Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

# Immunotherapy for the Treatment of Hematologic Malignancies

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Henry Ford Cancer Institute

AAEM American Academy of Emergency Medicine — Champion of the Emergency Physician

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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# Disclosures

- Research funds: Merck, GSK, TG therapeutics
- Advisory Board: Karyopharm therapeutics
- I will be discussing non-FDA approved indications during my presentation.



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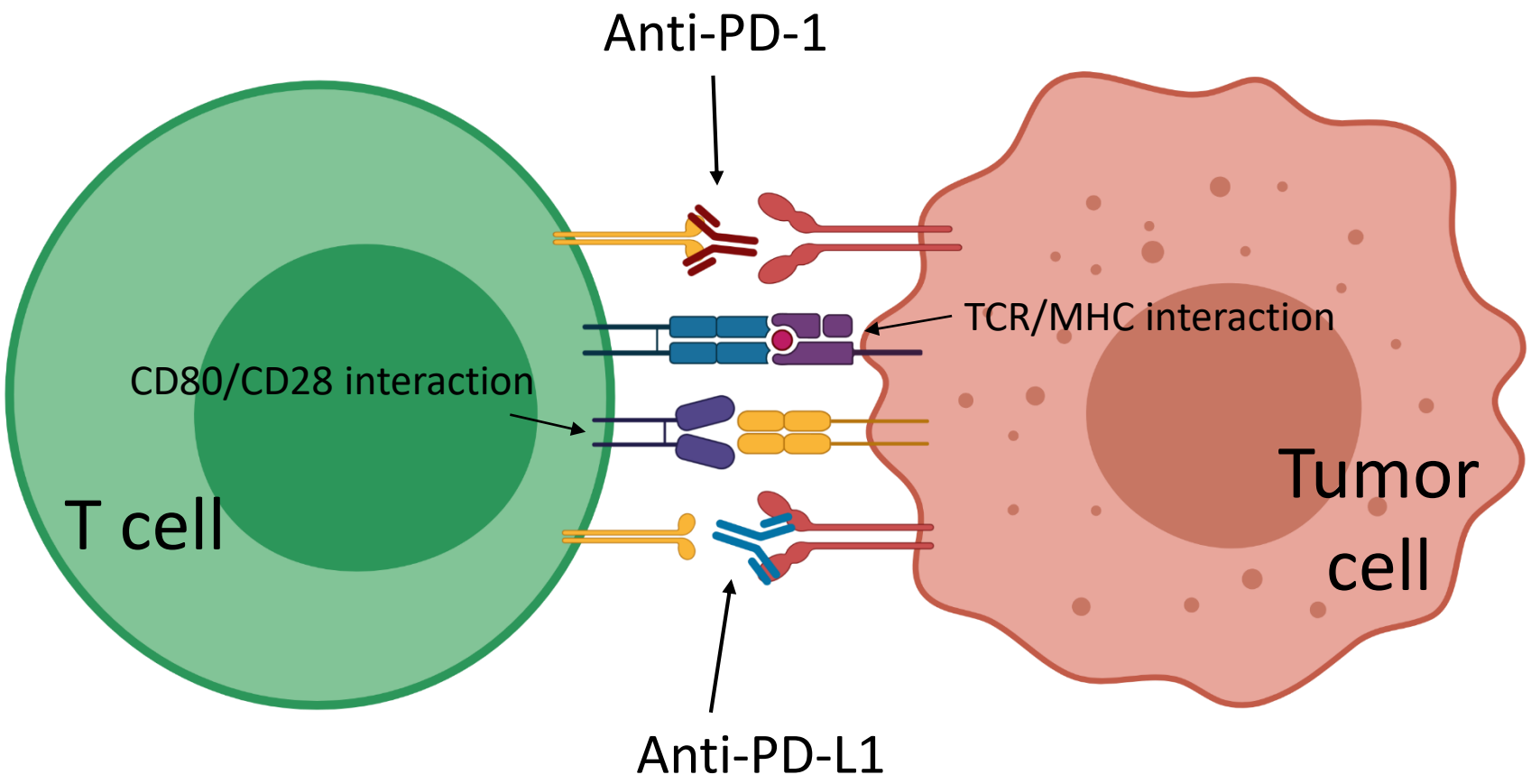
# Outline: Major immunotherapies under development

- Immune checkpoint inhibitors
- Antibody-drug conjugates
- Bispecifics
- Cellular therapies



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# Immune checkpoint inhibitors






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# FDA-approved checkpoint inhibitors: lymphoma

| Drug | Indication | Dose |
|---|---|---|
| Nivolumab | Classical **Hodgkin lymphoma**, relapsed after HSCT and brentuximab vedotin or ≥3 previous therapies | 240 mg Q2W or<br>480 mg Q4W |
| Pembrolizumab | Adult relapsed/refractory classical **Hodgkin lymphoma**<br><br>Pediatric refractory **cHL** or **cHL** relapsed after ≥2 lines of therapy | 200 mg Q3W or 400 mg Q6W adults<br><br>2 mg/kg (up to 200 mg) Q3W (pediatric) |
| Pembrolizumab | Adult/pediatric refractory **primary mediastinal large B-cell lymphoma** or relapsed after 2 previous therapies** | 200 mg Q3W or 400 mg Q6W adults<br><br>2 mg/kg (up to 200 mg) Q3W (pediatric) |

**Not recommended for patients with PBMCL that require urgent cytoreductive therapy.



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# Efficacy of approved checkpoint inhibitors: lymphoma

| Study | Treatment | Patient population | Overall response rate | Complete response rate | Landmark OS |
|---|---|---|---|---|---|
| CheckMate 205 | Nivolumab | Brentuximab vedotin-naïve **cHL** | 65% | 29% | 1-year: 92% |
| | | Bretuximab vedotin after auto-HCT **cHL** | 68% | 13% | 1-year: 93% |
| | | Bretuximab vedotin before/after auto-HCT **cHL** | 73% | 12% | 1-year: 90% |
| KEYNOTE-087 | Pembrolizumab | **cHL** progressed after ASCT and BV | 78.3% | 26% | 3-year: 86.3% |
| | | **cHL** after salvage chemo and BV, ineligible for ASCT | 64.2% | 26% | 3-year: 85.7% |
| | | **cHL** progressed after ASCT without BV treatment | 71.7% | 31.7% | 3-year: 87.6% |
| KEYNOTE-013 | Pembrolizumab | **PMBCL** with relapse/ineligible for ASCT | 48% | 33% | 1-year: 65% |
| KEYNOTE-170 | Pembrolizumab | **PMBCL** ineligible for ASCT with progression on ≥ 2 previous therapies | 45% | 13% | 1-year: 58% |

*cHL: Classical Hodgkin lymphoma; PMBCL: primary mediastinal B cell lymphoma*

Armand, J Clin Oncol 2018; Zinzani, ASH 2019.



