Scottish Consensus Clinical Management Guideline for Classical Hodgkin Lymphoma

***Consensus Group**

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Document Control

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MDT

All patients should be discussed at an MDT. Individual patient circumstances may dictate an alternative approach to that outlined in this guidance.

Clinical Trials

Entry into clinical trial should be considered where possible.

Essential Initial Investigations

Essential diagnostic and baseline investigations should be carried out as per BSH guideline: Guideline for the first-line management of Classical Hodgkin lymphoma – A British Society for Haematology guideline (2022)[1] https://onlinelibrary.wiley.com/doi/10.1111/bjh.18083

Note:
Baseline PET-CT scan recommended for all patients treated with curative intent.
Bone marrow trephine biopsy not required if PET-CT scan undertaken.

Other Investigations

Echocardiogram or cardiac MUGA scan: as per local guidance.

Pulmonary function tests (including assessment of diffusion capacity): recommended at base line in patients due to receive a bleomycin-containing chemotherapy regimen but if no history of lung disease, respiratory symptoms or smoking history may not be necessary in all. Should not delay initiation of therapy in patients without a prior respiratory disorder.

Irradiated Blood Components

Patients with Classic Hodgkin Lymphoma should be flagged to blood transfusion service / blood bank as requiring irradiated blood components (current advice is for life-long requirement).

Fertility Preservation

Around 50% of patients diagnosed with cHL are aged 15-44yrs. In Scotland around 33 women of child-bearing age are diagnosed each year and of those, about 50% are aged 15-24yrs.

Fertility preservation should be discussed with all patients and referral to appropriate Reproductive Medicine services considered.

When considering treatment, especially where multiple options are available, it may be relevant to consider that escBEACOPDac is more likely to cause infertility than ABVD[1].

Prognostic Scoring Systems in Classical Hodgkin Lymphoma

Early stage:

EORTC risk factors in localised disease

A. Favourable (patients must have all features)

1. Clinical stage 1 or 2
2. Maximum of three nodal areas involved
3. Age less than 50 yrs
4. ESR< 50 mm/h
5. Mediastinal/thoracic ratio ≤ 0.35 at D5/6

B. Unfavourable (If any present)

1. Clinical stage 2 with 4 or more nodal areas involved
2. Age ≥ 50 yrs
3. ESR ≥50 mm/h without B symptoms or > 30 mm/h with B symptoms
4. Mediastinal/thoracic ratio > 0.35 at D5/6

GHSG: (German Hodgkins Study Group) - risk factors for stage IIA unfavourable:

(Any risk factor present confers unfavourable risk status: all absent = favourable risk)

1. Large mediastinal mass > 0.33 at D5/6 on CXR
2. Extranodal disease
3. ESR >50 mm/h without B symptoms or > 30 mm/h with B symptoms
4. Three or more nodal areas

Advanced stage:

