



## The 65th ASH Annual Meeting Abstracts

## ORAL ABSTRACTS

## 627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

**CD19-Targeting CAR T-Cell Therapy in Transformed Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma: A Descar-T and US Collaborative Study**

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**Introduction:** Patients with histological transformation (HT) of Waldenström macroglobulinemia (WM) who relapse or are refractory (R/R) have a poor prognosis with standard chemoimmunotherapy, notably patients who are unable to undergo high dose chemotherapy (HCT) and autologous stem cell transplantation (ASCT) or who relapse after HCT/ASCT. CD19-targeted chimeric antigen receptor (CAR) T-cell therapies can lead to durable responses in relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) and thus may represent a promising therapeutic option in R/R transformed WM (tWM); however, data from pivotal trials is lacking. This study aimed to evaluate the efficacy and safety of anti-CD19 CAR T-cells in real-world patients with R/R tWM.

**Methods:** We retrospectively identified patients with biopsy-proven transformed WM/lymphoplasmacytic lymphoma treated with axicabtagene ciloleucl (axi-cel) or tisagenlecleucl (tisa-cel) in the French DESCAR-T registry (NCT04328298) and 2 US centers. The primary endpoint was best complete response rate (CRR). Secondary outcomes were best overall response rate (ORR), progression-free survival (PFS), overall survival (OS) and safety. Responses were assessed according to the Lugano 2014 criteria at 1 month, 3 months and 6 months. Subsequent assessments were per institutional practice. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded according to the ASTCT 2019 consensus criteria. Hematological toxicity and infections were graded according to the NCI CTCAE (version 5.0).

**Results:** Between June 2017 and May 2023, 22 patients (18 from DESCAR-T centers and 4 from US centers) with R/R tWM were treated with anti-CD19 CAR T-cells (13 axi-cel and 9 tisa-cel). Median age at WM diagnosis was 58 years (range 35-72). MYD88<sup>L265P</sup> and CXCR4 mutations were present in 85% (11/13) and 29% (2/7) of patients with available data, respectively. Patients received a median of 1 prior line of treatment (range, 0-4) for WM and 2 prior lines (range, 1-4) for HT. Eight patients

had received prior ASCT (2 for WM and 6 for HT) and 1 patient allogeneic SCT. The median time from WM to HT diagnosis was 4.5 years (range, 0-32) and 26 months (range, 3-90) from HT diagnosis to CAR T infusion. Of note, CNS involvement was present in 3 patients at DLBCL relapse before CAR T-cell therapy. At time of infusion, the median age was 66 years (range, 41-82) and 8 patients (36%) were older than 70 years. Median Eastern Cooperative Oncology Group (ECOG) was 1 (range, 0-2). Bridging therapy was administered to 16 patients (73%). Following bridging therapy, 6 patients had progressive disease (PD), 4 stable disease (SD) and 6 were responders (2 complete responses (CR) and 4 partial responses (PR)). After CAR T-cell infusion, best CRR was 82% and best ORR was 95%. The ORR/CRR was 95%/77% at 1 month, 76%/71% at 3 months and 68%/68% at 6 months. Seventeen patients (78%) experienced CRS, including 2 grade 3 (all after axi-cel), and 9 ICANS occurred (41%), including 1 grade 3 and 1 grade 4 (all after axi-cel). Eight patients (36%) presented infections, including 3 grade 3 and 1 grade 4. Neutropenia was reported in 78% (grade 3-4 = 68%), thrombocytopenia in 86% (grade 3-4 = 45%) and anemia in 86% (grade 3-4 = 32%) of patients. After a median follow-up of 17 months (range, 1-47), the 1-year PFS and OS were 70% and 84% respectively (figure). Five deaths were reported, 4 due to progressive disease and 1 from SARS-CoV-2 infection.

**Conclusion:** This study shows a high efficacy of anti-CD19 CAR T-cell therapy in R/R tWM with no unexpected toxicity. Longer follow-up is needed to confirm the long-term efficacy of CAR T-cells in tWM.