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# **In development:** Immune checkpoint inhibitors in AML

| Study | Population | Treatment(s) | ORR | Median OS (months) | Status |
|---|---|---|---|---|---|
| NCT02775903 | Untreated AML | Azacitidine + durvalumab | 20% | 13.0 | Active, not recruiting |
| | | Azacitidine | 23% | 14.4 | |
| NCT02397720 | Relapsed/refractory AML | Azacitidine + nivolumab | 33% | 6.4 | Recruiting |
| | | Azacitidine + nivolumab + ipilimumab | 44% | 10.5 | |
| NCT02768792 | Relapsed/refractory AML | HiDAC followed by pembrolizumab | 46% | 8.9 | Active, not recruiting |
| NCT02845297 | Relapsed/refractory AML | Azacitidine + pembrolizumab | 31% | 10.8 | Recruiting |
| | Newly diagnosed AML, ≥ 65 years of age | | 70.5% | 13.1 | |

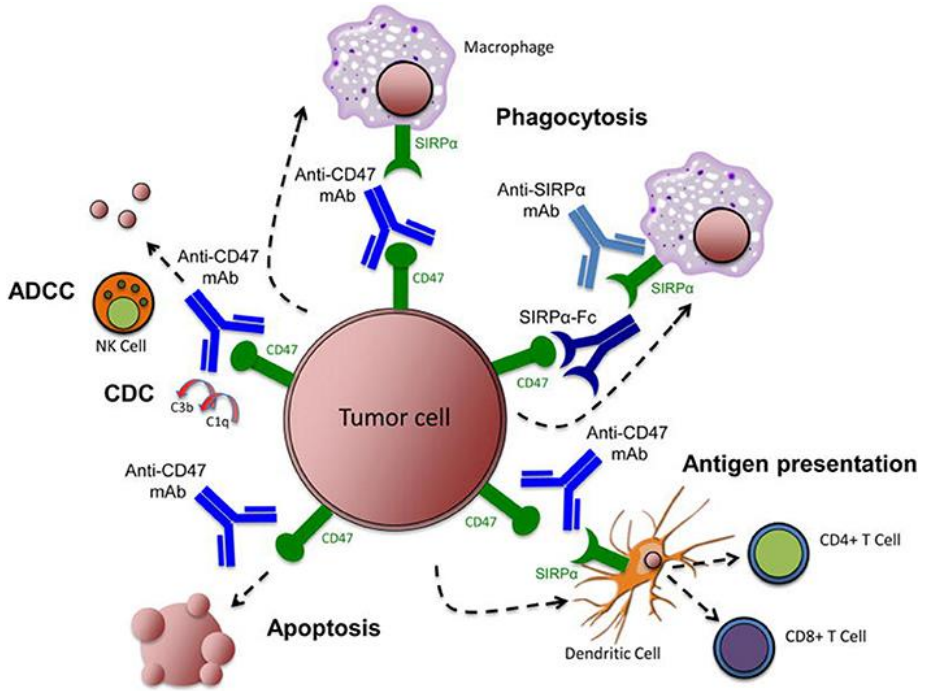
ASH 2019: Zeidan, Daver, Zeidner, Gojo.

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# **In development:** Macrophage checkpoint: CD47

| Treatment | Populations | ORR | CRR | Median DOR |
|---|---|---|---|---|
| Azacitidine + magroliumab | Untreated MDS | 91.7% | 50% | NR (>4.9 months) |
| | Untreated AML | 63.6% | 41% | NR (>5.8 months) |

- CD47 is expressed on some cancer cells
- CD47 signaling through SIRPα prohibits macrophage phagocytosis of cancer cells – "don't eat me"
- Blocking interaction of CD47 and SIRPα promotes adaptive immune responses and boosts tumor cell phagocytosis




Sallman, ASH 2019.
Zhang, Front Immunol 2020.

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# Outline

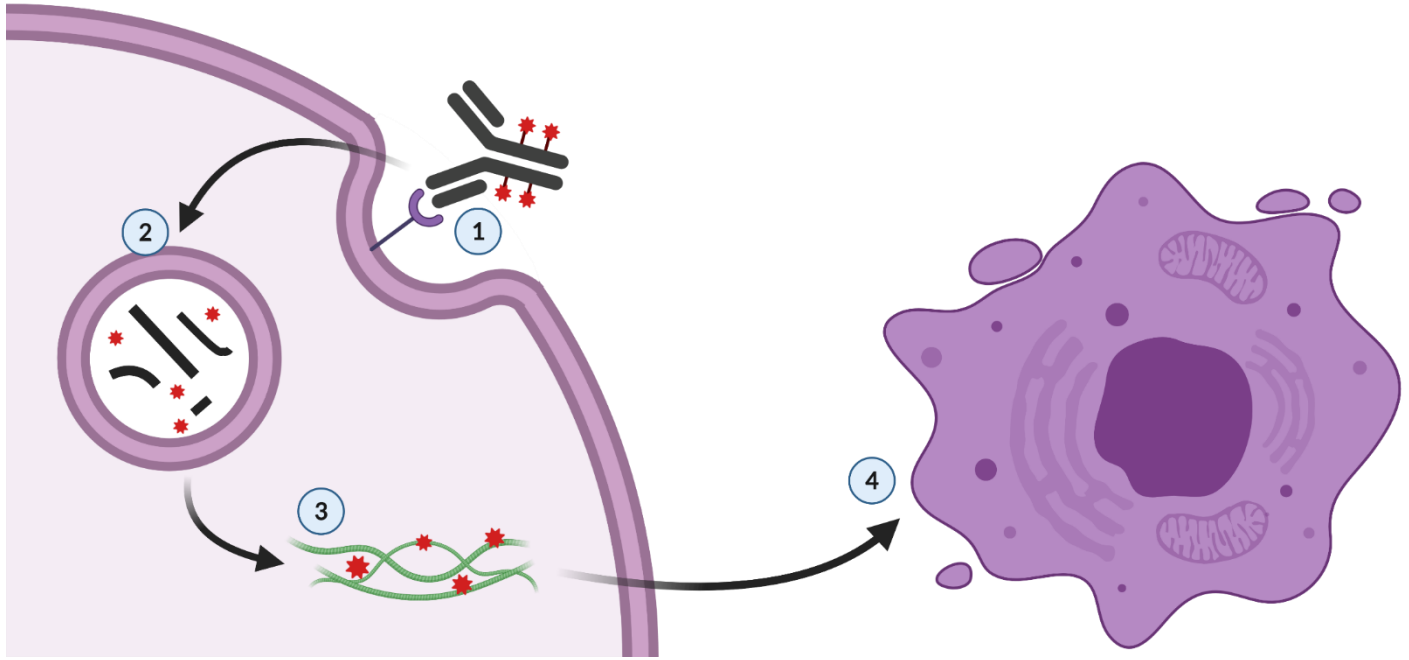
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- Bispecifics
- Cellular therapies



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# Antibody-drug conjugates

1. Antibody binds to receptor on tumor cell
2. ADC is internalized and broken down
3. Drug payload performs its MOA (here, microtubule disruption)
4. Apoptosis is induced in target cell






