Clinical Practice Guideline Webinar – Immunotherapy for the Treatment of Lymphoma

Monday, January 25, 2021
5 – 6 p.m. EST

Jointly provided by Postgraduate Institute for Medicine and the Society for Immunotherapy of Cancer

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Webinar Agenda

5:00 – 5:05 p.m. ET  Overview: Welcome and Introductions

5:05 – 5:45 p.m. ET  Presentation and discussion of guideline content

5:45 – 5:55 p.m. ET  Question and Answer Session

5:55 – 6:00 p.m. ET  Closing Remarks
How to Submit Questions

• Click the “Q&A” icon located on at the bottom of your Zoom control panel
• Type your question in the Q&A box, then click “Send”
• Questions will be answered in the Question & Answer session at the end of the webinar (as time permits)
Webinar faculty

Michael R. Bishop, MD
University of Chicago

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The University of Texas
MD Anderson Cancer Center

Stephen M. Ansell, MD, PhD
Mayo Clinic Cancer Center
Outline

• Introduction to lymphoma
• Management of B-cell non-Hodgkin lymphoma
• Management of Hodgkin lymphoma, chronic lymphocytic leukemia and T cell lymphoma
• Toxicity management
Lymphoma

- Most common type of hematologic cancer
- Estimated 85,720 new cases and 20,910 deaths in 2020
- Treatment modalities include chemotherapy, radiotherapy, stem cell transplantation, targeted therapies and immunotherapy
Guideline development

• *The Institute of Medicine’s Standards for Developing Trustworthy Practice Guidelines* were used to develop these recommendations

• Panel consisted of 12 participants, including medical oncologists, a pediatric oncologist, a nurse practitioner, and a patient advocate

• Recommendations come from literature evidence, supplemented with clinical experience of the panel members where necessary

• Consensus defined as ≥75% agreement
Guideline development

Position article and guidelines

Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of lymphoma

Sattva S Neelapu¹, Sherry Adkins¹, Stephen M Ansell², Joshua Brody³, Mitchell S Cairo⁴, Jonathan W Friedberg⁵, Justin P Kline⁶, Ronald Levy⁷, David L Porter⁸, Koen van Besien⁹, Michael Werner¹⁰ and Michael R Bishop⁶

Author affiliations +

Abstract

The recent development and clinical implementation of novel immunotherapies for the treatment of Hodgkin and non-Hodgkin lymphoma have improved patient outcomes across subgroups. The rapid introduction of immunotherapeutic agents into the clinic, however, has presented significant questions regarding optimal treatment scheduling around existing chemotherapy/radiation options, as well as a need for improved understanding of how to properly manage patients and recognize toxicities. To address these challenges, the Society for Immunotherapy of Cancer (SITC) convened a panel of experts in lymphoma to develop a clinical practice guideline for the education of healthcare professionals on various aspects of immunotherapeutic treatment. The panel discussed subjects including treatment scheduling, immune-related adverse events (irAEs), and the integration of immunotherapy and stem cell transplant to form recommendations to guide healthcare professionals treating patients with lymphoma.
General recommendations for lymphoma

• **Clinical trials** should be strongly considered as a treatment option at each stage of therapy for eligible patients with lymphoma.

• All patients newly diagnosed with lymphoma should receive initial imaging via **FDG-PET/CT**.

• Patients should be routinely administered **complete blood count (CBC) and serum IgG tests**. Infection precautions may be considered in patients with decreased neutrophil and absolute lymphocyte counts from CBC tests, as well as low levels of serum IgG.

• All patients with newly diagnosed lymphoma should receive assessment of their **cardiovascular history** and risk factors prior to receiving potentially cardiotoxic therapies.
Outline

• Introduction to lymphoma
• Management of B-cell non-Hodgkin lymphoma
• Management of Hodgkin lymphoma, chronic lymphocytic leukemia and T cell lymphoma
• Toxicity management
Diffuse Large B-cell Lymphoma Case

• 47 yo male who presented with stage IVB DLBCL with bulky retroperitoneal lymphadenopathy of up to 15 cm in size

• Had partial response after 4 cycles of DA-EPOCH-R but progressed after cycle 6

• After 1 cycle of R-DHAP he had increasing back pain and a CT scan revealed progressive disease

