EUROPEAN HEMATOLOGY ASSOCIATION

EHA-ISHBT Hematology Tutorial

Self-assessment Case – Session [11]

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Hyderabad, India
March 1-3, 2024

Introduction

- A 27 year-old man presented with weight loss and night sweats for 6 months.
- Examination showed cervical & axillary lymphadenopathy. No organomegaly
- FBC showed
  - WBC 16 x 10^9/l, Neutro- 92%, Lymphocytes- 5%
  - Hb 94 g/l, MCV 90 fl
  - Platelet count 351 x 10^9/l
  - ESR 60
- Normal Creat & LFT. Albumin 35 g/L

PET- CT

- Generalised lymphadenopathy both above and below the diaphragm
- Mediastinal mass — 8 cm x 10 cm
- Multiple hepatic and splenic lesions
- FDG avid Bone lesions in multiple bones

LN Biopsy- Classical Hodgkin Lymphoma

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Questions can be answered by scanning the QR on your phone to access Slido.

For each question you have 15 seconds.

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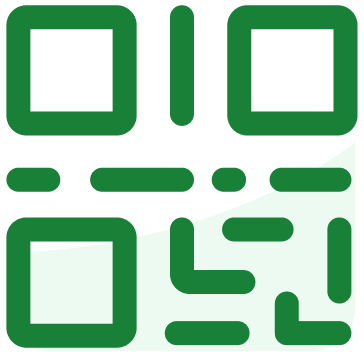

Join at slido.com
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Q1) Based on the information, what is the stage of lymphoma?

1. Stage I
2. Stage II
3. Stage III
4. Stage IV
5. Not possible to assess from this data

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11.31 Based on the information, what is the stage of lymphoma?

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HODGKIN LYMPHOMA STAGING[1]

Table 1

Definitions of Stages in Hodgkin Lymphoma[2]

Stage I Involvement of a single lymph node region (I) or localized involvement of a single extralymphatic organ or site (I_E).

Stage II Involvement of two or more lymph node regions on the same side of the diaphragm (II) or localized involvement of a single associated extralymphatic organ or site and its regional lymph node(s), with or without involvement of other lymph node regions on the same side of the diaphragm (II_E).

Note: The number of lymph node regions involved may be indicated by a subscript (eg, II_3).

Stage III Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized involvement of an associated extralymphatic organ or site (IIIE), by involvement of the spleen (III_S), or by both (III_{E+S}).

Stage IV Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or isolated extralymphatic organ involvement with distant (nonregional) nodal involvement.

A No systemic symptoms present

B Unexplained fevers >38°C; drenching night sweats; or weight loss >10% of body weight (within 6 months prior to diagnosis)

[1] For additional information regarding the staging of Hodgkin lymphoma, refer to: Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano Classification. J Clin Oncol 2014;32:3059-3068.

[2] FDG-PET scans are useful for upstaging in stage I–II disease. If there is FDG-PET positivity outside of disease already identified, further clinical investigation is recommended to confirm or refute the observation. FDG-PET scans may demonstrate increased avidity in lymphoid tissue unrelated to lymphoma in persons with HIV, particularly if HIV is not well-controlled (i.e. acute/subacute HIV infection, advanced immunosuppression and or viremia) and in the presence of opportunistic infections.

*NCCN 2024

STAGING/RISK CLASSIFICATION OF CHL[m]

Stage	Bulky Mediastinal Disease[m] or >10 cm Adenopathy	ESR >50 or # Sites >3	Type
IA/IIA	No	No	Favorable Disease
	No	Yes	Favorable/Unfavorable Disease
	Yes	Yes/No	Unfavorable Disease
IB/IIB	Yes/No	Yes/No	Unfavorable Disease
III–IV	Yes/No	N/A	Advanced Disease

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Q2) Which of the following is not expressed by RS cell of Classical Hodgkin Lymphoma?

1. CD 15
2. CD 30
3. CD 79a
4. PDL1 expression
5. PAX5

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11.32 Which of the following is not expressed by RS cell of Classical Hodgkin Lymphoma?

