



EPICS

CURRENT AND FUTURE STATE OF CAR T IN EUROPE

Key Highlights

- > On 20 June 2019, Aptitude Health gathered a group of lymphoma and CAR T-cell therapy experts to attend the closed-session Emerging Paradigms in Care Series (EPICS) panel meeting
- > The goals of the expert panel were to discuss current clinical practices and latest developments with CAR T in lymphoma, and gain a better understanding of challenges facing the real-world adoption of this novel treatment across Europe

Time	Topic	Speaker/Moderator
16.30 – 16.45	Welcome, Introductions, and Meeting Objectives • Round-robin – Experiences With CAR T	Chadi Nabhan, MD, MBA, FACP
16.45 – 16.55	Update on CAR T: Highlights From EHA and ICML	Marie José Kersten, MD, PhD
16.55 – 17.10	What Differentiates Various CAR T-Cellular Products?	Catherine Thieblemont, MD, PhD
17.10 – 17.55	Discussion: Differences and Similarities Between the 2 Approved CAR T-Cellular Products in the Real World	All
Patient Journey		
17.55 – 18.05	Sharing Experiences: The Patient Journey in the US	Sattva Neelapu, MD
18.05 – 18.10	Sharing Experiences: The Patient Journey in France	Catherine Thieblemont, MD, PhD
18.10 – 18.35	Discussion: The Patient Journey in Europe	All
18.35 – 18.50	<i>Working Dinner</i>	
CAR T Experience in the US – How Will It Translate in the EU?		
18.50 – 18.55	Sharing Experiences: Real-World CAR T Adoption and Reimbursement in the US	Sattva Neelapu, MD
18.55 – 19.05	Sharing Experiences: Commercial Challenges and Learnings From the US Market	Sattva Neelapu, MD
19.05 – 19.35	Discussion: Challenges in Administration and Reimbursement in the EU	All
Future of CAR T in the EU		
19.35 – 19.45	New Developments in CAR T	Max Topp, MD
19.45 – 19.55	Point-of-Care CAR T Therapy in the EU	Julio Delgado, MD, PhD
19.55 – 20.20	Discussion: Future of CAR T in the EU	All
20.20 – 20.30	Summary and Closing Remarks	Chadi Nabhan, MD, MBA, FACP

- > Chair: Catherine Thieblemont, MD, PhD
 - Hôpital Saint-Louis, Paris, France
- > Moderator: Chadi Nabhan, MD, MBA, FACP
 - Aptitude Health, Atlanta, United States
- > Paolo Corradini, MD
 - Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
- > Julio Delgado, MD, PhD
 - Hospital Clínic de Barcelona, Spain
- > Marie José Kersten, MD, PhD
 - Academic Medical Center, Amsterdam, The Netherlands
- > Kim Linton, MBChB, PhD
 - University of Manchester, United Kingdom
- > Tom van Meerten, MD, PhD
 - University Medical Center Groningen, The Netherlands
- > Sattva Neelapu, MD
 - MD Anderson Cancer Center, Houston, United States
- > Max Topp, MD
 - University of Würzburg, Germany



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Update on CAR T: Key Highlights
From ASCO, EHA, and ICML

> **EHA PS943:** Safety and efficacy of tisagenlecleucel in pediatric and young adults –

