Periphere T Zell Lymphome
Aktuelle Therapiestrategien und neue Ansätze

Lorenz Trümper, President, German Lymphoma Alliance e.V.,
UniversitätsKrebszentrum G-CCC, Universitätsmedizin Göttingen
AG T Zell Lymphome der GLA e.V./ ehem. DSHNHL

Gerald Wulf, Bertram Glaß, Thomas Weber, Bettina Altmann, Marita Ziepert, Markus Loeffler, Raphael Koch, Andreas Rosenwald, Norbert Schmitz, Michael Pfreundschuh
T-cell lymphoma: WHO classification

WHO 2016:

new: **follicular T-cell lymphoma (FTCL)**

new (provisional): **indolent T-cell lymphoproliferative disorder (LPD) of the GI tract and primary cutaneous acral CD8+ TCL**

renamed: **EATL-2: monomorphic epitheliotrophic intestinal TCL (MEITL)**
What are the challenges for diagnosis?

- ≥10% of patients receive an incorrect diagnosis\(^2\)
- In one analysis, diagnostic agreement between hematopathologists varied by subtype, ranging from 72% to 97%\(^3\)
- Over 1/3 of cases cannot be further classified and are diagnosed as PTCL-NOS\(^4\)

**Diagnosis is based on evaluation of:**
- Histological features\(^1\)
  - Tumor tissue biopsy
- Immunohistochemistry
- Flow cytometry
- Molecular genetics
- Cytogenetics

**Workup to assess staging and prognosis include:**\(^1\)
- History and physical exam
- CBC with differential
- Bone marrow biopsy ± aspirate
- LDH and uric acid
- Comprehensive metabolic panel
- PET/CT scan and/or C/A/P CT
- Tests for HIV, HTLV-1, HBV, and HBC

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2. Cheson BD. *Clinical Advances in Hematology and Oncology*. 2011;9(suppl 26);
PFS and OS vary by subtype as well as by IPI and PIT score

PTCL outcomes in the modern era: Swedish Lymphoma Registry (pts diagnosed 2000–2009)

ALKu, anaplastic large cell lymphoma kinase unknown; EN, extranodal; IPI, International Prognostic Index; PFS, progression-free survival; PIT, Prognostic Index for T-cell lymphoma; pts, patients; sp, subcutaneous panniculitis-like; TCL, T-cell lymphoma

CHOP as back-bone chemotherapy in aggressive lymphoma: still valid in PTCL

Schmitz et al., Blood 2010;116(18):3418-3425

McKelvey et al.
Cancer 1976 Oct;38(4):1484-93

Hydroxyldaunomycin (Adriamycin) combination chemotherapy in malignant lymphoma

Study undertaken by the Southwest Oncology Group
Supported by Operations Office Grant—CA16943 and Statistical Office Grant—CA12014.

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>ORR [%]</th>
<th>CRR [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morabito</td>
<td>297</td>
<td>76</td>
<td>56</td>
</tr>
<tr>
<td>Savage</td>
<td>199</td>
<td>76-90</td>
<td>55-70</td>
</tr>
<tr>
<td>Lee</td>
<td>84</td>
<td>59</td>
<td>47</td>
</tr>
<tr>
<td>Lopez-G.</td>
<td>174</td>
<td>64</td>
<td>49</td>
</tr>
<tr>
<td>Sung</td>
<td>52</td>
<td>63</td>
<td>17</td>
</tr>
<tr>
<td>Delmer</td>
<td>57</td>
<td></td>
<td>46</td>
</tr>
</tbody>
</table>
pTNHL – very few data…

Clinical data sets?

- retrospective analyses (subgroups)
- phase I/II clinical trials (relapse)
- Few “true“ phase III clinical trials

ACT-1 (NLG)
DSHNHL 2006 1A (in coop w. LYSA)
ACT-2 / DSHNHL 2006 1B (w. NLG)
GEM-P (UK) vs CHOP
Ro-CHOP (LYSA)

2 large international registries

Kombinationstherapie mit innovativen Substanzen bei peripheren T NHL
# ACT-2 study

