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Congress Coverage: ASH 2021 – Focus on Leukemia and MDS

Full Report

December 15, 2021

Report Contents

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Meeting Snapshot

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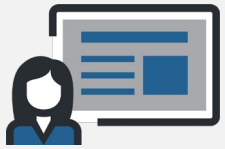
Virtual Closed-Door Roundtable

DATE:
December 15, 2021



DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in leukemia

- 5 from US
- 4 from EU

LEUKEMIA-SPECIFIC DISCUSSIONS on therapeutic advances and their application in clinical decision-making

Panel Consisting of 5 US and 4 European Leukemia Experts

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Jae Park, MD
Memorial Sloan Kettering Cancer Center

Amir Fathi, MD
Massachusetts General Hospital

CHAIR:
Elias Jabbour, MD
MD Anderson Cancer Center

Naval Daver, MD
MD Anderson Cancer Center

Guillermo Garcia-Manero, MD
MD Anderson Cancer Center

Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil, FMedSci
Queen Elizabeth Hospital

CO-CHAIR:
Nicola Gökbuget, MD
Goethe University Hospital

Valeria Santini, MD
University of Florence

Josep-Maria Ribera, MD, PhD
Hospital Germans Trias i Pujol

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Meeting Agenda

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Time (CST)	Topic	Speaker/Moderator
1.00 PM – 1.05 PM	**Welcome and Introductions**	Elias Jabbour, MD, and Nicola Gökbuget, MD
1.05 PM – 1.15 PM	**New Developments in MDS**	Guillermo Garcia-Manero, MD, and Valeria Santini, MD
1.15 PM – 1.45 PM	*Discussion and Key Takeaways*	*All* *Moderator: Elias Jabbour, MD*
1.45 PM – 2.00 PM	**Advances in AML: Newly Diagnosed**	Amir Fathi, MD, and Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil, FMedSci
2.00 PM – 2.25 PM	*Discussion and Key Takeaways*	*All* *Moderator: Elias Jabbour, MD*
2.25 PM – 2.35 PM	**Advances in AML: Relapsed/Refractory**	Naval Daver, MD
2.35 PM – 3.00 PM	*Discussion and Key Takeaways*	*All* *Moderator: Elias Jabbour, MD*
3.00 PM – 3.05 PM	Break	
3.05 PM – 3.15 PM	**Advances in ALL: Newly Diagnosed**	Josep-Maria Ribera, MD, PhD
3.15 PM – 3.35 PM	*Discussion and Key Takeaways*	*All* *Moderator: Nicola Gökbuget, MD*
3.35 PM – 3.45 PM	**Advances in ALL: Relapsed/Refractory**	Jae Park, MD
3.45 PM – 4.10 PM	*Discussion and Key Takeaways*	*All* *Moderator: Nicola Gökbuget, MD*
4.10 PM – 4.15 PM	**Summary and Closing Remarks**	Elias Jabbour, MD, and Nicola Gökbuget, MD

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Congress Highlights

Updates on MDS

Initial Results of Phase I/II Study of Azacitidine in Combination with Quizartinib for Patients with Myelodysplastic Syndrome and Myelodysplastic/Myeloproliferative Neoplasm with *FLT3* or *CBL* Mutations

Tareq Abuasab, et al, #1536

EPICS

STUDY POPULATION

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

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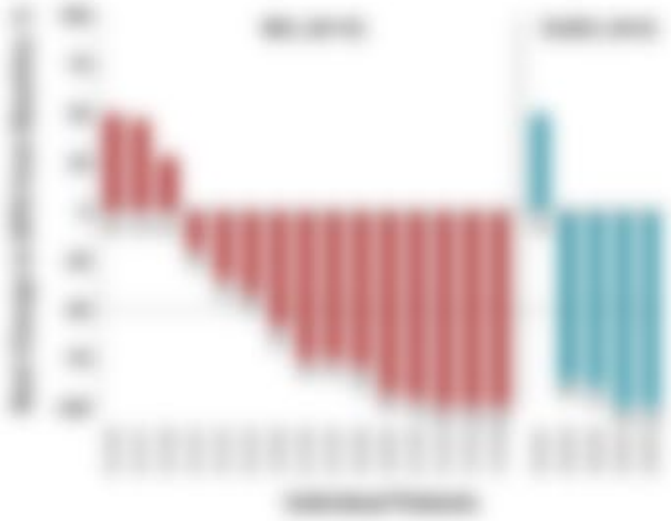

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Ivosidenib Monotherapy Is Effective in Patients With IDH1 Mutated Myelodysplastic Syndrome (MDS): The Idiome Phase II Study By the GFM Group

