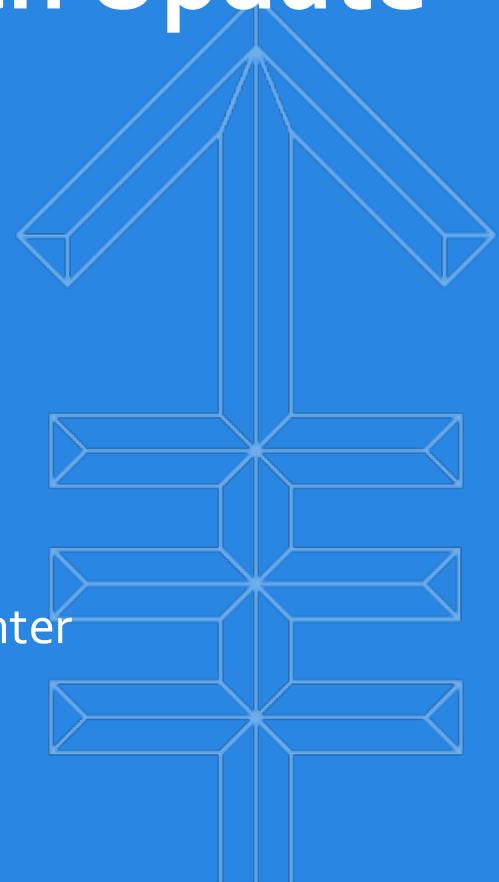




Memorial Sloan Kettering
Cancer Center™

Clinical Trials and Research Update

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Cutaneous T-cell Lymphoma Studies: General Goals

More Potent/Effective Treatments

Less Toxic Treatments

Better Understanding of the Illness

Increase Cures

↓
Longer Remissions

More Remissions

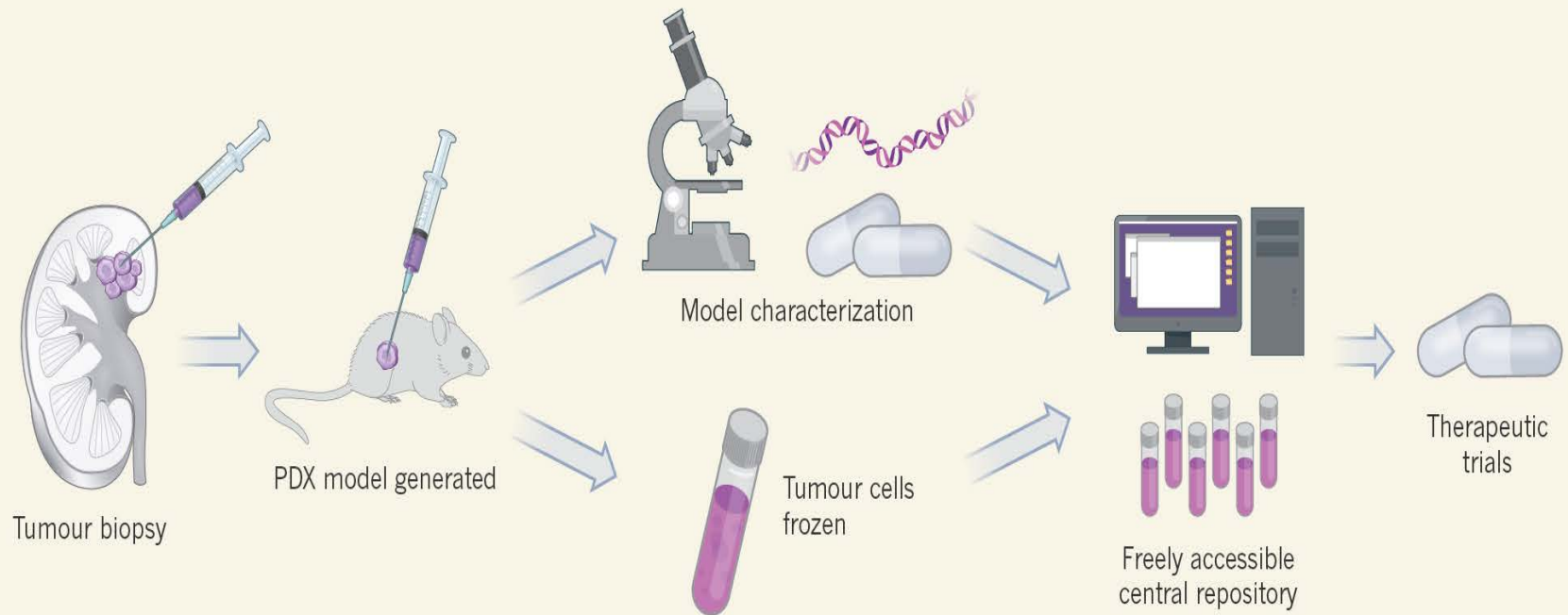
Less Symptoms

Better Quality of Life

Registries

Laboratory/Translational Studies

Patient-derived xenografts to model human cancer



Collaborative network

Bringing us all together for greater impact

CL International Consortium, ***CLIC, a multinational, interdisciplinary, project-based research alliance*** of CL expert centers worldwide to generate large-scale clinical and translational data for greater impact

- Initiated as ISCL-based interest in early 2013, officially supported by EORTC, USCLC, and other regional CL organizations
- Although inclusive in concept, the participants/sites are primarily determined by proposed projects, funding, and commitment





Cutaneous Lymphoma International Consortium (CLIC): an International Alliance for Large-Scale Collaborative Investigations in Cutaneous Lymphoma

55+ centers
Derm, Onc, Path



Clinical Trials

- Clinical trials are usually testing a new treatment on people
 - New Medication
 - New test (HTS, MRD)
- Usually the goal is to find better and/or additional treatments
 - Brand new treatment
 - Existing treatment for a new indication
 - New combination of existing treatments
 - Existing treatment in a better way
- **Informed Consent**



Clinical Trials: Phase I/Early phase

- Determine the correct dose/schedule for further studies
- Often very new drugs
- Might be a new combinations of existing drugs
- Learn about side effects
- Might be unknown therapeutic benefit
- Usually for patients in whom some conventional options have been tried.



