The Ongoing Evolution of Cancer Drug Therapy: What will impact your practice?

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Oncology New Drug Approvals
July 2023 - August 2024

- Quizartinib
- Talquetamab-tgvs
- Elranatamab-bcmm
- Toripalimab-tpzi
- Fruquintinib
- Repotrectinib
- Capivasertib
- Nirogacestat
- Eflornithine
- Lifileucel
- Tovorafenib
- Nogapenekin alfa inbakicept-pmln
- Tarlatamab-dlle
- Imetelstat
- Afamitresgene autoleucel
- Vorasidenib

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

Oncology (Cancer) / Hematologic Malignancies Approval Notifications

Resources for Information | Approved Drugs

Oncology (Cancer) / Hematologic Malignancies Approval Notifications

Ongoing | Cancer Accelerated Approvals

Verified Clinical Benefit | Cancer Accelerated Approvals

Withdrawn | Cancer Accelerated Approvals

Other | Cancer Accelerated Approvals

FDA does not issue approval announcements for every approval or drug label update that occurs in oncology and hematology. Please refer to Drugs@FDA for the latest approvals and prescribing information for specific products.

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Webpage	Description	Date
FDA approves vorasidenib for Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation	On August 6, 2024, the Food and Drug Administration approved vorasidenib (Voranigo, Servier Pharmaceuticals LLC), an isocitrate dehydrogenase-1 (IDH1) and isocitrate dehydrogenase-2 (IDH2) inhibitor, for adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection.	8/6/2024
FDA grants accelerated approval to afamitresgene autoleucel for unresectable or metastatic synovial sarcoma	On August 2, 2024, the Food and Drug Administration granted accelerated approval to afamitresgene autoleucel (TECELRA, Adaptimmune, LLC), a melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T cell immunotherapy, for adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are	8/2/2024

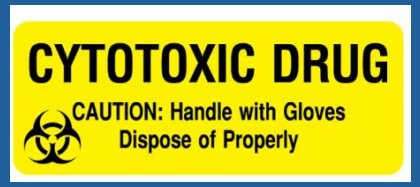
Content current as of:
08/06/2024

Regulated Product(s)
Drugs
Oncology

https://www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notifications

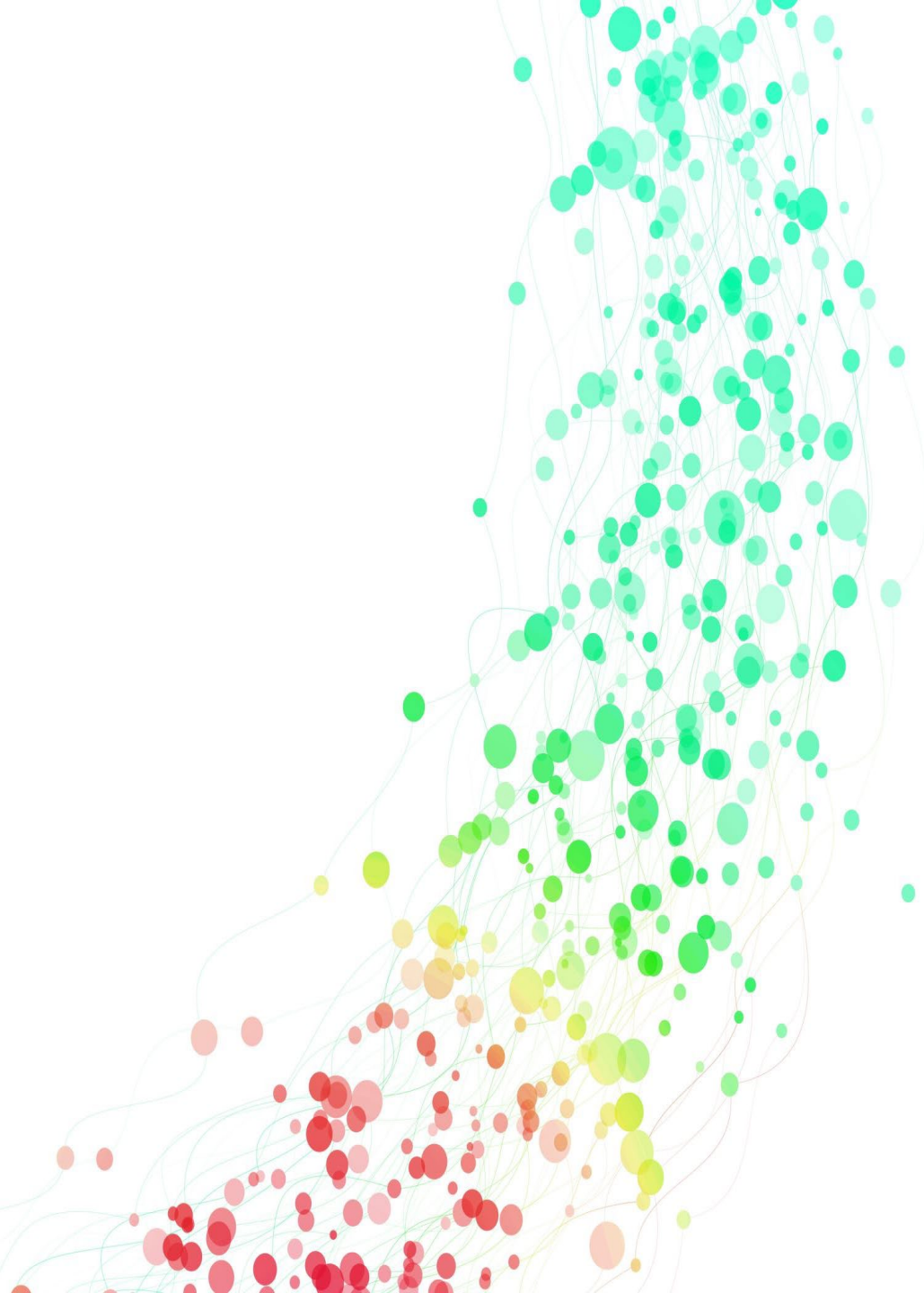
Strategies for Cancer Drug Therapy: 2024

Chemotherapy



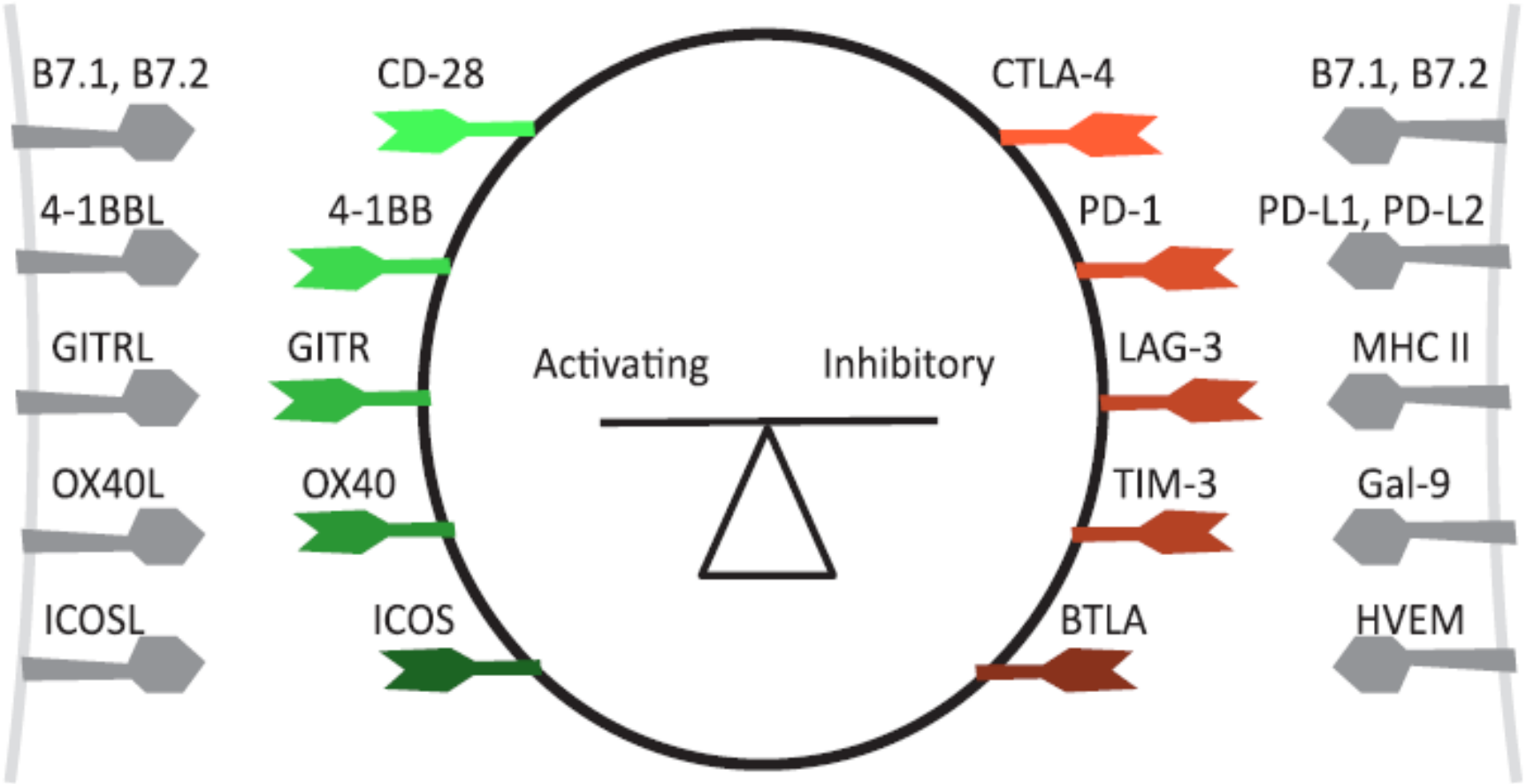
Immunotherapy

"Targeted" Therapy



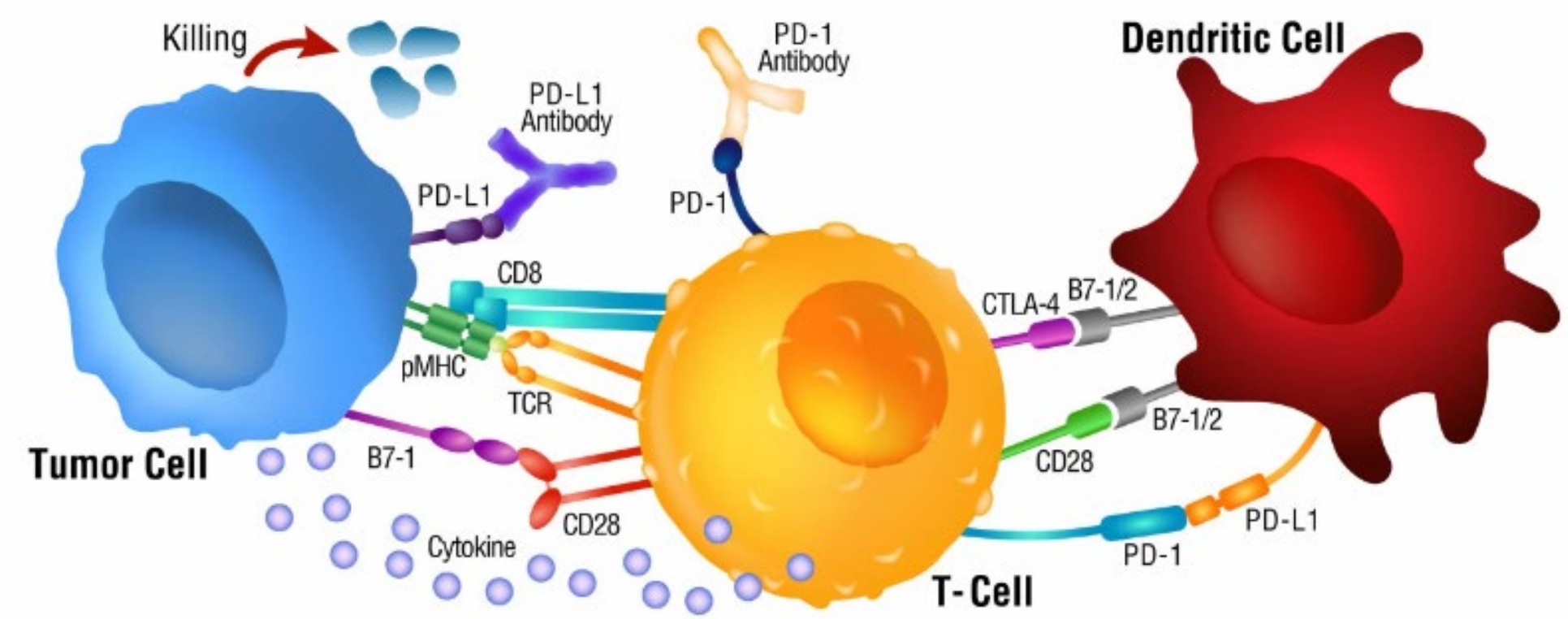
Optimization of the Immune Response: **Regulation of T cells**

Optimizing T-cell **Regulation** with Immune Checkpoint Inhibitors



Callahan MK, et al. Clinic Dermatology 2013;31:191-99

Strategies to Optimize Immune Response: **Immune Checkpoint Inhibitors**



How many immune check point inhibitors are currently marketed in the US for cancer treatment.

