EUROPEAN HEMATOLOGY ASSOCIATION

EHA-TSH Hematology Tutorial

Peripheral T cell Lymphoma, NOS case
Session: How I treat PTCL NOS patients
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Ankara, Türkiye
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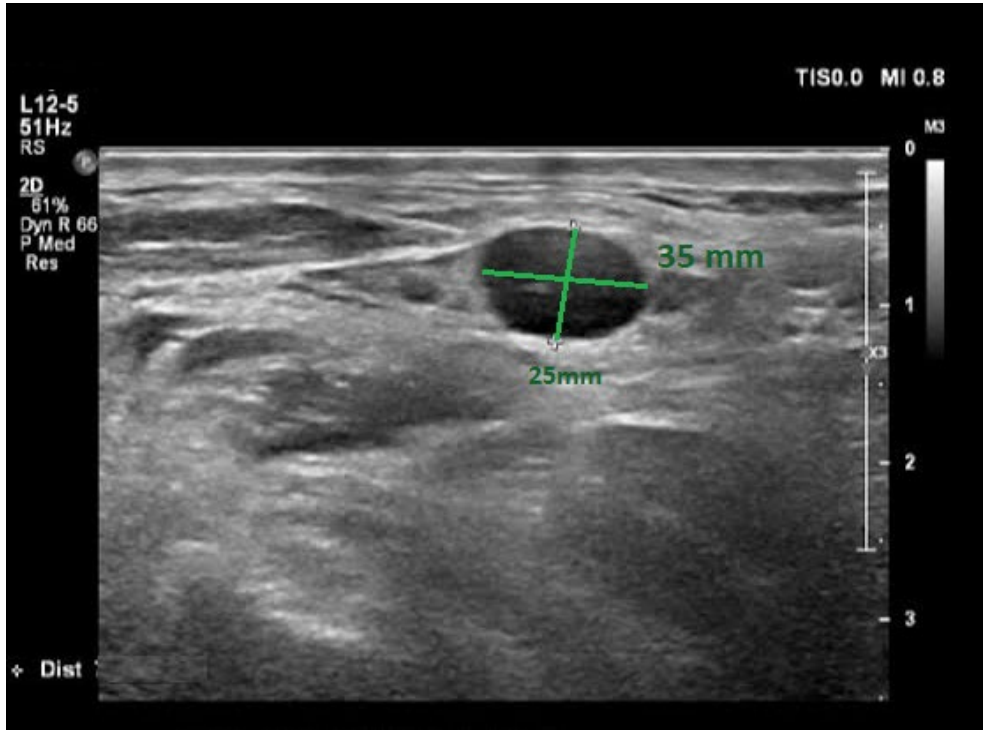
Disclosure

- Turkish Society of Hematology (registration)

