

**ESMO PRECEPTORSHIP  
ON LYMPHOMA**

**27-28 NOVEMBER 2015  
LUGANO, SWITZERLAND**

# Systemic T-cell lymphomas

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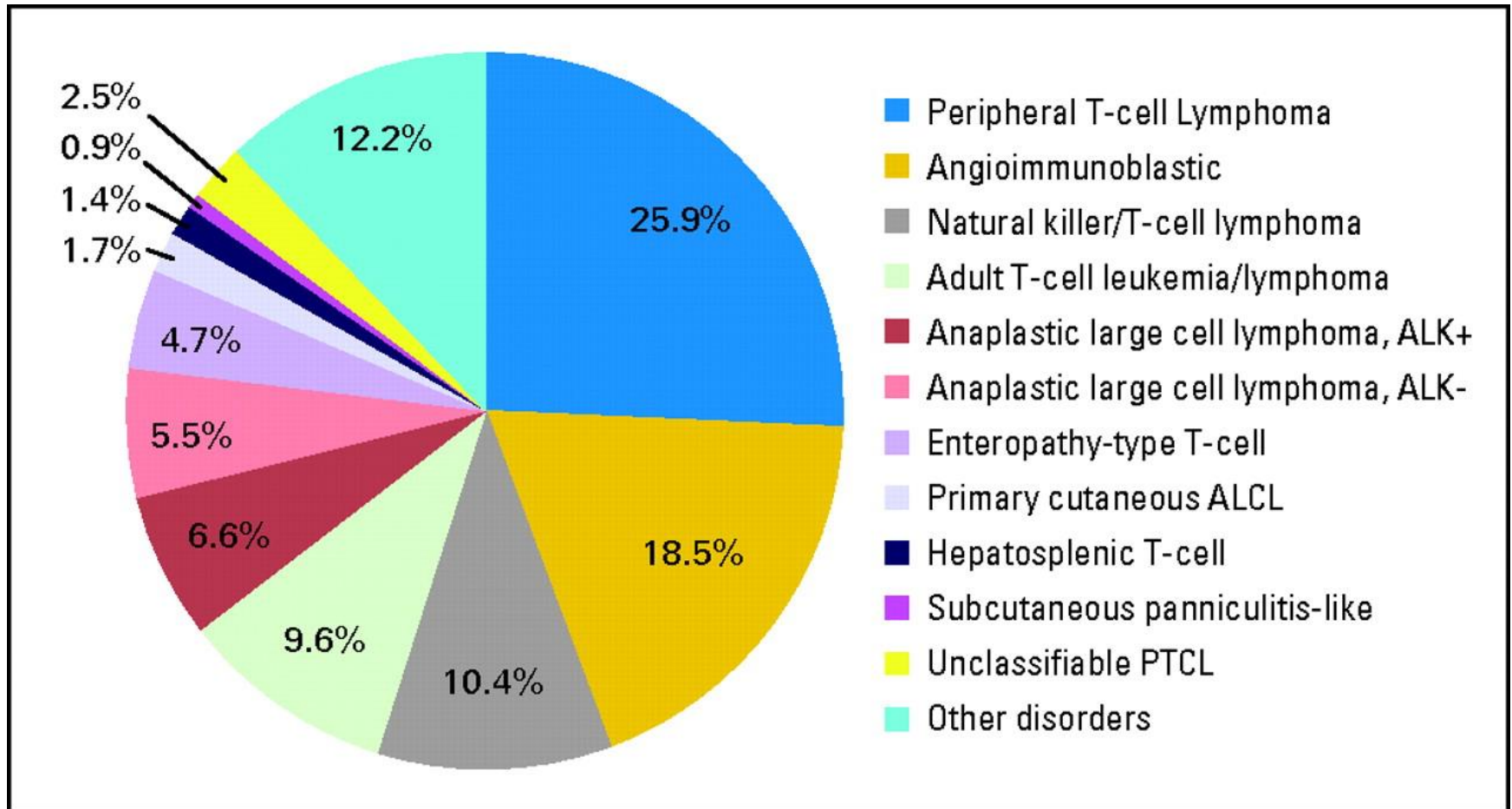
# Epidemiology

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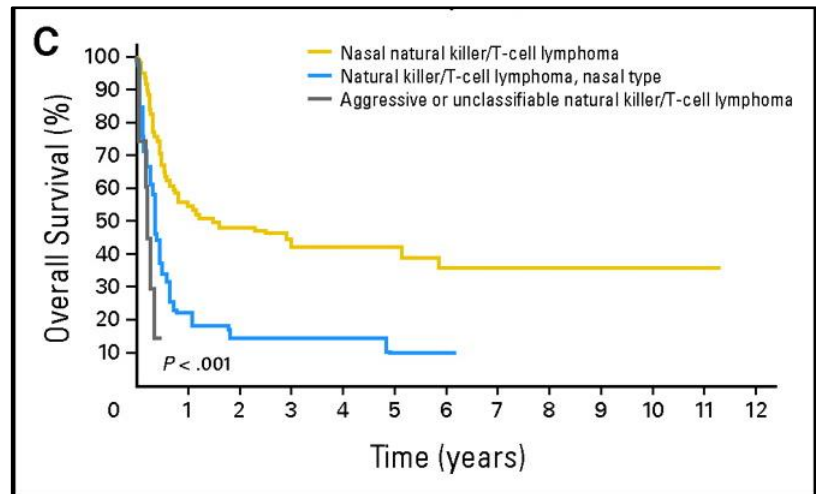
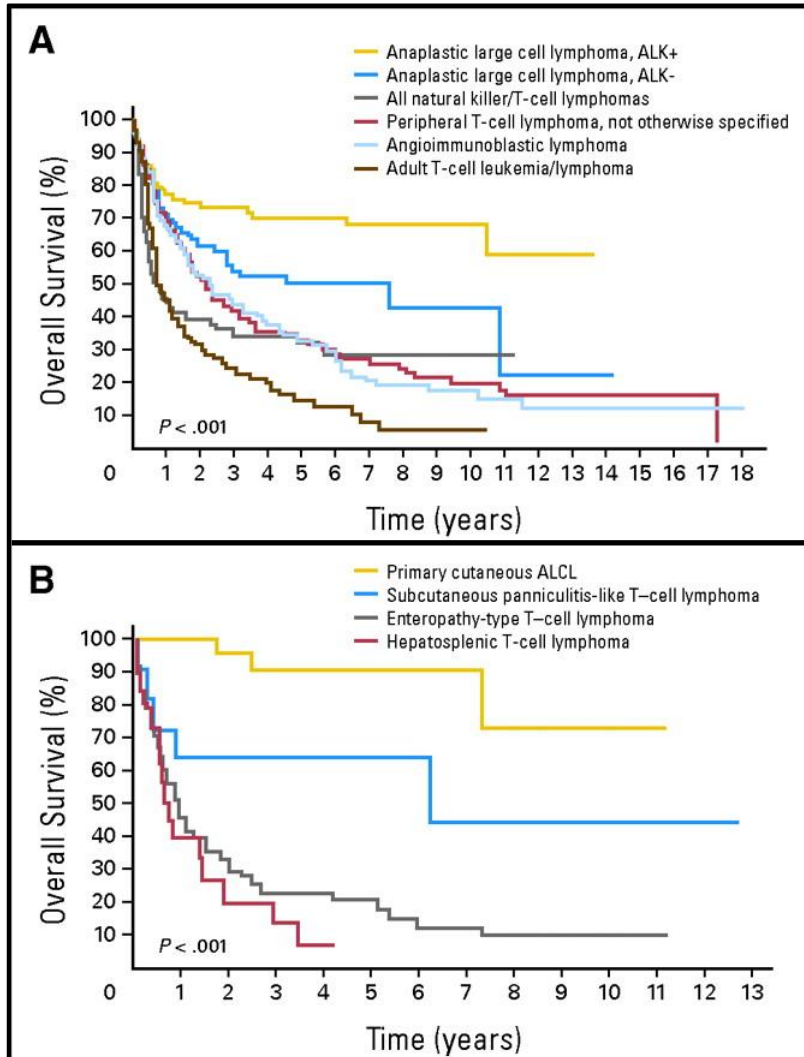
- ▶ Arise from post-thymic T-cells or mature NK-cells
- ▶ 10-15% of all non-Hodgkin lymphomas
- ▶ Incidence in Europe 1-2/100,000 per year
- ▶ Nodal subtypes most frequent in Europe
- ▶ PTCL more common in Asia due to EBV-associated ENKTCL
- ▶ Occurs in all age groups
- ▶ Median age around 55 years, but varies with subtype



