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Congress Coverage: ASH 2021 – Focus on Lymphoma

December 17, 2021

Report Contents

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Meeting Snapshot

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VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
December 17, 2021

SELECTED ASH ABSTRACT PRESENTATIONS by key experts

INSIGHT REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in lymphoma

- 4 from US
- 3 from Europe

LYMPHOMA-SPECIFIC DISCUSSIONS on latest research updates, therapeutic advances, and their application in clinical decision-making

Panel Consisting of 4 US and 3 European Lymphoma Experts

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Matthew Lunning, DO, FACP
University of Nebraska Medical Center

John N. Allan, MD
Weill Cornell Medicine

Stefan Barta, MD, MS, MRCPCUK
Penn Medicine

CHAIR:
Brad Kahl, MD
Washington University School of Medicine

John Gribben, MD, DSc, FRCP, FRCPath
Cancer Research UK Barts Centre

Pier Luigi Zinzani, MD, PhD
University of Bologna Institute of Hematology and Medical Oncology

Olivier Tournilhac, MD, PhD
Clermont Auvergne University

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Meeting Agenda

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Time (EST)	Topic	Speaker/Moderator
1.30 PM – 1.35 PM	**Welcome and Introductions**	Brad Kahl, MD
1.35 PM – 1.50 PM	**Advances in DLBCL/Aggressive B-Cell Lymphoma**	Matthew Lunning, DO, FACP
1.50 PM – 2.15 PM	*Discussion and Key Takeaways*	All Moderator: Brad Kahl, MD
2.15 PM – 2.25 PM	**Advances in CAR T**	John N. Allan, MD
2.25 PM – 2.50 PM	*Discussion and Key Takeaways*	All Moderator: Brad Kahl, MD
2.50 PM – 3.00 PM	**Advances in FL**	Olivier Tournilhac, MD, PhD
3.00 PM – 3.10 PM	**Advances in MCL and MZL**	Pier Luigi Zinzani, MD, PhD
3.10 PM – 3.35 PM	*Discussion and Key Takeaways*	All Moderator: Brad Kahl, MD
3.35 PM – 3.45 PM	Break	
3.45 PM – 3.55 PM	**Evolving Use of BTK Inhibitors in CLL**	John Gribben, MD, DSc, FRCP, FRCPath
3.55 PM – 4.20 PM	*Discussion and Key Takeaways*	All Moderator: Brad Kahl, MD
4.20 PM – 4.30 PM	**Role of Fixed-Duration and MRD-Guided Strategies in CLL**	Stefan K. Barta, MD, MS, MRCPCUK
4.30 PM – 4.55 PM	*Discussion and Key Takeaways*	All Moderator: Brad Kahl, MD
4.55 PM – 5.00 PM	**Wrap-up and Close**	Brad Kahl, MD

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Advances in DLBCL/Aggressive B-Cell Lymphoma

Congress Highlights From ASH 2021

Phase III POLARIX: Pola–R-CHP vs R-CHOP in Patients With Previously Untreated DLBCL

Tilly H, et al. 2021, ASH #LBA-1

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STUDY POPULATION

EFFICACY

Phase II LOTIS-3: Planned Interim Analysis of Loncastuximab Tesirine Plus Ibrutinib in Patients With Advanced DLBCL

Carlo-Stella C, et al. 2021, ASH #54

EPICS

STUDY POPULATION

EFFICACY

RE-MIND2: Observational, Retrospective Cohort Study of Systemic Therapies for R/R DLBCL

Nowakowski GS, et al. 2021, ASH #183

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BACKGROUND

Phase II: R2 as Frontline Chemo-Free Therapy for Elderly, Frail Patients With DLBCL

Gini G, et al. 2021, ASH #305

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STUDY POPULATION

DOSING

Phase II KEYNOTE-170: Final Analysis of Pembrolizumab in R/R PMBCL

Zinzani PL, et al. 2021, ASH #306

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STUDY POPULATION

Phase II/III Alliance A051701: DA-EPOCH-R ± Venetoclax in Previously Untreated Double-Hit Lymphoma

Abramson JS, et al. 2021, ASH #523

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STUDY POPULATION

Phase II: Acalabrutinib Window Prior to Frontline Therapy in Untreated Aggressive B-Cell Lymphoma – Preliminary Results and Correlatives of Response to Acalabrutinib

Roschewski M, et al. 2021, ASH #524

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STUDY POPULATION AND METHODS

EFFICACY

Phase Ib/II: Preliminary Analysis of Glofitamab Plus Polatuzumab Vedotin in R/R DLBCL

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Hutchings M, et al. 2021, ASH #525

STUDY POPULATION AND METHODS

Phase II: Naratuximab Emtansine Plus Rituximab in DLBCL and Other NHL

Levy MY, et al. 2021, ASH #526

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STUDY POPULATION

EFFICACY

Phase II/III UNITY-NHL Cohort: Umbralisib and Ublituximab ± Bendamustine in R/R DLBCL

Burke JM, et al. 2021, ASH #527

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STUDY POPULATION

EFFICACY

Phase Ib/II: Updated Results of Mosunetuzumab Plus Polatuzumab Vedotin in R/R Aggressive B-Cell NHL

Budde LE, et al. 2021, ASH #533

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STUDY POPULATION AND METHODS

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Advances in DLBCL/Aggressive B-Cell Lymphoma

Key Insights

Key Takeaways: Advances in DLBCL/Aggressive B-Cell Lymphoma

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Polatuzumab vedotin advances into early therapy

LBA-1: The POLARIX Study – Pola–R-CHP vs R-CHOP therapy in patients with previously untreated DLBCL (Tilly H. et al)

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Key Takeaways: Advances in DLBCL/Aggressive B-Cell Lymphoma

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Other studies in the newly diagnosed space did not impact current treatment practices

#305: R2 as frontline chemo-free therapy for elderly, frail patients with DLBCL. A phase II study of

Key Takeaways: Advances in DLBCL/Aggressive B-Cell Lymphoma

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Emerging data in the R/R setting are seen as “door-opening” for novel therapy modalities (1/2)

