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Risk of Secondary Breast Cancer in Female Non-Hodgkin Lymphoma Survivors: 40 Years of Follow-Up Assessed by Treatment Modality

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Purpose/Objective(s): Survivors of non-Hodgkin lymphoma (NHL) are at increased risk of treatment associated secondary malignancies. We quantified the risk of developing a secondary breast cancer (SBC) in female NHL survivors with over 40 years of follow-up, and evaluated differences in risk by treatment modality.

Materials/Methods: Standardized incidence ratios (SIR, observed-to-expected [O/E] ratio), which accounts for patient years at risk, and absolute excess risk of SBC were assessed in 65,123 female patients diagnosed with NHL as a first malignancy between 1975 and 2016 in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Only invasive disease was considered SBC, ductal carcinoma in situ was excluded. Follow up was available through 2016. SIRs were also evaluated for patients stratified by age at and latency from diagnosis.

Results: In all, 7,010 (10.8%) patients received radiotherapy alone (RT), 30,393 (46.7%) received chemotherapy alone (CT), and 7,845 (12.0%) received chemotherapy and radiation (CRT). In total, there were 1,480 female SBCs with NHL survivors having a lower incidence of SBC than the endemic rate (O/E 0.91, 95% CI 0.87-0.96, $P < 0.05$). Patients treated with RT were at a higher risk of SBC than those who did not receive RT (O/E 1.02, 95% CI 0.93-1.12 vs O/E 0.87, 95% CI 0.82-0.93 respectively; $P < 0.05$). When stratified by treatment groups (No therapy, RT alone, CT alone, and CRT) there was a significantly higher risk of SBC in the CRT group than any other treatment group (O/E 1.18, 95% CI 1.03-1.34, $P < 0.05$). When patients were stratified by age at diagnosis, there was a significantly increased risk of SBC in patients who were diagnosed at age < 25 years irrespective of RT status with O/E ratios of 3.07 and 3.97 in the RT and no RT groups, respectively. However, there was no significant difference between these two treatment groups. This effect decreased with increasing age at diagnosis of NHL. The risk of developing SBC was significantly higher at > 10 years from NHL diagnosis (O/E 1.12) compared to < 10 years (O/E 0.82).

Conclusion: This is the largest study to examine SBC risk in patients with NHL. These results demonstrate that survivors of NHL have a lower incidence of invasive breast cancer compared to the general population. Patients treated with RT did have an increased risk over those with no RT; however, this did not exceed endemic breast cancer rate. The use of CRT and time > 10 years from NHL diagnosis were associated with higher risk of developing an SBC. Importantly, women diagnosed with NHL < 25 yrs of age had a higher rate of SBCs regardless of RT use. These results may help inform breast cancer screening protocols for women with a history of NHL.

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Efficacy and Toxicity of Alternative Radiation Treatment Schemes for Patients With Hematologic Malignancies: A Collaborative ILROG COVID Era Report

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Purpose/Objective(s): The COVID19 pandemic required radiation oncologists (ROs) to consider shorter treatment courses to minimize patient and staff exposure and conserve healthcare resources. Hematologic ROs adopted hypofractionated radiation therapy (hRT) regimens according to guidelines published by the International Lymphoma Radiation Oncology Group (ILROG). We report for the first time the preliminary efficacy and toxicity of these novel hypofractionated regimens in the treatment of hematologic malignancies.

Materials/Methods: We conducted a multicenter, multinational retrospective study under the direction of the ILROG. All patients receiving hRT according to ILROG guidelines from 1/1/2020 to 8/31/2020 were included. Patient and treatment details were abstracted from separate institutional databases. Toxicity was graded using CTCAE v5.0.

Results: Ninety-three patients from 4 institutions treated with 114 RT courses were included. Patient and treatment details are displayed in Table 1. Median follow up for the cohort was 179 days, and 77 patients (82%) were alive at last follow up. Maximal toxicity experienced by patients included Grade 1 (n=16), Grade 2 (n=1) and Grade 3 (n=1) toxicities. Of 80 sites with response assessment within the RT field, 69% of patients achieved a complete response (n=55), 20% partial response (n=16), 9% stable disease (n=7), and 2% progressive disease (n=2). No COVID19 infections during or after RT have been documented in this patient cohort.

Conclusion: HRT according to ILROG guidelines resulted in low rates of acute toxicity and reasonable short-term treatment efficacy. Longer follow up and comparison with control groups is needed to draw more definitive conclusions and will be presented at the Annual Meeting.

Abstract 2625 – Table 1

	N (%)
Age in years at RT start (median, range)	68 (31-94)
Sex (male)	44 (47)
ECOG (median, range)	1 (0-4)
Diagnosis (n=93)	
Classic Hodgkin Lymphoma	3 (3)
Diffuse Large B Cell	15 (16)
Mantle Cell	6 (7)
Marginal Zone	12 (13)
Follicular Grade 1-2	15 (16)
Follicular Grade 3 (A and 3B)	1 (1)
Multiple Myeloma	13 (14)
Solitary Plasmacytoma	1 (1)

(Continued)

Abstract 2625 – Table 1 (Continued)