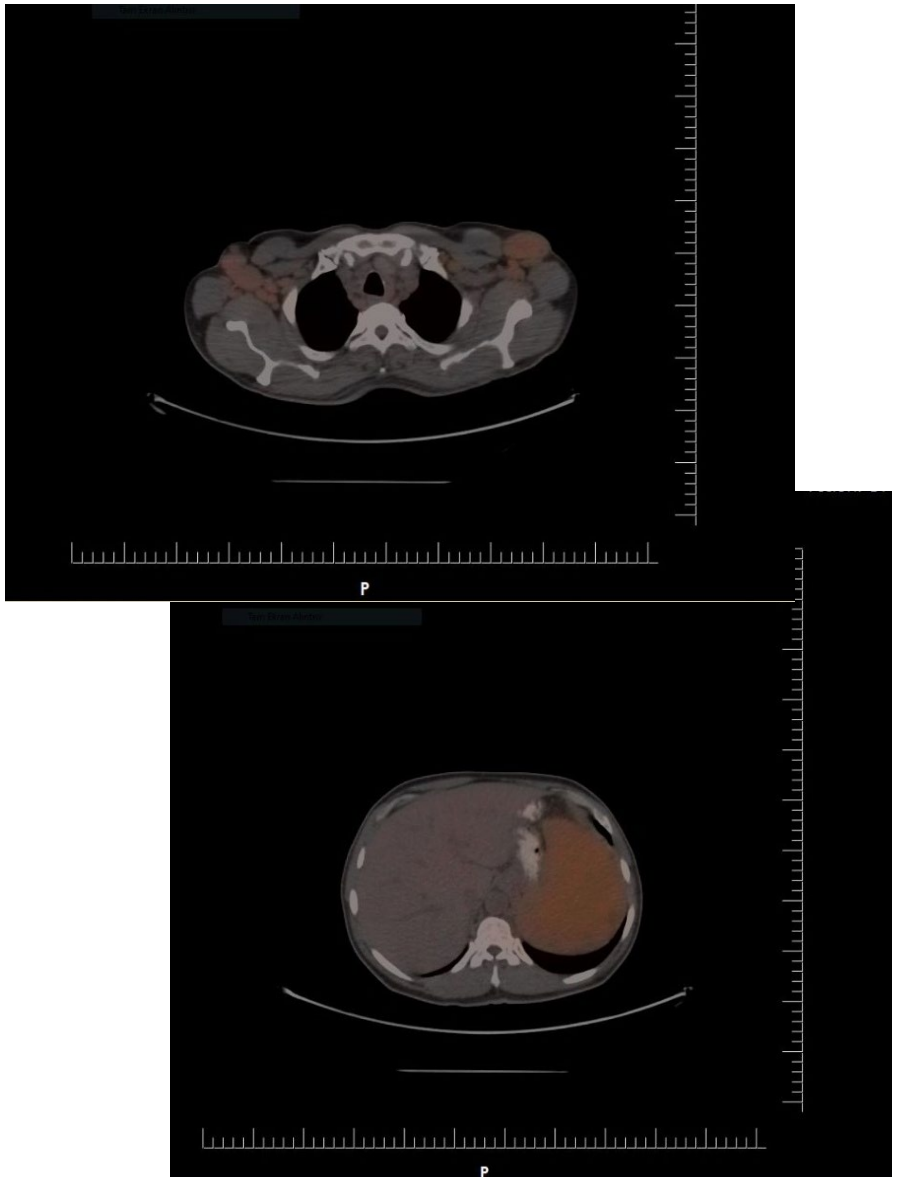
Clinical history

- A 66-year-old woman was admitted for lumps in both inguinal folds (2021)
- Her blood count on admission was normal except for mild anemia (Hb: 110 g/ L), no B symptoms were present



Imaging

- PET/CT revealed no cervical lymphanopathy but showed axillary, interpectoral hypermetabolic adenopathies largest of which was 3.5 x 2.5 cm. Also, abdominopelvic sections showed masses largest of which measured approximately 4.5 x 4 cm in dimension with SUVmax measuring up to 14.1.
- Splenomegaly and splenic involvement (+)



Clinical history

- Histopathological examination of the inguinal mass was consistent with peripheral T cell lymhpoma, NOS:
- Diffuse infiltrate of medium-sized lymphoid cells with irregular and hyperchromatic nuclei, and large lymphoid cells with irregular and vesicular nuclei with prominent nucleoli. These atypical lymphocytes had diffuse CD3 and multifocal CD4, CD8, PD-1 and CD278 expression
  - EBV-encoded RNAs in situ hybridization (EBER) was negative
  - Ki proliferation index was 40- 50 %
  - with a 2 % CD30 expression
- Bone marrow biopsy was negative for PTCL involvement

- LDH was elevated by 2 x upper limit
- ECOG performance status: 2
- IPI score: 4- high risk (expected 5-y OS: 22 %)
  - > 60
  - ECOG> 1
  - LDH elevated
  - Stage III- IV