Marie Sebert, et al, #62

EPICS

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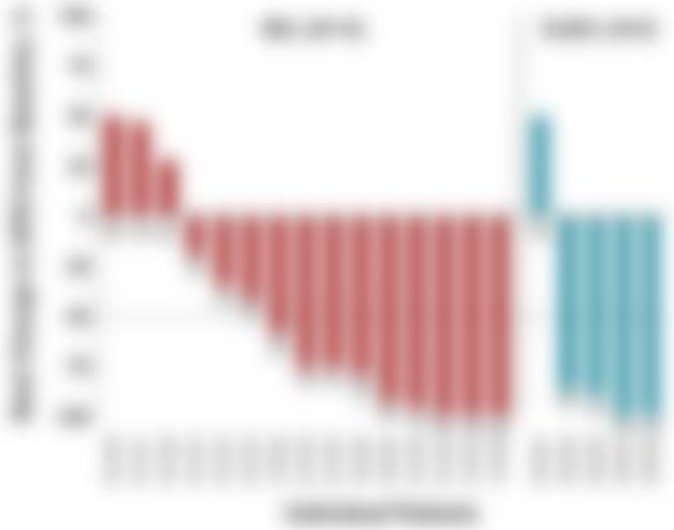

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Enasidenib (ENA) Is Effective in Patients with IDH2 Mutated Myelodysplastic Syndrome (MDS): The Ideal Phase II Study By the GFM Group

Lionel Ades, et al, #63

EPICS

STUDY POPULATION

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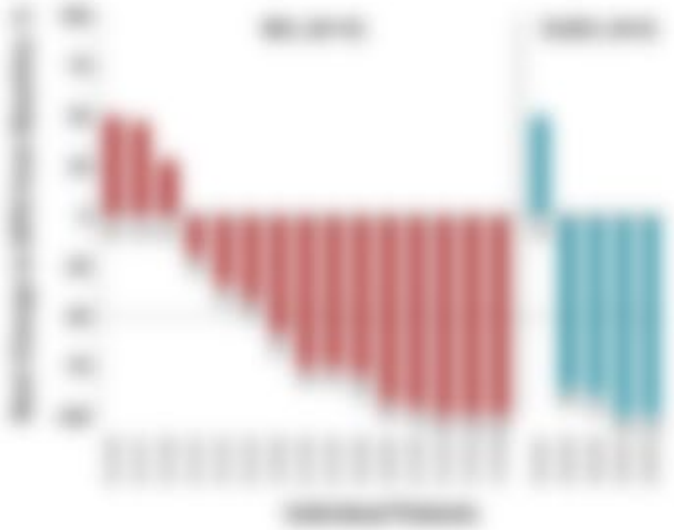

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Long Term Follow-up and Combined Phase 2 Results of Eprenetapopt (APR-246) and Azacitidine (AZA) in Patients with *TP53* mutant Myelodysplastic Syndromes (MDS) and Oligoblastic Acute Myeloid Leukemia (AML)

David A. Sallman, et al, #246

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STUDY POPULATION

Combined Cohorts (n=100)

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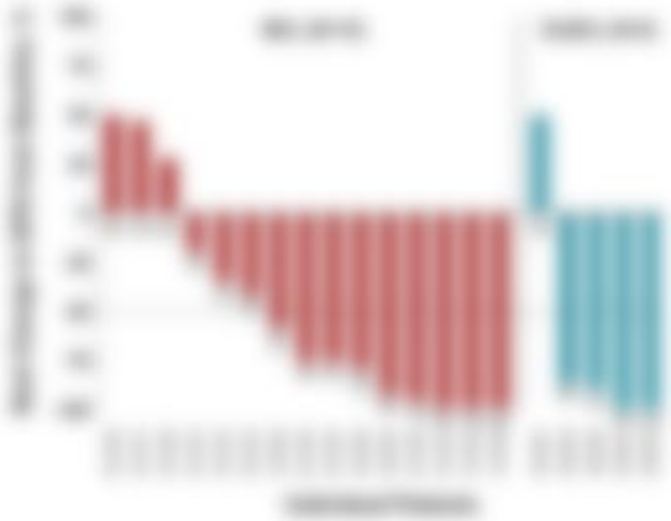

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Molecular International Prognosis Scoring System for Myelodysplastic Syndromes

Elsa Bernard, et al, #61

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STUDY POPULATION

Background

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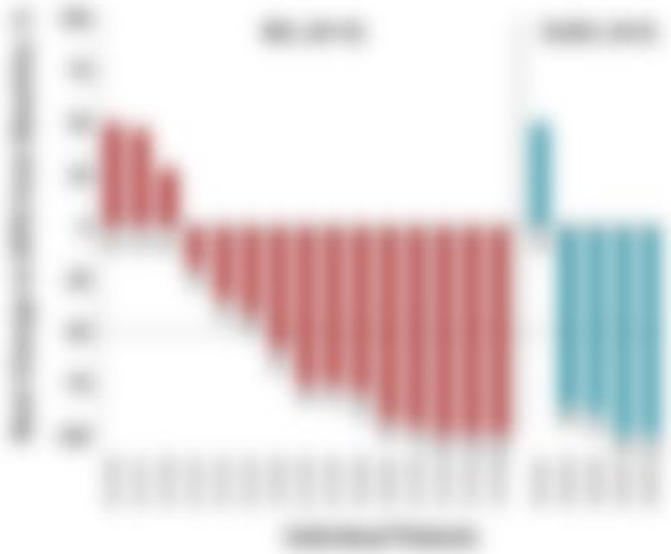

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Evorpacept (ALX148), a CD47-Blocking Myeloid Checkpoint Inhibitor, in Combination with Azacitidine: A Phase 1 / 2 Study in Patients with Myelodysplastic Syndrome (ASPEN-02)