Response and progression rates according to treatment arm

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>OR rate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 x CHOP - 14 (n = 58)</td>
<td>35/58 (60%)</td>
<td>(47% ; 73%)</td>
</tr>
<tr>
<td>6 x CHOP - 14 + A (n = 58)</td>
<td>42/58 (72%)</td>
<td>(59% ; 83%)</td>
</tr>
<tr>
<td>Total (n = 116)</td>
<td>77/116 (66%)</td>
<td>(57% ; 75%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CR/u rate</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>25/58 (43%)</td>
<td>13/58 (22%)</td>
</tr>
<tr>
<td>35/58 (60%)</td>
<td>9/58 (16%)</td>
</tr>
<tr>
<td>60/116 (52%)</td>
<td>22/116 (19%)</td>
</tr>
</tbody>
</table>
## ACT-2 trial

Types of infections during chemotherapy (grade 3-5)

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>6 x CHOP-14 (n=17)</th>
<th>6 x CHOP-14 + A (n=38)</th>
<th>Total (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial</td>
<td>10/17 (59%)</td>
<td>12/38 (32%)</td>
<td>22/55 (40%)</td>
</tr>
<tr>
<td>Fungal</td>
<td>1/17 (6%)</td>
<td>4*/38 (11%)</td>
<td>5*/55 (9%)</td>
</tr>
<tr>
<td>Viral</td>
<td>0/17 (0%)</td>
<td>19**/38 (50%)</td>
<td>19**/55 (35%)</td>
</tr>
</tbody>
</table>

* 1 Aspergillus  
** 14 CMV

Note: several types of infections can be specified for one infectious event

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DSHNHL 07-DEC-2015
ACT-2 trial
OS according to treatment arm

Median observation time: 43 months

- 6xCHOP-14 (n=58)
- 6xCHOP-14 + A (n=58)

p=0.120

DSHNHL 07-DEC-2015
CHOP+ Alemtuzumab

- Endauswertung der ACT-1 + ACT-2 Studie
- 252 Patienten, 18-80 Jahre; CHOP vs A-CHOP

Figure 1:

Event free survival

Progression free survival

Overall survival
ACT-1/2 Final Analysis

- Bulky Disease & Male gender: Signifikante RF in multivariater Analyse

Table 2: Multivariate analysis (Hazard Ratio, [95% CI], p-value) adjusting for IPI risk factors, bulky disease and gender

<table>
<thead>
<tr>
<th>Factor</th>
<th>EFS</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 x CHOP-14 + A vs. 6 x CHOP-14</td>
<td>0.8 ([0.6 – 1.1]; 0.196)</td>
<td>0.8 ([0.6 – 1.1]; 0.246)</td>
<td>1.2 ([0.8 – 1.6]; 0.370)</td>
</tr>
<tr>
<td>Age &gt; 60</td>
<td>1.4 ([1.0 – 1.9]; 0.046)</td>
<td>1.3 ([0.9 – 1.8]; 0.128)</td>
<td>1.5 ([1.1 – 2.2]; 0.018)</td>
</tr>
<tr>
<td>LDH &gt; UNV</td>
<td>1.1 ([0.8 – 1.5]; 0.621)</td>
<td>1.1 ([0.8 – 1.5]; 0.599)</td>
<td>1.1 ([0.8 – 1.6]; 0.535)</td>
</tr>
<tr>
<td>ECOG &gt; 1</td>
<td>2.1 ([1.5 – 3.1]; &lt;0.001)</td>
<td>2.3 ([1.6 – 3.3]; &lt;0.001)</td>
<td>2.7 ([1.8 – 4.0]; &lt;0.001)</td>
</tr>
<tr>
<td>Stage III/IV</td>
<td>1.1 ([0.7 – 1.8]; 0.722)</td>
<td>1.4 ([0.8 – 2.5]; 0.179)</td>
<td>1.6 ([0.9 – 3.1]; 0.137)</td>
</tr>
<tr>
<td>Extralymph. involvem. &gt; 1</td>
<td>1.5 ([1.1 – 2.2]; 0.010)</td>
<td>1.4 ([1.0 – 2.0]; 0.042)</td>
<td>1.4 ([1.0 – 2.1]; 0.048)</td>
</tr>
<tr>
<td>Bulky disease</td>
<td>2.1 ([1.4 – 3.2]; 0.001)</td>
<td>2.0 ([1.3 – 3.1]; 0.002)</td>
<td>3.0 ([1.9 – 4.7]; &lt;0.001)</td>
</tr>
<tr>
<td>Male gender</td>
<td>2.5 ([1.8 – 3.5]; &lt;0.001)</td>
<td>2.6 ([1.9 – 3.7]; &lt;0.001)</td>
<td>2.6 ([1.8 – 3.7]; &lt;0.001)</td>
</tr>
</tbody>
</table>
Schematic representation of ALCL entities and their genetic-associated aberrations.