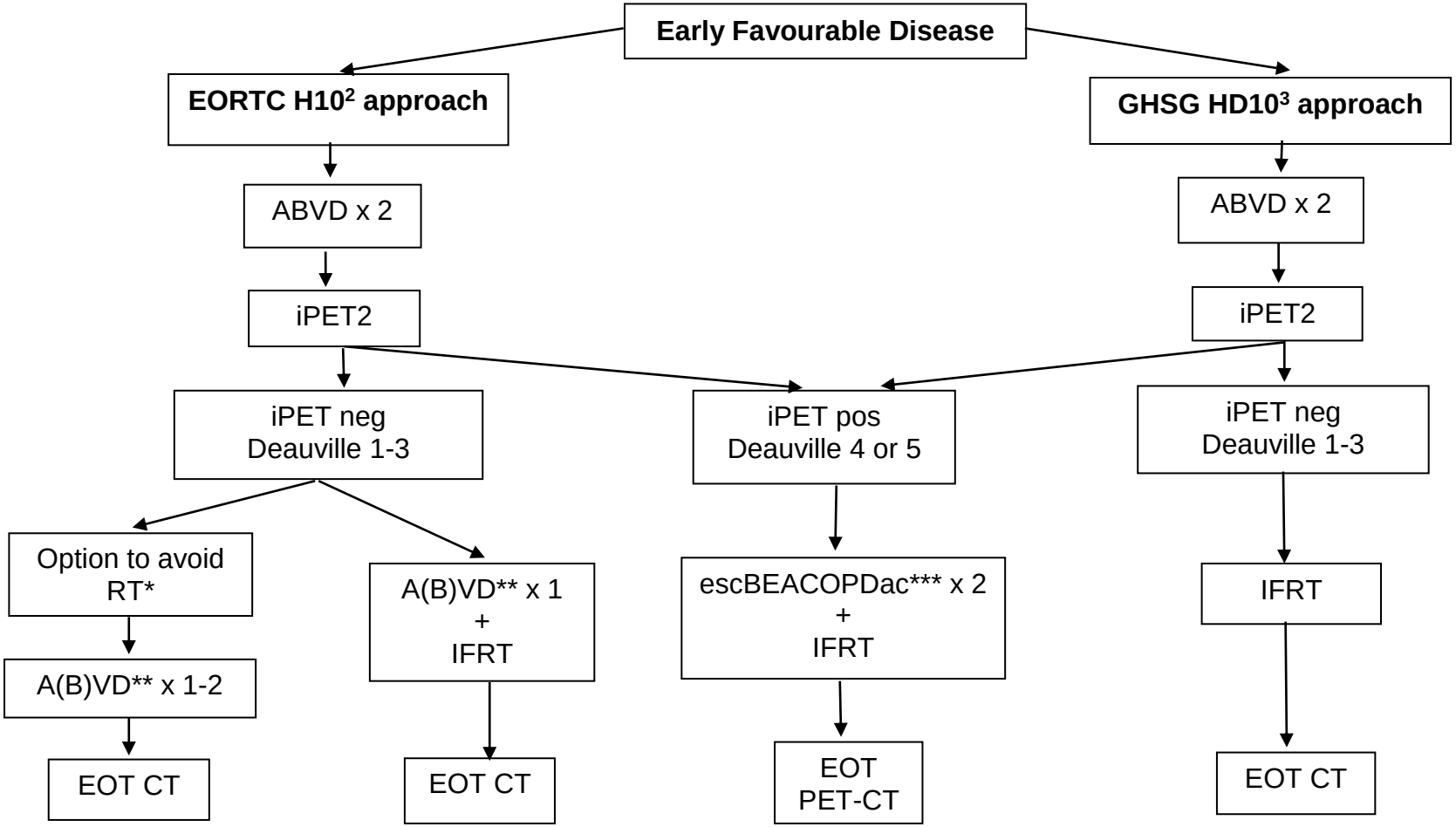
International Prognostic Score (Hasenclever Score)

1. Age > 45 yrs
2. Male sex
3. Serum Albumin < 40g/l
4. Hb < 105 g/l
5. Stage 4 disease
6. Leucocytosis i.e WCC >15 x 10^9/l
7. Lymphopenia i.e. < 0.6 x 10^9/l or < 8% of total WCC

Management of Early Stage Disease (clinical stage IA/IIA)

Assess Risk Factors using EORTC or GHSG criteria – Early Favourable / Early Unfavourable

Consider trial availability (patients <18 years may be eligible for paediatric trials).
Patients <26 years may benefit from TCT services.
Patients unfit for chemotherapy: consider involved site radiotherapy (ISRT) alone.