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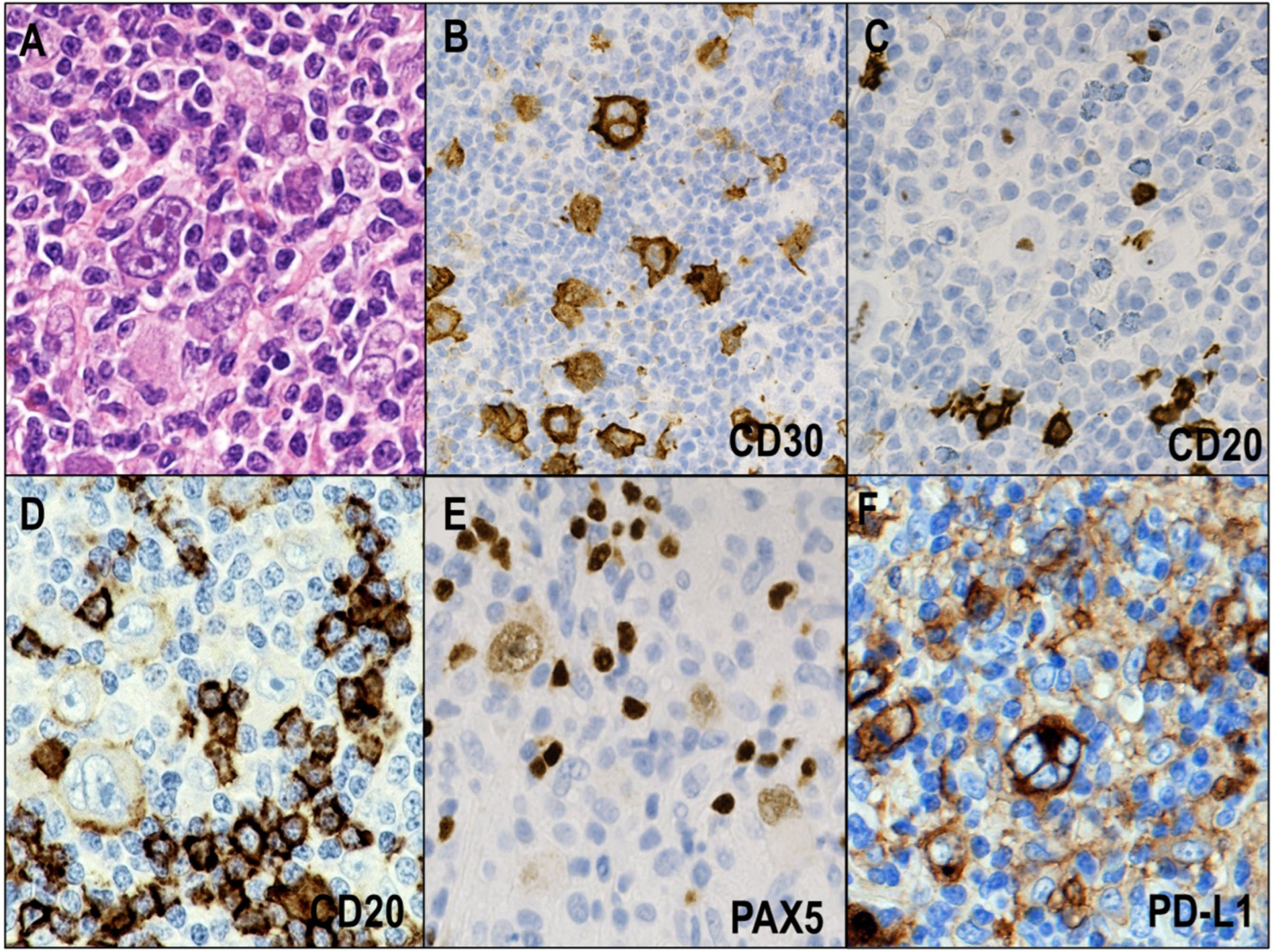

Figure 1. Histological and immunohistochemical features of classic Hodgkin lymphoma (CHL).

(**A**) CHL is histologically composed of Hodgkin and Reed–Sternberg (HRS) cells and abundant reactive bystander cells (HE × 400).

(**B**) HRS cells are universally positive for CD30 (×400).

(**C**,**D**) HRS cells are negative or weakly positive for CD20 (×400).

(**E**) HRS cells typically show weak expression of PAX5 (×400).