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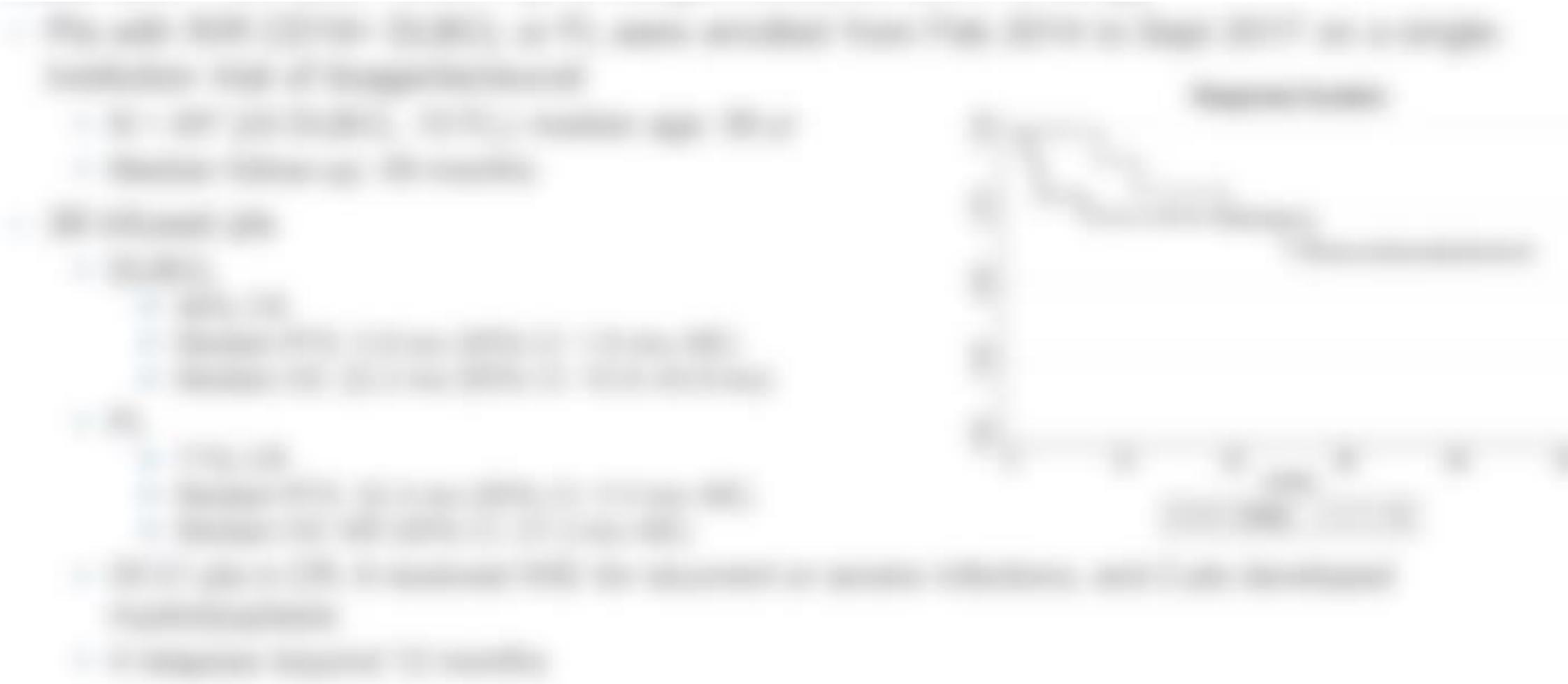
> **EHA S1600:** Real-world results on CD19 CAR T for 60 French patients included in a

[The following text is heavily blurred and illegible.]

> **Axi-cel**

- **ASCO 7562:** High baseline metabolic tumor volume is associated with decreased and less-

> **ICML 090:** Four-year follow-up of tisagenlecleucel (E.A. Chong)



> **EHA PS1067:** Preliminary results of earlier steroid use in pts treated with axi-cel in ZUMA-1 cohort

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CONGRESS HIGHLIGHTS: PRELIMINARY RESULTS FROM THE TRANSCEND STUDY (1/2)

> TRANSCEND NHL-001: Ongoing phase I study evaluating the safety and

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CONGRESS HIGHLIGHTS: PRELIMINARY RESULTS FROM THE TRANSCEND STUDY (2/2)

> **ASCO 7516:** Preliminary results in MCL (M. Wang)

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> **EHA PF440:** Survey assessing knowledge gaps and educational needs for

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**Differences and Similarities
Between the 2 Approved CAR
T-Cellular Products in the Real
World**

