Peripheral T-cell Lymphomas (PTCL)[1]

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[1] This algorithm contains the following subtypes: PTCL - not otherwise specified, angioimmunoblastic T-cell lymphoma (AITL), anaplastic large cell lymphoma, anaplastic lymphoma kinase (ALK) positive and ALK negative and enteropatic associated T-cell lymphoma (EATL). The following subtypes are not included in this algorithm: T-cell prolymphocytic leukemia (T-PLL), T-cell large granular lymphocytic leukemia (T-LGL), primary cutaneous anaplastic large-cell lymphoma (ALCL), breast implant-associated (BIA)-ALCL and all other cutaneous T-cell lymphoma [see Cutaneous T-cell Lymphoma (CTCL) algorithm].

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Note: Consider Clinical Trials as treatment options for eligible patients.

PATHOLOGIC DIAGNOSIS[1]

ESSENTIAL:

- Hematopathology review of all slides with at least one paraffin block or 15 unstained slides representative of the tumor. Re-biopsy if consult material is nondiagnostic.
- Adequate morphology and immunophenotyping to establish diagnosis
  - Flow cytometry immunophenotypic studies: CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD16, CD25, CD26, CD14, CD45, CD52, CD56, CD57, CD94, TCRbeta, TCRgamma, CD30, and TRCB1
  - Paraffin Panel: CD20, CD4, CD8, CD3, CD30 and/or other pan-T-cell markers (CD2, CD5, CD7, CD43), Ki-67, EBER

OF USE IN CERTAIN CIRCUMSTANCES TO DETERMINE SUBGROUP:

- TBX21/CXCR3/GATA3 and CCR4 to assess PTCL-TBX21 and PTCL-GATA3 plus ICOS and PD1 to exclude lymphomas with follicular helper phenotype (in cases of PTCL- NOS)
- BetaF1, TCR delta (gamma/delta T-cell lymphomas and subcutaneous panniculitis-like T-cell lymphoma)
- CD10, BCL-6, PD1, CXCL13, CD21, ICOS, and IDH2 R172K (AITL)
- CD15, ALK1, EMA (anaplastic T-cell lymphoma)
- CD103, CD56 (EATL)
- CD1a, CD34, TdT (T lymphoblastic lymphoma)
- TCL-1, FOXP3, CD25 (T-cell prolymphocytic leukemia and adult T-cell leukemia/ lymphoma)
- FISH studies to detect DUSP22 and TP63 (ALK negative ALCL)
- Molecular studies to detect clonality of the *TCR* genes
- NGS studies (end lymphoma panel) to assess the mutational landscape

STRONGLY RECOMMENDED:

- Fine needle aspiration (FNA) or core biopsy for tissue array/banking by protocol

INITIAL EVALUATION

ESSENTIAL:

- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen
  - Consider Dermatology consult for comprehensive skin assessment if cutaneous involvement is present or suspected
  - Performance status
  - B symptoms (Unexplained fever > 38°C during the previous month; Recurrent drenching night sweats during the previous month; Weight loss > 10 percent of body weight ≤ 6 months of diagnosis)
  - Calculation of International Prognostic Index (see Appendix A)
- CBC with differential, BUN, creatinine, albumin, AST, bilirubin, serum calcium, alkaline phosphatase, uric acid, LDH
- Beta-2-microglobulin
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBaAg, HCVAb)
- HTLV 1/2 serology
- HLH work-up including EBV by PCR, ferritin, fibrinogen, triglycerides, and cytokine 12 profile including IL-2sR (sCD25)
- Chest x-ray (AP & LAT)
- Unilateral or bilateral bone marrow biopsy with aspirate
- MUGA scan or echocardiogram
- PET/CT
- Lifestyle risk assessment[2]

OF USE IN SELECTED CASES:

- CT head or MRI with contrast
- EBV with PCR
- Pregnancy test
- Stool guaiac, if anemic
- Lumbar puncture, if paranasal sinus, testicular, parameningeal, orbit, CNS, paravertebral, bone marrow or HIV lymphoma
- Serum immunoelectrophoresis (SIEP)
- Discuss fertility options and sperm banking for patients of child bearing potential [refer to Fertility Preservation Prior to Cancer Treatment (Women) algorithm]