(**F**) HRS cells are highly associated with PD-L1 expression (×400).

Cancers **2022**, *14*(11), 2647;

Q3) In the IPS staging system for Hodgkin Lymphoma, which of the following is NOT a criteria?

1. LDH
2. Absolute lymphocyte count
3. Serum Albumin
4. Haemoglobin
5. Age

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11.33 In the IPS staging system for Hodgkin Lymphoma, which of the following is NOT a criteria?

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Review of Case again…. Classical Hodgkin Lymphoma

- A 27 year-old man presented with weight loss and night sweats for 6 months.
- Examination showed cervical & axillary lymphadenopathy. No organomegaly
- FBC showed
  - WBC 16 x 10^9/l, Neutro- 92%, Lymphocytes- 5%
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  - ESR 60
- Normal Creat & LFT. Albumin 35 g/l
- PET CT- Generalised lymphadenopathy, Mediastinal mass — 8 cm x 10 cm, Multiple hepatic and splenic lesions and FDG avid Bone lesions in multiple bones

Q4) What is International Prognostic Score (IPS) for this patient

1. IPS 3
2. IPS 4
3. IPS 5
4. IPS 6
5. IPS 7

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11.34 What is International Prognostic Score (IPS) for this patient

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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)**

†From: Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med 1998;339:1506-1514. Copyright © 1998

IPS 6- Predicted 5 year PFS- 42%, Estimated OS- 56%

*NCCN 2024

Further course

- Patient was treated with BV-AVD (Brentuximab + Adrimaycin, Vinblastine, Dacarbazine) therapy as first line
- Achieved complete remission on PET CT after 2 cycles
- Completed 6 cycles with BV-AVD. Required G-CSF support
- On follow up for >2 years and keeping remission

Q5) Which of the following is NOT true about the ECHELON -1 trial?

1. BV+ AVD resulted in a superior PFS as compared to ABVD
2. BV+AVD resulted in a superior OS as compared to ABVD
3. BV+AVD had less neutropenia as compared to ABVD
4. BV+AVD group had fewer second cancers and subsequent therapies as compared to ABVD
5. BV+AVD group had higher incidence of peripheral neuropathy than ABVD

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11.35 Which of the following is NOT true about the ECHELON -1 trial?

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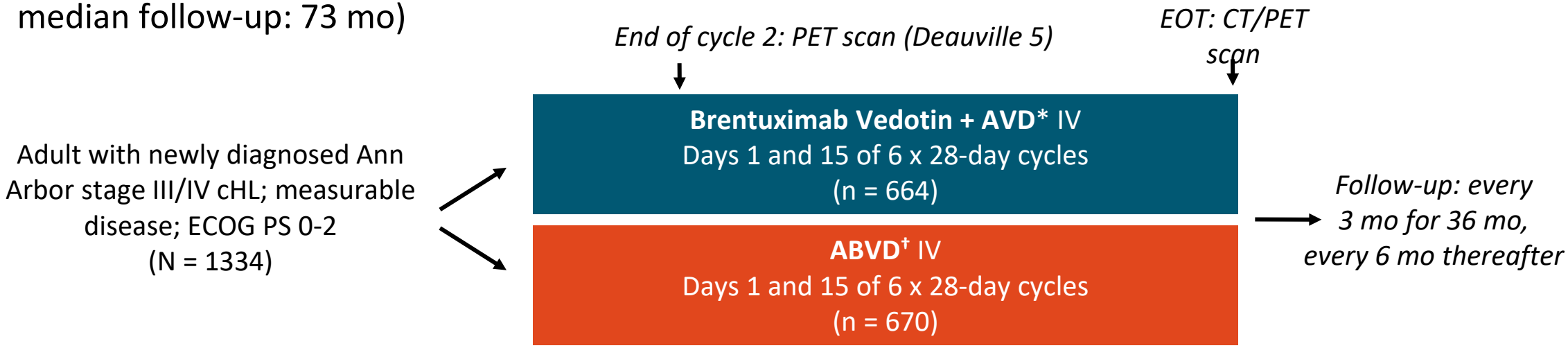
ECHELON-1 Updated Analysis: Study Design

- Updated analysis of international, open-label phase III trial (data cutoff: June 1, 2021; median follow-up: 73 mo)



