
بسم الله الرحمن الرحيم

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Treatment Approach in a Case of Hodgkin Lymphoma

“A Panel Discussion”

Case Presentation

- 28-year-old male
- **Chief Complaint**: Fatigue, persistent fever, and unexplained weight loss over the past 3 months

- The patient reports recurrent fevers (up to 39°C) for the past 3 months, occurring mostly at night and accompanied by drenching night sweats.
- He has lost approximately 8 kg unintentionally over the same period.
- He also notes occasional itching and a persistent cough for the past 2 months.
- No significant past medical history or family history of cancer.

Physical Examination:

- Thin, fatigued appearance
- Multiple enlarged, non-tender lymph nodes palpable in the neck, axillae, and inguinal regions

Laboratory Tests:

CBC: Mild anemia (hemoglobin 10.5 g/dL)

ESR: Elevated (60 mm/hr).

LDH: Elevated (450 U/L).

Liver and kidney function tests: Normal.

Biopsy:

Excisional biopsy of a cervical lymph node reveals **classic Hodgkin lymphoma, nodular sclerosis subtype**, with the presence of Reed-Sternberg cells.

Imaging:

PET-CT Scan: Confirms widespread lymph node involvement with high metabolic activity and mediastinal mass >10 cm.

Q1

Pretreatment Evaluation

Essential:

- History & physical (H&P) including: B symptoms (unexplained fever >38°C; drenching night sweats; or weight loss >10% of body weight within 6 mo of diagnosis), alcohol intolerance, pruritus, fatigue, performance status, and examination of lymphoid regions, spleen, and liver
- Complete blood count (CBC), differential
- Erythrocyte sedimentation rate (ESR)
- Comprehensive metabolic panel, lactate dehydrogenase (LDH), and liver function test (LFT)
- Human immunodeficiency virus (HIV) testing (See NCCN Guidelines for Cancer in People with HIV)
- Pregnancy test for those of childbearing potential prior to cytotoxic chemotherapy or radiation therapy (RT)
- FDG-PET/CT scan (skull base to mid-thigh or vertex to feet in selected cases)[c,d]
- Counseling: Fertility/psychosocial[e] and smoking cessation (See NCCN Guidelines for Smoking Cessation)

Useful in selected cases:

- Fertility preservation[e,f]
- Pulmonary function tests ([PFTs] including diffusing capacity of the lung for carbon monoxide [DLCO])[g] if ABVD[h,i] is being used
- Hepatitis B/C testing (encouraged)
- Diagnostic CT[j] (contrast-enhanced)
- Chest x-ray (encouraged, especially if large mediastinal mass)
- Adequate bone marrow biopsy if there are unexplained cytopenias other than anemia and negative FDG-PET[k]
- Echocardiogram or multigated acquisition (MUGA) scan and consideration of atorvastatin[1] if anthracycline-based chemotherapy is indicated
- MRI of select sites, with contrast unless contraindicated
- FDG-PET/MRI (skull base to mid-thigh) without contrast

Diagnostic CT

- CT is considered diagnostic if it is enhanced with oral and/or IV contrast. CT component of a conventional FDG-PET/CT is often not IV contrast-enhanced. Although the diagnostic CT will often be of the neck/chest/abdomen/pelvis, at minimum include the areas identified as abnormal on FDG-PET/CT.

Diagnostic CT

- In some settings, a low-dose CT is performed at the time of PET (primarily for attenuation correction of PET images), and this may not adequately characterize the anatomy. A diagnostic-quality CT (ie, higher photon strength) can better characterize ambiguous PET findings and/or determine the size of a mediastinal or other large tumor mass.

Bone marrow evaluation

- Bone marrow aspirate and biopsy is generally **not** required, because it has little or no therapeutic consequences.
- Some experts suggest bone marrow examination only when unexplained cytopenias are present in the setting of a PET that is negative for bone marrow involvement.

Bone marrow evaluation

- A homogeneous pattern of uptake in the marrow should not be assumed to be marrow involvement.
- Some experts interpret PET/CT lesions at ≥3 skeletal sites as bone marrow involvement.

Lumbar puncture

- For patients with neurologic symptoms or signs, the CNS should be evaluated by lumbar puncture with cytology and by MRI.

Staging:

Based on the diagnostic findings, the patient is diagnosed with **Stage IIIB Hodgkin lymphoma**:

Stage III: Lymph node involvement on both sides of the diaphragm (cervical, mediastinal, and inguinal regions)

B Symptoms: Fever, night sweats, and weight loss

Q2

Prognosis

International Prognostic Score (IPS) 1 point per factor (advanced disease)†

- Albumin <4 g/dL
- Hemoglobin <10.5 g/dL
- Male
- Age ≥45 years
- Stage IV disease
- Leukocytosis (white blood cell count ≥15,000/mm^3)
- Lymphocytopenia (lymphocyte count <8% of white blood cell count, and/or lymphocyte count <600/mm^3)

0 points:88% FFP and 98% OS
1 point:84% FFP and 97% OS
2 points:80% FFP and 91% OS
3 points:74% FFP and 88% OS
4 points:67% FFP and 85% OS
5 to 7 points:62% FFP and 67% OS

Q3

- What would be your preferred initial treatment regimen for this patient?

Preferred regimens:

Stage III–IV

- Nivolumab-AVD[r,y,z] (category 1)
  or
  BrECADD + G-CSF[r] (category 1) (for ages 18-61 y)

Useful in Certain Circumstances

- BV-AVD + G-CSF[r] (category 1)
  (if not a candidate for CPI; contraindicated in those with neuropathy)

  or

  ABVD[h,y] x 2 cycles[r] (category 1) (if BV and CPI not available or contraindicated) → Restage with FDG-PET/CT[c,aa] →
  - Deauville 1–3[s] → AVD x 4 cycles[bb] (adapted from RATHL)[5]
  - Deauville 4–5[s,v] → BrECADD + G-CSF[r,x] x 3 cycles → Restage with FDG-PET/CT[c]

Nivolumab plus AVD (preferred)

- N+AVD achieved better outcomes with less toxicity than BV+AVD in a phase 3 trial (S1826) of patients with advanced-stage cHL.
- Previously, BV+AVD was shown to be superior to ABVD in the ECHELON-1 trial.

