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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Improved Survival of R/R Double Hit/Triple Hit Lymphoma in the Era of CD19 Chimeric Antigen T Cell (CART) Therapy

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Introduction: DH/THL also classified as high-grade B cell lymphomas (HGBCL) with MYC and BCL2 and/or BCL6 rearrangements have higher risk of progression after initial treatment and poor response to salvage therapies compared to diffuse large B cell lymphoma (DLBCL), NOS. Recently, CART cell therapy has shown encouraging responses in treatment of relapsed refractory (R/R) DLBCL. In this retrospective study, we evaluated whether survival of (R/R) DH/THL is improved in the CART era.

Methods: In this multicenter retrospective study, adult pts (pts) with R/R DH/THL after anthracycline-based therapy were included. Demographic and clinical variables were obtained from electronic health records. Study objectives was overall

survival (OS) at 2 year landmark. We utilized full propensity score matching to compare progression free survival (PFS) and OS of CART with 2 nd line chemoimmunotherapy.

Results: 278 DH/THL pts treated between 2010-2020 were included. Median age was 63 years (range 52-74), 163 (58%) were male, 119 (43%) were classified as DLBCL and 116 (42%) as HGBCL; 40 (14%) were transformed from follicular lymphoma. 225 (82%) had advanced stage, 161 (67%) had elevated LDH, 85 (33%) had bulky disease, 74 (59%) had B symptoms. 105 (38%) pts treated for relapsed disease before 2018 were included in the pre-CART era cohort. 168 (60%) pts treated from 2018 onwards were included in the CART era cohort. 102 (60%) pts in CART cell era received CART cells, 40 (14%) received polatuzumab vedotin (pola), 10 (3.5%) received loncastuximab tesirine, tafasitamab and bispecific antibody each. Characteristics at relapse were similar in both groups.

Median follow up was 8.9 (0.2-146) months. 2-year OS estimate was 36% (CI $_{95}$: 30-42%) in entire population. Patients treated in CART cell era had significantly higher OS (2 yr OS: 43% [CI $_{95}$: 35-53]) compared to pts treated in pre-CART cells era (2-year OS: 24% [CI $_{95}$: 16-34], p=0.0006) (Figure 1).

In multivariable analyses, increasing age (HR = 1.02 (CI $_{95}$: 1.01, 1.04), p=0.003), extranodal disease (HR = 1.41 (CI $_{95}$: 1.00, 1.99), p<0.001), elevated LDH (HR = 1.57 (CI $_{95}$: 1.11, 2.24), p=0.01) were associated with inferior OS. Increasing time to relapse (HR = 0.98 (CI $_{95}$: 0.97, 0.99), p<0.001) was associated with superior OS. BCL6 rearrangement did not affect OS. When adjusted for these factors, treatment with CART cells was associated with higher 2 yr OS (HR = 0.33 (CI $_{95}$: 0.22, 0.49), p<0.001). Treatment with polatuzumab (HR = 1.07 (CI $_{95}$: 0.71, 1.6), p=0.07) was not significantly associated with OS in univariable analysis.

102 pts underwent CART cell therapy at any point for relapse; 94 (93%) were refractory to prior chemotherapy. 62 (60%) responded and 52 (50%) had CR after CART cells. 2-year PFS and OS after CART cell therapy were 28% (CI $_{95}$: 19-40) and 40% (CI $_{95}$: 30-53), respectively. Increasing time to CART was associated with inferior OS (HR: 1.02 (CI $_{95}$: 1.0-1.03, p=0.03) but not PFS (HR: 1.02 (CI $_{95}$: 0.99-1.04), p=0.2).

219 (79%) pts received curative intent salvage chemotherapy for 2 nd line. 2-year PFS and OS were 15% (CI $_{95}$: 11-20) and 38% (CI $_{95}$: 31-45), respectively. 21 pts received CART cell therapy for 2 nd line. 2 year PFS and OS in this small number of pts were 52% (CI $_{95}$: 35-79) and 70% (CI $_{95}$: 52-94), respectively. Due in part to the small number of pts who received CART cells in 2 nd line, we utilized full propensity score matched analysis to compare each patient in CART cell group to all possible matched controls in salvage chemotherapy group. Variables matched were age, LDH, extra nodal disease and time to relapse. In propensity score matched analysis, pts who received CART cells had significantly higher 2 year PFS (HR: 10.5 (CI $_{95}$: 3.4-17.5), p=002) and 2 year OS (HR: 7.5 (CI $_{95}$: 1.4-13), p=0.01).

