EUROPEAN HEMATOLOGY ASSOCIATION

EHA-MSH Hematology Tutorial

Self-assessment Case – Session 6: Imaging in Hodgkin Lymphoma

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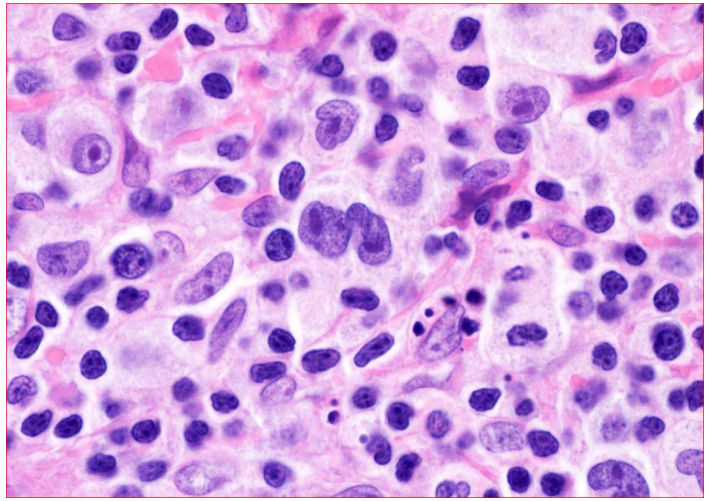
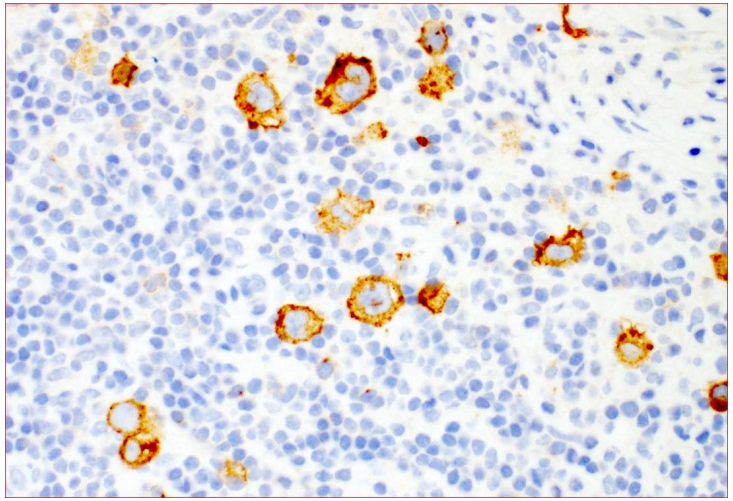
Introduction

- 18-year-old male patient presents with symptoms of itching and weight loss
- Physical examination → lymphadenopathy (cervical, supraclavicular [right and left])
- Pathology of the cervical node:



MGG IHC staining



CD30 IHC staining

Question 1: What is the most likely diagnosis?

1. Infectious mononucleosis (EBV)
2. $CD30^+$ T-cell lymphoma
3. Hodgkin lymphoma
4. Diffuse large B-cell lymphoma

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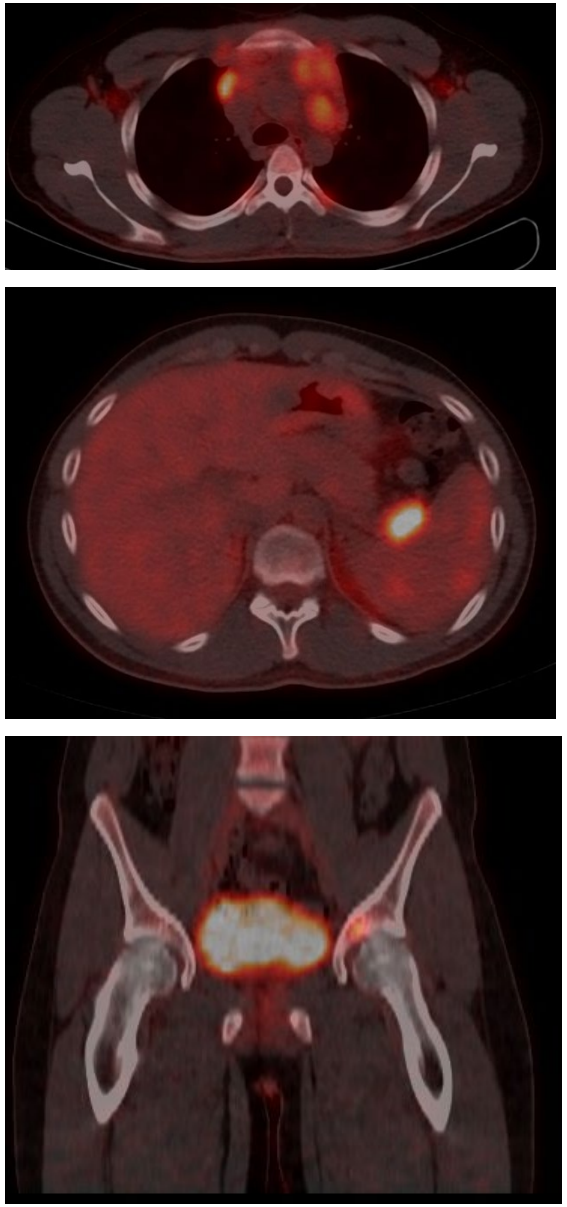
3. **Hodgkin lymphoma**
4. Diffuse large B-cell lymphoma