Immune Checkpoint Inhibitors (ICI) Marketed in the USA (August 2024)

Cytotoxic T Lymphocyte

- Ipilimumab
- Tremelimumab

PD-1 inhibition:

- Nivolumab
- Pembrolizumab
- Cemiplimab
- Dostarlimab
- Retifanlimab
- **Toripalimab (FDA approved 10/23) → current indication nasopharyngeal cancer**

PD-L1 inhibition:

- Atezolizumab
- Avelumab
- Durvalumab

Combination LAG-3 and PD1:

- Relatlimab (LAG-3 inhibitor) + nivolumab (PD-1 inhibitor)

Monoclonal Antibodies in Clinical Practice

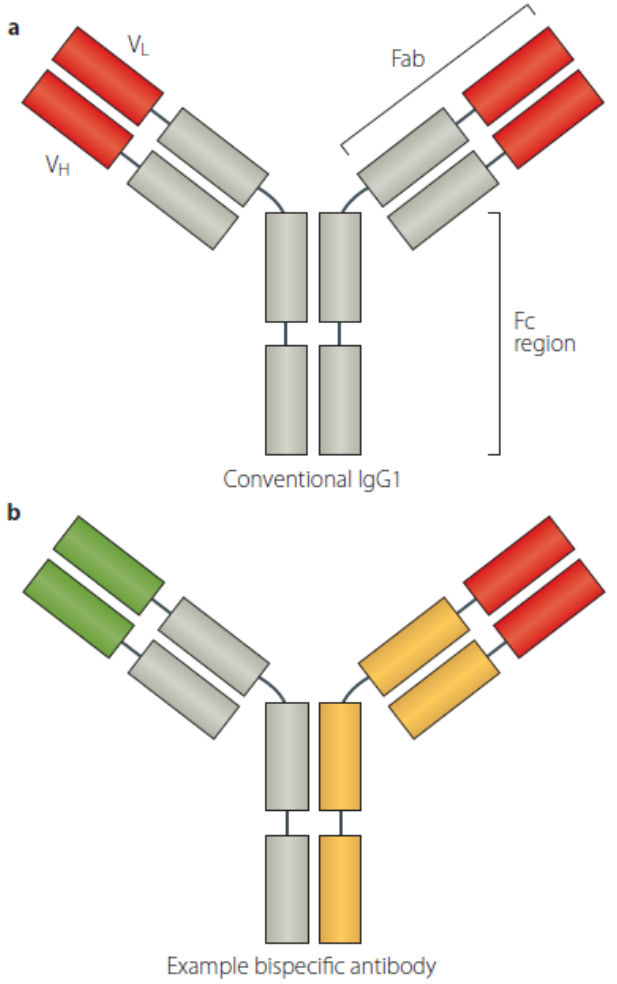
- Unconjugated monoclonal antibody
- Conjugated monoclonal antibody
- Bispecific antibody → bispecific agents

Bispecific Agents in Cancer

- **Bispecific agent** is an **artificial protein** that can simultaneously bind to **two different types of antigens** or **two different epitopes of the same antigen**.

- **Structural types:**
  - Bispecific monoclonal antibody
  - Bispecific proteins

- Potential **mechanisms of action of select agents:**
  - Forcing association of protein complexes
  - Interfering with receptor signaling
  - Inactivating signal ligands
  - Recruiting and activating of immune cells



Bispecific Agents in Cancer: **Current Strategies** in Oncology and Hematology

- Forcing of associated protein complexes

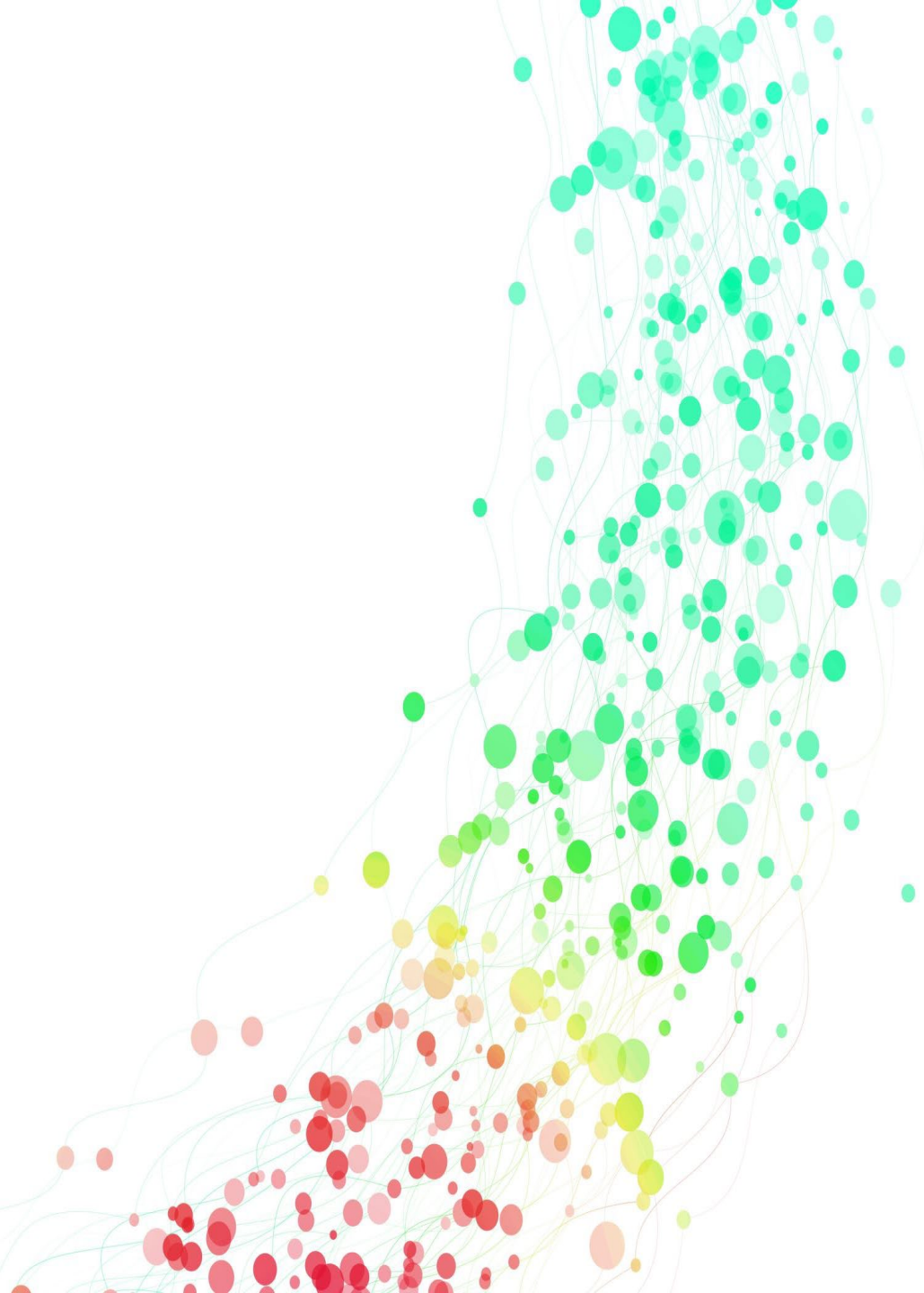
  Example: Emicizumab in hemophilia a

- Interfering with receptor signaling

  Example: Amivantamab in NSCLC with EGFR Exon 20 insertion mutations

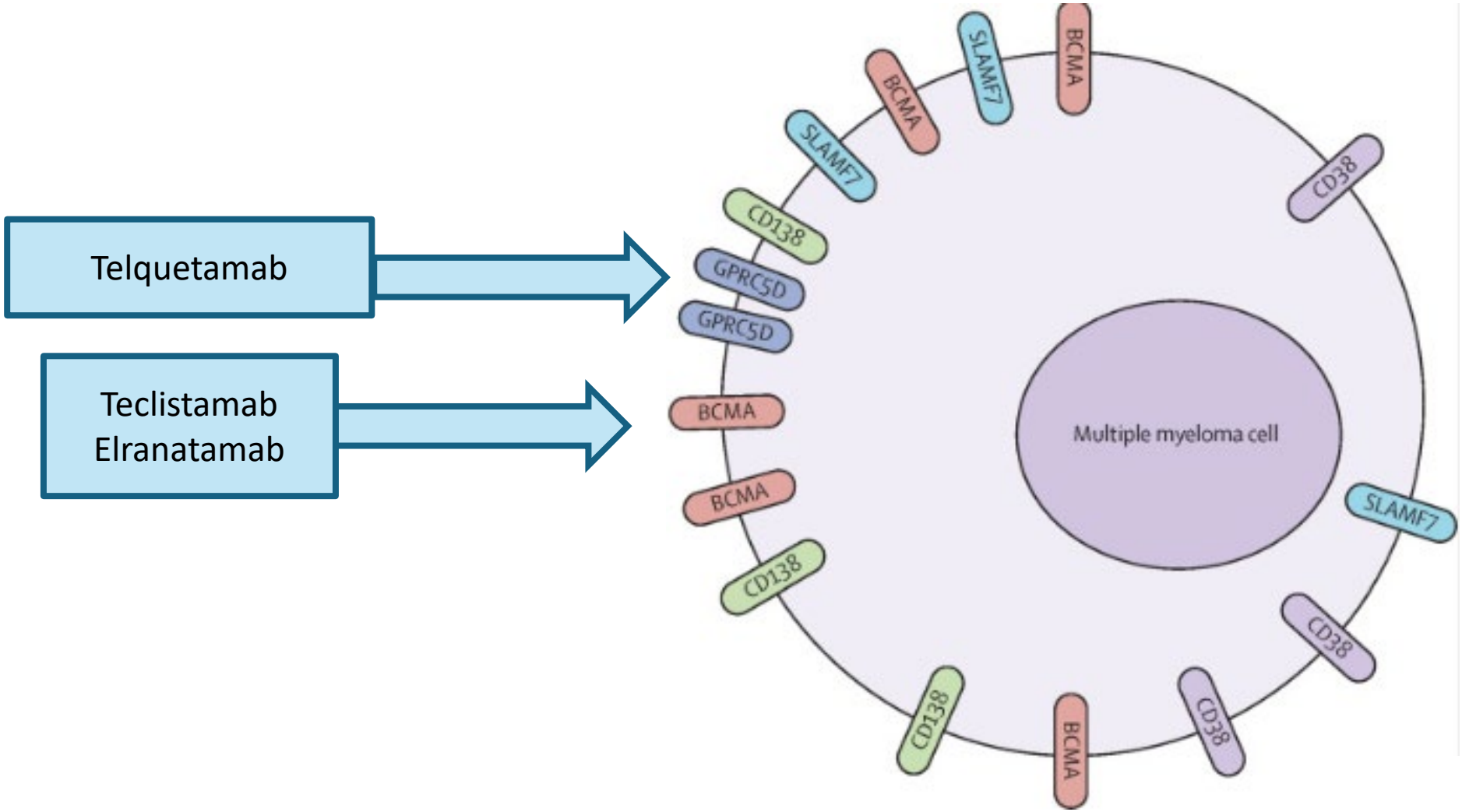
- Recruiting and activating immune cells

  Example: Bispecific T cell engagers



Optimization of the Immune Response: **Recruitment of T cells**

Bispecific T Cell Engagers: Targets in Multiple Myeloma

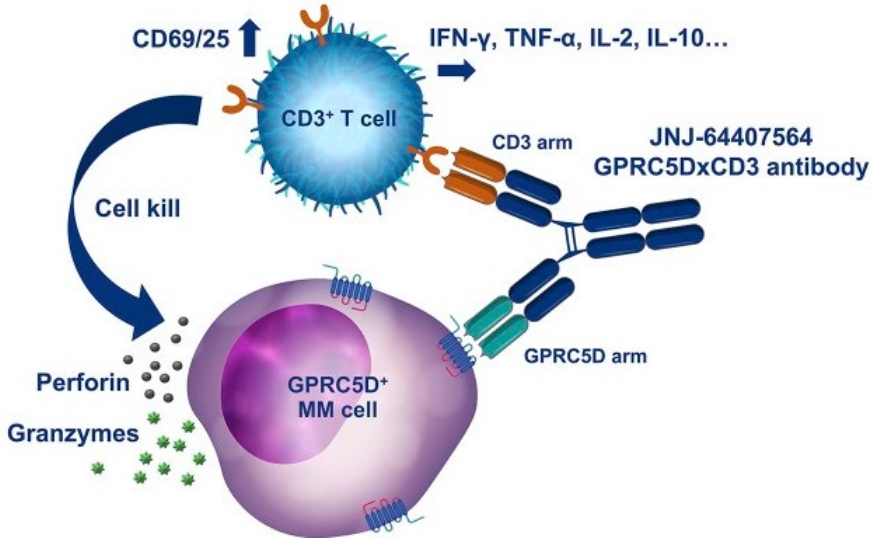


van de Donk, Niels WCJ, et al. Lancet Hematol 2021;8(6):e446-e461.