• Treatment options approved for 2\textsuperscript{nd} or 3\textsuperscript{rd} line DLBCL:
  • CAR T-cell therapy
  • Polatuzumab + bendamustine + rituximab
  • Tafasitamab + lenalidomide

• What is the best treatment option for this patient?
Treatment of NHL

Immunotherapy options include:

- Monoclonal antibodies
  - Rituximab
  - Obinutuzumab
  - Mogamulizumab-kpkc
  - Tafasitamab-cxix
- Antibody-drug conjugates
  - Ibritumomab tiuxetan
  - Brentuximab vedotin
  - Polatuzumab vedotin-piix

- Cellular therapies
  - Axicabtagene ciloleucel
  - Tisagenlecleucel
  - Brexucabtagene autoleucel
- Immunomodulators
  - Lenalidomide
- Immune checkpoint inhibitors
  - Pembrolizumab
Rituximab

Anti-CD20 antibody

- **Approved for:**
  - R/R low grade or follicular CD20-positive B-cell NHL as a single agent
  - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first-line chemotherapy and, in patients achieving a CR or PR to rituximab + chemotherapy, as single-agent maintenance
  - Non-progressing low-grade CD20-positive B-cell NHL as single agent after first-line cyclophosphamide, vincristine and prednisone
  - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP or other anthracycline chemotherapy
Obinutuzumab

Anti-CD20 antibody

• Approved for:
  • R/R follicular lymphoma after rituximab, in combination with bendamustine, followed by obinutuzumab monotherapy
  • Previously untreated stage II bulky, III or IV follicular lymphoma, in combination with chemotherapy, followed by obinutuzumab monotherapy if achieving at least a PR
Tafasitamab-cxix

Anti-CD19 antibody

• Approved for: R/R DLBCL in combination with lenalidomide for patients ineligible for autoSCT

• Fc engineering enhances ADCC and ADP compared to unmodified IgG

• Panel noted tafasitamab + lenalidomide as a treatment option for second-line treatment of transplant-ineligible DLBCL
Ibritumomab tiuxetan
Anti-CD20 antibody + $^{90}$Y

- Delivers cytotoxic radiation to CD20-expressing cells

- Approved for:
  - R/R low-grade or follicular NHL
  - Follicular NHL with a PR or CR to first-line chemotherapy

- Requires additional handling/safety considerations, since radioactive

- Dosing in units of millicurie (mCi) per kg
Polatuzumab vedotin-piiq
Anti-CD79b antibody + monomethyl auristatin E

• Approved for:
  • R/R DLBCL after at least two prior therapies, in combination with rituximab and bendamustine

• Committee recommends PV as the third-line treatment for patients with DLBCL who are ineligible for CAR T therapy.
Axicabtagene ciloleucel, tisagenlecleucel and brexucabtagene autoleucel

CD19 CAR T therapies

<table>
<thead>
<tr>
<th>Agent</th>
<th>Approved indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axicabtagene ciloleucel</td>
<td>R/R large B cell lymphomas after 2+ prior therapies</td>
</tr>
<tr>
<td>Tisagenlecleucel</td>
<td>R/R large B cell lymphomas after 2+ prior therapies</td>
</tr>
<tr>
<td>Brexucabtagene autoleucel</td>
<td>R/R MCL</td>
</tr>
</tbody>
</table>

Axi-cel and brexu-cel have the same CAR construct; however, the manufacturing of brexu-cel involves enrichment of specific lymphocytes to improve therapeutic potential.
Recommendations for DLBCL

First-line treatment
- Adults: R-CHOP
- Pediatric: rituximab + FAB chemotherapy

Second-line treatment
- Transplant eligible: chemoimmunotherapy regimen that includes rituximab, followed by autoSCT if CR achieved
- Transplant-ineligible: no consensus. Options: lenalidomide, lenalidomide + tafasitamab, polatuzumab vedotin + BR, or salvage chemoimmunotherapy

Third-line treatment (or later)
- Anti-CD19 CAR T therapy
- CAR-ineligible: polatuzumab vedotin + rituximab + bendamustine
DLBCL Case Study

• The first-line regimen for newly diagnosed DLBCL in adult patients should be R-CHOP or R-CHOP-like regimens.

• For the second-line therapy of DLBCL, transplant-eligible patients should receive a chemoimmunotherapy regimen that includes rituximab followed by autoSCT consolidation if CR is achieved.