See Page 3: Induction therapy

[1] Review MD Anderson approved biomarkers

[2] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

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INDUCTION THERAPY

Stages I - IV →

- CD30-positive
  - CHP-Bv
- CD30-negative
  - EPOCH **or** CHOEP **or** CHOP
- NK/T cell lymphoma
  - Stage I/II: DeVIC with ISRT[1]
  - Stage III/IV: SMILE **or** DDGP **or** P-GEMOX
- CTCL: Refer to Cutaneous T-cell Lymphoma (CTCL) algorithm
- Large cell transformation CTCL[2]
  - Brentuximab vedotin (if CD30-positive) **or**
  - Romidepsin **or**
  - Pralatrexate **or**
  - Gemcitabine **or**
  - Liposomal doxorubicin
  - Consideration for ISRT[1] in limited cutaneous lesions with LCT
  - Multiagent chemotherapy as for PTCL
- Hepatosplenic T-cell lymphoma and EATL
  - HCVAD **or**
  - Dose adjusted EPOCH
- ALK positive and negative anaplastic large-cell lymphoma (ALCL)
  - Limited stage CHP-Bv plus with or without ISRT[1]
  - Other options: CHOEP or CHOP with or without ISRT[1]
- Special circumstances: limited stage ALK positive ALCL or ALK negative DUSP22 positive ALCL
  - Abbreviated course chemotherapy with ISRT[1]

INTERIM RESPONSE

→ After 2-4 cycles, repeat all positive studies[3]

- Complete or partial response[4,5] →
  - Complete current treatment
  - See Page 4 for evaluation, response, treatment and follow up
- No response or progressive disease[4,5] → See Page 5 for refractory or relapse therapy

ALK = anaplastic lymphoma kinase
CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone
CHOEP = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone
CHP-Bv = cyclophosphamide, doxorubicin, prednisone, brentuximab vedotin
DeVIC = dexamethasone, etoposide, ifosfamide, carboplatin
DDGP = cisplatin, dexamethasone, gemcitabine, pegaspargase
DMILE = steroid, methotrexate, ifosfamide, L-asparaginase, etoposideEPOCH = etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin
P-GEMOX = pegaspargase, gemcitabine, oxaliplatin
HCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone
ISRT = involved site radiation therapy

[1] Radiation therapy can be considered for limited stage patients with abbreviated systemic therapy, or to sites of bulk or incomplete response after systemic therapy completion
[2] Refer to Cutaneous T-cell Lymphoma (CTCL) algorithm
[3] PET scans should be used to assess residual abnormalities on CT scan, especially if done pretreatment
[4] Partial response includes a biological measure of disease: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.
[5] For response assessment, refer to: Cheson, B. D., Fisher, R. I., Barrington, S. F., Cavalli, F., Schwartz, L. H., Zucca, E., & Lister, T. A. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, *32*(27), 3059-3067. doi: 10.1200/JCO.2013.54.8800

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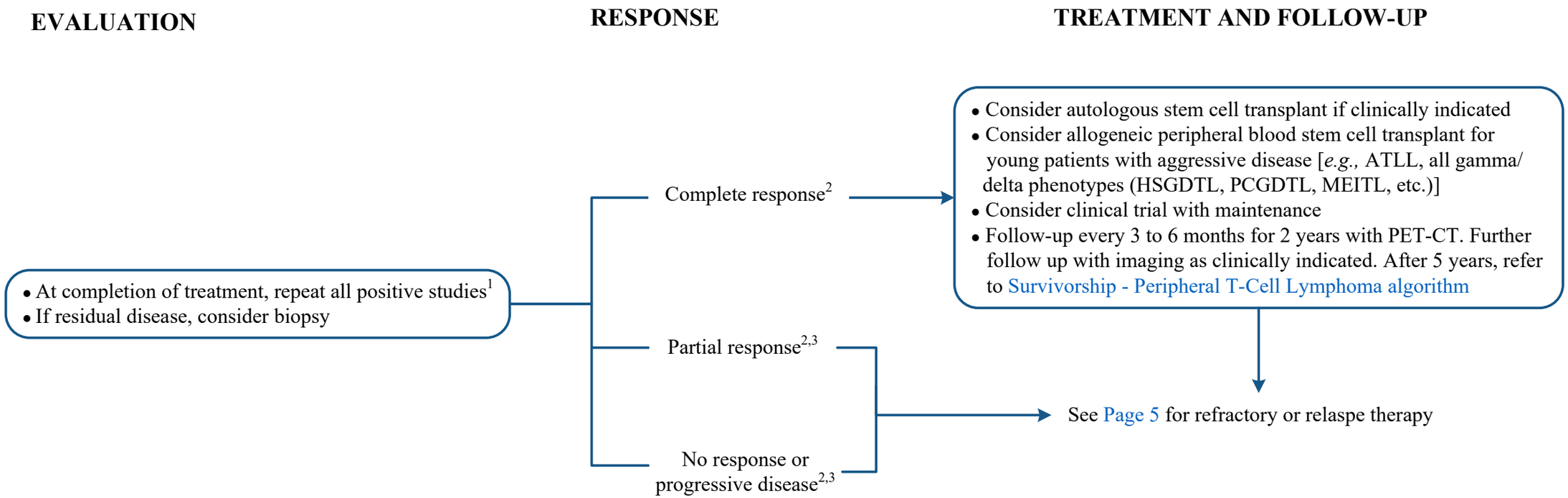
Note: Consider Clinical Trials as treatment options for eligible patients.



