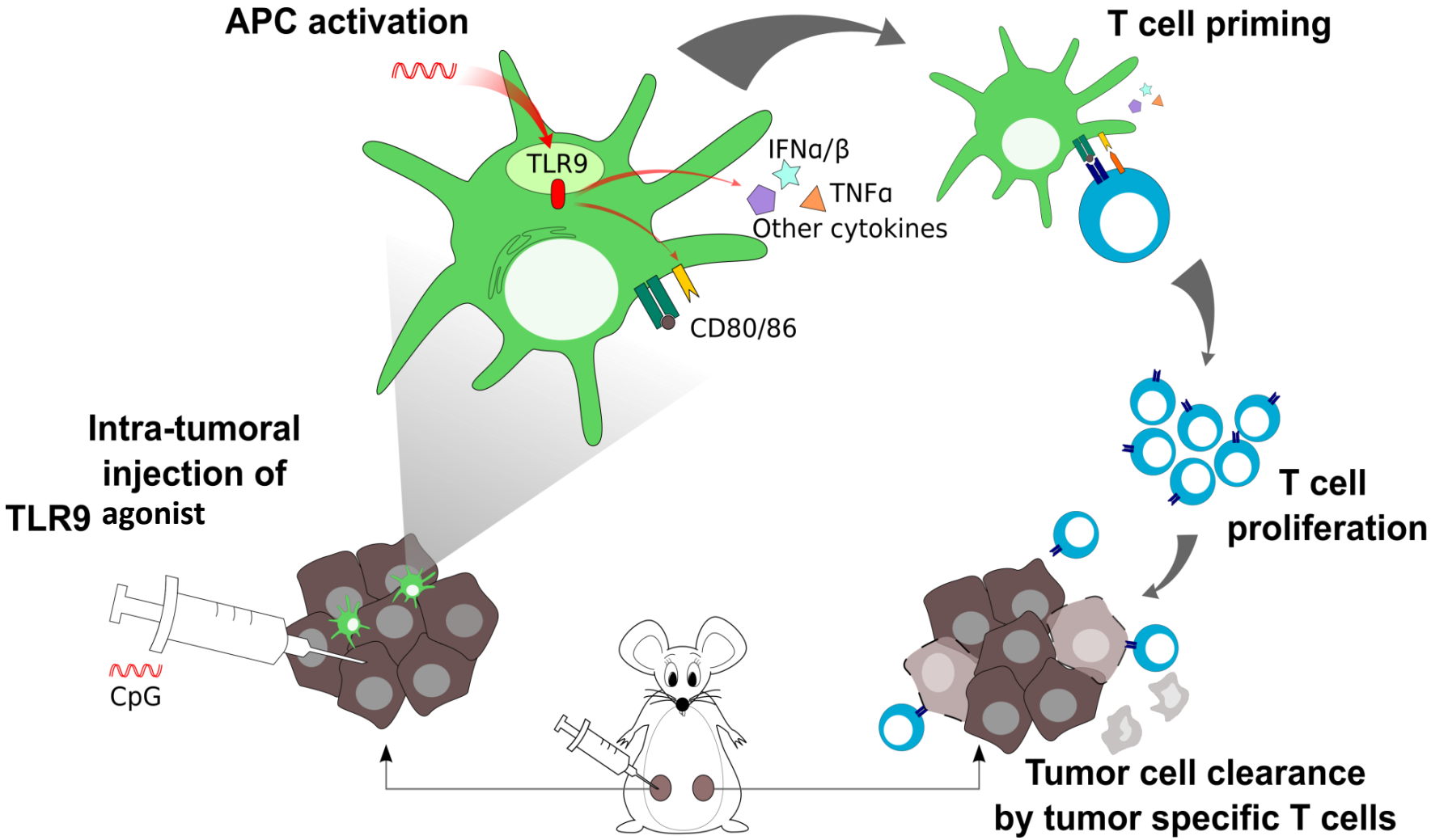
Mechanism of CpG (TLR9 Agonist)



