Controversies and Approaches to T-cell Lymphoma Therapy in 2016

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Lymphoma Service
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Financial Disclosures

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• Consultant to: Celgene, Bristol-Myers Squibb, Millennium Pharmaceuticals, Seattle Genetics, Spectrum Pharmaceuticals
T and NK Lymphomas

- Subtypes/Unusual subtypes/Prognosis
- “Standard” upfront approaches
- Newer Approaches
- Relapse
  - Strategies
  - Therapies
### Proportion of Major T-cell Subtypes: North America

<table>
<thead>
<tr>
<th>Registry</th>
<th>PTCL-NOS</th>
<th>AITL</th>
<th>ALCL, ALK +</th>
<th>ALCL, ALK -</th>
<th>NK/T</th>
<th>ATL</th>
<th>EATL</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPTCL (NA)</td>
<td>34%</td>
<td>16%</td>
<td>16%</td>
<td>8%</td>
<td>5%</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>BCCA</td>
<td>59%</td>
<td>5%</td>
<td>6%</td>
<td>9%</td>
<td>9%</td>
<td>NA*</td>
<td>5%</td>
</tr>
<tr>
<td>COMPLETE</td>
<td>34%</td>
<td>15%</td>
<td>11%</td>
<td>8%</td>
<td>6%</td>
<td>2%</td>
<td>3%</td>
</tr>
</tbody>
</table>

“Less Common” Subtypes of TCL

NK/T-cell Lymphoma

2/3-3/4 are Stage I/II

ATLL

OS by Subtype

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Response</th>
<th>Consolidation phase</th>
<th>Regimen</th>
<th>Response</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>CHOP</td>
<td>CR</td>
<td>Chemotherapy</td>
<td>CR</td>
<td>DOD</td>
<td></td>
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<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Chemotherapy</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Auto BMT</td>
<td>CR</td>
<td>DOD</td>
<td></td>
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<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Auto BMT</td>
<td>CR</td>
<td>DOD</td>
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<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Chemotherapy</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Allo BMT</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>PR</td>
<td>Auto PBSC</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>PR</td>
<td>Auto PBSC</td>
<td>Failure</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Chemotherapy</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>Failure*</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Allo BMT</td>
<td>NE</td>
<td>TRD</td>
<td></td>
</tr>
<tr>
<td>CHOP</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>CR</td>
<td>Chemotherapy</td>
<td>CR</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>PR</td>
<td>Allo BMT</td>
<td>NE</td>
<td>TRD</td>
<td></td>
</tr>
<tr>
<td>Platinum-Ara-C based</td>
<td>PR</td>
<td>Auto PBSC</td>
<td>CR</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>CHOP</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>Platinum-Ara-C based</td>
<td>PR</td>
<td>Auto PBSC</td>
<td>CR</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
<tr>
<td>CHOP-like</td>
<td>Failure</td>
<td>—</td>
<td>—</td>
<td>DOD</td>
<td></td>
</tr>
</tbody>
</table>
MSKCC Experience with Hepatosplenic TCL
Non-CHOP induction-HSCT

Overall Survival N=19

Median OS: 59.2 mo


Overall Survival by Induction

Median OS
- ICE/IVAC upfront: Not Reached
- Other: 21.7 months
- Allo N=8
- Auto N=4
Swedish National Registry: PFS in 755 patients with PTCL.