Guillermo Garcia-Manero, et al, #2601

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STUDY POPULATION

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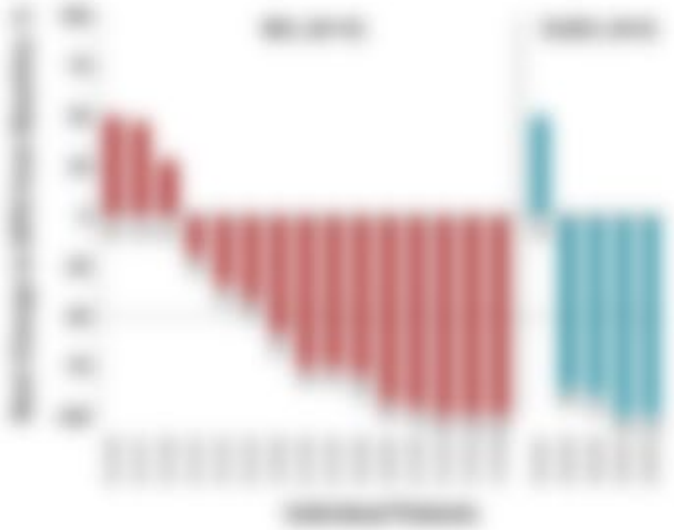

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

CPX 351 As First-Line Treatment in Higher-Risk MDS. A Phase II Trial By the GFM

Pierre Peterlin, et al, #243

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STUDY POPULATION

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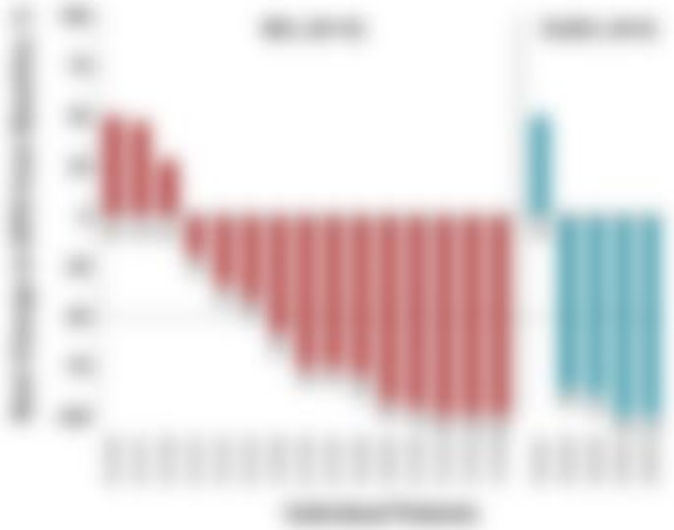

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Pevonedistat (PEV) + Azacitidine (AZA) Versus Aza Alone As First-Line Treatment for Patients with Higher-Risk Myelodysplastic Syndromes (MDS)/Chronic Myelomonocytic Leukemia (CMML) or Acute Myeloid Leukemia (AML) with 20–30% Marrow Blasts: The Randomized Phase 3 PANTHER Trial (NCT03268954)

Mikkael A. Sekeres, et al, #242

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STUDY POPULATION

PANTHER (P-3001): global, open-label, multi-center, randomized phase 3 trial (NCT03268954)

Background

- Phase I dose-escalation study of VLS-101, a RIDR1-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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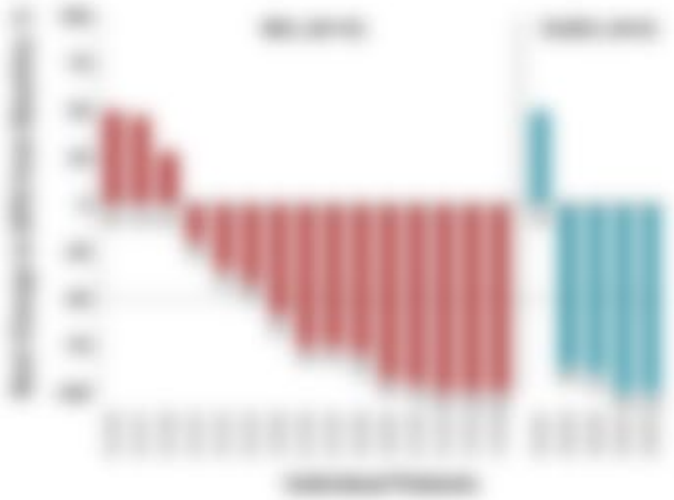

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

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Discussion Summary

Updates on MDS

New Developments in MDS

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MDS with mutations

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Congress Highlights

Updates on Newly Diagnosed AML

Phase 3, Open-Label, Randomized Study of Gilteritinib and Azacitidine Vs Azacitidine for Newly Diagnosed *FLT3*-Mutated Acute Myeloid Leukemia in Patients Ineligible for Intensive Induction Chemotherapy

