The Emerging Role of Immunotherapy for the Treatment of Relapsed/Refractory Diffuse Large B-cell Lymphoma

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Disclosures

I have nothing to disclose.
Objectives

1. Discuss the role of novel monoclonal antibodies for patients with relapsed refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL)

2. Review the outcomes associated with bispecific antibody therapy in R/R DLBCL

3. Describe ongoing research with checkpoint inhibitors in R/R DLBCL
Cancer Incidence...The Bad and the Good

American Cancer Society 2020 Statistics
- 1.8 million new cancer diagnoses
- 606,000 cancer deaths

Hematologic malignancies
- Acute leukemia
  - 26,090 new cases; 10,370 deaths
- Lymphoma
  - 85,720 new cases; 20,910 deaths
- Multiple myeloma
  - 32,270 new cases; 12,830 deaths
Cancer Incidence...The Bad and the Good

Decrease in mortality

– 29%
– 2.9 million fewer deaths

Why?

– Lung cancer
  • Decrease smoking
  • Decrease mortality
– Breakthroughs!
  • Hematological & lymphoid

Siegel R. Ca Cancer J Clin 2020; 70-7-30
Diffuse Large B-Cell Lymphoma

Cancer Stat Facts: NHL — Diffuse Large B-Cell Lymphoma (DLBCL)
Accessed 6/23/20
Non-Hodgkin’s Lymphoma (NHL)

DLBCL
- Most common subtype

Heterogeneous disease
- Germinal center B cell (GCB)
  - 70-80% cure rate
- Activated B cell (ABC)
  - 40% cure rate
DLBCL Therapy Options

Initial therapy
- R-CHOP + radiation
- 20-50% refractory or will relapse

R/R Disease
- Transplant candidate?
- Non-transplant candidate?
R/R DLBCL Therapy Options

HSCT Candidate
- Second line therapy
- 50% relapse

Non-HSCT Candidate
- Second line therapy
- 30-40% response

Crump M et al. Blood; 2017; 130 1800-1808
SCHOLAR-1

Pooled data
- Two phase III trials
- Two observational cohorts

Patient groups
- Progressive disease
- Stable disease as best response
- Relapsed ≤ 12 months post HSCT

Crump, M et al. Blood 2017; 130(16): 1800-1808
SCHOLAR-1: Outcomes for R/R DLBCL

Refractory disease
  ◦ No response to therapy
  ◦ Relapse in ≤12 months post HSCT

Pooled data
  ◦ Two phase III trials
  ◦ Two observational cohorts

Patient groups
  ◦ Progressive disease
  ◦ Stable disease as best response
  ◦ Relapsed ≤12 months post HSCT
## SCHOLAR-1

<table>
<thead>
<tr>
<th></th>
<th>Pooled patients evaluated (N = 523)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Response rate, % (95% CI)</strong></td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>26 (21-31)</td>
</tr>
<tr>
<td>CR</td>
<td>7 (3-15)</td>
</tr>
<tr>
<td>PR</td>
<td>18 (13-23)</td>
</tr>
<tr>
<td>OS</td>
<td>6.3 months</td>
</tr>
<tr>
<td><strong>Response rate by refractory category</strong></td>
<td></td>
</tr>
<tr>
<td>Primary refractory</td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>20 (11-34)</td>
</tr>
<tr>
<td>CR</td>
<td>3 (1-11)</td>
</tr>
<tr>
<td>Refractory to second line or later</td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>26 (17-39)</td>
</tr>
<tr>
<td>CR</td>
<td>10 (5-20)</td>
</tr>
<tr>
<td>Relapse ≤ 12 months post HSCT</td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>34 (24-45)</td>
</tr>
<tr>
<td>CR</td>
<td>15 (6-31)</td>
</tr>
</tbody>
</table>

Crump, M et al. Blood 2017; 130(16): 1800-1808
CAR T-cell Therapy

First relapse
- Partial response (PR) the secondary therapy
  - Regardless of eligibility for HSCT