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# FDA-approved antibody-drug conjugates

| Drug | Target antigen | Indication |
|---|---|---|
| Brentuximab vedotin | CD30 | **Classical Hodgkin lymphoma,** relapsed after HSCT or ≥2 previous therapies |
| | | **Cutaneous anaplastic large cell lymphoma** or **CD30+ mycosis fungoides** ≥ 1 previous therapies |
| | | **Classical Hodgkin lymphoma** - first line with combination chemo |
| | | **Classical Hodgkin lymphoma** consolidation after auto-HSCT |
| Inotuzumab ozogamicin | CD22 | Relapsed/refractory/MRD+ **B-cell ALL** |
| Polatuzumab vedotin (w/ bendamustine & rituximab) | CD79b | **DLBCL** ≥ 2 previous therapies |
| Gemtuzumab ozogamicin | CD33 | **R/R or newly-diagnosed CD33+ AML** in adults or pediatric patients |
| Belantamab mafodotin | BCMA | **R/R multiple myeloma** after ≥ 4 prior therapies |



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# Efficacy of approved ADCs – brentuximab vedotin

| Study | Treatment(s) | Patient population | Overall response rate | Complete response rate | Landmark OS |
|---|---|---|---|---|---|
| NCT00848926 | Brentuximab vedotin | Relapsed/refractory Hodgkin lymphoma after failed auto-SCT | 75% | 33% | 5-year: 41% |
| NCT00866047 | Brentuximab vedotin | Relapsed/refractory systemic anaplastic large cell lymphoma | 86% | 66% | 5-year: 60% |
| ECHELON-1 | Brentuximab vedotin + doxorubicin, vinblastine, and dacarbazine | Previously untreated stage III or IV Hodgkin lymphoma | 2-year modified PFS rate: 82.1% | | |
| | Doxorubicin, bleomycin, vinblastine, and dacarbazine | | 2-year modified PFS rate: 77.2% | | |
| AETHERA | Brentuximab vedotin | Unfavorable-risk relapsed or primary refractory classic Hodgkin lymphoma after auto-SCT | Median PFS: 42.9 months | | |
| | Placebo | | Median PFS: 24.1 months | | |

Chen, Blood 2016; Pro, Blood 2017; Connors, N Engl J Med 2018; Moskowitz, Lancet 2015.

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# Efficacy of approved ADCs

| Study | Treatment(s) | Patient population | Key outcomes |
|---|---|---|---|
| INO-VATE | Inotuzumab ozogamicin | Relapsed/refractory **B cell precursor ALL** | CR/CRi rate: 73.8% vs 30.9%<br>Median OS: 7.7 vs 6.2 months<br>2-year OS: 22.8% vs 10% |
| | Standard-of-care chemo | | |
| GO29365 | Polatuzumab vedotin + bendamustine & rituximab | Relapsed/refractory **DLBCL** | CRR: 40.0% vs 17.5%<br>Median PFS: 9.5 vs 3.7 months<br>Median OS: 12.4 vs 4.7 months |
| | Bendamustine & rituximab | | |
| ALFA-0701 | Gemtuzumab ozogamicin + daunorubicin + cytarabine | De novo acute **myeloid leukemia** | CR/CRp rate: 81.5% vs 73.6%<br>Median OS: 27.5 vs 21.8 months<br>Median EFS: 17.3 vs 9.5 months |
| | Daunorubicin + cytarabine | | |
| DREAMM-2 | Belantamab mafodotin | R/R **multiple myeloma** after IMiD, PI, and anti-CD38 | ORR: 31%<br>Median PFS: 2.9 months |

Sehn, J Clin Oncol 2020; Kantarjian, Cancer 2019; Lambert, Haematologica 2018.

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# **In development:** Novel ADCs in clinical trials

| Trial | Indication | Treatment(s) | ADC target antigen | Phase |
|---|---|---|---|---|
| NCT03544281 | R/R multiple myeloma | GSK2857916 + lenaolidomide + dexamethasone | BCMA | 2 |
| | | GSK2857916 + bortezomib + dexamethasone | | |
| NCT03386513 | CD123+ AML, BPDCN or ALL | IMGN632 | CD123 | 1/2 |
| NCT03424603 | R/R B cell malignancies | STRO-001 | CD74 | 1 |
| NCT03682796 | R/R B cell lymphoma | TRPH-222 | CD22 | 1 |
| NCT04240704 | CLL or NHL | JBH492 | CCR7 | 1 |
| NCT03833180 | Pre-treated hematologic malignancies | VLS-101 | ROR1 | 1 |



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# Outline

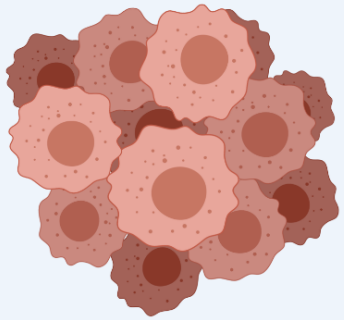
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# Bispecifics in immunotherapy

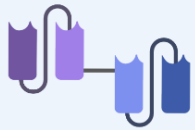
## Target 1: Tumor



Explored targets include:
CD19, CD20, EGFR, BCMA, CEA, FAP, EpCAM, CD123 …

## Immune cell engagers

Bispecific killer cell engagers



Bispecific T cell engagers



Bispecific antibodies



Nanobody-scFv



## Target 2: Immune cell

T cells



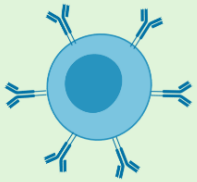
NK cells



Macrophages



B cells



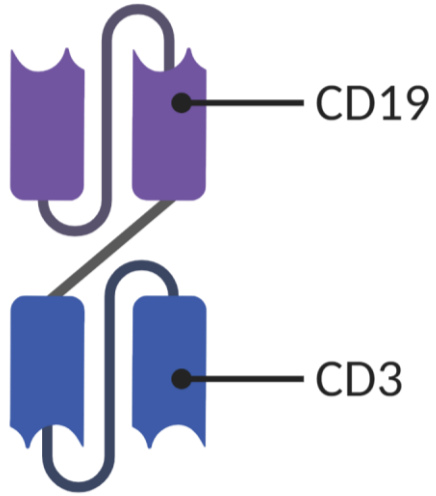
*Commonly CD3 on T cells, CD16 for NK and macrophages, etc*

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# Clinical use of immune cell engagers

| Drug | Indications |
|---|---|
| Blinatumomab | Relapsed/refractory B-ALL |
| | B-ALL in 1st or 2nd complete response with MRD ≥ 0.1% |



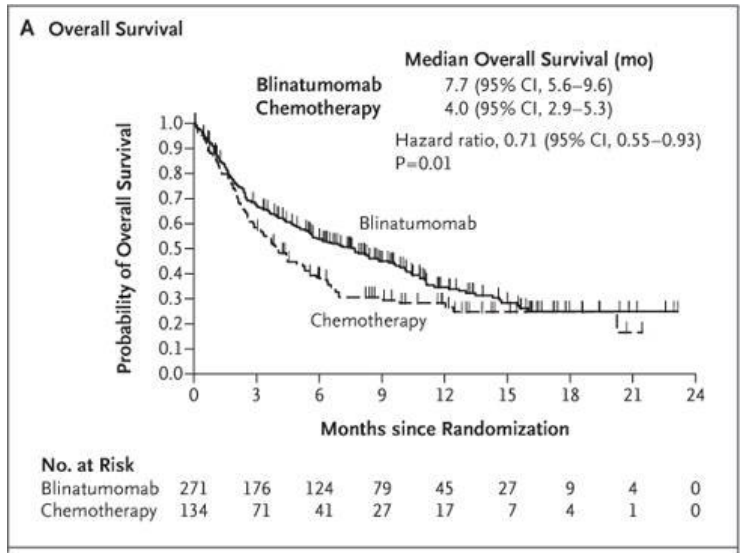

[Blinatumomab prescribing information.]