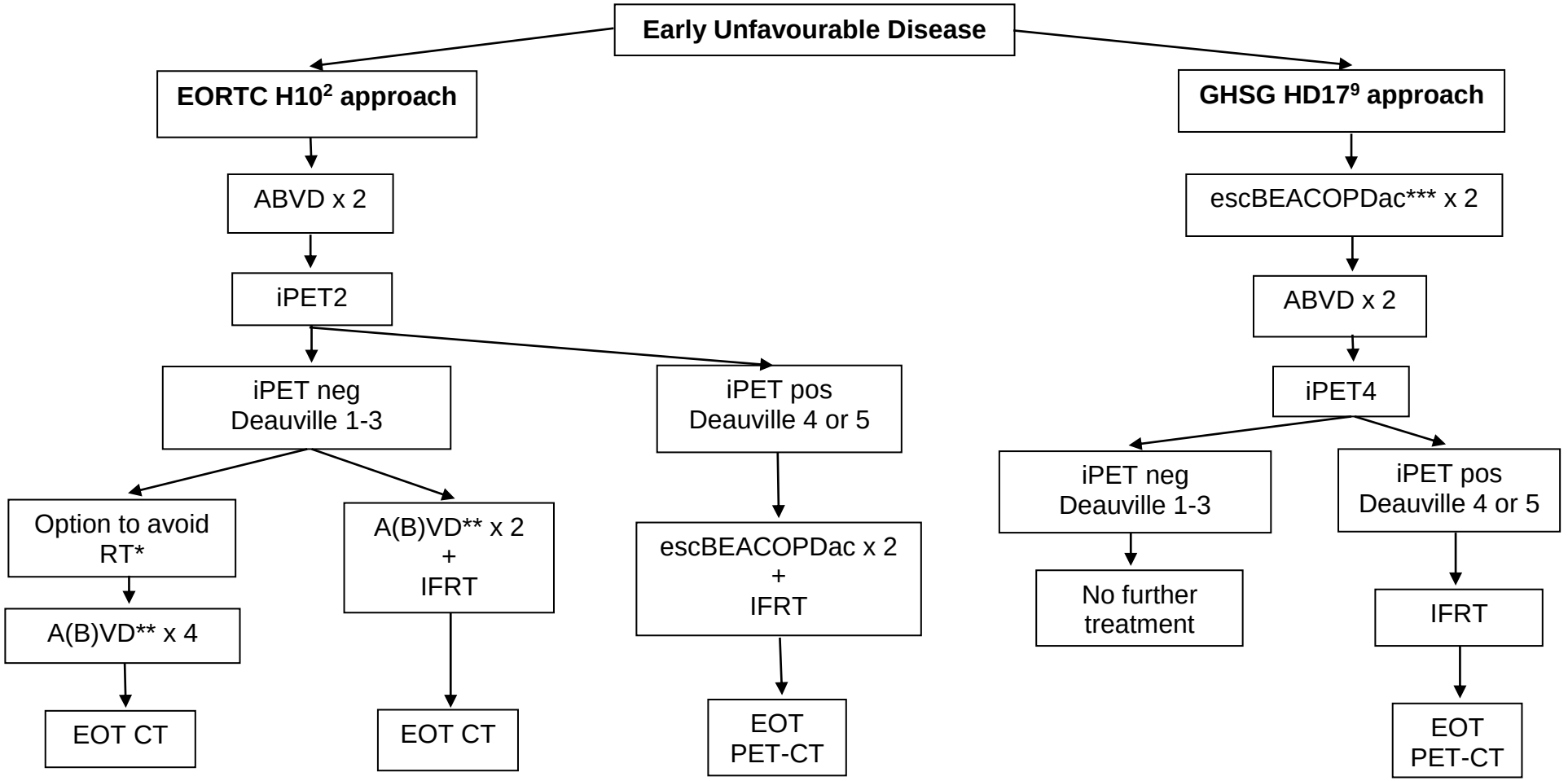
iPET 2 = interim PET-CT after 2 x chemo, IFRT = Involved field radiotherapy, EOT CT = End of Treatment CT, EOT PET-CT = End of Treatment PET-CT

* it is reasonable to omit RT in iPET 2 neg patients in some circumstances, although there is an increased risk of relapse (RAPID[4] study)

**it is now common practice to omit Bleomycin following iPET 2 neg result, extrapolating data from RATHL[5] study

***escBEACOPDac is less myelosuppressive, with some reduced risk of infertility when compared with escBEACOPP and has been shown to have similar efficacy[6,7,8]

Management of Early Stage Disease (clinical stage IA/IIA)



