New CARs in Town

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Faculty Disclosure

• Larry W. Buie declares no existence of a financial interest in any amount related to the content of this activity.

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Need for Additional Therapies in Hematologic Malignancies

Relapsed and refractory disease, following treatment with conventional and targeted therapies or bone marrow transplantation, is associated with a poor prognosis.

Learning Objectives

At the conclusion of this activity, participants should be better able to:

1. Recognize currently approved CAR (Chimeric Antigen Receptor) T-cell therapies and their place in therapy
2. Identify novel CAR targets and treatments
3. Recognize relevant clinical trial data for CAR therapies in development
4. Recognize common toxicities associated with CAR T-cell therapies and identify appropriate management strategies
Chimeric Antigen Receptor T-Cells (CAR Ts)

- CAR design
  - CD3ζ signaling element
  - Costimulatory receptor
  - Targeted single chain variable fragment

- Major histocompatibility independent mechanism

Pre-Conditioning Chemotherapy

- Improves antitumor activity
  - Depletion of leukocytes
  - Decrease in regulatory T-cells
  - Decreased indoleamine production
- Tumor debulking
  - Reduction in tumor antigen
- Cyclophosphamide and fludarabine
  - Increase T-cell expansion
  - Improved disease-free survival

T-Cell Expansion and Persistence

# Updates in FDA Approved CAR T-Cell Products

## FDA Approved CAR T-Cell Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Co-Stimulatory Domain</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tisagenlecleucel (Kymriah®)</td>
<td>41BB</td>
<td>Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse</td>
</tr>
<tr>
<td>Tisagenlecleucel (Kymriah®)</td>
<td>41BB</td>
<td>Adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy</td>
</tr>
<tr>
<td>Axicabtagene cileoleucel (Yescarta™)</td>
<td>CD28</td>
<td>Adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy</td>
</tr>
<tr>
<td>Brexucabtagene autoleucel (TECARTUS™)</td>
<td>CD28</td>
<td>Relapsed or Refractory Mantle Cell Lymphoma</td>
</tr>
</tbody>
</table>

Updated Results: Tisagenlecleucel in ALL (ELIANA)

Single Cohort, Phase II, Multicenter, Global Study

N=79
Pediatric and adults
Relapsed or refractory B-cell ALL

Leukapheresis
Conditioning
T-Cell Infusion

Primary Endpoint: Overall Response Rate

Secondary Endpoints: CR rates, MRD response, duration of remission, EFS, OS, Kinetics, Safety

ALL = acute lymphoblastic leukemia

Longer Follow-Up with Sustained Efficacy

<table>
<thead>
<tr>
<th>ORR, %</th>
<th>82</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR, %</td>
<td>62</td>
</tr>
<tr>
<td>CRi, %</td>
<td>20</td>
</tr>
<tr>
<td>MRD response, %</td>
<td>98</td>
</tr>
<tr>
<td>Duration of response, months</td>
<td>Not reached</td>
</tr>
<tr>
<td>Median OS</td>
<td>Not reached</td>
</tr>
<tr>
<td>OS-18 months, %</td>
<td>70</td>
</tr>
<tr>
<td>RFS-18 months, %</td>
<td>66</td>
</tr>
</tbody>
</table>

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Tisagenlecleucel in Lymphoma (Juliet)

**International, Phase II, Multicenter**

- **N=111 DLBCL**
- At least two lines of therapy (rituximab and an anthracycline)
- Relapse after or ineligible for auto transplant

**Primary Endpoint: Best Overall Response Rate**

**Secondary Endpoints: response duration, OS, safety, cellular kinetics**


Tisagenlecleucel in Lymphoma Results

<table>
<thead>
<tr>
<th>ORR, %</th>
<th>52</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR, %</td>
<td>40</td>
</tr>
<tr>
<td>PR, %</td>
<td>12</td>
</tr>
<tr>
<td>Median Duration of Response, months</td>
<td>Not reached</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>Not Reached</td>
</tr>
<tr>
<td>Median OS, months</td>
<td>12 months</td>
</tr>
<tr>
<td>OS-12 months, predicted</td>
<td>40%</td>
</tr>
</tbody>
</table>

Updated Results: Axicabtagene Ciloleucel in Lymphoma (ZUMA-1)

International, Phase II, Multicenter

N=101
DLBCL
Primary mediastinal B-Cell Lymphoma
Transformed follicular lymphoma

Leukapheresis
Conditioning
T-Cell Infusion

Primary Endpoint: Objective Response

Secondary Endpoints: response duration, PFS, OS, safety, biomarker assessments

ORR, %  83
CR, %  58
PR, %  25
Median time to response, months  1.0
Median DOR, months  11.1
Median PFS, months  5.3
Median OS, months  NR