Conclusions:

Survival of r/r DH/THL appears to have improved in the era of CART cell therapy. About 2/3 of pts refractory to chemotherapy respond to CART cells, and in multivariable analysis, receipt of CART cells was associated with improved OS. Increasing time to CART cells was associated with inferior survival. In a propensity score matched analysis utilizing full matching, CART cell therapy in 2 nd line was associated with significantly higher 2 year PFS and OS compared to curative intent salvage therapy. Other CD 19 and CD 20 targeting agents approved after CART cell therapy might contribute to favorable survival, effect of these agents could not be assessed because of small numbers.

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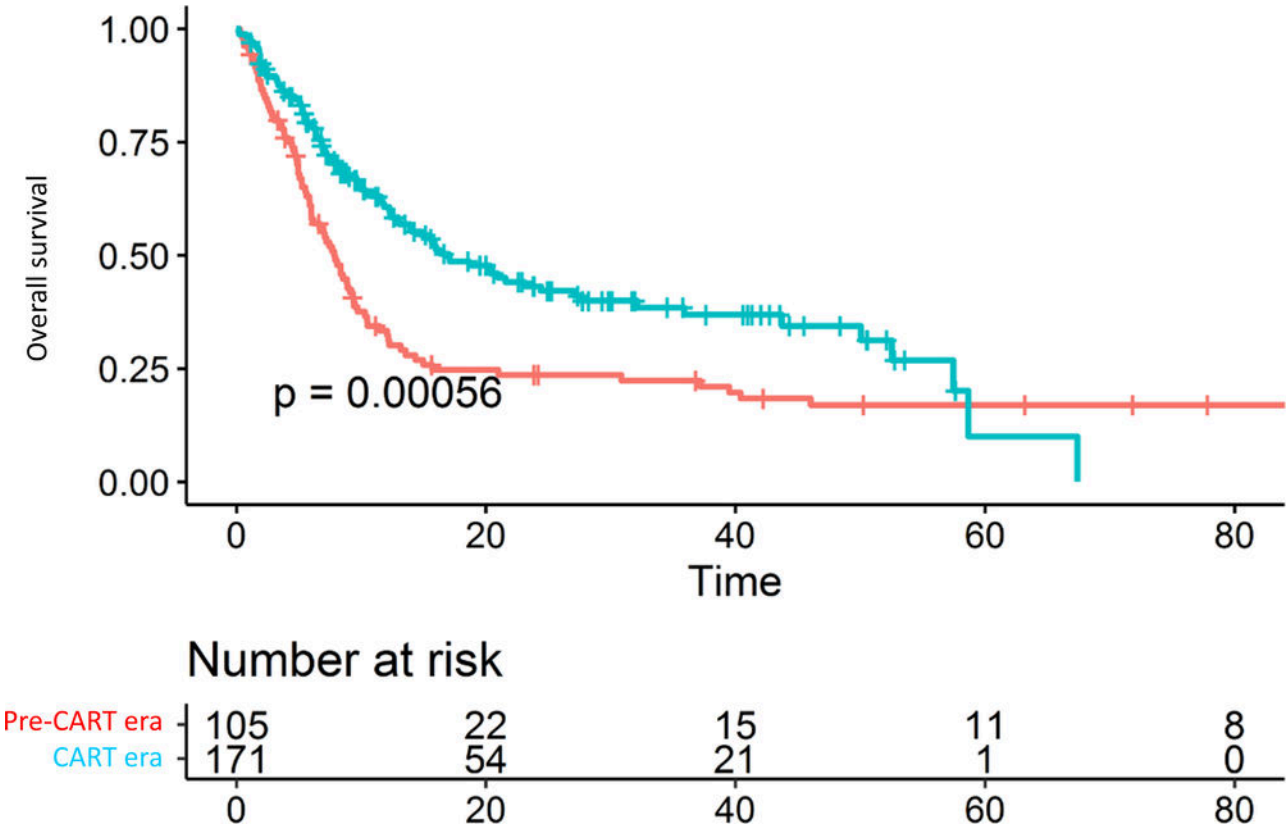

Figure 1

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