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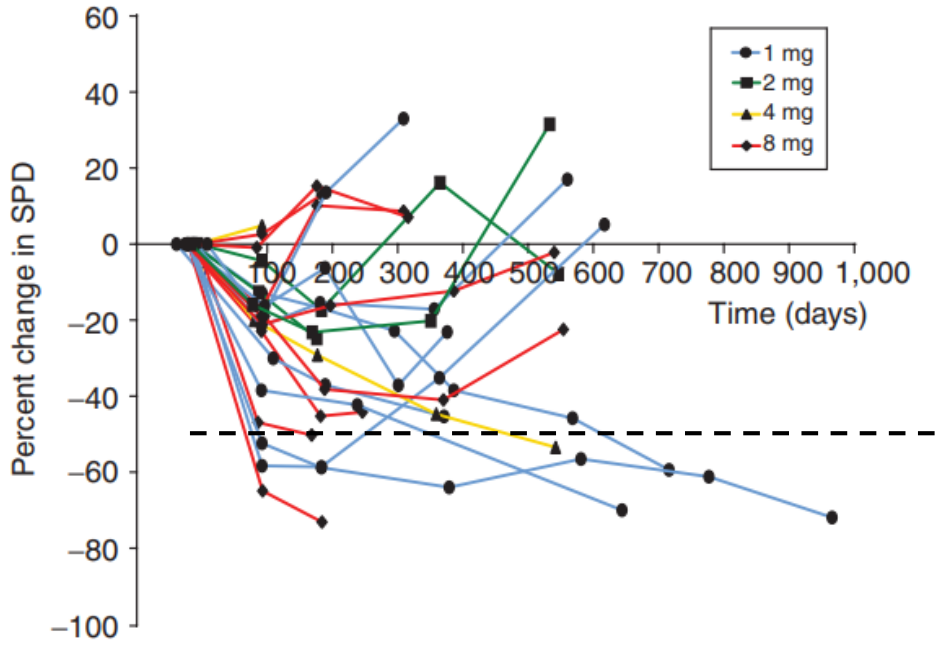
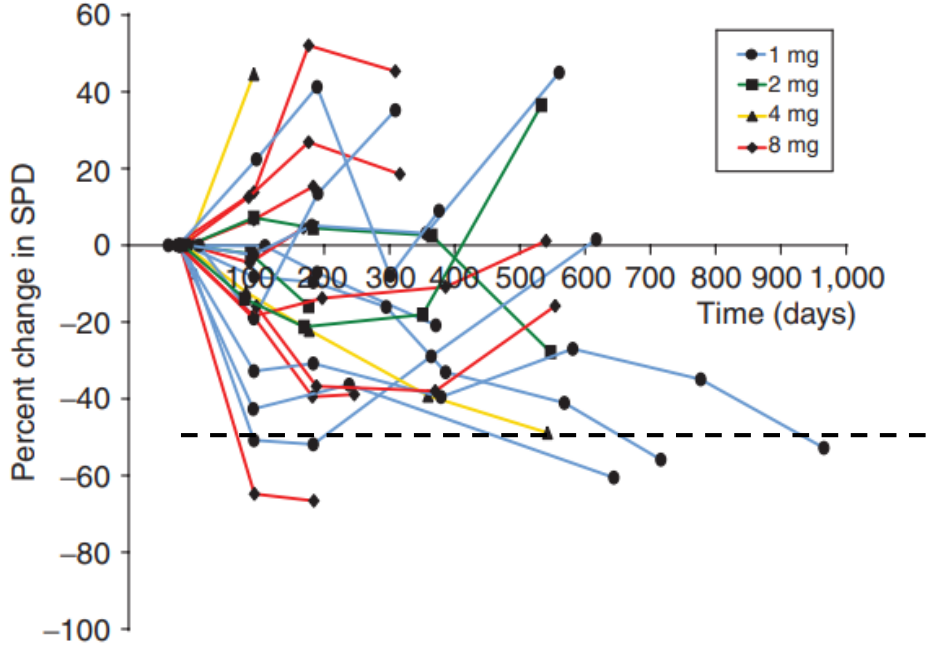
Clinical Responses Were Durable; Can Deepen Over Time

