EUROPEAN HEMATOLOGY ASSOCIATION

EHA-TSH Hematology Tutorial

Self-assessment Case – Session 4: Treatment Approaches in R/R PTCL

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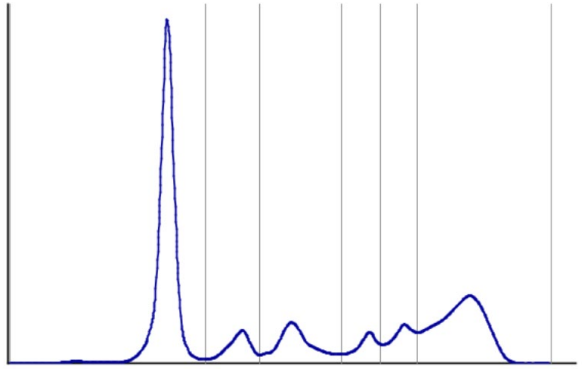
Disclosures

- The presenter has no conflicts of interest to disclose as related to companies or products mentioned in this presentation

Introduction

- 49-year-old male
- Fluctuating cervical and inguinal adenopathy (6 months' duration)
- Rash for 1 month; fever and night sweats (B symptoms)
- Leukocytes: 13.3 × 10^9/L; Hb: 122 × 10^9/L; platelets: 269 × 10^9/L
- Circulating plasma cells: 3%
- LDH: 400 IU/L (normal is < 250 IU/L)
- Gamma globulins: 20.7 g/L
- Presence of a weak $CD4^+$ T-cell population that has completely lost surface expression of CD3; partial loss of CD7 and CD26
  - A small proportion express CD10 (~ 10%)
  - There is also a small contingent of circulating plasma cells
- T-cell clone positive; B-cell clone weakly-positive

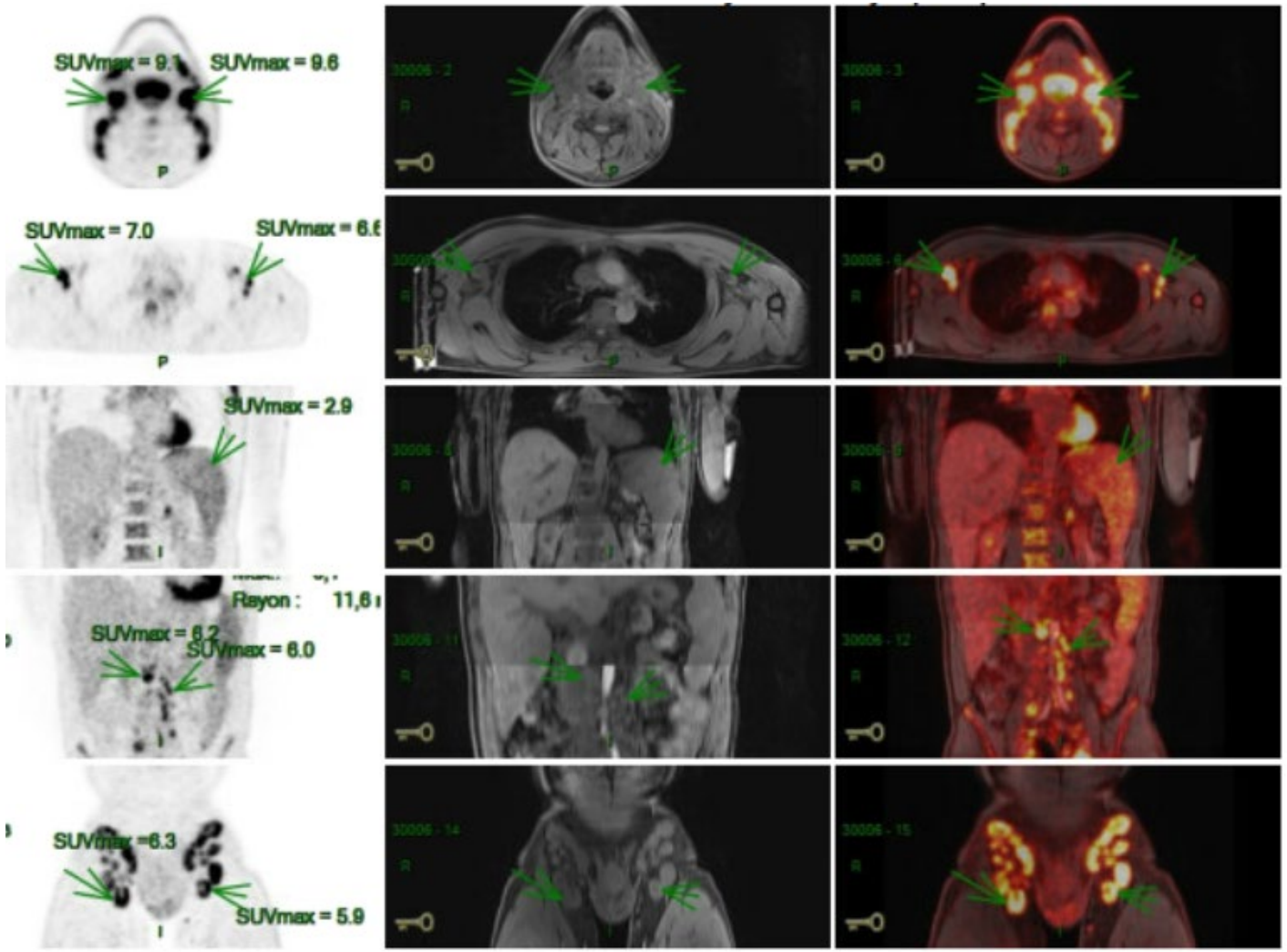
Serum electrophoresis showing hypergammaglobulinemia