The NEW ENGLAND JOURNAL of MEDICINE

Nivolumab in Advanced Hodgkin's Lymphoma

A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Nivolumab+AVD in Advanced-Stage Classic Hodgkin's Lymphoma by A.F. Herrera et al. (published October 17, 2024)

In this trial, researchers assessed the efficacy and safety of nivolumab plus chemotherapy with doxorubicin, vinblastine, and dacarbazine (N+AVD), as compared with brentuximab vedotin plus AVD (BV+AVD), in patients with newly diagnosed classic Hodgkin's lymphoma.

Combination chemotherapy has been the standard treatment of **advanced-stage classic Hodgkin's lymphoma** for decades.

CONCLUSIONS

In adolescents and adults with previously untreated, stage III or IV classic Hodgkin's lymphoma, N+AVD improved progression-free survival, as compared with BV+AVD, and had a better side-effect profile.

Overall Survival with Brentuximab Vedotin in Stage III or IV Hodgkin's Lymphoma

Ansell SM et al. DOI: 10.1056/NEJMoa2206125

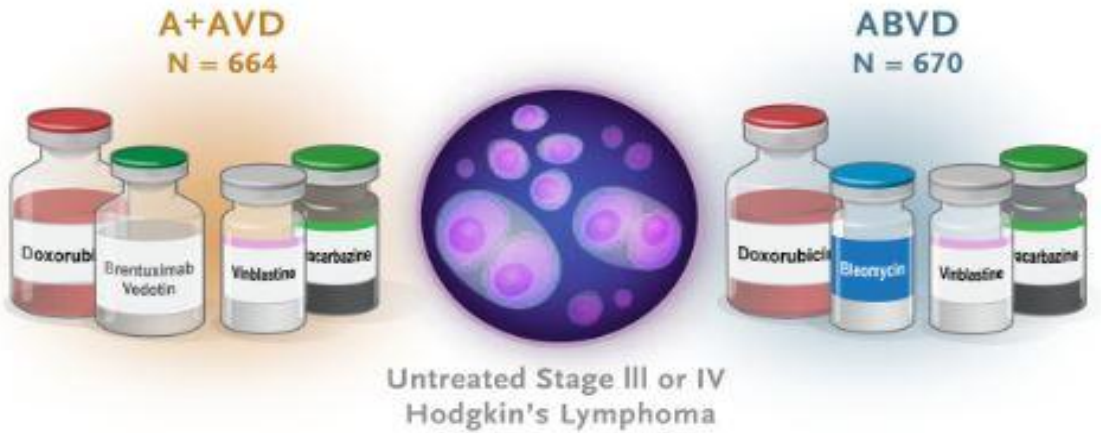
CLINICAL PROBLEM

In the ECHELON-1 trial involving patients with newly diagnosed stage III or IV Hodgkin's lymphoma, first-line treatment with the antibody–drug conjugate brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine (A+AVD) offered a benefit in modified progression-free survival over standard treatment with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). Data on overall survival are needed.

CLINICAL TRIAL

Design: The phase 3, multicenter, open-label, randomized ECHELON-1 trial examined the efficacy and safety of A+AVD, as compared with ABVD, in adult patients with previously untreated stage III or IV Hodgkin's lymphoma.

Intervention: 1334 patients were randomly assigned to receive A+AVD or ABVD on days 1 and 15 of each 28-day cycle for up to six cycles. The key secondary end point was overall survival. (The primary end point, modified progression-free survival, was reported previously.)



RESULTS

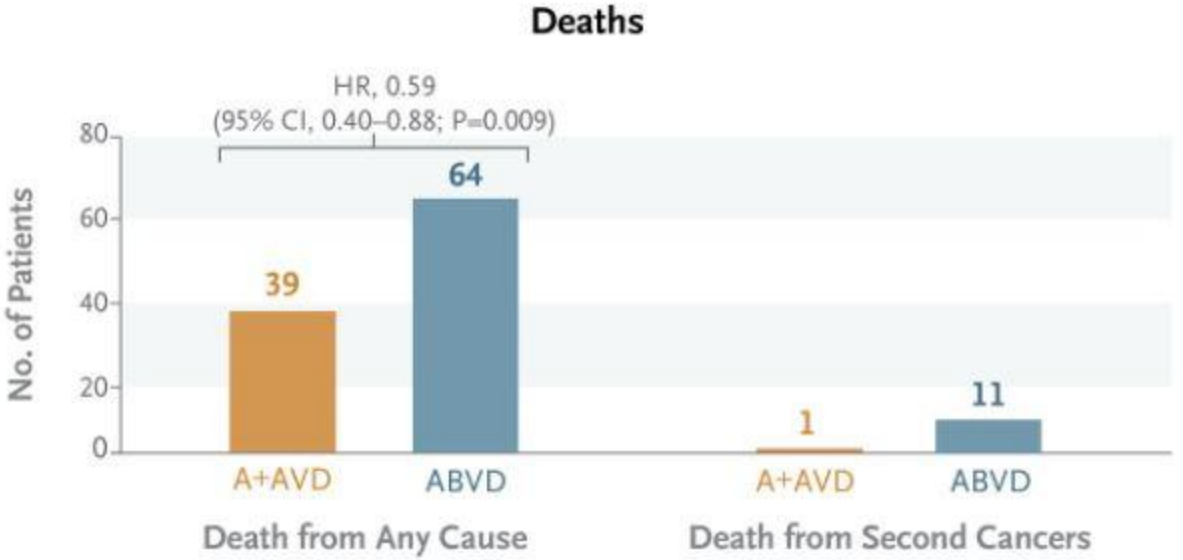
Efficacy: During a median follow-up of 73 months, overall survival significantly favored A+AVD over ABVD.