PET/CT staging

Ann Arbor stage IV:
Based on bone localization and lymph nodes above and below diaphragm

FDG-PET MIP



PET/CT axial images

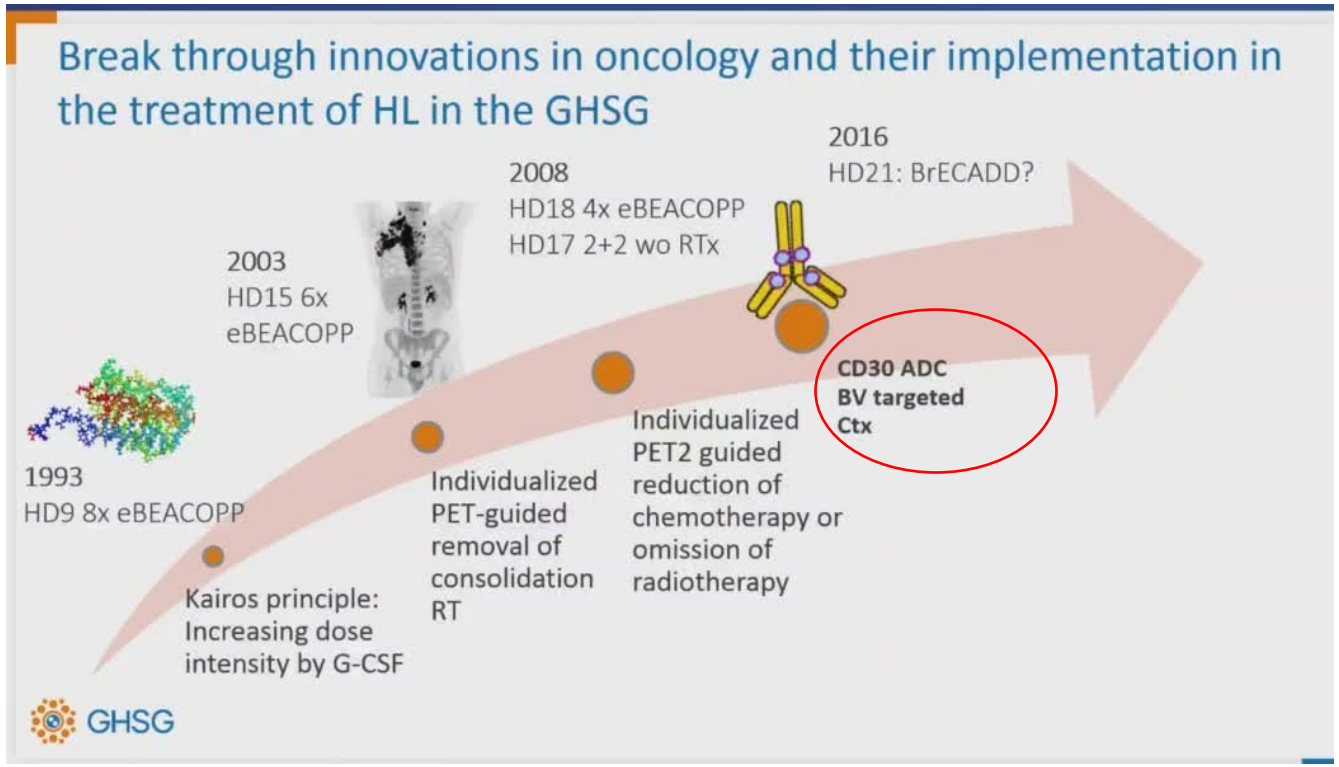
Question 2: What treatment for advanced-stage Hodgkin lymphoma do you recommend in this patient?