Eunice S. Wang, et al, #700

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STUDY POPULATION

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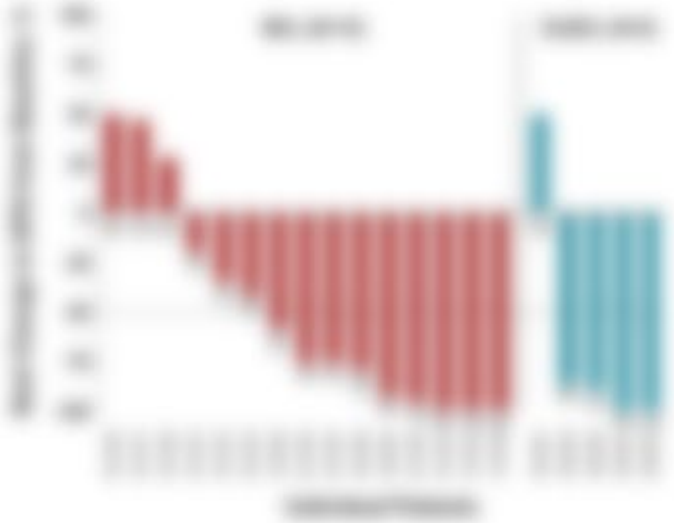

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Impact of *FLT3* Mutation Clearance After Front-Line Treatment with Gilteritinib Plus Azacitidine, or Gilteritinib or Azacitidine Alone in Patients with Newly Diagnosed AML: Results from the Phase 2 / 3 Lacewing Trial

Eunice S. Wang, et al, #3445

EPICS

STUDY POPULATION

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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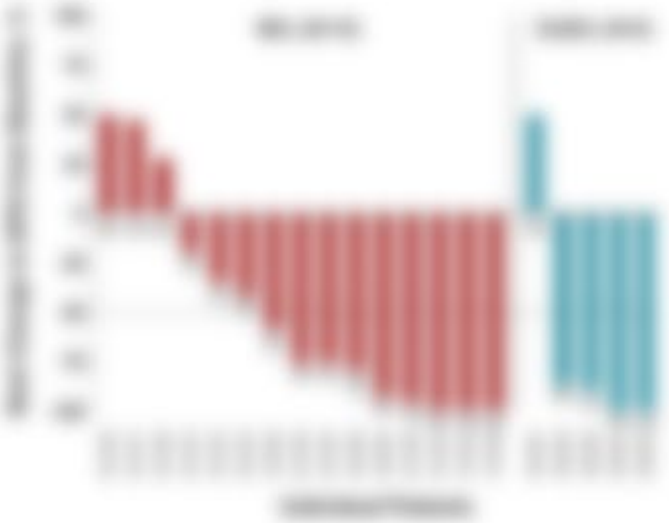
Table 2. Post-Treatment MRD Status by Cohort in Patients With Post-Baseline Samples Who Achieved



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.

AGILE: A Global, Randomized, Double-Blind, Phase 3 Study of Ivosidenib + Azacitidine Versus Placebo + Azacitidine in Patients with Newly Diagnosed Acute Myeloid Leukemia with an *IDH1* Mutation

Pau Montesinos, et al, #697

EPICS

STUDY POPULATION

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- Phase I dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
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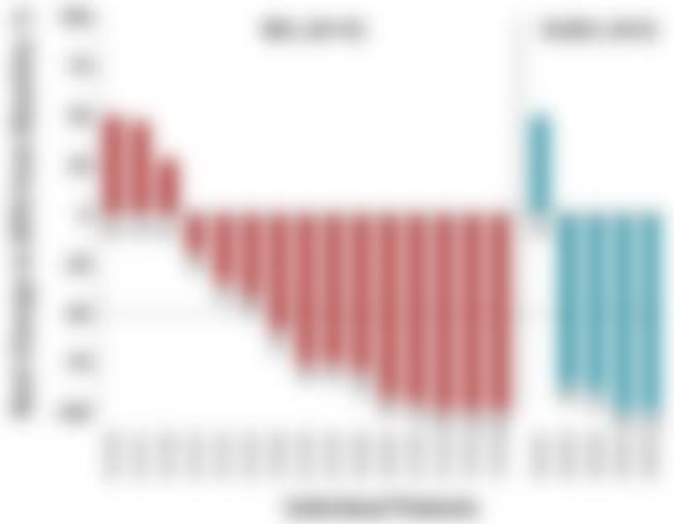
EFS in the intent-to-treat population



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 and Expansion Study of Eprenetapopt (APR-246) in Combination with Venetoclax (VEN) and Azacitidine (AZA) in *TP53*-Mutant Acute Myeloid Leukemia (AML)

Guillermo Garcia-Manero, et al, #3409

EPICS

STUDY POPULATION

Background

- Phase I dose-escalation study of VLX-101, a PKDR1-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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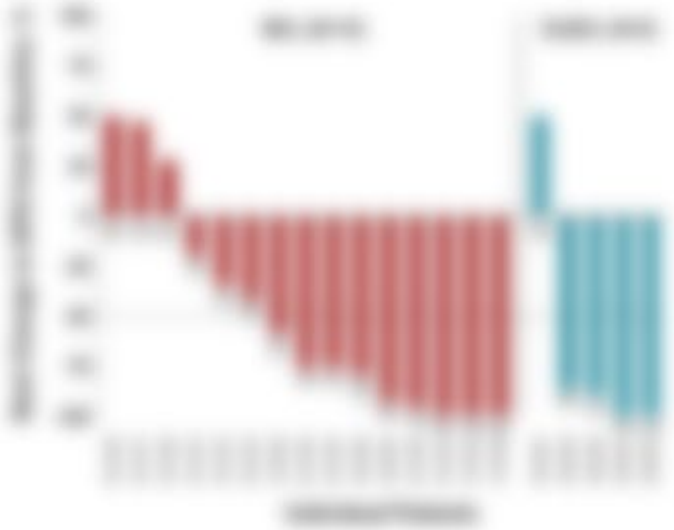