Overall Response



Distal Response



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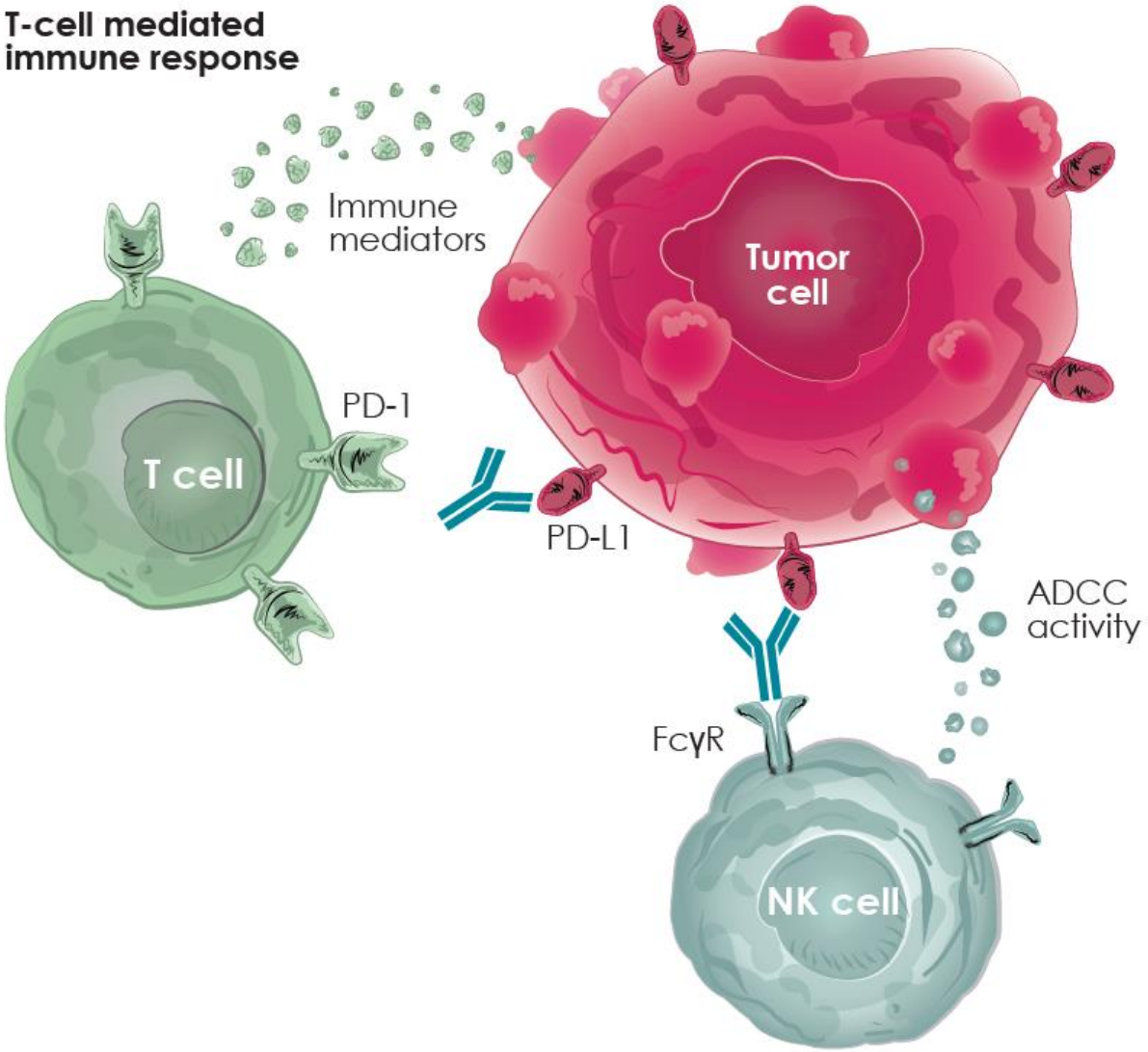
Frank MJ, et al. *Cancer Discov*. 2018;8(10):1258-1269.

Approaches to Enhance Immune Therapy



Chen R, et al. *Hematol Oncol*. 2017:35:67.

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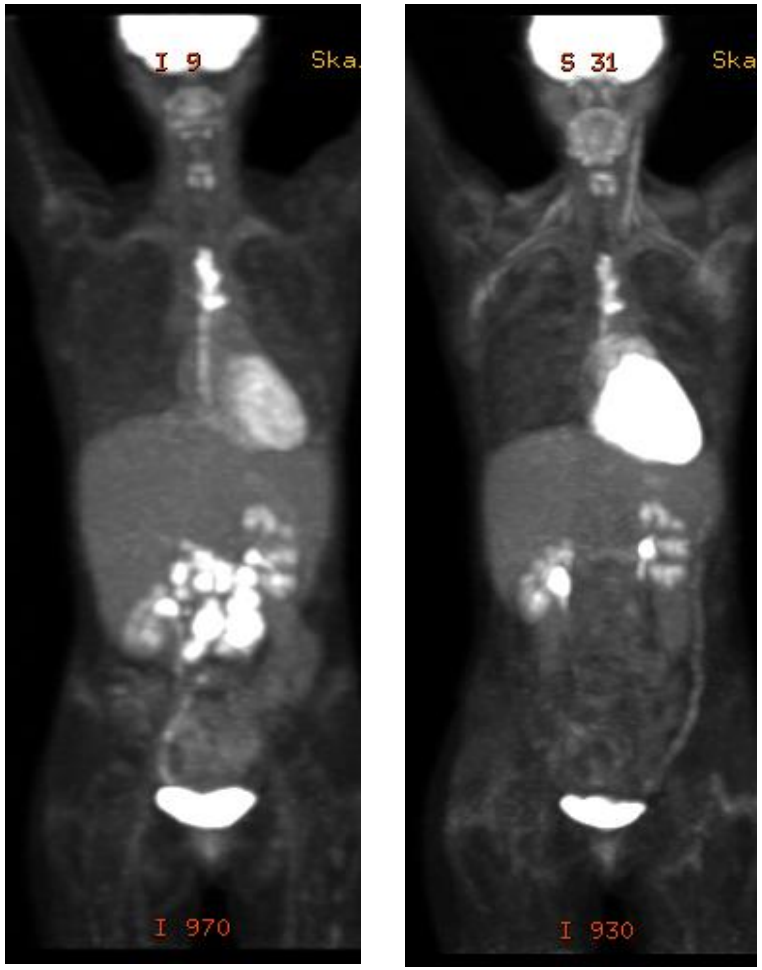
Does Blocking PD-1 signaling work? Highly Effective in Hodgkin Lymphoma

