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ANTI-CD19 CAR T-CELL THERAPY FOR PATIENTS WITH RICHTER SYNDROME: A LYSA STUDY FROM THE DESCAR-T REGISTRY

H. BENSABER[1], E. BACHY[2], R. DULERY[3], D. BEAUVAIS[4], T. GASTINNE[5], B VILLEMAGNE[6], L. ROULIN[7], E. PAUBELLE[8], P. FEUGIER[9], E. FERRANT[2], C. CASTILLA-LLORENTE[10], T. LONGVAL[11], E. GAT[12], A. FAYARD[1], J-O. BAY[1], S. LE GOUILL[13], R HOUOT[14] and R. GUIEZE[1]

[1]Department of Hematology and Cell Therapy, Estaing University Hospital, Clermont-Ferrand, France, [2]Department of Hematology, Lyon Sud Hospital, Pierre-Benite, France, [3]Department of Hematology, Saint-Antoine Hospital, Paris, France, [4]Department of Hematology, University Hospital of Lille, Lille, France, [5]Hematology Department, Nantes University Hospital, Nantes, France, [6]Clinical Hematology, Hospital of Vendée, La Roche-sur-Yon, France, [7]Department of Hematology, Henri Mondor Hospital, Creteil, France, [8]Department of Hematology, University Hospital of Amiens, Amiens, France,[9]Department of Hematology, University Hospital of Nancy, Nancy, France, [10]Department of hematology, Gustave Roussy Institute, Villejuif, France, [11]Department of Hematology, Versailles Hospital, Le Chesnay-Rocquencourt, France, [12]LYSARC, The Lymphoma Academic Research Organisation, Lyon Sud Hospital, Pierre-Benite, France, [13]Curie Institute, Paris, France, [14]Department of Hematology, University Hospital of Rennes, Rennes, France

Lysa Lysarc DESCAR-T

I. INTRODUCTION

Richter syndrome (RS) refers to the onset of aggressive lymphoma, mostly diffuse large B-cell lymphoma (DLBCL), in patients with chronic lymphocytic leukemia (CLL). The outcome of RS patients is usually very poor with short survival (typically < 1 year) due to chemoresistance. Indeed, chemoimmunotherapy regimens used in *de novo* DLBCL failed to induce a significant complete remission rate (CRR) (R-CHOP, 7%; ofatumumab-CHOP, 27%)[1,2]. CD19-targeted chimeric antigenic receptor (CAR) T-cell therapy such as axicabtagene ciloleucel (axi-cel) and tisagenlecleucel (tisa-cel) have been transformative for patients with relapsed/refractory DLBCL.

II. AIM

We aimed to investigate the efficacy and safety profile of CD19-CAR T-cell therapy, axi-cel and tisa-cel for patients with Richter syndrome

III. METHOD

We conducted an analysis of the DESCAR-T registry which collects real-life data of patients treated with approved anti-CD19 therapies (axi-cel and tisa-cel) since July 1th, 2018 in France. We selected patients with biopsy-proven RS of DLBCL histology, treated by tisa-cel or axi-cel, in either the frontline or relapse setting. Data regarding prior CLL history were collected in addition to the DESCAR-T registry data. The data cut-off was April 26th, 2023. The primary endpoint was best CRR according to Cheson IWG 2014 (Lugano Classification) after CAR-T cell infusion. Secondary endpoints were overall survival (OS), progression-free survival (PFS), overall response rate (ORR), incidence and grading of immune effector cell-associated neurotoxicity syndrome (ICANS), cytokine release syndrome (CRS) (ASTCT Consensus) and hematological toxicity incidence (NCI CTCAE v5.0).

IV. RESULTS

CD19-directed CAR T-cell therapy was planned for 17 patients from November 12th, 2019 to July 26th, 15 were infused and subsequently included in the present analysis (1 patient refused the infusion and 1 was not infused due to disease progression).

Patients characteristics	
N	15
Median age	61 years (range 42-76)
Sex ratio M/F	1.5

CLL genomic features	
Del17p	2/10 (20%)
Del11q	6/9 (67%)
Complex Karyotype	3/7 (43%)
TP53 mutation	5/8 (62%)
Unmutated IGVH	5/7 (71%)

Prior therapeutic lines for CLL before RS	
Median number	2 (0-9)
Abstention	3 (20%)
Chemo-immunotherapy	9 (60%)
Ibrutininb	9 (60%)
Venetoclax	4 (27%)

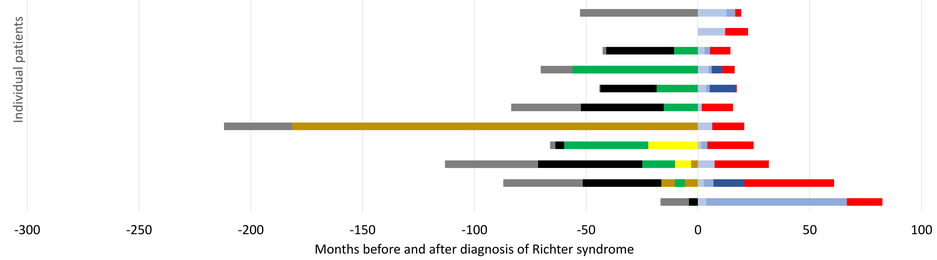
Richter syndrome features	
Median prior lines of therapy for RS	3
Patients with ≥ 1 prior lines of therapy for RS before infusion	13 (87%)
Median time from CLL diagnosis to RS	7 years (0-22)

Infusion of CART	
Bridge therapy before CART	13 (87%)
Disease status prior CAR T-cell infusion	
Progression	8 (53%)
Complete response	1 (7%)
Partial response	3 (20%)
Stable	2 (13%)
Non evaluated	1 (7%)
Axi-cel	7 (47%)
Tisa-cel	8 (53%)

Following CAR T-cell infusion with axi-cel (7 patients) or tisa-cel (8 patients), best CRR was 47% and best ORR was 53%. One-year PFS rate was 48.9% and one-year OS rate was 46.6%. After a median follow-up of 11.7 months (range, 0-23), 8 (53%) patients were alive, 7 (47%) patients died (3 from acute toxicity and 4 from disease progression).

Response after infusion of CART	
CRR	47%
ORR	53%

Treatment with duration of response of each line for CLL and Richter syndrome (n=15 patients)



Toxicity of CAR T cells

V. CONCLUSIONS

CD19-directed CAR T-cell therapy showed high response rates in our series of heavily pretreated RS patients.

Frequency of CAR T-cell-specific adverse events was in the range of what is observed in *de novo* DLBCL while severity appeared higher.

Our observations suggested that CART-cell should be considered in Richter Syndrome R/R

VI. REFERENCES

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VIII. CONTACT INFORMATION

Romain Guieze, MD, PhD
Department of Hematology and Cell Therapy, Estaing University Hospital
1 Rue Lucie et Raymond Aubrac, 63100 Clermont-Ferrand, France
rguieze@chu-clermontferrand.fr