Second relapse and beyond
- If not previously given

ZUMA-1
- ORR 81% (49%CR; 32%PR)

JULIET
- ORR 52% (40% CR; 12% PR)

ORR = overall response rate
Monoclonal Antibodies

POLATUZUMAB VEDOTIN
TAFASITAMAB
Polatuzumab vedotin

Antibody drug conjugate
  ◦ Toxin – monomethylauristatin E (MMAE)
  ◦ Targets CD79

Indication
  ◦ Patients with relapsed or refractory DLBCL after at least two prior therapies

Polivy [package insert]. South San Francisco CA: Genetech, Inc.; 2019
Polatuzumab vedotin
Mechanism of Action

Polatuzumab vedotin

Multi-center trial relapsed refractory DLBCL

- Polatuzumab ± bendamustine and rituximab (BR)
  - At least 1 prior regimen
  - Not eligible for transplant

- Efficacy
  - Complete response
  - Duration of response

- Patient characteristics
  - Median age 69 years (30-86)
  - Median number of prior therapies 2 (1-7)
Polatuzumab vedotin

<table>
<thead>
<tr>
<th>Response</th>
<th>Polatuzumab + BR n = 40</th>
<th>BR n=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective response at the end of treatment</td>
<td>18 (45%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p = 0.026</td>
</tr>
<tr>
<td>Progression Free Survival (PFS)</td>
<td>8 months</td>
<td>2 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p = &lt;0.001</td>
</tr>
<tr>
<td>Overall Survival (OS)</td>
<td>12 months</td>
<td>5 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p = &lt;0.0023</td>
</tr>
</tbody>
</table>

Survival benefit observed

- GCB and non-GCG
- Double expresser status

Sehn LH, Blood 2018; 132 Abstract 1683
Polatuzumab vedotin
Reported Toxicities

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Grades P+BR</th>
<th>Grade &gt;3 P+BR</th>
<th>All Grades BR</th>
<th>Grade &gt;3 BR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>49</td>
<td>42</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>49</td>
<td>40</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>Anemia</td>
<td>47</td>
<td>24</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>40</td>
<td>0</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>38</td>
<td>4.4</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>18</td>
<td>2.2</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>33</td>
<td>2.2</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>22</td>
<td>16^</td>
<td>15</td>
<td>2.6^</td>
</tr>
</tbody>
</table>

^ = fatal outcomes; 2 P+BR; 1 BR

Sehn LH, Blood 2018; 132 Abstract 1683
Tafasitamab (MOR208)

CD19 antigen activity
- Enhances B-cell antigen receptor signaling
  - PI3K
  - Bruton’s tyrosine kinase
- Tumor proliferation and survival
- Preserved during lymphoma treatment

Monoclonal antibody
- Directly induces cytotoxicity
  - Disrupting B-cell antigen signaling
Tafasitamab (MOR208) R/R NHL

Phase IIa
- Multi-center, open, single arm trial
- Tafasitamab 12 mg/kg
  - Days 1, 8, 15, 22 of a 28 day cycle
  - Two planned cycles
    - More therapy if response
- Pre-medications: antipyretics, anti-histamine, H1 receptor blocker & steroid

Enrollment
- 35 DLBCL & 34 FL

NHL = Non-Hodgkin’s Lymphoma; FL = follicular lymphoma
Jurczak W. Annals of Oncology; 2018 29: 1266-1272
## Tafasitamab (MOR208) R/R NHL

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>DLBCL (%)</th>
<th>FL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 35</td>
<td>n = 34</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td>71</td>
<td>62</td>
</tr>
<tr>
<td><strong>Ann Arbor Stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stages I-II</td>
<td>4 (11)</td>
<td>5 (15)</td>
</tr>
<tr>
<td>Stages III-IV</td>
<td>30 (86)</td>
<td>29 (85)</td>
</tr>
<tr>
<td><strong>Prior lines of therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12 (34)</td>
<td>13 (38)</td>
</tr>
<tr>
<td>2</td>
<td>8 (23)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>3</td>
<td>9 (26)</td>
<td>5 (15)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>6 (17)</td>
<td>12 (35)</td>
</tr>
<tr>
<td><strong>Duration of response most recent treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>26 (74)</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Rituximab refractory</td>
<td>24 (69)</td>
<td>17 (50)</td>
</tr>
<tr>
<td>Post HCST</td>
<td>4 (11)</td>
<td>6 (18)</td>
</tr>
</tbody>
</table>
## Tafasitamab (MOR208) R/R NHL