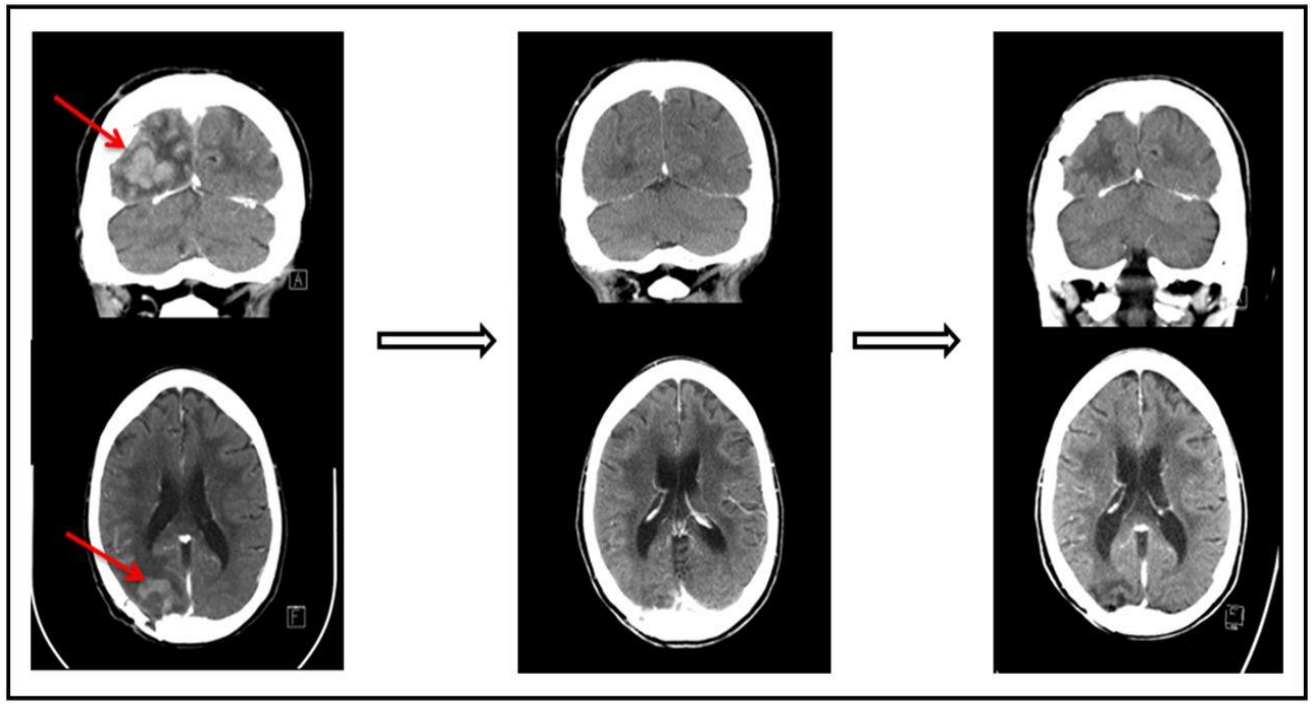


42-year-old female – Hodgkin lymphoma

26-year-old male – Hodgkin lymphoma

Courtesy of SM Ansell, Mayo Clinic

Promising Results with Anti-PD1 in Patients with Primary Refractory PCNSL



- 13% of PCNSL patients have translocations at 9p24.1
- 67% have copy number gains
- All 4 patients responded

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Nayak L, et al. *Blood*. 2017;129(23):3071-3073.

Scorecard for PD-1 Blockade in Lymphoma

- Hodgkin's Disease: FDA approved fourth line, 65% ORR
- PMBCL: FDA approved third line, 45% ORR
- PCNSL: Impressive results in small series

- NK/T Cell: Positive anecdotes
- Mediastinal Grey Zone: Positive anecdotes
- Richter's Transformation: Positive anecdotes

- FL: Disappointing
- DLBCL: Disappointing

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Other Interesting Antibody Targets

Naked Antibodies	Bispecific Antibodies	Antibody-Drug Conjugates
CD 40	CD 3-19*	CD 79b
CD 137	CD 3-20	CD 30*
CD 27	CD 3-BCMA	
CD 47		
CD 22		
CCR 4*		
CD38*		
SlamF7 (CD319)*		