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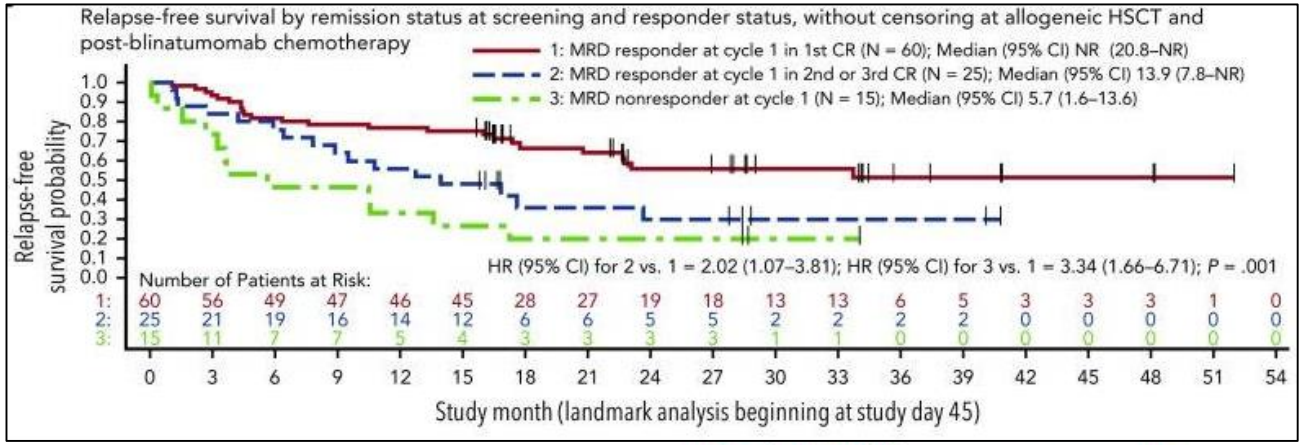
# Blinatumomab in R/R B-ALL

| Trial | Patient population | Treatment | Key outcomes |
|---|---|---|---|
| NCT02013167 | Adults with R/R B-ALL | Blinatumomab | Median OS: 7.7 vs 4.0 months<br>Median DOR: 7.3 vs 4.6 months |
| | | Chemotherapy | |
| NCT01207388 | Adults with MRD+ B-ALL | Blinatumomab | Complete MRD response rate: 78%<br>Median OS: 36.5 months |

R/R B-ALL




MRD+ B-ALL




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# Dosing regimens for blinatumomab

| | Cycle | | Patients weighing 45 kg or more (Fixed-dose) | Patients weighing less than 45 kg (BSA-based dose) |
|---|---|---|---|---|
| MRD-positive B-ALL | Induction cycle 1 | Days 1-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 14-day treatment-free interval | 14-day treatment-free interval |
| | Consolidation cycles 2-4 | Days 1-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 14-day treatment-free interval | 14-day treatment-free interval |

| | Cycle | | Patients weighing 45 kg or more (Fixed-dose) | Patients weighing less than 45 kg (BSA-based dose) |
|---|---|---|---|---|
| R/R B-ALL | Induction cycle 1 | Days 1-7 | 9 mcg/day | 5 mcg/m$^2$/day (not to exceed 9 mcg/day) |
| | | Days 8-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 14-day treatment-free interval | 14-day treatment-free interval |
| | Induction cycle 2 | Days 1-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 14-day treatment-free interval | 14-day treatment-free interval |
| | Consolidation cycles 3-5 | Days 1-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 14-day treatment-free interval | 14-day treatment-free interval |
| | Continued therapy cycles 6-9 | Days 1-28 | 28 mcg/day | 15 mcg/m$^2$/day (not to exceed 28 mcg/day) |
| | | Days 29-42 | 56-day treatment-free interval | 56-day treatment-free interval |

Blinatumomab prescribing information.

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# Dosing regimens for blinatumomab – R/R B-ALL

Induction cycle 1





7-day low-dose infusion

21-day normal dose infusion

14 days treatment-free

Induction 2, Consolidation





28-day continuous infusion

14 days treatment-free

Blinatumomab prescribing information.

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# Common side effects of T cell engagers

## Cytokine release syndrome

- Characterized by initial flu-like symptoms, which progress into a shock-like syndrome with elevation in cytokine levels
- Patients display fever, vascular leakage, and organ dysfunction
- Variable onset and course
- Pre-treatment with dexamethasone required
- Management:
  - IL-6 and IL-6R antagonism
  - Corticosteroids
  - Other cytokine receptor antagonists

## B cell aplasia

- Due to current clinical agents targeting CD19, which is expressed by both normal and neoplastic B cells
- May result in hypogammaglobulinemia
- Increased risk of infection
- Managed through administration of intravenous immunoglobulin

**Stay tuned:** more information on toxicity management later in this program

## Neurotoxicity

- Also known as "immune effector cell-associated neurotoxicity syndrome" (ICANS)
- Manifests as confusion, delirium, seizures, cerebral edema
- Largely unknown mechanisms
- Incidence increases with more doses, increased age, more prior therapies
- Management:
  - Supportive care for low-grade
  - Corticosteroids for higher-grade

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# **In development:** Novel immune cell engagers in clinical trials

| Trial | Indication | Treatment | Target antigens | Phase |
|---|---|---|---|---|
| NCT03214666 | HR myelodysplastic syndromes, R/R AML, systemic mastocytosis | GTB-3550 (TriKE) | CD16, IL-15, CD33 | 1/2 |
| NCT03516591 | High-risk myelodysplastic syndromes | AMV564 | CD33, CD3 | 1 |
| NCT03739606 | CD123+ R/R blood cancers | Flotetuzumab | CD123, CD3 | 2 |
| NCT02730312 | CD123+ R/R blood cancers | XmAb14045 | CD123, CD3 | 1 |
| NCT03888105 | R/R B cell NHL | Odronextamab | CD20, CD3 | 2 |
| NCT03309111 | Previously treated multiple myeloma | GBR 1342 | CD38, CD3 | 1/2 |
| NCT03761108 | R/R multiple myeloma | REGN5458 | BCMA, CD3 | 1/2 |