# T-cell lymphoma subtypes



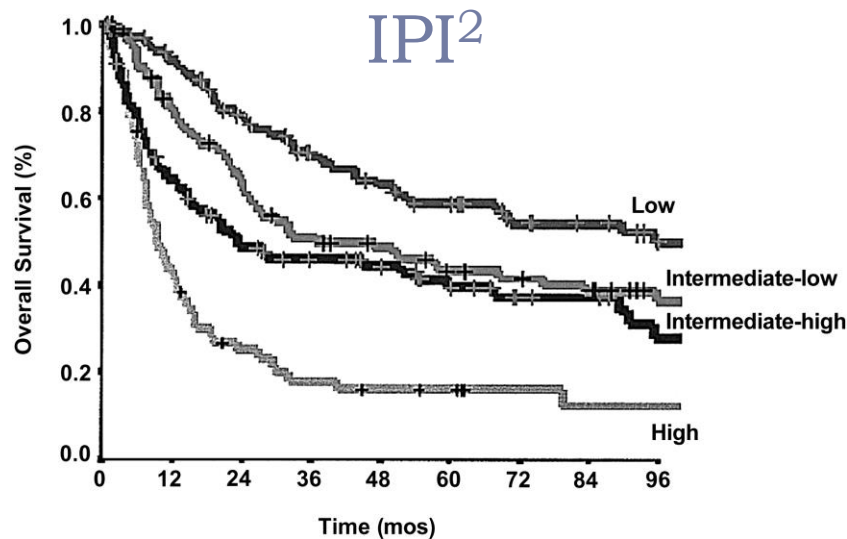
# Overall survival – common subtypes



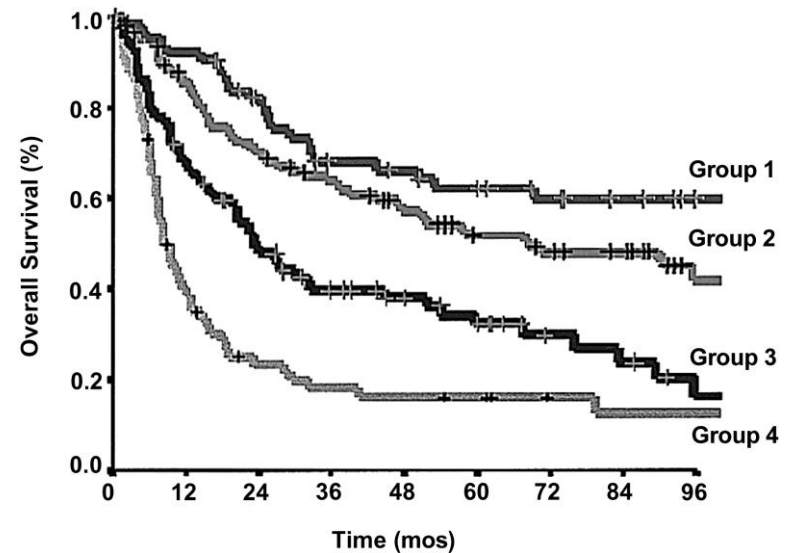
# Staging and risk stratification

## Lugano classification<sup>1</sup>

- ▶ Ann Arbor stage I-IV
- ▶ CeCT
- ▶ PET/CT (if FDG-avid)
- ▶ BMB
- ▶ EBV assessment



## PIT<sup>3</sup>



Age, PS, LDH,  
BM involvement

1. Cheson B, *et al.* JCO 2014, 32, 3059-68.
2. Shipp M, *et al.* NEJM 1993; 329, 987-94.
3. Gallamini A, *et al.* Blood 2004;103:2474-2479

# All systemic T-cell lymphoma patients should be treated within clinical trials

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- ▶ Due to the rarity of the disease and due to the many subtypes which are clinically very different:
- ▶ There are very few studies available and very little evidence from randomised trials
- ▶ For the lack of better options, CHOP is the backbone of most treatment protocols

