APTITUDE HEALTH

EPICS

CURRENT AND FUTURE STATE OF CAR T IN EUROPE

Key Highlights

BACKGROUND

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- 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

AGENDA

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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	*Working Dinner*	
	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

FACULTY

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- 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

CONGRESS HIGHLIGHTS: KEY ABSTRACTS IN ALL

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

CONGRESS HIGHLIGHTS: KEY ABSTRACTS IN DLBCL (1/3)

EPICS

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

CONGRESS HIGHLIGHTS: KEY ABSTRACTS IN DLBCL (2/3)

EPICS

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

CONGRESS HIGHLIGHTS: KEY ABSTRACTS IN DLBCL (3/3)

EPICS

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

CONGRESS HIGHLIGHTS: SAFETY MANAGEMENT

EPICS

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

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

EPICS

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

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

EPICS

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

CONGRESS HIGHLIGHTS: KNOWLEDGE GAPS

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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)

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- Dr Thieblemont highlighted in her presentation several fundamental differences between

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

	JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]

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

EPICS

	JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
[illegible]	[illegible]	[illegible]

Axicabtagene ciloleucel CHMP assessment report. 2018. www.ema.europa.eu; Tisagenlecleucel CHMP assessment report. 2018. www.ema.europa.eu; Kymriah [summary of product characteristics]. Dublin, Ireland: Novartis Europharm Limited. https://www.ema.europa.eu/en/documents/product-information/kymriah-epar-product-information_en.pdf

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

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	JULIET Phase II, single-arm, open-label	ZUMA-1 Phase II, single-arm, open-label
[illegible]	[illegible]	[illegible]

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Schuster S, et al. *N Engl J Med.* 2019;380:45-56; Locke FL, et al. *Lancet Oncol.* 2019:20:31-42.

DISCUSSION: DIFFERENCES AND SIMILARITIES BETWEEN CAR T-CELLULAR PRODUCTS

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

DISCUSSION: SELECTING A PRODUCT IN THE REAL WORLD

EPICS

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

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

EPICS

- 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)

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

DISCUSSION: CRITERIA FOR OPTIMAL PATIENT SELECTION

EPICS

- 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

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- 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