Clinical Trials: Phase II

- Phase II clinical trials test efficacy of a therapy, cannot determine superiority to a standard therapy
- Usually already know “best” dose and side effects
 - Scenario A
 - Test the anti-tumor effect of a new drug
 - Scenario B
 - Evaluate the effectiveness of a new combination or approach to therapy

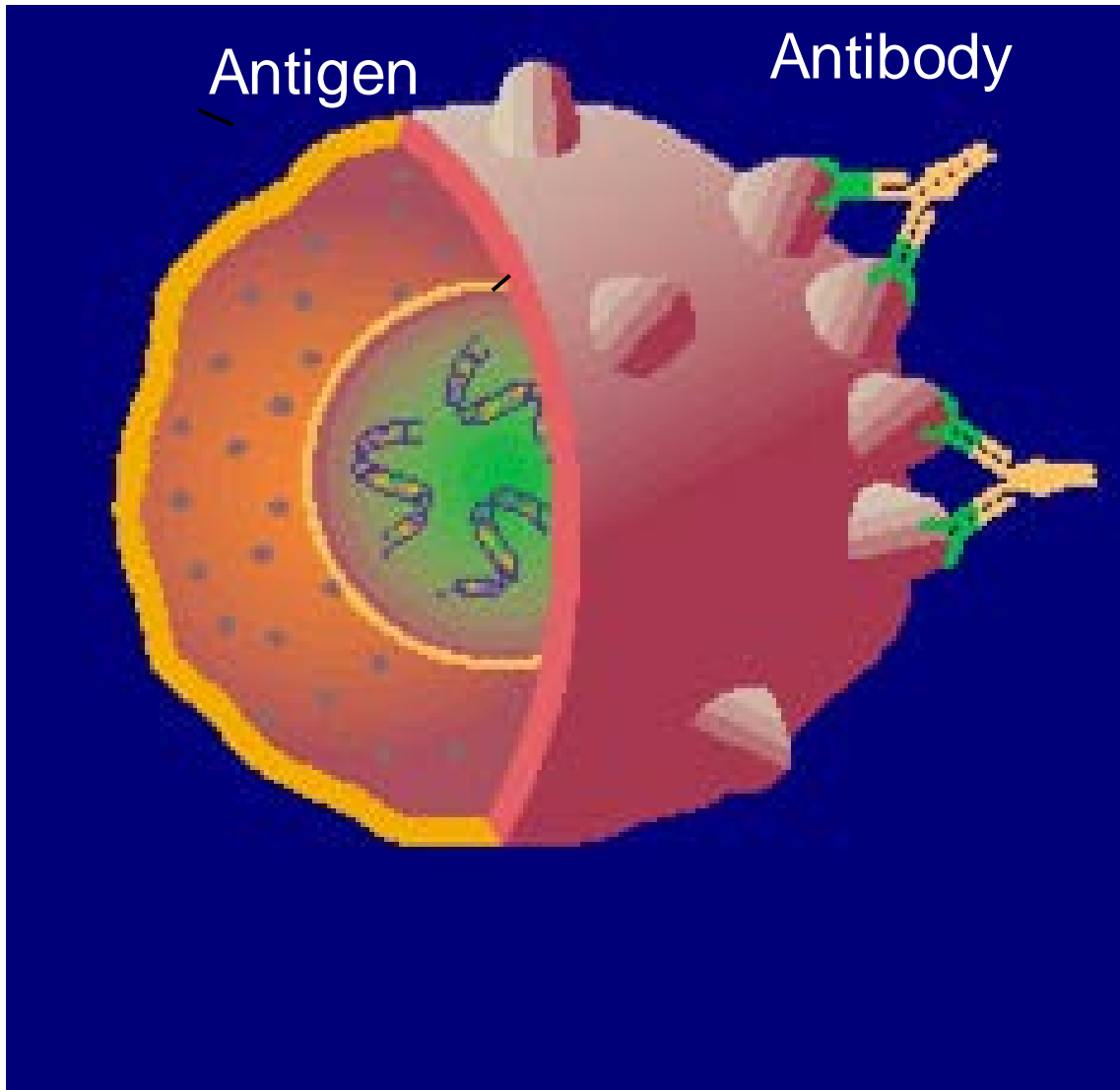


Clinical Trials: Phase III

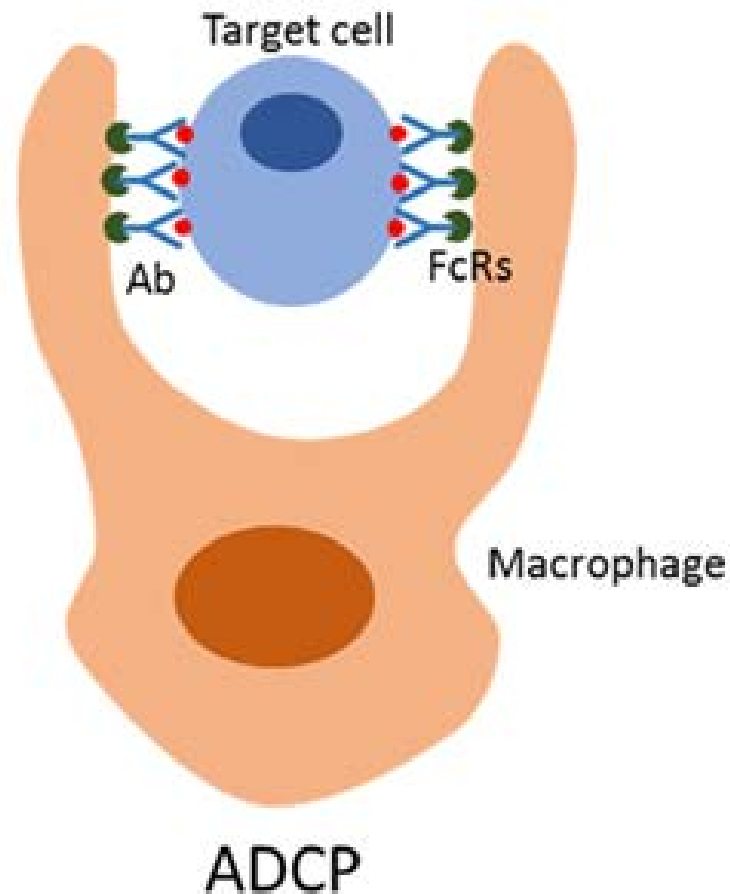