*FDA Approvals

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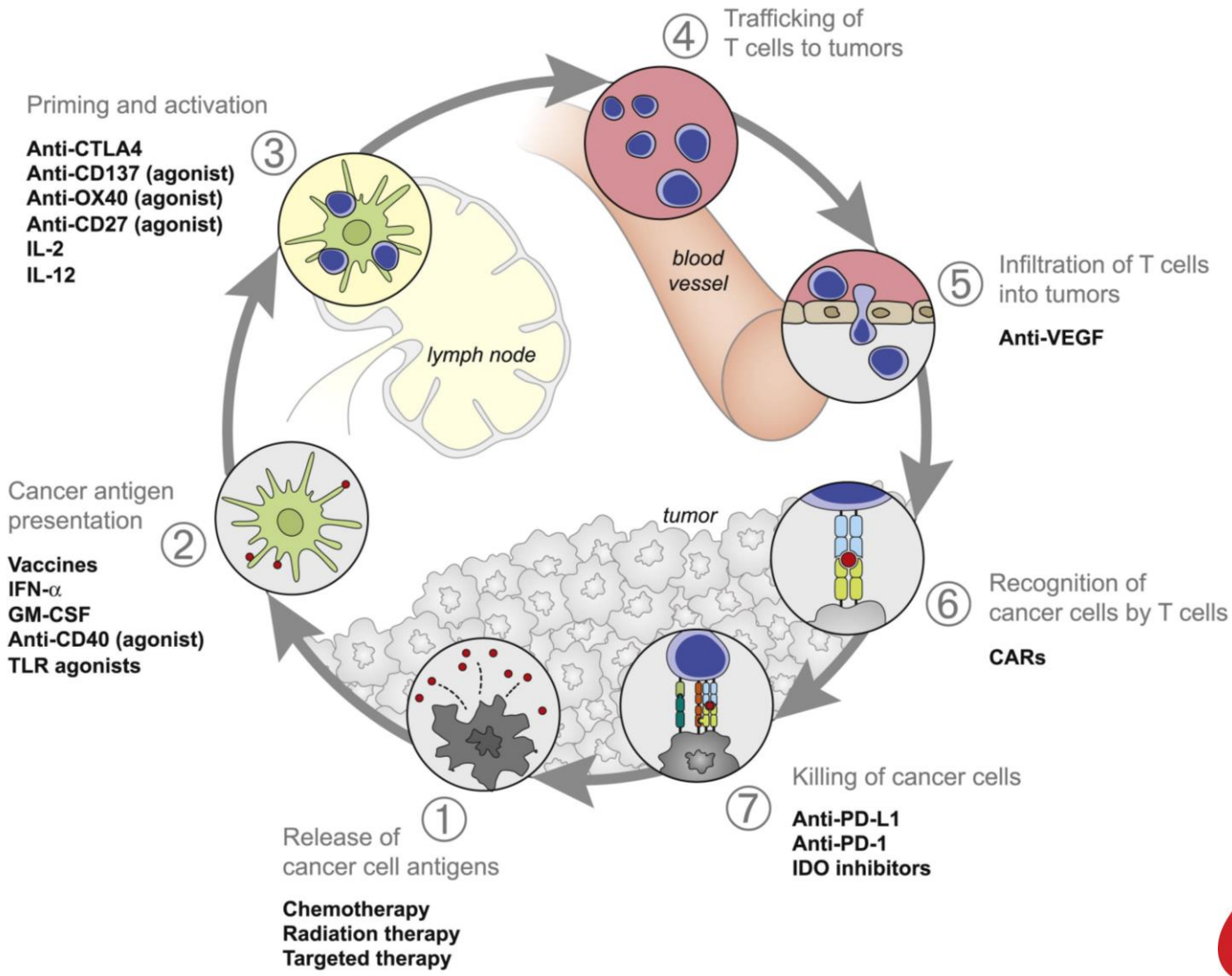
Combination Approaches



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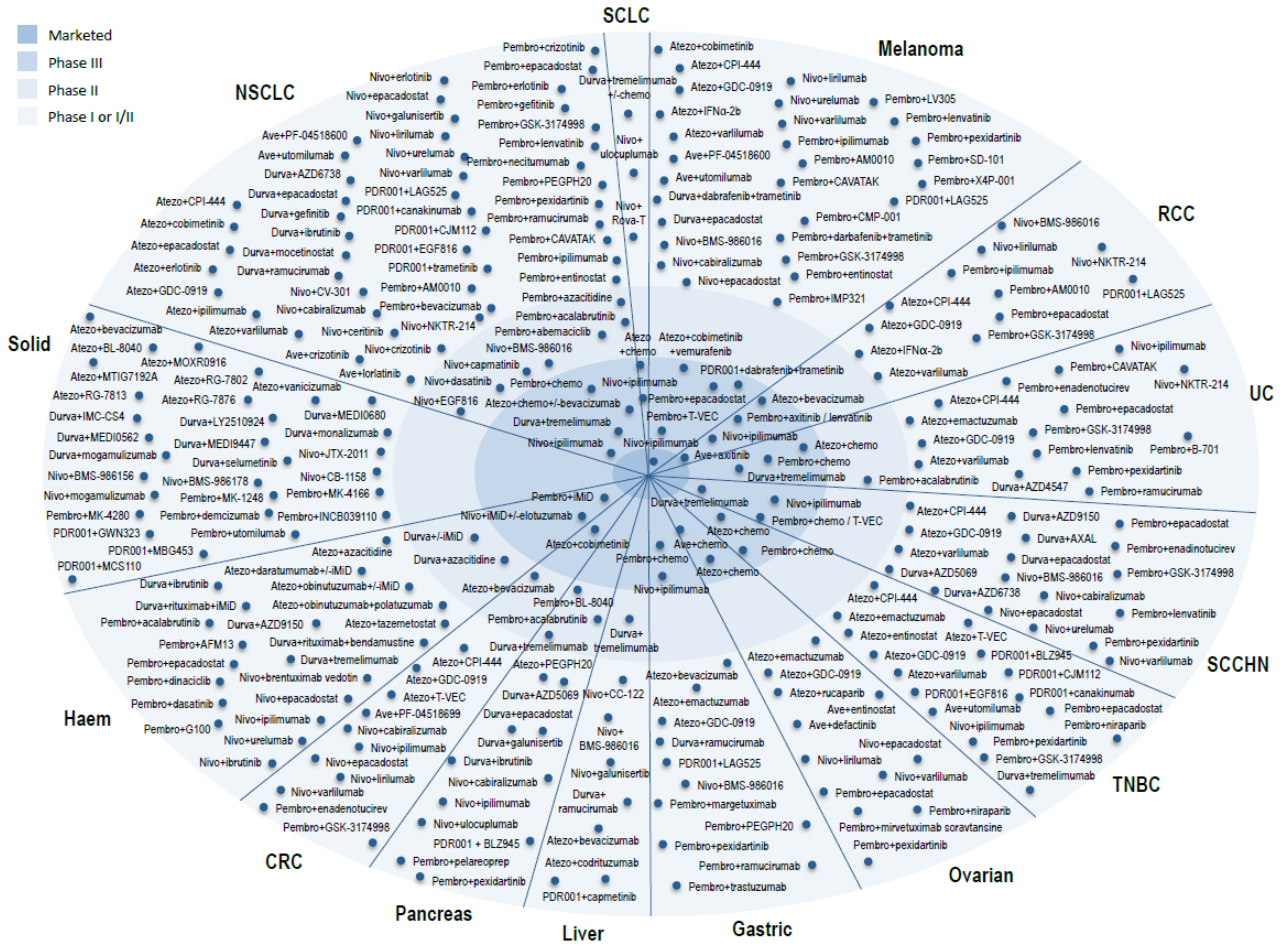
Chen DS, et al. *Immunity.* 2013;39(1):1-10.