Clinical history

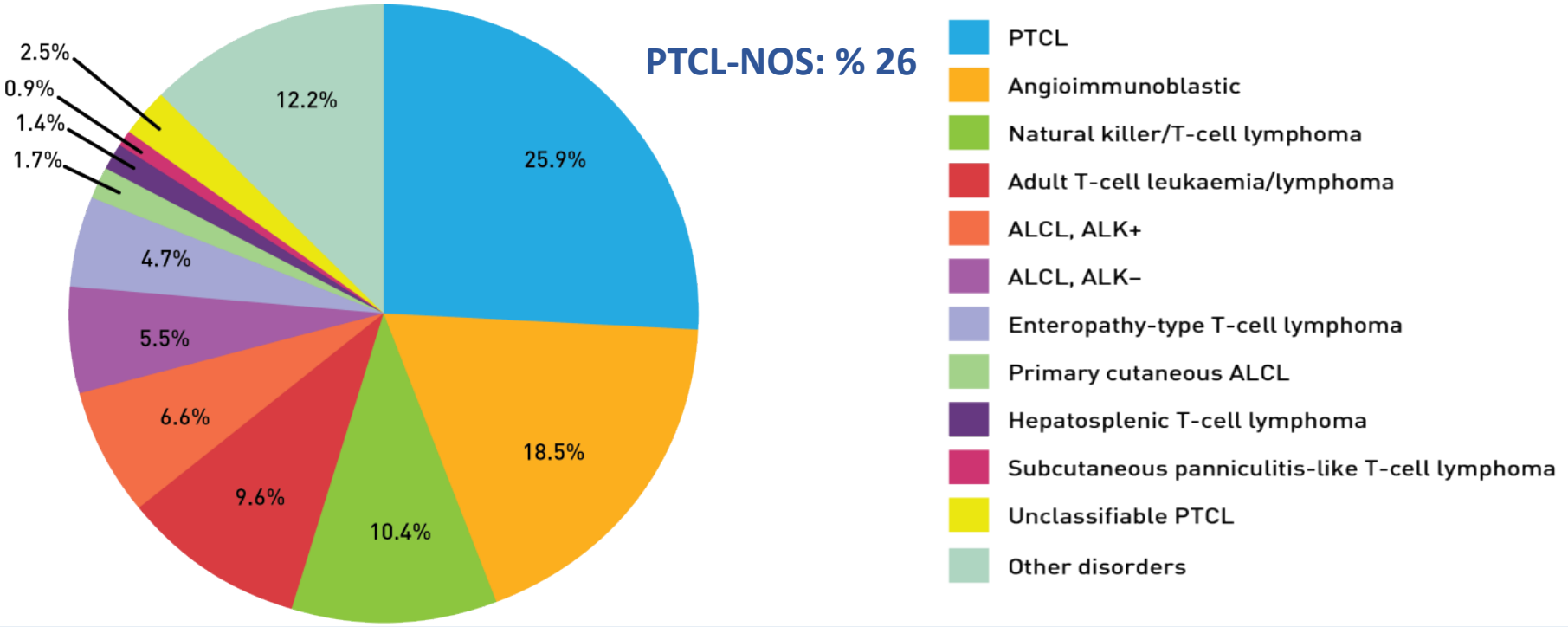
- CHOP14 chemotherapy was introduced
- Then CHOP21 due to intolerance
- After 3 courses, PET/ CT improved greatly:
- Few abdominal adenopathies largest of which is in about 1.3 cm in diameter (Deauville score: 1). Bone marrow expresses minimally increased diffuse FDG uptake –secondary to chemotherapy-, SUVmax measuring up to 2.4

Clinical history

- By the end of the 4th cycle, 8.04 x 10^6/ kg (divided in two) autologous stem cells were collected via G-CSF
- 6 courses completed and the end of treatment PET/ CT was consistent with CR
- As soon as CR1 was achieved, the patient underwent consolidative ASCT
- Still in CR

Discussion

- Peripheral T cell lymphomas constitute 10- 15 % of all lymphomas
- There are more than 30 subtypes



Vose J, et al. J Clin Oncol 2008;26:4124–30

Discussion

- About 90 % have cytogenetic abnormality:
  - t(7; 14)
  - t(11;14)
  - İnv(14), t(14;14)
  - +7q/ 8q/ 17q/ 22q
  - -4q/ 5q/ 6q/ 9p/ 10q/ 12q/ 13q
- None of them are pathognomonic!
- TCR transclocations also frequent