- Primary endpoint: modified PFS per independent review
  - 2-yr PFS rate with BV + AVD vs ABVD: 82.1% vs 77.2% (HR: 0.77; 95% CI: 0.60-0.98; *P* = .04)

- Current analysis
  - Key secondary endpoint: α-controlled, event-driven OS analysis
  - LTFU assessments: OS for PET2+ vs PET2- patients; investigator-assessed PFS; subsequent tx; safety

*BV + AVD: BV 1.2 mg/kg, doxorubicin 25 mg/m^2, vinblastine 6 mg/m^2, dacarbazine 375 mg/m^2. †ABVD: doxorubicin 25 mg/m^2, bleomycin 10 U/m^2, vinblastine 6 mg/m^2, dacarbazine 375 mg/m^2.

Ansell. ASCO 2022. Abstr 7503. Connors. NEJM. 2018;378:331. NCT01712490.

ECHELON-1 Updated Analysis: OS and PFS

OS Outcome	BV + AVD (n = 664)	ABVD (n = 670)
OS events, n	39	64
Estimated 6-yr OS, % (95% CI)	93.9 (91.6-95.5)	89.4 (86.6-91.7)

PFS Outcome	BV + AVD (n = 664)	ABVD (n = 670)
PFS events, n	112	159
Estimated 6-yr PFS, % (95% CI)	82.3 (79.1-85.0)	74.5 (70.8-77.7)

- Addition of brentuximab vedotin to AVD significantly reduced risk of death by 41% vs ABVD (HR: 0.59; 95% CI: 0.40-0.88; log-rank *P* = .009), with median OS not reached
- Comparable OS benefit observed in multivariate analysis adjusting for baseline disease and demographic characteristics (HR: 0.53; 95% CI: 0.34-0.83)
  - Covariates most strongly associated with OS: age, non-white race, ECOG PS, PET2 status
- Across subgroups defined by baseline disease and demographic factors, OS benefit was generally consistent with brentuximab vedotin + AVD
- BV + AVD significantly reduced risk of progression or death by 32% vs ABVD (HR: 0.68; 95% CI: 0.53-0.86; log-rank *P* = .002)

Ansell. ASCO 2022. Abstr 7503.