DIFFERENCES BETWEEN JULIET AND ZUMA-1 (1/4)

> Dr Thieblemont highlighted in her presentation several fundamental differences between

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DIFFERENCES BETWEEN JULIET AND ZUMA-1 (2/4)

JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
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<p>Primary endpoint: Overall survival (OS)</p> <p>Secondary endpoints: Progression-free survival (PFS), Time to next treatment (TTNT), Quality of life (QoL)</p>	<p>Primary endpoint: Overall survival (OS)</p> <p>Secondary endpoints: PFS, TTNT, QoL</p>
<p>Population: Newly diagnosed, relapsed, or refractory multiple myeloma</p> <p>Intervention: Carfilzomib, lenalidomide, and dexamethasone</p>	<p>Population: Newly diagnosed, relapsed, or refractory multiple myeloma</p> <p>Intervention: Carfilzomib, lenalidomide, and dexamethasone</p>
<p>Comparison: Standard of care (SOC)</p>	<p>Comparison: SOC</p>
<p>Statistical significance: p < 0.001 for OS</p>	<p>Statistical significance: p < 0.001 for OS</p>

DIFFERENCES BETWEEN JULIET AND ZUMA-1 (3/4)

JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
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DIFFERENCES BETWEEN JULIET AND ZUMA-1 (4/4)

JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
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DISCUSSION: DIFFERENCES AND SIMILARITIES BETWEEN CAR T-CELLULAR PRODUCTS

> Experts stressed that a direct comparison of clinical efficacy and safety data between the

> Reiterating the difficulties of direct comparisons, experts expressed no strong preference for the

DISCUSSION: EXPERIENCES FROM REAL-WORLD PRACTICE (1/2)

- > Efficacy of tisagenlecleucel and axi-cel is in line with what is expected from clinical trials

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*Postmeeting note: Gauthier J, et al. ASH 2018. Abstract 299.

DISCUSSION: EXPERIENCES FROM REAL-WORLD PRACTICE (2/2)

> Dropout rates are higher (up to 60%) than in pivotal trials (big problem!). Main reason: long wait

> Optimal patient selection for CAR T-cell therapy is viewed as a moving target, as experts are still in the

DISCUSSION: THE PLACE OF CAR T IN THE TREATMENT ALGORITHM

> Standards establishing how CAR T-cell therapy might best fit within current treatment algorithms for

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The Patient Journey in Europe