Vega F, Modern Pathology, 2022

- PTCL- NOS is a heterogeneous disease
- Molecular studies defined at least 2 subtypes:
  - GATA3 (poorer prognosis)
  - TBX1
- Patients presenting with high IPI, advanced stage (III-IV) or elderly respond poorly with a poor outcome

Discussion

- Primary tx: many centers use CHOP and then consolidate with an autologous transplant in first remission
- BV-CHP could be used for any PTCL that expresses CD30
- Any less intense treatment is inferior to CHOPlike regimens
- Median time to progression is 6.7 months

  Mak V, et al. *J Clin Oncol.* 2013;31(16):1970-1976. 2. Lunning M, et al. *J Clin Oncol*. 2013;31(16):1922-1927
- 5y survival is about 30 %

Discussion

- Should we still add etoposide to CHOP?

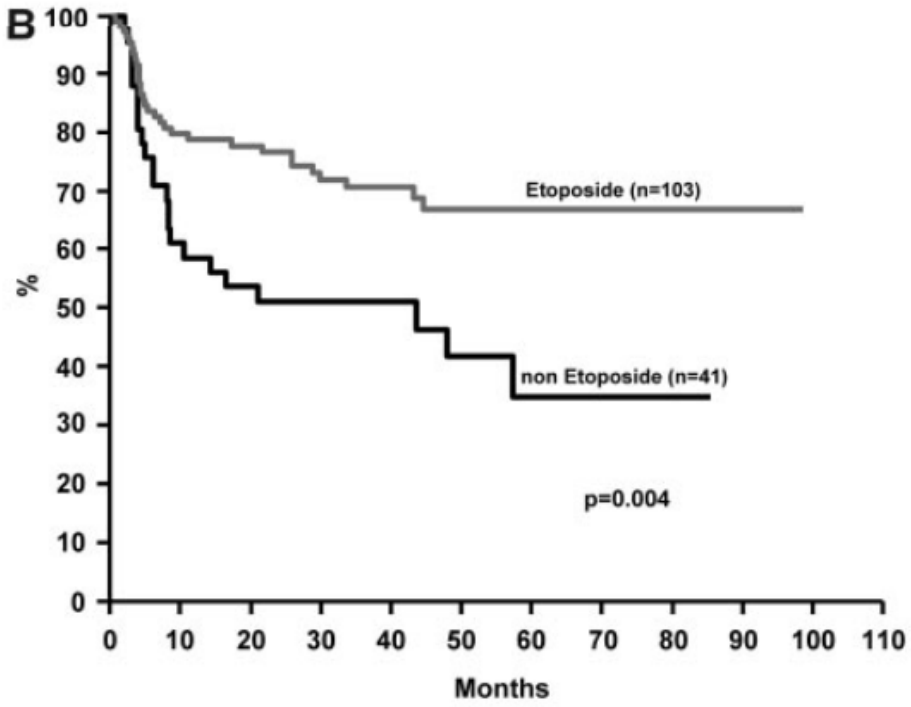


Fig 1: EFS for all T cell lymphomas

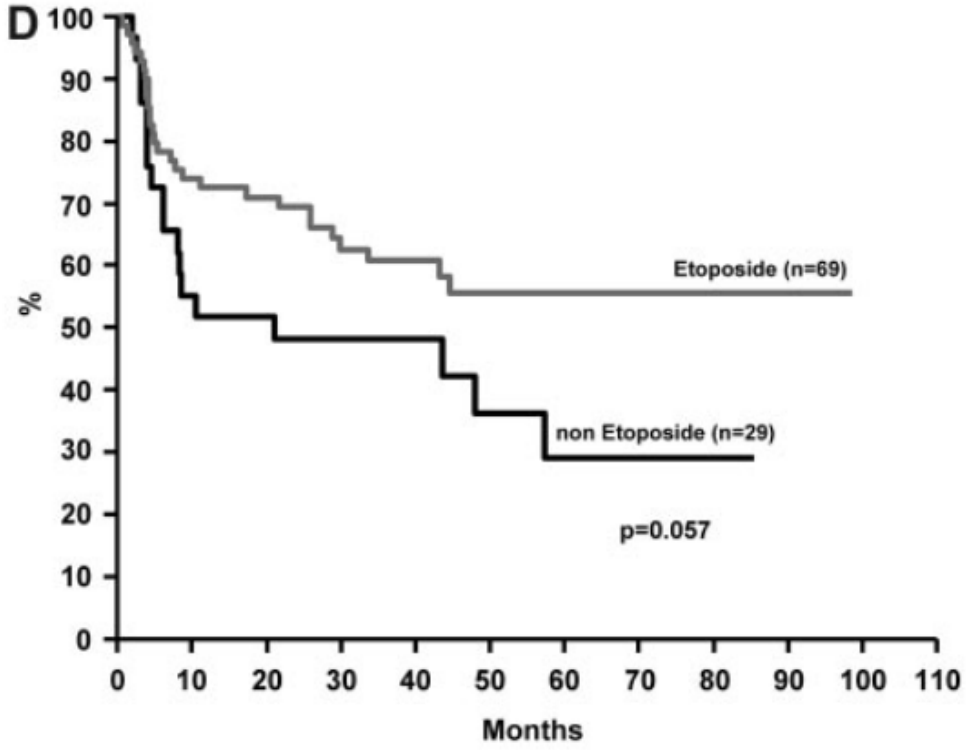


Fig 2: EFS for major PTCL subtypes (PTCL-NOS, AITL, ALK-/ ALCL)

Scmitz et al, Blood, 2010

CHOP vs CHOEP

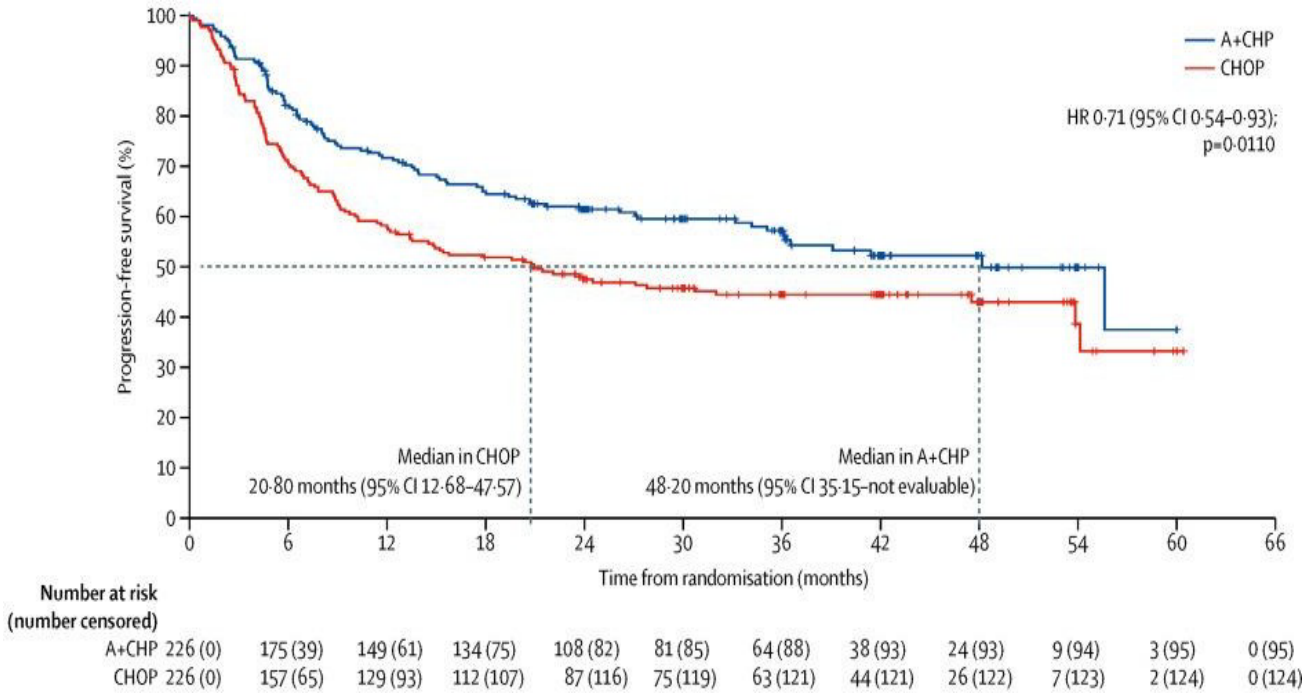
- Etoposide is not easy to tolerate
  - Sepsis, heavy myelosupression etc
- The EFS advantage does not translate to OS
- Younger/ fit patients with normal LDH may benefit from it
- No advantage for patiens > 60 y
- Older patients may do better with CHOP instead