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[3] Partial response includes a biological measure of disease: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.

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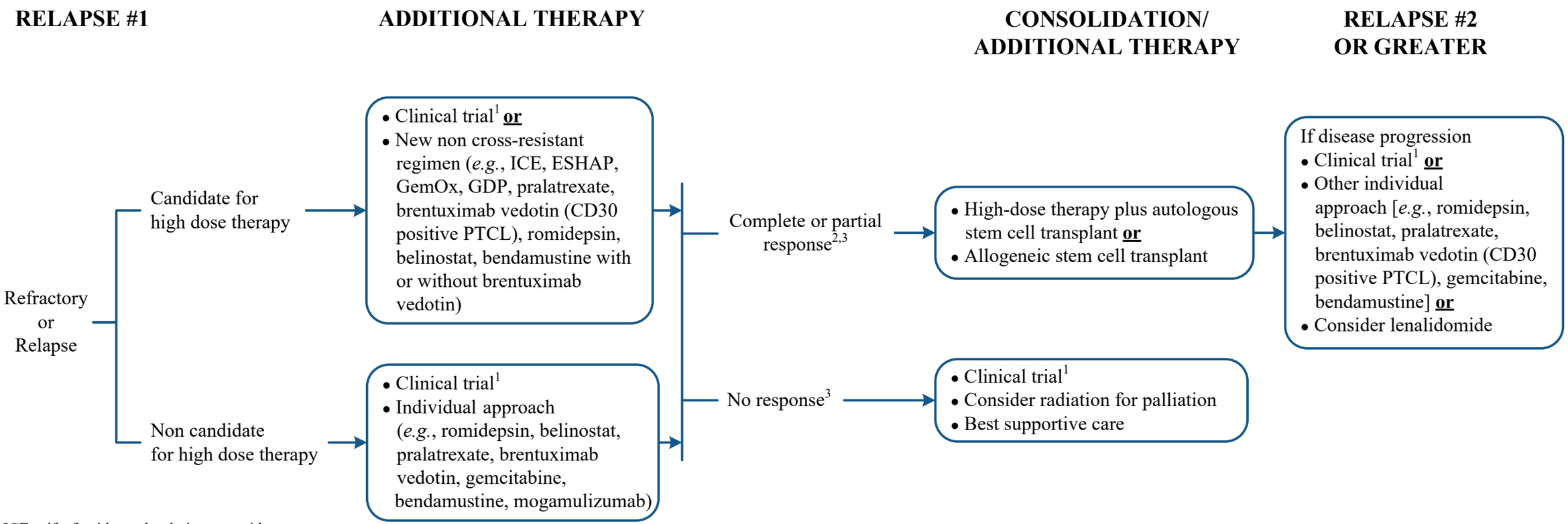

ICE = ifosfamide, carboplatin, etoposide
ESHAP = etoposide, methylprednisolone, high dose cytarabine, cisplatin
GemOx = gemcitabine and oxaliplatin
GDP = gemcitabine, dexamethasone, and cisplatin

[1] Clinical trials or individual regimens: patients who progress after three successive regimens are unlikely to derive additional benefit from currently utilized combination chemotherapy regimens, except for patients with a long disease-free interval

[2] Partial response includes a biological measure of disease: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.

[3] For response assessment, refer to: Cheson, B. D., Fisher, R. I., Barrington, S. F., Cavalli, F., Schwartz, L. H., Zucca, E., & Lister, T. A. (2014). Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. *Journal of Clinical Oncology*, *32*(27), 3059-3067. doi: 10.1200/JCO.2013.54.8800

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APPENDIX A: International Prognostic Index for PTCL-U[1]

Risk Factors	Prognostic Risk	Number of Risk Factors
• Age > 60 years • Serum LDH > 1 times normal • Performance status 2 – 4 • Bone marrow involvement	• Group 1 • Group 2 • Group 3 • Group 4	0 1 2 3 or 4

[1] Other prognostic scoring systems have been proposed and validated, but none are currently used to impact PTCL treatment algorithm

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