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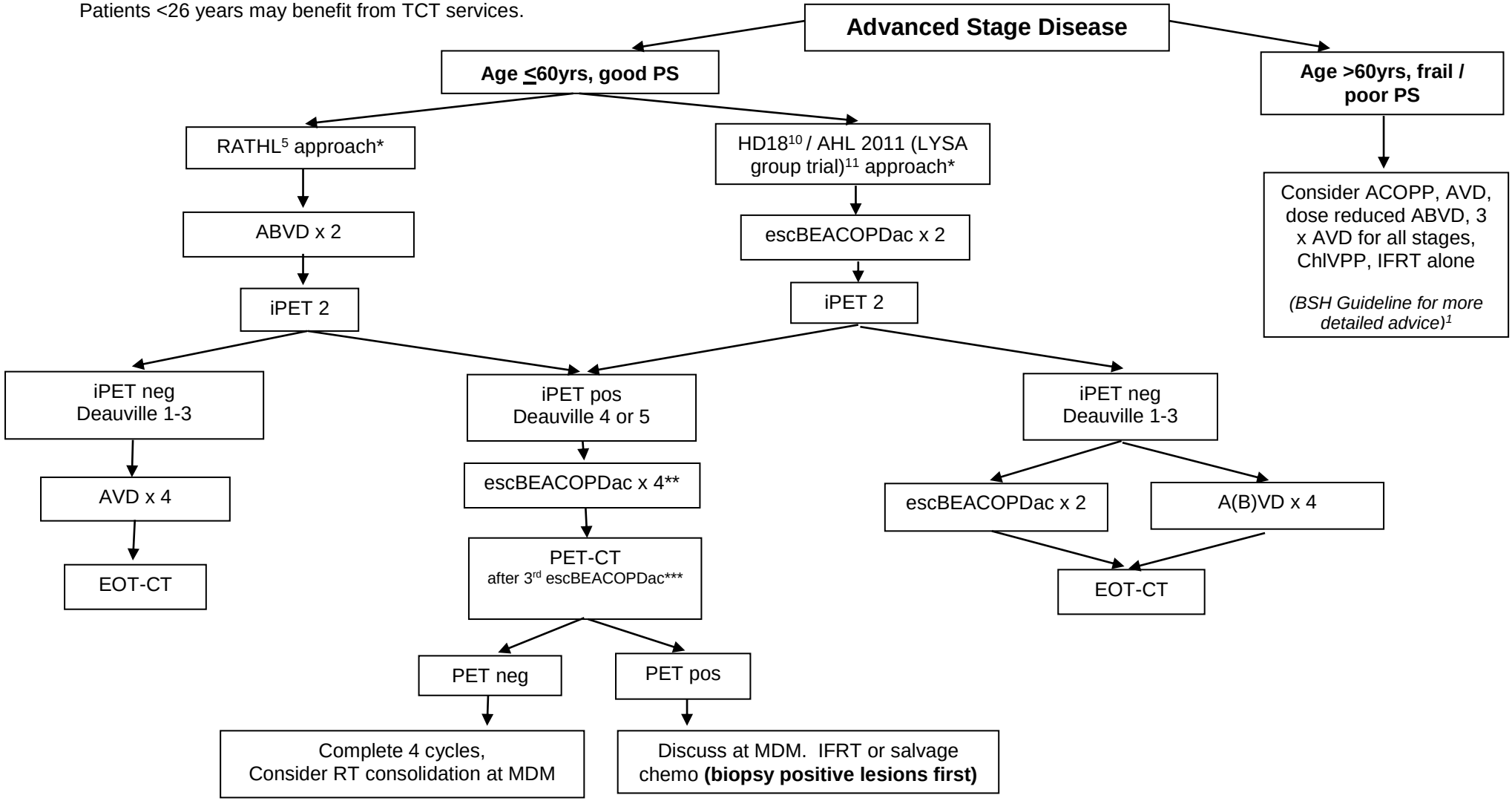
Management of Advanced Stage Disease
(clinical stage IIB, III and IV)

Consider trial availability (patients <18 years may be eligible for paediatric trials).
Patients <26 years may benefit from TCT services.