Talquetamab-tgvs
(approved in August 2023)

Bispecific T-cell engaging antibody that binds to:

- CD3 receptor on T-cells
- **GPRC5D (G protein-coupled receptor, family C, group 5, member D)**



Current indication:

Treatment of adult patients with **relapsed or refractory myeloma** who have received **at least four prior lines of therapy** including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Pillarisetti K, et al. Blood 2020. Talquetamab package insert accessed 7.24.2024.

Talquetamab: Refractory or Relapsed Myeloma

Method:

- **Phase 1, open-label, multicenter study**
  - Dose-escalation (part 1) and dose-expansion (part 2)
- Patients with heavily pretreated relapsed or refractory myeloma.
- Evaluated intravenous weekly, intravenous every other week, subcutaneously weekly, subcutaneous every other week, or subcutaneous monthly

Treatment:

  - Talquetamab initiated at dose of 0.5 mcg/kg in part 1
  - **Step-up dosing** used to mitigate CRS.
  - **Pre-treatment** with glucocorticoid, antihistamine, acetaminophen required during all step-up doses and prior to initial full dose.

Objectives:

- Primary endpoint: frequency and type of DLSE (part 1), AE, laboratory abnormalities
- Secondary endpoint included: Response, pharmacokinetics, pharmacodynamics, immunogenicity.

Results:

- Patients that had received 405 mcg every week: RR 70%
- Patients that had received 800 mcg every other week: RR 64%

Chari A, et al. NEJM 2022:387:2232. **(MONUMENTAL)**

Talquetamab: Toxicities in Refractory / Relapsed Myeloma

Talquetamab **(all doses intravenous)** N=102

Event	Any Grade	Grade ≥ 3
Hematologic		
anemia	58%	33%
neutropenia	47%	26%
lymphopenia	52%	47%
thrombocytopenia	35%	13%
Cytokine release syndrome	49%	5%
Skin-related events	24%	0
Dysquesia	37%	NA
Fatigue	36%	1%
Nail-related events	20%	0
Headache	34%	2%

Chari A et al. *N Engl J Med*. 2022;387(24):2232-2244.

Talquetamab: Toxicities in Refractory / Relapsed Myeloma

Talquetamab (**405 mcg weekly subcutaneous**) N = 30

Event	Any Grade	Grade ≥ 3
Hematologic		
anemia	60%	30%
neutropenia	67%	60%
lymphopenia	40%	40%
thrombocytopenia	37%	23%
Cytokine release syndrome	77%	3%
Skin-related events	67%	0
Dysgeusia	63%	NA
Fatigue	33%	3%
Nail-related events	57%	0
Pyrexia	33%	0

Chari A et al. *N Engl J Med*. 2022;387(24):2232-2244.

Talquetamab-tgvs

Classification:

- Bispecific GPRC5D and CD3 T-cell engager

Indication:

- Treatment of adult patients with relapsed or refractory multiple myeloma who have received **at least four prior lines of therapy** including a proteasome inhibitor, IMID, anti-CD38 monoclonal antibody.

Dose is determined by schedule (weekly or biweekly):

- The table below outlines the recommended **weekly** schedule

Dose Schedule	Day	Dose	
Step-up dosing	Day 1	Step-up dose 1	0.01 mg/kg SC
	Day 4	Step-up dose 2	0.06 mg/kg SC
	Day 7	First treatment dose	0.4 mg/kg SC
Weekly dosing	One week post first treatment dose, then weekly thereafter	Subsequent treatment doses	0.4 mg/kg SC

Talquetamab package insert. Accessed 9.5.2023

Talquetamab-tgvs: Targeting **GPRC5D**

Talquetamab-Induced Grover's Disease

Mindy Kresch BS,[a] Sophie Guénin MSc,[a,b] Adnan Mubasher MD,[b] Emily Elbogen PA,[b] Mark Lebwohl MD[b]

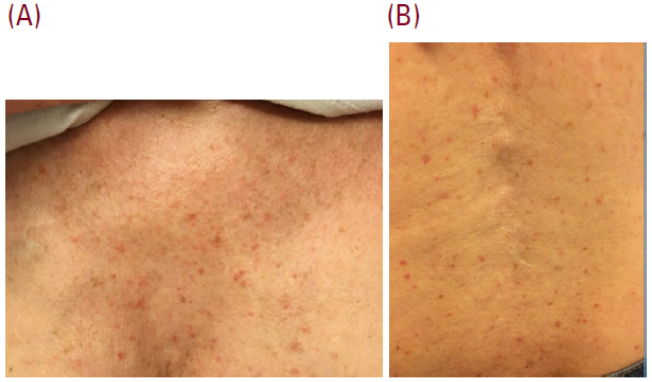
[a]New York Medical College, Valhalla, NY

[b]The Kimberly and Eric J. Waldman Department of Dermatology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY

INTRODUCTION

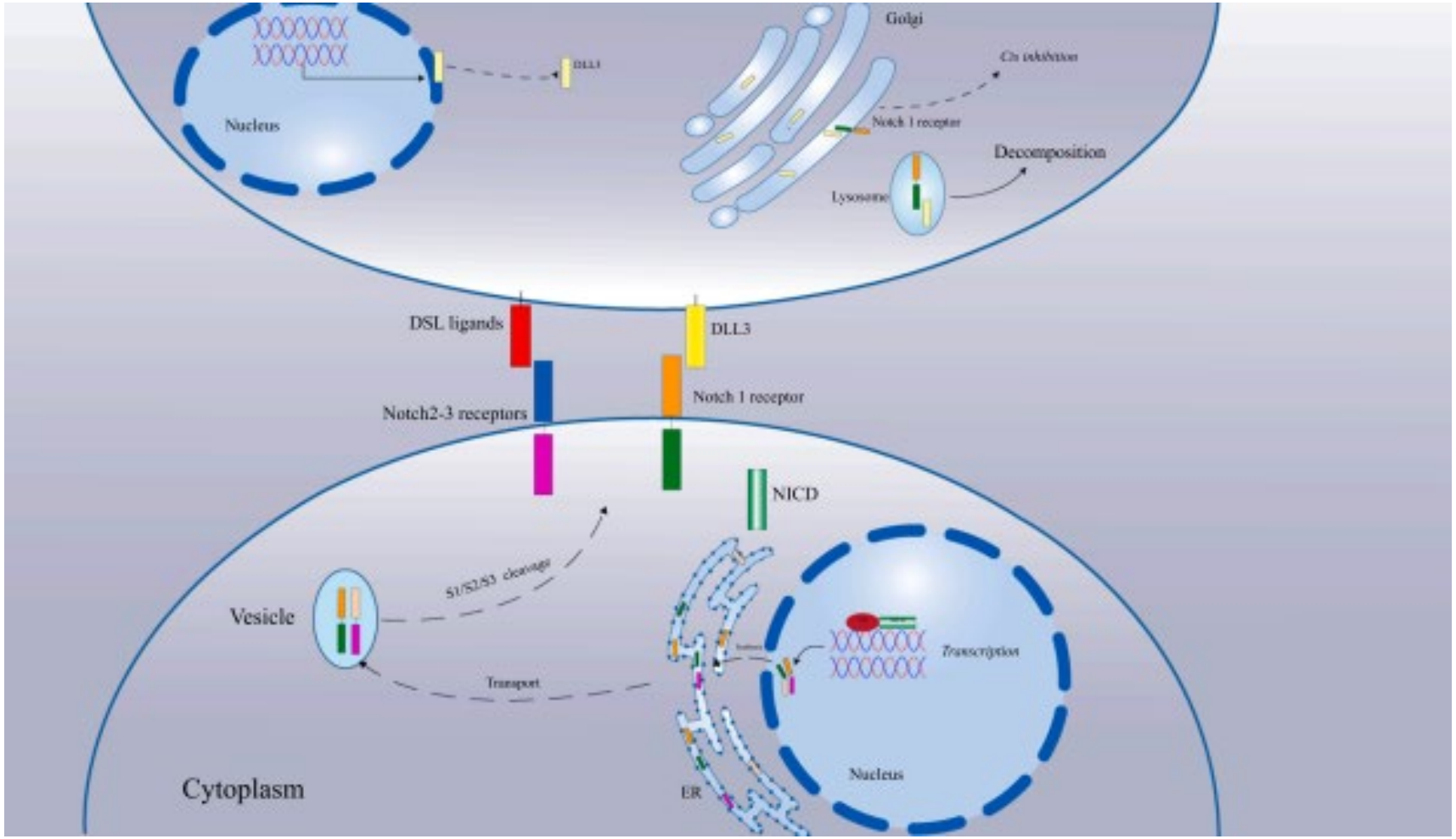
First reported in 1970, transient acantholytic dermatosis (TAD), also known as Grover disease (GD), is a rare transient dermatosis of largely unknown etiology.[1] It commonly occurs as grouped pruritic, papulovesicular skin eruptions on the trunk of men over the age of 40.[1] The histopathologic hallmark of the disease is acantholysis which is frequently accompanied by varying degrees of dyskeratosis and perivascular lymphohistiocytic infiltrate.[2,3] While the pathophysiology of disease is largely unknown, it has been reported to be associated with triggers such as heat, sweat, sunlight, medications, and neoplasms, specifically hematological malignancies.[4,5] GD also appears to be associated with states of immune modulation that occur in solid organ transplantation or in patients treated withinterleukin-4, cetuximab, vemurafenib,

FIGURE 1. Grover's Disease Induced by Talquetamab treatment in 74-year-old female. (A) Papular, non-pruritic rash on patient sternal chest. (B) Diffusely distributed papular rash on patient mid- and lumbar back.



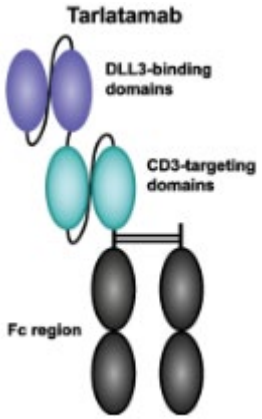
Kresch M, et al. J Drugs Dermatol 2023;22(8):828-9.