Safety: Deaths associated with second cancers and pulmonary toxicity were more common with ABVD than with A+AVD. However, the incidence of myelotoxic effects was greater with A+AVD. In addition, peripheral neuropathy occurred more frequently with A+AVD; most cases resolved or ameliorated by the end of follow-up.

LIMITATIONS AND REMAINING QUESTIONS

- The large disparity in deaths from second cancers is unexplained.
- Cause of death was investigator-assessed, and contextual information was not always provided.

Links: Full Article | NEJM Quick Take | Editorial



CONCLUSIONS

Patients with previously untreated stage III or IV Hodgkin's lymphoma who received A+AVD (brentuximab vedotin plus doxorubicin, vinblastine, and dacarbazine) had significantly longer overall survival than those who received standard treatment with ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine).

- N+AVD is contraindicated in patients with rheumatoid arthritis, inflammatory bowel disease, and other autoimmune illnesses that require immunosuppressive therapy.

- Some experts offer BrECADD (BV, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) to selected fit patients ≤60 years who have advanced-stage cHL with adverse prognostic features, based on results from the HD21 trial (BrECADD was superior to escalated BEACOPP).

Q4

- Alternatives

Alternatives

- When nivolumab is contraindicated or not available, the preferred initial treatment varies by age and comorbidities.

≤60 years

- BV+AVD
  - BV+AVD is contraindicated in patients with moderate pre-existing peripheral neuropathy.

RATHL – In the RATHL trial, patients with a complete response (CR) after two cycles of ABVD received four cycles of AVD (ie, bleomycin omitted) .

BrECADD – BrECADD is acceptable for fit patients ≤60 years with adverse prognostic features.

>60 years

- Sequential BV-AVD-BV.
  - Sequential BV-AVD-BV involves a lead-in with single-agent BV to provide early disease control, followed by six cycles of AVD, and then four final cycles of consolidation with single-agent BV. The regimen minimizes neurotoxicity by sequential (rather than simultaneous) treatment with BV and AVD, and it reduces or delays relapses with four final cycles of BV consolidation therapy.

- The initial treatment was **ABVD**.

Mid-Treatment Assessment

- After 3 cycles of ABVD, a mid-treatment PET/CT shows debulked mediastinal mass (PET score 3)with no new lesions.

Q5

- How important is interim PET/CT in guiding treatment decisions?

- Response is judged using the five-point (Deauville) scoring system according to the Lugano classification :
  - **Complete response (CR)** – PET score 1 to 3
  - **Less than CR** – PET score 4 to 5; consider biopsy to exclude an alternative diagnosis (eg, infection, another malignancy).

- In this case, the favorable response justified continuing ABVD (total 6 courses).

- Post-treatment PET/CT reveals complete response.

Q6

- What is the role of RT?

RADIATION THERAPY

- Radiation therapy (RT) is not routinely used to treat patients with advanced-stage cHL.
- There is no demonstrated benefit from consolidative RT after achieving complete response with chemotherapy in patients with bulky disease.

Bulky disease

- There is no persuasive evidence that consolidative radiation therapy (RT) is beneficial for patients with bulky cHL (>10 cm or >1/3 of the chest diameter) who achieve a complete response (CR) to chemotherapy.

Q7

- Surveillance

Surveillance

- The patient should be seen every three months in the first year, every four to six months in the second year, and then annually.
- Imaging should be limited to avoid unnecessary radiation exposure.
- If clinically indicated, CT can be obtained up to every six months for the first two years (ie, ≤4 CTs total) or if relapse is suspected. To reduce radiation exposure and avoid false-positive results, PET should be performed only for a suspected relapse.

	Follow-up After Completion of Treatment Up to 5 Years
Interim H&P	• Every 3–6 mo for 1–2 y, then every 6–12 mo until year 3, then annually.
Vaccines	• Annual influenza vaccine and other vaccines as clinically indicated (see NCCN Guidelines for Survivorship).
Laboratory studies[2]:	▸ CBC, platelets, ESR (if elevated at time of initial diagnosis), chemistry profile as clinically indicated. ▸ Thyroid-stimulating hormone (TSH) at least annually if RT to neck.
Counseling	Reproduction, health habits, psychosocial, cardiovascular, breast awareness, skin cancer risk, end-of-treatment discussion (see NCCN Guidelines for Survivorship).
Imaging	• Imaging should only be obtained if significant clinical concern for relapse or as mandated if enrolled in an active protocol. ▸ If imaging is necessary, it may include diagnostic CT at 3- to 6-month intervals for up to 2 years as clinically indicated, or after 2 years if relapse is suspected. ▸ FDG-PET/CT should only be done if last FDG-PET/CT was Deauville 4–5, to confirm CR at the end of all prescribed therapy including RT. Once negative, repeat FDG-PET/CT should not be done unless evaluating suspicious findings on H&P or CT. • Surveillance FDG-PET/CT should not be done routinely due to risk for false positives. Management decisions should not be based on FDG-PET scan alone; clinical or pathologic correlation is needed.