Axicabtagene Ciloleucel in Lymphoma: Updated Results

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One of These Is Not Like the Others…KTE-X19

Brexucabtagene Autoleucel (KTE-X19): The Back Story

- Mantle Cell Lymphoma (MCL) is a Non-Hodgkin Lymphoma (NHL) with an aggressive course
  - Typically treated with chemotherapy or targeted therapies, including Bruton’s tyrosine kinase (BTK) inhibitors
  - Relapse/refractory disease is associated with worse outcomes
  - Not all patients are eligible or will tolerate stem cell transplantation
- Response with axicabtagene ciloleucel (KTE-C19) has been observed
  - CR for 17 months at data cutoff from ZUMA-1
- Many patients will have a leukemic phase, which may limit the number of T-cells in the product
  - KTE-X19 is manufactured with removal of CD19+ tumor cells to limit T-cell activation and exhaustion in the ex vivo manufacturing process

ZUMA-2: Brexucabtagene Autoleucel in R/R MCL

Multicenter, Phase II, Open-Label

N=68 Dx of R/R MCL → Leukapheresis → Conditioning → T-Cell Infusion → Primary Endpoint: Objective Response

Secondary Endpoints: response duration, PFS, OS, safety, and QOL

ZUMA-2 Results

Brexucabtagene Autoleucel Induces durable responses in patients with R/R MCL with high risk disease, including those progressing on or refractory to BTK-inhibitor therapies.

Toxicity Comparisons Among CD19 Directed CAR T-Cells

<table>
<thead>
<tr>
<th>CAR T-Product, Disease, N</th>
<th>CRS - Any Grade</th>
<th>CRS – ≥ Grade 3</th>
<th>Neurotoxicity Any Grade</th>
<th>Neurotoxicity ≥ Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tisagenlecleucel, ALL, N=75</td>
<td>67 (89%)</td>
<td>56 (75%)</td>
<td>30 (40%)</td>
<td>10 (13%)</td>
</tr>
<tr>
<td>Tisagenlecleucel, Lymphoma, N=111</td>
<td>64 (58%)</td>
<td>24 (22%)</td>
<td>23 (21%)</td>
<td>13 (12%)</td>
</tr>
<tr>
<td>Axicabtagene Ciloleucel, Lymphoma, N=108</td>
<td>88 (81%)</td>
<td>12 (11%)</td>
<td>37 (34%)</td>
<td>35 (33%)</td>
</tr>
<tr>
<td>Brexucabtagene Autoleucel, MCL, N=68</td>
<td>62 (91%)</td>
<td>10 (15%)</td>
<td>43 (63%)</td>
<td>21 (31%)</td>
</tr>
</tbody>
</table>

B-Cell Maturation Antigen (BCMA) as a Target

- Multiple Myeloma is currently not a curable disease
- BCMA is expressed by mature B-lymphocytes
  - Necessary for survival of plasma cells
- Overexpression is associated with progression of multiple myeloma
  - Upregulation of nuclear factor kappa-B pathways
  - Upregulation of genes that promote survival, growth, angiogenesis, metastasis, and immunosuppression
- BCMA overexpression is associated with a poor response to treatment and poorer overall prognosis
- Soluble BCMA may be useful to monitor response to treatment

Anti-BCMA CAR T-Cell Therapy: bb2121

Open Label, Phase I, Multicenter, dose escalation and dose expansion

N=33
R/R Multiple Myeloma
At least 3 prior lines of therapy including proteasome inhibitor, immunomodulatory agent, and *daratumumab

Leukapheresis
Lymphodepletion
T-Cell Infusion

Primary Endpoint: Safety

Secondary Endpoints: response rates, duration of response
Exploratory Endpoints: MRD negative response, OS, PFS, serum BCMA levels, bb2121 quantification

*daratumumab and refractoriness to most recent line of therapy required for dose expansion participation

Best Responses Among Individual Patients

Objective Response Rate: 85%, 45% with CR or stringent CR

bb2121 Leads to Longer PFS at the Optimized Dose

Median time to response: 1 month
Median PFS: 11.8 months
bb2121: Cellular Kinetics

Phase II KarMMa:
Idecabtagene Vicleucel (bb2121)

Open Label, Phase II, Multicenter

N= R/R Multiple Myeloma
At least 3 prior lines of therapy including proteasome inhibitor, immunomodulatory agent, and daratumumab

Leukapheresis
Lymphodepletion
T-Cell Infusion
Multiple dosing levels

Primary Endpoint: ORR

Secondary Endpoints: CR, safety, duration of response, PFS, OS, MRD, QOL, duration of response