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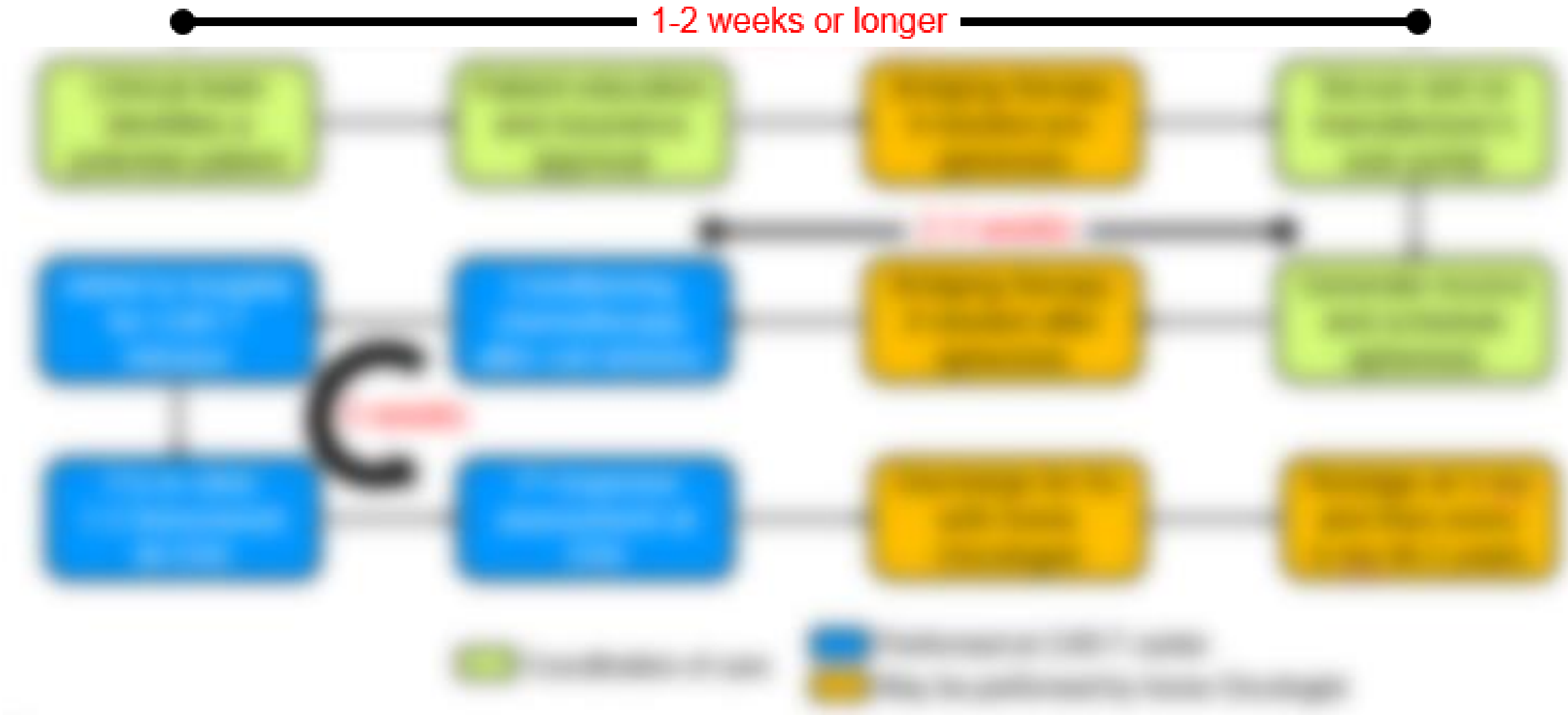
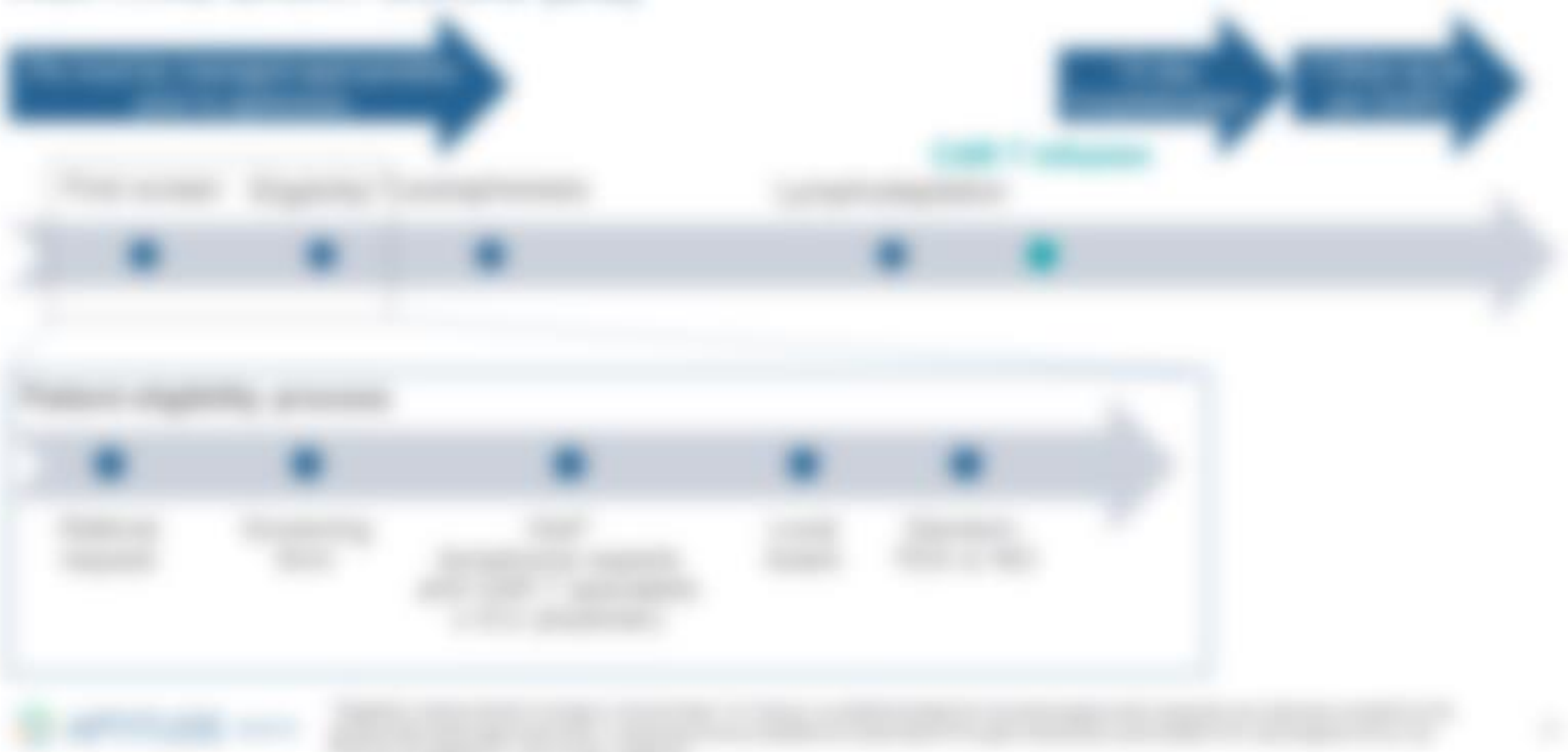