CD, cluster of differentiation; Hb, hemoglobin; IU, international units; LDH, lactose dehydrogenase.

PET–MRI

Baseline PET–MRI of the patient



PET–MRI, positron emission tomography–magnetic resonance imaging; SUV_{max}, maximum standardized uptake value.

Question 1: What is the next step?

1. Start chemotherapy, the T-cell lymphoma diagnosis is obvious
2. Bone marrow aspiration to rule out a myeloma
3. Lymph node biopsy
4. Skin biopsy
5. Sequence the circulating T cells

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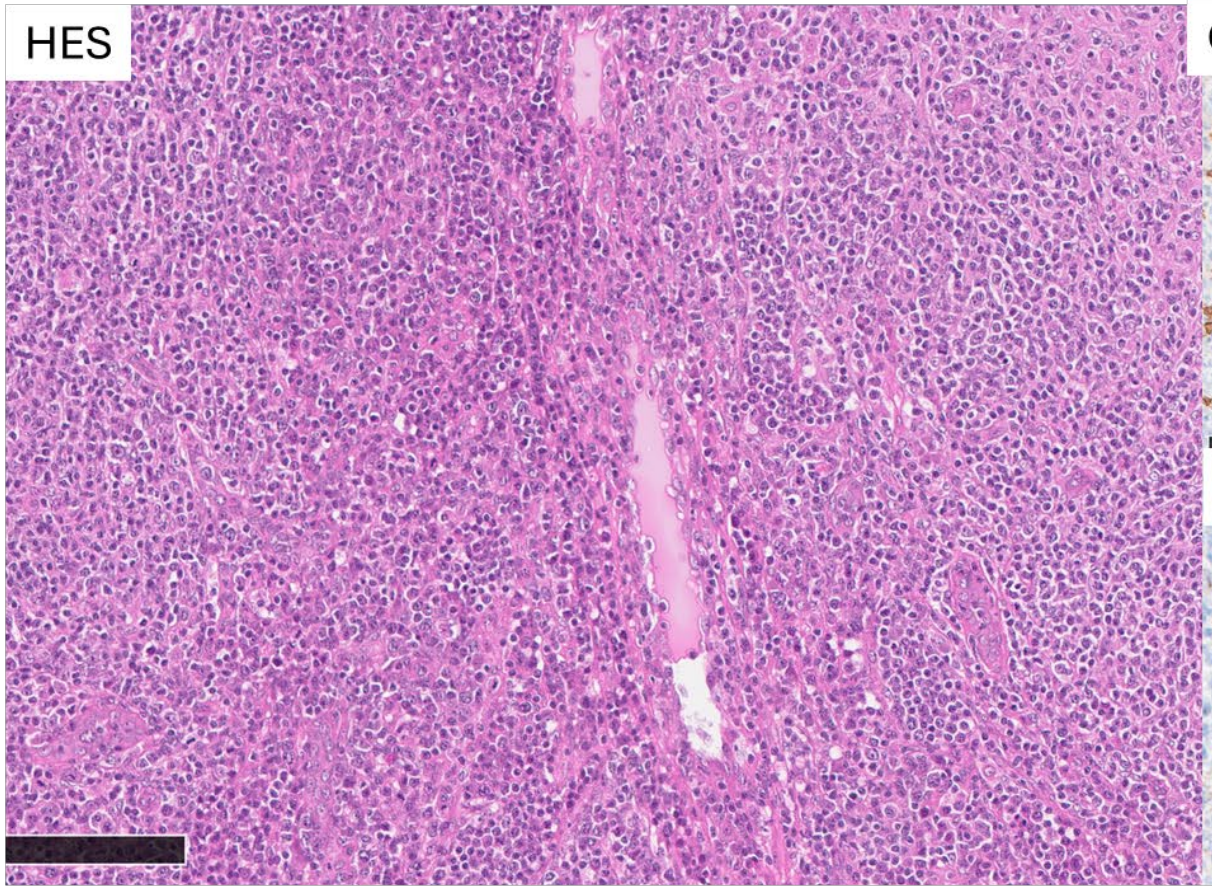
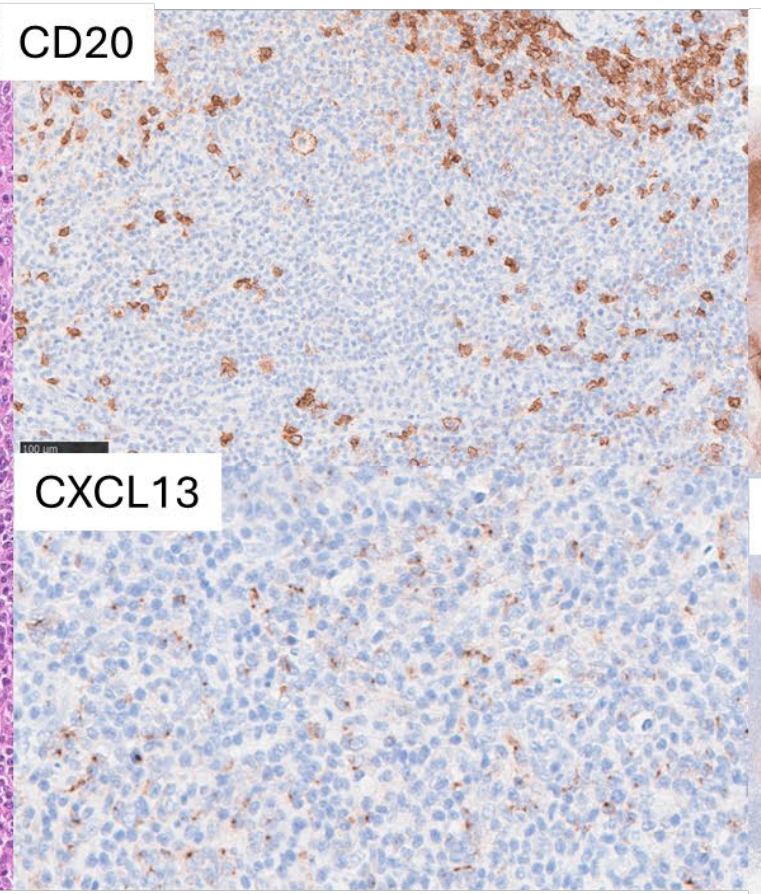
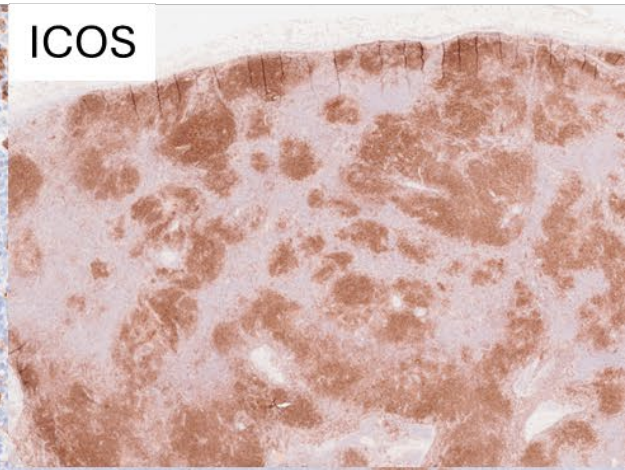
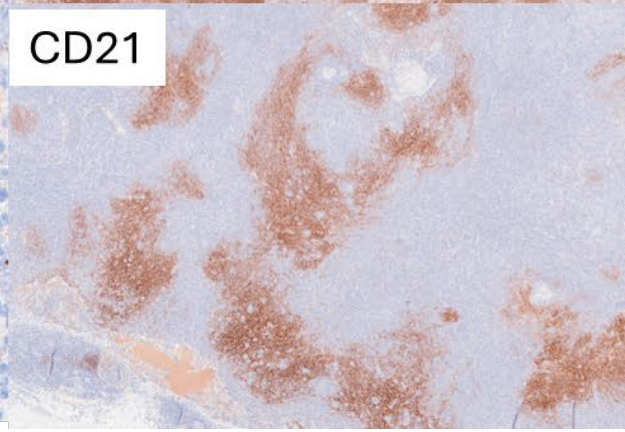
Lymph node biopsy









Question 2: A diagnosis of TFHL is supported by the presence of which of the following?