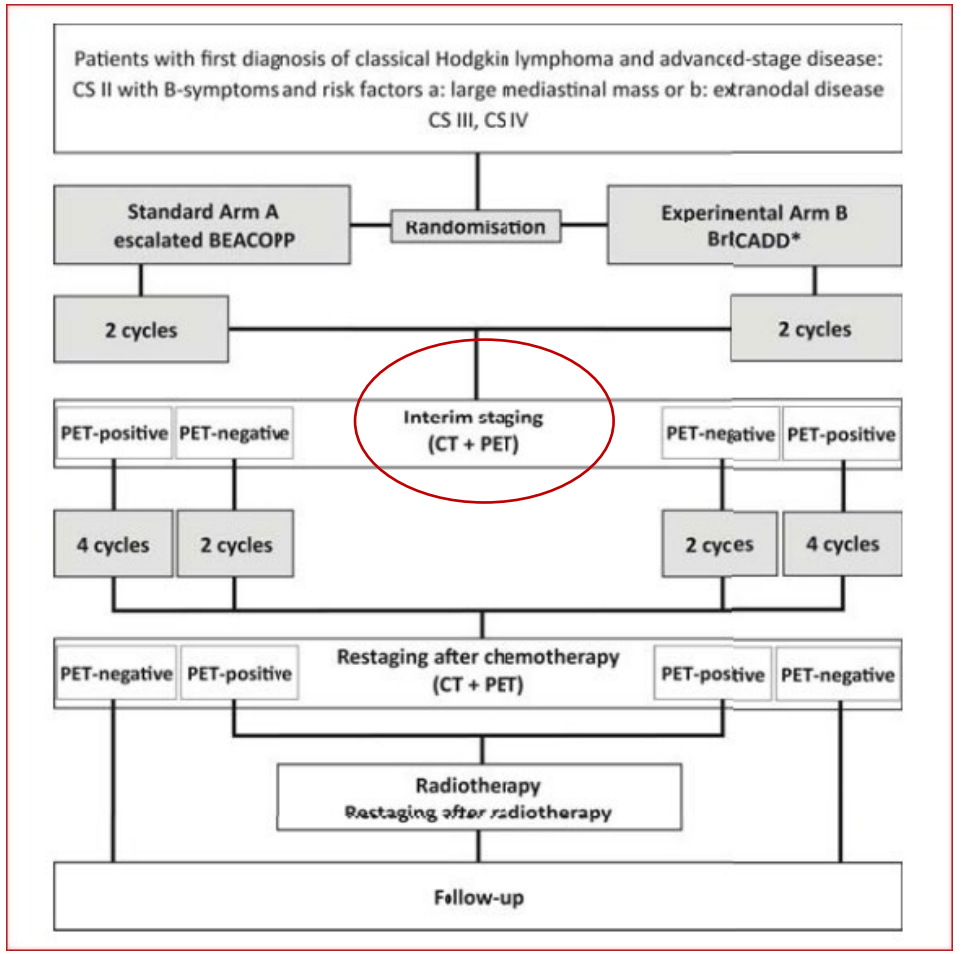
1. 6–8 cycles of ABVD
2. PET-2-guided ABVD
3. 6 cycles of escalated BEACOPP
4. PET-2-guided escalated BEACOPP
5. Treatment in clinical trial HD21

Question 2: What treatment for advanced-stage Hodgkin lymphoma do you recommend in this patient?

1. 6–8 cycles of ABVD
2. PET-2-guided ABVD
3. 6 cycles of escalated BEACOPP
4. PET-2-guided escalated BEACOPP
5. **Treatment in clinical trial HD21**

German Hodgkin Study Group (GHSG): HD 21





Randomization for experimental arm (BrECADD)

Question 3: Interim PET assessment

How should we score in this patient?