THE PATIENT JOURNEY IN FRANCE: EXPERIENCE FROM HÔPITAL SAINT-LOUIS (1/2)

- 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)



DISCUSSION: THE PATIENT JOURNEY IN EUROPE (1/3)

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

DISCUSSION: THE PATIENT JOURNEY IN EUROPE (2/3)

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

DISCUSSION: THE PATIENT JOURNEY IN EUROPE (3/3)

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

DISCUSSION: PATIENT REGISTRY AND DATA CAPTURE

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- 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

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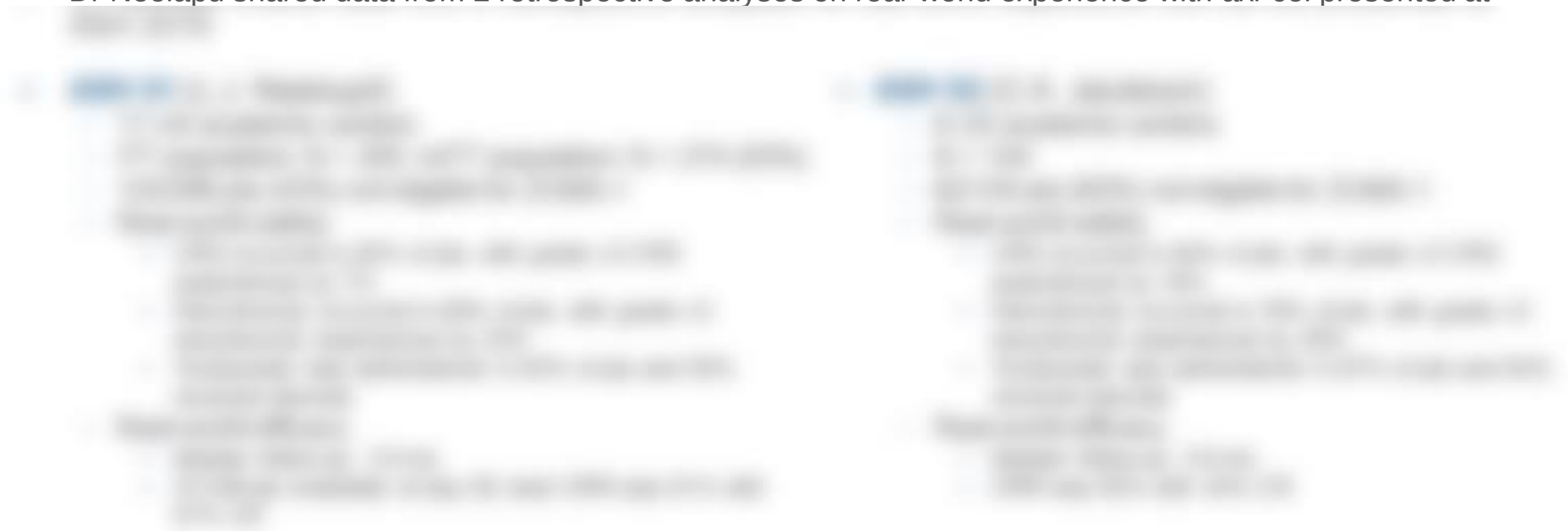
> Dr Neelapu shared data from 2 retrospective analyses on real-world experience with axi-cel presented at



SHARING EXPERIENCES: COMMERCIAL CHALLENGES AND LEARNINGS FROM THE US MARKET

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

DISCUSSION: PAYER LANDSCAPE

	US	Europe
[illegible]	[illegible]	[illegible]

DISCUSSION: CHALLENGES IN IMPLEMENTING CAR T IN EUROPE

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- 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