Slide credit: clinicaloptions.com

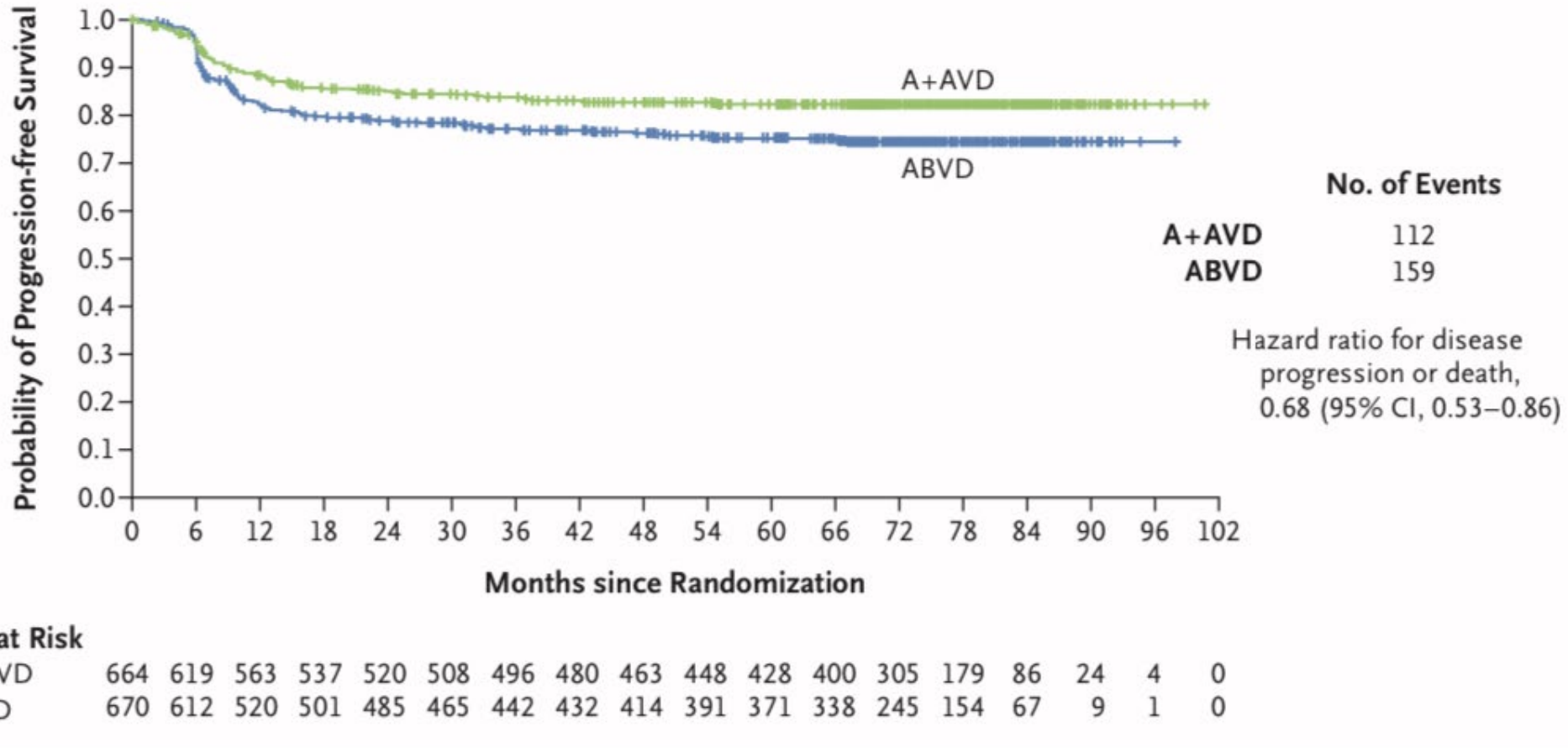


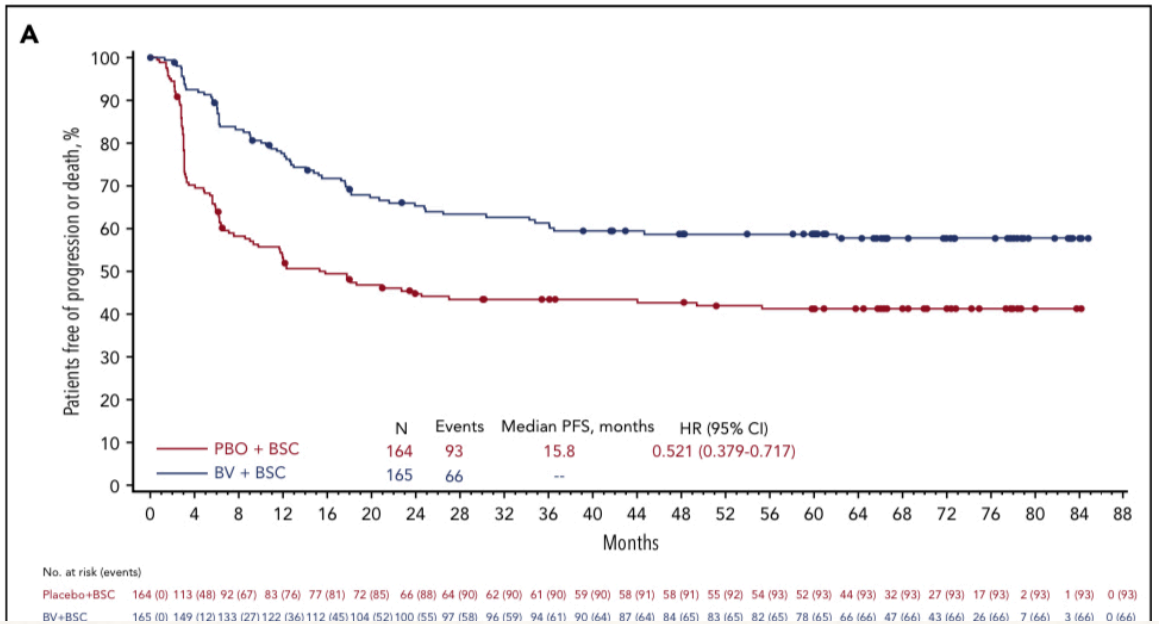
Figure 3. Progression-free Survival According to Investigator Assessment (Intention-to-Treat Population).