	N (%)
Mycosis Fungoides	5 (5)
Peripheral T cell	1 (1)
Leukemia (including myeloid sarcoma)	8 (9)
Other	13 (14)
Therapy Intent (n = 114)	
Definitive	25 (22)
Consolidative	12 (11)
Salvage	4 (4)
Palliative	70 (60)
Bridge to CAR T-cell therapy	3 (3)
If prior systemic therapy (ST) (n = 54)	
Prior ST regimens > 3	22 (19)
Response to ST (n = 59)	
CR	13 (22)
PR	7 (12)
SD	1 (2)
PD	38 (64)
Treatment site (n = 114)	
Head and neck	23 (21)
Thorax	30 (26)
Abdomen	5 (4)
Pelvis	21 (18)
Extremity	23 (20)
Central Nervous System	11 (10)
Other	1 (1)
Radiation Dose in Gy (median, range)	4 (4-39)
Fractions (median, range)	1 (1-13)
Dose/Fractionation (n = 114)	
4 Gy / 1 fx;	57 (50)
8 Gy / 1 fx;	12 (11)
8 Gy / 2 fxs;	6 (5)
12 Gy / 3 fxs;	13 (11)
18 Gy / 6 fxs;	1 (1)
20 Gy / 5 fxs;	3 (3)
25 Gy / 5 fxs;	7 (6)
27 Gy / 9 fxs;	5 (4)
30 Gy / 6 fxs;	5 (4)
36 Gy / 12 fxs;	4 (4)
39 Gy / 13 fxs;	1 (1)
Prior RT received in field	20 (18)
Concurrent ST (n = 118)	8 (7)

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Factors Affecting Outcome of Bridging Radiotherapy (RT) Before CAR-T for High Grade Lymphoma

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Purpose/Objective(s): CD19 CAR-T therapy is the most effective salvage in chemo-refractory high-grade NHL. During manufacturing many patients (pts) require bridging therapy to halt disease progression and RT is one of the options due to its potential to control chemo-refractory disease. However, data guiding selection of pts who may benefit from bridging RT is limited and choice is usually made on the basis of disease extent only. In this study we examined factors which may affect outcome after RT bridging and CAR-T therapy

Materials/Methods: We reviewed all pts treated with bridging RT prior to CAR-T therapy in our institution from April 2019-January 2021. Data collected included pt characteristics, disease and treatment details, outcomes including relapse and survival.

Results: 27 pts received bridging RT. Median age was 57 years (19-79), 63% were male and 89% a performance status of 0-1. Table 1 shows disease & RT treatment details. 23 pts were infused (1 not infused due to infection and 3 pending). All but 1 completed planned RT and RT was well tolerated; only 1 pt had grade 3 toxicity. Of 23 pts available for outcome analysis, 22 had PET-CT after RT prior to CAR-T. 21 (91.3%) had partial metabolic response (PMR) or complete metabolic response (CMR) in RT field, but 12 of these had progressive disease out of field. At a median follow-up of 8.8 months (0.6-20.6); 12 pts have relapsed; 2 in-field; 5 out-of-field and 5 in both. 16 (69.6%) pts achieved local control with CMR (12; 52.2%) or PMR (4; 17.4%). Median PFS was 5.1 months (95% CI 0.0-11.9 months) and median OS was 17.8 months (95% CI 12.7-22.9 months). On Cox regression analysis bulky disease was associated with a significantly worse PFS (HR 1.05; 95% CI 1.0-1.07; P=0.05) and OS (HR 1.07; 95% CI 1.01-1.13; P=0.027). Relapse was less common in pts achieving CMR at some point compared to pts who did not (3/10 vs 9/13; $\chi^2=0.06$). Relapse rate at 12 months was higher with SUV max > 20 (8/13 vs 4/10, $\chi^2=0.3$); but was not affected by bulky disease (< 5 cms: 5/10; \geq 5 cms 7/13, $\chi^2=0.9$), CTV size (< 220 cm³: 4/9; \geq 220 cm³: 5/9; $\chi^2=0.6$), RT dose (< 30 Gy: 3/7, \geq 30 Gy: 9/15; $\chi^2=0.5$) and extent of disease included in RT field (all: 6/12, part: 6/11, $\chi^2=0.83$).

Conclusion: RT bridging prior to CAR-T therapy is an effective and well tolerated with 69.9% achieving local control. RT did not result in complications preventing infusion. Bulky disease, CTV size, RT dose, and RT extent did not affect local control. SUV max > 20 showed a trend towards a worse relapse rate and bulky disease was associated with a worse PFS and OS.

Abstract 2626 – Table 1

Disease	RT dose		Site	
De novo	19 (70.4%)	< 20 Gy	2 (7.4%)	Abdomen/pelvis 11 (40.7%)
Transformed	8 (29.6%)	20-30 Gy	7 (25.9%)	Axilla 1 (3.7%)
Bulk (\geq 5cms)		\geq 30 Gy	17 (63%)	Bone 4 (14.8%)
< 5cms	11 (40.7%)	NA	1 (3.7%)	Mediastinum 5 (18.5%)
\geq 5cms	16 (59.3%)	RT technique		Head & neck 5 (18.5%)
SUV max		IMRT	16 (59.3%)	Testes 1 (3.7%)
< 20	10 (37%)	3D-conformal	1 (3.7%)	RT field
\geq 20	17 (63%)	Simple	8 (29.6%)	All active dis 14 (51.9%)
		NA	2 (7.4%)	Main dis 13 (48.1%)

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