FOLLOW-UP AFTER COMPLETION OF TREATMENT AND MONITORING FOR LATE EFFECTS

Follow-up and Monitoring After 5 Years[II,1]

- Interim H&P: Annually
  - Annual blood pressure, aggressive management of cardiovascular risk factors.
  - Annual influenza vaccine and other vaccines as clinically indicated (see NCCN Guidelines for Survivorship).
  - For guidance on COVID-19 vaccination, please see the CDC for Use of COVID-19 Vaccines in the US.
  - For guidance on general recommendations for vaccination in patients with cancer, see NCCN Guidelines for the Prevention and Treatment of Cancer-Related Infections.
  - For guidance on the adolescent and young adult population, see NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.
- Cardiovascular symptoms may emerge at a young age.
  - Consider stress test/ECHO at 10-year intervals or per institutional guidelines after treatment is completed.
  - Consider carotid ultrasound at 10-year intervals or per institutional guidelines if neck irradiation.
- Laboratory studies:
  - CBC, platelets, chemistry profile annually
  - TSH at least annually if RT to neck
  - Biannual lipids
  - Annual fasting glucose
- Annual breast screening: Initiate at age 40 years or 8 years post-therapy, whichever comes first, if chest or axillary radiation. The NCCN Hodgkin Lymphoma Guidelines Panel recommends breast MRI in addition to mammography for individuals assigned female at birth with intact breast tissue[mm] who received irradiation to the chest between ages 10–30 years, which is consistent with the American Cancer Society (ACS) Guidelines. Consider referral to a breast specialist.
- Perform other routine surveillance tests for cervical, colorectal, endometrial, lung, and prostate cancer as per the NCCN Guidelines for Detection, Prevention, and Risk Reduction and the ACS Cancer Screening Guidelines.
- Counseling: Reproduction, health habits, psychosocial, cardiovascular, breast awareness, and skin cancer risk (see NCCN Guidelines for Survivorship).
- Treatment summary and consideration of transfer to PCP.
- Consider a referral to a survivorship clinic.

- Six months post-treatment, the patient develops recurrence (multiple FDG-avid lymph nodes on PET/CT).

Q8

- What are the next steps for managing this relapsed case?

Biopsy

- Diagnosis of relapsed cHL generally requires biopsy of a suspicious mass.
- A repeat biopsy may not be required for patients with early recurrence in the setting of incomplete response, especially with persistence of constitutional symptoms. However, if the disease was unusually resistant to initial therapy, a biopsy may be warranted to confirm the initial diagnosis of cHL and exclude other diseases.

- The goal of treatment of relapsed or refractory cHL should be to achieve long-term disease control/cure, while limiting toxicity and complications of therapy. In most cases, long-term disease-free survival requires autologous hematopoietic cell transplantation (HCT).

The most common salvage chemotherapy regimens for r/r cHL are:

- ICE
- Gemcitabine-containing regimens:
  - GVD
  - GDP
  - BeGEV
- DHAP
- Targeted chemotherapy (eg, brentuximab vedotin [BV] plus bendamustine)

PRINCIPLES OF SYSTEMIC THERAPY
Relapsed or Refractory Disease

Classic Hodgkin Lymphoma

- **Consider the following when selecting re-induction or subsequent therapy:**
  - **Clinical trial enrollment**
  - **Referral to a center with expertise**

Primary Refractory Disease or Relapse (within any time frame) (Candidate for or Not a Candidate for HDT/ASCR)		**Additional Considerations for Relapsed/ Refractory CHL (Not a Candidate for HDT/ ASCR)**
Second-Line and Subsequent Therapy[n,o] (in alphabetical order)	**Therapy for Disease Refractory to at Least 3 Prior Lines of Subsequent Therapy (in alphabetical order)**	• Individualized treatment is necessary. • For localized relapse, consolidative ISRT should be strongly considered. • Refer to or consult a center with expertise. • Single-agent palliative therapy options include: ▸ CPI: ◊ Nivolumab[27,28] ◊ Pembrolizumab[29,30] ▸ Non-CPI containing regimen: ◊ Bendamustine[15] ◊ BV[5] ◊ Everolimus[20] ◊ ISRT[f] ◊ Gemcitabine[31] ◊ Lenalidomide[23] ◊ Vinblastine[24]
CPI-containing regimens • BV-Nivolumab[1] • GVD-Pembrolizumab[2] • ICE-Nivolumab[3] • ICE-Pembrolizumab[4] <u>Non-CPI-containing regimens</u> • BV[5] • BV-bendamustine[6] • DHAP (dexamethasone, cisplatin, high-dose cytarabine)[7,8] • Gemcitabine/bendamustine/vinorelbine[9] • GVD (gemcitabine, vinorelbine, liposomal doxorubicin)[10] • ICE (ifosfamide, carboplatin, etoposide)[8,11,12] • ICE-BV[13] • IGEV (ifosfamide, gemcitabine, vinorelbine)[14]	• Bendamustine[15] • Bendamustine-carboplatin-etoposide[16] • Decitabine-pembrolizumab[17,18,19] • GCD (gemcitabine, cisplatin, dexamethasone)[21] • GEMOX (gemcitabine, oxaliplatin)[22] • ISRT[d] • Vorinostat-pembrolizumab[25]	

General Guidelines for Checkpoint Inhibitors (CPI) for Relapsed or Refractory CHL[32,33]

- Post-allogeneic HCT, patients can receive either nivolumab or pembrolizumab. There are limited data regarding the use of CPI following allogeneic HCT. If a CPI is used, the HCT regimen will need to be carefully considered.
- Checkpoint inhibitors can be continued despite progression on imaging if patients are deriving clinical benefit, as imaging progression may be indicative of immune flare rather than true progression.[34]

Q9

- Autologous HCT

- **Autologous HCT** — Autologous HCT should be considered the treatment of choice for most patients with r/r cHL.
- Sustained remissions after HCT can be achieved in more than one-half of patients with r/r cHL.

- Benefits from HCT compared with chemotherapy alone are especially marked in the following categories of patients:
  - Early relapse (<12 months after completion of initial therapy)
  - Generalized systemic relapse, or the presence of other poor prognostic markers
  - Second (or later) relapse
  - Refractory cHL (ie, induction failure after initial chemotherapy)

- **Eligibility for autologous HCT**

  - **Performance status** – Eastern Cooperative Oncology Group (ECOG) performance status ≤2
  - **Medical fitness** – Adequate cardiac, pulmonary, kidney, and liver function, and appropriate psychosocial support
  - **Age** – Age limits for autologous HCT vary by institution and are not absolute, but some experts suggest autologous HCT for patients ≤70 or ≤75 years of age.