#54: Planned interim analysis of a phase II study of loncastuximab tesirine plus ibrutinib in patients with advanced DLBCL (LOTIS-3)

Key Takeaways: Advances in DLBCL/Aggressive B-Cell Lymphoma

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Emerging data in the R/R setting are seen as “door-opening” for novel therapy modalities (2/2)

#525: Glofitamab in combination with polatuzumab vedotin: Phase Ib/II preliminary data support manageable

Key Takeaways: T-Cell Lymphoma

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Initial data with anti-CD47 agents in hematologic malignancies are promising

#3560: CD47-blocker TTI-622 shows single-agent activity in patients with advanced R/R lymphoma: Update from the ongoing first-in-

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Advances in CAR T

Congress Highlights From ASH 2021

Phase III BELINDA: Tisa-Cel vs SOC as Second-Line Therapy for R/R Aggressive B-Cell NHL

Bishop MR, et al. 2021, ASH #LBA-6

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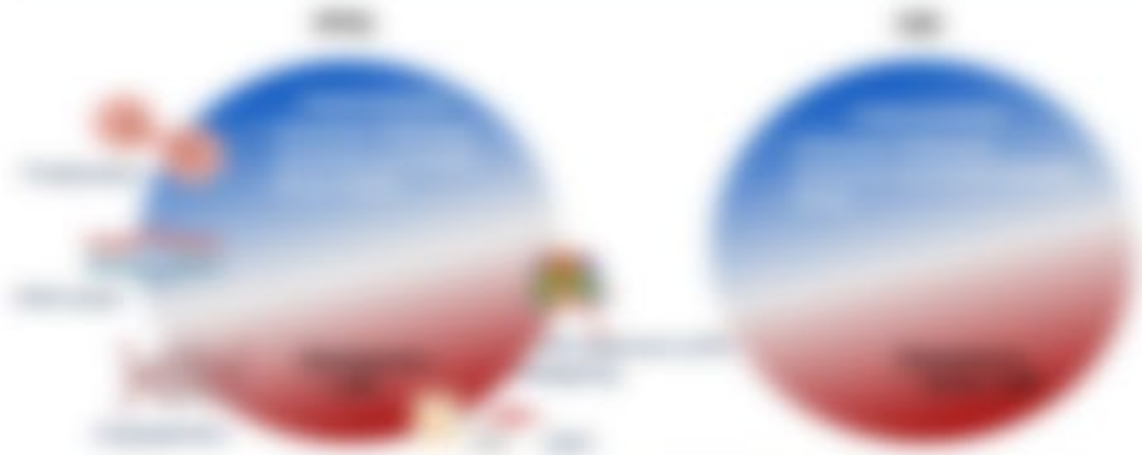
STUDY POPULATION



Phase III ZUMA-7: Primary Analysis of Axi-Cel vs SOC for R/R LBCL

Locke F, et al. 2021, ASH #2

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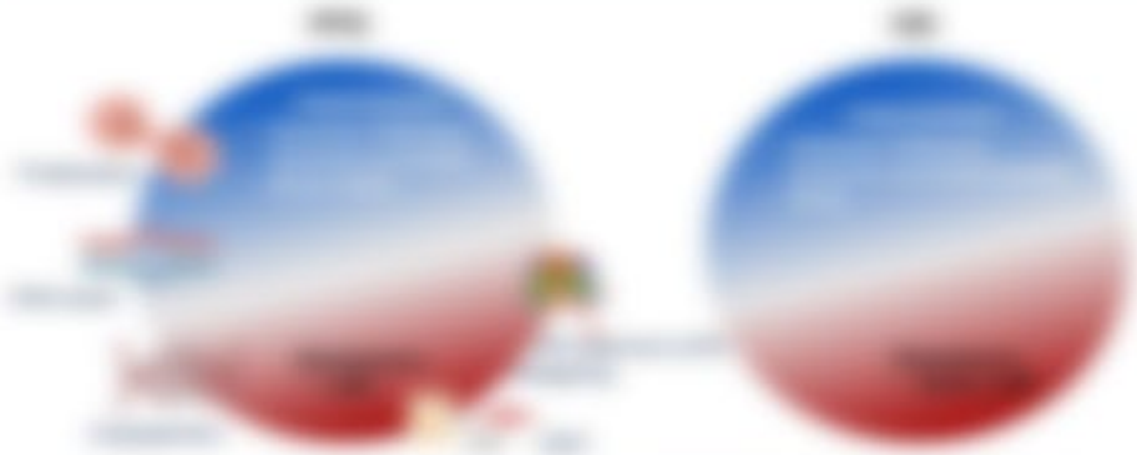
STUDY POPULATION



Phase III TRANSFORM: Liso-Cel vs SOC With Salvage CT Followed by ASCT as Second-Line Treatment in Patients With R/R LBCL

Kamdar M, et al. 2021, ASH #91

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STUDY POPULATION

Real-world (DESCAR-T Registry): A Propensity Score-Matched Comparison of Axi-Cel and Tisa-Cel for R/R DLBCL

Bachy E, et al. 2021, ASH #92

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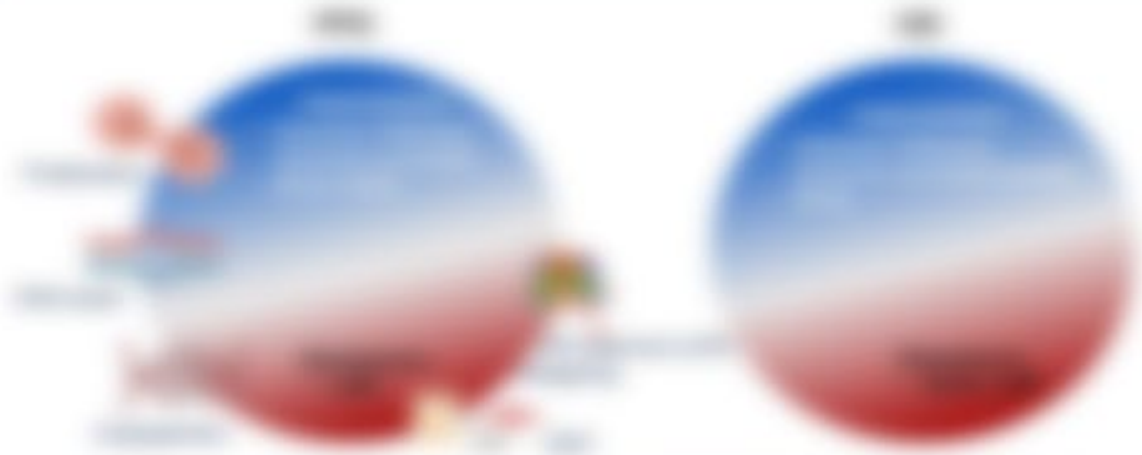
STUDY POPULATION