1. Visual score using Deauville assessment
2. Visual score using International Harmonization Project[1] for response criteria in lymphoma clinical trials
3. Quantitative assessment using SUV_{max}
4. Quantitative assessment using metabolic tumor volume

Cheson BD. The International Harmonization Project for response criteria in lymphoma clinical trials. Hematol Oncol Clin North Am. 2007; 21: 841-854.

Question 3: Interim PET assessment

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3. Quantitative assessment using SUV_{max}
4. Quantitative assessment using metabolic tumor volume

Feedback

- The Lugano classification for PET assessment says that visual scoring with Deauville is the current standard of care

Barrington SF, et al. Role of imaging in the staging and response assessment of lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol. 2014; 32: 3048-3058.

Deauville score

- FDG uptake related to mediastinal blood pool and liver
- ‘Use visual assessment, with PET/CT images scaled to fixed SUV display and color table’

Score of 1–3

- Complete metabolic response

Score of 4 or 5

- Partial metabolic response/stable disease or progression of disease
  → treatment failure!

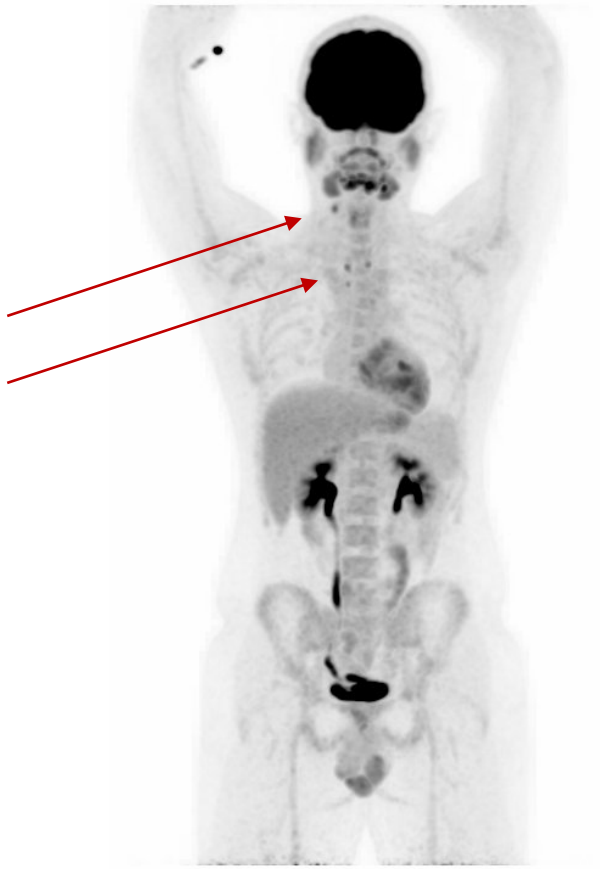
Evaluation after 2 cycles of BrECADD (6 weeks)

PET before treatment

PET after 2 cycles of BrECADD

Deauville score 2:
Complete metabolic remission

Evaluation after 4 cycles of BrECADD (12 weeks)



- **Viral infection; slight cough**
- Possible reactive lymph nodes cervical and mediastinal involvement

Repeat PET/CT after 4 weeks

- Complete metabolic response
- Deauville score of 1

PET/CT after the 4th cycle, during viral infection

Repeat PET/CT scan after recovery from viral infection

Question 4: How should we proceed in this patient?

1. Go for cycles 5 and 6
2. Go for consolidation with radiotherapy
3. Wait and see
4. Maintenance with brentuximab vedotin

Question 4: How should we proceed in this patient?

1. Go for cycles 5 and 6
2. Go for consolidation with radiotherapy
3. **Wait and see**
4. Maintenance with brentuximab vedotin

Feedback

- The HD21 protocol describes that patients will be given a total of 4 cycles when PET is negative after 2 cycles

NIH U.S. National Library of Medicine
ClinicalTrials.gov

ClinicalTrials.gov Identifier: NCT02661503.