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# Outline

- Immune checkpoint inhibitors
- Antibody-drug conjugates
- Bispecifics
- Cellular therapies



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# Comparing T cell engagers and CAR T therapy

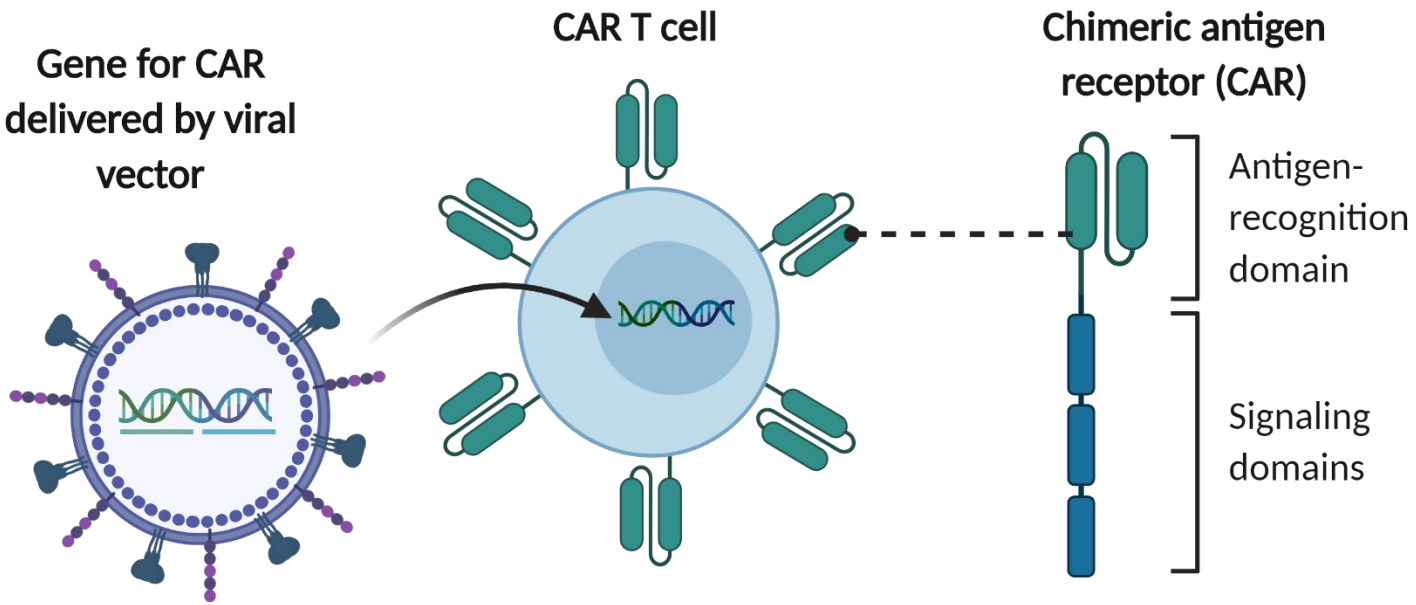
| | CAR T cells | T cell engagers (BiTEs) |
|---|---|---|
| **Structure** | Synthetic gene construct encoding an scFv against tumor antigen linked to activation/costimulatory motifs | Recombinant protein with two specificities: one for tumor antigen and one for T cell antigen (usually CD3) |
| **Effector cell types** | Engineered CD8+ and CD4+ T cells | Endogenous CD8+ and CD4+ T cells |
| **Immune synapse** | Atypical | Typical |
| **Serial killing** | Yes | Yes |
| **Killing mechanisms** | Perforin and granzyme B, Fas-Fas-L, or TNF/TNF-R | Perforin and granzyme B |
| **Trafficking** | Active | Passive |
| **Clinical applications** | Pre-treatment lymphodepletion followed by a single infusion | No lymphodepletion; repeat administration and continuous infusions. |
| **Specificity** | Manufactured for each patient | "Off-the-shelf" |

Slaney, Cancer Disc 2018.

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# Chimeric antigen receptors

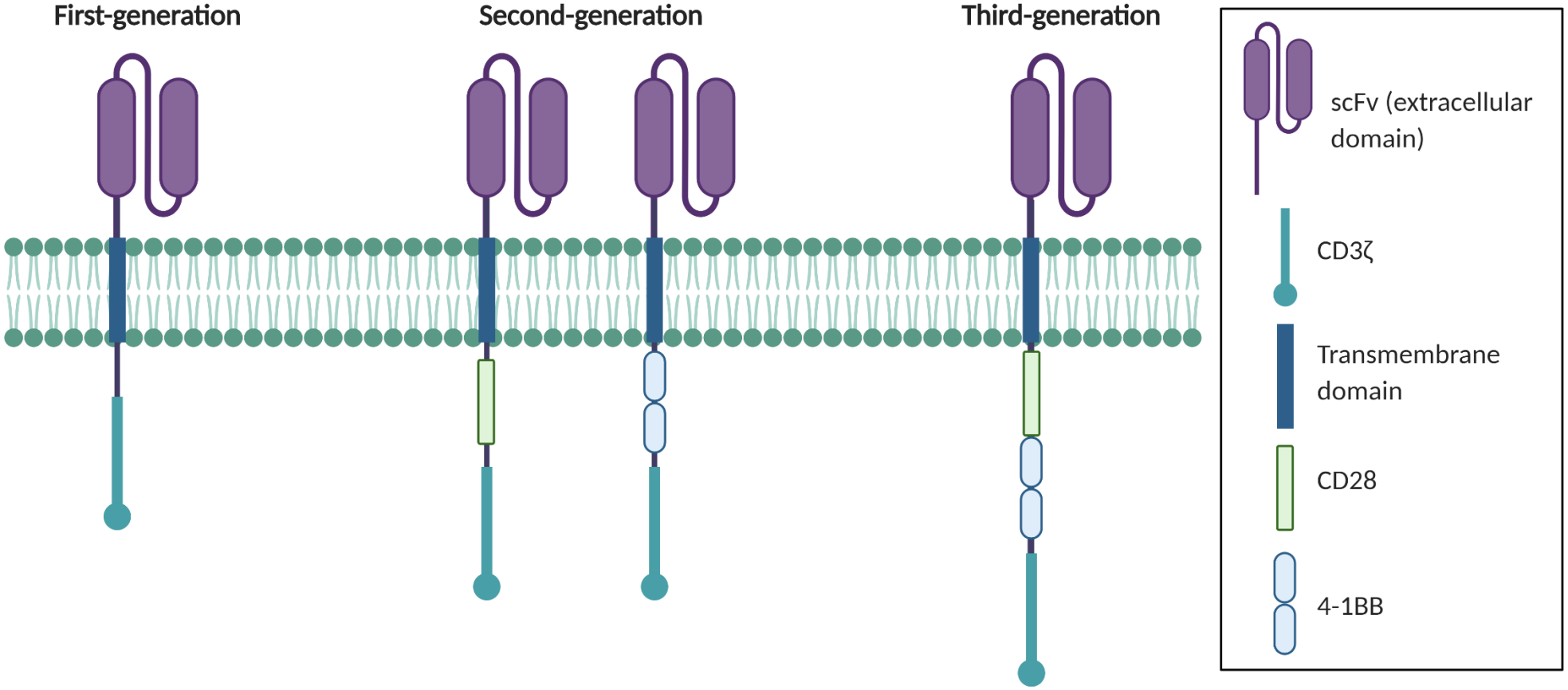
- Overcome immune tolerance
- Targets surface molecules in native conformation
- Independent of antigen presenting cell and MHC complex