1. *TET2* mutation
2. *RHOA p.G17V*
3. *SETD2* mutation
4. *NPM1* mutation
5. t(2;5) translocation

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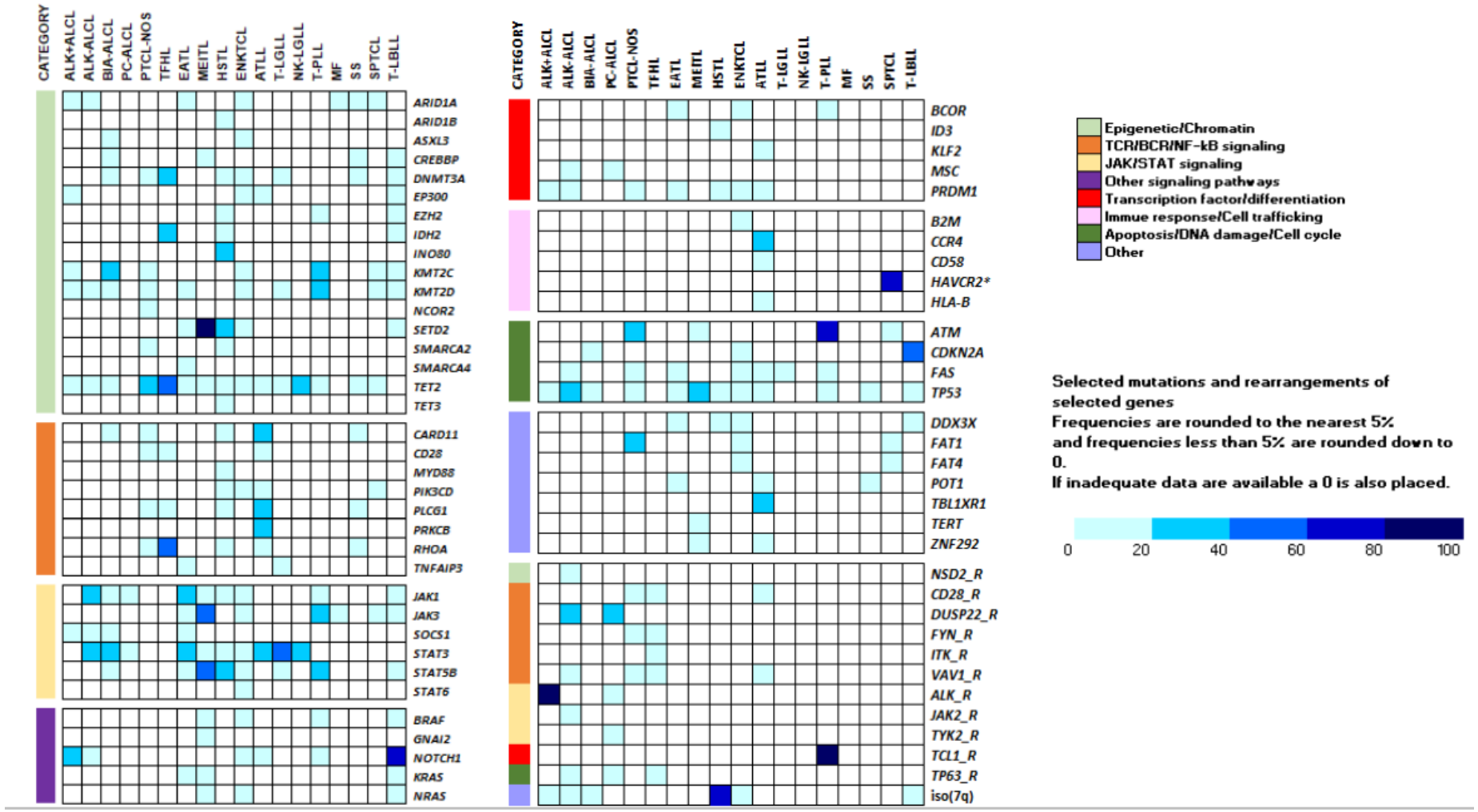
PTCL molecular landscape



de Leval, EHA 2024.

Molecular status of the patient

Tumor

- *TET2 p.R1261C*: 19.6%
- *TET2 p.R1465X*: 26.6%
- *RHOA p.G17V*: 17.4%

Question 3: Which treatment do you recommend?

1. CHOEP for 6 cycles plus allogeneic SCT
2. Bortezomib plus lenalidomide plus dexamethasone (VRd or RVd)
3. CHOEP for 6 cycles plus autologous SCT
4. Romidepsin
5. Azacitidine

CHOP, cyclophosphamide, doxorubicin, vincristine, prednisolone; CHOEP, cyclophosphamide, doxorubicin, vincristine, etoposide, prednisolone;