©2014 by American Society of Hematology
### PTCL: Outcomes by Subtype and IPI

<table>
<thead>
<tr>
<th>PTCL subtype</th>
<th>5-year OS*</th>
<th>5-year FFS*</th>
<th>5-year OS by IPI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0-1</td>
</tr>
<tr>
<td>PTCL-NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPTCL</td>
<td>32%</td>
<td>20%</td>
<td>50%</td>
</tr>
<tr>
<td>BCCCA</td>
<td>35%</td>
<td>29%</td>
<td>64%</td>
</tr>
<tr>
<td>AITL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPTCL</td>
<td>32%</td>
<td>18%</td>
<td>56%</td>
</tr>
<tr>
<td>BCCCA</td>
<td>36%</td>
<td>13%</td>
<td>NR</td>
</tr>
<tr>
<td>ALC L ALK−</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPTCL</td>
<td>49%</td>
<td>36%</td>
<td>74%</td>
</tr>
<tr>
<td>BCCCA</td>
<td>34%</td>
<td>28%†</td>
<td>66%†</td>
</tr>
<tr>
<td>ALC L ALK+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPTCL</td>
<td>70%</td>
<td>60%</td>
<td>90%</td>
</tr>
<tr>
<td>BCCCA</td>
<td>58%</td>
<td>28%†</td>
<td>66%†</td>
</tr>
</tbody>
</table>


(1990-2002)
(1981-2000)
ALCL OS based on genetic subtype

B

Overall Survival by Genetic Subtype

Gene rearranged
- ALK
- DUSP22
- TP63
- /-/-

Percent Survival

0 10 20 30 40 50 60 70 80 90 100

0 24 48 72 96 120 144 168 192 216 240

Months After ALCL Diagnosis

p<0.0001

Initial Treatment for the more common Peripheral T-cell Lymphomas
**CHOP-Based Treatment for Peripheral (Mature) T / NK Lymphomas**

**Always**
- Anaplastic Large Cell-ALK-1 positive

**Never**
- Mycosis fungoides
- Sezary syndrome

**Sometimes**
- Peripheral T-cell lymphoma NOS
- Angioimmunoblastic T-cell lymphoma
- Anaplastic Large Cell-ALK-1 positive
- Enteropathy-type intestinal lymphoma
- Subcutaneous panniculitis-like T-cell
- Anaplastic large cell lymphoma
- Lymphomatoid papulosis
- T-cell large granular lymphocytic
- Extranodal NK / T-cell lymphoma-nasal
- Hepatosplenic T-cell lymphoma
- NK / T-cell leukemia / lymphoma
- Adult T-cell leukemia / lymphoma
- T-cell prolymphocytic leukemia
## First-line treatment of PTCL: CHOP+ and non-CHOP

<table>
<thead>
<tr>
<th>Citation</th>
<th>regimen</th>
<th>n</th>
<th>PTCL</th>
<th>ORR/CR</th>
<th>% PFS/EFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallamani Blood 2007</td>
<td>A-CHOP</td>
<td>24</td>
<td>14</td>
<td>75/71</td>
<td>48 (2 yr)</td>
</tr>
<tr>
<td>Simon et al BJH 2010</td>
<td>VIP-rABVD</td>
<td>43</td>
<td>28</td>
<td>58/44</td>
<td>45 (2 yr)</td>
</tr>
<tr>
<td>Kim et al Eur J Ca 2012</td>
<td>Bortez + CHOP</td>
<td>46</td>
<td>16</td>
<td>76/65</td>
<td>35 (PTCL 31%)</td>
</tr>
<tr>
<td>Mahadevan et al Cancer 2012</td>
<td>PEGS</td>
<td>20</td>
<td>10</td>
<td>39/24</td>
<td>14 (2 yr) In untreated</td>
</tr>
<tr>
<td>Advani et al ASH 2013</td>
<td>CEOP-Pral</td>
<td>33</td>
<td>21</td>
<td>70/52</td>
<td>39 (2 yr)</td>
</tr>
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</table>
Adding Etoposide to CHOP: German Prospective High-Grade NHL Studies

<table>
<thead>
<tr>
<th>PTCL Subtype</th>
<th>n</th>
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<tbody>
<tr>
<td>ALCL, ALK+</td>
<td>78</td>
</tr>
<tr>
<td>ALCL, ALK-</td>
<td>113</td>
</tr>
<tr>
<td>PTCL-NOS</td>
<td>70</td>
</tr>
<tr>
<td>AITL</td>
<td>28</td>
</tr>
<tr>
<td>Other</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>320</td>
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</table>