**Disclosures Di Blasi:** BMS: Consultancy; *abbvie*: Honoraria; *Incyte*: Honoraria; *Pfizer*: Honoraria; *Kite Gilead*: Consultancy, Honoraria; *Novartis*: Consultancy, Honoraria; *Janssen*: Consultancy. **Cheminant:** *Amgen*: Honoraria; *Innate Pharma*: Research Funding; *AstraZeneca*: Other: Travel accommodations and Meeting inscription; *Abbvie*: Research Funding. **Gros:** *Gilead*: Consultancy, Other: Travel and accommodation expenses; *Milteny*: Consultancy; *BMS*: Consultancy; *Novartis*: Consultancy, Other: Travel and accommodation expenses. **Bachy:** *Pfizer*: Honoraria, Other: Personal Fees; *Hospices Civils de Lyon Claude Bernard Lyon 1 University*: Current Employment; *Takeda*: Honoraria; *Bristol Myers Squibb*: Honoraria, Other: Personal Fees, Research Funding; *Incyte*: Honoraria; *Novartis*: Honoraria, Other: Personal Fees; *Amgen*: Research Funding; *Roche*: Consultancy, Honoraria; *Kite, a Gilead Company*: Honoraria, Other: Personal Fees. **Treon:** *Eli Lilly*: Consultancy, Research Funding; *Janssen*: Consultancy, Research Funding; *BeiGene*: Consultancy, Research Funding; *Bristol Myers Squibb*: Consultancy, Research Funding; *Abbvie/Pharmacyclics*: Consultancy, Research Funding. **Reshef:** *Takeda*: Consultancy, Honoraria, Research Funding; *Atara Biotherapeutics*: Consultancy, Research Funding; *Bristol Myers Squibb*: Honoraria, Research Funding; *Gilead Sciences*: Consultancy, Honoraria, Other: Travel support, Research Funding; *J&J*: Research Funding; *Jasper*: Consultancy; *Capstan*: Consultancy; *MidaTech*: Consultancy; *Orca*: Consultancy; *SyntheKine*: Consultancy, Research Funding; *CareDx*: Research Funding; *Precision Biosciences*: Research Funding; *Bayer*: Consultancy; *TScan*: Consultancy, Research Funding; *Regeneron*: Consultancy; *Instil Bio*: Consultancy; *Incyte*: Consultancy, Research Funding; *Allogene*: Consultancy; *Quell Biotherapeutics*: Consultancy; *Sanofi*: Research Funding; *Immatics*: Research Funding; *TCR2*: Research Funding. **Castillo:** *AstraZeneca*: Consultancy, Research Funding; *Loxo*: Consultancy, Research Funding; *Abbvie*: Consultancy, Research Funding; *BeiGene*: Consultancy, Research Funding; *Pharmacyclics*: Consultancy, Research Funding; *Kite*: Consultancy; *Mustang Bio*: Consultancy; *Cellectar*: Consultancy, Research Funding. **Houot:** *Kite/Gilead*, *Novartis*, *Bristol-Myers Squibb/Celgene*, *ADC Therapeutics*, *Incyte*, *Milteny*: Consultancy; *Kite/Gilead*, *Novartis*, *Incyte*, *Janssen*, *MSD*, *Takeda*, *F. Hoffmann-La Roche Ltd*: Honoraria.

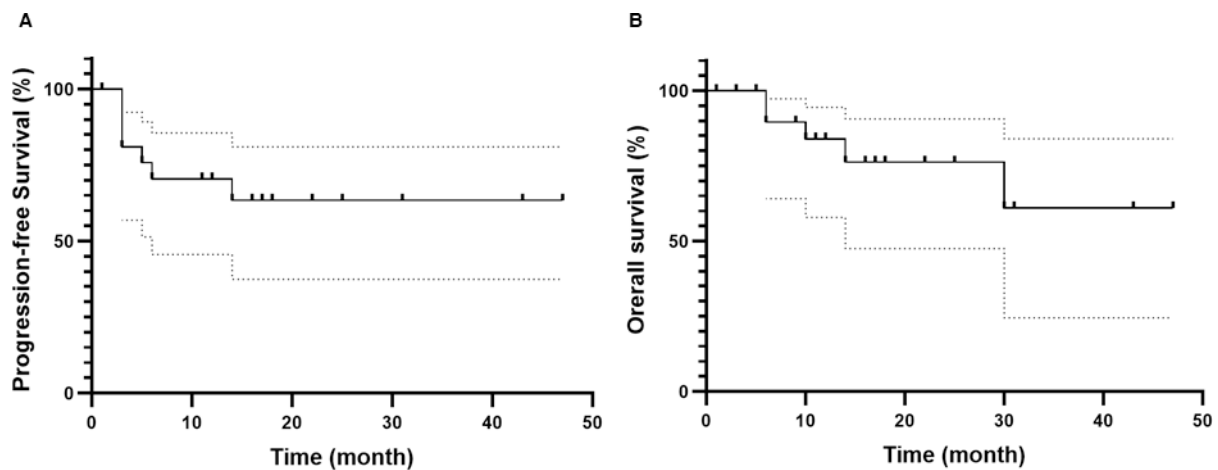


Figure 1

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