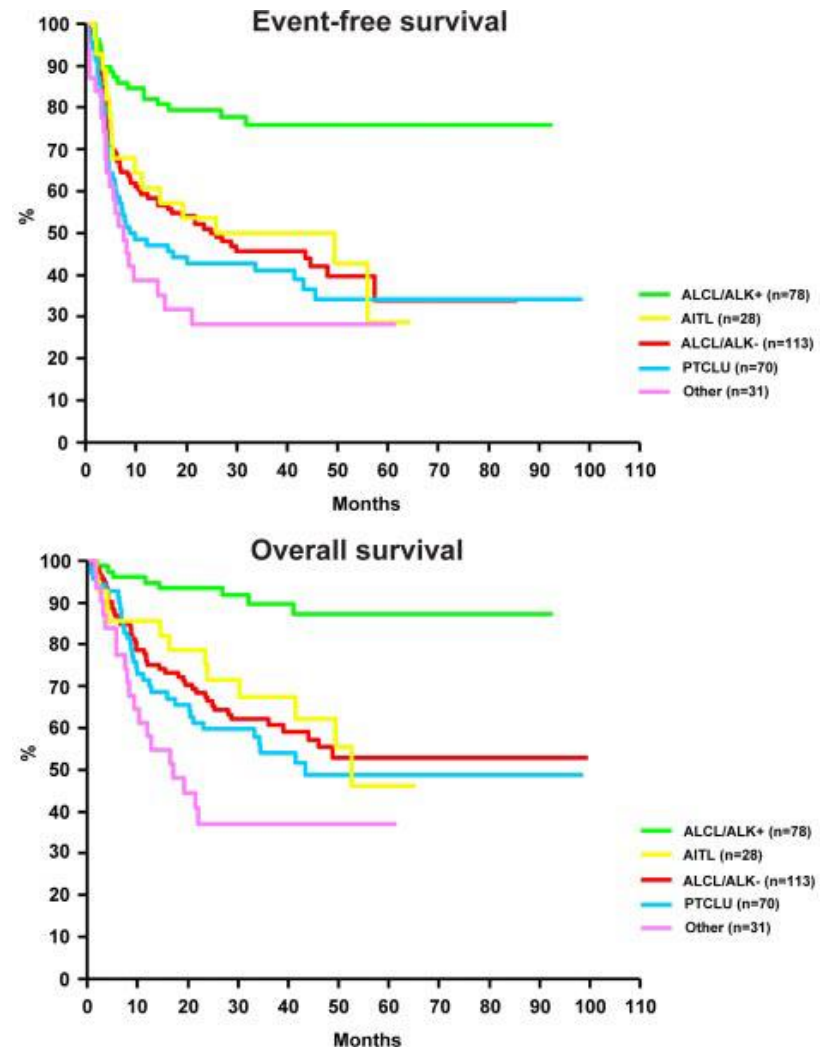


Nodal PTCL  
PTCL-NOS, AITL, ALCL ALK+, ALCL ALK-

First-line therapy

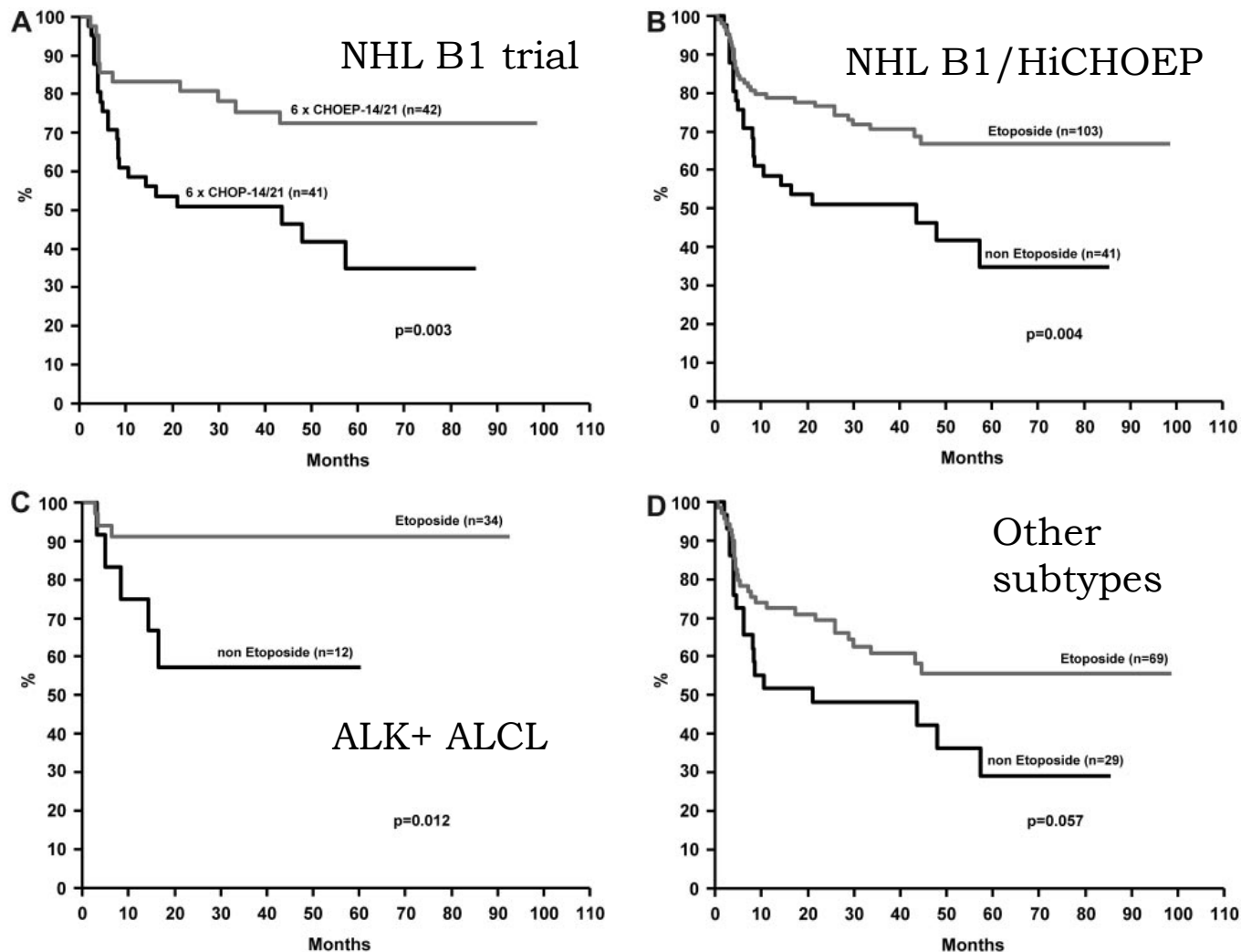
# German DSHNHL retrospective data

- ▶ 343 T-cell lymphoma patients treated in German trials 1993-2007
- ▶ Treatment was 6-8 cycles of CHOP or CHOEP
- ▶ 3-year EFS and OS were
  - ▶ 75.8% and 89.8% (ALK+ ALCL)
  - ▶ 50.0% and 67.5% (AITL)
  - ▶ 45.7% and 62.1% (ALK- ALCL)
  - ▶ 41.1% and 53.9% (PTCL-NOS)
- ▶ IPI useful in predicting outcomes
- ▶ Etoposide improved outcomes in younger patients



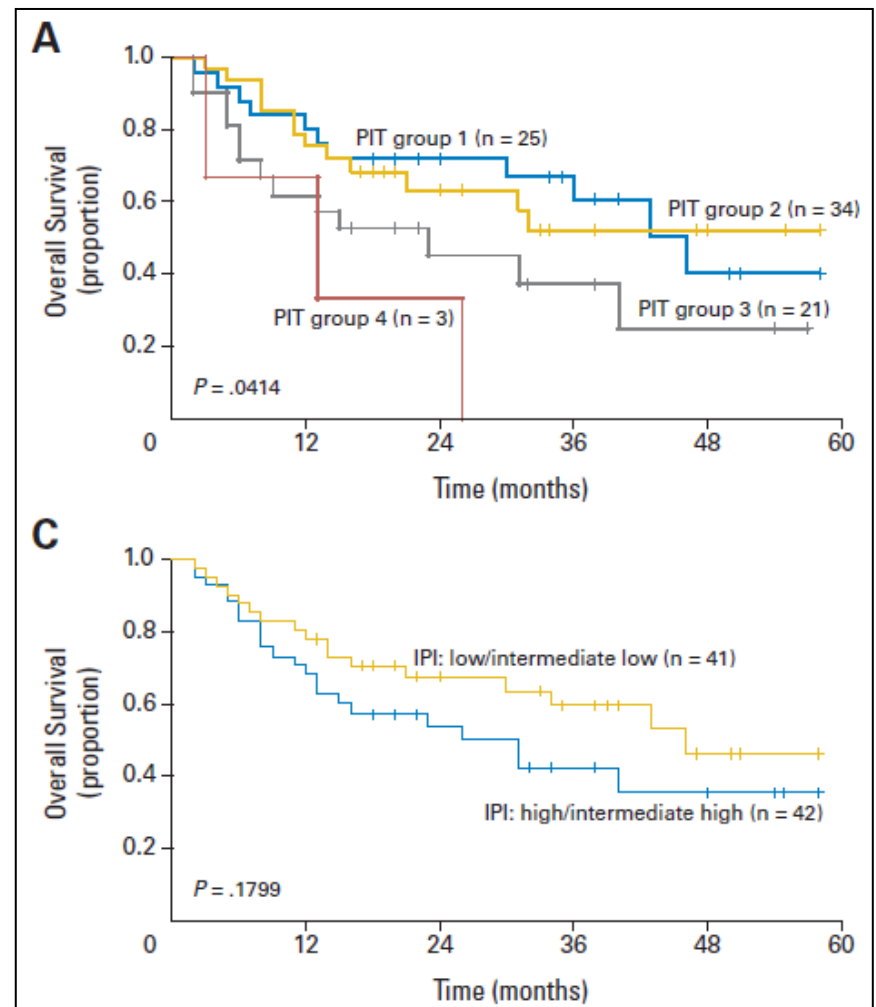
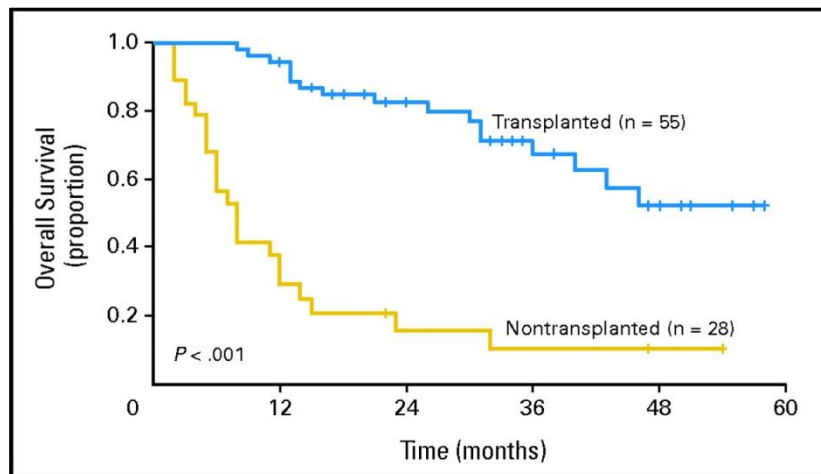