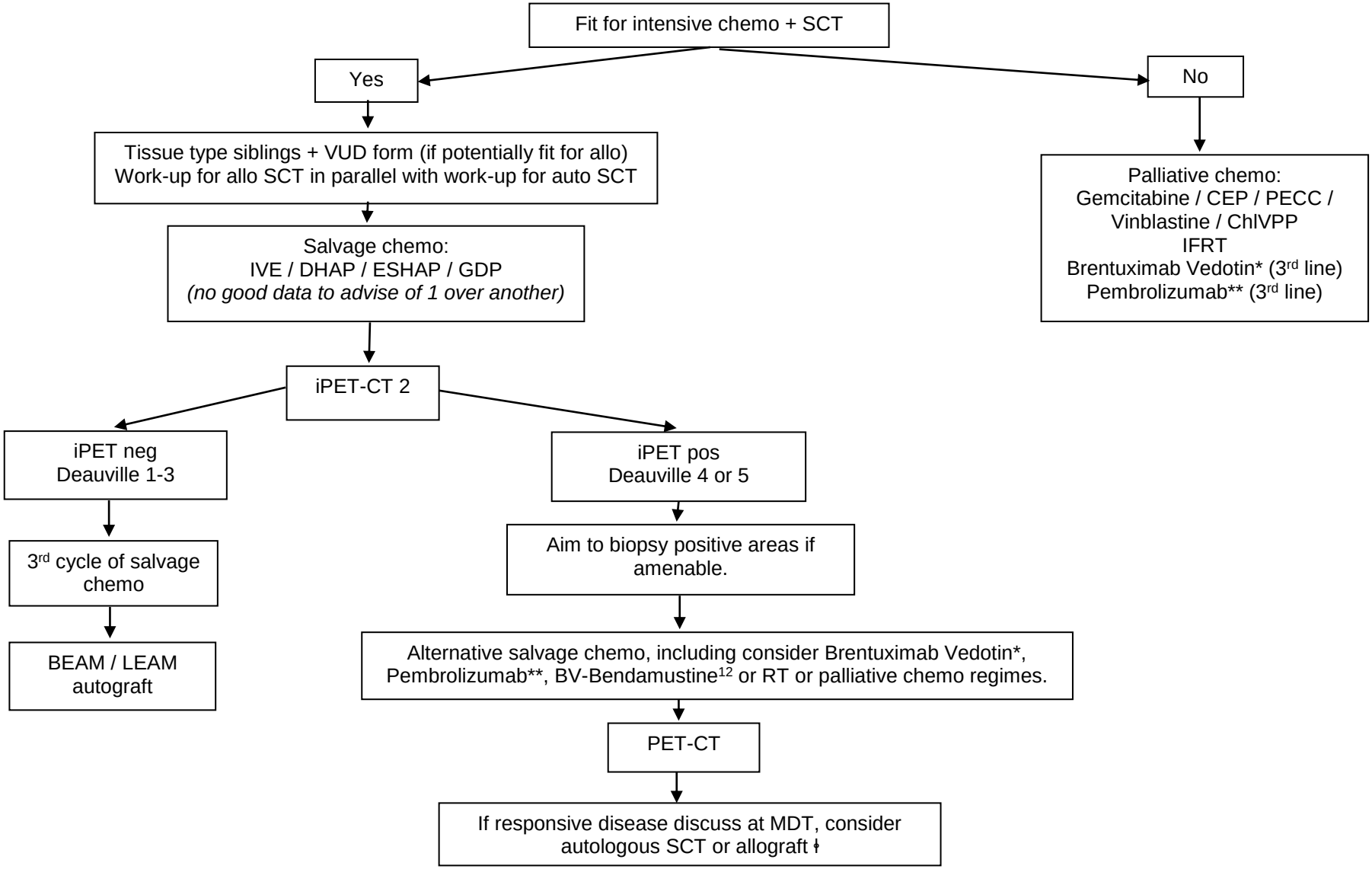


*Hasenclever ≥3 have increased risk iPET2 pos and higher 5 yr relapse rate as does stage IV disease – consider HD18 approach with these patients. Starting with escBEACOPDac may also offer possibility of shorter treatment duration and may have lower risk of cardiac toxicity with reduced overall anthracycline dose.