Targeting DLL3 in Small Cell Lung Cancer



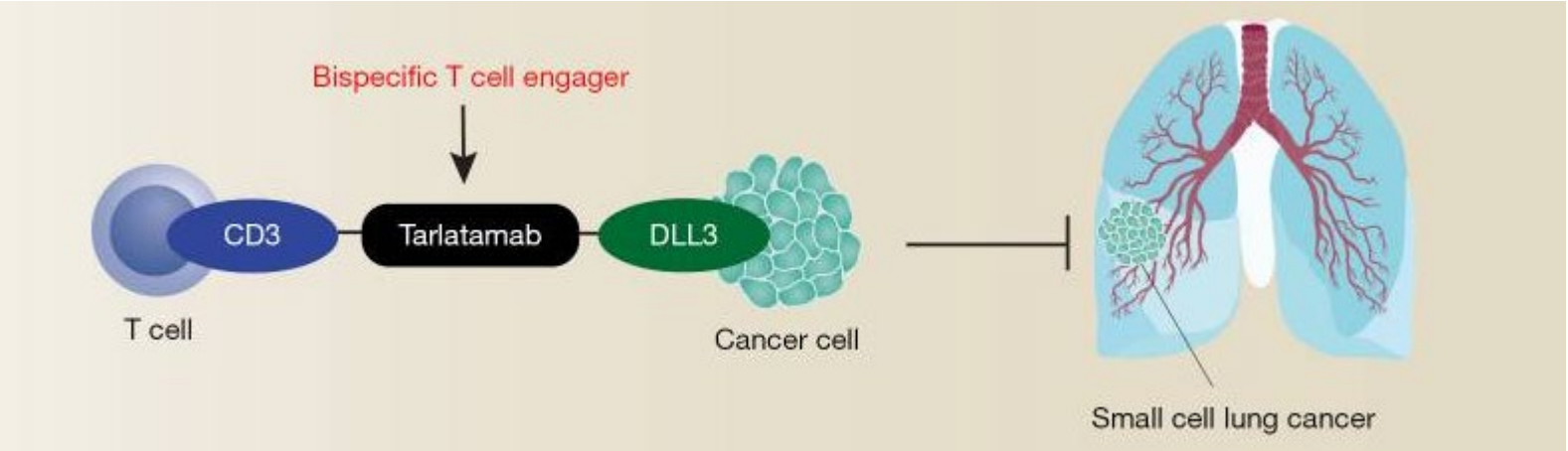
Yang W, et al. Critical Rev Oncol Hematol 2023;191:104136.

Tarlatamab-dlle: Bispecific T Cell Engager
(approved in May 2024)



Bispecific protein that targets both:

- CD3 on T cells
- DLL3 (delta-like ligand 3)



Tang D, Kang R. Transl Lung Cancer Res 2023

Tarlatamab: Refractory or Relapsed Extensive Stage Small Cell Lung Cancer

Method:

- Phase 2, open-label, international trial
- Patients with previously treated small-cell lung cancer
- Three-part trial:
  - **Part 1:** Dose comparison assessment randomly assigned 1:1 ration to receive tarlatamab10 mg or 100 mg IV
  - **Part 2**: Patients enrolled only at selected dose of part I → until total of 100 patients (part I and 2) enrolled at selected dose
  - **Part 3**: evaluation of safety of tarlatamab when inpatient monitoring during cycle 1 was reduced from 48 to 24 hours after the infusion.

Treatment:

- Step dose of tarlatamab 1 mg IV on cycle 1, day 1
- Target dose (either 10 mg or 100 mg) on cycle 1, day 8, and cycle 1, day 15
- Target dose every 14 days of a 28-day cycle (2 doses per cycle)

Objectives:

- Primary endpoint: Objective response (complete and partial)
- Secondary endpoint: DOR, disease control, duration disease control, PFS, OS, AE, pharmacokinetics, immunologic response.

Ahn MJ, et al. NEJM 2023:389:2063. **(DeLLphi-301)**

Tarlatamab: Refractory or Relapsed Extensive Stage Small Cell Lung Cancer

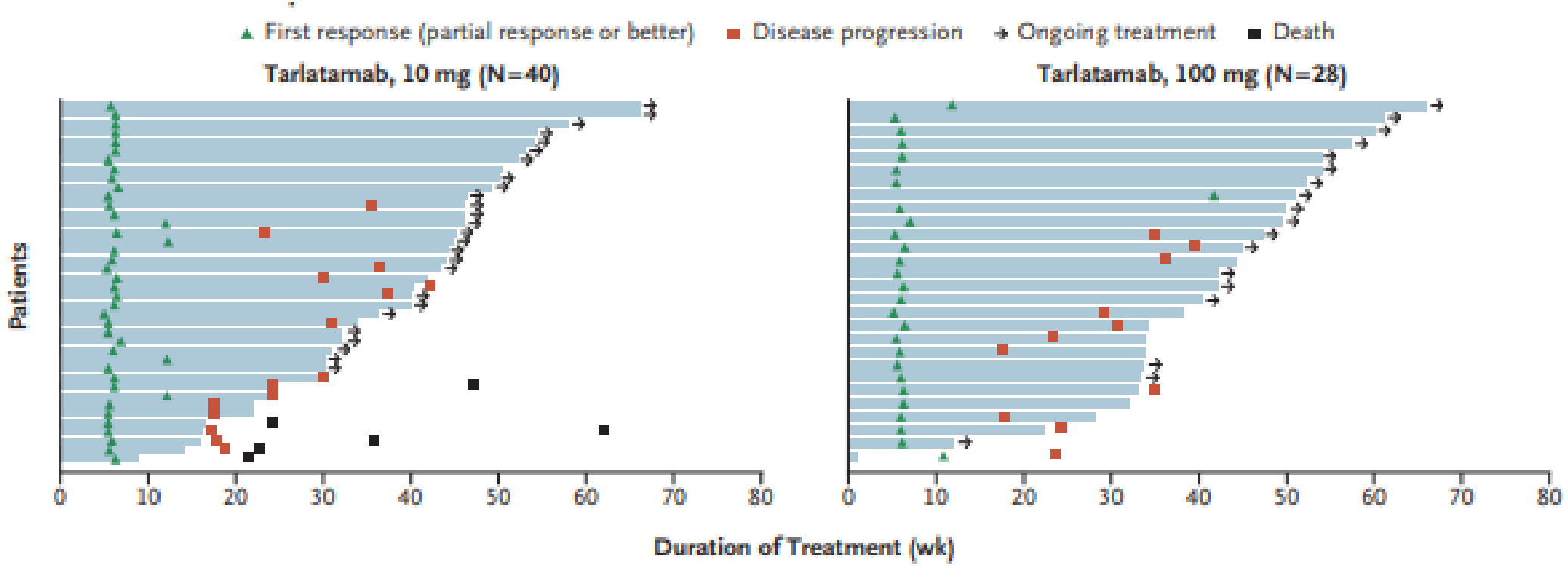
Treatment Response (Phase 2 DeLLphi-301)

Variable	Tarlatamab, 10 mg (N=100)	Tarlatamab, 100 mg (N=88)
ORR	40%	32%
Median DOR	NE (5.9 – NE)	NE (6.6 – NE)
Median PFS	4.9 months	3.9 months
Disease Control	70%	63%

Ahn MJ, et al. NEJM 2023:389:2063. **(DeLLphi-301)**

Tarlatamab: Refractory or Relapsed Extensive Stage Small Cell Lung Cancer

Onset and Duration of Response



Ahn MJ, et al. NEJM 2023:389:2063. **(DeLLphi-301)**

Tarlatamab: Refractory or Relapsed Extensive Stage Small Cell Lung Cancer

Adverse Events

Adverse Event	Tarlatamab 10 mg		Tarlatamab 100 mg Part 1 (N= 87)
	Part 1 and 2 (N=99)	Part 3, reduced monitoring (N=34)	
CRS	49%	56%	61%
ICANS	7%	12%	28%
Neutropenia	18%	12%	28%
Event leading to discontinuation during treatment	7%	9%	7%

Ahn MJ, et al. NEJM 2023:389:2063. **(DeLLphi-301)**

Tarlatamab-dlle

Classification:

- Bispecific DLL3 –directed CD3 T-cell engager

Indication:

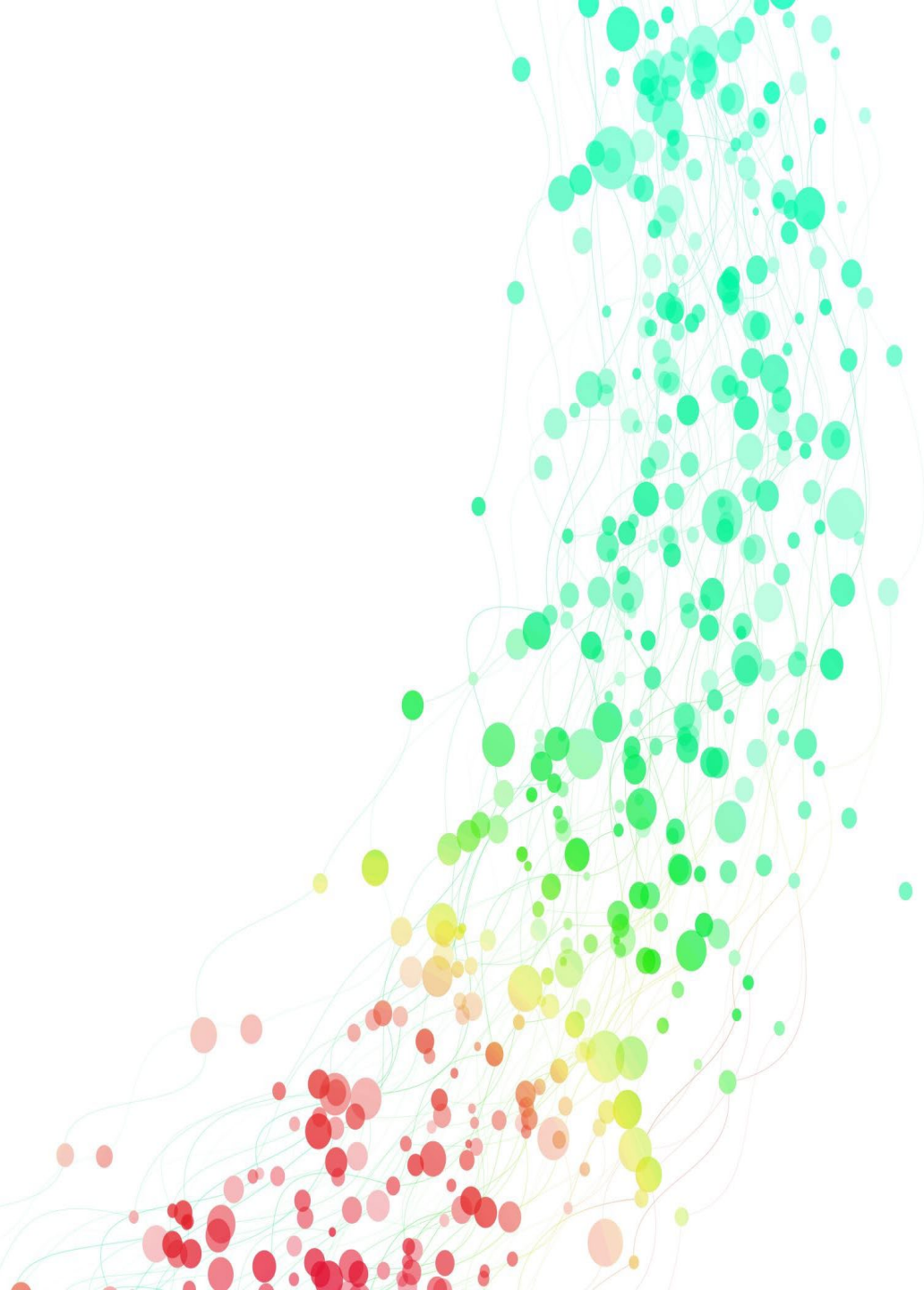
- Treatment of adults with **extensive-stage small cell lung cancer** with disease progression on or after platinum-based chemotherapy.
- Approved under accelerated approval based on results of the DeLLphi-301 clinical trial.