# German DSHNHL retrospective data



# Reimer et al.

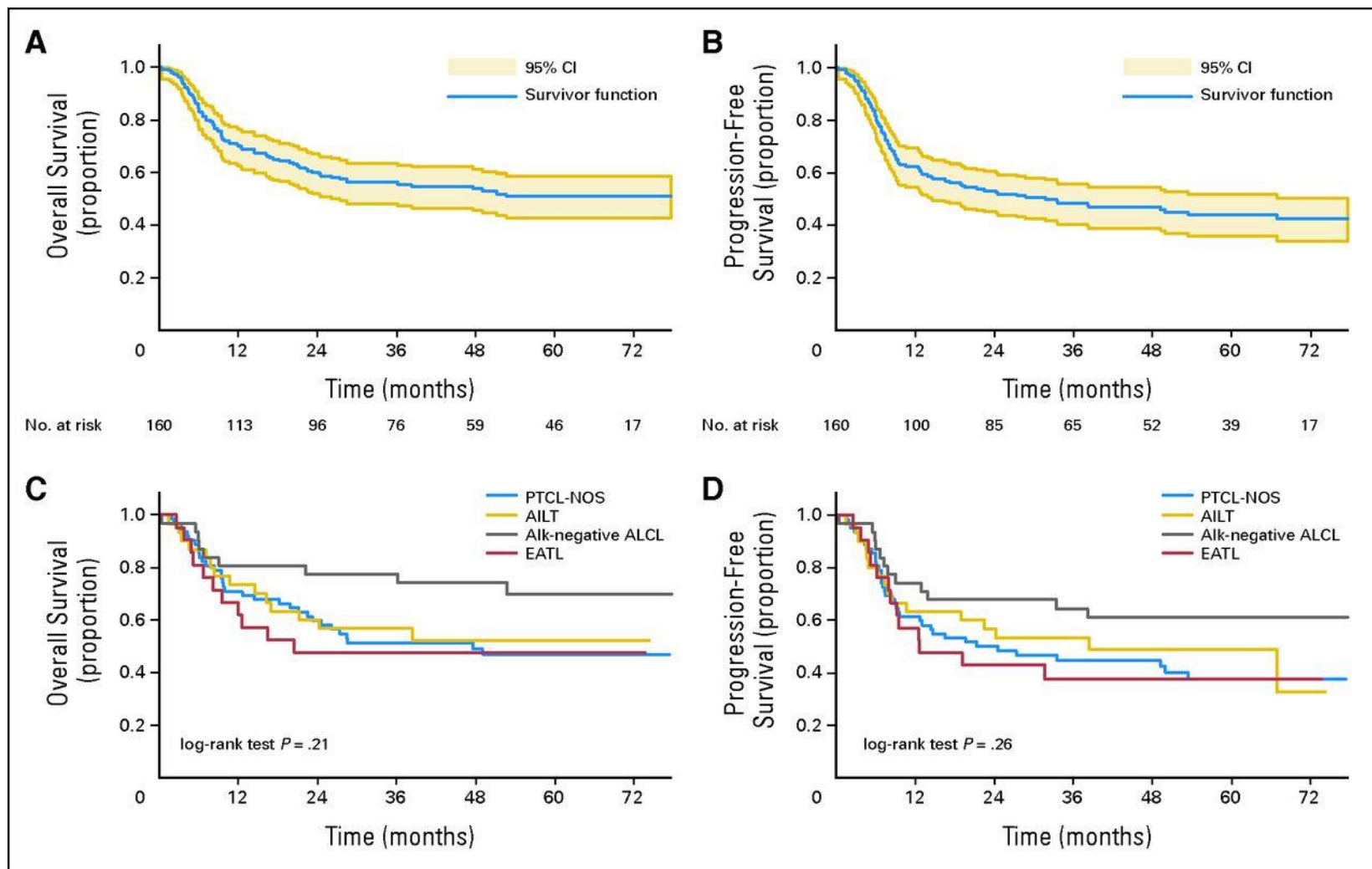
- ▶ 83 PTCL patients
  - ▶ PTCL-NOS = 32
  - ▶ AITL = 27
  - ▶ ALK- ALCL = 13
- ▶ 4-6 x CHOP
- ▶ Cy-TBI + ASCT if responsive
- ▶ ORR 66%, CR 56%



# Nordic NLG-T-01 trial

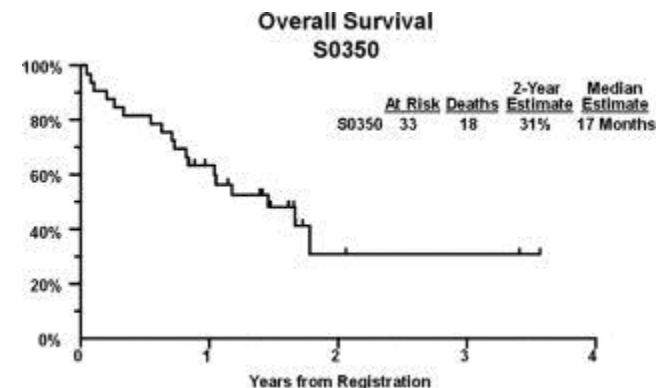
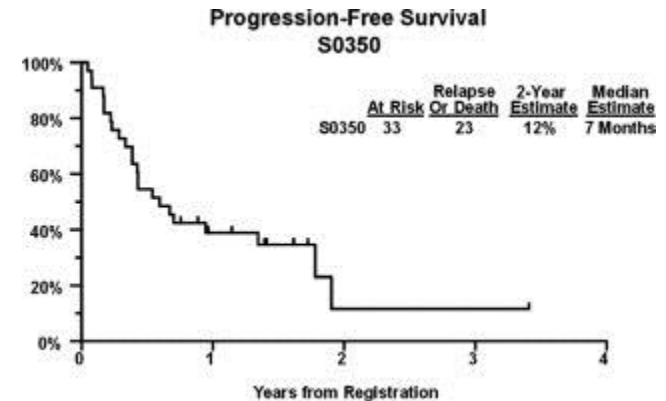
- ▶ **160 patients PTCL**
- ▶ **ALK+ ALCL excluded**
- ▶ **Age 18-67 years**  
**(median 57 years)**