Discussion: ECHELON- II

- Double-blind
- Randomized
- Phase III
- CD 30 expression > % 10
- BV- CHP vs CHOP, Q3E for 6- 8 cycles
- Primary endpoint: PFS
- Better PFS, better OS
- Comparable toxicity
- Fast FDA approval

Disease Diagnosis, n (%)	BV+CHP (n = 226)	CHOP (n = 226)
sALCL	162 (72)	154 (68)
ALK+	49 (22)	49 (22)
ALK-	113 (50)	105 (46)
PTHL-NOS	29 (13)	43 (19)
AITL	30 (13)	24 (11)
ATLL	4 (2)	3 (1)
EATL	1 (0)	2 (1)

Horwitz et al, Lancet 2019

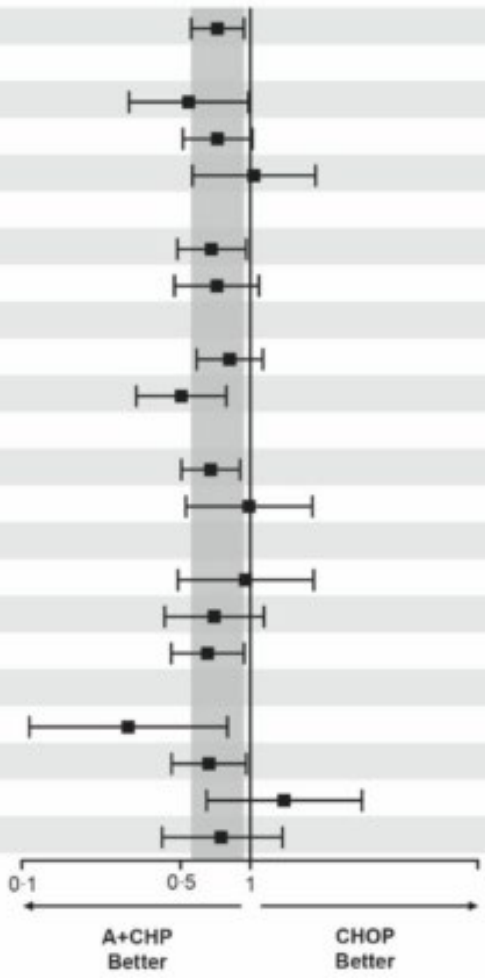


- Adding BV to CHP
- Significant PFS advantage

- HR: 0.71, p=0.011

B.

ITT Subgroups	Event/N A+CHP	Event/N CHOP	Hazard Ratio (95% CI)
Overall	95/226	124/226	0·71 (0·54, 0·93)
IPI Score			
0–1	18/52	27/48	0·53 (0·29, 0·97)
2–3	56/141	77/145	0·71 (0·50, 1·00)
4–5	21/33	20/33	1·03 (0·55, 1·92)
Age			
<65 years	54/157	75/156	0·67 (0·47, 0·95)
≥65 years	41/69	49/70	0·70 (0·46, 1·08)
Gender			
Male	59/133	80/151	0·80 (0·57, 1·13)
Female	36/93	44/75	0·49 (0·31, 0·78)
Baseline ECOG Status			
0/1	76/174	105/179	0·66 (0·49, 0·89)
2	19/51	19/47	0·98 (0·51, 1·87)
Disease Stage			
I/II	15/42	19/46	0·95 (0·48, 1·88)
III	29/57	35/67	0·69 (0·42, 1·14)
IV	51/127	70/113	0·64 (0·45, 0·93)
Disease Indication			
ALK-positive sALCL	5/49	16/49	0·29 (0·11, 0·79)
ALK-negative sALCL	50/113	60/105	0·65 (0·44, 0·95)
AITL	18/30	13/24	1·40 (0·64, 3·07)
PTCL-NOS	19/29	31/43	0·75 (0·41, 1·37)