Dose:

- Cycle 1, Day 1: tarlatamab 1 mg IV over 1 hour
- Cycle 1, Day 8 and 15: tarlatamab 10 mg IV over 1 hour
- Then tarlatamab 10 mg IV over 1 hour q 14 days

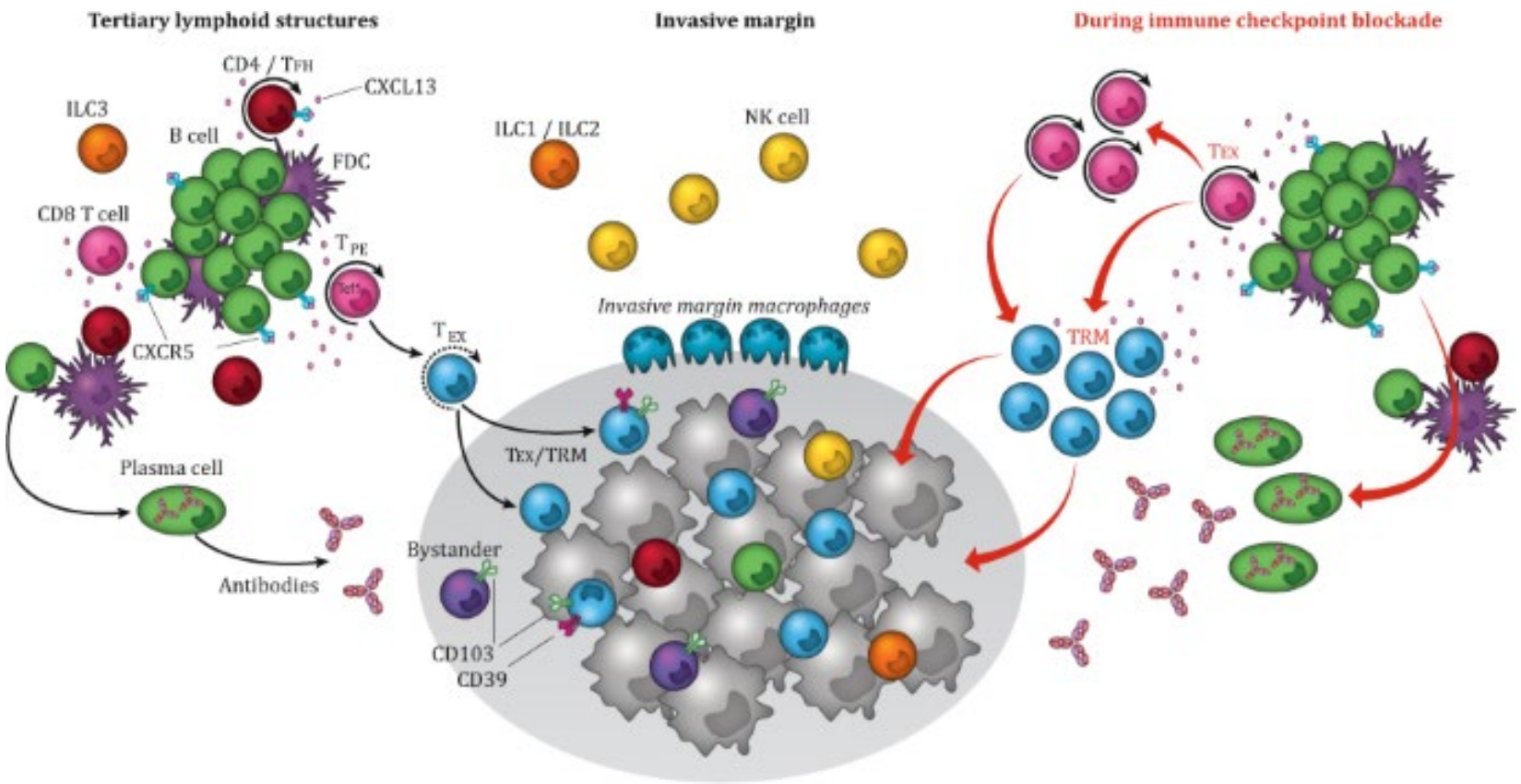
Warnings:

- **Boxed Warning: cytokine release syndrome (CRS) and n**eurologic toxicity (including ICANS)
- Cytopenia
- Hepatotoxicity
- Hypersensitivities
- Embryo-fetal toxicity



Optimizing the Immune Response to Cancer: **Adoptive Cellular Immunotherapy**

Tumor-Infiltrating Lymphocytes (TIL)



Paijens ST, et al. Cellular & Molecular Immunology 2021;18(4):842-859.

Lifileucel

(approved February 16, 2024)

Classification:

- Tumor-derived autologous T cell immunotherapy

Indication:

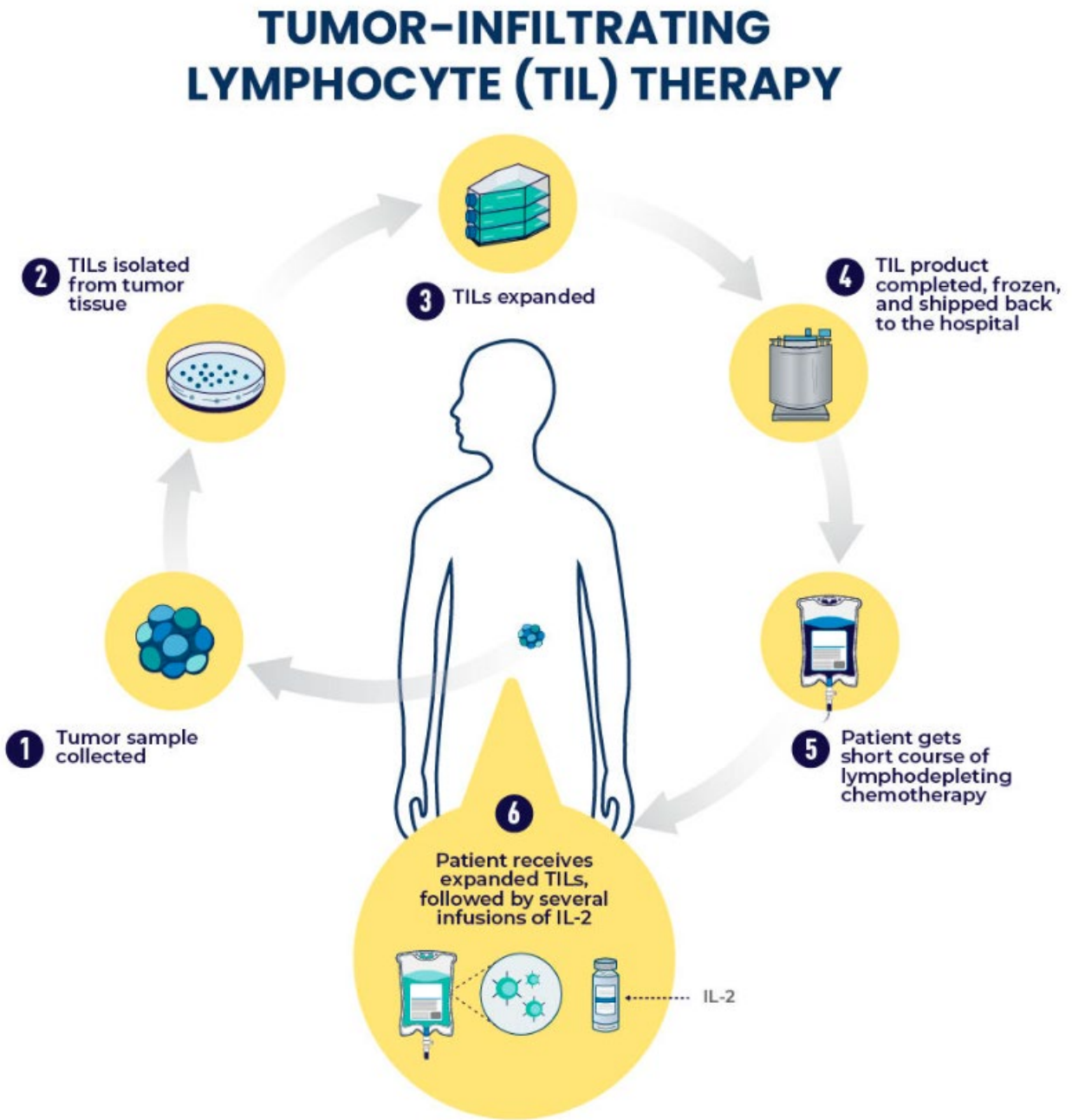
- Adults with unresectable or metastatic melanoma previously treated with PD-1 inhibitor, and if BRAF V600 +, a BRAF inhibitor ± MEK inhibitor.

Strategy*:

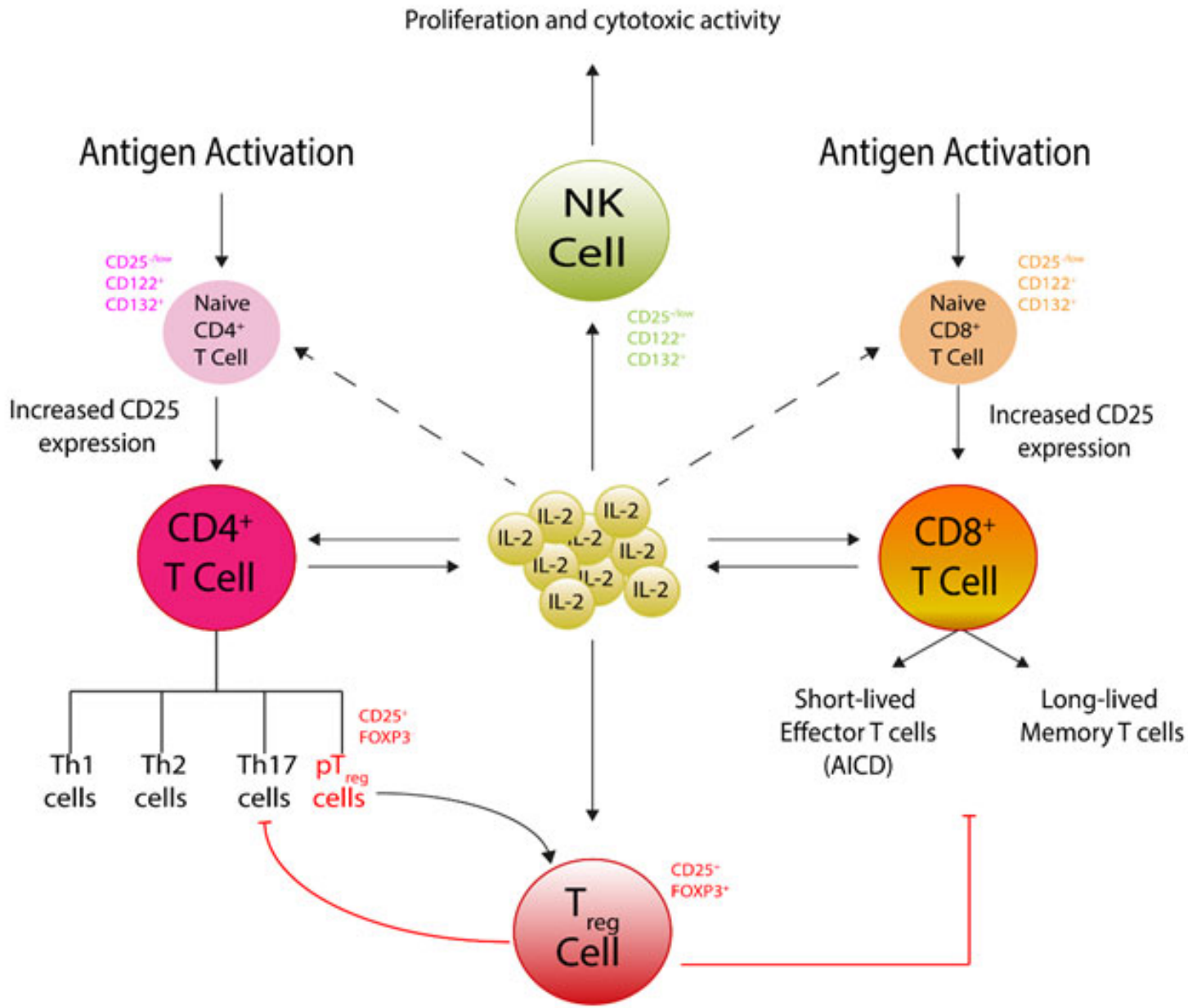
- Harvesting T cells that have infiltrated patient's tumor
- Generation of tumor infiltrating lymphocytes (TILs)
- Lymphodepletion (cyclophosphamide and fludarabine)
- Lifileucel (recommended lifileucel dose is 7.5×10^9 to 72×10^9 viable cells)
- Aldesleukin (support cell expansion in vivo)

* Administer lifileucel in an inpatient hospital setting with an intensive care facility.