Autologous HCT conditioning

- No specific preparative regimen is considered the standard of care for autologous HCT in r/r cHL.
- The choice of conditioning regimen is influenced by patient comorbidities, short- and long-term toxicities, and institutional preferences.
- **BEAM** (BCNU, etoposide, cytarabine, melphalan)
- Acceptable alternative regimens include:
  - **CBV** (cyclophosphamide, BCNU, etoposide)
  - **Bu/Cy** (busulfan, cyclophosphamide)
  - **Bu/Mel** (busulfan, melphalan)

Tandem autologous HCT

- No randomized studies have directly compared tandem (ie, sequential) autologous HCT with single autologous HCT for r/r cHL. However, uncontrolled prospective studies have demonstrated no clear benefits for tandem transplantation, even for patients with adverse prognostic features.

Maintenance therapy

- Maintenance therapy may benefit certain patients after autologous HCT for r/r cHL.
- **Brentuximab vedotin maintenance** — For patients who undergo autologous HCT and are at higher risk of relapse , brentuximab vedotin (BV) maintenance therapy improves progression-free survival (PFS) when compared with observation alone. There is no proven benefit for BV maintenance for patients at lower risk of relapse or for patients who received BV as a component of initial treatment for cHL.
- high-risk features:
  - Primary refractory cHL or relapse <12 months after initial therapy
  - Less than complete response (CR) to most recent salvage therapy
  - B symptoms at relapse
  - Relapse with extranodal disease
  - Two or more salvage therapies

PD-1 blockade maintenance

- Maintenance therapy with a PD-1 inhibitor may provide clinical benefit following autologous HCT for r/r cHL.

Q10

- RT

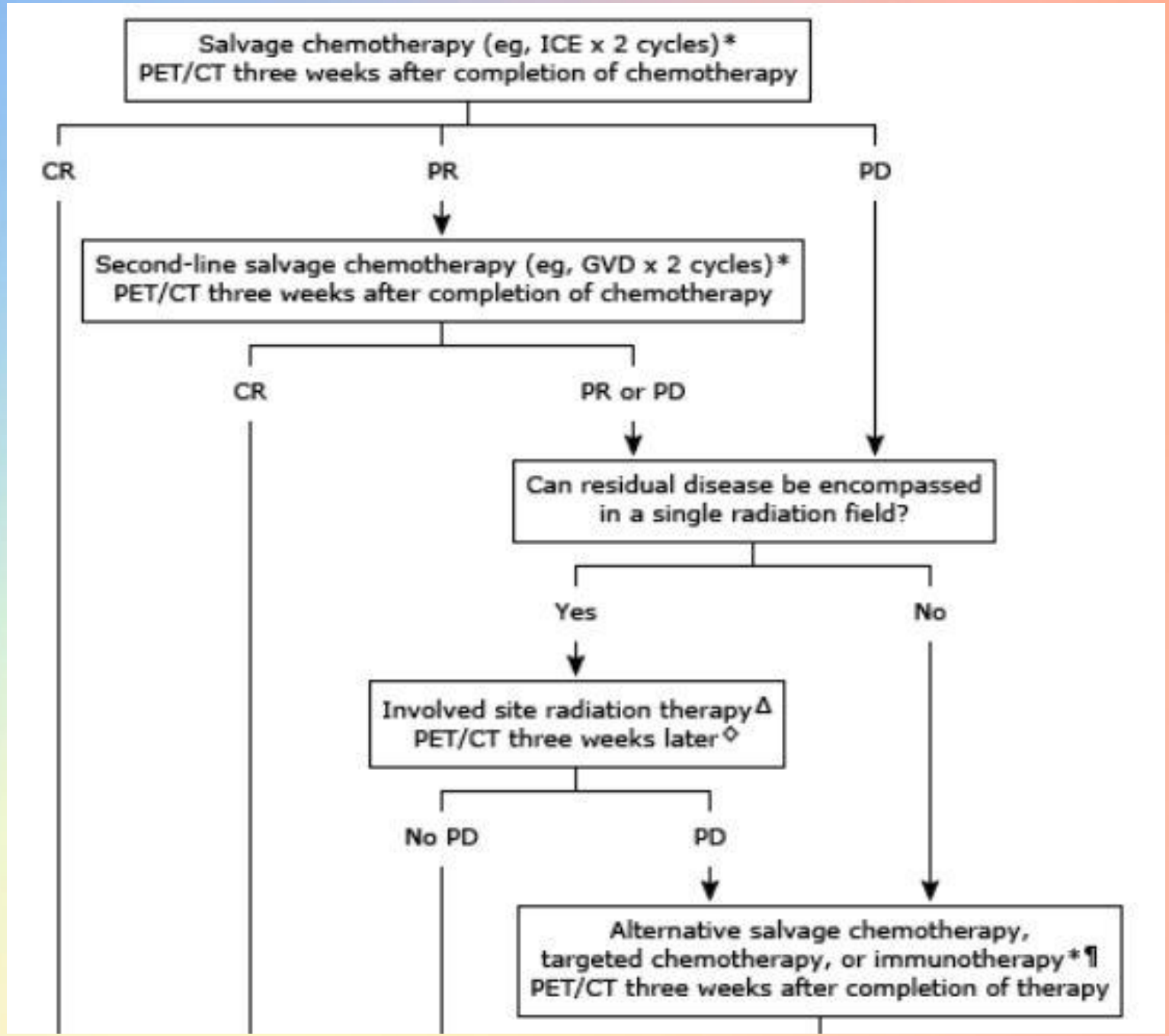
Radiation therapy (RT)