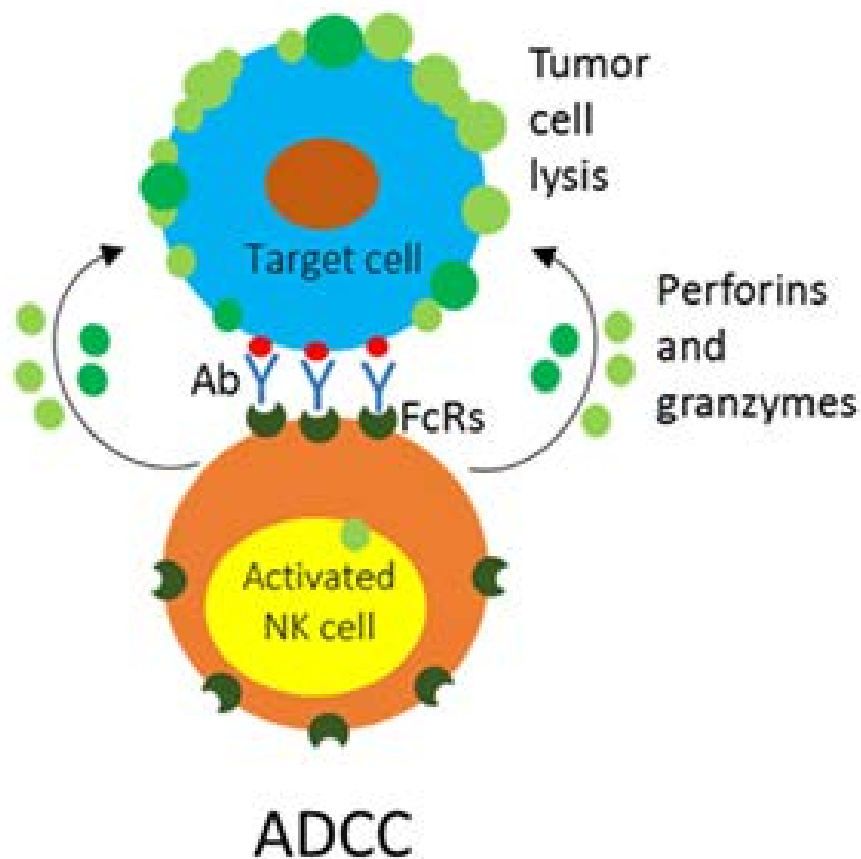
- A randomized comparison of a standard regimen to a new treatment
 - Patient might get one or another treatment (usually you do not get to choose)
 - Placebo control studies are unusual in CTCL
 - If an experimental therapy looks better in a Phase II study, we are often not sure without a phase 3



Types of Treatment: Antibodies

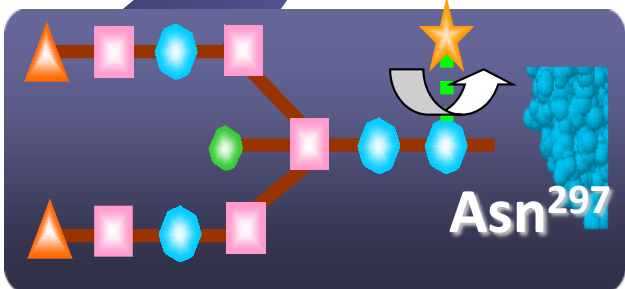
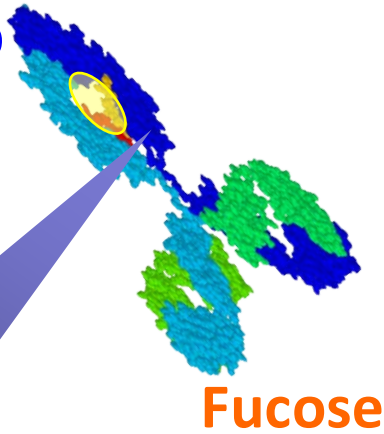