Philippe Gaulard, and Laurence de Leval Blood
2016;127:175-177

©2016 by American Society of Hematology
Overall survival in patients with ALCL, stratified by rearrangements of ALK, DUSP22, and TP63. −/−/−, triple-negative cases lacking all 3 rearrangements
OS and PFS by SCT status.

Barbara Pro et al. Blood 2017;130:2709-2717
Patients who were in remission and in follow-up at study closure.
The Phase 3 ECHELON-2 Trial: Results of a Randomized, Double-Blind, Active-Controlled Study of Brentuximab Vedotin and CHP (A+CHP) Versus CHOP in Previously Untreated Subjects with CD30-Expressing Peripheral T-Cell Lymphomas (PTCL)

Steven Horwitz, Owen A O’Connor, Barbara Pro, Tim Illidge, Michelle Fanale, Ranjana Advani, Nancy L Bartlett, Jacob Haaber Christensen, Franck Morschhauser, Eva Domingo-Domenech, Giuseppe Rossi, Won Seog Kim, Tatyana Feldman, Anne Lennard, David Belada, Árpád Illés, Kensei Tobinai, Kunihiro Tsukasaki, Su-Peng Yeh, Andrei Shustov, Andreas Hüttmann, Kerry J Savage, Sam Yuen, Swaminathan Iyer, Pier Luigi Zinzani, Zhaowei Hua, Meredith Little, Shangbang Rao, Joseph Woolery, Thomas Manley, Lorenz Trümper

American Society of Hematology Annual Meeting; San Diego, California, December 1-4, 2018, Abstract #997
Key Eligibility Criteria
- Age ≥18 years
- CD30-expression (≥10% cells)
- Previously-unreotated PTCL:
  - Systemic ALCL (sALCL)* including ALK(+) sALCL with IPI ≥2, ALK(-) sALCL
  - PTCL-NOS, AITL, ATLL, EATL, HSTCL

Stratification Factors
- IPI score (0-1 vs. 2-3 vs. 4-5)
- Histologic subtype (ALK-positive sALCL vs. all other histologies)

*targeting 75% (±5%) ALCL per EU regulatory commitment

EOT
PET

A+CHP
(A) brentuximab vedotin 1.8 mg/kg +
(C) cyclophosphamide 750 mg/m² +
(H) doxorubicin 50 mg/m² +
(P) prednisone 100 mg (Days 1-5)

+ placebo vincristine
Q3W for 6 to 8 cycles

CHOP
(C) cyclophosphamide 750 mg/m² +
(H) doxorubicin 50 mg/m² +
(O) vincristine 1.4 mg/m² +
(P) prednisone 100 mg (Days 1-5)

+ placebo brentuximab vedotin
Q3W for 6 to 8 cycles

Per investigator discretion:
GCSF primary prophylaxis, consolidative RT and SCT

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase ATLL, adult T-cell leukaemia/lymphoma; EATL, enteropathy-associated T-cell lymphoma; EOT, end of treatment; GCSF, granulocyte-colony stimulating factor; HSTCL, hepatosplenic T-cell lymphoma; IPI, international prognostic index
Endpoints and Analysis Populations

Endpoints
Type 1 error control for primary and all key secondary endpoints

• **Primary Endpoint**
  ◦ Progression-Free Survival (PFS) per blinded independent review of PFS
    - ASCT or RT consolidation not an event if preplanned by investigator

• **Secondary Endpoints**
  ◦ Overall survival (OS)
  ◦ PFS per BICR in sALCL subjects
  ◦ Complete remission (CR) rate
  ◦ Objective remission rate (ORR)
  ◦ Safety

Analysis Populations

• **Efficacy**
  ◦ Intention-to-treat (ITT)

• **Safety**
  ◦ All subjects who received any amount of brentuximab vedotin or any component of CHOP

* PFS events = PD, death, or subsequent systemic therapy to treat residual or progressive disease
* Lymphoma response criteria Cheson 2007
## Summary of Treatment