• The third-line treatment for DLBCL in fit patients should be anti-CD19 CAR T cell therapy.
  • Anti-CD19 CAR T-cell therapy should be considered prior to tafasitamab + lenalidomide therapy in CART-eligible patients

• Patients who are ineligible for third-line anti-CD19 CAR T cell therapy should instead receive polatuzumab vedotin-piiq+ rituximab+bendamustine.
  • Bendamustine should be avoided prior to apheresis in CART-eligible patients
# Recommendations for MCL

<table>
<thead>
<tr>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment (or later)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transplant-eligible:</strong> No consensus</td>
<td><strong>No consensus</strong></td>
<td><strong>No consensus</strong></td>
</tr>
<tr>
<td><strong>Options:</strong> chemoimmunotherapy + autoSCT or chemoimmunotherapy alone</td>
<td><strong>Options:</strong> brexucabtagene autoleucel, proteasome inhibitors, BTK inhibitors, BTK inhibitors + rituximab, or lenalidomide + rituximab</td>
<td></td>
</tr>
<tr>
<td><strong>Transplant-ineligible:</strong> chemoimmunotherapy + rituximab maintenance</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Recommendations for FL

**First-line treatment**
- **Low tumor burden: no consensus**
- **Options include:** *rituximab, lenalidomide* + *rituximab*, or *chemoimmunotherapy*
- **High tumor burden:** chemoimmunotherapy

**Second-line treatment**
- Options will vary and should be decided on case-by-case basis, factoring in:
  - Prior therapies
  - Time of relapse
  - Tumor bulk
  - Age
  - Comorbidities

**Third-line treatment (or later)**

**Notes:**
- When anti-CD20 antibody is indicated, *rituximab* should be used over *obinutuzumab*
- If relapse occurs <6 months after *rituximab*, *obinutuzumab* should be used
- If relapse occurs >6 months after *rituximab*, re-administration of *rituximab* can occur
# Recommendations for MZL

<table>
<thead>
<tr>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment (or later)</th>
</tr>
</thead>
</table>
| Low tumor burden: rituximab monotherapy | Options will vary and should be decided on case-by-case basis, factoring in:  
  • Prior therapies  
  • Time of relapse  
  • Tumor bulk  
  • Age  
  • Comorbidities | High tumor burden: chemoimmunotherapy |

- Low tumor burden: **rituximab** monotherapy
- High tumor burden: chemoimmunotherapy

Options will vary and should be decided on case-by-case basis, factoring in:
- Prior therapies
- Time of relapse
- Tumor bulk
- Age
- Comorbidities
Recommendations for PMBCL

**First-line treatment**
- DA-R-EPOCH

**Second-line treatment**
- Transplant eligible: chemoimmunotherapy regimen that includes *rituximab*, followed by autoSCT if CR achieved.
- Transplant-ineligible: no consensus. Options: *lenalidomide, lenalidomide + tafasitamab, polatuzumab vedotin + BR, or salvage chemoimmunotherapy.*

**Third-line treatment (or later)**
- No consensus.
- Options: *axicabtagene cilocelel, BV + pembrolizumab, salvage chemoimmunotherapy.*
### Recommendations for BL - pediatric

<table>
<thead>
<tr>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment (or later)</th>
</tr>
</thead>
</table>
| • **Rituximab-containing** chemoimmunotherapy, with either FAB or BFM backbone | • **Rituximab-containing** chemoimmunotherapy  
• Options: R-ICE or R-CYVE | • Patients should receive stem cell transplant if eligible. |


Recommendations for BL - adult

**First-line treatment**
- **Rituximab-containing** chemoimmunotherapy.
- Options: rituximab + CODOXM/IVAC alternating with rituximab + HyperCVAD, rituximab + LMB

**Second-line treatment**
- Similar **rituximab-containing** chemoimmunotherapy
- Consolidation similar to DLBCL

**Third-line treatment (or later)**
Outline

• Introduction to lymphoma
• Management of B-cell non-Hodgkin lymphoma
• Management of Hodgkin lymphoma, chronic lymphocytic leukemia and T cell lymphoma
• Toxicity management
Hodgkin lymphoma case

