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ELEVENTH ANNUAL MEETING

Salvage Radiotherapy in Relapsed/Refractory Large B-Cell Lymphoma After CAR T-Cell Therapy Failure

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INTRODUCTION

- While chimeric antigen receptor (CAR) T-cell therapy can lead to durable remission in many patients with relapsed/refractory (rel/ref) large B cell lymphoma (LBCL), the majority will develop progressive disease, necessitating effective salvage strategies.
- We sought to describe our experience with salvage radiation therapy (SRT) relative to other therapies in patients with rel/ref LBCL post-CD19-targeted CAR T-cell therapy failure.

AIM

- Estimate local control following SRT in patients with rel/ref LBCL after failure of commercial CD19 CAR T-cell therapy.
- Compare outcomes between SRT alone, systemic therapy, and combined modality therapy (CMT). All three categories were defined at the time of the first salvage therapy following CAR T-cell therapy failure.
- Evaluate the impact of radiation field size on survival.

METHOD

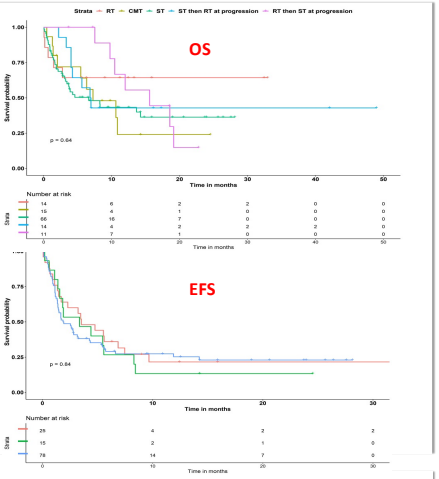
- A multi-institutional retrospective study was conducted in a database of 352 consecutive LBCL patients who received axicabtagene ciloleucel (axi-cel) or tisagenlecleucel (tisa-cel) between 2017 and 2021.
- Patients who relapsed following CAR T-cell therapy and received salvage therapies [RT alone, systemic therapy alone, or combined modality therapy (CMT)] were identified and analyzed.
- The CMT cohort included only patients who had been planned for both RT and systemic therapy as a first salvage regimen, regardless of the response to either.
- A separate analysis was then conducted for patients who were treated with comprehensive versus focal RT.

RESULTS

- A total of 120 patients with post-CAR T relapsed LBCL received salvage therapies (RT alone, 25 patients; CMT, 15 patients; systemic therapy alone, 80 patients).
- **Median follow-up after CAR T**: 10.2 mo (IQR: 5.2-20.9 months].
- **Median follow-up after salvage:** 5.6 mo (IQR: 1.9-12.1 months)
- **Median time from CAR T to PCF**
  - 3.0 mo (IQR: 1.1-5.1 mo)
- **Sites of failure**
  - **78% failed in previous sites of disease (n=93)**
    - **30% in these sites alone**
    - **48% concurrent with de novo sites**
- The median OS from the time of salvage therapy was not reached for the RT group, 7.3 months for the CMT group, 6.6 months for the systemic therapy group, 6.9 months for the systemic therapy then RT group, and 15.6 months for the RT then systemic therapy group (p=0.6).
- The median EFS was 3.5 months for the RT group, 3.3 months for the CMT group, and 1.9 months for the systemic therapy group (p=0.84).
- **54 patients received any SRT to total of 93 sites**
  - **Median dose: 30 Gy (range, 4-50.4 Gy)**
  - **Median fx: 10 (range, 1-28 fx)**
- **1 y-local control (in field) for the 81 assessable sites was > 80%.**
- **in-field PFS for bulky sites (≥5 cm as per PET/CT) as compared to non-bulky sites was not statistically different (p= 0.6):**
  - **bulky sites were not treated to higher BED_{10} (>30 Gy) as compared to non-bulky sites (p=0.7).**

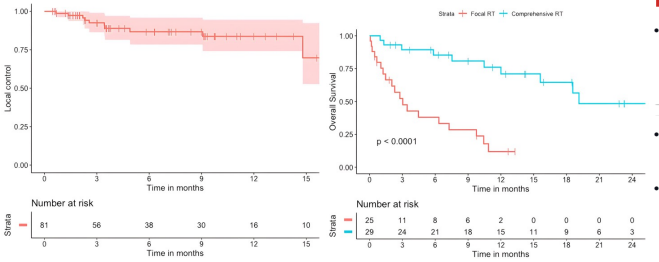
Patient Characteristics

	Overall (n=120)	SRT (n=25)	CMT (n=15)	ST (n=80)
Median age (range)	62 (15-81)	63 (43-81)	62 (40-78)	62 (15-79)
ECOG 0-1	100 (83.4%)	21 (84.0%)	11 (73.3%)	68 (85.1%)
Stage I-II	49 (40.8%)	16 (64.0%)	6 (40.0%)	27 (33.8%)
Extranodal disease	91 (75.8%)	18 (72.0%)	12 (80.0%)	61 (76.3%)
CNS disease	20 (16.7%)	5 (20.0%)	2 (13.3%)	13 (16.3%)
Bulky (>5 cm, non-CNS)	31 (31.0%)	5 (25.0%)	5 (38.5%)	21 (31.3%)
Elevated LDH	71 (59.2%)	8 (32.0%)	11 (73.3%)	52 (65.0%)
Bridging therapy	58 (48.3%)	12 (48.0%)	8 (53.3%)	38 (47.5%)
Axi-cel (vs. tisa-cel)	82 (68.3%)	14 (56.0%)	10 (66.7%)	58 (72.5%)
CR post-CAR T	51 (42.5%)	12 (48.0%)	5 (33.3%)	34 (42.5%)
ORR (CR+PR)	84 (70.0%)	20 (80.0%)	11 (73.3%)	53 (66.3%)



RESULTS

- **54 patients received SRT**
  - **Comprehensive: 29 patients (median 36.7 Gy)**
    - **Median OS: 19 mo**
  - **Focal: 25 patients (median 30 Gy)**
    - **Median OS: 3 mo**
- **26 of the 29 patients who received comprehensive RT had only a single site of disease, but survival for the 3 patients with >1 site of disease was not statistically different (p=0.17).**
- **Twenty-three of 29 patients who received comprehensive RT had limited-stage disease. Among these, there was no difference in median OS among the patients who received RT alone vs. those who received RT followed by additional therapies (log-rank p= 0.2).**
- **On multivariate survival analysis, achieving PR or CR post-CAR T (HR=0.5, 95% CI: 0.3-0.9, p= 0.01) was independently associated with superior OS.**
- **Advanced-stage disease (HR=2.2, 95% CI: 1.3-3.8, p= 0.004; HR=2.3, 95% CI: 1.4-3.6, p= <0.001) and elevated LDH (HR=2.9, 95% CI: 1.7-5.3, p= <0.001; HR=1.7, 95% CI: 1.1-2.7, p= 0.01) at the time of receiving salvage therapy were independent factors associated with a shorter OS and shorter EFS, respectively.**



CONCLUSIONS

- Our findings suggest that RT is a viable therapeutic strategy that can provide local control for LBCL relapsed post-CAR-T cell therapy, particularly in patients with limited-stage relapsed disease who were treated with comprehensive RT.
- High tumor burden at the time of salvage therapy is associated with worse outcomes.
- Future prospective studies should investigate combination of RT with other novel strategies, including lenalidomide, polatuzumab vedotin, loncastuximab tesirine, bispecific antibodies, and/or consolidation with allogeneic HSCT to optimize patient outcomes.