<table>
<thead>
<tr>
<th>Response</th>
<th>DLBCL (%)</th>
<th>FL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 35</td>
<td>N =34</td>
</tr>
<tr>
<td>CR</td>
<td>2 (6)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>PR</td>
<td>7 (20)</td>
<td>7 (21)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>5 (14)</td>
<td>16 (47)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>11 (31)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>ORR</td>
<td>9 (26)</td>
<td>10 (29)</td>
</tr>
<tr>
<td>Median time to response</td>
<td>2 months</td>
<td>2.8 months</td>
</tr>
<tr>
<td>Median duration of response</td>
<td>20 months (1-26.5)</td>
<td>NR</td>
</tr>
<tr>
<td>Response &gt; 12 months</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Median PFS (median follow up 21 months)</td>
<td>2.7 months</td>
<td>8.8 months</td>
</tr>
</tbody>
</table>
## Tafasitamab (MOR208) R/R NHL

<table>
<thead>
<tr>
<th>Safety</th>
<th>DLBCL (%)</th>
<th>FL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade ≥ 3</td>
<td>19 (54)</td>
<td>9 (27)</td>
</tr>
<tr>
<td><strong>Hematological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>6 (17)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>2 (6)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Anemia</td>
<td>3 (9)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Non-hematological</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2 (6)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td><strong>Infusion reactions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1/2</td>
<td>4 (11)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Grade 3/4</td>
<td>0</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>
Tafasitamab + lenalidomide (L-MIND) in R/R DLBCL

Phase II

- Multi-center, open, single arm trial

Tafasitamab 12 mg/kg

- Days 1, 8, 15, 22 of a 28 day cycles 1-3
- Cycles 4 and beyond – days 1, 15
- 12 cycles combination therapy
  - Monotherapy if response

Pre-medications

- Antipyretics, anti-histamine, H1 receptor blocker, steroid & merperidine

Lenalidomide

- Days 1-21 of each cycle

Salls G. Lancet, published online June 5 2020
doi.org/10.1016/S1470-2045(20)30225-4
## Tafasitamab + lenalidomide (L-MIND) in R/R DLBCL

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>DLBCL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 81</td>
</tr>
<tr>
<td>Age, years</td>
<td>72 (62-76)</td>
</tr>
<tr>
<td>Ann Arbor Stage</td>
<td></td>
</tr>
<tr>
<td>Stages I-II</td>
<td>20 (25)</td>
</tr>
<tr>
<td>Stages III-IV</td>
<td>61 (75)</td>
</tr>
<tr>
<td>Previous anti-CD20 therapy</td>
<td>81 (100)</td>
</tr>
<tr>
<td>Primary refractory</td>
<td>15 (19)</td>
</tr>
<tr>
<td>Rituximab refractory</td>
<td>34 (42)</td>
</tr>
<tr>
<td>Previous HSCT</td>
<td>9 (11)</td>
</tr>
<tr>
<td>&gt;3</td>
<td></td>
</tr>
<tr>
<td>IPI at screening</td>
<td></td>
</tr>
<tr>
<td>0-2 (low – intermediate risk)</td>
<td>40 (49)</td>
</tr>
<tr>
<td>3-5 (intermediate high – high risk)</td>
<td></td>
</tr>
</tbody>
</table>

Salls G. Lancet, published online June 5 2020
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**Response**