• A 27 year old male presents with stage IVA nodular sclerosis Hodgkin lymphoma.
• He has diffuse lymphadenopathy; liver, lung and splenic lesions and multiple bone lesions on PET scan.
• He receives brentiximab vedotin + AVD x 6 cycles and has a CR.
• He has a biopsy proven relapse 9 months later.
• He receives ICE chemotherapy followed by an autologous stem cell transplant and brentuximab vedotin for 1 year.
• The patient relapses again 6 months after completing 16 cycles of brentuximab vedotin and is treated with nivolumab.
• He has a CR and is offered an allogenic transplant, but declines.
• He remains in remission 4 years later.
## Approved immunotherapies for Hodgkin lymphoma

<table>
<thead>
<tr>
<th>Agent</th>
<th>Therapy type</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brentuximab vedotin</td>
<td>ADC</td>
<td>First-line stage III-IV cHL (combination with doxorubicin, vinblastine and dacarbazine)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consolidation therapy for cHL after autoSCT and high risk of relapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R/R cHL after autoSCT</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>ICI</td>
<td>R/R cHL after autoSCT and brentuximab vedotin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R/R cHL after 3+ prior therapies</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>ICI</td>
<td>R/R cHL after 3+ prior therapies</td>
</tr>
</tbody>
</table>
Brentuximab vedotin

Anti-CD30 antibody + monomethyl auristatin E

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study design</th>
<th>Patient population</th>
<th>Enrolled patients</th>
<th>Primary endpoint</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECHELON-1</td>
<td>Randomized phase III; comparator: ABVD</td>
<td>First line stage III or IV cHL</td>
<td>1334</td>
<td>Modified PFS</td>
<td>2-yr PFS: 82.1 vs 77.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2-yr OS: 96.6 vs 94.9%</td>
</tr>
<tr>
<td>AETHERA</td>
<td>Randomized phase III; comparator: BSC</td>
<td>cHL at high risk of relapse after autoSCT</td>
<td>329</td>
<td>PFS</td>
<td>5-yr PFS: 59 vs 41%</td>
</tr>
<tr>
<td>NCT00848926</td>
<td>Phase II, single-arm</td>
<td>R/R cHL with prior autoSCT</td>
<td>102</td>
<td>ORR</td>
<td>ORR: 75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CR rate: 34%</td>
</tr>
</tbody>
</table>

**Recommended uses in HL:**
- Pre-autoSCT with chemotherapy, ICI, or monotherapy
- First-line stage III-IV with AVD
- Third-line treatment

Moskowitz, Blood 2018.
Younes, J Clin Oncol 2012.
Nivolumab and pembrolizumab

Anti-PD-1 antibodies

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study design</th>
<th>Patient population</th>
<th>Enrolled patients</th>
<th>Primary endpoint</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CheckMate 205</td>
<td>Phase II single-</td>
<td>R/R cHL with prior autoSCT +/- BV</td>
<td>243</td>
<td>ORR</td>
<td>ORR: 69%</td>
</tr>
<tr>
<td></td>
<td>arm, nivolumab</td>
<td></td>
<td></td>
<td></td>
<td>Median PFS: 14.7 mo</td>
</tr>
<tr>
<td>NCT02572167</td>
<td>Phase I/II single-</td>
<td>R/R cHL second-line</td>
<td>62</td>
<td>CR rate</td>
<td>CR rate: 61%</td>
</tr>
<tr>
<td></td>
<td>arm, nivolumab +</td>
<td></td>
<td></td>
<td></td>
<td>ORR: 83%</td>
</tr>
<tr>
<td></td>
<td>BV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KEYNOTE-087</td>
<td>Phase II single-</td>
<td>R/R cHL</td>
<td>210</td>
<td>ORR and safety</td>
<td>ORR: 69%</td>
</tr>
<tr>
<td></td>
<td>arm, pembrolizumab</td>
<td></td>
<td></td>
<td></td>
<td>6-month PFS: 72.4%</td>
</tr>
</tbody>
</table>

Recommended uses in HL:
- Pre-autoSCT with BV
- Third-line treatment
Recommendations for HL