THE PATIENT JOURNEY IN THE US

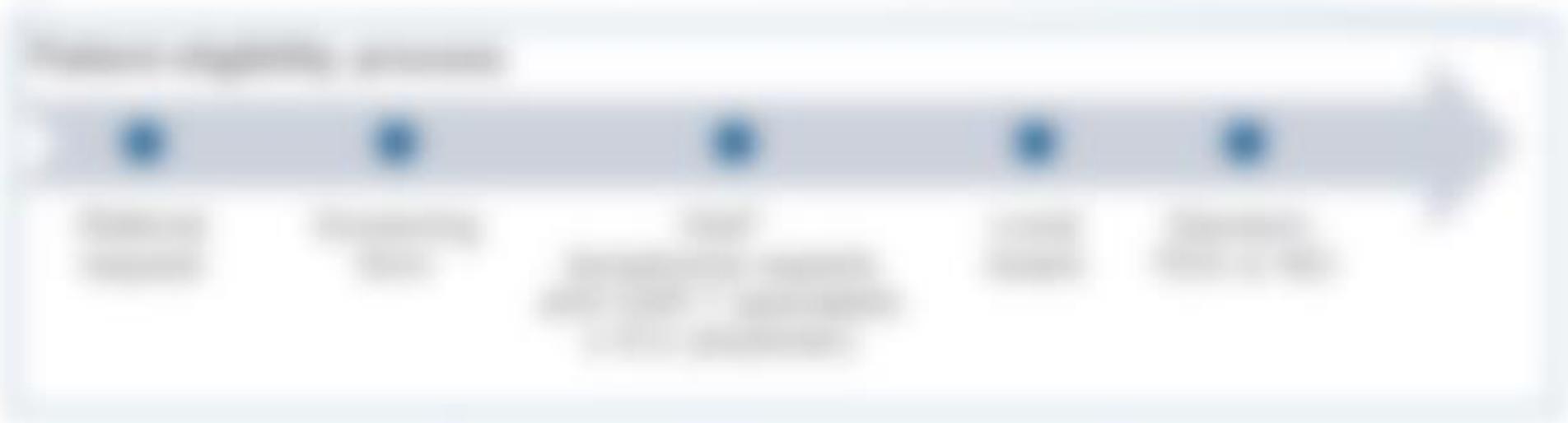
1-2 weeks or longer



THE PATIENT JOURNEY IN FRANCE: EXPERIENCE FROM HÔPITAL SAINT-LOUIS (1/2)

> Dr Thieblemont summarized real-world results from 60 French patients included in a temporary

THE PATIENT JOURNEY IN FRANCE: EXPERIENCE FROM HÔPITAL SAINT-LOUIS (2/2)



> In addition to clinical challenges such as managing toxicities, the patient journey for CAR T-cell

> Experts stressed the need for more data, to gain an overall understanding of the factors impacting the ultimate

> Given the hype induced by media, experts are faced with challenging patient expectations before,

DISCUSSION: PATIENT REGISTRY AND DATA CAPTURE

> Experts noted the importance of establishing high-quality data registries to collect standardized long-term data



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**Challenges in Administration and
Reimbursement in the EU**

SHARING EXPERIENCES: REAL-WORLD CAR T ADOPTION AND REIMBURSEMENT IN THE US

> Dr Neelapu shared data from 2 retrospective analyses on real-world experience with axi-cel presented at

ASCO 2022
Abstract 7500
Real-world experience with axi-cel in the US
Dr Neelapu presented data from a retrospective analysis of 100 patients who received axi-cel for relapsed and refractory diffuse large B-cell lymphoma (R/R DLBCL) in the United States. The study included patients from various geographic regions and healthcare settings. Key findings include a high rate of CAR T cell manufacturing success, with approximately 90% of patients receiving their treatment. The overall response rate was high, with a significant number of patients achieving complete remission. The study also highlighted the challenges of reimbursement and access to CAR T cell therapy in the real-world setting.

ASCO 2022
Abstract 7501
Real-world experience with axi-cel in the US
Dr Neelapu presented data from a second retrospective analysis of 100 patients who received axi-cel for R/R DLBCL in the US. This study focused on the impact of reimbursement and access on treatment outcomes. It found that patients who received axi-cel had significantly better outcomes compared to those who did not, despite the challenges of reimbursement. The study emphasized the need for improved reimbursement policies to ensure that all eligible patients have access to this life-saving therapy.

SHARING EXPERIENCES: COMMERCIAL CHALLENGES AND LEARNINGS FROM THE US MARKET

> Dr Neelapu discussed barriers to real-world CAR T adoption in the US

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DISCUSSION: PAYER LANDSCAPE

US	Europe
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DISCUSSION: CHALLENGES IN IMPLEMENTING CAR T IN EUROPE

> Experts discussed challenges associated with uptake and scale-up of CAR T-cell therapy in Europe



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Future of CAR T in the EU

(1/4)

> **ICML 118:** Phase I, first-in-human clinical trial of third-generation CD19-targeted 19-28Z/4-

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(2/4)

- > **ICML 117:** Novel BAFF-R CAR T-cell therapy for CD19 antigen-loss relapsed B-cell

[Blurred text area containing abstract details of the ICML 117 presentation, including study objectives and preliminary results.]