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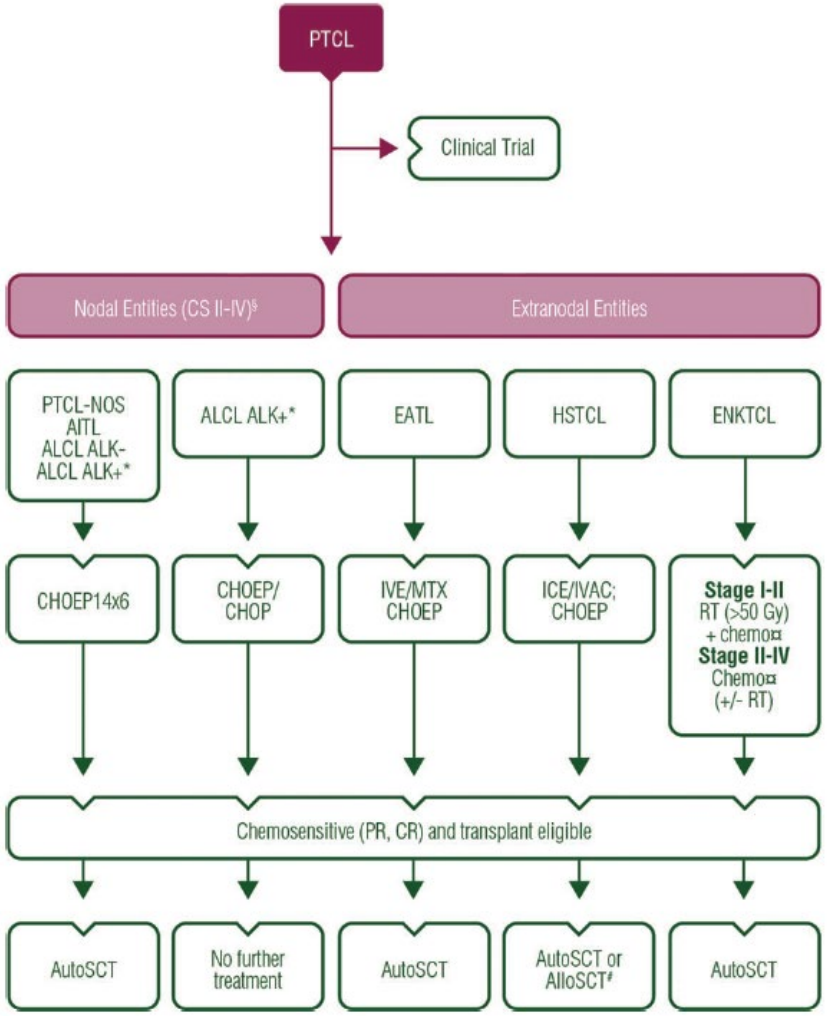
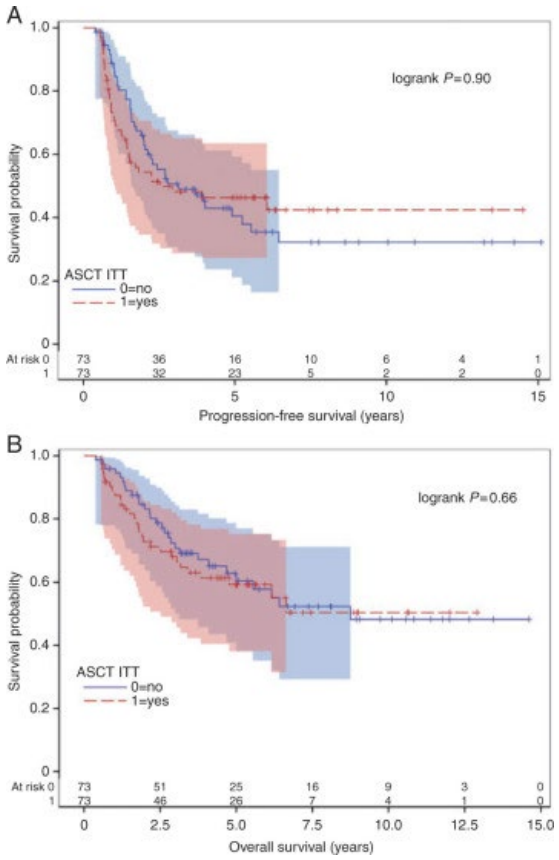
ESMO guidelines (2015)



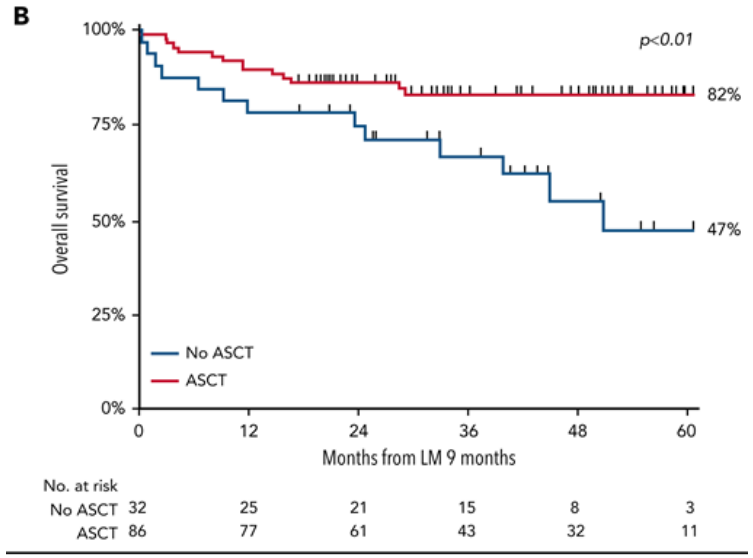
What about frontline autologous SCT?