Tick marks indicate censored data.

N Engl J Med 2022;387:310-20.

Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial

Lancet 2015; 385: 1853–62



blood® Brief Report

CLINICAL TRIALS AND OBSERVATIONS

Five-year PFS from the AETHERA trial of brentuximab vedotin for Hodgkin lymphoma at high risk of progression or relapse

Blood. 2018;132(25):2639-2642

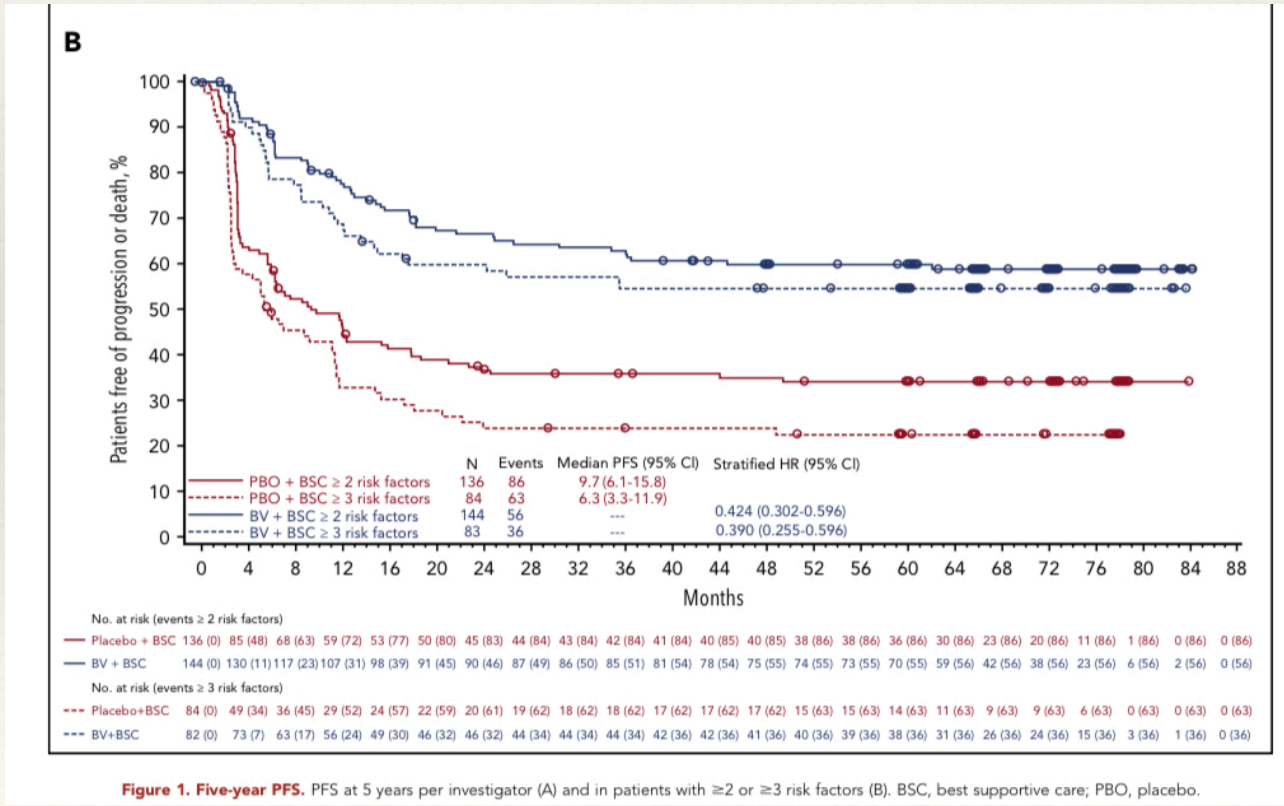


Figure 1. Five-year PFS. PFS at 5 years per investigator (A) and in patients with ≥2 or ≥3 risk factors (B). BSC, best supportive care; PBO, placebo.

Q6) Which of the following is TRUE about Pembrolizumab in Hodgkins Lymphoma?