<table>
<thead>
<tr>
<th>First-line treatment</th>
<th>Second-line treatment</th>
<th>Third-line treatment (or later)</th>
</tr>
</thead>
</table>
| Stage I-II: doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) | • Salvage chemotherapy or immunotherapy, and autoSCT if eligible. Pre-autoSCT options include:  
  • **Brentuximab vedotin**  
  • Ifosfamide + carboplatin + etoposide  
  • **Brentuximab vedotin** + **nivolumab**  
  • **Brentuximab vedotin** monotherapy | • **No consensus. Options:**  
  • **Salvage chemotherapy or immunotherapy** + autoSCT if eligible  
  • **PD-1 inhibitor therapy**  
  • **Brentuximab vedotin** |
| Stage III-IV: no consensus. Options:  
  • ABVD  
  • **Brentuximab vedotin**, doxorubicin, vinblastine and dacarbazine (A-AVD) | | |

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Hodgkin lymphoma case

1. Brentuximab vedotin is standardly included in initial chemotherapy combinations
2. Brentuximab vedotin should be given as consolidation therapy after autologous stem cell transplantation in high-risk patients
3. Anti-PD1 antibodies are standard of care in relapsed Hodgkin lymphoma patients post autologous transplant
4. Consider allogeneic transplant or a clinical trial if the disease progresses
Recommendations for PTCL

First-line treatment
- CD30+: no consensus
- Options: BV + CHP, chemotherapy, chemotherapy + autoSCT
- CD30-negative: chemotherapy + autoSCT

Second-line treatment
- Eligible for transplant: no consensus.
- Options: chemotherapy + autoSCT, chemotherapy + alloSCT, HDAC inhibitors
- CD30+, SCT-ineligible: BV up to 16 doses
- CD30-, SCT-ineligible: HDAC inhibitors

Third-line treatment (or later)
### Approved therapies for CLL

<table>
<thead>
<tr>
<th>Agent</th>
<th>Treatment type</th>
<th>Indication(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>Anti-CD20 antibody</td>
<td><strong>Untreated</strong> CD20-positive CLL in combination with FC&lt;br&gt;<strong>R/R</strong> CD20-positive CLL in combination with FC</td>
</tr>
<tr>
<td>Obinutuzumab</td>
<td>Anti-CD20 antibody</td>
<td><strong>Untreated</strong> CLL in combination with chlorambucil</td>
</tr>
<tr>
<td>Ofatumumab</td>
<td>Anti-CD20 antibody</td>
<td><strong>Untreated</strong>, fludarabine-ineligible CLL in combination with chlorambucil&lt;br&gt;<strong>Relapsed</strong> CLL in combination with FC&lt;br&gt;<strong>Extended treatment</strong> of CLL in CR or PR after 2+ prior therapies&lt;br&gt;CLL <em>refractory</em> to fludarabine and alemtuzumab</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Anti-CD52 antibody</td>
<td><strong>Untreated</strong> or R/R CLL</td>
</tr>
</tbody>
</table>

*The panel did not reach consensus on preferred regimens for the first-line or second-line treatment of CLL. Options include targeted therapy (if eligible) and chemoimmunotherapy regimens, which may include rituximab, obinutuzumab, ofatumumab, and alemtuzumab.*
Outline

• Introduction to lymphoma
• Management of B-cell non-Hodgkin lymphoma
• Management of Hodgkin lymphoma, chronic lymphocytic leukemia and T cell lymphoma
• Toxicity management
### “Black box” warnings on lymphoma immunotherapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Warning due to</th>
<th>Therapy</th>
<th>Warning due to</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab</td>
<td>• Autoimmune conditions</td>
<td>Ibritumomab tiuxetan</td>
<td>• Severe infusion reactions</td>
</tr>
<tr>
<td></td>
<td>• Severe infusion reactions</td>
<td></td>
<td>• Severe cytopenia</td>
</tr>
<tr>
<td></td>
<td>• Anaphylaxis</td>
<td></td>
<td>• Severe cutaneous/mucocutaneous reactions</td>
</tr>
<tr>
<td></td>
<td>• Cancer</td>
<td></td>
<td>• Do not administer if altered biodistribution</td>
</tr>
<tr>
<td></td>
<td>• Infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axicabtagene ciloleucel</td>
<td>• CRS</td>
<td>Lenalidomide</td>
<td>• Embryo-fetal toxicity</td>
</tr>
<tr>
<td></td>
<td>• ICANS</td>
<td></td>
<td>• Significant neutropenia, thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>• Do not administer if active infection or inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brexucabtagene autoleucel</td>
<td>• CRS</td>
<td>Rituximab and biosimilars</td>
<td>• Severe infusion reactions</td>
</tr>
<tr>
<td></td>
<td>• ICANS</td>
<td></td>
<td>• TLS</td>
</tr>
<tr>
<td></td>
<td>• Do not administer if active infection or inflammation</td>
<td></td>
<td>• Severe mucocutaneous reactions</td>
</tr>
<tr>
<td>Brentuximab vedotin</td>
<td>• PML</td>
<td>Tisagenlecleucel</td>
<td>• PML</td>
</tr>
<tr>
<td>Obinutuzumab</td>
<td>• Hepatitis B reactivation</td>
<td></td>
<td>• Hepatitis B reactivation</td>
</tr>
<tr>
<td></td>
<td>• PML</td>
<td></td>
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</table>
Cytokine release syndrome