No

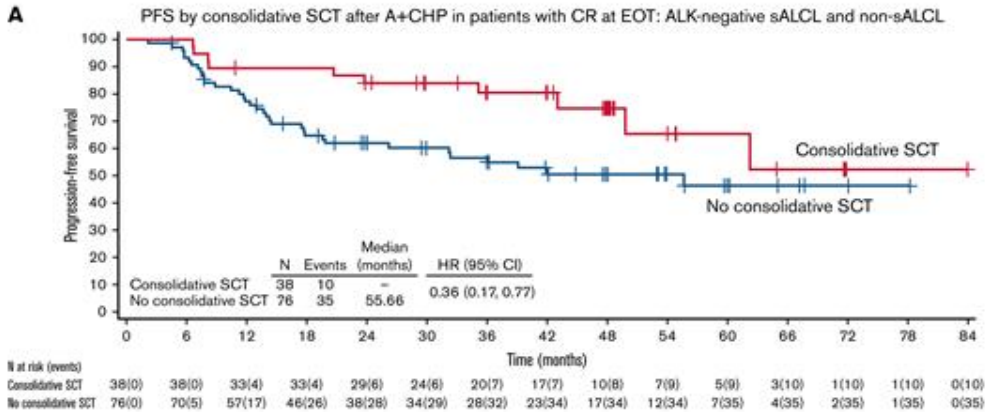


Fossard G, et al. Ann Oncol. 2018;29:715-23

Yes



Brink M, et al. Blood. 2022;140:1009-19



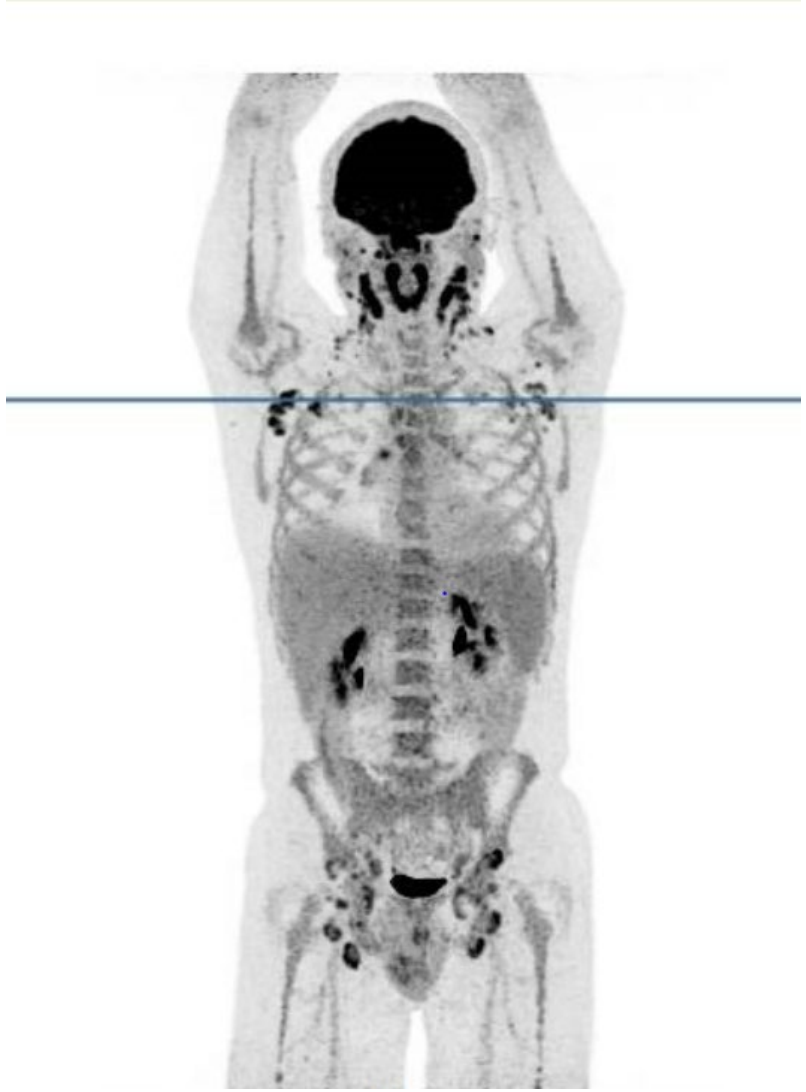
Savage KJ, et al. Blood Adv. 2022;6:5550-5

« TRANSCRIPT»

An open label, controlled, randomized multicentric international study evaluating the benefit of autologous stem cell transplantation after complete response in frontline setting patients with T cell lymphoma.

Treatment

- The patient received 4 cycles of CHOEP
  - Achieved partial response
- Patient received 2 cycles of DHAC
- Hematopoietic stem cell collection
- Progressive disease after 2 cycles of DHAC
- A new lymph node biopsy shows the location of the TFHL



DHAC, dexamethasone, cytarabine, carboplatin.