1. Pembrolizumab did not have a better PFS compared to BV in relapsed refractory Hodgkins in Keynote 204 Phase 3 trial
2. Pembrolizumab was not evaluated in those who had received prior BV in Keynote 087 phase 2 trial
3. Pembrolizumab had a Higher ORR than BV in keynote 204
4. Less than 50% achieved a ORR in keynote 087 with Pembrolziumab in relapsed refractory Hodgkins
5. Pembrolizumab had lower incidence of pneumonitis than BV in keynote 204

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11.36 Which of the following is TRUE about Pembrolizumab in Hodgkins Lymphoma?

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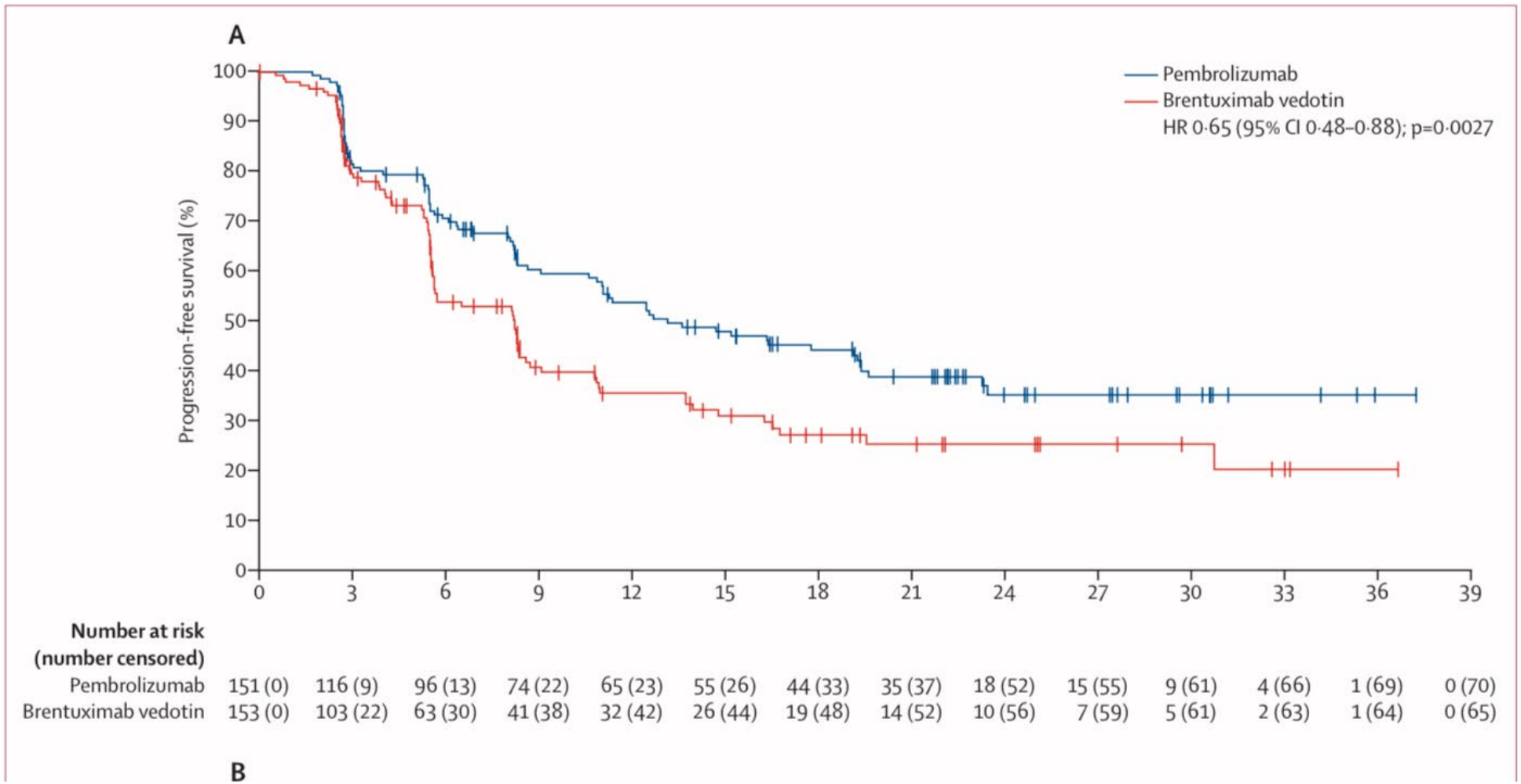
Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