Prospective multicenter studies in PTCL

<table>
<thead>
<tr>
<th></th>
<th>CHOP</th>
<th>CHOEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>83</td>
<td>118</td>
</tr>
<tr>
<td>PTCL</td>
<td>39%</td>
<td>39%</td>
</tr>
<tr>
<td>AITL</td>
<td>33%</td>
<td>19%</td>
</tr>
<tr>
<td>ALCL</td>
<td>16%</td>
<td>19%</td>
</tr>
<tr>
<td>IPI 1</td>
<td>14%</td>
<td>28%</td>
</tr>
<tr>
<td>IPI 2</td>
<td>35%</td>
<td>32%</td>
</tr>
<tr>
<td>IPI 3</td>
<td>45%</td>
<td>19%</td>
</tr>
<tr>
<td>IPI 4-5</td>
<td>6%</td>
<td>21%</td>
</tr>
<tr>
<td>Med Age</td>
<td>47</td>
<td>57</td>
</tr>
<tr>
<td>ORR</td>
<td>79%</td>
<td>82%</td>
</tr>
<tr>
<td>CR</td>
<td>39%</td>
<td>51%</td>
</tr>
</tbody>
</table>

Reimer, P. et al et al. JCO vol 27, Jan 2009
CHOEP-ASCT Nordic Lymphoma Group

ND PTCL, N = 166
Med Age-57 years
ALK+/ALCL excluded

CHOEP x 4-6
CR
PR

HDT/ASCT
N = 115
90 CR 3-month post

PFS, largest subtypes

Subtype | 5 yr PFS | 5 yr OS
---|---|---
ALCL | 61 | 70
AITL | 47 | 52
PTCL | 38 | 49
EATL | 38 | 48

D’Amore et al. JCO 2012 Sep 1;30(25):3093-9
Autologous stem cell transplantation as first-line therapy in PTCL

**Swedish Registry**

<table>
<thead>
<tr>
<th></th>
<th>Auto-SCT ITT (n = 128)</th>
<th>Non-auto-SCT (n = 124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 yr OS</td>
<td>48%</td>
<td>26%</td>
</tr>
<tr>
<td>5 yr PFS</td>
<td>41%</td>
<td>20%</td>
</tr>
</tbody>
</table>

2. Mehta et al. CLLM 2013 Dec;13(6):664-70
Prognosis by Interim PET

Casulo et al., Leukemia & Lymphoma, October 2013; 54(10): 2163–2167
## Type of Therapy by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Tx/palliation</td>
<td>46</td>
<td>6</td>
</tr>
<tr>
<td>RT</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>CHT</td>
<td>564</td>
<td>71</td>
</tr>
<tr>
<td>HDT</td>
<td>158</td>
<td>20</td>
</tr>
</tbody>
</table>

★ Includes
- ALL subtypes
- Tx in CR1/PR1 + Relapse

 Courtesy of Monica Bellei and Massimo Federico
Brentuximab Beyond Relapsed ALCL

<table>
<thead>
<tr>
<th>PTCL</th>
<th>Best Clinical Response</th>
<th>Overall Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR n (%)</td>
<td>PR n (%)</td>
</tr>
<tr>
<td>Mature T-/NK-cell (n=34)</td>
<td>8 (24)</td>
<td>6 (18)</td>
</tr>
<tr>
<td>AITL (n=13)</td>
<td>5 (38)</td>
<td>2 (15)</td>
</tr>
<tr>
<td>PTCL-NOS (n=21)</td>
<td>3 (14)</td>
<td>4 (19)</td>
</tr>
</tbody>
</table>