EFFICACY

SAFETY



Phase II ZUMA-5: Long-term Follow-up of Axi-Cel in R/R iNHL

Neelapu SS, et al. 2021, ASH #93

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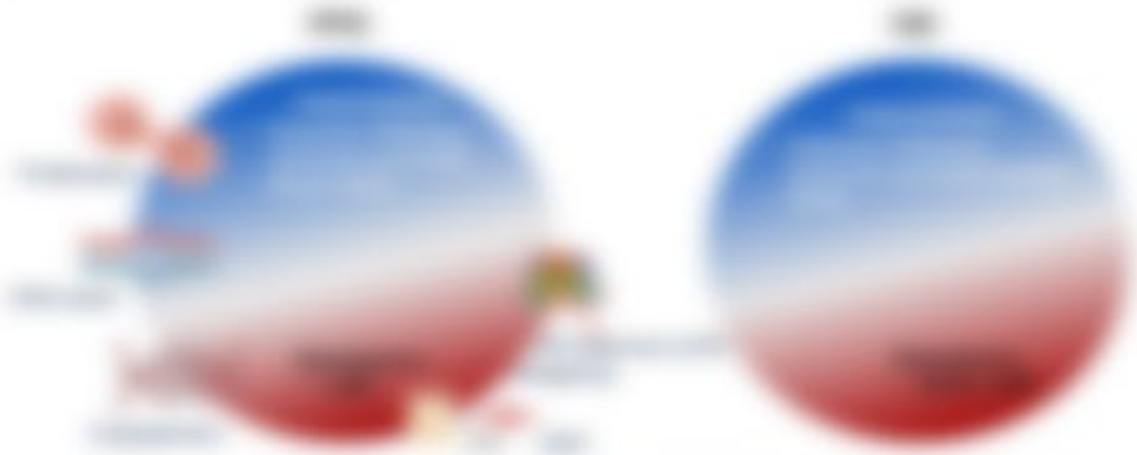
STUDY POPULATION



Phase II ELARA Subgroup Analysis: Tisa-Cel in Adult Patients With High-Risk R/R FL

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Thieblemont C, et al. 2021, ASH #131

STUDY POPULATION

Real World: Impact of Comorbidities on Outcomes and Toxicity in Patients Treated With CAR T in DLBCL

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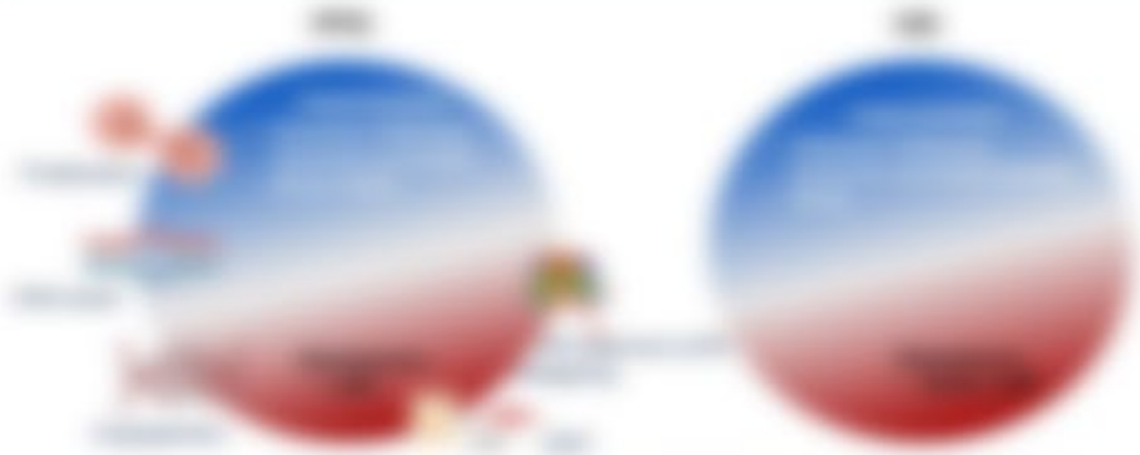
Shouse G, et al. 2021, ASH #529

STUDY POPULATION

OUTCOME



Real World: Impact of Age and Specific Organ Dysfunction in Patients Treated With Axi-Cel in LBCL

Locke F, et al. 2021, ASH #530

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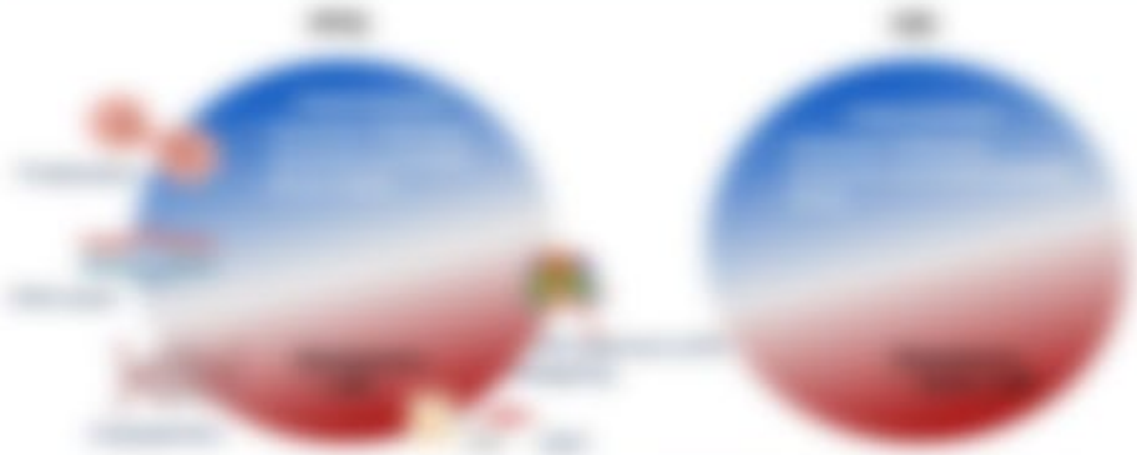
STUDY POPULATION