Antibodies can help the immune system eliminate cancer cells



Mogamulizumab (KW-0761); anti-CCR4

Mogamulizumab



Modified (defucosylated Fc)
to make it more potent

Mavoric Study

People with MF/SS
Stage IB – IVB
after ≥ 1 prior
systemic Tx

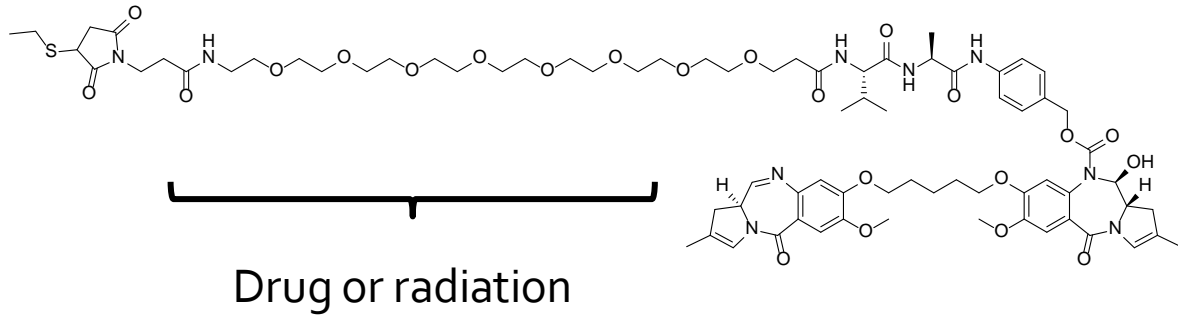
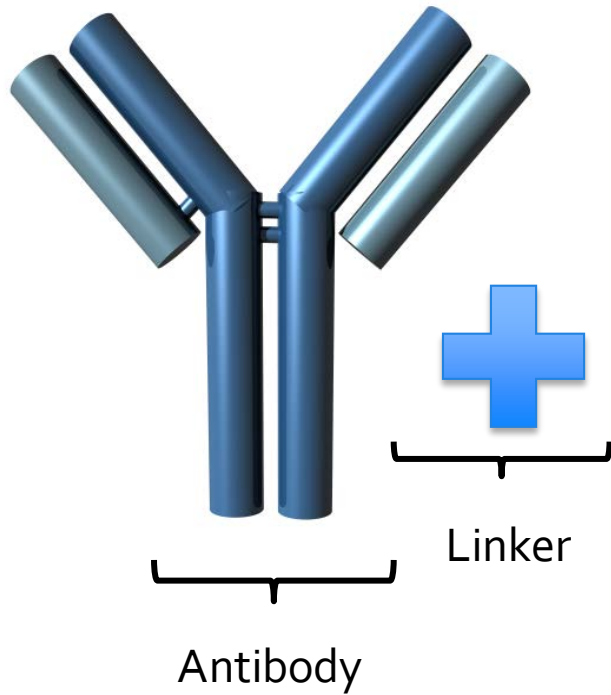
Randomization

Moga
IV

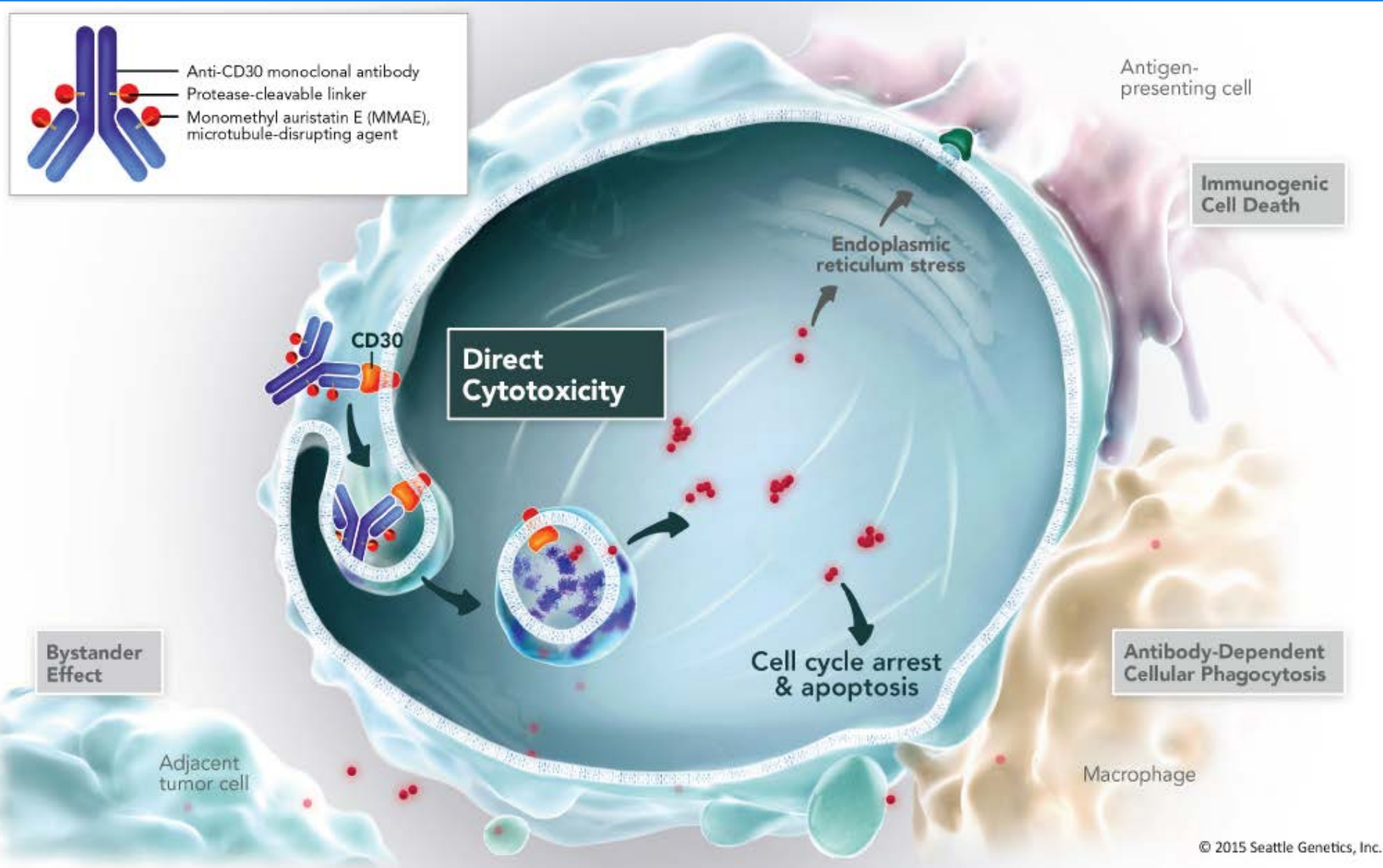
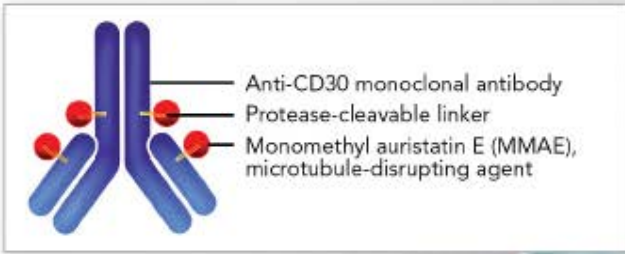
Vorinostat
400 mg PO
daily