Increasing Complexity > 800 CT with PD-L1/PD1



Adapted from Vanessa Lucey, CRI

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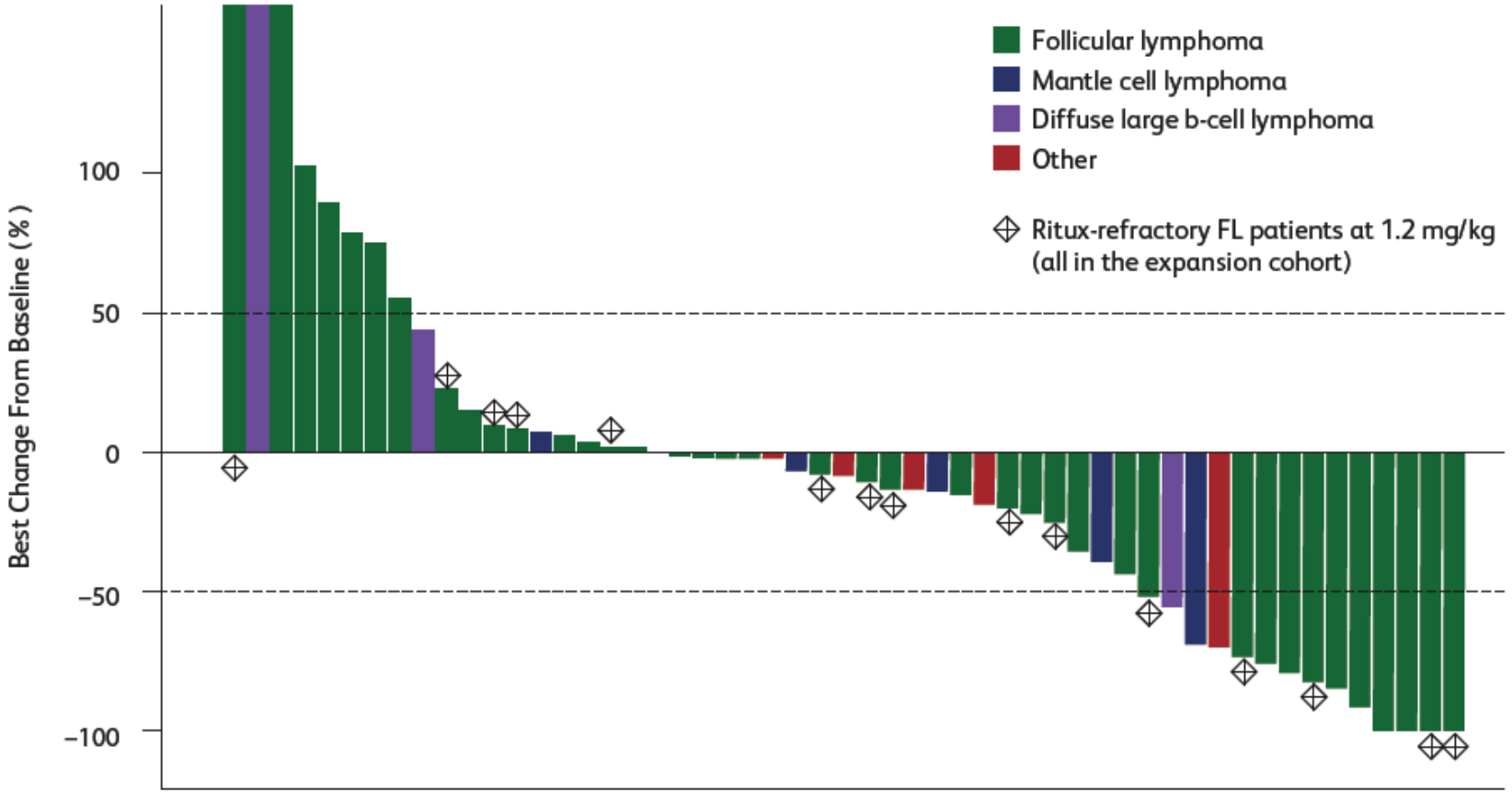
Anti-CD 137 Plus Rituximab in Relapsed Lymphoma