Outpatient control (after 6 months)

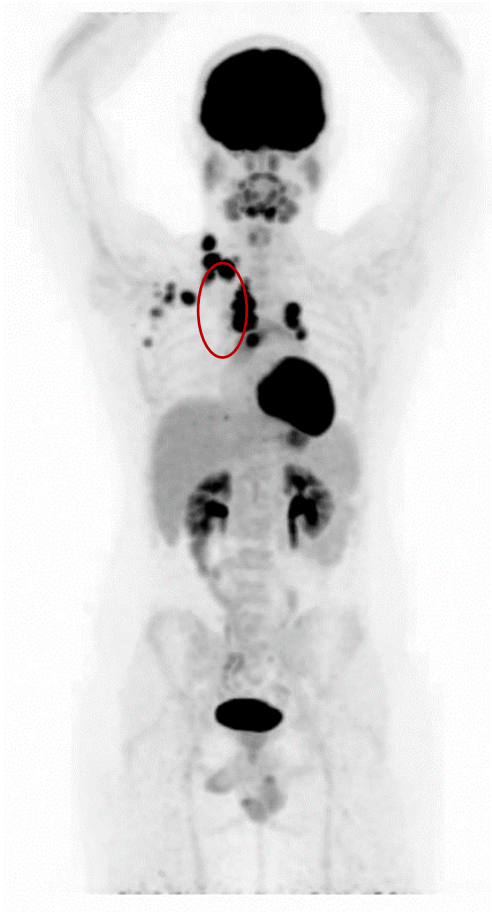
- Good recovery, but new lymphoadenopathies in the right-cervical region

Differential diagnosis

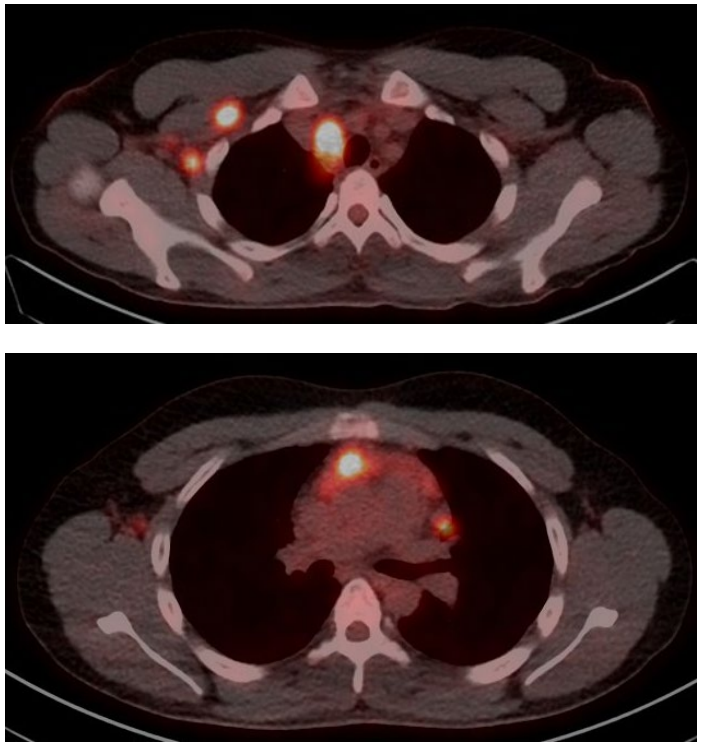
- Viral infection
- Sarcoidosis
- Relapsed Hodgkin lymphoma

Next step: new PET/CT?

