The Role of Radiotherapy in Older Adults with DLBCL

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Disclosures

• Consultant and Advisory Board for Concerto HealthAI
Agenda

• Definitions of Radiotherapy (RT) for limited stage DLBCL
  – IFRT, ISRT, INRT
  – IMRT vs 3D-CRT
• Dose Changes

• RICOVER-60 (and the role of RT to bulky disease)

• Combined modality therapy (SWOG studies)
Definitions of Fields

Radiation Fields

• Involved Field
  – Based on 2D (bony) anatomy
  – Includes entire lymph node region

• Involved Site
  – Based on 3D anatomy (GTV→CTV→PTV)
  – Includes original extent of disease with a margin to account for imaging limitations and disease specifics

• Involved Node
  – Based on 3D anatomy (GTV→CTV→PTV)
  – Includes original extent of disease with margin
Phase III Trial on RT Dose
Radiotherapy and Oncology 2011;100:86

640 Sites of Aggressive NHL
82% DLBCL
67% stage I-II
73% as post-chemo consolidative RT
10% received Rituximab

30 Gy vs 40-45 Gy

Median f/u 5.6 yrs:

<table>
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<tr>
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<th>30 Gy (n=319)</th>
<th>40-45 Gy (n=321)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>5y FFLP</td>
<td>82%</td>
<td>84%</td>
<td>0.66</td>
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<tr>
<td>5y OS</td>
<td>64%</td>
<td>68%</td>
<td>0.29</td>
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30 Gy in 15 fractions
40-45 Gy in 20-23 fractions

Courtesy of Chris Kelsey
Side Effects

• Short Term:
  – Radiation Dermatitis, local hair loss, fatigue,
  – Head and Neck: dysphagia, odynophagia, taste change, xerostomia, (head and neck)
  – Chest: esophagitis, cough
  – Abdomen: nausea/vomiting, diarrhea, cramps
• Long Term:
  – Second malignancy (lower risk in older adults)
  – Head/Neck: dry eye, dry mouth, dental cavities, hypothyroidism
  – Chest: radiation pneumonitis, heart disease
  – Abdomen: small bowel obstruction
Evolution of Delivery of RT
Standard of Care for this case

**Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients with aggressive CD20+ B-cell lymphomas: a randomised controlled trial (RICOVER-60)**

- 4 armed study looking at 6 vs 8 cycles of CHOP +/- Rituximab.
- Radiotherapy was given to bulky disease and extranodal sites.
- Arm 3 (R-CHOP-14) was the winning arm with 3 yr EFS 66.5%.

Is Consolidative RT needed?

• To answer the question of whether RT is needed to bulky or extranodal sites?
  – An amendment to the Initial RICOVER-60 trial which continued the winning arm (R-CHOPx6) but without the consolidative RT
  – This was then compared to the initial group that included RT

Held et al. JCO 2014.
Can RT be used to decrease systemic toxicity

**SWOG S8736**

- Randomized trial of CHOP x 8 vs CHOP x 3 + IFRT
- 5 yr PFS and OS favored combined modality arm
- However a report in 2001 (only in abstract form) with 10 yr follow up showed survival curves began to overlap.
- Many assumed this due to higher risk of late relapse in RT arm.

**SWOG S0014**

- Phase 2 study of RCHOP x 3 + IFRT in patients with at least 1 high risk IPI feature.
- 4 yr PFS an OS were 88% and 92%
- No long term follow-up.

Miller et al. NEJM 1998

Persky et al. JCO 2008
Continued Risk of Relapse Independent of Treatment Modality in Limited-Stage Diffuse Large B-Cell Lymphoma: Final and Long-Term Analysis of Southwest Oncology Group Study S8736

Stephens et al. JCO 2016
PFS in RICOVER-60 study
Screening Geriatric Assessment

• Could a GA have helped us decide which standard to use for this patient?
• Should we be worried about late relapse in a patient with lower life expectancy?
GA-based treatment decision proposal?

Screening Geriatric Assessment

- After pre-phase treatment?
  - Fit
    - R-CHOP-14 x 6 per RICOVER-60
  - Pre-frail
    - R-CHOP-14 x 3/4 + ISRT (dose dependent on interim PET) Per SWOG S0014
  - Frail
    - Palliative Care
Summary

- Multidisciplinary care of older adults with DLBCL is critical
- Radiation delivery has improved from the days of 2D-IFRT
- Now has lower toxicity and better tolerability.
- Radiotherapy should be used to sites of bony involvement and bulky disease.
- R-CHOP x 3/4 + ISRT may be a good option for patients who are pre-frail or may have difficulty tolerating 6 cycles of R-CHOP.
- Screening Geriatric Assessments should be used and studied in this patient population.