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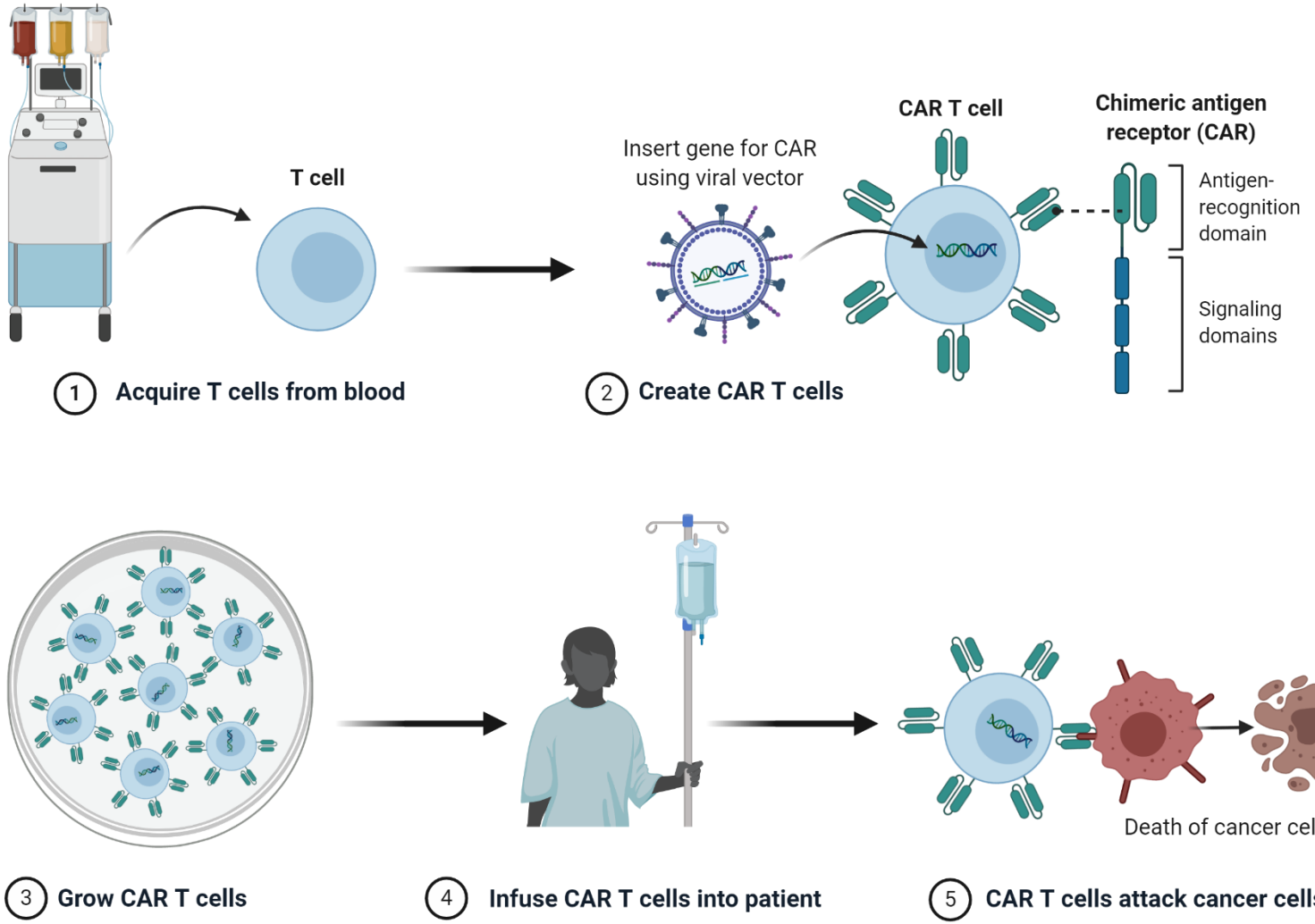
# Evolution of CAR constructs




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# CAR T manufacturing and administration




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# FDA-approved CAR T cell therapies

| Drug | Target/co-stimulatory domain | Indication | Dose |
|---|---|---|---|
| Axicabtagene ciloleucel | CD19/CD28 | Adults with r/r large **B-cell lymphoma**, Including diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, DLBCL arising from follicular lymphoma, and R/R follicular lymphoma | 2 x $10^6$ CAR-positive, viable T cells per kg bodyweight (up to 2x$10^8$) |
| Tisagenlecleucel | CD19/4-1BB | Patients ≤25 yr with refractory **B-cell acute lymphoblastic leukemia** or in 2+ relapse | 0.2-0.5x$10^6$ CAR-positive, viable T cells per kg if under 50 kg<br>0.1-2.5x$10^8$ CAR-positive, viable T-cells if over 50 kg |
| Tisagenlecleucel | CD19/4-1BB | Adults with r/r large **B-cell lymphoma** after 2+ therapies Including DLBCL, high-grade B-cell lymphoma, DLBCL arising from follicular lymphoma | 0.6-6.0 x $10^8$ CAR-positive, viable T cells |
| Brexucabtagene autoleucel | CD19/CD28 | Adults with **mantle cell lymphoma** (MCL) who have not responded to or who have relapsed following other treatments | 2 x $10^6$ CAR-positive, viable T cells per kg bodyweight (up to 2x$10^8$) |
| Lisocabtagene maraleucel | CD19/4-1BB | Adults with R/R large **B-cell lymphoma** after at least 2 prior therapies | 50-110 x $10^6$ CAR-positive viable T cells (1:1 CD4:CD8) |
| Idecabtagene vicleucel | BCMA/4-1BB | Adults with R/R **multiple myeloma** after 4+ prior therapies | 300-460x$10^6$ CAR-positive T cells |



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# Comparing clinical trials of CD19 CAR T therapies

| Trial | Indication | Treatment(s) | ORR | Landmark OS | Grade 3+ toxicity rates |
|---|---|---|---|---|---|
| ZUMA-2 | R/R mantle cell lymphoma | Brexucabtagene autoleucel (KTE-X19) | 86%<br>CRR: 57% | 1-year: 86% | CRS: 18%<br>NE: 46% |
| ZUMA-1 | Refractory large B cell lymphoma | Axicabtagene ciloleucel | 83%<br>CRR: 58% | 2-year: 50% | CRS: 11%<br>NE: 32% |
| JULIET | R/R diffuse large B cell lymphoma | Tisagenlecleucel | 52%<br>CRR: 40% | 1-year: 49% | CRS: 22%<br>NE: 12% |
| ELIANA | R/R B cell acute lymphoblastic leukemia | Tisagenlecleucel | 82%<br>CRR: 62% | 18-month: 70% | CRS: 48%<br>NE: 13% |

Wang, ASH 2019; Locke, Lancet Oncol 2019; Schuster, N Engl J Med 2019; Grupp, Biol Blood Mar Trans 2019.