1. Shinkawa et al. *J Biol Chem* 2003;278:3466; 2. Ishii et al. *Clin Cancer Res* 2010;16:1520; 3. Niwa et al. *Cancer Res* 2004;64:2127; 4. Matsushita T, *Korean J Hematol* 2011;46(3):148-150; 5. Ishida et al. *Clin Cancer Res* 2003;9:3625; 6. Ishida et al. *Clin Cancer Res* 2004;10:5494; 7. Duvic et al. *Blood* 2015;125:1883-1889.

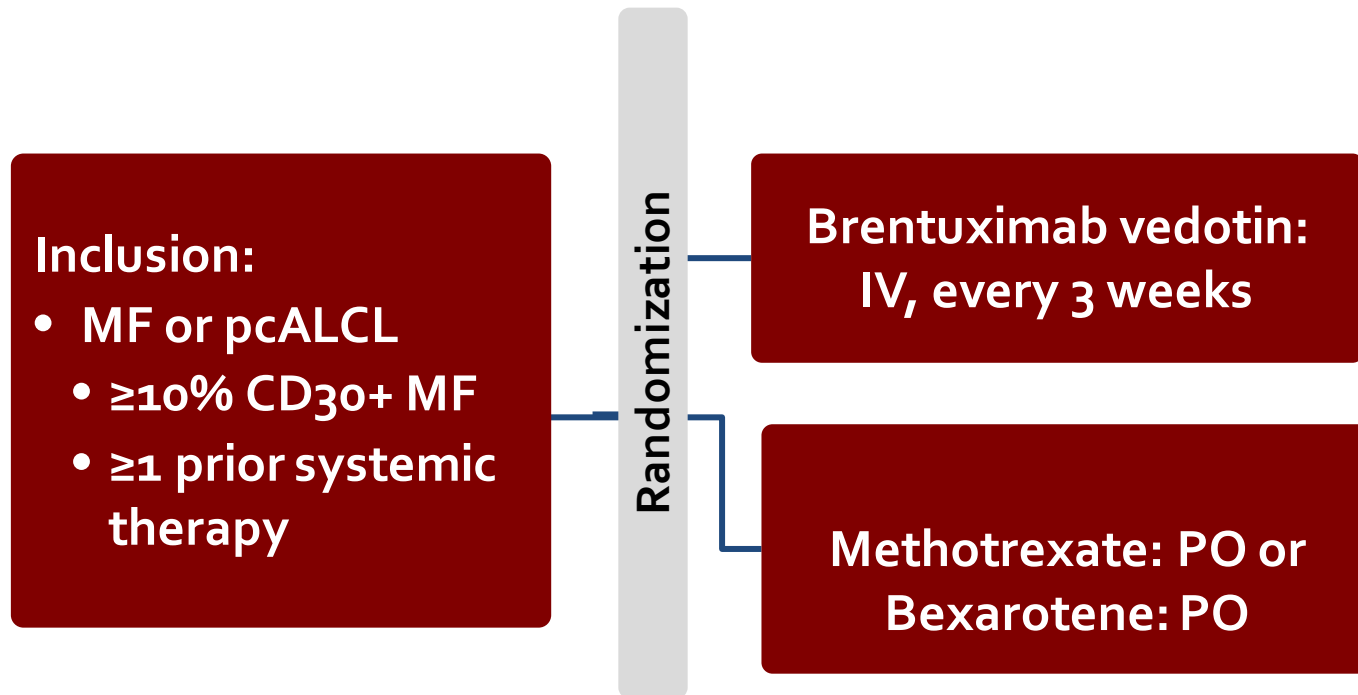
Antibody drug conjugates (ADC)