### Best Overall Response at Each Dosing Level

<table>
<thead>
<tr>
<th></th>
<th>Ide-Cel 150 X 10^6 (n=4)</th>
<th>Ide-Cel 300 X 10^6 (n=70)</th>
<th>Ide-Cel 450 X 10^6 (n=54)</th>
<th>All patients (n=128)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, %</td>
<td>50</td>
<td>69</td>
<td>82</td>
<td>73</td>
</tr>
<tr>
<td>CR rate, %</td>
<td>25</td>
<td>29</td>
<td>39</td>
<td>33</td>
</tr>
<tr>
<td>MRD negative, %</td>
<td>25</td>
<td>24</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>VGPR</td>
<td>25</td>
<td>14</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td>PR</td>
<td>0</td>
<td>26</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Median DoR, m</td>
<td>--</td>
<td>9.9</td>
<td>11.3</td>
<td>10.6</td>
</tr>
<tr>
<td>Median PFS, m</td>
<td>--</td>
<td>5.8</td>
<td>11.3</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Median time to first response: 1 month  
Median time to CR: 2.8 months

### CRS with Idacabtagene Vicleucel

<table>
<thead>
<tr>
<th>CRS Outcome</th>
<th>Ide-Cel 150 X 10^6 (n=4)</th>
<th>Ide-Cel 300 X 10^6 (n=70)</th>
<th>Ide-Cel 450 X 10^6 (n=54)</th>
<th>All patients (n=128)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 CRS event, n (%)</td>
<td>2 (50)</td>
<td>53 (76)</td>
<td>52 (96)</td>
<td>107 (84)</td>
</tr>
<tr>
<td>Maximum Grade, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1/2</td>
<td>2 (50)</td>
<td>49 (70)</td>
<td>49 (91)</td>
<td>100 (78)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>2 (3)</td>
<td>3 (6)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>1 (1)</td>
<td>0</td>
<td>1 (&lt; 1)</td>
</tr>
<tr>
<td>Grade 5</td>
<td>0</td>
<td>1 (1)</td>
<td>0</td>
<td>1 (&lt; 1)</td>
</tr>
<tr>
<td>Median Onset, days (range)</td>
<td>7 (2-12)</td>
<td>2 (1-12)</td>
<td>1 (1-10)</td>
<td>1 (1-12)</td>
</tr>
<tr>
<td>Median Duration, days (range)</td>
<td>5 (3-7)</td>
<td>4 (2-28)</td>
<td>7 (1-63)</td>
<td>5 (1-63)</td>
</tr>
<tr>
<td>Tocilizumab Use, n (%)</td>
<td>1 (25)</td>
<td>30 (43)</td>
<td>36 (67)</td>
<td>67 (52)</td>
</tr>
<tr>
<td>Corticosteroid Use, n (%)</td>
<td>0</td>
<td>7 (10)</td>
<td>12 (22)</td>
<td>19 (15)</td>
</tr>
</tbody>
</table>
Neurotoxicity with Idacabtagene Vicleucel

<table>
<thead>
<tr>
<th>Neurotoxicity Outcome</th>
<th>Ide-Cel 150 X 10⁶ (n=4)</th>
<th>Ide-Cel 300 X 10⁶ (n=70)</th>
<th>Ide-Cel 450 X 10⁶ (n=54)</th>
<th>All patients (n=128)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 neurotoxicity event, n (%)</td>
<td>0</td>
<td>12 (17)</td>
<td>11 (20)</td>
<td>23 (18)</td>
</tr>
<tr>
<td>Maximum Grade, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>0</td>
<td>7 (10)</td>
<td>5 (9)</td>
<td>12 (9)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>0</td>
<td>4 (6)</td>
<td>3 (6)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>1 (1)</td>
<td>3 (6)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Median Onset, days (range)</td>
<td>--</td>
<td>3 (1-10)</td>
<td>2 (1-5)</td>
<td>2 (1-10)</td>
</tr>
<tr>
<td>Median Duration, days (range)</td>
<td></td>
<td>3 (2-26)</td>
<td>5 (1-22)</td>
<td>3 (1-26)</td>
</tr>
<tr>
<td>Tocilizumab Use, n (%)</td>
<td>--</td>
<td>0</td>
<td>3 (6)</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Corticosteroid Use, n (%)</td>
<td>--</td>
<td>2 (3)</td>
<td>8 (15)</td>
<td>10 (8)</td>
</tr>
</tbody>
</table>