NEW DEVELOPMENTS IN CAR T: HIGHLIGHTS FROM ICML (1/4)

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

NEW DEVELOPMENTS IN CAR T: HIGHLIGHTS FROM ICML (2/4)

EPICS

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

NEW DEVELOPMENTS IN CAR T: HIGHLIGHTS FROM ICML (3/4)

EPICS

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

NEW DEVELOPMENTS IN CAR T: HIGHLIGHTS FROM ICML (4/4)

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

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

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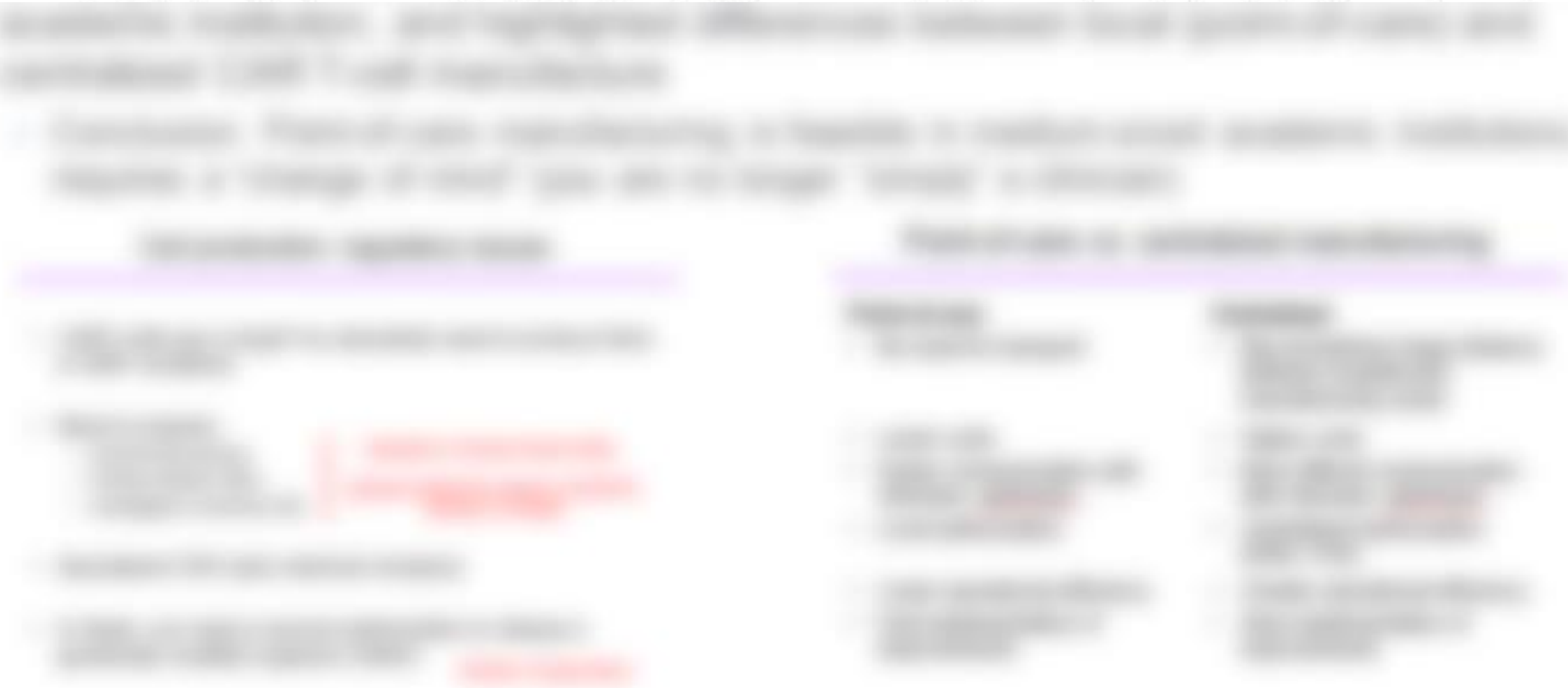
> Dr Delgado described the implementation of a CAR T-cell production system within his



DISCUSSION: NEXT STEPS IN CAR T

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

DISCUSSION: COMPETITIVE LANDSCAPE (1/2)

EPICS

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

DISCUSSION: COMPETITIVE LANDSCAPE (2/2)

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

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Abbreviations

ABBREVIATIONS (1/2)

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- 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)

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- 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