<table>
<thead>
<tr>
<th>Response</th>
<th>DLBCL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective response</strong></td>
<td>48 (60)</td>
</tr>
<tr>
<td>Best objective response</td>
<td></td>
</tr>
<tr>
<td><strong>CR</strong></td>
<td>34 (43)</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>14 (18)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>11 (14)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>13 (16)</td>
</tr>
<tr>
<td>Median duration of response (n = 48)</td>
<td>21.7 months</td>
</tr>
<tr>
<td>c-MYC translocations (7)</td>
<td>3 CR</td>
</tr>
<tr>
<td></td>
<td>1 PR</td>
</tr>
</tbody>
</table>
# Tafasitamab + lenalidomide (L-MIND) in R/R DLBCL

<table>
<thead>
<tr>
<th>Safety</th>
<th>Grade 1-2 (%)</th>
<th>Grade 3 (%)</th>
<th>Grade 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematological events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (1)</td>
<td>22 (27)</td>
<td>17 (21)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>11 (14)</td>
<td>10 (12)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Anemia</td>
<td>22 (27)</td>
<td>6 (7)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Non-hematological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All rash</td>
<td>22 (27)</td>
<td>7 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (32)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Asthenia</td>
<td>17 (21)</td>
<td>2 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Cough</td>
<td>17 (21)</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>18 (22)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Decrease appetite</td>
<td>16 (20)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>hypokalemia</td>
<td>10 (12)</td>
<td>4 (5)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>
Tafasitamab + lenalidomide (L-MIND) in R/R DLBCL

Conclusion
- Suggest synergy of tafasitamab + lenalidomide

Notable responses
- Refractory disease
- Refractory to rituximab
- Germinal center B-cell disease

Safety
- Infusion reactions most common
- Neutropenia common
  - Short duration
  - Responds to GCSF

Compatible with CAR T-cell therapy?

Salls G. Lancet, published online June 5 2020
doi.org/10.1016/S1470-2045(20)30225-4
Learning Assessment (Are you still with me?)

Which of the following statements about monoclonal antibodies therapies in DLBCL is TRUE?

1. Infusion related reactions are uncommon in newer agents than traditional anti-CD20 agents
2. Tafasitamab + lenalidomide reported significant toxicities and the combination should be avoided
3. Tafasitamab has activity in both FL and DLBCL as a single agent
4. All statements are TRUE

text SallyBarbour693 to 22333

www.pollev.com/sallybarbour693
Which of the following statements about monoclonal antibodies therapies in DLBCL is TRUE?

- Infusion related reactions are uncommon in newer agents than traditional anti-CD20 agents
- Tafasitamab + lenalidomide reported significant toxicities and the combination should be avoided
- Tafasitamab has activity in both FL and DLBCL as a single agent

All statements are TRUE
Bispecific Antibodies

BLINATUMOMAB
MOSUNETUZUMAB
Blinatumomab

- CD19
- Tumor Cell
- BiTE
- CD3
- T Cell
- Redirected Lysis
Blinatumomab in R/R DLBCL

Phase I

- 38 R/R NHL patients
  - 18 (47%) FL; 13 (34%) MCL; 5 (13%) DLBCL; 2 other
- ORR 69% across all subtypes
  - ORR 55% for DLBCL
  - Maximum tolerated dose 60 µg/m²/day CIWI 4-8 weeks
- Median response duration
  - 404 days (95% CI, 207-1129 days)
- Safety
  - 22% experience grade 1-3 neurologic toxicity
  - Reversible and manageable

FL – follicular lymphoma, MCL = mantle cell lymphoma
Blinatumomab in R/R DLBCL Long Term Outcomes

Survival (n = 38)
- Median OS 4.6 years (14.6 days – 10.7 years)
- Median PFS 6.7 months (0-10.3 years)

Target dose critical
- Patients treated ≥60 μg/m²/day
  - OS 5.8 years (4 months -10.3 years)
- Patients treated ≤60 μg/m²/day
  - OS 1.1 year (14.6 days -10.6 years)
  - Hazard ratio 0.3 (95% CI, 0.2-0.8; P = 0.007)
Blinatumomab in R/R DLBCL
Long Term Outcomes