PET/CT 8 months after 4 cycles of BrECADD



FDG/PET MIP



FDG-PET/CT axial images;
cervical and mediastinal region

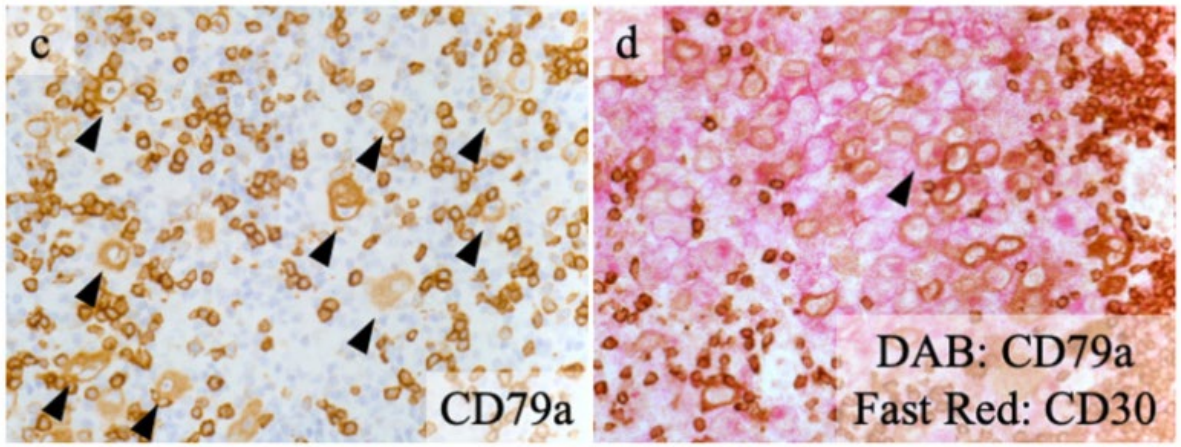
Suspected relapsed Hodgkin lymphoma?

New lymph-node extirpation!

Pathology report (lymph nodes)

Confirmation and explanation of relapse

In conclusion, we found CD79a-positivity in CHL to be associated with older age. In addition, CD79a-positive CHL patients had a poorer survival rate than CD79a-negative CHL patients. No positive correlation was observed between CD79a and CD20 expression. Our study suggests that CD79a-positive CHL involves unique clinicopathological features compared with CD79a-negative CHL. Further studies are needed to clarify the characteristics of CD79a-positive CHL, especially in Japan, where many patients are older at onset.



Sakatani A, et al. Clinicopathological significance of CD79a expression in classic Hodgkin lymphoma. J Clin Exp Hematop. 2020; 60: 78-86.

Question 5: Relapse of classical Hodgkin lymphoma 8 months after 4 cycles BrECADD

Which second-line therapy?

1. DHAP-BEAM/ASCT
2. IGEV or ICE
3. Pembrolizumab

Question 5: Relapse of classical Hodgkin lymphoma 8 months after 4 cycles BrECADD

Which second-line therapy?

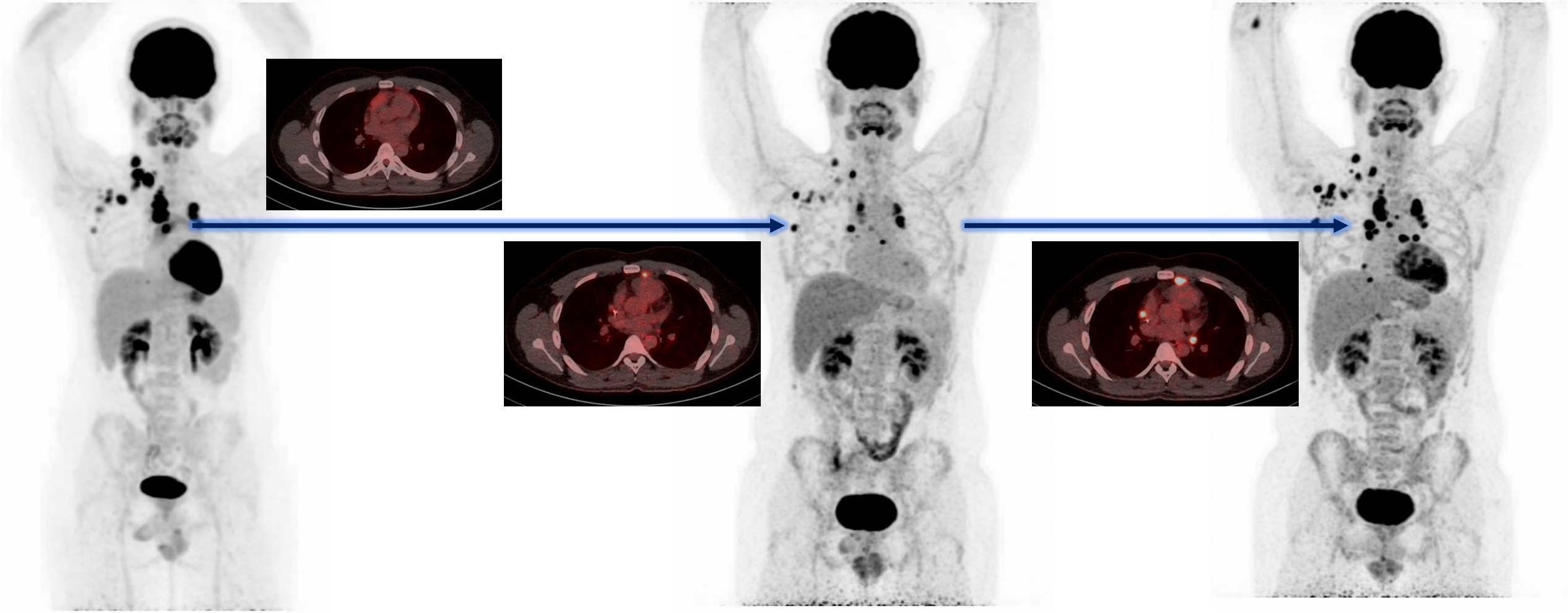
1. **DHAP-BEAM/ASCT**
2. IGEV or ICE
3. Pembrolizumab