Key takeaways: VLX-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Updated Survival and Response Analyses from a Phase 1 Study of Ivosidenib or Enasidenib Combined with Induction and Consolidation Chemotherapy in Patients with Newly Diagnosed AML with an *IDH1* or *IDH2* Mutation

Eytan M. Stein, et al, #1276

EPICS

STUDY POPULATION

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- Phase 1 dose-escalation study of VLS-101, a ROR1-targeting ADC, in patients with heavily pretreated MCL and DLBCL
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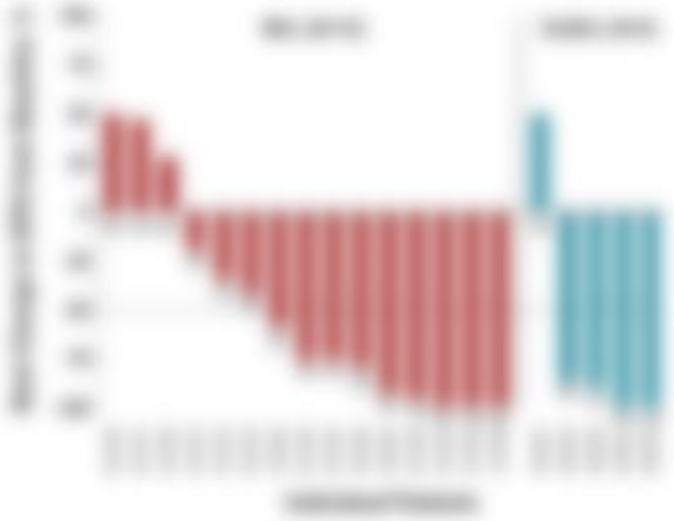

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

Real-World Experience of CPX-351 As First-Line Treatment in 188 Patients with Acute Myeloid Leukemia

Christina Rautenberg, et al, #33

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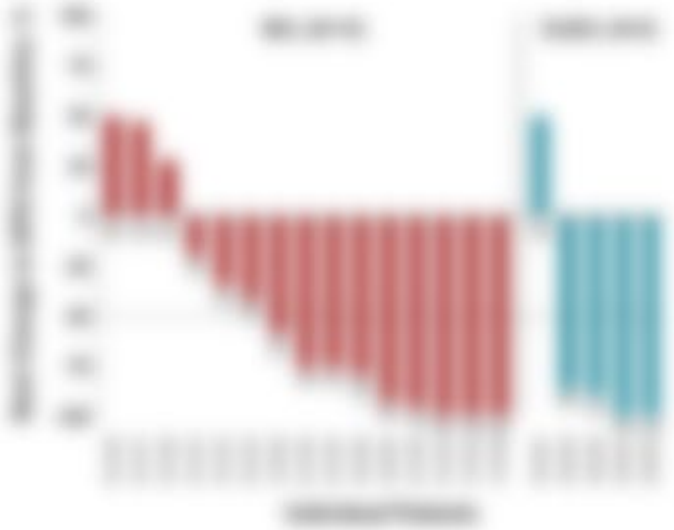

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Long-Term Overall Survival (OS) with Oral Azacitidine (Oral-AZA) in Patients with Acute Myeloid Leukemia (AML) in First Remission after Intensive Chemotherapy (IC): Updated Results from the Phase 3 QUAZAR AML-001 Trial

Andrew H. Wei, et al, #871

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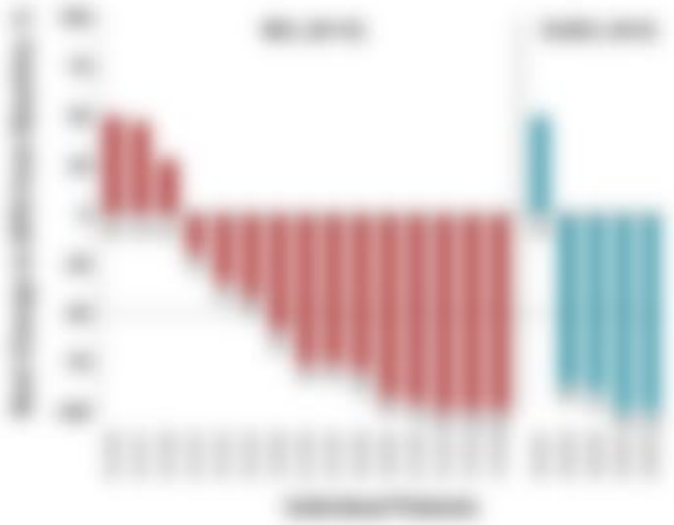

Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

A Phase II Study of 5-Azacytidine (AZA) and Venetoclax As Maintenance Therapy in Patients with Acute Myeloid Leukemia (AML) in Remission