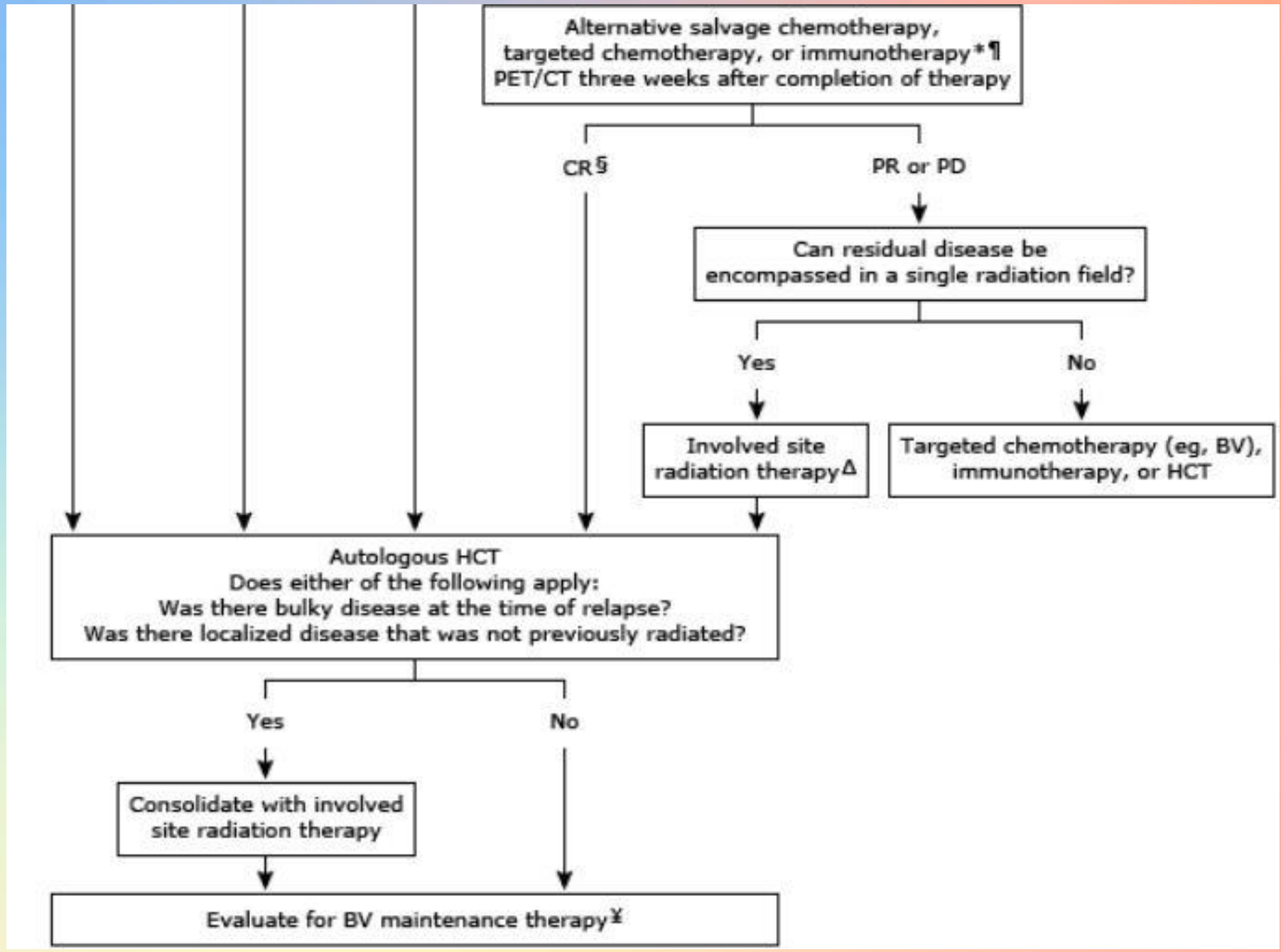
- **Indications for radiation** — The decision to offer RT must balance the potential improvement of local disease control against the potential for long-term toxicity, including second malignancies and cardiovascular morbidity.
- For patients undergoing autologous HCT:
  - Consolidative RT may be administered **prior** to transplantation for patients who had a PR (by PET/CT) to salvage chemotherapy with residual disease that can be encompassed in a radiation port.
  - Consolidative RT may be used **after** autologous HCT for patients who had bulky disease at the time of relapse and for select patients with non-bulky disease that can be encompassed in a radiation field.
- There are no randomized trials indicating a survival benefit, but several studies have shown that adjuvant irradiation can control limited residual disease and may contribute to improved prognosis.