- Younger than 60
- Females
- IPI other than 4-5
- Anaplastic large cell lymphoma subtype is OK but there is less certainty for other subtypes

RoCHOP vs CHOP

- Newly diagnosed PTCL
- Stage I- IV
- Age: 18- 80

- Neither PFS nor OS better
  - Age
  - Sex
  - IPI
  - Histology
  - Nodal subtype
- Toxicity increased (especially hematologic)

Journal of Clinical Oncology 40, no. 3 (January 20, 2022) 242-251.

Discussion: Autologous Hematopoetic Cell Transplant

- Response to first line CHOP based chemo is high, but not sustained
- PFS is usually short, many specialists consider consolidation w ASCT
- Randomized controlled studies are lacking
  - PTCL- NOS with **low/ low- intermediate** risk
  - 5 y OS with frontline ASCT: % 74 vs 49 %
  - 5 y OS with standart chemotherapy: less than 30 %

AUTOLOGOUS YES OR NO?

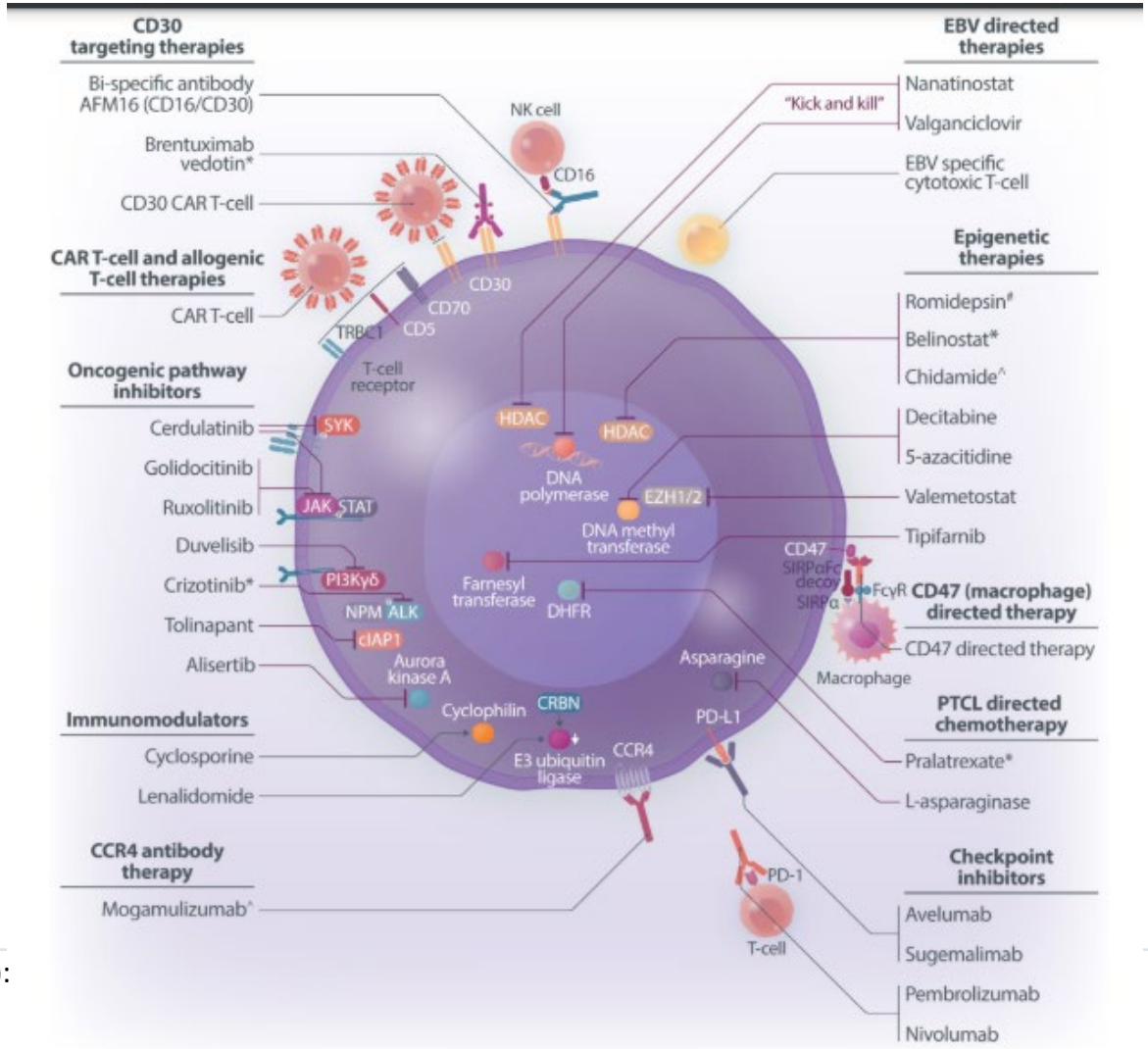
Trial	N	Pre ASCT response	Post ASCT	Go w/ ASCT?
Danish/Swedish Registry [1] Cederleuf et al. 2017	232	CR	2-y PFS %67 2-y OS %80	N
Retrospective LYSA [2] Fossard et al 2018	269	CR/PR	5-y PFS %45 5-y OS %60	N
COMPLETE study [3] **Prospective** Park et al 2019	119 (Nodal PTCL)	CR	2 y OS %87.6 (vs <%70.2) (p = .06)	N
Retrospective [4] Garcia-Sancho et al, 2022	174	CR	**5-y PFS %63** **(vs 49%) (p=0.04)**	**Y**
Retrospective Registry [5] Brink et al 2022	219 (Nodal PTCL)	CR/PR	**5-y OS %78** **(vs %45) (p=0.35)**	**Y**
Prospective [6] Savage et al (E2 subgroup)	114 (CHP-BV) 97 (CHOP)	CR	**5-y PFS %63 (vs %46)** 5-y PFS %49 (vs %51)	**Y** N