- ORR - 23%, CR - 8%, PR - 15%
- Well tolerated, no DLTs
- Elevated LFTs

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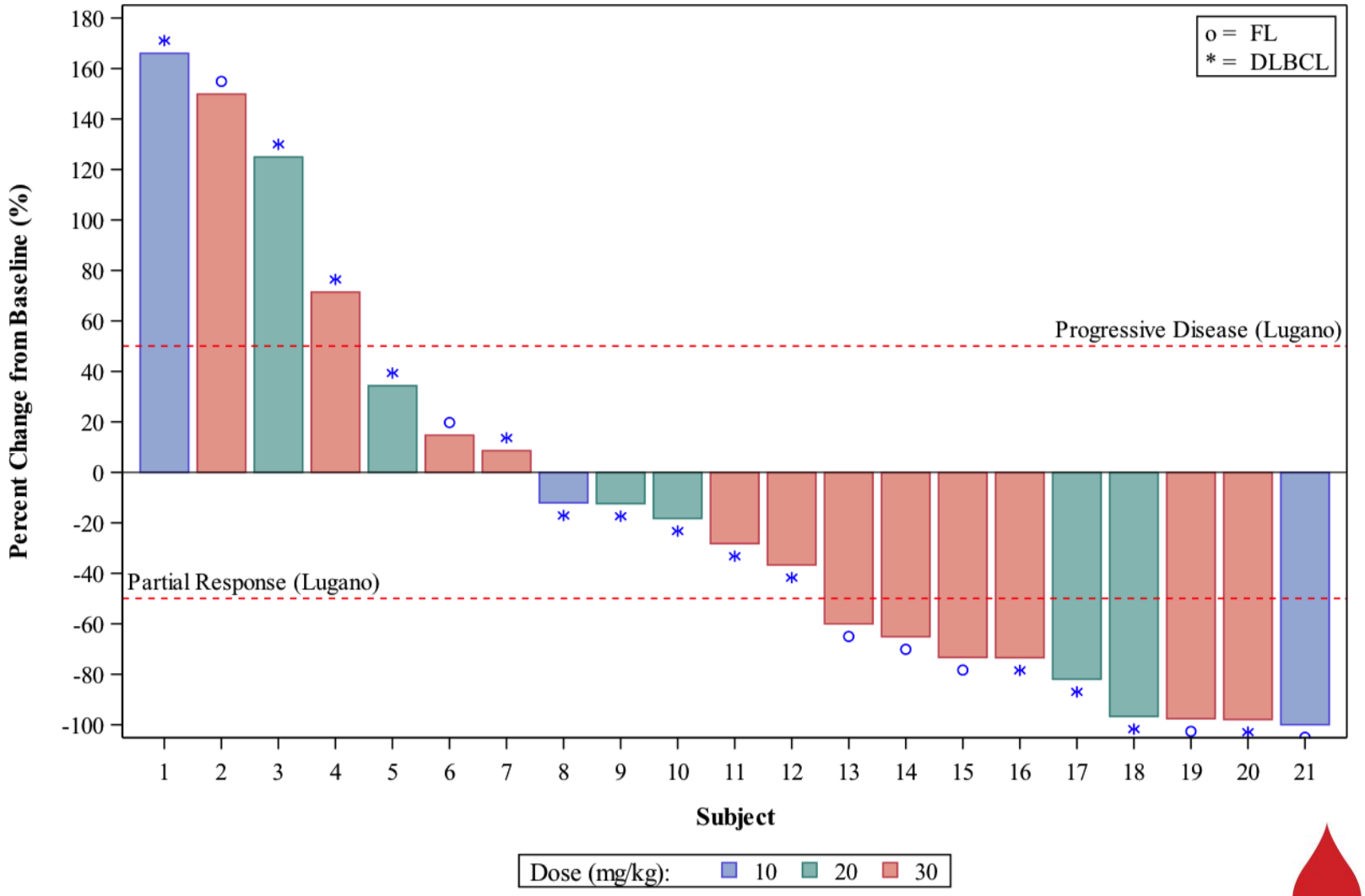
Gopal A, et al. *Hematol Oncol*. 2017;35(S2):260.

Anti CD47 plus Rituximab



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Advani RH, et al. *J Clin Oncol*. 2013;31(1):88-94.

Search for Synergy: Two-Tumor Model

No Treatment	CpG Alone	CpG + Effective Ab
		

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Houot R, et al. *Blood*. 2009;113(15):3546-3552.