BV + CH-P

N=26
Median F/U 21.4 mos
Est 1 yr PFS 71%

Horwitz S M et al. Blood 2014;123:3095-3100
Fanale et al JCO Oct 1, 2014:3137-3143;
A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Brentuximab Vedotin and CHP (A+CHP) Versus CHOP in the Frontline Treatment of Patients with CD30-positive Mature T-cell Lymphomas

**ECHELON-2; NCT01777152**

- **Randomize**
  - PTCL-CD30+ (≥ 10%)
  - If ALK+ ALCL IPI >2

- **RESTAGE C4**

- **Placebo+ CHOP” x 6-8 cycles**

- **BV + CH-P” x 6-8 cycles**

- **F/U Progression Death**

N=300
Primary endpoint: improvement in PFS
Romidepsin-CHOP Phase I-II PFS

1 year estimated PFS 63.9% (95%CI 35.4 – 82.5)

Median Follow-up 10 months
n=27
CR 15/27 (55.6%)
ORR 20/27 (74%)

Delarue et al ASH 2014
Phase III Ro-CHOP Study

- International randomized, open-label study
- Principal objective: PFS improvement
- Planned accrual: 420 patients
**Untreated PTCL: Phase III Trials**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Patient Population</th>
<th>Primary Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alemtuzumab + CHOP-14 + G-CSF vs CHOP-14 + G-CSF</td>
<td>Newly diagnosed PTCL</td>
<td>EFS</td>
<td>Completed</td>
</tr>
<tr>
<td>Brentuximab vedotin + CHP vs CHOP</td>
<td>CD30+ PTCL</td>
<td>PFS</td>
<td>Ongoing</td>
</tr>
<tr>
<td>CHOP → pralatrexate</td>
<td>Newly diagnosed PTCL</td>
<td>PFS, OS</td>
<td>Closed</td>
</tr>
<tr>
<td>Romidepsin + CHOP vs CHOP</td>
<td>Newly diagnosed PTCL</td>
<td>PFS</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Belinostat + CHOP or Pralatrexate + CHOP vs CHOP</td>
<td>Newly diagnosed PTCL</td>
<td>PFS</td>
<td>Planned</td>
</tr>
<tr>
<td>Lenalidomide + CHOEP</td>
<td>Newly diagnosed PTCL</td>
<td>CR</td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

- Broad attempts to add drug X to CHOP for all (or at least many) subtypes of PTCL
- Endpoints: Improvements in PFS (months not years)
Relapsed T-cell Lymphoma
Algorithmic Approach to Patients with Relapsed PTCL (NOS, AITL, ALCL)

- **Transplantation soon** (Donor known; patient eligible)
  - Combination chemotherapy (ICE, other combinations)
    - Allogeneic stem-cell transplantation
      - Adequate response
      - Donor known and eligible
      - No donor available
    - Transplantation unclear (Donor unknown; patient may or may not be eligible)
      - Clinical trial or single agent
    - Transplantation never (Physician or patient determines patient ineligible)
      - Clinical trial or single agent
- Transplantation never (Physician or patient determines patient ineligible)
  - Clinical trial or single agent
  - Clinical trial or single agent

Luning et al. *J Clin Oncol*, 2013;31:
Retrospective Analyses of Stem-cell Transplantation in Relapsed PTCL: MSKCC

ASCT as 2\textsuperscript{nd} line
N=40

Median PFS 6 months by ITT

Response to ICE 70\% (28/40)
Received ASCT 68\% (27/40)

Allogeneic SCT, Any line Transplanted only
N=34

2 year OS 61\%

TRM 18\%

Horwitz et al, ASH Annual Meeting Abstracts 2005;106:2679
Allogeneic Transplantation in T-cell Lymphoma: MSKCC

- N=65
- 2 Year OS: 59%
- 2 Year PFS: 48%
- Median PFS 20.26 mo

N. Mehta-Shah et al ASH 2015
Autologous Transplantation in Relapsed PTCL

CIBMTR: PFS excluding pt in CR1 (Most patients ALCL)

The Stanford Experience Auto

MSKCC

- Benefits are unclear. Most single institution studies show low PFS rates while registry data suggests better outcomes.