Safety

◦ Hospitalization
  ◦ Infections: pneumonia, sepsis, catheter infection, diarrhea
    ◦ Median time to hospitalization 234 days (5-3151 days)
    ◦ IVIG supplementation – 4 patients

◦ Cancer
  ◦ Breast, stomach, cervical cancers (2.5-6.25 years)

Dufner V; Blood Advances. 2019; 3 (16): 2491-2498
Blinatumomab in Newly Diagnosed DLBCL

Interim phase II analysis

- R-chemotherapy
  - R-CHOP, R-DA-EPOCH, R-CHOEP
- Blinatumomab
  - Cycle 1: 9 μg/m²/day x7 days → 28 μg/m²/day x7 days → 112 μg/m²/day x42 days → 28 days rest
  - Cycle 2: 9 μg/m²/day x7 days → 28 μg/m²/day x7 days → 112 μg/m²/day x14 days

Katz D. Blood (2019) 134 (Supplement_1): 4077
Blinatumomab in Newly Diagnosed DLBCL

Outcomes (n= 28)
- ORR 25/28 (89%)
- No metabolic response (n= 4)
  - All had objective response post blinatumomab
- Minimal residual disease (MRD)
  - 9/13 convert to MRD (-) post blinatumomab

Safety
- Grade ≥3 adverse events
  - 11% neurologic, 14% neutropenia, 14% neutropenic fever
  - 2 patients discontinued treatment
Mosunetuzumab

Bispecific monoclonal antibody
- CD3 cross-linked to CD20

Interim phase Ib analysis (N = 218)
- Indolent and aggressive lymphoma
- R/R DLBCL (87/124)
  - 12 prior CAR T-cell therapy
- Dose escalation cycle 1 on days 1, 8, 15
  - 1, 2 and 60 mg administered
  - Cycle 2 fixed dose day 1 out of 21 days
- Maximum 17 cycles
Mosunetuzumab

Interim phase Ib analysis

- Efficacy aggressive NHL
  - ORR 37.1 % and CR 19.4% aggressive

- Durability of response
  - 70.8% that achieved CR maintained at 16 months

- Previous CAR T-cell therapy
  - ORR 38.9% with CR 22.2%

Mosunetuzumab

Safety

- CRS 28.4 % - majority grade I/II
  - 3 patients required tocilizumab
- Neurological – 44%
  - Grade 1, 28.0%; Grade 2, 12.8%; Grade 3, 3.2%
  - Headache, insomnia, dizziness
Which of the following toxicities can be seen in patients receiving bispecific antibodies?

1. Cytokine release syndrome
2. Constipation
3. Weight loss
4. Secondary AML
Which of the following toxicities can be seen in patients receiving bispecific antibodies?

Cytokine release syndrome  A
Constipation             B
Weight loss              C
Secondary AML           D
Checkpoint Inhibitors

PEMBROLIZUMAB
NIVOLUMAB
Pembrolizumab Maintenance after Autologous HSCT

Phase 2 open label multi-center trial
- Setting of minimal residual disease
- PD-1 blockade early may prevent early relapse

Treatment
- Within 60 days of HSCT
- Pembrolizumab 200 mg every 3 weeks

Outcome
- Progression free survival increase
  - 60% → 80%
Pembrolizumab Maintenance after Autologous HSCT

Patients (n = 29)
- Median age 57 years (22-76 years)
- Median previous therapies 2

Disease status
- Prior/Post HSCT
  - CR 18 (62%) → CR 25 (86%)

Outcomes (n= 28)
- 10 patients relapsed
  - Median 5 months (3-18 months)
  - CR 59% (95% CI, 34-76%) at 18 months
  - Failed to meet 80%

Pembrolizumab Maintenance after Autologous HSCT

Outcomes (n= 28)
- 10 patients relapsed
  - Median 5 months (3-18 months)
  - CR 59% (95% CI, 34-76%) at 18 months
  - Failed to meet 80%