- ▶ **6 x CHOEP14**
- ▶ **If CR/PR (131 pts) →**  
**HCT/ASCT (115 pts)**



# Nodal PTCL

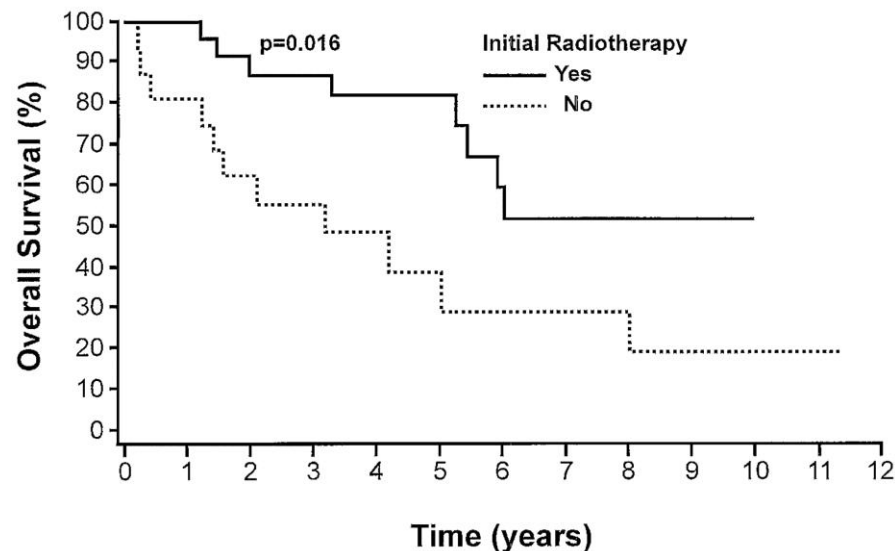
- ▶ CHOEP followed by HDC/ASCT in responding patients is an evidence-based approach with long-term disease-free survival in a substantial proportion of patients
- ▶ PEGS (cisplatin, etoposide, gemcitabine and prednisolone) gave ORR 39% and 2-year PFS 14%<sup>1</sup>
- ▶ Low-risk IPI ALK+ ALCL show favourable outcomes (5-year disease-free survival 60-80%) without HDC/ASCT<sup>2</sup>



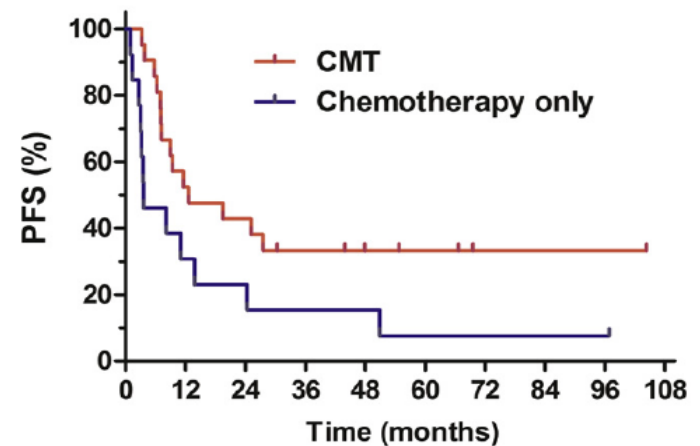
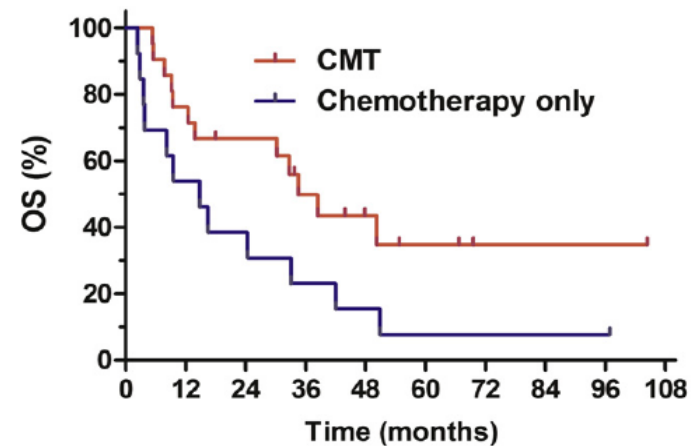
# Localised nodal PTCL

- ▶ This is a very rare condition
- ▶ Retrospective data support the use of shortened chemotherapy followed by radiotherapy:

41 patients with localised disease identified by the International PTCL project:



34 patients with stage I-II PTCL-NOS treated with CMT (21) or chemotherapy only (13)



1. Mahadevan D, et al. Cancer 2013;119:371-9.
2. Zhang XM, et al. IJROBP 2013; 85: 1051-56.

Nodal PTCL  
PTCL-NOS, AITL, ALCL ALK+, ALCL ALK-

Relapsed and refractory disease

# Relapsed/refractory nodal PTCL

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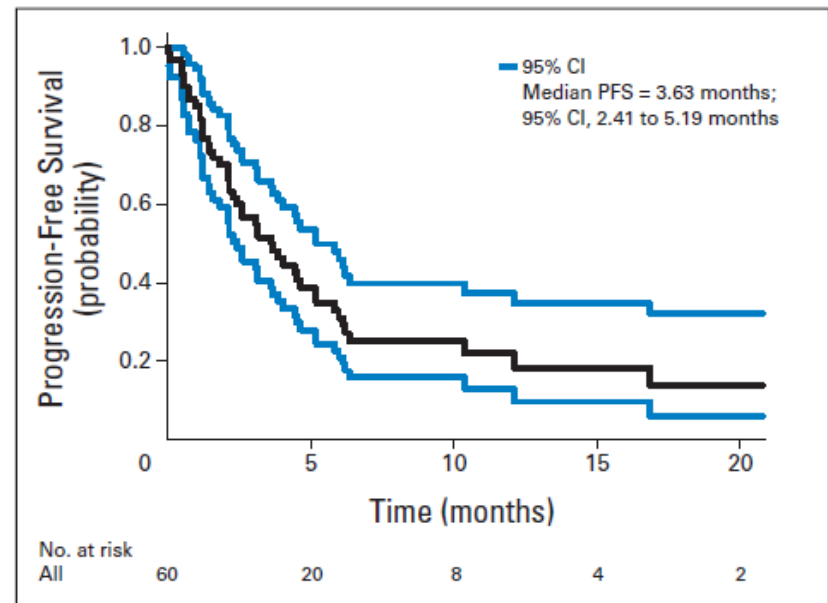
- ▶ No established standard of care
- ▶ Only one globally approved salvage treatment
  - ▶ Brentuximab vedotin for r/r ALCL
- ▶ Two drugs approved in the US for r/r PTCL
  - ▶ Romidepsin
  - ▶ Pralatrexate
- ▶ Other drugs with some single-agent activity
  - ▶ Gemcitabine
  - ▶ Bendamustine
  - ▶ Mogamulizumab
- ▶ RIC-alloSCT is a potentially curative option in patients with R/R disease who achieve remission<sup>1,2</sup>