Lifileucel package insert.2.2024



https://www.cancer.gov/news-events/cancer-currents-blog/2024/fda-amtagvi-til-therapy-melanoma


Proliferation and cytotoxic activity
Antigen Activation
Antigen Activation
NK Cell
CD25-/low CD122+ CD132+
Naive CD4+ T Cell
CD25-/low CD122+ CD132+
Naive CD8+ T Cell
CD25-low CD122+ CD132+
Increased CD25 expression
Increased CD25 expression
CD4+ T Cell
IL-2
CD8+ T Cell
CD25+ FOXP3
Th1 cells
Th2 cells
Th17 cells
pTreg cells
Short-lived Effector T cells (AICD)
Long-lived Memory T cells
CD25+ FOXP3+
Treg Cell

Capillary Leak Syndrome: Clinical Sequalae

Decrease in intravascular blood volume:

- Decrease blood pressure
- Increase heart rate
- Decrease perfusion of tissues and organs resulting in the clinical sequelae including, but not limited to,:
  - ↑ creatinine
  - ↑ LFT (transaminases and bili)
  - ↓ absorption from skin and GI track

Increase in extravascular fluid:

- Edema
- Weight gain (fluid)

Lifileucel: A Tumor-Infiltrating Lymphocyte Therapy

Methods:

- Phase 3, multicenter, open-label trial in patients with unresectable stage IIIC or IV melanoma randomized to **TILs vs ipilimumab**

Treatment arms:

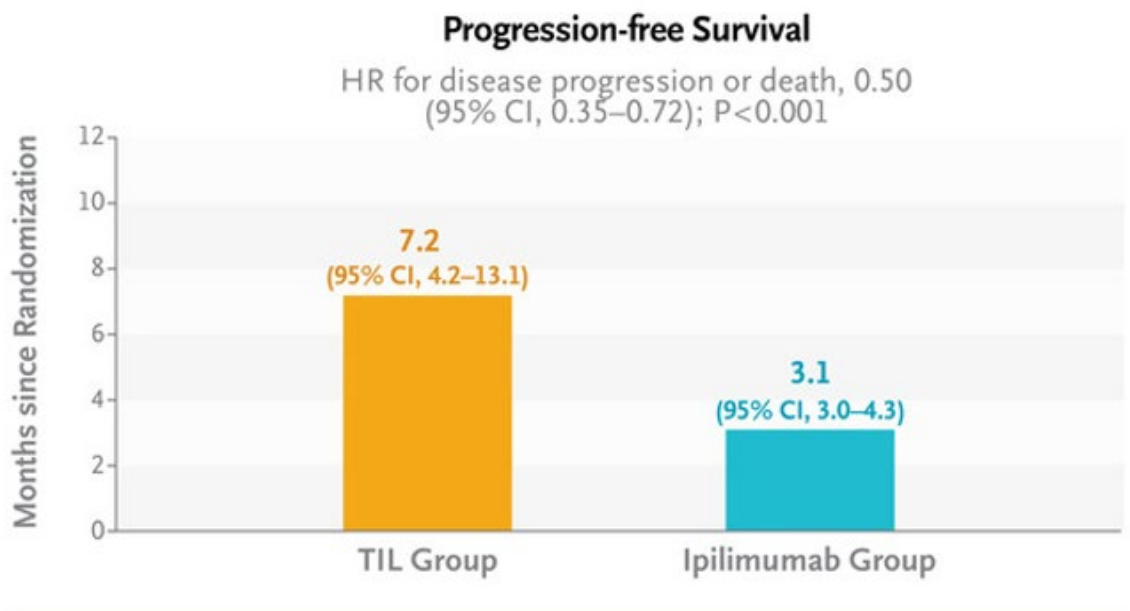
- TILS: nonmyeloablative, lymphodepleting chemotherapy (Flu/Cy) → TILs (minimum of 5 x 10^9) → high-dose aldesleukin (interleukin 2 or IL2)
- ICI: Ipilimumab 3 mg/kg IV q 3 weeks for a maximum of 4 doses

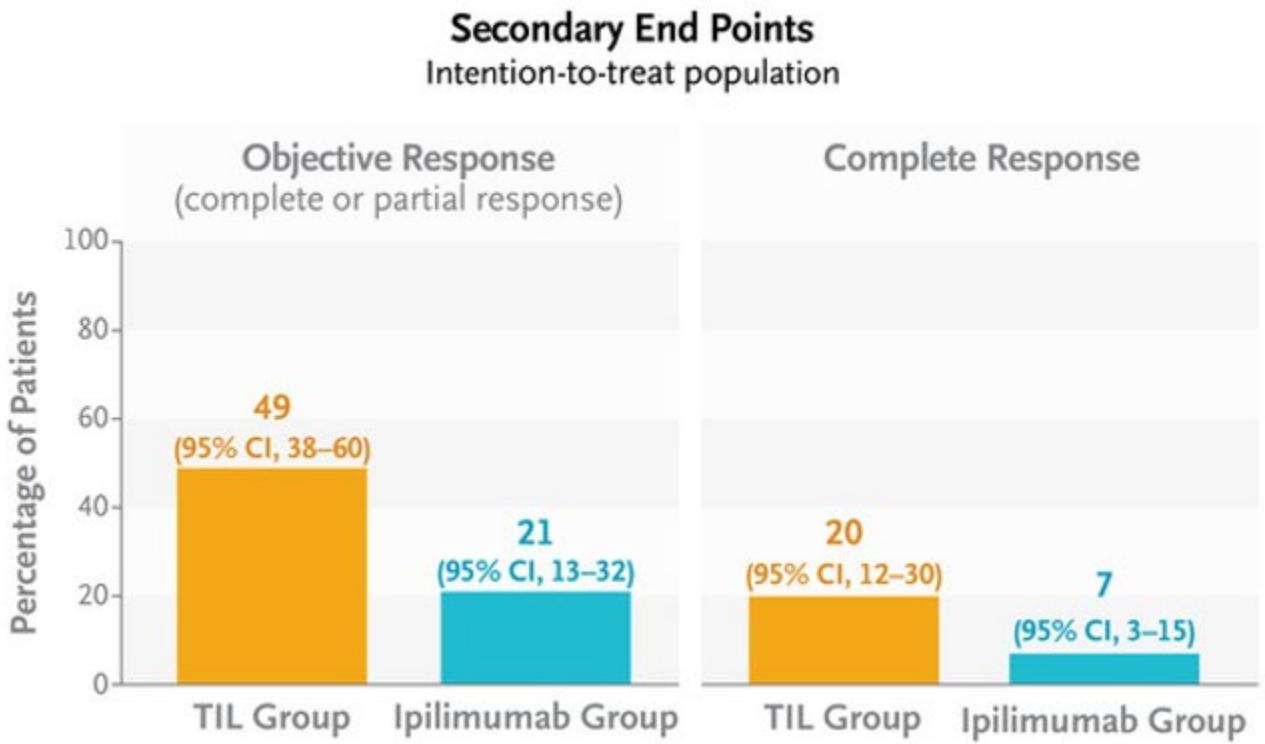
Endpoints:

- Primary endpoint: progression free survival
- Secondary endpoints: ORR, CR

Rohaan MW, et al. NEJM 2022;387(23):2113-2125.

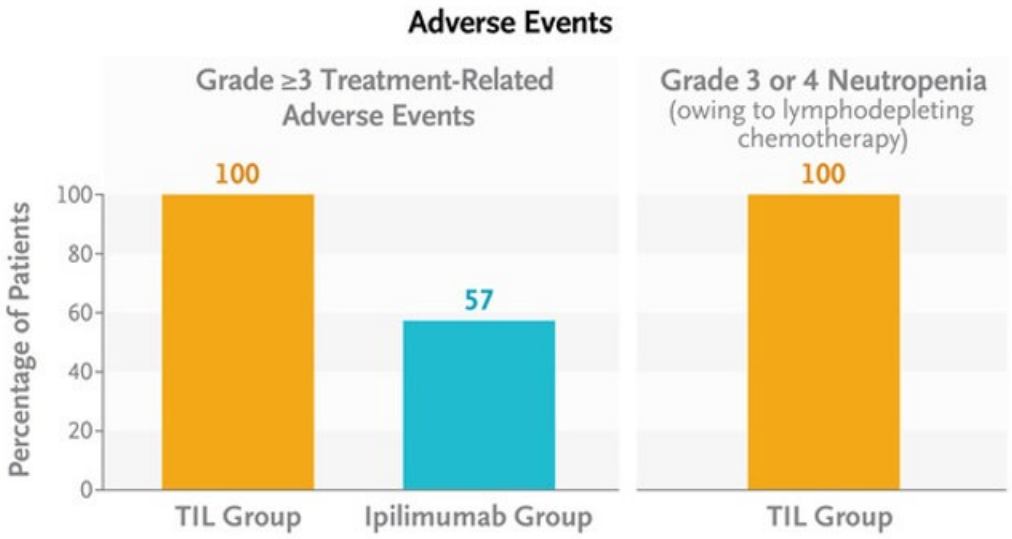
Lifileucel: Response in Melanoma





Rohaan MW, et al. NEJM 2022;387(23):2113-2125.

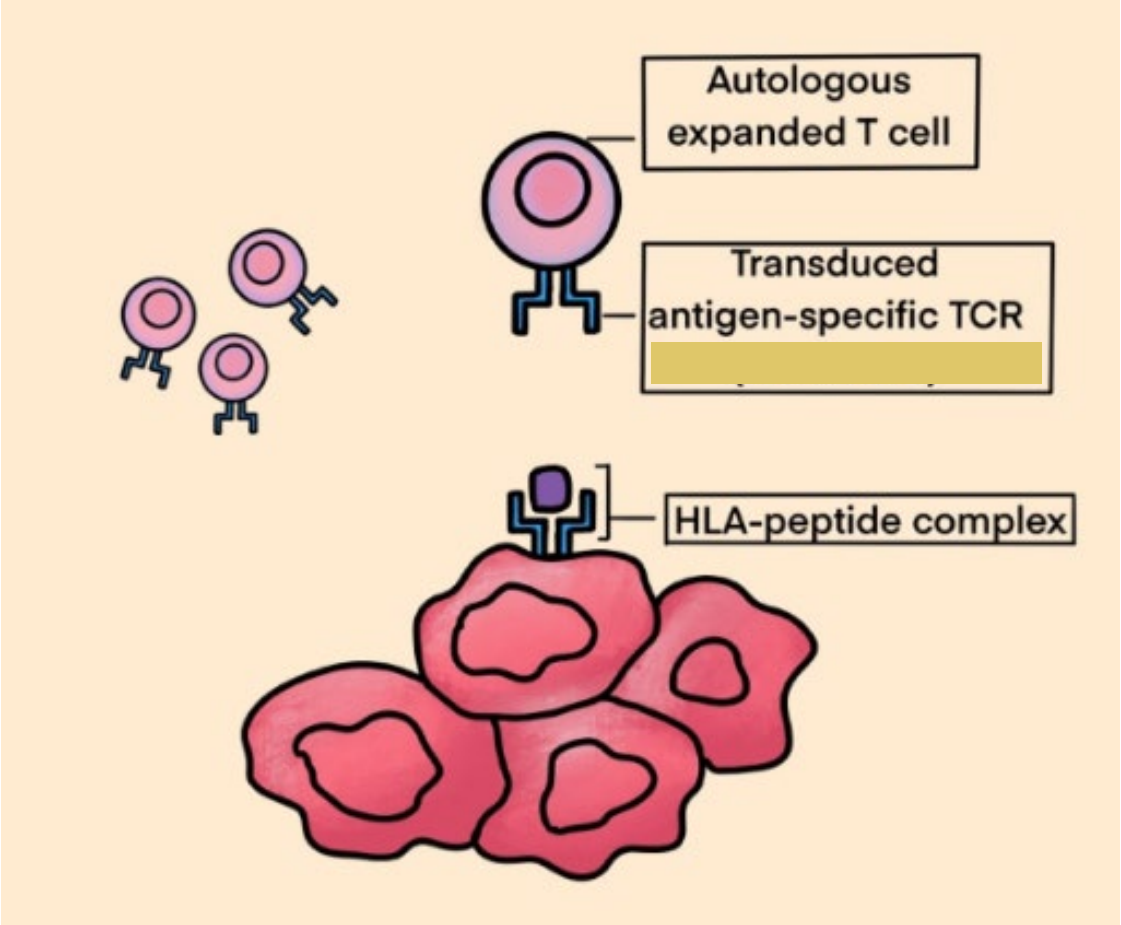
Lifileucel: Toxicity in Melanoma



- Myelosuppression in patient treated with TILs was attributed to lymphodepleting chemotherapy.
- **Capillary leak syndrome (CLS) associated with IL2 seen in 30%.**
- Autoimmune toxicities seen in TILs group included:
  - Skin hypopigmentation (11%)
  - Uveitis (8%)
  - Hearing impairment (4%)

Rohaan MW, et al. NEJM 2022;387(23):2113-2125.