<table>
<thead>
<tr>
<th></th>
<th>A+CHP (N=226)</th>
<th>CHOP (N=226)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure to study drug, n</strong></td>
<td>223</td>
<td>226</td>
</tr>
<tr>
<td>Number of subjects treated by cycle, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 cycles</td>
<td>156 (70)</td>
<td>140 (62)</td>
</tr>
<tr>
<td>8 cycles</td>
<td>40 (18)</td>
<td>44 (19)</td>
</tr>
<tr>
<td>Median relative dose intensity (brentuximab vedotin or vincristine), %</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td><strong>Subsequent therapy, n</strong></td>
<td>226</td>
<td>226</td>
</tr>
<tr>
<td>Systemic therapy for residual or progressive disease, n (%)</td>
<td>59 (26)</td>
<td>94 (42)</td>
</tr>
<tr>
<td>Palliative radiation, n (%)</td>
<td>10 (4)</td>
<td>8 (4)</td>
</tr>
</tbody>
</table>
Progression-free Survival

- 3-yr PFS:
  - A+CHP: 57% (42%)
  - CHOP: 44% (55%)

- Events:
  - A+CHP: 95 (42%)
  - CHOP: 124 (55%)

- HR (95% CI) and P:
  - A+CHP: 0.71 (0.54, 0.93), P = 0.011

- Median PFS (95% CI):
  - A+CHP: 48.2 mo (35.2, NE)
  - CHOP: 20.8 mo (12.7, 47.6)

- Median Follow-up:
  - 36.2 months
Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>A+CHP</th>
<th>CHOP</th>
<th>Deaths</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>51 (23%)</td>
<td>73 (32%)</td>
<td>75th percentile</td>
<td>0.66 (0.46, 0.95)</td>
<td>0.0244</td>
</tr>
<tr>
<td>Median follow-up</td>
<td>42.1 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Not reached 17.5 mo
## Prespecified Subset Analyses: PFS

<table>
<thead>
<tr>
<th>ITT Subgroups</th>
<th>A+CHP Event/N</th>
<th>CHOP Event/N</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>95/226</td>
<td>124/226</td>
<td>0.71 (0.54, 0.93)</td>
</tr>
<tr>
<td><strong>IPI Score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>18/52</td>
<td>27/48</td>
<td>0.53 (0.29, 0.97)</td>
</tr>
<tr>
<td>2–3</td>
<td>66/141</td>
<td>116/141</td>
<td>0.71 (0.50, 1.00)</td>
</tr>
<tr>
<td>4–5</td>
<td>21/33</td>
<td>20/33</td>
<td>1.03 (0.55, 1.92)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>54/157</td>
<td>75/156</td>
<td>0.67 (0.47, 0.95)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>41/69</td>
<td>49/70</td>
<td>0.70 (0.46, 1.08)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>59/133</td>
<td>80/151</td>
<td>0.80 (0.57, 1.13)</td>
</tr>
<tr>
<td>Female</td>
<td>36/93</td>
<td>44/75</td>
<td>0.49 (0.31, 0.78)</td>
</tr>
<tr>
<td><strong>Baseline ECOG Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0/1</td>
<td>76/174</td>
<td>105/179</td>
<td>0.66 (0.49, 0.89)</td>
</tr>
<tr>
<td>2</td>
<td>19/51</td>
<td>19/47</td>
<td>0.98 (0.51, 1.87)</td>
</tr>
<tr>
<td><strong>Disease Stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>15/42</td>
<td>19/46</td>
<td>0.95 (0.48, 1.88)</td>
</tr>
<tr>
<td>III</td>
<td>29/57</td>
<td>35/67</td>
<td>0.69 (0.42, 1.14)</td>
</tr>
<tr>
<td>IV</td>
<td>51/127</td>
<td>70/113</td>
<td>0.64 (0.45, 0.93)</td>
</tr>
<tr>
<td><strong>Disease Indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALK-positive sALCL</td>
<td>5/49</td>
<td>16/49</td>
<td>0.29 (0.11, 0.79)</td>
</tr>
<tr>
<td>ALK-negative sALCL</td>
<td>50/113</td>
<td>60/105</td>
<td>0.65 (0.41, 0.95)</td>
</tr>
<tr>
<td>AITL</td>
<td>18/30</td>
<td>13/24</td>
<td>1.40 (0.64, 3.07)</td>
</tr>
<tr>
<td>P'TCL-NOS</td>
<td>19/29</td>
<td>31/43</td>
<td>0.75 (0.41, 1.37)</td>
</tr>
<tr>
<td>PFS (FD, Death)</td>
<td>84/226</td>
<td>103/226</td>
<td>0.75 (0.56, 1.00)</td>
</tr>
</tbody>
</table>