Feedback

- Current second-line treatment options include reinduction chemotherapy and ASCT

Evaluation after 2 cycles of DHAP

- Aiming for complete metabolic remission before ASCT



September of 2020: FDG-PET MIP

- Progression of disease
- Deauville score of 5

November of 2020: FDG-PET MIP

- 2 cycles of DHAP
- Mixed response?

December of 2020: FDG-PET MIP

- 2 cycles of DHAP + 1 cycle of ICE[a]
- Progression of disease
- Deauville score of 5

[a]Following DHAP severe ototoxicity due to cisplatin.

Question 6: Relapse after BrECADD and refractory to DHAP/ICE

What is the next step in this patient?

1. Brentuximab vedotin
2. Pembrolizumab
3. Nivolumab
4. Dexamethasone
5. Radiotherapy

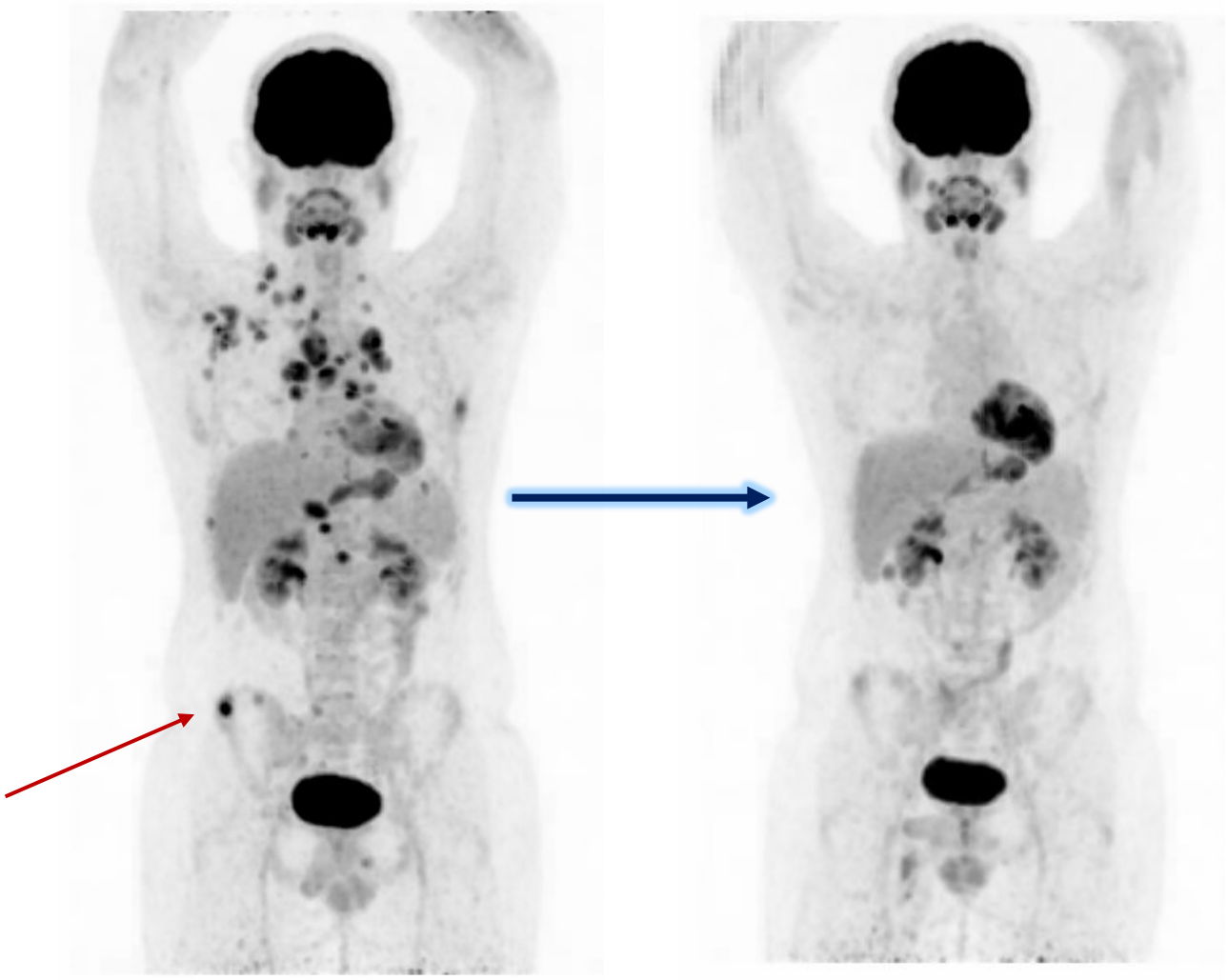
Question 6: Relapse after BrECADD and refractory to DHAP/ICE