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# CAR T side effects

- Cytokine Release Syndrome (CRS)
- Neurotoxicity
  - ICANS: Immune effector cell-associated neurotoxicity syndrome
  - NE: Neurologic events
- B cell aplasia
- Macrophage Activation Syndrome (MAS)/HLH

**Stay tuned:** more information on toxicity management later in this program



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# CAR T side effects - CRS

**Cytokine Release Syndrome symptoms**

**Gastrointestinal**
- Nausea/vomiting
- Diarrhea
- Anorexia



**Skin**
- Rash



**Respiratory**
- Tachypnea
- Hypoxia
- Pulmonary edema



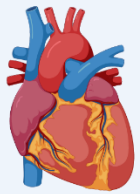
**Constitutional**
- Fever +/- rigors
- Malaise/fatigue
- Myalgias
- Arthralgias
- Headache



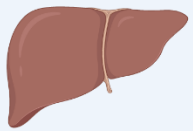
**Coagulation**
- Elevated D-dimer
- Hypofibrinogenemia +/- bleeding



**Cardiovascular**
- Tachycardia
- Hypotension
- Capillary leak
- Widened pulse presssure
- Increased cardiac output (early)
- Potentially diminished cardiac output (late)



**Hepatic dysfunction**
- Transaminitis
- Hyperbilirubinemia



**Renal function**
- Azotemia



*Symptoms often mimic sepsis, but treatment of CRS is quite different*



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# Eligibility considerations for CAR

- Disease
  - Relative stability during CAR T manufacturing (~2-6 weeks)
  - Bridging therapy (chemo, RT, steroids, lenalidomide, ibrutinib)
  - CNS control
- Patient
  - Adequate cell counts
  - DVT, bleeding, infection, neuro disorders
  - Functional status: at screen vs. day of CAR T infusion
- Other
  - Social support,  reimbursement
  - Availability of tocilizumab for CRS management



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# **In development:** Novel CAR T therapies in clinical trials

| Trial | Indication | Treatment | Target antigen | Phase |
|---|---|---|---|---|
| NCT03971799 | R/R pediatric AML | CD33CART | CD33 | 1/2 |
| NCT04186520 | R/R B cell malignancies | CAR-20/19 T cells | CD19, CD20 | 1/2 |
| NCT04109482 | R/R BPDCN, AML, HR MDS | MB-102 | CD123 | 1/2 |
| NCT03287817 | Diffuse large B cell lymphoma | AUTO3 | CD19, CD22 | 1/2 |
| NCT02690545 | R/R HL and NHL | ATLCAR.CD30 | CD30 | 1/2 |



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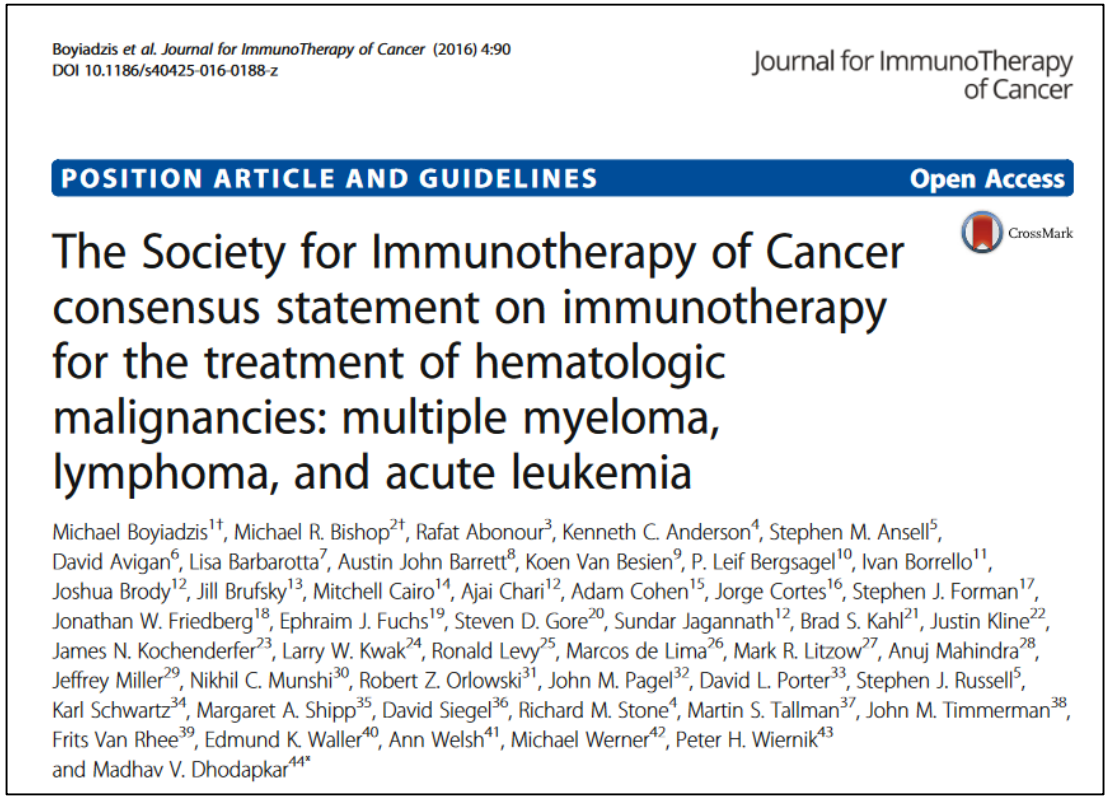
# Conclusions

- Many immunotherapy options for hematological malignancies
- Checkpoint inhibitors for Hodgkin lymphoma and PMBCL – high response rate, excellent tolerance, durable responses if CR
- Blinatumomab and inotuzumab for ALL – effective salvage, deeper remissions
- Polatuzumab vedotin for DLBCL – effective salvage, potential to become frontline
- CAR T therapy – ever-increasing indications; patient selection and toxicity management still concerns