• Common with CAR T therapy but can occur with other immunotherapies.
• Management includes tocilizumab and corticosteroids.
Neurotoxicity

- Also called CAR-T Related Encephalopathy Syndrome (CRES) or IEC-associated neurologic syndrome (ICANS)
- Manifests as confusion, delirium, seizures, cerebral edema
- Largely unknown mechanisms
- Incidence increases with more doses, increased age, more prior therapies
- Management options:
  - Supportive care
  - Corticosteroids

<table>
<thead>
<tr>
<th>Neurotoxicity Domain</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICE score</td>
<td>7-9</td>
<td>3-6</td>
<td>0-2</td>
<td>0</td>
</tr>
<tr>
<td>Depressed level of consciousness</td>
<td>Awakens spontaneously</td>
<td>Awakens to voice</td>
<td>Awakens to tactile stimulus</td>
<td>Unrousable</td>
</tr>
<tr>
<td>Seizure</td>
<td>N/A</td>
<td>N/A</td>
<td>Any clinical seizure/on EEG</td>
<td>Prolonged/life-threatening seizure</td>
</tr>
<tr>
<td>Motor Findings</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Hemi or paraparesis, deep focal motor weakness</td>
</tr>
<tr>
<td>Raised ICP/cerebral edema</td>
<td>N/A</td>
<td>N/A</td>
<td>Focal edema on imaging</td>
<td>Diffuse cerebral edema on imaging, cranial N palsy, Cushing’s triad, Decorticate posture</td>
</tr>
</tbody>
</table>

Infusion reactions

• Can be allergic or non-allergic
• Allergic reactions uncommon, but can lead to anaphylaxis
• Infusion reactions are common, particularly when mAbs are administered after SCT
• Most infusion reactions occur with first dose of therapy
• Among lymphoma immunotherapies, rituximab has highest incidence of infusion reactions, up to 77%
Tumor lysis syndrome

• Result of a sudden and massive release of metabolites after widespread lysis of tumor cells

• Particularly high risk in hematologic cancers with high tumor burden

• Management approaches include:
  • Prophylactic hydration
  • Prophylactic hypouricemic agents, like allopurinol
  • Dialysis
Patients with viral infections

• Reactivation of hepatitis B infection has been reported after certain antibody therapies, including rituximab and BV

• Panel recommends **not treating patients with active viral infections** with CAR T therapy or alloSCT

• Patients should be **evaluated for HBV/HCV** prior to immunotherapy, and antivirals should be initiated if positive

• Patients with **HIV can be considered** for immunotherapy if their HIV is well-controlled
Conclusions

• **Clinical trials** should be strongly considered as a treatment option at each stage of therapy for eligible patients with lymphoma.

• The immunotherapy options for B-NHL are broad include rituximab as a standard for newly diagnose disease. CAR T cells have emerged as the preferred option for relapsed/refractory disease while polatuzumab vedotin is available for CAR-ineligible patients.

• Brentuximab vedotin has been incorporated into both frontline and second-line therapies for HL. Checkpoint inhibitors are standard options in the relapsed/refractory settings

• Careful consideration, monitoring and management are necessary when immunotherapies are utilized in lymphoma.
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• Click the “Q&A” icon located on at the bottom of your Zoom control panel
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Faculty:
Stephan Grupp, MD, PhD – Children’s Hospital of Philadelphia and U. of Pennsylvania
Matthew J. Frigault, MD, MSc – Massachusetts General Hospital
Frederick L. Locke, MD – Moffitt Cancer Center
Bianca D. Santomasso, MD, PhD – Memorial Sloan Kettering Cancer Center

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