# Single-agent Gemcitabine

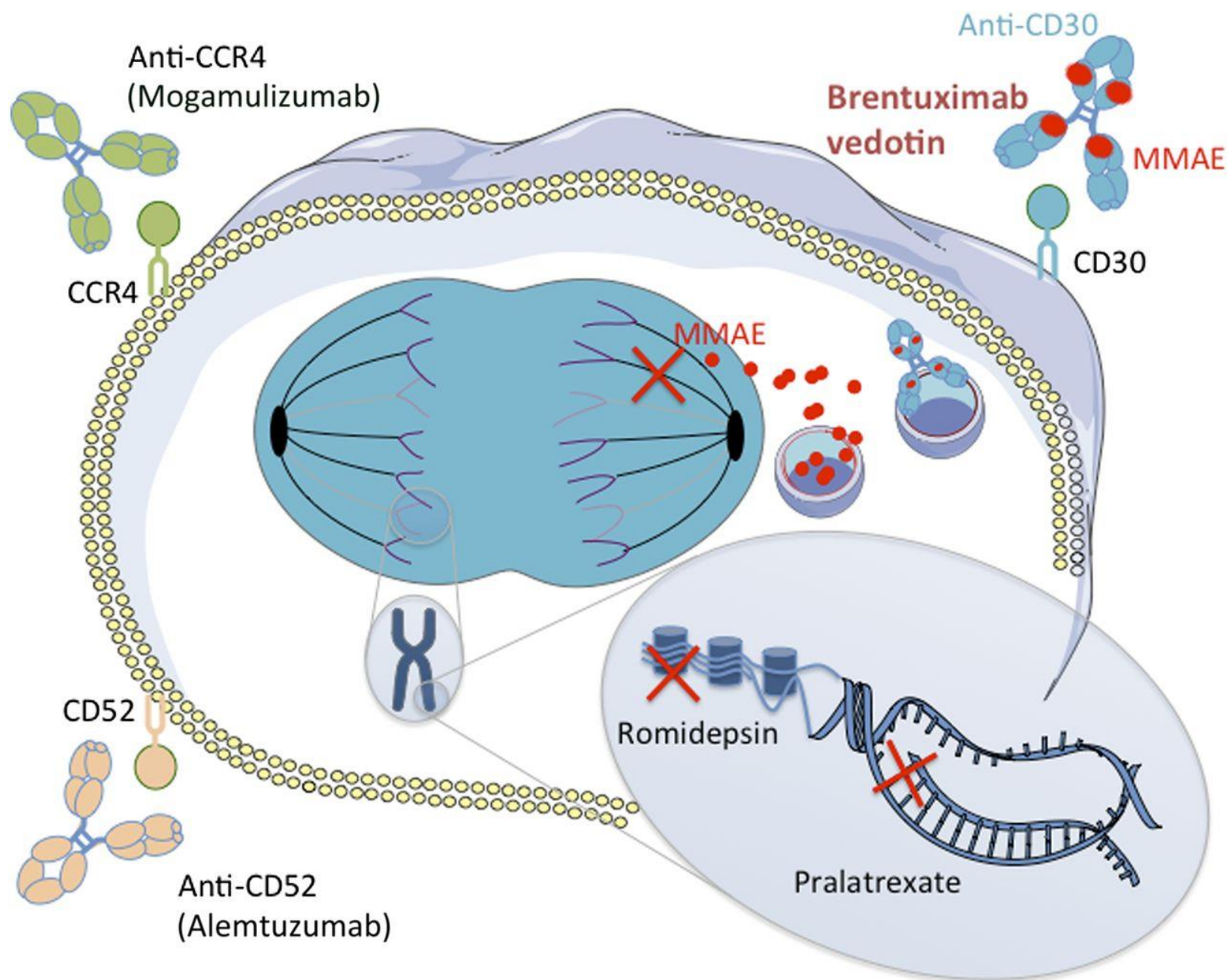
- ▶ 20 PTCL patients
- ▶ 2-8 prior treatments (median 3)
- ▶ Gemcitabine 1200 mg/m<sup>2</sup> on days 1, 8, 15 in 28-day cycles
- ▶ ORR 55%, CR 30%
- ▶ Median duration of CR 34 months (15-120 months)
- ▶ PRs were short-lived

## BENTLY trial

- ▶ Bendamustine 120 mg/m<sup>2</sup> days 1-2 in 21-day cycles
- ▶ 60 patients with r/r PTCL
  - ▶ 32 AITL, 23 PTCL-NOS
- ▶ Not heavily pretreated
  - ▶ Lines of therapy 1-3, median 1
- ▶ ORR 50%, CR 28%
- ▶ Median DoR 3.5 months!