What is the next step in this patient?

1. Brentuximab vedotin
2. **Pembrolizumab**
3. Nivolumab
4. Dexamethasone
5. Radiotherapy

Feedback

- Due to an indication for immune checkpoint inhibitors, pembrolizumab can be prescribed before ASCT
- However, we tried brentuximab vedotin since it was already part of the patient's treatment



February of 2021: FDG-PET MIP

- 2 cycles of brentuximab vedotin
- Progression of disease
- Deauville score of 5
- New bone lesions

March of 2021: FDG-PET MIP

- 2 cycles of pembrolizumab
- Complete metabolic response
- Deauville score of 2 (iliac bone right)

- No response on brentuximab vedotin; severe peripheral neuropathy
- Hours after first cycle of pembrolizumab, very severe pain
- After 2 cycles of pembrolizumab → complete metabolic response

Question 7: Pembrolizumab 200 mg every 3 weeks

For how long should we continue pembrolizumab in this patient?

1. Until complete remission
2. Until progression of disease
3. For 12 months
4. For 24 months

Question 7: Pembrolizumab 200 mg every 3 weeks

For how long should we continue pembrolizumab in this patient?

1. Until complete remission
2. Until progression of disease
3. For 12 months
4. **For 24 months**

Feedback

All KEYNOTE trials with pembrolizumab have used it for a maximum of 2 years as monotherapy

Chen R, et al. Phase II study of the efficacy and safety of pembrolizumab for relapsed/refractory classic Hodgkin lymphoma. J Clin Oncol. 2017; 35: 2125-2132.

Overview of clinical trials: Immune checkpoint inhibitors

- Chen R, et al. Pembrolizumab in relapsed or refractory Hodgkin lymphoma: 2-year follow-up of KEYNOTE-087. Blood. 2019; 134: 1144-1153
- Herrera AF, et al. Brentuximab vedotin plus nivolumab after autologous haematopoietic stem-cell transplantation for adult patients with high-risk classic Hodgkin lymphoma: a multicentre, phase 2 trial. Lancet Haematol. 2023; 10: e14-e23
- Kuruvilla J, et al. Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study. Lancet Oncol. 2021; 22: 512-524
- Lynch RC, et al. Concurrent pembrolizumab with AVD for untreated classic Hodgkin lymphoma. Blood. 2023; 141: 2576-2586

Discussion and conclusions

- Treatment for Hodgkin lymphoma is PET-guided
- PFS > 90%
  - De-escalation to diminish acute and long-term side effects
- For patients with relapse:
  - Brentuximab vedotin (antibody–drug conjugate) and immune checkpoint inhibitors have been shown to be very effective

References

- Barrington SF, et al. Role of imaging in the staging and response assessment of lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol. 2014; 32: 3048-3058
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- Sakatani A, et al. Clinicopathological significance of CD79a expression in classic Hodgkin lymphoma. J Clin Exp Hematop. 2020; 60: 78-86
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