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Real World (DESCAR-T Registry and Lysa Group): KTE-X19 in R/R MCL

Herbaux C, et al. 2021, ASH #743

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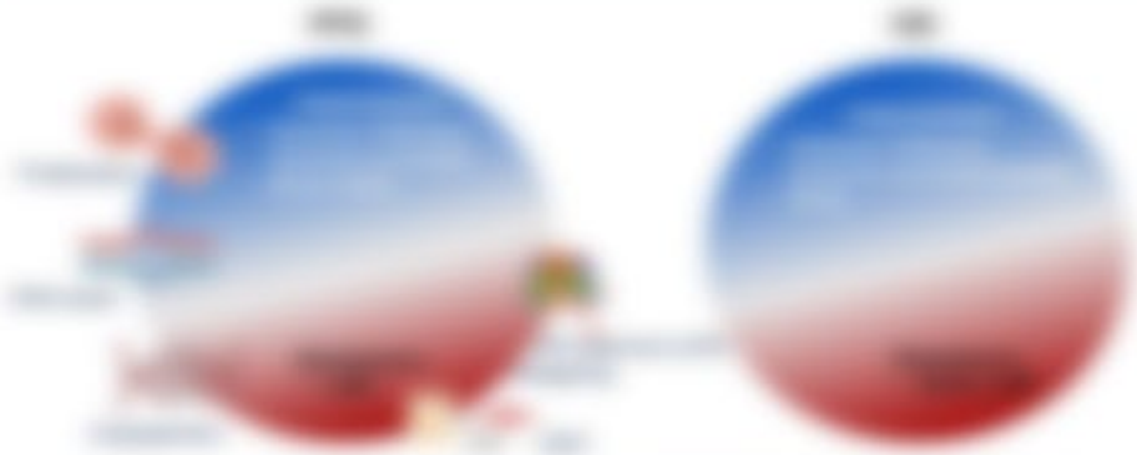
STUDY POPULATION



Real World (US Lymphoma CAR T Consortium): Brexu-Cel in R/R MCL

Wang Y, et al. 2021, ASH #744

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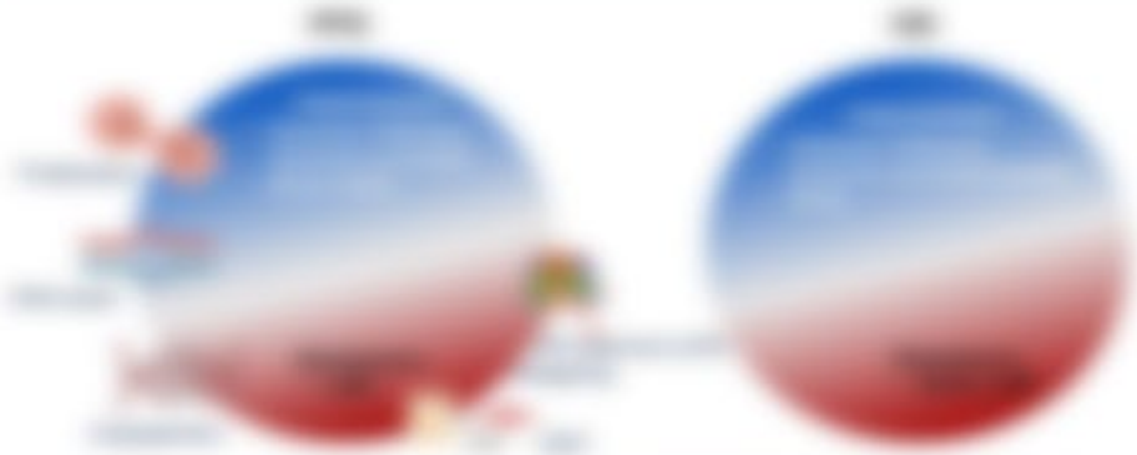
STUDY POPULATION



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Advances in CAR T

Key Insights

Key Takeaways: CAR T

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Experts are excited about using CAR T in the second-line setting for R/R LBCL

Key Takeaways: CAR T

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The 3 second-line CAR T trials differed substantially with regard to study design and patient characteristics

Key Takeaways: CAR T

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Comorbidities and predictors for CAR T outcomes in real-world practice in DLBCL/LBCL

Key Takeaways: CAR T

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CAR T comparison in indolent NHL

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Advances in Indolent NHL

Congress Highlights From ASH 2021

Phase II CITADEL-204: Primary Analysis of Parsaclisib in Patients With R/R MZL

Phillips T, et al. 2021, ASH #44

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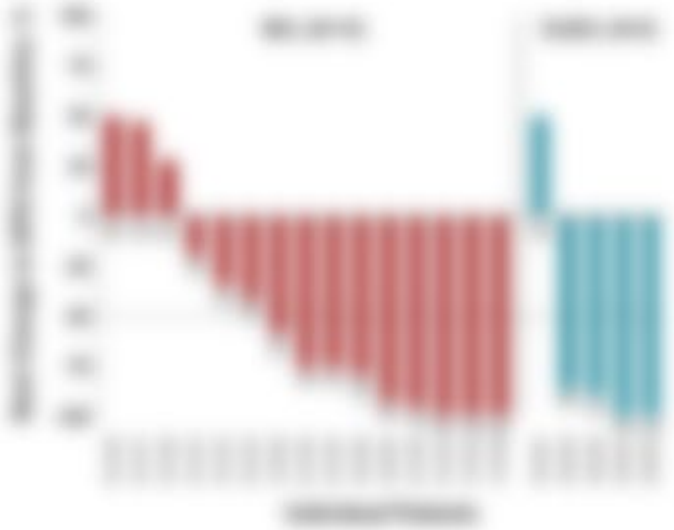
Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for MCL cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 23 weeks to 58 weeks



Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase II UNITY-NHL Cohort: Umbralisib and Ublituximab in R/R MZL

Chavez JC, et al. 2021, ASH #45

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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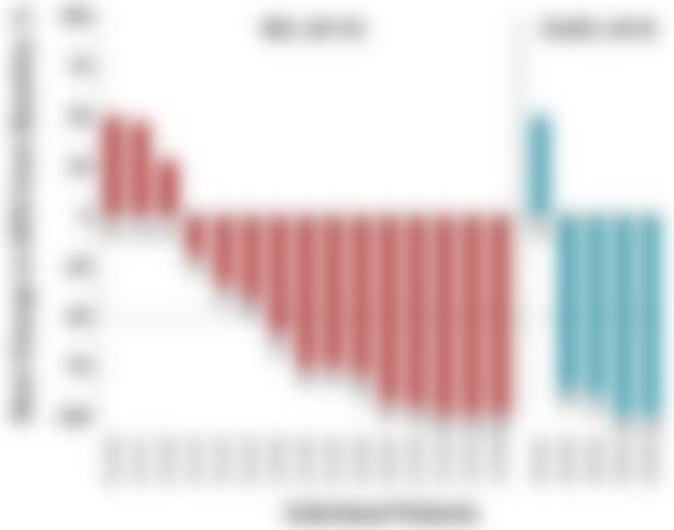

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Phase I/II: Mosunetuzumab for Patients With R/R FL Who Have Received ≥2 Prior Lines of Therapy

Budde LE, et al. 2021, ASH #127

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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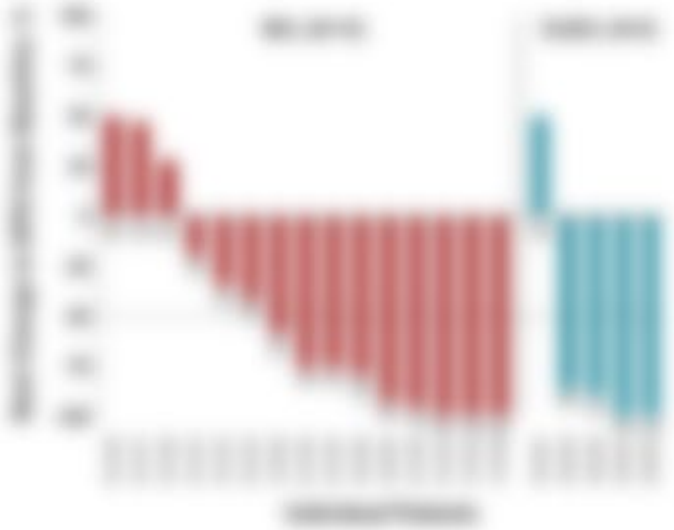

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase I/II: Glofitamab ± Obinutuzumab in Patients With Multiple R/R FL

Morschhauser F, et al. 2021, ASH #128

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
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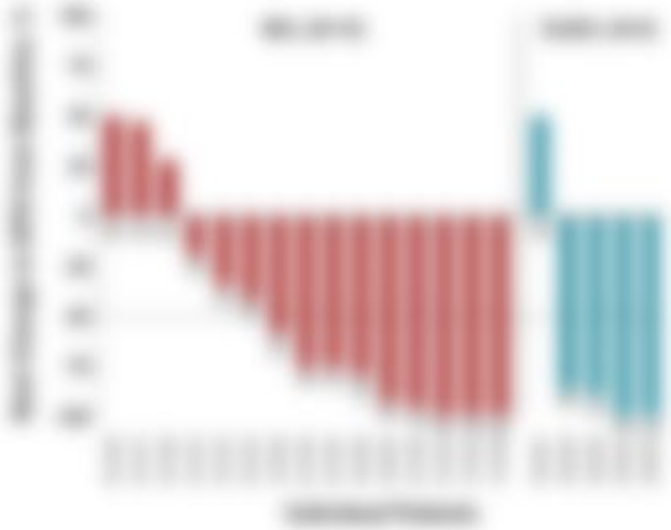

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Phase Ib: Initial Results of Mosunetuzumab Plus Lenalidomide in Patients With R/R FL

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Morschhauser F, et al. 2021, ASH #129

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
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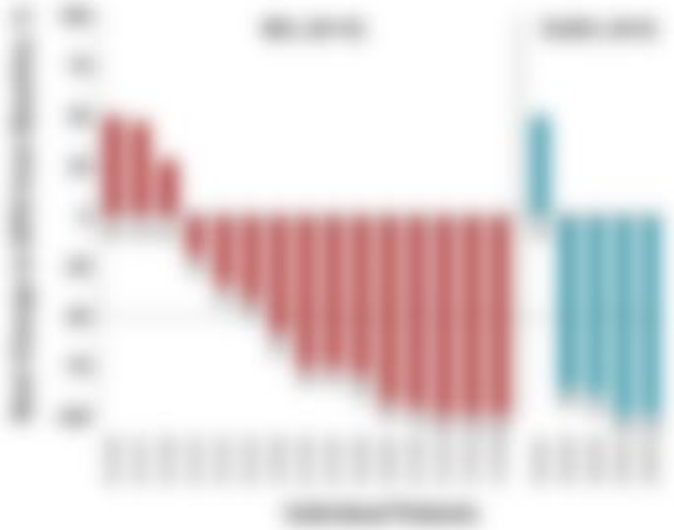

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase I/II: Preliminary Analysis of Glofitamab Step-up Dosing in Patients With R/R MCL, for Most of Whom BTKi Had Failed