Engineered **T Cell Receptor (TCR)** Therapy

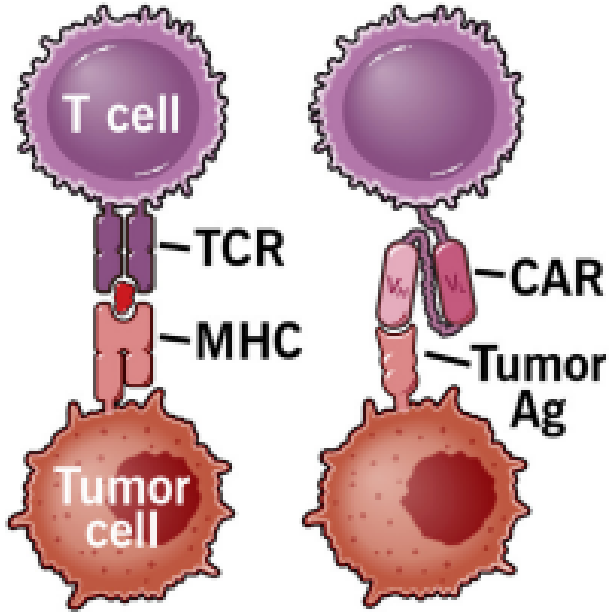


Dalal S, et al. Int J Mol Sci 2024;25(2)

Afamitresgene autoleucel

(approved August 2, 2024)

- Genetically modified T cell immunotherapy
- T cells are collected from the patient's blood → modified to express T cell receptor that targets the **MAGE-A4 protein in synovial sarcoma cancer cells.**



Ligon JA, et al. Transplantation and Cellular Therapy 2024

Afamitresgene autoleucel

Classification:

- A melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T cell immunotherapy.

Indication:

- Treatment of adults with unresectable or metastatic synovial sarcoma
  - who have received prior chemotherapy
  - Are positive for HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P or HLA-A*02:06P
  - Whose tumors express MAGE-A4 antigen

Strategy:

- Leukapheresis → T cells for afamitresgene autoleucel manufacturing
  - CD4+ and CD8+ T cells were transduced with lentiviral vector to express affinity enhanced TCR recognizing the MAGE-A4→ expansion
- Lymphodepletion (fludarabine, cyclophosphamide)
- Afamitresgene autoleucel (2.68 $x10^9$ – 10 x 10^9 MAGE-A4 TCR positive T cells) infusion

Afamitresgene autoleucel

Methods:

- Phase 2 trial (SPEARHEAD), including 3 cohorts
- **Cohort 1:** patients with HLA-A*02 with metastatic or unresectable synovial sarcoma or myxoid round cell liposarcoma expressing MAGE-A4 and who had received at least one previous line of chemotherapy.

Treatment:

- Single dose of afami-cel after lymphodepletion

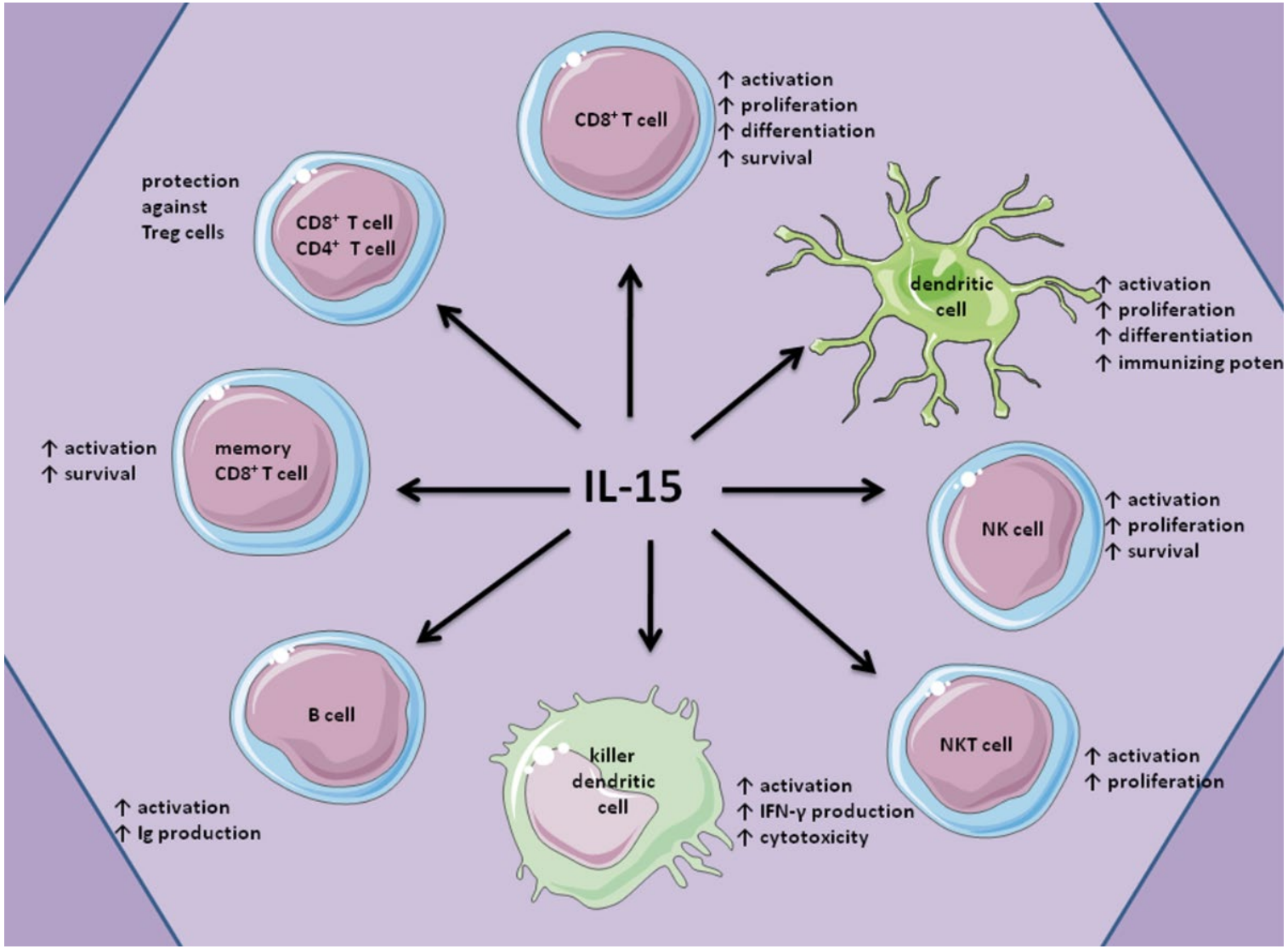
Endpoints / Results (Cohort 1):

- ORR → 37% (n=52)
  - ORR in patients with synovial sarcoma (n=44) → 39%
  - ORR in patients with myxoid round cell liposarcoma (n=8) → 25%
- Adverse events:
  - CRS → 71 %
  - Cytopenia associated with lymphodepletion

Cohort 1: D'Angelo SP, et al. Lancet 2024;403:1460-71.

Optimizing the Immune Response to Cancer: **Cytokines**

Immunotherapy: Optimizing **Interleukin 15**



Jakobisiak M, et al. Cytokine & Growth Factor Reviews 2011; 22:99-108.

Nogapendekin alfa inbakicept (NAI)

Mechanism:

- Interleukin-15 receptor **agonist → "super agonist"**
- Fusion protein of human 1L 15 variant bound to a dimeric human IL-15Rα human IgG Fc.
- May act synergistically with BCG
- Intravesical administration **ONLY**

Indication:

- Used in combination with BCG for the treatment of adult patients with **BCG-unresponsive non-muscle invasive bladder cancer** with carcinoma in situ with or without papillary tumors.

Note: also known as N-803 if you are looking in the literature

Nogapendekin alfa inbakicept package insert. Accessed 5.14.2024

Nogapendekin alfa inbakicept (NAI)
(approved April 2024)

Methods:

- Phase 2/3 study (QUILT-3.032)
- Single-arm, multicenter trial of patients with BCG-unresponsive, high risk non-muscle invasive bladder cancer with carcinoma in situ with or without Ta/T1 papillary disease following resection.

Treatment:

- Nogapendekin alfa inbakicept induction **via intravesical instillation with BCG** → maintenance for up to 37 months. (Cohort A, Cohort B)
- NAI alone (Cohort C)

Endpoints / Results (Cohort A):

- CR rate: 71% (N=82 patients)
- Median DOR 26.6 months

Chamie K, et al. NEJM Evid 2022; 2(1)

Nogapendekin alfa inbakicept
(approved April 2024)

Indication:

- In combination with BCG in the treatment of adults with BCG-unresponsive nonmuscle invasive bladder cancer with carcinoma in situ with or without papillary tumors.

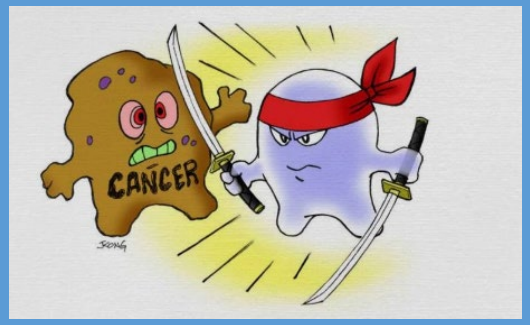
Treatment:

- Induction: NAI 400 mcg administered intravesically with BCG once a week for 6 weeks. (A second course of induction may be administered if CR in not achieved at month 3)
- Maintenance: NAI 400 mcg administered intravesically with BCG once a week for 3 weeks at months 4, 7, 10, 13, and 19.

Nogapendekin alfa inbakicept package insert. Accessed 5.20.2024

Drug Therapy for Cancer: 2024

Chemotherapy



Immunotherapy

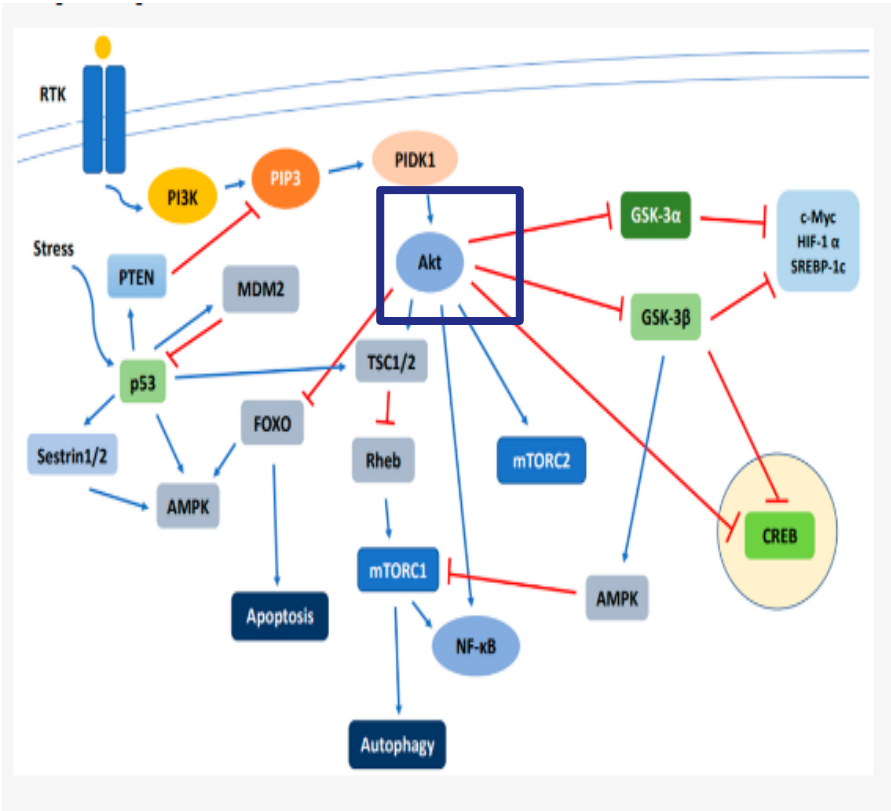
"Targeted" Therapy

Capivasertib
(approved November 2023)

Mechanism of action:

- Small molecule **inhibitor of all three AKT isoforms (AKT1, AKT2, AKT3)**
- Inhibits phosphorylation of AKT downstream substrates

* AKT activation in cancer may be the result of upstream signaling pathways, mutations in AKT1, loss of PTEN function, and/or mutation is PIK3CA.