Future CAR T-Cell Approaches

- Many CAR T-cell products in the pipeline
  - Lisocabtagene maraleucel
  - JNJ-4528
- Dual Target CAR T-Cell therapies
  - CD19/CD22
- Combinations with checkpoint inhibitors
- Allogeneic CAR T-cell therapy
- Off-the-shelf options
- CAR T-cells for solid tumors
  - Understanding differences in tumor microenvironment
  - T-cell sequestration

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Switching Gears:
CAR T-Cell Toxicity: Balancing Benefits with Risk

CRS Pathophysiology

- Most common toxicity of cellular immunotherapy
- Triggered by activation and expansion of T cells
- Complex pathophysiology
  - IL-2, soluble IL-2Rα, INFγ, IL-6, soluble IL-6R, and GM-CSF
  - Monocyte and macrophage activation
  - Dendritic cell activation

**Clinical Symptoms**

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constitutional</td>
<td>Fever, rigors, malaise, fatigue, anorexia, myalgias, arthralgias, nausea, vomiting</td>
</tr>
<tr>
<td>Skin</td>
<td>Rash</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting, diarrhea</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Tachypnea, hypoxemia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia, widened pulse pressure, hypotension, increased cardiac output (early), diminished cardiac output (late)</td>
</tr>
<tr>
<td>Coagulation</td>
<td>Elevated D-dimer, hyprofibrinogenemia, bleeding</td>
</tr>
<tr>
<td>Renal</td>
<td>Azotemia</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Transaminitis, hyperbilirubinemia</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Headache, mental status changes, confusion, delirium, word finding difficulty, aphasia, hallucinations, tremor, dysmetria, altered gait, seizure</td>
</tr>
</tbody>
</table>

**ASTCT CRS Grading Consensus Guidelines**

<table>
<thead>
<tr>
<th>CRS Parameter</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Temp ≥ 38°C</td>
<td>Temp ≥ 38°C</td>
<td>Temp ≥ 38°C</td>
<td>Temp ≥ 38°C</td>
</tr>
<tr>
<td>Hypotension</td>
<td>None</td>
<td>Not requiring vasopressors</td>
<td>Requiring one vasopressor</td>
<td>Requiring multiple vasopressors</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>None</td>
<td>Low-flow oxygen</td>
<td>High flow oxygen</td>
<td>Positive pressure</td>
</tr>
</tbody>
</table>
CRS with CAR T-Cells

- High disease burden = increased antigen load = more toxicity
- Improved CAR constructs = more toxicity
  - Increased cytokine production
  - Increased T-cell activation and expansion
- Peaks within 1-2 weeks of cell infusion
- May or may not be associated with neurotoxicity


Biomarkers for CRS

- Barriers to biomarker utilization
  - Assays are not readily available
  - Severity of CRS is not predicted by cytokine levels
  - Panels need to measure multiple cytokines
- C-reactive protein (CRP)
  - Acute phase reactant
  - Produced in response to IL-6 production
  - Lag time is 1-2 days
  - Peak levels and fold increase in CRP may be predictive
- Ferritin is not predictive of CRS development but may indicate severity
- Hypofibrinogenemia

Variability in Cytokine Response

- Baseline cytokines are variable based on age, gender and ethnicity
- Disease burden
- Type of malignancy
- Relative and absolute changes in cytokine must be considered
- Presence of inflammatory disease
- Infection


Tocilizumab

- Humanized mAB targeting IL-6R
  - Inhibits IL-6 binding to both membrane-associated and soluble IL-6Rs
  - Inhibiting classical and proinflammatory trans-signaling
  - Side effects: transaminitis, thrombocytopenia, hyperlipidemia, and an increased risk of infection
- Effective treatment for CRS
  - Symptoms begin to clear within hours
  - Cytokines return to normal within 48 hours
  - Dose: 8 mg/kg IV once and may be repeated up to 4 doses
  - Must keep 2 doses per patient available per REMS for approved CAR T-cell therapies

FDA Approval of Tocilizumab for CRS

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Retrospective, pooled analysis of prospective clinical trials involving CTL019 and KTE-C19 in hematologic malignancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary objective</td>
<td>Characterize resolution of CRS (grade 3 or higher)</td>
</tr>
</tbody>
</table>
| Responders defined                  | • No fever or vasopressors required within 14 days of tocilizumab administration  
• No more than 2 doses of tocilizumab required  
• No drugs other than tocilizumab or corticosteroids used for treatment |
| Results                              |                                                                                                                   |
| Response Rate                       | 69%                                                                                                               |
| Median time to tocilizumab (days)   | 4                                                                                                                  |
| Median doses of tocilizumab         | 1                                                                                                                  |
| Median time to response (days)      | 4                                                                                                                  |
|                                      | KTE-C19, N=15                                                                                                      |
|                                      | 53%                                                                                                                |
|                                      | 3                                                                                                                  |
|                                      | 2                                                                                                                  |
|                                      | 4.5                                                                                                                |