Question 4: Which course of action do you recommend?

1. Perform autologous stem cell transplantation
2. Perform allogeneic stem cell transplantation
3. Include the patient in a clinical trial, if available
4. Propose 2 additional cycles of DHAC
5. Palliative care, given the poor prognosis of the refractory disease

Question 4: Which course of action do you recommend?

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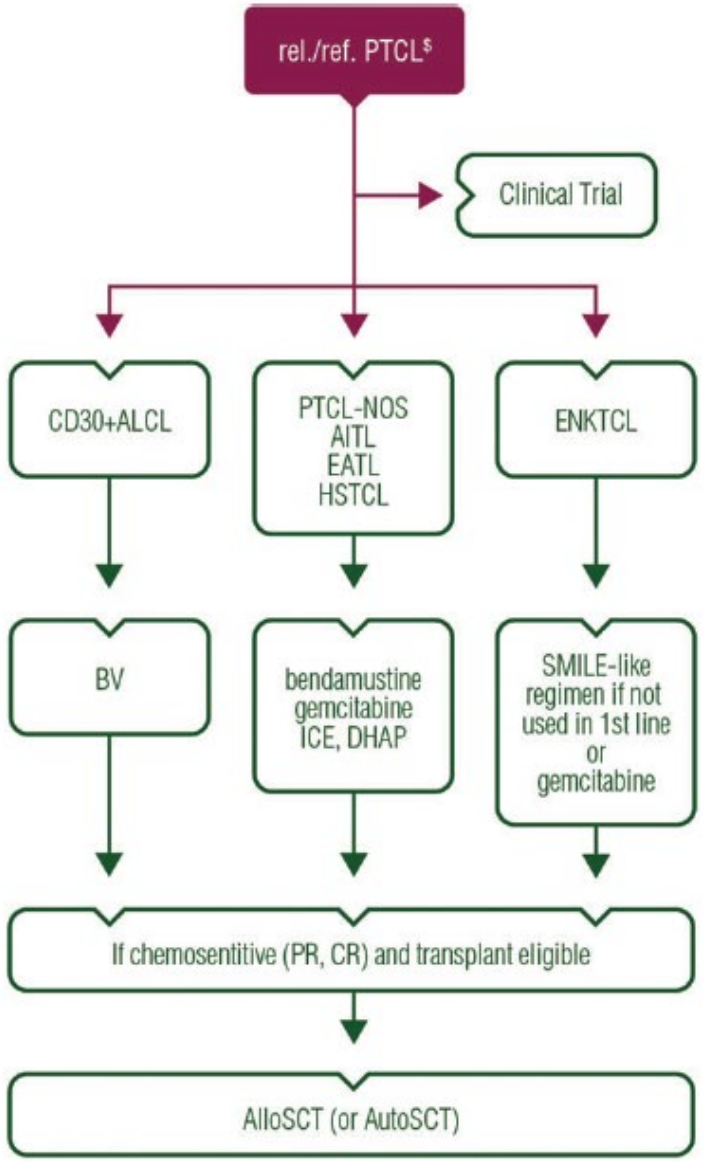
ESMO guidelines[1]

allogeneic stem-cell transplantation (alloSCT). A proposed treatment algorithm is summarised in Figure 1B. For relapsed/refractory nodal PTCL other than ALCL, inclusion into clinical trials is highly encouraged. Outside clinical trials, in fit patients, combination chemotherapy regimens such as DHAP (dexamethasone, high-dose cytarabine, cisplatin) or ICE (ifosphamide, etoposide, carboplatin) can be attempted in chemosensitive patients with an available donor, aiming at alloSCT as a potentially curative modality. In unfit patients, monotherapy with gemcitabine or bendamustine are generally well-tolerated, with an ORR of approximately 50% but with modest durations of response [30, 31]. Promising new drugs are under current

UK guidelines[2]

- All PTCL cases, both untreated and relapsed/refractory, should be considered for a clinical trial wherever possible (GRADE 1B).



1. d'Amore F, et al. Ann Oncol. 2015;26 Suppl 5:v108-15.
2. Fox CP, et al. Br J Haematol. 2022;196:507-52.

Ongoing treatment

- The patient was included in the ORACLE Study, randomized in the oral azacitidine arm
  - Patient received 6 cycles of azacitidine
- PET–CT showed complete response
- Allogeneic SCT was considered

Question 5: Regarding epigenetic-targeted therapies, which of the following statements is true?

1. Azacitidine has shown efficacy only in patients harboring a *TET2* mutation
2. Romidepsin targets DNA methylation
3. Romidepsin targets histone methylation
4. Azacitidine is a DNA methyltransferase inhibitor
5. Belinotat targets DNA acetylation

Question 5: Regarding epigenetic-targeted therapies, which of the following statements is true?