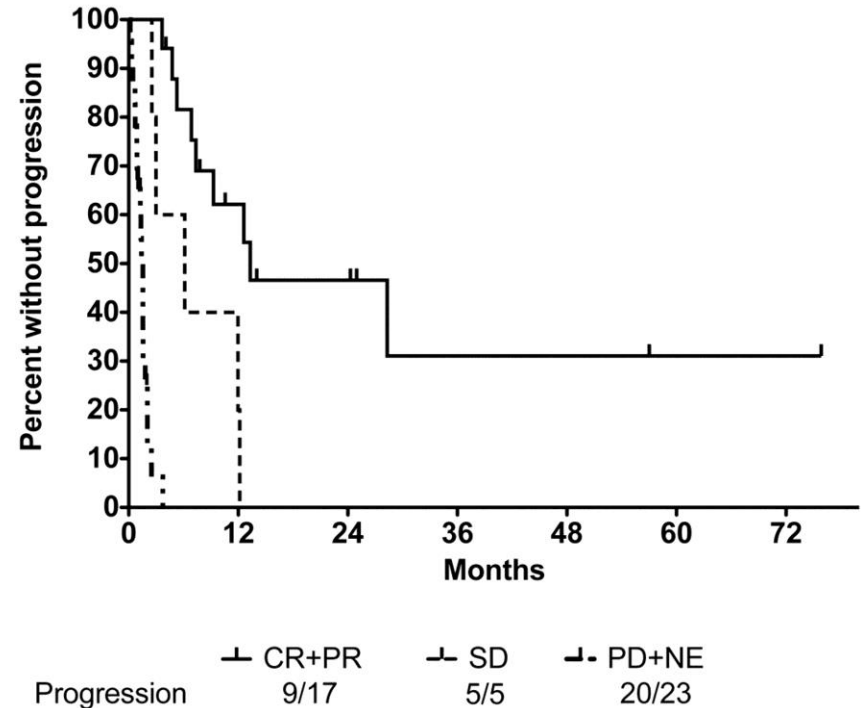






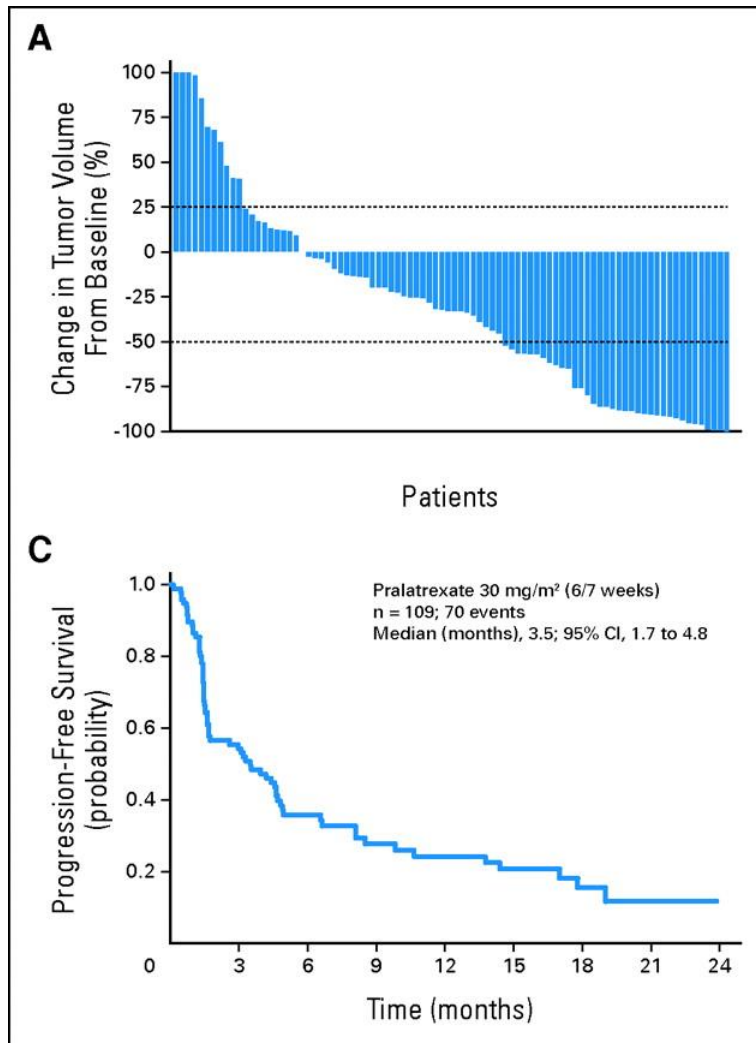
# Romidepsin phase II study

- ▶ 47 patients with r/r PTCL
  - ▶ 27 PTCL-NOS, 7 AITL
- ▶ Stages II-IV
- ▶ Median age 59 years
- ▶ 2-11 prior lines of therapy
- ▶ Administered 14 mg/m<sup>2</sup> iv. on days 1, 8 and 15 in 28-day cycles
- ▶ Treatment until progression
  - ▶ 1-57 cycles, median 3 cycles
- ▶ Most common side effects:
  - ▶ Nausea
  - ▶ Fatigue
  - ▶ Neutropenia, thrombocytopenia

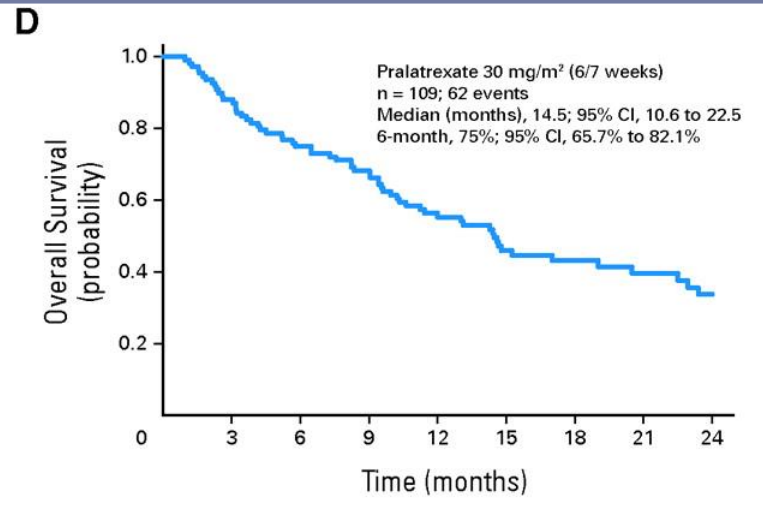


- ▶ ORR 38%, CR 18%
- ▶ Median DoR 8.9 months
- ▶ Median DoCR 29.7 months

# Pralatrexate – PROPEL phase II study

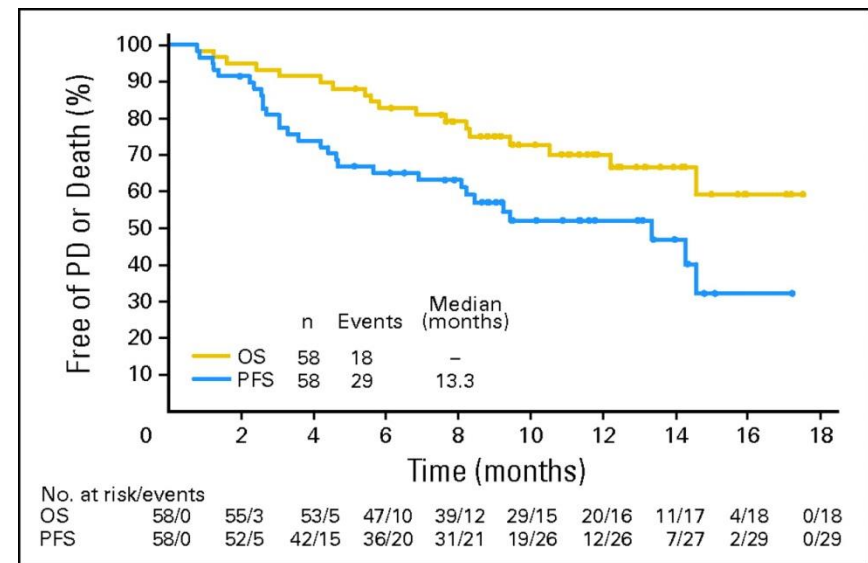
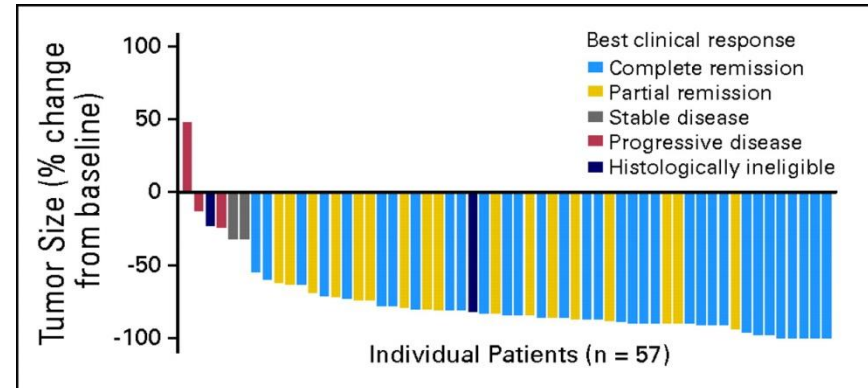


- ▶ 115 patients enrolled, 11 patients treated
  - ▶ 59 PTCL-NOS, 17 ALCL, 13 AITL
- ▶ 30 mg/m<sup>2</sup> iv. weekly for 6 weeks in 7-week cycles
- ▶ ORR 29%, CR 11%
- ▶ Median DoR 10.1 months
- ▶ Grade III-IV AEs:
  - ▶ thrombocytopenia (32%), mucositis (22%), neutropenia (22%), and anemia (18%)