Alexandre Bazinet, et al, #2326

EPICS

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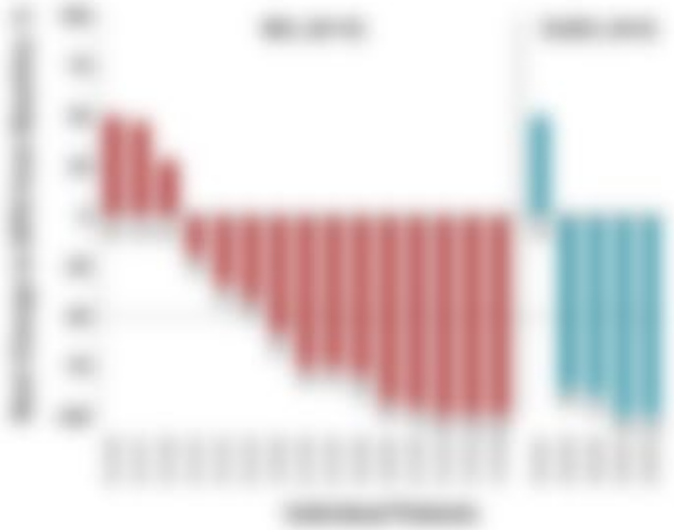


Key takeaways: VLS-101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced MCL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best histologies in which to test this agent.

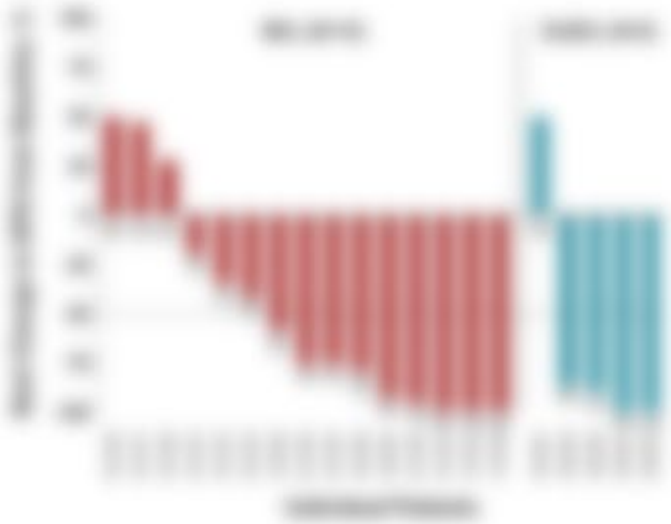
Long-Term Survival after Intensive Chemotherapy or Hypomethylating Agents in AML Patients Aged 70 Years and Older: A Large Patient Data Set Study from Dataml, SAL and Pethema European Registries

Christian Recher, et al, #872

EPICS

STUDY POPULATION

A All Patients B Royston and Parmar adjusted HR



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
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Phase I/II Study of Azacitidine (AZA) With Venetoclax (VEN) and Magrolimab (Magro) in Patients (pts) with Newly Diagnosed Older/Unfit or High-Risk Acute Myeloid Leukemia (AML) and Relapsed/Refractory (R/R) AML

Naval Daver, et al, #371

EPICS

STUDY POPULATION

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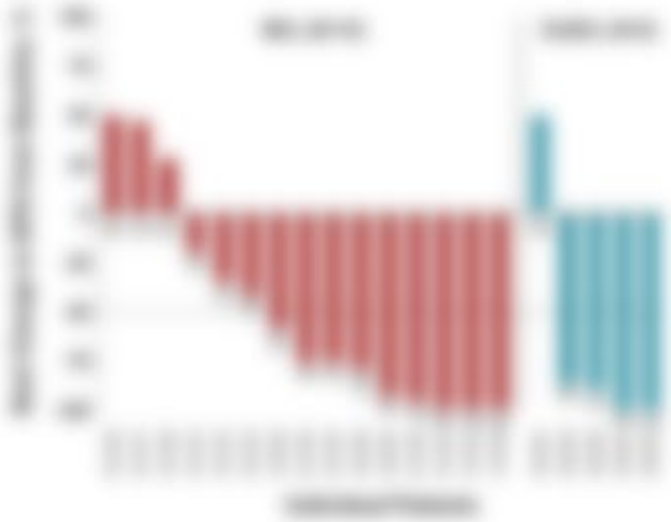

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Azacitidine, Venetoclax and Pevonedistat As Frontline Therapy for Patients with Secondary Acute Myeloid Leukemia Who Are Unfit for Intensive Chemotherapy: Results from a Phase I/II Study

Nicholas J. Short, et al, #2349

EPICS

STUDY POPULATION

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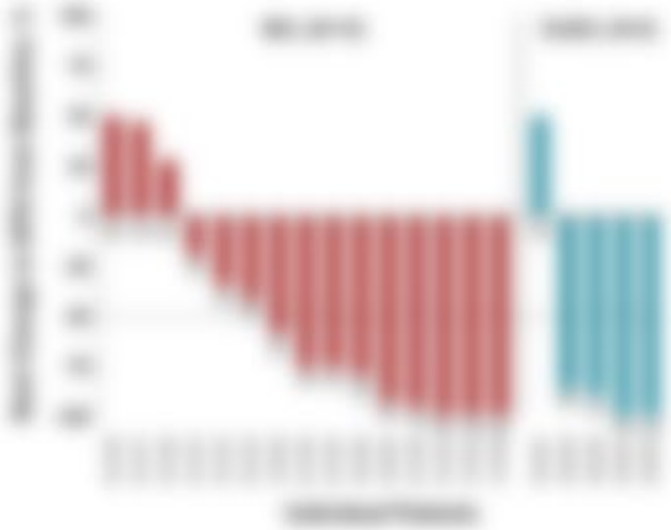
Figure 1 – (A) Overall survival and (B) relapse-free survival for the entire cohort