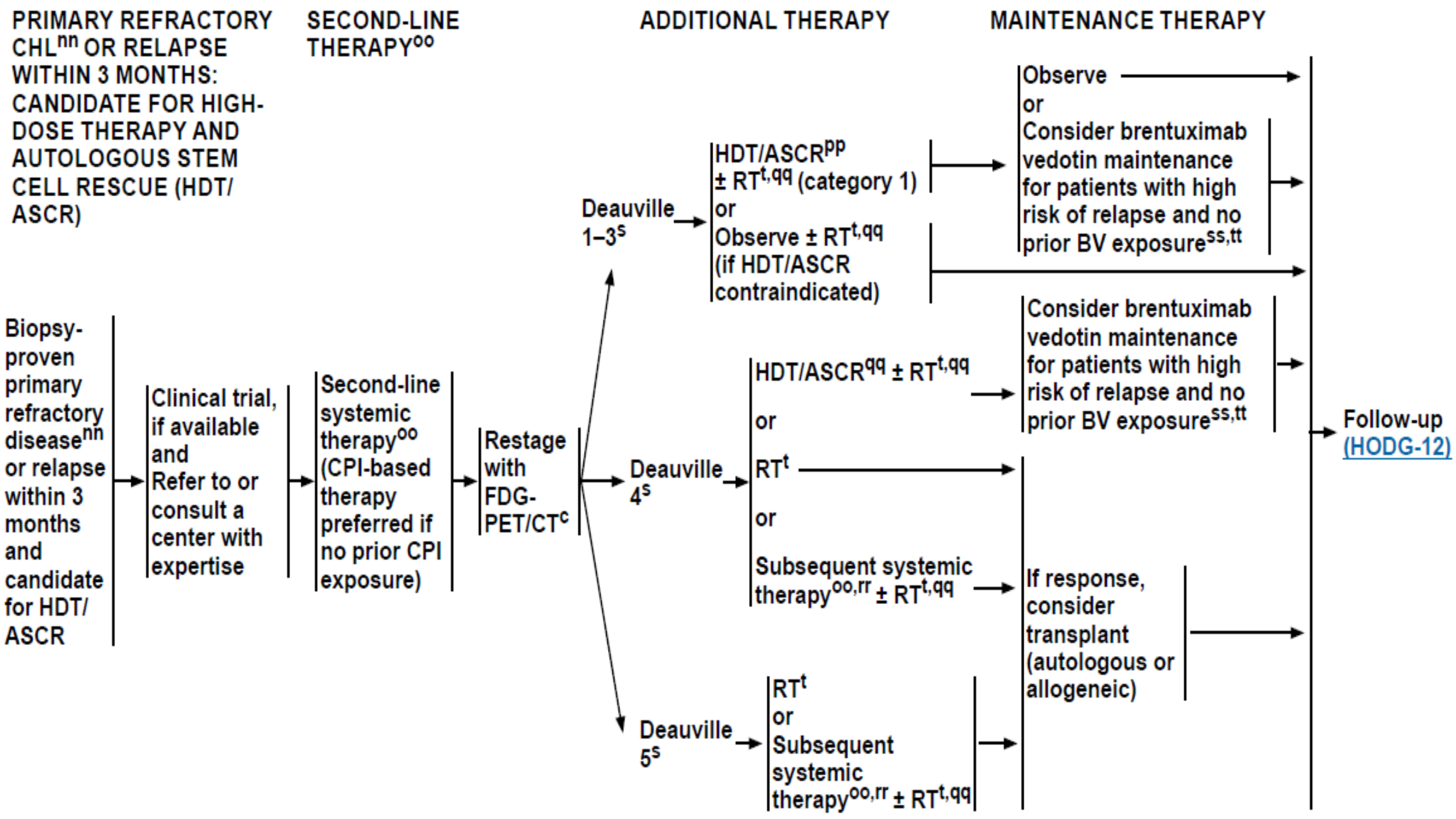
Radiation therapy (RT)

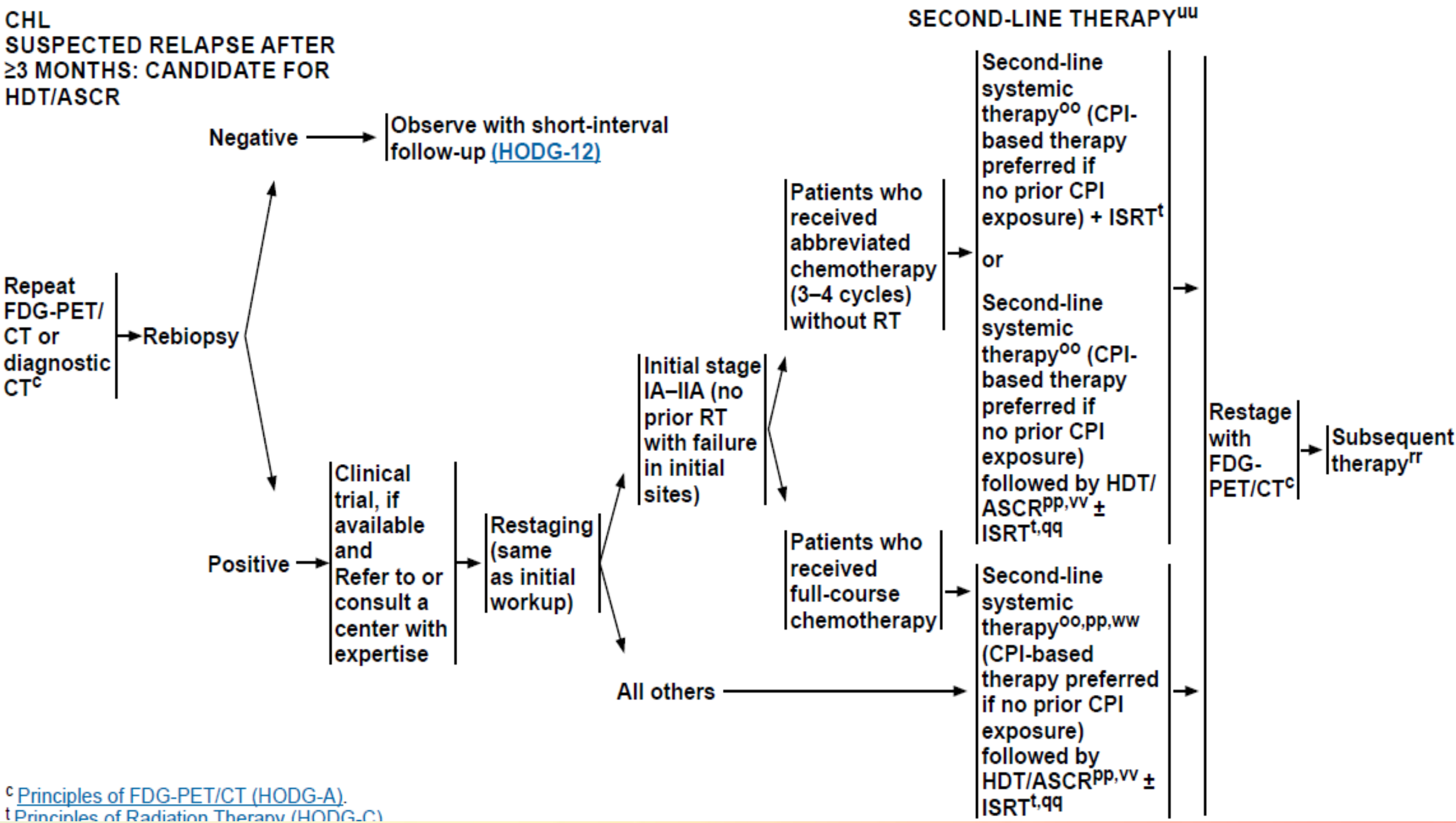
- Late first relapse – Salvage chemotherapy followed by RT may be an option for select patients with a late (generally at least several years after completion of initial treatment), localized, asymptomatic, first recurrence of cHL.
- Palliation without curative intent – RT, with or without systemic chemotherapy or targeted chemotherapy, may provide relief of symptoms in select patients who are not able to undergo chemotherapy and/or HCT with curative intent.