0.1 \[\text{A+CHP Better}\] \[0.5\] \[1\] \[\text{CHOP Better}\]
PFS: censored at time of consolidative ASCT or RT

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Events</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A+CHP</td>
<td>81 (36%)</td>
<td>0.71 (0.53, 0.94)</td>
<td>0.017</td>
</tr>
<tr>
<td>CHOP</td>
<td>111 (49%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treatment-Emergent Peripheral Neuropathy

Peripheral Neuropathy (PN)*

<table>
<thead>
<tr>
<th>Subjects (%)</th>
<th>A+CHP</th>
<th>CHOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Subjects, n (%)

<table>
<thead>
<tr>
<th></th>
<th>A+CHP (N=223)</th>
<th>CHOP (N=226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-emergent PN, n</td>
<td>117</td>
<td>124</td>
</tr>
<tr>
<td>Resolution† of all PN events</td>
<td>58 (50)</td>
<td>79 (64)</td>
</tr>
<tr>
<td>Ongoing PN at last follow-up</td>
<td>61 (52)</td>
<td>45 (36)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>44 (72)</td>
<td>32 (71)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>15 (25)</td>
<td>12 (27)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

†Resolution was defined as resolved/recovered with or without sequelae; or return to baseline or lower severity as of the latest assessment for pre-existing events

*Includes the preferred terms of peripheral sensory neuropathy, paraesthesia, peripheral motor neuropathy, muscular weakness, peripheral sensorimotor neuropathy, hypoaesthesia, dysaesthesia, areflexia, burning sensation, peroneal nerve palsy, polyneuropathy, autonomic neuropathy, gait disturbance, muscle atrophy, and neuralgia.
Summary and Conclusions

- ECHELON-2 first prospective trial in PTCL to show OS benefit over CHOP
- A+CHP provided clinically meaningful improvement in PFS and OS versus CHOP
  - 29% reduction in the risk of a progression event
    - 3-yr PFS: A+CHP 57% versus CHOP 44%
  - 34% reduction in the risk of death
- A+CHP has a comparable safety profile to CHOP
- FDA approved brentuximab vedotin in combination with CHP for adults with previously-untreated sALCL or other CD30-expressing PTCL, including AITL and PTCL-NOS in November, 2018
Upfront transplant in PTCL

DSS, disease-specific survival


5 y OS by subtype:
- ALK-neg: 70%
- AITL: 52%
- NOS: 47%
- EATL: 48%

5 y PFS by subtype:
- ALK-neg: 61%
- AITL: 49%
- NOS: 38%
- EATL: 38%

Updated analysis with 10 y median follow-up:
- ALK-neg ALCL 10 y: OS 48%; PFS 48%; DSS 67%
long-term outcome of pts. with r/r PTCL and conventional chemotherapy, excluding SCT

n=153; populational based (British Columbia Cancer Agency Lymphoid Cancer) 1976-2010 recipients of stem cell transplantation excluded

allogeneic stem cell transplantation for r/r PTCL
Wulf et al., BMT 2018, in press

Göttingen 51
Hamburg 36
Homburg 5
Marburg 3
accrual stopped 08.2013 for futility

first-line treatment of mature (peripheral) T-cell lymphoma (PTCL) for patients ≤60 years

inclusion criteria
- Peripheral T-cell lymphoma, unspecified
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large cell lymphoma, ALK negative
- Extranodal NK/T-cell lymphoma, nasal type
- Enteropathy type T-cell lymphoma
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis type T-cell lymphoma
- all stages and IPI except stage I with aIPI 0

= At diagnosis, patients are randomized to allogeneic or autologous transplantation (tx). Donor search (family or unrelated) will be initiated only in patients randomized to allogeneic transplantation. Patients randomized to allogeneic tx but without a donor will receive autologous tx. Peripheral blood stem cells are harvested after DHAP in patients who are to receive autologous tx (randomized or crossed over [dotted line ••• in the diagram] from the allogeneic transplant arm because no donor is available).