Other Alternatives for Prevention and Treatment of CRS

• Prophylactic tocilizumab?
• CAR T-cell dose refinement
• Siltuximab
  • binds IL-6
• Anakinra
  • IL-1 receptor antagonist
• Point of care cytokine measurement
• Incorporation of suicide genes

Pathophysiology of ICANS

• Passive diffusion of cytokines into the brain
  • High serum levels of IL-6 and IL-15 associated with severe neurotoxicity
• Trafficking of T cells into the CNS
  • Presence of CAR T-cells in cerebrospinal fluid from patients with neurotoxicity
• Disruption of blood brain barrier
  • Elevated protein levels
• Secondary cortical irritation
  • Diffuse generalized slowing consistent with encephalopathy on EEG
  • Seizure activity
• MRI and CT scans are usually negative
  • Exceptions: cerebral edema

Characterization of ICANS

• Typically manifests as toxic encephalopathy
  • Earliest signs are diminished attention, language disturbance, impaired handwriting
  • Severe CRES is associated with seizures, mental obtundation, increased ICP, and cerebral edema
• May be biphasic
  • Phase I: typically within first 5 days
    • Fever and other CRS symptoms present
    • Typically shorter duration and lower grade
    • Responsive to anti-IL-6 therapy
  • Phase II: delayed neurotoxicity occurring during weeks 3-4 after CAR T-cell therapy
    • Longer duration and higher grade neurotoxicity
    • Anti-IL-6 therapy is not effective!
ASTCT ICANS Grading Consensus Guidelines

<table>
<thead>
<tr>
<th>Domain</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICE</td>
<td>7-9</td>
<td>3-6</td>
<td>0-2</td>
<td>Unable to perform</td>
</tr>
<tr>
<td>Level of Consciousness</td>
<td>Awakens spontaneously</td>
<td>Awakens to voice</td>
<td>Awakens with tactile stimulus</td>
<td>Unarousable</td>
</tr>
<tr>
<td>Seizure</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Seizure resolving with intervention</td>
</tr>
<tr>
<td>Motor Findings</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Deep focal motor weakness</td>
</tr>
<tr>
<td>Increased ICP/cerebral edema</td>
<td>N/A</td>
<td>N/A</td>
<td>Focal/Local Edema</td>
<td>Diffuse cerebral edema; Papilledema</td>
</tr>
</tbody>
</table>

Management of ICANS

<table>
<thead>
<tr>
<th>Grade</th>
<th>Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Supportive care, IV fluids&lt;br&gt;Withhold oral intake&lt;br&gt;Management of agitation&lt;br&gt;Neurology consult: papilledema assessment, lumbar puncture, MRI, EEG&lt;br&gt;If associated with CRS, consider anti-IL-6 therapy</td>
</tr>
<tr>
<td>2</td>
<td>Dexamethasone 10 mg IV q6h or methylprednisolone 1 mg/kg IV q12h&lt;br&gt;Consider transfer to ICU</td>
</tr>
<tr>
<td>3</td>
<td>Transfer to ICU&lt;br&gt;Corticosteroids, continue until grade 1 ICANS then taper&lt;br&gt;Acetazolamide</td>
</tr>
<tr>
<td>4</td>
<td>Consider mechanical ventilation&lt;br&gt;Seizure management&lt;br&gt;High dose corticosteroids&lt;br&gt;Management of increased ICP and papilledema</td>
</tr>
</tbody>
</table>
Zuma 1, Cohort 4: Early Steroid Use May Reduce Severe Toxicities without Compromising Efficacy

- Early steroid intervention
  - Grade 1 CRS
  - Grade 1 ICANS
  - No improvement with 3 days of supportive care
- Primary endpoint
  - Severity or CRS and ICANS
- Results
  - ≥ Grade 3 CRS or ICANS was lower than cohorts 1 and 2
  - Responses were similar
  - No effects on CAR T-cell expansion

Key Takeaways

- Approved CAR T-cell therapies have long-term data that support their use in patients with relapsed/refractory B-cell malignancies.
- There are many CAR T-cell products in development, including those that are targeting new antigens, such as BCMA.
- Toxicity remains a concern with CAR T-cell therapies, with the most significant being CRS and neurotoxicity.
- Early intervention with steroids may reduce toxicity of CAR T-cell therapy without affecting efficacy outcomes.
Thank You