Lancet Oncol 2021; 22: 512–24

John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson,



New Therapy Model for Hodgkin Lymphoma

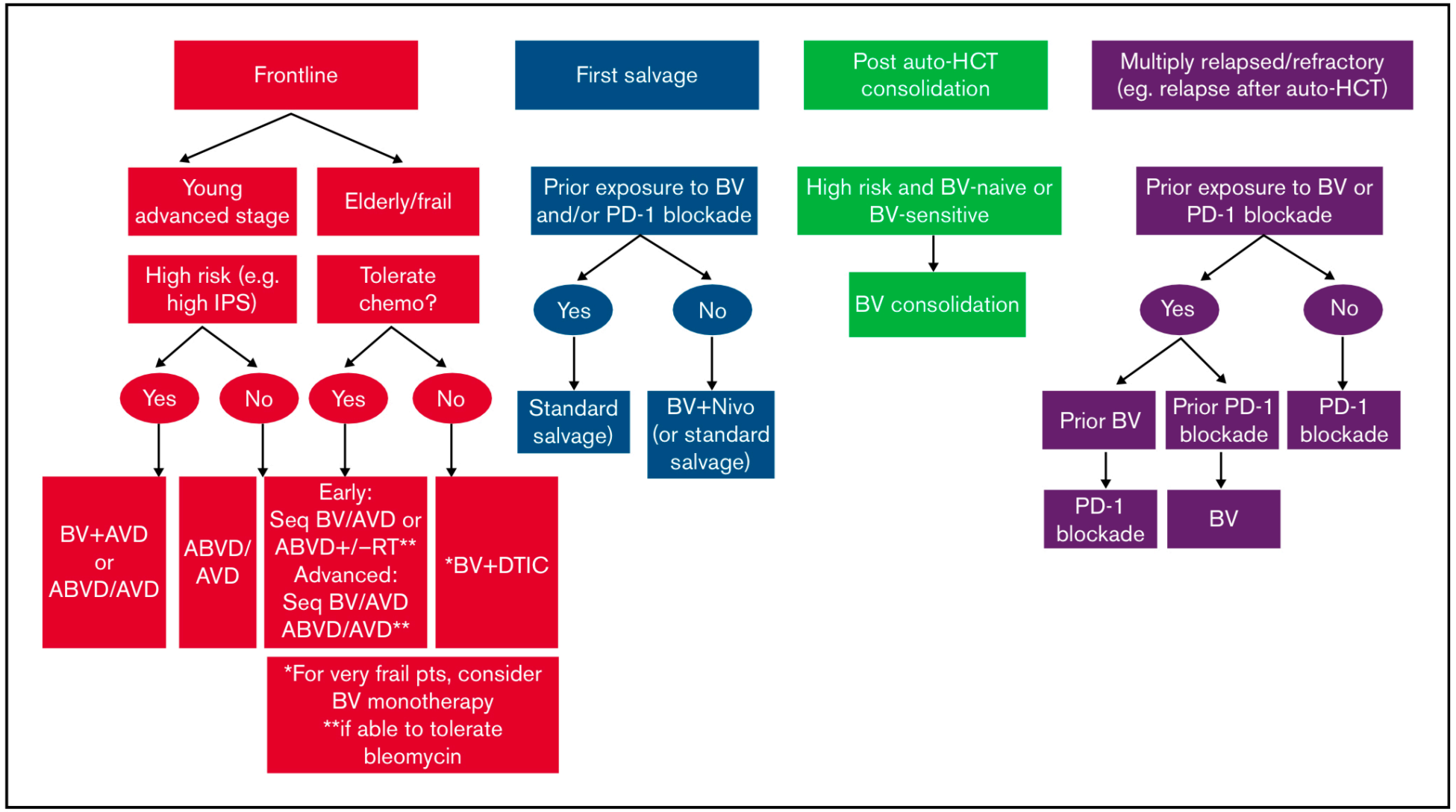


Figure 1. How we incorporate novel agents into treatment of classical Hodgkin lymphoma.

*Blood, 19 AUGUST 2021, VOLUME 138,NUMBER 7