Phillips T, et al. 2021, ASH #130

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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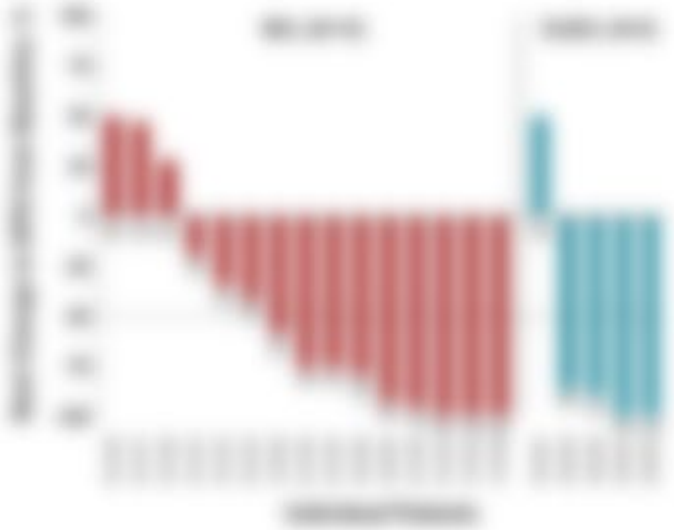

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Phase III MCL R2 Elderly Trial: R2 Maintenance After First-Line Immunochemotherapy in MCL

Ribrag V, et al. 2021, ASH #379

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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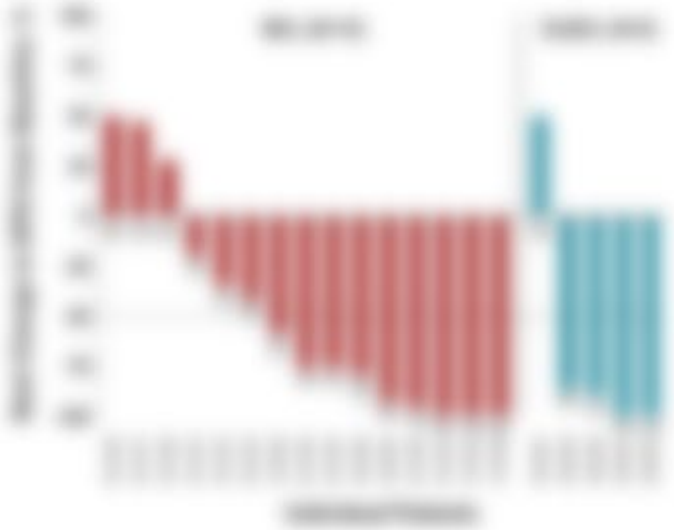

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase I/II BRUIN: Updated Results With Pirtobrutinib in Previously Treated MCL

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Wang M, et al. 2021, ASH #381

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
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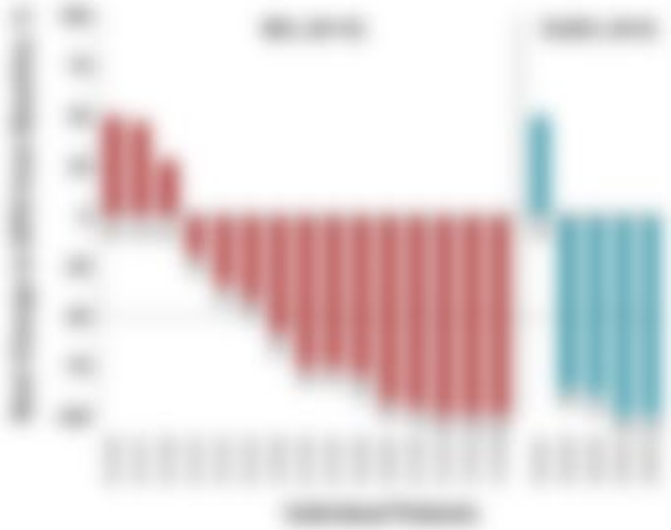

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase II CITADEL-205: Primary Analysis of Parsaclisib in Patients With R/R MCL Not Previously Treated With BTKi

Mehta A, et al. 2021, ASH #382

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Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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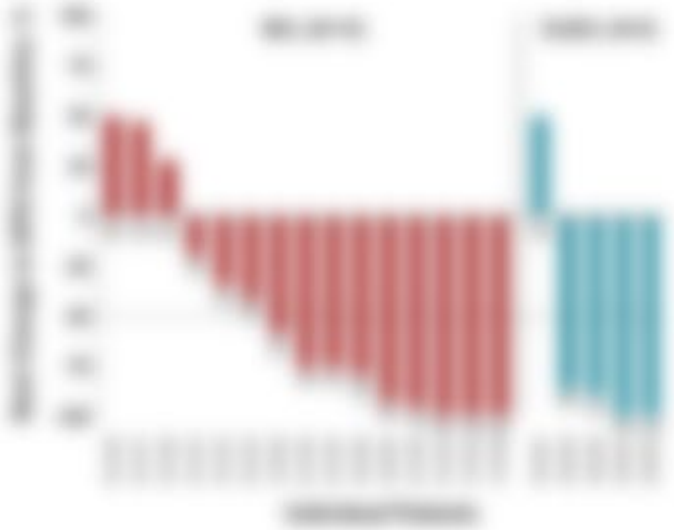

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase III FOLL12 Subset Analysis: RB or R-CHOP in Post-induction Management of Treatment-Naive Advanced FL

Luminari S, et al. 2021, ASH #811

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Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
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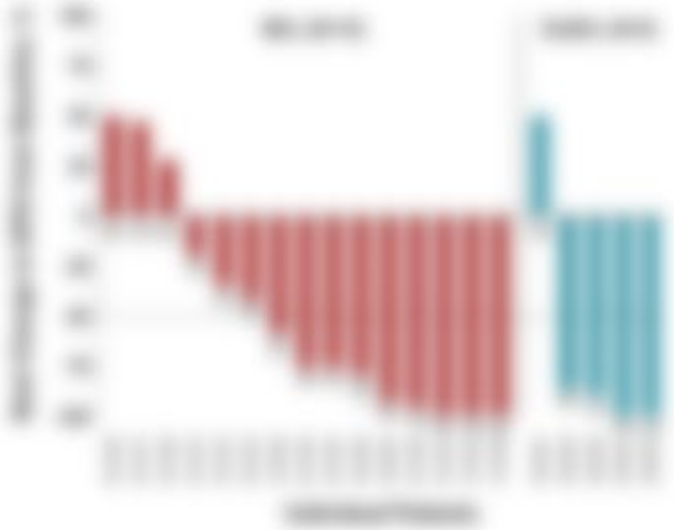


Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase III MAGNIFY: Completed Induction Phase Analysis of R2 Followed by Maintenance in R/R Indolent NHL

Lansigan F, et al. 2021, ASH #812

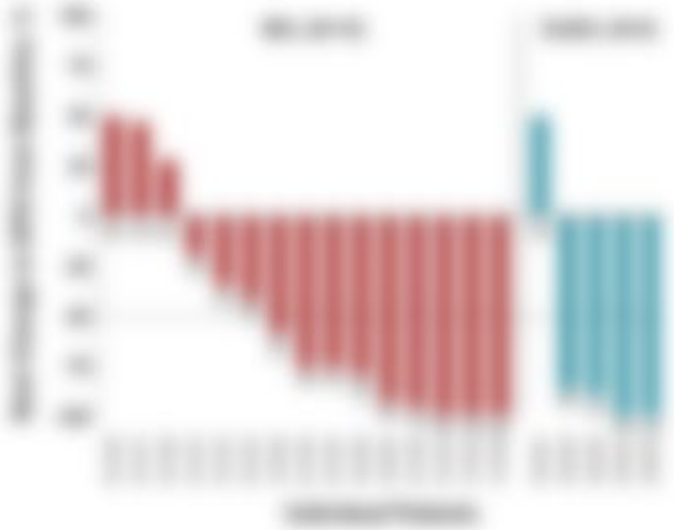
EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
- Primary objective was to refine estimates of MTD and recommended dosing regimen

Results

- 32 patients were enrolled, including 15 patients with MCL
- DLTs were G4 neutropenia and G3 diarrhea
- G4 neutropenia occurred in 28% of patients; G-CSF successfully ameliorated neutropenia
- On-study reversible G3 neuropathy occurred in 9% of patients; no G4 neuropathy occurred
- ORR was 47% (3 CR, 4 PR) for MCL cohort and 80% (2 CR, 2 PR) for DLBCL cohort
- 8 responding patients have ongoing responses ranging from 23 weeks to 58 weeks



Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Phase II CITADEL-203: Primary Analysis of Parsaclisib in Patients With R/R FL

EPICS

Lynch RC, et al. 2021, ASH #813

Background

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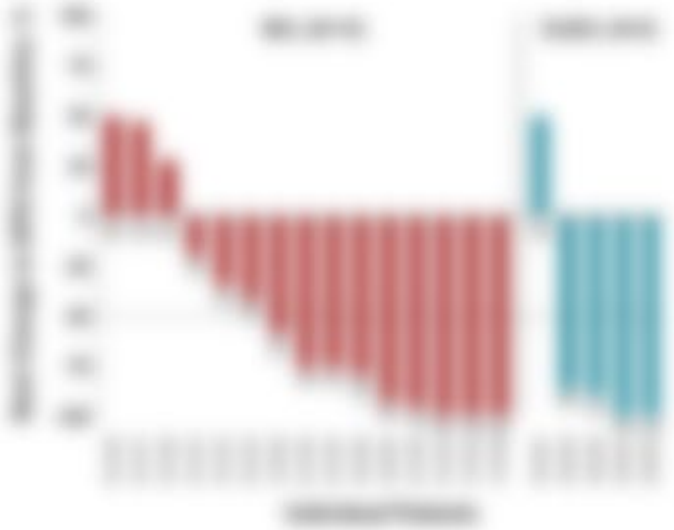

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Phase II PrECOG 0403: Frontline Venetoclax Plus Obinutuzumab and Bendamustine in Patients With High Tumor Burden FL

Portell CA, et al. 2021, ASH #814

EPICS

Background

- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
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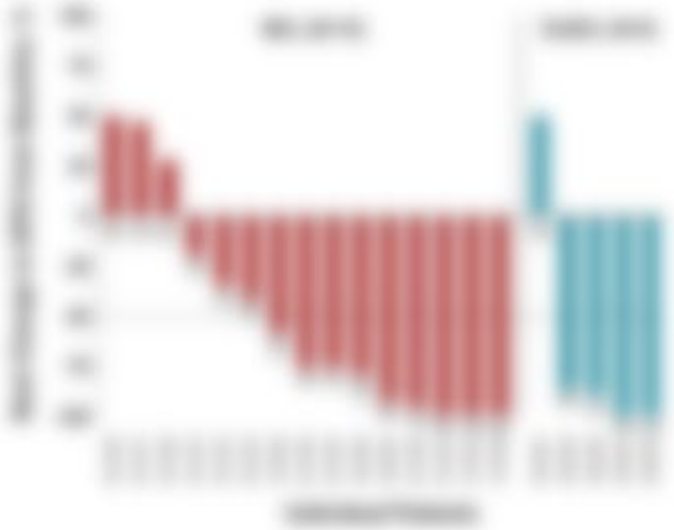

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Phase III RESORT Long-term Follow-up: Comparison of 2 Different Rituximab Dosing Strategies for Low Tumor Burden FL

Kahl BS, et al. 2021, ASH #815

EPICS

Background

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- Primary objective was to refine estimates of MTD and recommended dosing regimen

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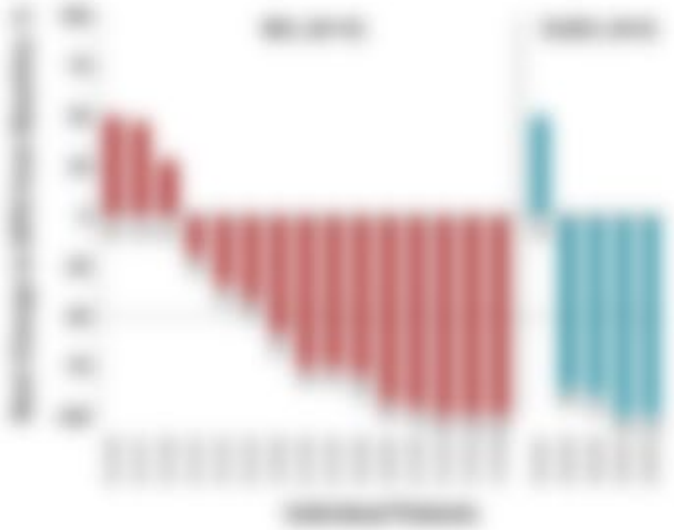