ASCT = autologous stem cell transplantation; SCT = allogeneic stem cell transplantation

DSHNHL: http://www.dshnhl.org/
AATT study: updated results of the interim analysis
OS according to treatment arm

Schmitz et al. ASCO 2015
## AATT study: cause of death after SCT

<table>
<thead>
<tr>
<th></th>
<th>autoSCT (n=30)</th>
<th>alloSCT (n=28)</th>
<th>Total (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Salvage treatment</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>NRM</td>
<td>0</td>
<td>8*</td>
<td>8</td>
</tr>
</tbody>
</table>

* includes one patient with PTLD

Schmitz et al. ASCO 2015
EDO-S101

- is a functional **pan-HDAC inhibitor**
- is a functional **alkylating agent**
- causes cell cycle arrest
- reduces proteins of the DSB repair system
- increases pro-apoptotic BIM
- reduces anti-apoptotic proteins (XIAP, Mcl-1)
- triggers the classical pathway of apoptosis
- works synergistically with proteasome inhibitors

Phase IB/II, n=30

PFS-3 years
pTNHL – CAR T problems

• *Fratricide* (or soricide)

• NB: Less of a problem in CD19/20 directed B cell depletion

• *Specific antigens* (TAA) beyond idiootype
SUGGESTED TREATMENT REGIMENS

First-line Therapy:
• Clinical trial
• ALCL
  ◦ Preferred regimen
    ◦ Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) (category 1)
  ◦ Other recommended regimens
    ◦ CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
    ◦ CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone)
    ◦ Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
• Other histologies
  ◦ Preferred regimens (in alphabetical order)
    ◦ Brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, and prednisone) for CD30+ histologies
    ◦ CHOEP
    ◦ CHOP
    ◦ Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
  ◦ Other recommended regimens (in alphabetical order)
    ◦ CHOP followed by IVE (ifosfamide, etoposide, epirubicin) alternating with intermediate-dose methotrexate [Newcastle Regimen] [studied only in patients with EATL]
    ◦ HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with high-dose methotrexate and cytarabine (category 3)

First-line Consolidation:
• Consider consolidation with high-dose therapy and stem cell rescue.

ESMO guidelines 2015:
Treatment algorithm for PTCL

2015 ESMO proposed treatment algorithm for frontline PTCL
Participation in a clinical trial is recommended whenever possible

**Nodal entities (CS II–IV)**
- PTCL-NOS, AITL, ALK− ALCL, ALK+ ALCL†
  - CHOEP 14 ×6

**Extranodal entities**
- ALK+ ALCL†
  - CHOEP/CHOP
- EATL
  - IVE/MTX CHOEP
- HSTCL
  - ICE/IVAC; CHOEP
- ENKTCL
  - Stage I–II
  - RT (>50 Gy) + Chemo§
  - Stage II–IV
  - Chemo§ (± RT)

If chemosensitive (CR, PR) and transplant-eligible
- ASCT
- No further treatment
- ASCT
- ASCT or AlloSCT‡
- ASCT

*Stage I: shortened chemotherapy schedule (e.g. 3 courses) followed by curatively intended radiotherapy. †ALK+ ALCL with a high-risk profile (e.g. IPI >2) should be considered for ASCT consolidation, while ASCT in low-risk profile patients is not recommended. §If donor available. SMILE or AspaMetDex.

CS, clinical stage; ICE, ifosfamide + etoposide + carboplatin; IVAC, ifosfamide + cytarabine + etoposide; IVE/MTX, ifosfamide + vincristine + etoposide/methotrexate; RT, radiotherapy

Mitglieder AG T-NHL 11/2017

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Uniklinik Heidelberg, Med. Klinik V
Klinikum der Universität München, Med. Klinik III
Universitätsklinikum Tübingen, Institut f. Pathologie u. Neuropathologie
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Klinikum Nürnberg, Paracelsus Medizinische Privatuniversität

n=27, 18 Institutionen
Studientreffen der GLA e.V. – ULM 2017, Göttingen 2018
Nächster Termin: Münster, November 2019
Leipzig, November 2020

AGs Aggressive B, T Zell Lymphome
Dank an alle Studienteilnehmer, Studienteams Patienten & ihre Familien
www.german-lymphoma-alliance.de
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