# Brentuximab vedotin

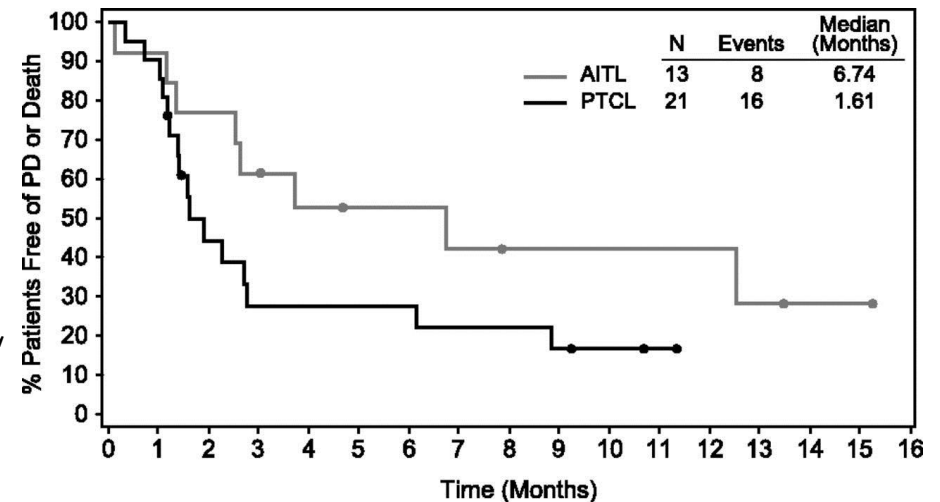
- ▶ Anti-CD30 antibody linked to MMAE
- ▶ 58 patients with heavily pretreated r/r ALCL<sup>1</sup>
- ▶ BV 1.8 mg/kg q3w
- ▶ ORR 86%, CR 58%
- ▶ Median DoR 12.6 months
- ▶ Median DoCR 13.2 months



1. Pro B, et al. JCO 2012; 30:2190-2196.  
 2. Horwitz SM, et al. Blood 2014; 123(20): 3095-3100.

- ▶ Anti-CD30 antibody linked to MMAE

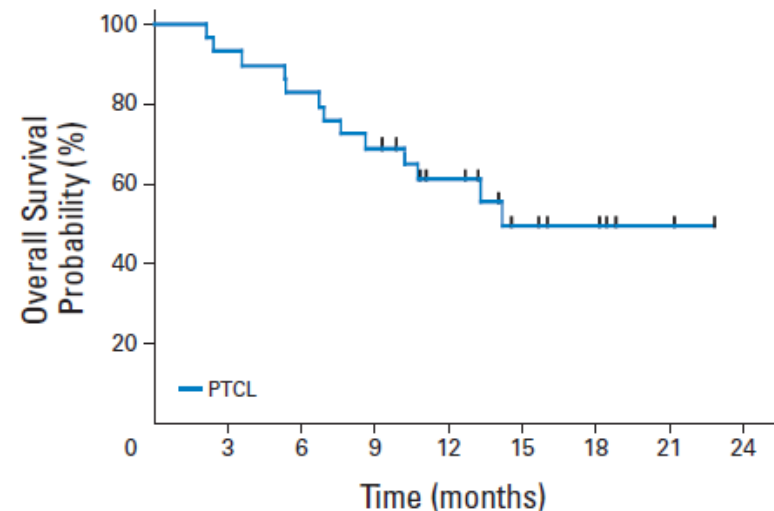
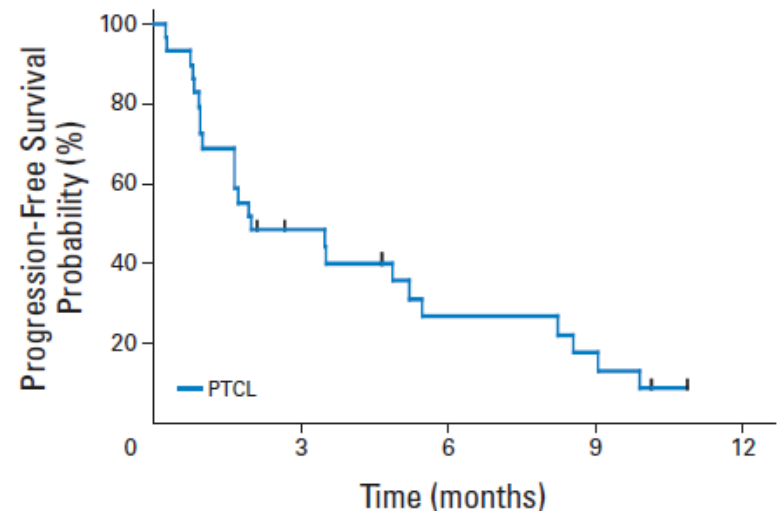
- ▶ A more recent study also showed activity in other CD30 positive sPTCL
- ▶ 35 patients: 22 PTCL & 13 AITL
- ▶ ORR 41%, CR 24%



1. Pro B, et al. JCO 2012; 30:2190-2196.
2. Horwitz SM, et al. Blood 2014; 123(20): 3095-3100.

# Mogamulizumab

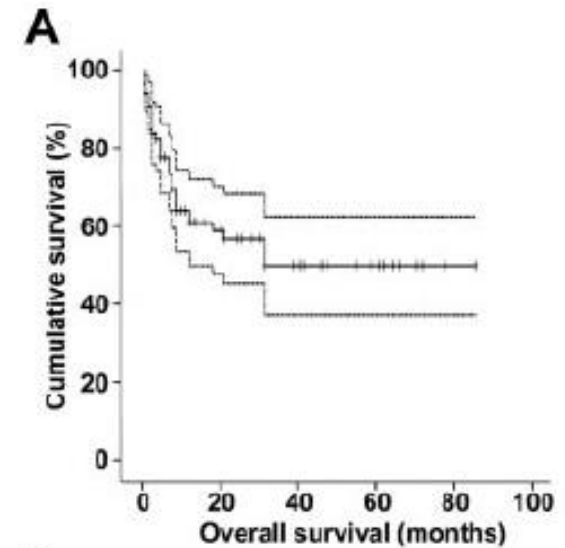
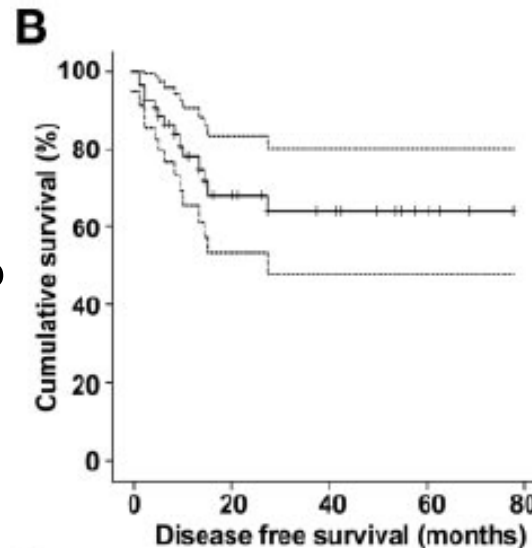
- ▶ 30% to 65% of patients with PTCL express CCR4 on the tumour cells
- ▶ Mogamulizumab is an anti-CCR4 antibody
- ▶ Like Alemtuzumab it enhances antibody-dependent cytotoxicity
- ▶ 29 PTCL
  - ▶ 19 PTCL-NOS, 12 AITL
- ▶ Heavily pretreated
  - ▶ 1-6 systemic lines, median 2)
- ▶ Mogamulizumab 1 mg/kg weekly for 8 weeks
- ▶ ORR 34%, CR 17%



# Extranodal NK/T-cell lymphoma

# NK/T cell lymphoma

- ▶ The SMILE regimen is the new standard of care
  - ▶ Dexamethasone, methotrexate, ifosfamide, L-asparaginase, etoposide
- ▶ 43 newly diagnosed and 44 relapsed patients
- ▶ 56% stage III-IV, 43% IPI 3-5
- ▶ ORR 78%
- ▶ CR 56%
- ▶ 5-year OS 50%
- ▶ 4-year DFS 64%







Thank you!