Ongoing Clinical Trials of *in situ* Vaccination at Stanford

- Ibrutinib + intratumoral TLR9 + low-dose radiation in previously treated patients with indolent lymphoma (NCT02927964)
- Anti-Ox40 monoclonal antibody + intratumoral TLR9 + low-dose radiation in patients with indolent lymphoma (NCT03410901)

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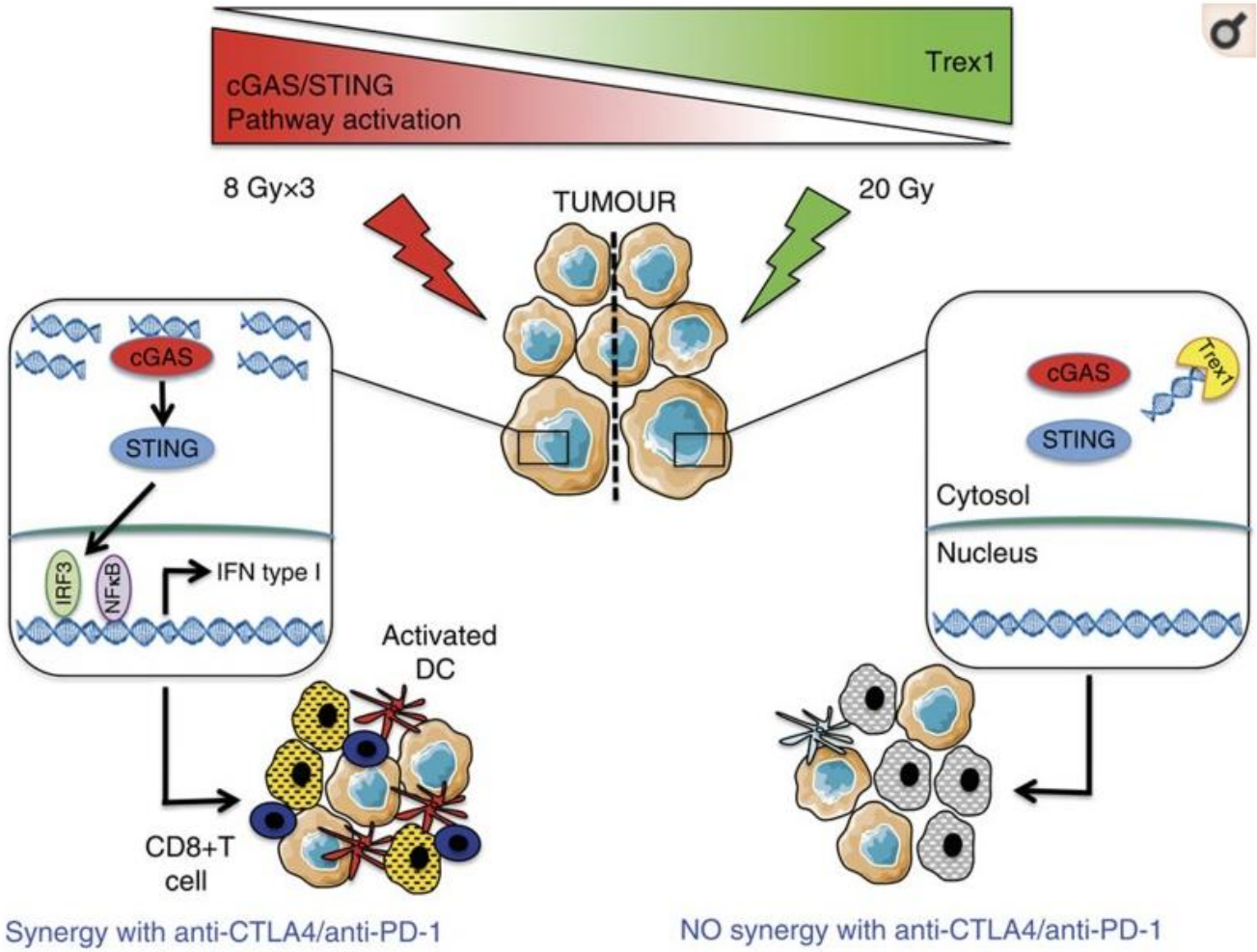
Combining Low-Dose XRT with Immunotherapy



Vanpouille-Box C, et al. *Nat Commun*. 2017;8:15618.

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Conclusions

- The immune system interacts with lymphoma potentially either to aid or impede the tumor.
- Locally injected immune modulators can trigger systemic anti-tumor immune responses.
- Checkpoint blockade works well in HD and perhaps in other lymphomas with amplified PDL1 genes.
- Antibodies against other targets are promising.
- Synergistic combinations of immune modulators with other therapies are actively being sought.

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PANEL DISCUSSION/Q&A SESSION

Integration of Immunotherapy into Treatment for Hematological Malignancies

MEDICAL EDUCATION FOR BETTER OUTCOMES

Postgraduate Institute for Medicine

Jointly provided by The Leukemia & Lymphoma Society, RMEI Medical Education, LLC, and Postgraduate Institute for Medicine.

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