(3/4)

> **ICML 120:** CD19-targeted CAR T cell therapy with concurrent ibrutinib for CLL after prior



(4/4)

> **ICML 122:** Liso-cel plus durvalumab (anti-PD-L1) in R/R aggressive B-cell NHL

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NEW DEVELOPMENTS IN CAR T: POINT-OF-CARE CAR T THERAPY IN THE EU

> Dr Delgado described the implementation of a CAR T-cell production system within his

The image contains two blurred diagrams illustrating CAR T-cell production systems. The left diagram shows a process flow with a red box labeled "POINT-OF-CARE CAR T". The right diagram shows a similar process flow with a red box labeled "POINT-OF-CARE CAR T".

DISCUSSION: NEXT STEPS IN CAR T

> Experts reviewed promising strategies and bioengineering solutions to maximize CAR T outcomes,

- > Experts have a favorable opinion of bispecific T-cell engagers in lymphoma; unlike CAR Ts, they are

DISCUSSION: COMPETITIVE LANDSCAPE (2/2)

> ADCT-402 (loncastuximab tesirine) is perceived as considerably active with durable CRs in a

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Abbreviations

ABBREVIATIONS (1/2)

- > 1L – first line
- > 2L – second line
- > ADC – antibody-drug conjugate
- > AE – adverse event
- > ALC – absolute lymphocyte count
- > ALL – acute lymphoblastic leukemia
- > ANC – absolute neutrophil count
- > APC – absolute phagocyte count
- > ASCO – American Society of Clinical Oncology
- > ASCT – autologous stem cell transplant
- > ASH – American Society of Hematology
- > allo-SCT – allogeneic stem cell transplantation
- > auto-SCT – autologous stem cell transplantation
- > axi-cel – axicabtagene ciloleucel
- > CAR – chimeric antigen receptor
- > CIBMTR – Center for International Blood and Marrow Transplantation Research
- > CLL – chronic lymphocytic leukemia
- > CMS – Centers for Medicare & Medicaid Services
- > CNS – central nervous system
- > CR – complete remission
- > CRi – complete remission with incomplete blood count recovery
- > CRP – C-reactive protein
- > CRS – cytokine release syndrome
- > ctDNA – circulating tumor DNA
- > DL – dose level
- > DLBCL – diffuse large B-cell lymphoma
- > DOR – duration of response
- > EBMT – European Society for Blood and Marrow Transplantation
- > ECOG PS – Eastern Cooperative Oncology Group performance status
- > EFS – event-free survival
- > EHA – European Hematology Association
- > EMA – European Medicines Agency
- > FACT – Foundation for the Accreditation of Cellular Therapy
- > FDA – US Food and Drug Administration
- > FL – follicular lymphoma

ABBREVIATIONS (2/2)

- > HBV – hepatitis B virus
- > HEOR – health economics and outcomes research
- > Hgb – hemoglobin
- > ICANS – immune cell-associated neurologic syndrome
- > ICML – International Conference on Malignant Lymphoma
- > ICU – intensive care unit
- > IL – interleukin
- > IRC – independent review committee
- > ITT – intention-to-treat
- > IV – intravenous
- > IVIG – intravenous immunoglobulin
- > liso-cel – lisocabtagene maraleucel
- > MCL – mantle cell lymphoma
- > mITT – modified intention-to-treat
- > MRD – minimal residual disease
- > NA – not available
- > NE – not evaluable
- > NR – not reported
- > NHL – non-Hodgkin lymphoma
- > NK – natural killer
- > ORR – overall response rate
- > OS – overall survival
- > PD – progressive disease
- > PD-L1 – programmed cell death protein 1 ligand 1
- > PFS – progression-free survival
- > PMBCL – primary mediastinal B-cell lymphoma
- > PR – partial remission
- > pts – patients
- > REMS – Risk Evaluation and Mitigation Strategy
- > R/R – relapsed/refractory
- > RWE – real-world evidence
- > SCT – stem cell transplantation
- > SmPC – summary of product characteristics
- > TFL – transformed follicular lymphoma
- > TTR – time to response
- > WM – Waldenström macroglobulinemia