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Question 6: Which of the following is the best course of action regarding allogeneic SCT in patients with R/R PTCL?

1. Perform aSCT only in patients with complete response
2. Perform aSCT only with a matched related donor
3. Perform aSCT only with bone marrow cells
4. Perform aSCT only in a fit patient
5. Perform aSCT only in patients who have undergone myeloablative conditioning

*aSCT, allogeneic SCT

R/R, relapsed/refractory.

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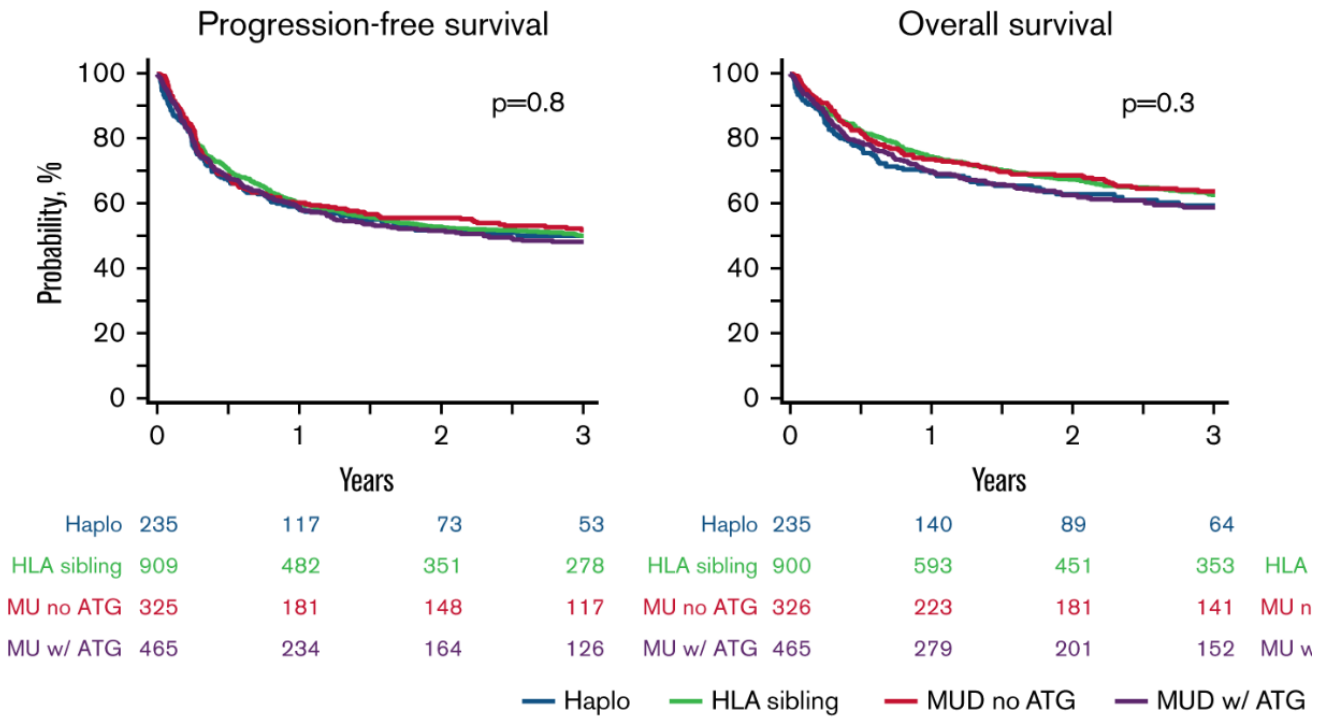
Donor type does not affect outcome



		OS	PFS
At 1 y	CR	79 (76-82)	68 (65-71)
	Partial remission	70 (66-74)	55 (51-59)
	Resistant/untreated	61 (55-65)	45 (39-50)
	P	<.0001	<.0001
At 3 y	CR	68 (65-71)	57 (53-60)
	Partial remission	59 (54-63)	47 (42-51)
	Resistant/untreated	49 (4455)	36 (31-41)
	P	<.0001	<0001

haplo, haploidentical; HLA, human leukocyte antigen; MUD, matched unrelated donor; OS, overall survival; PFS, progression free survival; y, year(s).

Hamadani M, et al. Blood Adv. 2022;6:920-30.

Donor type does not affect outcome

Source of stem cells	HR	*P* value
BM	1.00	0.022
Cord blood	1.44 (0.76–2.73)	
PBSC	0.69 (0.41–1.14)	

BM, bone marrow; PBSC, peripheral blood stem cell.
Mamez AC, et al. J Hematol Oncol. 2020;13:56.

Ongoing treatment

- Unfortunately, the patient progressed before allogeneic SCT was performed
- Patient was included in a second clinical trial:
  - Patient reached partial response after 4 cycles of the experimental drug
  - Received allogeneic SCT with a matched unrelated donor
- Patient is in sustained complete response after 3 years, with 100% donor chimerism

References

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