**RATHL approach, if iPET2 positive may be an option for some to continue with ABVD x 4 + IFRT eg if not fit for escBEACOPDac

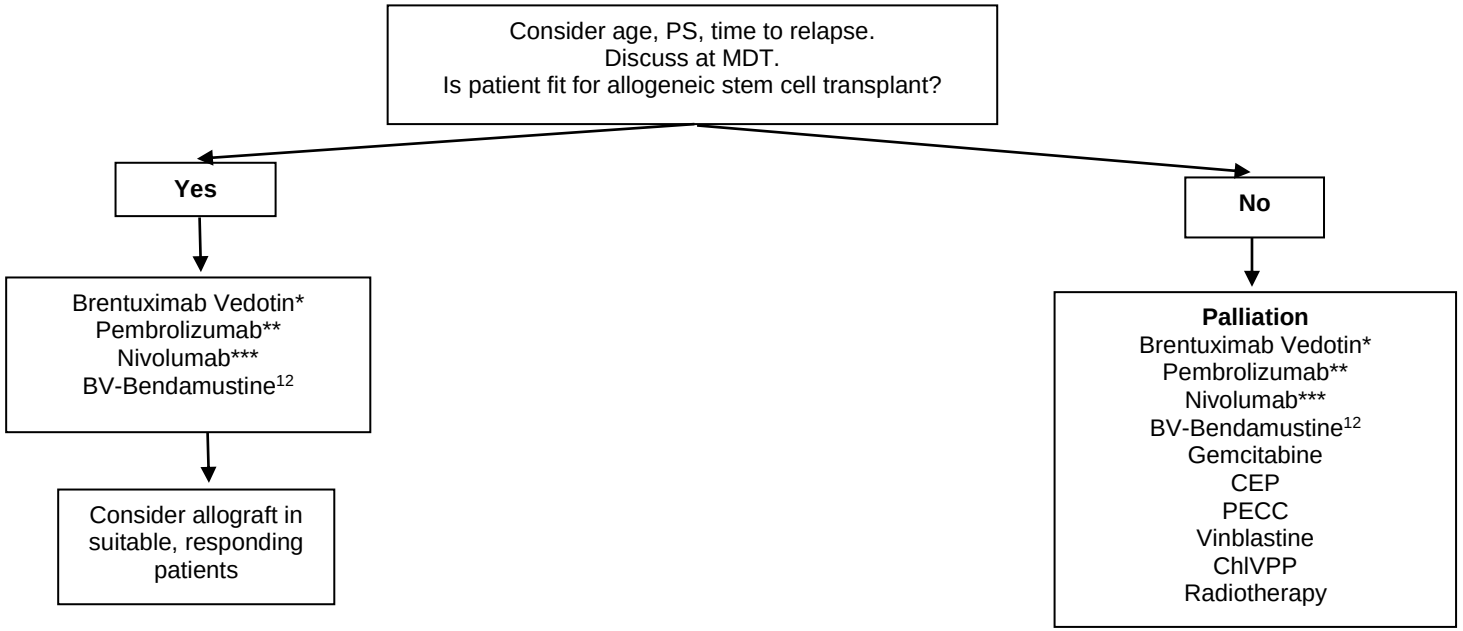
***May consider doing earlier PET-CT if concerns re-response.

Management of Relapsed or Refractory Disease
(No Previous Autologous Stem Cell Transplant)



ǂ Progression to Autograft requires proven ongoing chemo-sensitive disease, ideally with complete metabolic response, but if not achievable may still be benefit to autograft if has been a very good partial response.

Management of Relapse Following Autologous Stem Cell Transplant



Patients who have relapsed after ASCT are eligible for either Brentuximab vedotin (SMC approval No. 845/12) or Pembrolizumab (SMC approval No. 2380).
Patients who have relapsed after ASCT and Brentuximab are eligible for Nivolumab (SMC approval No. 1240/17).

***Treatment with Brentuximab Vedotin**

- After four cycles of Brentuximab vedotin carry out a PET scan. Only continue with Brentuximab vedotin if there is a benefit to the patient.
- If transplant is a possibility please discuss with transplant centre as soon as practical.

****Treatment with Pembrolizumab**

- Reported cases of early increase in tumour size and new lesions, followed by later response. In trials if still progressive disease after 12 weeks then treatment discontinued. Otherwise continue until toxicity, disease progression or allo SCT, to a maximum duration of 2 years.

*****Treatment with Nivolumab**

- Must have had previous Brentuximab Vedotin and ASCT to be eligible.
- Caution in patients being considered for allo SCT as early data suggests increased incidence of Acute GVHD + increased transplant related mortality.
- If responding, continue until toxicity, disease progression or allo SCT.

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