- Young, fit patient
- High risk disease
- Chemosensitivity

- ASCT

Discussion

- **Figure: Systemic agents approved, previously studied, or under investigation in peripheral T-cell lymphomas/mature T/NKlymphomas.** *Approved in the USA; brentuximab vedotin (BV) is globally approved in relapsed/refractory (R/R) anaplastic large cell lymphoma (ALCL) and for front-line treatment in CD30+ PTCL; BV-CHP (BV, cyclophosphamide, doxorubicin, prednisolone) in Europe approved in ALCL only. #Romidepsin was previously approved in the USA/Canada but withdrawn following report of the negative findings of the phase III, RO-CHOP (romidepsin, cyclophosphamide, doxorubicin, vincristine, predisone) versus CHOP study; pralatrexate is not approved in Europe. ^Approved outside the USA, mogamulizumab is approved in Japan only for CCR4+ R/R PTCL (and adult T-cell leukemia/lymphoma [positive for human T-lymphotropic virus 1]); chidamide is approved in China only for R/R PTCL.



Kerry J. Savage, Laurence de Leval, Haematologica, Vol. 108 No. 12 (2023): December, 2023 https://doi.org/10.3324/haematol.2023.282719

Current First Line Treatment of PTCL-NOS

- CHOP based chemo
- Add BV if CD30 > 10 %
- If CR1 achieved, and transplant eligible consolidate with ASCT
- If CR1 not reached → R/R treatment
- If CR reached but not transplant eligible → clinical trial or close observation

Thanks for your attention!