The Role of Radiotherapy in the Treatment of Non-Hodgkin Lymphoma

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Lymphomas (>> 60 histological subtypes)
- Hodgkin's Lymphoma
- Non-Hodgkin's Lymphomas
  - B Cell Lymphomas
    - indolent
      - follicular Lymphoma
      - MZL
    - aggressive
      - diffuse large B cell lymphoma
      - mantle cell lymphoma
    - highly aggressive
      - Burkitt's
  - T Cell Lymphomas
    - systemic
    - primary cutaneous
      - PTCL NOS
      - ALCL
      - NK/T
      - mycosis fungoides
      - Sézary syndrome
      - SMPTL

Early Stage Diffuse Large B Cell Lymphoma

NCCN Guidelines: Early Stage DLBCL

Stage I/II
- Non-bulky < 10 cm
  - RCHOP x 3 + RT
  - or
  - RCHOP x 6 + RT
  - or
  - RCHOP x 6
- Bulky > 10 cm
  - RCHOP x 6 +/- RT
**Prognostic Factors**

- Stage
- Tumor bulk
- Clinical factors: stage adjusted IPI
- Molecular factors: GCB, ABC, double-hit (myc, bcl2)....

**Role of RT in Early Stage DLBCL**

- Improve local control
- Spare chemotherapy
- Improve survival

**RT Improves Local Control in Early Stage DLBCL (1)**

**ECOG 1484**

- Pre- rituximab, pre-PET
- N = 243
- Bulky stage I, stage IE, II, IIE
- Bulky disease 31%
- CHOP x 8
- ONLY CR pts randomized
- 93 CR in OB, 75 CR in RT

Horning SJ, et al., Journal of Clinical Oncology 2004

**RT Improves Local Control in Early Stage DLBCL (2)**

**DFS**

- RT: 17 pts failed tx, 3 pts progressed in previously involved sites
- OB: 31 pts failed tx, 15 pts progressed in previously involved sites

Horning SJ, et al., Journal of Clinical Oncology 2004
RT is Chemo-sparing and Improves OS in Early Stage DLBCL

- Randomized study, pre-rituximab era
- CHOP x 8 vs CHOP x 3 + RT 40-55 Gy
- N=201 CHOP alone and 200 in CHOP + RT
- Stage I, IE (bulky disease included), non-bulky II or IIIE

Miller TP, et al., NEJM 1998

Addition of RT Improves Outcome in the Rituximab Era

- Retrospective study from MD. Anderson
- Stage I/II DLBCL, N= 190, RT given to 103 pts
- RCHOP x 6-8 +/- IFRT 30 – 36.9 Gy
- PFS at 5 yrs: 82% with RT, 78% without
- OS at 5 yrs: 92% with RT, 73% without
- RT is still beneficial in risk-factor-matched analysis (IPI, bulky, response to therapy)

Phan J., et al., Journal of Clinical Oncology 2010

RCHOP + IFRT for Early Stage DLBCL

- Single arm study, compared with the historical control
- Stage I, IE, Non-bulky stage II, or IIIE AND at least one of the risk factors (nonbulky stage II, age >60 years, PS >2, or elevated LDH)
- N = 60
- Treated with RCHOP x 3 + IFXRT 40-46 Gy for CR pts, 50-55Gy for PR pts

Role of RT in Early Stage DLBCL

- Improve local control
- Spare chemotherapy
- Improve survival

In both pre- and post- rituximab era, thus RT is an integral part of the first-line treatment for early stage DLBCL

- When RT is not feasible/suitable, full course of chemo (RCHOP x 6-8) is used
Primary Cutaneous B Cell Lymphoma

Cutaneous B Cell Lymphoma: New WHO-EORTC Classification

- Primary cutaneous marginal zone lymphoma
- Primary cutaneous follicle center lymphoma (including DLBCL)
- Primary cutaneous diffuse large B cell lymphoma, leg type
- Primary cutaneous diffuse large B cell lymphoma, other intravascular large B cell lymphoma

Willemze et al., Blood, 2005
Radiotherapy as Initial Treatment

<table>
<thead>
<tr>
<th></th>
<th>PCMZL n=25</th>
<th>PCFCL n=101</th>
<th>PCLBCL-LT n=27</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median</td>
<td>49</td>
<td>58</td>
<td>78</td>
</tr>
<tr>
<td>Extent</td>
<td></td>
<td></td>
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<tr>
<td>Solitary</td>
<td>36%</td>
<td>48%</td>
<td>44%</td>
</tr>
<tr>
<td>Localized</td>
<td>20%</td>
<td>45%</td>
<td>56%</td>
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<tr>
<td>Multifocal</td>
<td>44%</td>
<td>8%</td>
<td>0</td>
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<tr>
<td>Response to RT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>100%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>PR</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SD/PD</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Time to 1st relapse</td>
<td>16 mos</td>
<td>12 mos</td>
<td>17 mos</td>
</tr>
<tr>
<td>5-yr DFS</td>
<td>95%</td>
<td>97%</td>
<td>59%</td>
</tr>
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</table>

Senff et al., Arch Dermatol 2007

Outcome of Primary Cutaneous B Cell Lymphomas

<table>
<thead>
<tr>
<th></th>
<th>PCMZL (n = 21)</th>
<th>PCFCL (n = 17)</th>
<th>PCLBCL-LT (n = 50)</th>
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<tbody>
<tr>
<td>CR</td>
<td>100%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>PR</td>
<td>0</td>
<td>0</td>
<td>0</td>
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Rituximab for PCBCL

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<thead>
<tr>
<th></th>
<th>FCL</th>
<th>MZL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>ORR</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>CR</td>
<td>15 (71%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>PR</td>
<td>6 (29%)</td>
<td>3 (60%)</td>
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Morales et al., J Am Acad Dermatol 2008

Summary: PCBCL

- Radiotherapy provides definitive first-line treatment, with the exception of PCDLBCL-LT, which is treated with chemo as initial therapy
- Abbreviated irradiation is highly effective at relapse
- Rituximab is active in multi-lesional relapsed disease
THANK YOU!

Lymphomas (>> 60 histological subtypes)

Hodgkin's Lymphoma

Non-Hodgkin's Lymphomas

B Cell Lymphomas

T Cell Lymphomas

- follicular Lymphoma
- PTCL NOS
- PTCL NOS - ALCL
- mantle cell lymphoma
- diffuse large B cell lymphoma
- mycosis fungoides
- primary cutaneous
- Sezary syndrome
- MZL
- Burkitt's
- mycosis fungoides
- Sezary syndrome

systemic

primary cutaneous

indolent

aggressive

highly aggressive