- **Management of HCT-eligible first relapse or refractory classical Hodgkin lymphoma**


Salvage chemotherapy (eg, ICE x 2 cycles)*
PET/CT three weeks after completion of chemotherapy
CR
PR
PD
Second-line salvage chemotherapy (eg, GVD x 2 cycles)*
PET/CT three weeks after completion of chemotherapy
CR
PR or PD
Can residual disease be encompassed in a single radiation field?
Yes
No
Involved site radiation therapy Δ
PET/CT three weeks later ◇
No PD
PD
Alternative salvage chemotherapy, targeted chemotherapy, or immunotherapy*¶
PET/CT three weeks after completion of therapy


Alternative salvage chemotherapy, targeted chemotherapy, or immunotherapy*¶
PET/CT three weeks after completion of therapy
CR§
PR or PD
Can residual disease be encompassed in a single radiation field?
Yes
No
Involved site radiation therapy△
Targeted chemotherapy (eg, BV), immunotherapy, or HCT
Autologous HCT
Does either of the following apply:
Was there bulky disease at the time of relapse?
Was there localized disease that was not previously radiated?
Yes
No
Consolidate with involved site radiation therapy
Evaluate for BV maintenance therapy¥


PRIMARY REFRACTORY CHL[nn] OR RELAPSE WITHIN 3 MONTHS: CANDIDATE FOR HIGH-DOSE THERAPY AND AUTOLOGOUS STEM CELL RESCUE (HDT/ASCR)
SECOND-LINE THERAPY[oo]
ADDITIONAL THERAPY
MAINTENANCE THERAPY
Biopsy-proven primary refractory disease[nn] or relapse within 3 months and candidate for HDT/ASCR
Clinical trial, if available and Refer to or consult a center with expertise
Second-line systemic therapy[oo] (CPI-based therapy preferred if no prior CPI exposure)
Restage with FDG-PET/CT[c]
Deauville 1–3[s]
HDT/ASCR[pp] ± RT[t,qq] (category 1) or Observe ± RT[t,qq] (if HDT/ASCR contraindicated)
Observe or Consider brentuximab vedotin maintenance for patients with high risk of relapse and no prior BV exposure[ss,tt]
Deauville 4[s]
HDT/ASCR[qq] ± RT[t,qq] or RT[t] or Subsequent systemic therapy[oo,rr] ± RT[t,qq]
Consider brentuximab vedotin maintenance for patients with high risk of relapse and no prior BV exposure[ss,tt]
Deauville 5[s]
RT[t] or Subsequent systemic therapy[oo,rr] ± RT[t,qq]
If response, consider transplant (autologous or allogeneic)
Follow-up (HODG-12)



[c] Principles of FDG-PET/CT (HODG-A).
[t] Principles of Radiation Therapy (HODG-C)

- Patient received ICE as salvage chemotherapy, followed by ASCT.

- He achieved complete remission post-ASCT.

Relapse After ASCT

Case Details:

- Eighteen months post-ASCT, the patient develops recurrence (new FDG-avid lymph nodes on PET/CT).

Q11

- What is the best next step for this patient who has relapsed after ASCT?

ALLOGENEIC TRANSPLANTATION

- **Indications for allogeneic HCT**
  - medically-eligible patients who were previously treated with brentuximab vedotin (BV) and autologous HCT and who had only a partial response or progressive disease after immune checkpoint inhibition (ICI). (not for patients who had a complete response (CR) with ICI)

ALLOGENEIC TRANSPLANTATION

- Allogeneic HCT in patients who were previously treated with pembrolizumab may be associated with an increased risk for acute graft-versus-host disease (GVHD), hyperacute GVHD, chronic GVHD, hepatic sinusoidal obstructive syndrome (SOS, also called veno-occlusive disease) after reduced intensity conditioning, and glucocorticoid-requiring febrile syndrome (with an identified infectious disease).
- In settings where ICI is not available, allogeneic HCT may be considered for patients with r/r cHL following autologous HCT.

- **Allogeneic HCT conditioning** — RIC or NMA preparative regimens are preferred for allogeneic HCT in r/r cHL. Some institutions offer myeloablative allogeneic HCT in this setting.
- Preferred RIC regimen is fludarabine and melphalan; some centers add alemtuzumab to this regimen.
- RIC/NMA conditioning offers a survival advantage when compared with myeloablative approaches for allogeneic HCT in r/r cHL.

- Following allogeneic HCT
  - radiation therapy to localized or bulky disease that was not previously radiated
  - maintenance BV therapy to BV-naïve patients

Management Options:

- Re-induction Chemotherapy:
  - Brentuximab vedotin ± bendamustine or gemcitabine-based combinations.
- Allogeneic Stem Cell Transplantation (Allo-SCT):
  - Offers potential for long-term remission through graft-versus-lymphoma effects.
- Checkpoint Inhibitors:
  - Pembrolizumab or nivolumab for those ineligible for allo-SCT.
- Clinical Trials:
  - Investigational agents such as CAR T-cell therapy.


thank
you