Smith S, et al. JCO September 1, 2013 vol. 31 no. 25 3100-3109
## Approved Agents in Relapsed/Refractory PTCL

<table>
<thead>
<tr>
<th>Belinostat N=129</th>
<th>Outcomes</th>
<th>Romidepsin N=131</th>
<th>Pralatrexate N=109</th>
<th>Brentuxiambvedotin (ALCL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>Median prior Rx</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>26%</td>
<td>ORR</td>
<td>25%</td>
<td>29%</td>
<td>86%</td>
</tr>
<tr>
<td>11%</td>
<td>CR</td>
<td>15%</td>
<td>11%</td>
<td>59%</td>
</tr>
<tr>
<td>15%</td>
<td>PR</td>
<td>11%</td>
<td>18%</td>
<td>27%</td>
</tr>
<tr>
<td>8.4</td>
<td>Median duration of response</td>
<td>17 months</td>
<td>10.1 months</td>
<td>13.2 mos</td>
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<tr>
<td>1.6</td>
<td>Median PFS</td>
<td>4 months</td>
<td>3.5 months</td>
<td>14.6 mos</td>
</tr>
</tbody>
</table>

O’Connor OA, et al. JCO in press
Progression Free Survival: Relapsed/Refractory PTCL

### FDA Approved Agents for TCL ORR (%) by Lymphoma Subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Pralatrexate</th>
<th>Romidepsin</th>
<th>Belinostat</th>
<th>Brentuximab vedotin</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTCL, NOS</td>
<td>31</td>
<td>29</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>AITL</td>
<td>8</td>
<td>30</td>
<td>46</td>
<td>54</td>
</tr>
<tr>
<td>ALCL</td>
<td>29</td>
<td>24</td>
<td>15</td>
<td>86</td>
</tr>
</tbody>
</table>

O’Connor OA et al, ASCO 2013; Horwitz, S et al ICML 2013  
Horwitz S M et al. *Blood* 2014;123:3095-3100
NCCN Regimens for Relapsed TCL

SUGGESTED TREATMENT REGIMENS FOR PTCL-NOS AND EATL

Second-line Therapy (with intention to proceed to transplant) and Subsequent Therapy:
- Clinical trial preferred
- Preferred single agents/combination regimens
  - Single agents (alphabetical order)
    - Belinostat
    - Brentuximab vedotin for CD30+ PTCL
    - Pralatrexate
    - Romidepsin
  - Combination regimens (alphabetical order)
    - DHAP (dexamethasone, cisplatin, cytarabine)
    - ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin)
    - GDP (gemcitabine, dexamethasone, cisplatin)
    - GemOx (gemcitabine, oxaliplatin)
    - ICE (ifosfamide, carboplatin, etoposide)

Alternative Regimens:
- Single agents (alphabetical order)
  - Bendamustine
  - Gemcitabine
  - Lenalidomide
- Combination regimen
  - GVD (gemcitabine, vinorelbine, liposomal doxorubicin)

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Bendamustine in Relapsed TCL

Phase II BENTLY trial for relapsed/refractory PTCL (GOELAMS/LYSA)
- N = 60 (23 with PTCL-U, 32 with AITL)
- Schedule: 120 mg/m² on Days 1 and 2 q3w
- **ORR: 50%
  - 28% CR/CRu
- Median PFS: 3.6 mos
- Median OS: 6.2 mos
- Most frequent grade 3/4 AEs:
  - neutropenia,
  - infection
  - thrombocytopenia

A phase 2, multicentre, single-arm, open-label study of lenalidomide in relapsed or refractory PTCL: The EXPECT trial