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

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Advances in Indolent NHL

Key Insights

Key Takeaways: Indolent NHLs (FL, MCL, and MZL)

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Given COVID-19, experts prefer a wait-and-see approach over R2 maintenance

Key Takeaways: Indolent NHLs (FL, MCL, and MZL)

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There is a lot of excitement for bispecific antibodies in FL (1/2)

Key Takeaways: Indolent NHLs (FL, MCL, and MZL)

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There is a lot of excitement for bispecific antibodies in FL (2/2)

Key Takeaways: Indolent NHLs (FL, MCL, and MZL)

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Other emerging therapies – much promise, but nothing yet practice changing (1/2)

compared with ibrutinib

Key Takeaways: Indolent NHLs (FL, MCL, and MZL)

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Other emerging therapies – much promise, but nothing yet practice changing (2/2)

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Advances in CLL

Congress Highlights From ASH 2021

Phase III Alliance A041202: Long-term Follow-up of Ibrutinib-Based Regimens vs Chemo-Immunotherapy in Older Patients With Untreated CLL

Woyach JA, et al. 2021, ASH #639

EPICS

STUDY POPULATION

EFFICACY

Phase III SEQUOIA Interim Analysis: Zanubrutinib vs BR in Patients With Treatment-Naive CLL/SLL

Tam CS, et al. 2021, ASH #396

EPICS

STUDY POPULATION

EFFICACY

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Phase III ASCEND: 3-Year Follow-up of Acalabrutinib vs Rituximab Plus Idelalisib or Bendamustine in R/R CLL

Jurczak W, et al. 2021, ASH #393

EPICS

STUDY POPULATION

EFFICACY

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Phase III FLAIR Interim Analysis: Ibrutinib Plus Rituximab vs FCR in Untreated CLL

Hillmen P, et al. 2021, ASH #642

EPICS

STUDY POPULATION

SAFETY

Phase II: Long-term Follow-up of Ibrutinib Plus FCR as Initial Therapy for Younger Patients With CLL

Davids MS, et al. 2021, ASH #640

EPICS

STUDY POPULATION

EFFICACY

Phase I/II BRUIN: Updated Results With Pirtobrutinib in Previously Treated CLL/SLL

EPICS

Mato AR, et al. 2021, ASH #391

STUDY POPULATION

EFFICACY

Phase III CLL13: Venetoclax-Based Time-Limited Combination Treatments (RVe, Gve, GIVe) vs Standard CIT (FCR/BR) in Frontline CLL in Fit Patients

EPICS

Eichhorst B, et al. 2021, ASH #71

STUDY POPULATION AND METHODS

EFFICACY

SAFETY

Phase III GLOW: First Prospective Data on MRD Outcomes After Fixed-Duration Ibrutinib Plus Venetoclax vs Chlorambucil Plus Obinutuzumab for First-Line Treatment of CLL in Elderly and Unfit Patients

Munir T, et al. 2021, ASH #70

EPICS

STUDY POPULATION

PFS RATE

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Phase III CAPTIVATE MRD Cohort: 2-Year Post-randomization DFS Results of First-Line Ibrutinib Plus Venetoclax for CLL

Ghia P, et al. 2021, ASH #68

EPICS

STUDY POPULATION AND METHODS

3-YEAR PFS RATES AND uMRD

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Phase II FILO: Preliminary Results of Ibrutinib Plus Venetoclax vs FCR in Untreated Fit Patients With Intermediate-Risk CLL

Michallet AS, et al. 2021, ASH #641

EPICS

STUDY POPULATION

EFFICACY

APTITUDE HEALTH

Phase II Vision HO141: Primary Analysis of Time-Limited Venetoclax and Ibrutinib for Patients With R/R CLL Who Have uMRD

Niemann CU, et al. 2021, ASH #69

EPICS

STUDY POPULATION AND METHODS

SAFETY

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Phase II: Ibrutinib Plus Ublituximab and Umbralisib in Patients With CLL – a MRD-Driven, Time-Limited Approach

Roeker LE, et al. 2021, ASH #395

EPICS

STUDY POPULATION AND METHODS

EFFICACY

Phase III SEQUOIA Arm D: Early Results of Zanubrutinib Plus Venetoclax in Patients With Treatment-Naive CLL/SLL With Del(17p)

Tedeschi A, et al. 2021, ASH #67

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STUDY POPULATION AND ARM D DESIGN

EFFICACY

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Advances in CLL

Key Insights

Key Takeaways: CLL

EPICS

BTKi therapy continues to show excellent long-term results and dominance over chemo-immunotherapy (1/2)

#393: Three-year follow-up of the Ascend trial: acalabrutinib vs rituximab plus idelalisib or bendamustine in R/R CLL (Jurczak W. et al)

Key Takeaways: CLL

EPICS

BTKi therapy continues to show excellent long-term results and dominance over chemo-immunotherapy (2/2)

#640: Longer-term follow-up of a multicenter, phase II study of iFCR as initial therapy for younger patients with CLL (Davids MS, et al)

Key Takeaways: CLL

EPICS

Data on the non-covalent BTKi pirtobrutinib are very promising

Key Takeaways: CLL

EPICS

Fixed-duration and MRD-guided approach are very promising, but follow-up is too short to currently consider them SOC (1/3)

#67: Zanubrutinib in combination with venetoclax for patients with treatment-naïve CLL/SLL with del(17p): Early results from Arm D of the

Key Takeaways: CLL

EPICS

Fixed-duration and MRD-guided approach are very promising, but follow-up is too short to currently consider them SOC (2/3)

#70: First prospective data on MRD outcomes after fixed-duration ibrutinib plus venetoclax vs chlorambucil plus obinutuzumab for first-line

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Key Takeaways: CLL

EPICS

Fixed-duration and MRD-guided approach are very promising, but follow-up is too short to currently consider them SOC (3/3)

In summary, experts find fixed-duration and MRD-guided approaches very promising, but agree that follow-up is too short to currently

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