Antibody Drug conjugates

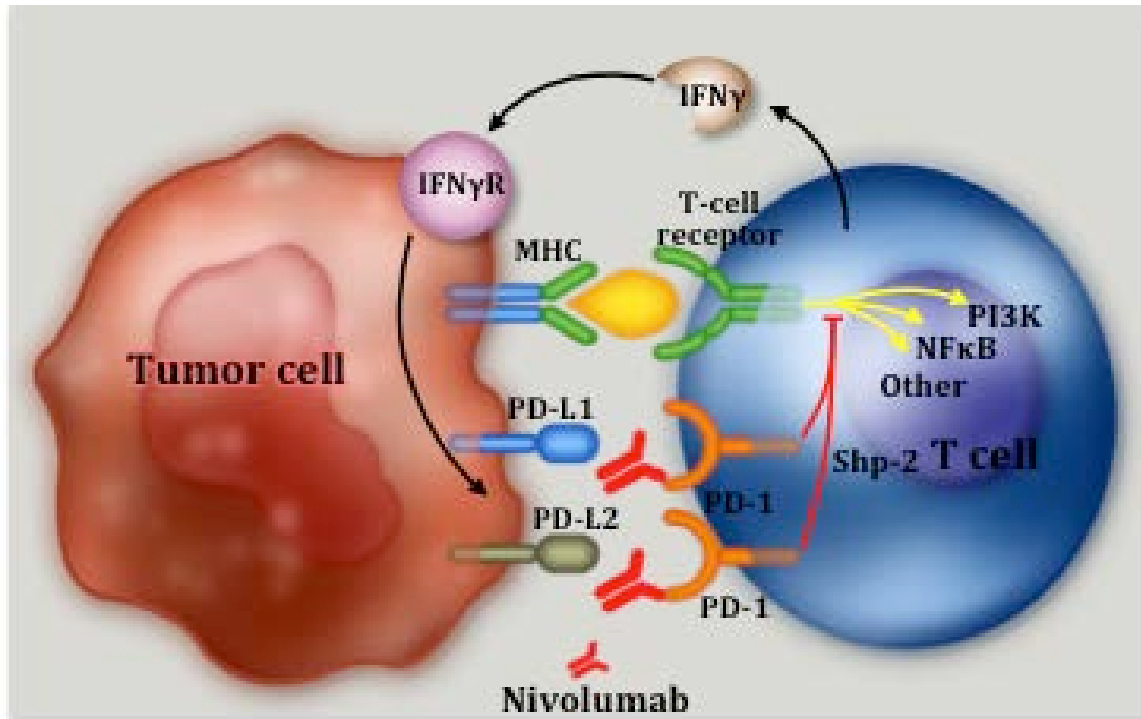


ALCANZA: Brentuximab Vedotin vs Standard Treatments



Immune Checkpoint Inhibitors

- PD-1 ligands block immune response on immune effector cells.¹
- PD-L1 on malignant cells and/or in the tumor microenvironment suppresses antitumor immunity.

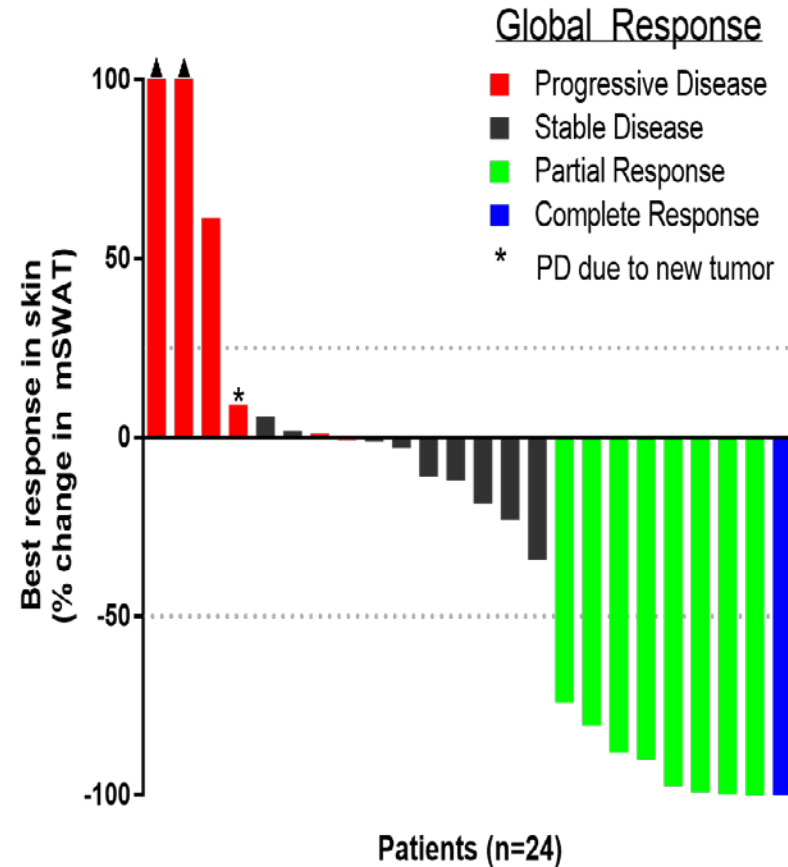


¹Francisco LM et al. J Exp Med 2009;206:3015-29.