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Iadademstat in Combination with Azacitidine Generates Robust and Long Lasting Responses in AML Patients (ALICE Trial)

Olga Salamero, et al, #3376

EPICS

STUDY POPULATION

Comparing Outcomes between Liposomal Daunorubicin/Cytarabine (CPX-351) and HMA + Venetoclax As Frontline Therapy in Acute Myeloid Leukemia

Justin Grenet, et al, #32

EPICS

STUDY POPULATION

CPX-351 **HMA/VEN**

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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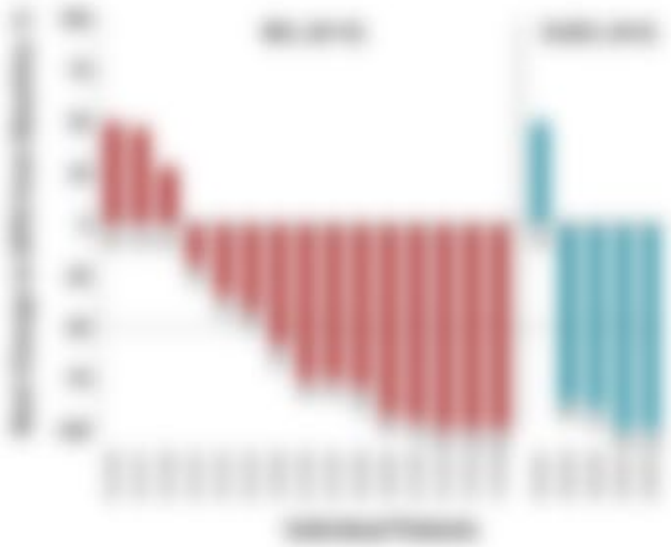

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Discussion Summary

Updates on Newly Diagnosed AML

Advances in AML (1/2)

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Newly Diagnosed AML

[illegible]

Advances in AML (2/2)

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Newly Diagnosed AML (cont)

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Congress Highlights

Updates on Relapsed/Refractory AML

Venetoclax in Combination with Gilteritinib Demonstrates Molecular Clearance of *FLT3* mutation in Relapsed/Refractory *FLT3*-Mutated Acute Myeloid Leukemia

Naval Daver, et al, #691

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STUDY POPULATION

Safety and Efficacy of Menin Inhibition in Patients (Pts) with MLL-Rearranged and NPM1 Mutant Acute Leukemia: A Phase (Ph) 1, First-in-Human Study of SNDX-5613 (AUGMENT 101)

Eytan Stein, et al, #699

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STUDY POPULATION

SNDX-5613 patients are heavily pretreated & have a poor prognosis

Outcomes for Patients with Late-Stage Mutant-*IDH2* (m*IDH2*) Relapsed/Refractory Acute Myeloid Leukemia (R/R AML) Treated With Enasidenib Vs Other Lower-Intensity Therapies in the Randomized, Phase 3 IDHentify Trial

Courtney D. DiNardo, et al, #1243

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STUDY POPULATION

A Prospective Phase 2 Study of Venetoclax and Low Dose Ara-C (VALDAC) to Target Rising Molecular Measurable Residual Disease and Early Relapse in Acute Myeloid Leukemia

Ing S. Tiong, et al, #1261

EPICS

STUDY POPULATION

A Phase II Study of CPX-351 Plus Venetoclax in Patients with Relapsed/Refractory (R/R) or Newly Diagnosed Acute Myeloid Leukemia (AML)

Kunhwa Kim, et al, #1275

EPICS

STUDY POPULATION

Safety and Efficacy from a Phase 1b/2 Study of IMGN632 in Combination with Azacitidine and Venetoclax for Patients with CD123-Positive Acute Myeloid Leukemia

Naval Daver, et al, #372

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STUDY POPULATION

Antileukemic Activity Observed
Across All Doses/Schedules

Place video here

Additional ASH Abstracts*

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Olutasidenib (FT-2102) in Combination with Azacitidine Induces Durable Complete Remissions in Patients with mIDH1

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Discussion Summary

Updates on Relapsed/Refractory AML

Advances in AML

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Relapsed/Refractory AML

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Congress Highlights

Updates on Newly Diagnosed ALL

Ponatinib and Chemotherapy in Adults with *De Novo* Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia. Final Results of Ponalfil Clinical Trial

J.M. Ribera, et al, #1230

EPICS

STUDY POPULATION

Updated Results of a Phase II Study of Ponatinib and Blinatumomab for Patients with Philadelphia Chromosome-Positive Acute Lymphoblastic Leukemia

N.J. Short, et al, #2298

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STUDY POPULATION

Updated Results from a Phase II Study of Mini-Hyper-CVD Plus Inotuzumab Ozogamicin, with or without Blinatumomab, in Older Adults With Newly Diagnosed Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia

N.J. Short, et al, #3400

EPICS

STUDY POPULATION

Fractionated Inotuzumab Ozogamicin Combined with Low-Intensity Chemotherapy Provides Very Good Outcome in Older Patients with Newly Diagnosed CD22+ Philadelphia Chromosome-Negative B-Cell Precursor Acute Lymphoblastic Leukemia: First Results from the EWALL-INO Study

P. Chevalier, et al, #511

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STUDY POPULATION

Response (N = 90)	N (%)

Final Induction Therapy Results of an Open Label Phase II Study Using Inotuzumab Ozogamicin for Induction Therapy, Followed By a Conventional Chemotherapy Based Consolidation and Maintenance Therapy in Patients Aged 56 Years and Older With Acute B-Lymphoblastic Leukemia (INITIAL-1 trial)

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Frontline Consolidation with Blinatumomab for High-Risk Philadelphia-Negative Acute Lymphoblastic Adult Patients. Early Results from the Graall-2014-QUEST Phase 2

N. Boissel, et al, #1232

EPICS

STUDY POPULATION

Patients (N=94)		SAE	N

Dose Reduced Chemotherapy in Sequence with Blinatumomab for Newly Diagnosed Older Patients With B-Precursor Adult Lymphoblastic Leukemia (ALL): Results of the Ongoing GMALL Bold Trial

N. Gökbuget, et al, #3399

EPICS

STUDY POPULATION

Table 1: Results of Remission Induction

Updated Results from a Phase II Study of Hyper-CVAD with Sequential Blinatumomab in Adults with Newly Diagnosed Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia

N.J. Short, et al, #1233

EPICS

STUDY POPULATION

Figure 1. Continuous remission duration (CRD) and overall survival

First Results of the Risk-Adapted, MRD-Stratified GMALL Trial 08/2013 in 705 Adults with Newly Diagnosed Acute Lymphoblastic Leukemia/Lymphoma (ALL/LBL)

N. Gökbuget, et al, #362

EPICS

STUDY POPULATION

Table 1: Total Outcome and Subgroups for ALL

	Total	B-ALL/Ph-	B-ALL/PH+	T-ALL	B/T SR[4]	B/T HR[4]

Genomic Data Improves Prognostic Stratification in Adult T-Cell Acute Lymphoblastic Leukemia Patients Enrolled in Measurable Residual Disease-Oriented Trials

C. Gonzalez-Gil, et al, #3486

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STUDY POPULATION

	% OS (95% CI)	

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Discussion Summary

Updates on Newly Diagnosed ALL

Advances in ALL: Newly Diagnosed

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Ph+ ALL – TKIs

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Congress Highlights

Updates on Relapsed/Refractory ALL

Long-Term Follow-up of the Combination of Low-Intensity Chemotherapy Plus Inotuzumab with or without Blinatumomab in Patients with Relapsed-Refractory Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia

F. Haddad et al, #3363

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STUDY POPULATION

Response, No. (%)

Outcome after Inotuzumab Ozogamicin for Patients with Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia and Extramedullary Disease

S. Kayser, et al, #3404

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STUDY POPULATION

Response after the first InO cycle (n=24)

Blinatumomab and Inotuzumab for Treatment of Multiply Relapsed Acute Lymphoblastic Leukemia: A Real-Life Campus ALL Study

M. Sciumè, et al, #3408

EPICS

STUDY POPULATION

The Efficacy and Safety of Low-Dose Inotuzumab Ozogamicin in Patients with Relapsed or Refractory Acute Lymphoblastic Leukemia: Interim Results of a Phase 4 Study

M. Özcan, et al, #1208

EPICS

STUDY POPULATION

$CD22^{low}/Bcl\text{-}2^{high}$ Expression Identifies Poor Response to Inotuzumab in Relapsed/Refractory Acute Lymphoblastic Leukemia

E. Diaz-Flores, et al, #614

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STUDY POPULATION

Impact of Allogeneic Hematopoietic Cell Transplantation (HCT) As Consolidation Following CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy for Treatment of Relapsed Acute Lymphoblastic Leukemia (ALL)

J.H. Park, et al, #3880

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STUDY POPULATION

High Effectiveness and Safety of Anti-CD7 CAR T-Cell Therapy in Treating Relapsed or Refractory T-Cell Acute Lymphoblastic Leukemia (T-ALL)

J. Yang, et al, #473

EPICS

STUDY POPULATION

Tandem CD19/CD22 Dual Targets CAR T-Cells Bridging Hematopoietic Stem Cells Transplantation Acquires Robust Remission for Relapsed and Refractory B Acute Lymphoblastic Leukemia Patients

W. Cui, et al, #1753

EPICS

Leukemia Status post CAR-T Infusion

STUDY POPULATION

Outcomes after Reinfusion of CD19-Specific Chimeric Antigen Receptor (CAR)-Modified T Cells in Children and Young Adults with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia

R.M. Myers, et al, #474

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STUDY POPULATION

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Discussion Summary

Updates on Relapsed/Refractory ALL

Advances in ALL: Relapsed/Refractory

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- For first salvage therapy, disease burden and kinetics of the disease are important in determining therapy choice. For high-burden