<table>
<thead>
<tr>
<th></th>
<th>ITT (N=54)</th>
<th>AITL (N=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Control</td>
<td>52% (28)</td>
<td>58% (15)</td>
</tr>
<tr>
<td>ORR</td>
<td>22% (12)</td>
<td>31% (8)</td>
</tr>
<tr>
<td>CR/Cru</td>
<td>11% (6)</td>
<td>15% (4)</td>
</tr>
<tr>
<td>PR</td>
<td>11% (6)</td>
<td>15% (4)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>30% (16)</td>
<td>27% (7)</td>
</tr>
<tr>
<td>POD</td>
<td>33% (18)</td>
<td>23% (6)</td>
</tr>
<tr>
<td>D/C without response assessment</td>
<td>15% (8)</td>
<td>19% (5)</td>
</tr>
</tbody>
</table>

IDH2 Mutations in T Cell Lymphoma

T follicular helper CD4+ cells (TFH)

- BCL6+
- CXCR5+
- PD1+

AG-221 (mIDH2 inhibitor)

TFH-like lymphoma (AITL and some PTCL-NOS)

IDH1/2 and Tet2 are mutually exclusive in AML but co-occur in TFH-like lymphoma

Expansion Cohorts

- AITL
- Glioma
- Non-glioma solid
PI3K in B-cell and T-cell Malignancies

- Antigen receptors, costimulatory molecules, cytokine receptors, and chemokine receptors can all trigger PI3K activation leading to AKT phosphorylation.
- Transcriptional profiling of PTCL-NOS cases identifies distinct subgroups based on high expression of either GATA3 or TBX21 (t-bet)
- GATA3-high tumors are enriched for PI3K-induced transcriptional signatures.

**Inhibition of AKT phosphorylation in CLL Cells from patients treated with duvelisib (PI3K δ/γ inhibitor)**

\[ \text{Iqbal J et al. Blood 2014;123:2915-2923} \]

**PTCL: Gata3 high tumors show a worse OS**

\[ \text{Patel et al., ASCO 2013 & Douglas et al. ASH 2013} \]
# IPI-145 Clinical Activity in TCL

<table>
<thead>
<tr>
<th>Population</th>
<th>Best Response, n (%)</th>
<th>Median Time to Response, months (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>CR</td>
</tr>
<tr>
<td>All TCL</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>PTCL</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>CTCL</td>
<td>18</td>
<td>0</td>
</tr>
</tbody>
</table>

Includes evaluable patients = at least 1 on-treatment response assessment or PD without assessment
CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease
ORR = CR + PR

- Clinical activity observed across PTCL and CTCL subtypes
  - PTCL: CRs in 1 EATCL and 1 PTCL NOS
    PRs in 2 AITCL, 2 SPTCL, 1 PTCL NOS, 1 ALCL (ALK-negative)
  - CTCL: PRs in 4 MF, 1 Sézary syndrome, and 1 MF-LCT

Horwitz et al. ASH 2014
Mature T-cell Lymphomas with Subtype Specific Approaches *We Think* are Better

- NK/T- Chemo + XRT for localized disease
- ATLL (HTLV-1 Associated)
  - Aggressive subtypes-Chemo-Allo strongly considered in CR1
  - Indolent subtypes-interferon + anti-retrovirals, Obs
- HSTCL- Chemo (non-CHOP) –Stem cell transplantation in CR1 (Allo > Auto)
- CTCL-approached as more indolent; palliative-maintenance therapies
PTCL: Initial Approach:

- Clinical Trial
  - Current: CHOP-like +X
  - Future: Novel regimen
- CHOEP-ASCT in CR1 for Most
  - ALCL
    - ALK+; -IPI
    - Dusp 22 rearranged?
    - Low IPI, Early Stage?
PTCL: Relapse

- Clinical Trial
  - Novel agents
  - Novel regimens
  - Standard agents
    - BV-ALCL
    - Others—little data to strongly suggest one over the other
- Intent for Transplantation
  - Allo > Auto
  - Depth of response > Durability
- No Intent for Transplantation
  - Durability > Depth of response