²Andorsky DJ et al. Clin Cancer Res 2011;17:4232-44



Pembrolizumab in CTCL: Responses seen across all clinical characteristics

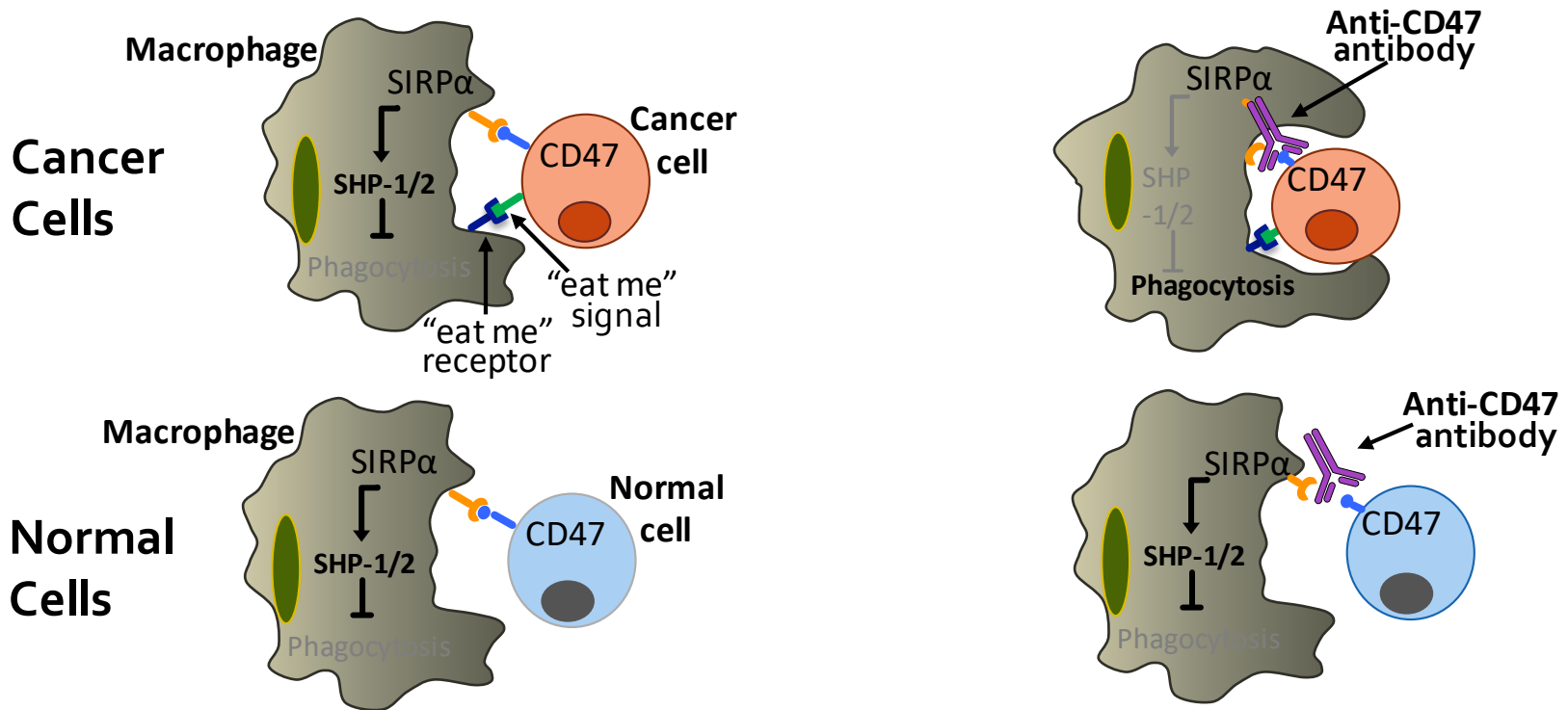


Overall response rate: 38%



CD47

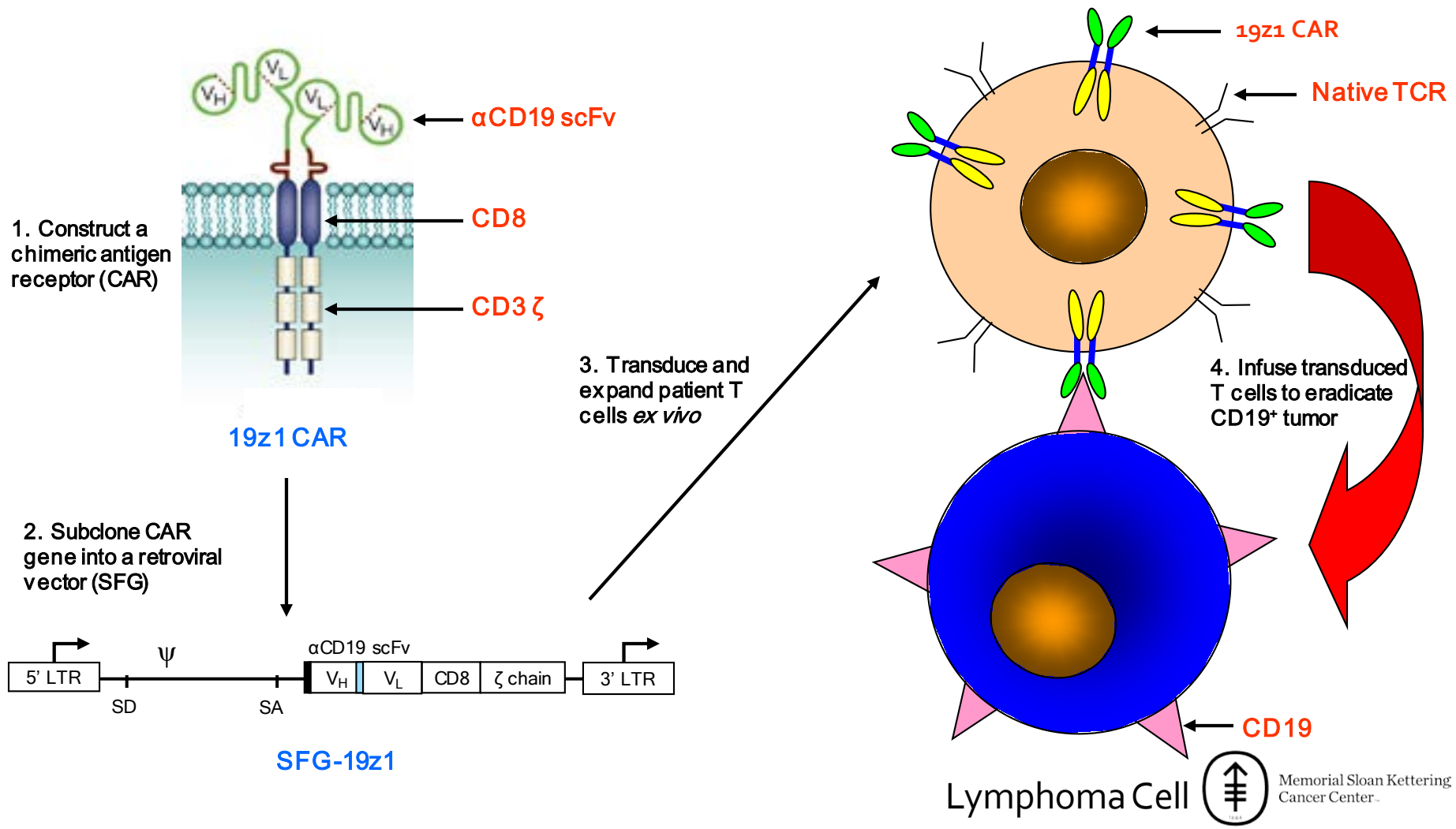
A Cancer Immune Checkpoint



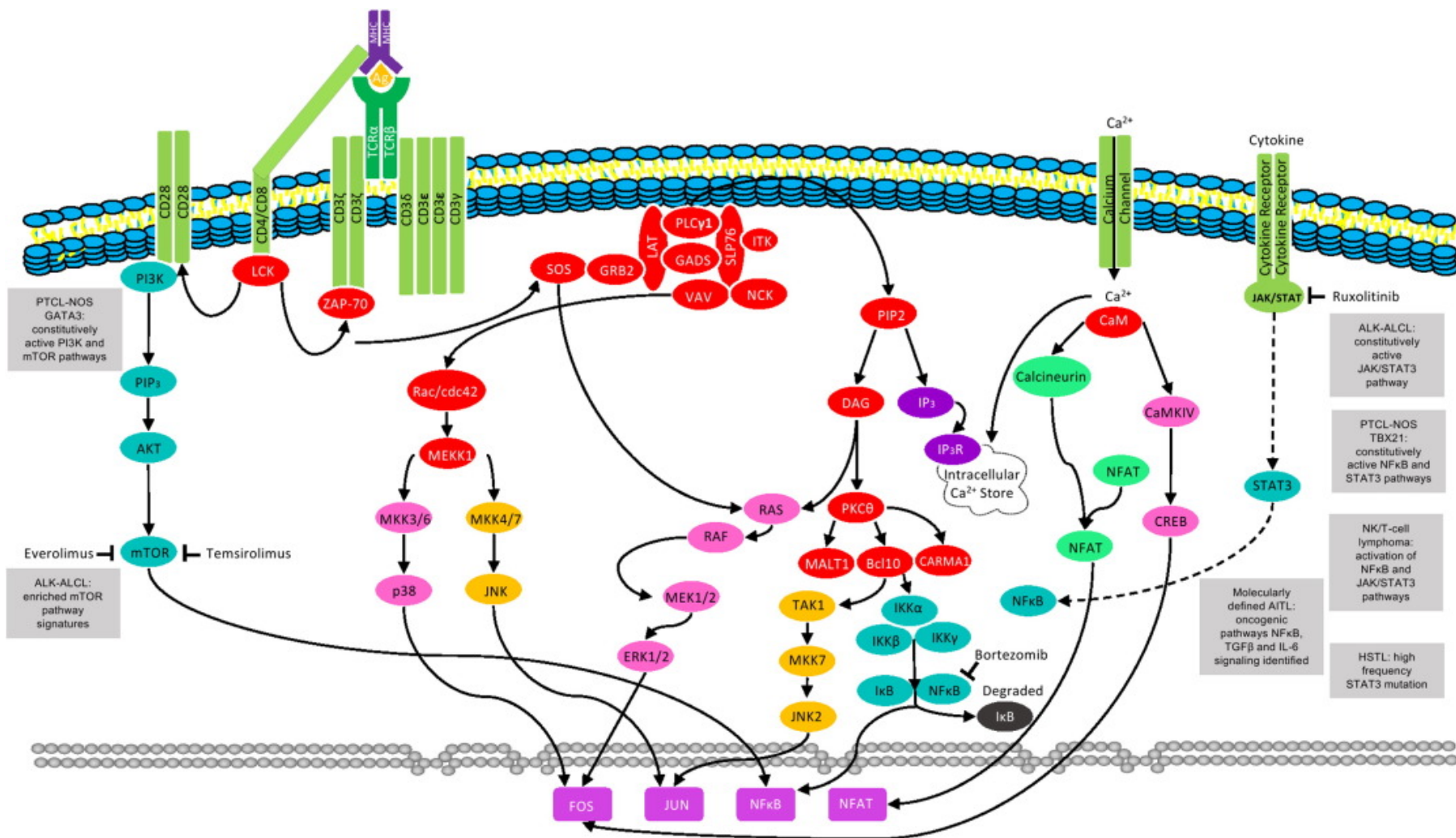
- CD47 sends a "don't eat me" signal to immune cells
- CD47 is expressed on a wide variety of cancers including CTCL
- **Antibodies that block the CD47 potently stimulate immune phagocytosis of cancer cells**



Generation of CD19-targeted Autologous T cells (CAR) for treatment of B cell Lymphoma



signaling pathways



Research in systemic therapies: Many

- Antibodies-many
- Antibody drug conjugates-many
- Immune checkpoint inhibitors
- CAR-T-maybe in the future
- Small molecules-many
- miRNA
- New skin directed therapies-Larissa (I think) will cover
- Others

Many exciting new approaches in CTCL

- **New drugs approved by the FDA**
- **New/improved technology** allowing us to learn more, help identify actionable targets, and modify/render agents more effective/safe
- **More encouraging treatment options** (many in the pipeline) with **Improved/more tumor-selective** therapies, less toxicity
- **Develop combination/sequential strategies to optimize anti-**

Working together at large scale for greater impact

survival outcomes

- Taking steps towards personalized, precision medicine