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# Additional Resources



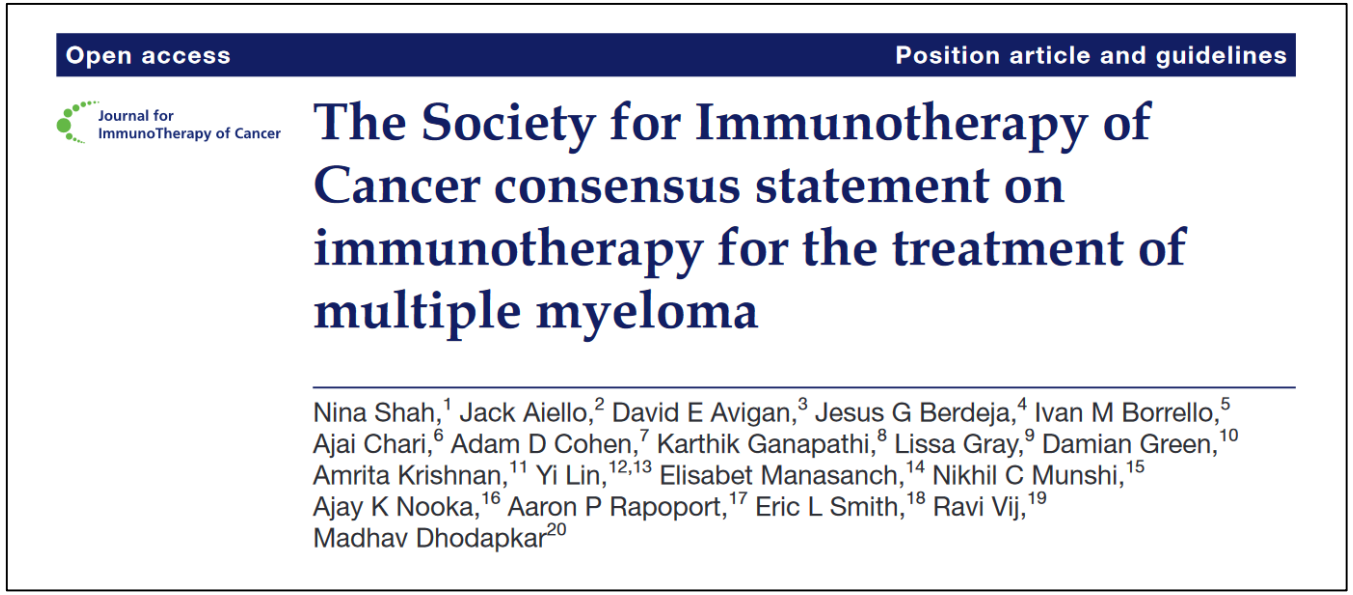
Boyiadzis *et al. Journal for ImmunoTherapy of Cancer* (2016) 4:90
DOI 10.1186/s40425-016-0188-z

Journal for ImmunoTherapy of Cancer

**POSITION ARTICLE AND GUIDELINES** **Open Access**

## The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of hematologic malignancies: multiple myeloma, lymphoma, and acute leukemia

Michael Boyiadzis[1†], Michael R. Bishop[2†], Rafat Abonour[3], Kenneth C. Anderson[4], Stephen M. Ansell[5], David Avigan[6], Lisa Barbarotta[7], Austin John Barrett[8], Koen Van Besien[9], P. Leif Bergsagel[10], Ivan Borrello[11], Joshua Brody[12], Jill Brufsky[13], Mitchell Cairo[14], Ajai Chari[12], Adam Cohen[15], Jorge Cortes[16], Stephen J. Forman[17], Jonathan W. Friedberg[18], Ephraim J. Fuchs[19], Steven D. Gore[20], Sundar Jagannath[12], Brad S. Kahl[21], Justin Kline[22], James N. Kochenderfer[23], Larry W. Kwak[24], Ronald Levy[25], Marcos de Lima[26], Mark R. Litzow[27], Anuj Mahindra[28], Jeffrey Miller[29], Nikhil C. Munshi[30], Robert Z. Orlowski[31], John M. Pagel[32], David L. Porter[33], Stephen J. Russell[5], Karl Schwartz[34], Margaret A. Shipp[35], David Siegel[36], Richard M. Stone[4], Martin S. Tallman[37], John M. Timmerman[38], Frits Van Rhee[39], Edmund K. Waller[40], Ann Welsh[41], Michael Werner[42], Peter H. Wiernik[43] and Madhav V. Dhodapkar[44*]



**Open access** **Position article and guidelines**

Journal for ImmunoTherapy of Cancer

## The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of multiple myeloma

Nina Shah,[1] Jack Aiello,[2] David E Avigan,[3] Jesus G Berdeja,[4] Ivan M Borrello,[5] Ajai Chari,[6] Adam D Cohen,[7] Karthik Ganapathi,[8] Lissa Gray,[9] Damian Green,[10] Amrita Krishnan,[11] Yi Lin,[12,13] Elisabet Manasanch,[14] Nikhil C Munshi,[15] Ajay K Nooka,[16] Aaron P Rapoport,[17] Eric L Smith,[18] Ravi Vij,[19] Madhav Dhodapkar[20]

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- Some figures created using Biorender.com




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# Case Studies



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- A 52 y/o male presented with abdominal pain. CT scan of abdomen showed mesenteric adenopathy around the pancreas and third portion of the duodenum. PET/CT scan showed very intense FDG uptake within multiple peripancreatic enlarged lymph nodes(LN) as well as multiple enlarged and conglomerated mesenteric LN. Mesenteric LN biopsy showed diffuse large B-cell lymphoma and minor background Follicular lymphoma, grade 3B. DLBCL was GC in origin, DPE, No C-MYC rearrangement.
- Patient received 6 cycles of R-CHOP and achieved functional CR by PET/CT scan. He underwent consolidation with high dose chemo/auto stem cell transplant. One year later, he had recurrent abdominal pain and had a PET scan that showed recurrent disease. He received salvage DHAP with CR after 2 cycles. He was offered allogenic stem cell transplant, but he declined. 6 months later he had a second recurrence.


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What would you do next:

A. Polatuzumab-Bendamustine-Rituximab
B. Tafasitamab + Lenalidomide
C. CD-19 directed CAR-T therapy
D. Selinexor
E. BCMA targeted CAR-T therapy



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# C. CD-19 directed CAR-T therapy



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- The patient received CAR-T therapy following lymphodepleting regimen of Fludarabine and Cyclophosphamide. 5 days later he presented with high fever, tachycardia, hypoxia requiring high flow nasal canula, severe hypotension requiring vasopressors.
- What treatment would you give:

A. Evaluate for infectious causes and treated with antibiotics if febrile neutropenic
B. Start Tocilizumab 8 mg/kg and dexamethasone
C. Dexamethasone
D. Comfort measures/goals of care discussion
E. A + B


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E. A + B



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55 y/o female presented with easy bruising and elevated white blood cell count of 20k, 50% of which are blasts. Flowcytometry showed markedly increased B lymphoblasts. Molecular testing for BCR/ABL fusion gene was negative. Patient was started on R-Hyper CVAD regimen. Bone marrow biopsy following cycle 2A showed a morphologic CR. MRD testing is positive at $1 \times 10^{3}$.

What would you do next:

A. Continue Hyper CVAD
B. Switch to Blinatumomab
C. Switch to Inotuzumab
D. Switch to FLAG-Ida
E. Switch to Gemtuzumab Ozogamicin



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# B. Switch to Blinatumomab



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