Safety
- 23 patients grade >3 adverse events
  - 6 patients discontinued due to toxicity

Neutropenia
- Most common grade ≥3
- Leukopenia, thrombocytopenia

Immune mediated grade ≥2
- 10 patients
- Pneumonitis, transaminitis and rash

Pembrolizumab Maintenance after Autologous HSCT

Adverse events

- Neutropenia
  - Most common grade ≥3
- Hematologic
  - Leukopenia, thrombocytopenia

Immune mediated grade ≥2

- 10 patients
  - Pneumonitis, transaminitis and rash
Combined Ipilimumab and Nivolumab Consolidation After HSCT (CPIT-001 Trial)

High risk hematologic malignancies
- Primary refractory, relapsed < 12 months from induction
- Multiple myeloma, peripheral T-cell lymphoma

Therapy: 14-28 days post HSCT
- Ipilimumab 1 mg/kg weeks 1, 4, 7, 10, 16, 22
- Nivolumab 3 mg/kg weeks 1, 4, 7, 10, 12, 14, 16, 18, 20, 22, 24, 26

Endpoint
- Safety, PFS and OS at 18 months

Skarbnik A. Blood. 2018; 132 (supplement 1): 256
## Combined Ipilimumab and Nivolumab Consolidation After HSCT (CPIT-001 Trial)

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
<th>Disease post HSCT</th>
<th>PFS 18 months</th>
<th>OS 18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Refractory Disease</td>
<td>7</td>
<td>CR 57% PR 43%</td>
<td>83%</td>
<td>100%</td>
</tr>
<tr>
<td>DLBCL Relapse &lt; 12 months post induction</td>
<td>7</td>
<td>CR 43% PR 57%</td>
<td>40%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Skarbnik A. Blood. 2018; 132 (supplement 1): 256
Combined Ipilimumab and Nivolumab Consolidation After HSCT (CPIT-001 Trial)

Safety
- Immune related adverse events (iAE)
  - 65% > grade 2; systemic steroids

Common iAE
- Colitis 58%, rash 48%, thrombocytopenia 45%, anemia 45%, transaminitis 32%
- 1 death secondary to pneumonitis

Time to iAE
- Median 4 weeks
- Resolution 1 week post steroid therapy

Response
- No correlation with development iAE, use of steroids

Skarbnik A. Blood. 2018; 132 (supplement 1): 256
Combined Ipilimumab and Nivolumab Consolidation After HSCT (CPIT-001 Trial)

Conclusions
- Benefit in primary refractory DLBCL
- Less benefit in early relapse patients
  - Most heavily pretreated
  - Toxicity profile manageable

Phase II trial
- Planned
The Final Learning Assessment

Which of the following statements accurately summarizes the use of checkpoint inhibitors post HSCT?

1. No benefit has been demonstrated over watching and waiting
2. Pembrolizumab, ipilimumab, nivolumab are all well tolerated post HSCT
3. Occurrences of iAE do not correlate with disease response
4. All patients with DLBCL should receive a checkpoint inhibitor

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Which of the following statements accurately summarizes the use of checkpoint inhibitors post HSCT?

- No benefit has been demonstrated over watching and waiting.
- Pembrolizumab, ipilimumab, nivolumab are all well tolerated post HSCT.
- Occurrences of iAE do not correlate with disease response.
- Occurrences of iAE do not correlate with disease response.
The Role of Immunotherapy in R/R DLBCL

Monoclonal antibodies
- Polatuzumab and tafasitamab
- Benefit in refractory patients with manageable toxicity

Bispecific antibodies
- Blinatumomab – activity in r/r patients
  - Doses higher than traditional dosing in leukemia
- Mosunetuzumab – promising agent under investigation

Checkpoint inhibitors
- Less clinical success
- Maintenance or in relapsed disease
- Phase II planned: nivolumab and ipilimumab
The Emerging Role of Immunotherapy for the Treatment of Relapsed/Refractory Diffuse Large B-cell Lymphoma

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