Systemic T-cell lymphomas

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Epidemiology

- 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\(^1\)
- Ann Arbor stage I-IV
- CeCT
- PET/CT (if FDG-avid)
- BMB
- EBV assessment

PIT\(^3\)

IPI\(^2\)
- Age, PS, LDH, BM involvement

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

- 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

- **NHL B1 trial**
  - 6 x CHOP-14/21 (n=42)
  - 6 x CHOP-14/21 (n=41)
  - $p=0.003$

- **NHL B1/HiCHOEP**
  - Etoposide (n=103)
  - non Etoposide (n=41)
  - $p=0.004$

- **ALK+ ALCL**
  - Etoposide (n=34)
  - non Etoposide (n=12)
  - $p=0.012$

- **Other subtypes**
  - Etoposide (n=89)
  - non Etoposide (n=29)
  - $p=0.057$

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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%\(^1\).
- Low-risk IPI ALK+ ALCL show favourable outcomes (5-year disease-free survival 60-80%) without HDC/ASCT\(^2\).

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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)

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

Relapsed and refractory disease
Relapsed/refractory nodal PTCL

- 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\(^1,2\)

Single-agent Gemcitabine

- 20 PTCL patients
- 2-8 prior treatments (median 3)
- Gemcitabine 1200 mg/m^2 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^2 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/m² 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/m2 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
- BV 1.8 mg/kg q3w
- ORR 86%, CR 58%
- Median DoR 12.6 months
- Median DoCR 13.2 months

Brentuximab vedotin

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

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

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!