Sun EJ, et al. Biomedicines 2021;9(11)

Capivasertib: HR+ Advanced Breast Cancer

Capitello-291

Methods:

- Phase 3 randomized, double-blind trial in individuals with ER+/HER2- advanced breast cancer **who have had a relapse or disease progression during or after therapy with aromatase inhibitor.**
  - Patient could have received CDK4/6 inhibitor therapy

Treatment:

- **Capivasertib + fulvestrant**
  - Capivasertib 400 mg PO BID x 4 days → 3 days off treatment each week over 28-day cycle
  - Fulvestrant 500 mg IM q 14 days x 3, then q 28 days
- **Placebo + fulvestrant**

Endpoints:

- Investigator-assessed PFS in overall population
- Investigator-assessed PFS in pts with AKT pathway-altered tumors (PIK3CA, AKT1, or PTEN)

Turner NC, et al. NEJM 2023:388:2058-70.

Capivasertib: HR+ Advanced Breast Cancer

Capitello-291

	Fulvestrant + Capivasertib	Fulvestrant (+ placebo)
In all patients:	N=355	N=353
Median PFS (95% CI)	7.2 months	3.6 months
In patients with AKT altered pathway:	N=155	N=134
Median PFS (95 % CI)	7.3 months	3.1 months

Turner NC, et al. NEJM 2023:388:2058-70.

Capivasertib: HR+ Advanced Breast Cancer

Capitello-291

Adverse Events: Capivasertib + Fulvestrant

Adverse Event (≥ 10%)	Any Grade %	Grade ≥ 3 %
Diarrhea	72.4	9.3
Rash	38.0	12.1
Nausea	34.6	0.8
Fatigue	20.8	0.6
Vomiting	20.6	1.7
Headache	16.9	0.3
Decreased appetite	16.6	0.3
Hyperglycemia	16.3	2.3
Stomatitis	14.6	2.0
Asthenia	13.2	1.1
Pruritis	12.4	0.6
Anemia	10.4	2.0
Urinary tract infection	10.1	1.4

Turner NC, et al. NEJM 2023:388:2058-70

Capivasertib

Current indication:

- In combination with fulvestrant, for adults with HR+, HER- locally advanced or metastatic breast **cancer with one or more PIK3CA/AKT/PTEN alterations following progression on at least one endocrine therapy.**

Dose and administration:

- Capivasertib 400 mg PO BID x 4 days**, followed by 3 days off**.
- Swallow tablets whole.
- Tablet sizes: 200 mg, 160 mg
- Dose modifications recommended with strong or moderate CYP3A inhibitors

Warning and Precautions:

- Hyperglycemia
- Diarrhea
- Cutaneous reactions
- Embryo-fetal toxicities

Capivasertib package insert. Accessed 12.8.2023

Evolution of Targeted Therapy for “**Less Common**” Cancer….new strategies.

Nirogacestat

(Approved November 2023)

Mechanism:

- **Gamma secretase inhibitor** that blocks proteolytic activation of the Notch receptor.

Indication:

- Adult patients with progressing **desmoid tumors** who require systemic treatment.

Wang L. NCI 2023, Nirogacestat package insert, accessed 12/5/2023

Eflornithine
(Approved December 2023)

Mechanism of action:

- Ornithine decarboxylase inhibitor

Indications:

- Adult and pediatric patients with **high-risk neuroblastoma** who have demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy.

Elfornithine package insert, accessed 12.14.2023

Tovorafenib

(Approved April 2024)

Mechanism:

- Oral, selective, **CNS-penetrant type II RAF kinase inhibitor** of mutant BRAF V600E, wild-type BRAF, and wild-type CRAF kinases.

Indication:

- Patients 6 months of age or older with relapsed or refractory **pediatric low-grade glioma (LGG)** harboring a BRAF fusion or rearrangement, or BRAF V600 mutation.

Capogiri M, et al. Frontiers Oncology 2023

Imetelstat
(Approved June 2024)

Mechanism:

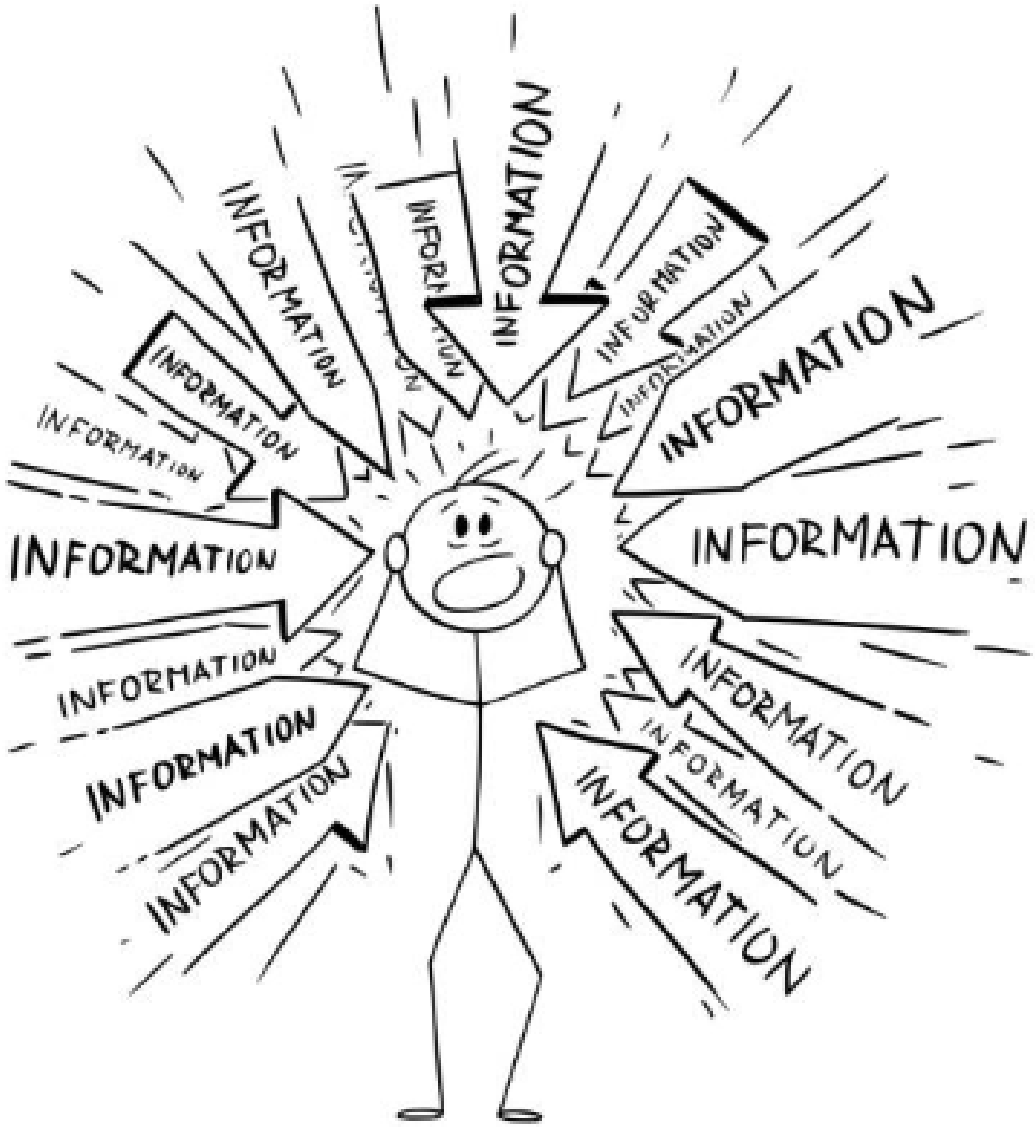
- Oligonucleotide telomerase inhibitor

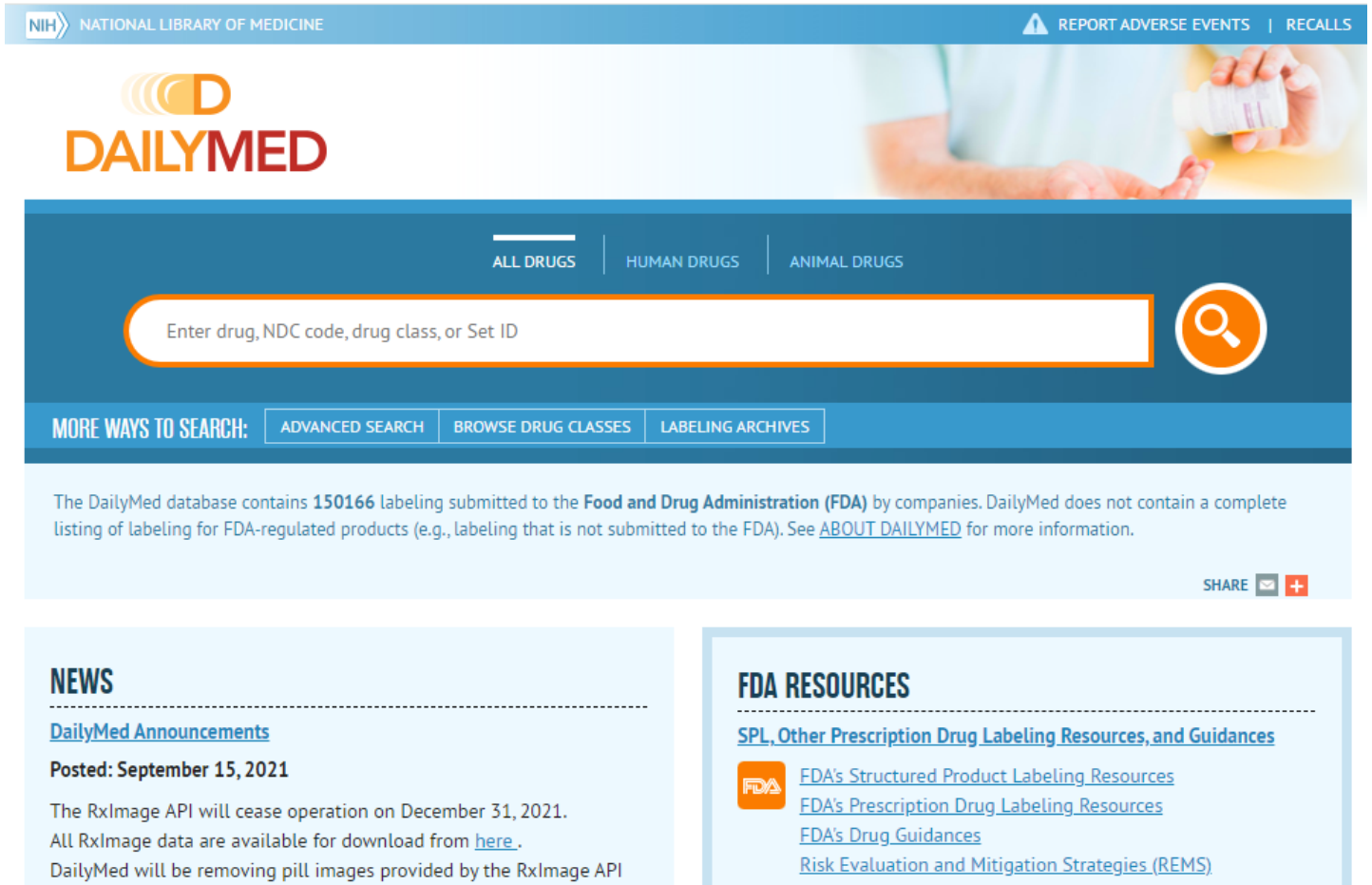
Indications:

- Adults with low- to intermediate-1 risk myelodysplastic syndrome with transfusion-dependent anemia requiring 4 or more units RBC over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents.

Imetelstat package insert. Accessed 7.2024

When it seems like there is just too much information …..





https://dailymed.nlm.nih.gov/dailymed/