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Conference Coverage: EHA 2022 – Focus on Lymphoma

June 16, 2022

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
June 16, 2022



**DISEASE STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
lymphoma
> 4 from US
> 4 from Europe



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

Panel Consisting of 4 US and 4 European Lymphoma Experts

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Paolo Caimi, MD
Case Comprehensive
Cancer Center



Matthew Lunning, DO, FACP
University of Nebraska
Medical Center



CHAIR:
Brad Kahl, MD
Washington University
School of Medicine



**Stefan Barta, MD, MS,
MRCP**
Penn Medicine



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



Georg Hess, MD
Johannes Gutenberg University



Olivier Tournilhac, MD, PhD
Clermont-Ferrand University



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



Meeting Agenda

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Time (EST/CEST)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM/15.00 – 15.05	Welcome and Introductions	Brad Kahl, MD
9.05 AM – 9.15 AM/15.05 – 15.15	Advances in DLBCL/Aggressive B-Cell Lymphoma	Matthew Lunning, DO, FACP
9.15 AM – 9.40 AM/15.15 – 15.40	Discussion and Key Takeaways	All
9.40 AM – 9.45 AM/15.40 – 15.45	Updates on T-Cell Lymphoma	Stefan K. Barta, MD, MS, MRCPCUK
9.45 AM – 10.00 AM/15.45 – 16.00	Discussion and Key Takeaways	All
10.00 AM – 10.05 AM/16.00 – 16.05	Advances in FL	Paolo Caimi, MD
10.05 AM – 10.10 AM/16.05 – 16.10	Advances in MCL	Georg Hess, MD
10.10 AM – 10.15 AM/16.10 – 16.15	Advances in MZL/Waldenström Macroglobulinemia	Pier Luigi Zinzani, MD, PhD
10.15 AM – 10.50 AM/16.15 – 16.50	Discussion and Key Takeaways	All
10.50 AM – 11.00 AM/16.50 – 17.00	BREAK	
11.00 AM – 11.10 AM/17.00 – 17.10	Evolving Therapies in CLL/SLL	Olivier Tournilhac, MD, PhD
11.10 AM – 11.30 AM/17.10 – 17.30	Discussion and Key Takeaways	All
11.30 AM – 11.40 AM/17.30 – 17.40	Role of Fixed-Duration and MRD-Guided Strategies in CLL	John Gribben, MD, DSc, FRCP
11.40 AM – 11.55 AM/17.40 – 17.55	Discussion and Key Takeaways	All
11.55 AM – 12.00 PM/17.55 – 18.00	Summary and Closing Remarks	Brad Kahl, MD



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Congress Highlights

Glofitamab in patients with R/R DLBCL: Pivotal phase II expansion results and analysis of immune correlates

Dickinson M, et al. 2022, EHA S220; Piccione E, et al. 2022, EHA P1210

STUDY POPULATION

> Pts with DLBCL and at least 2 prior therapies

Duration of CR



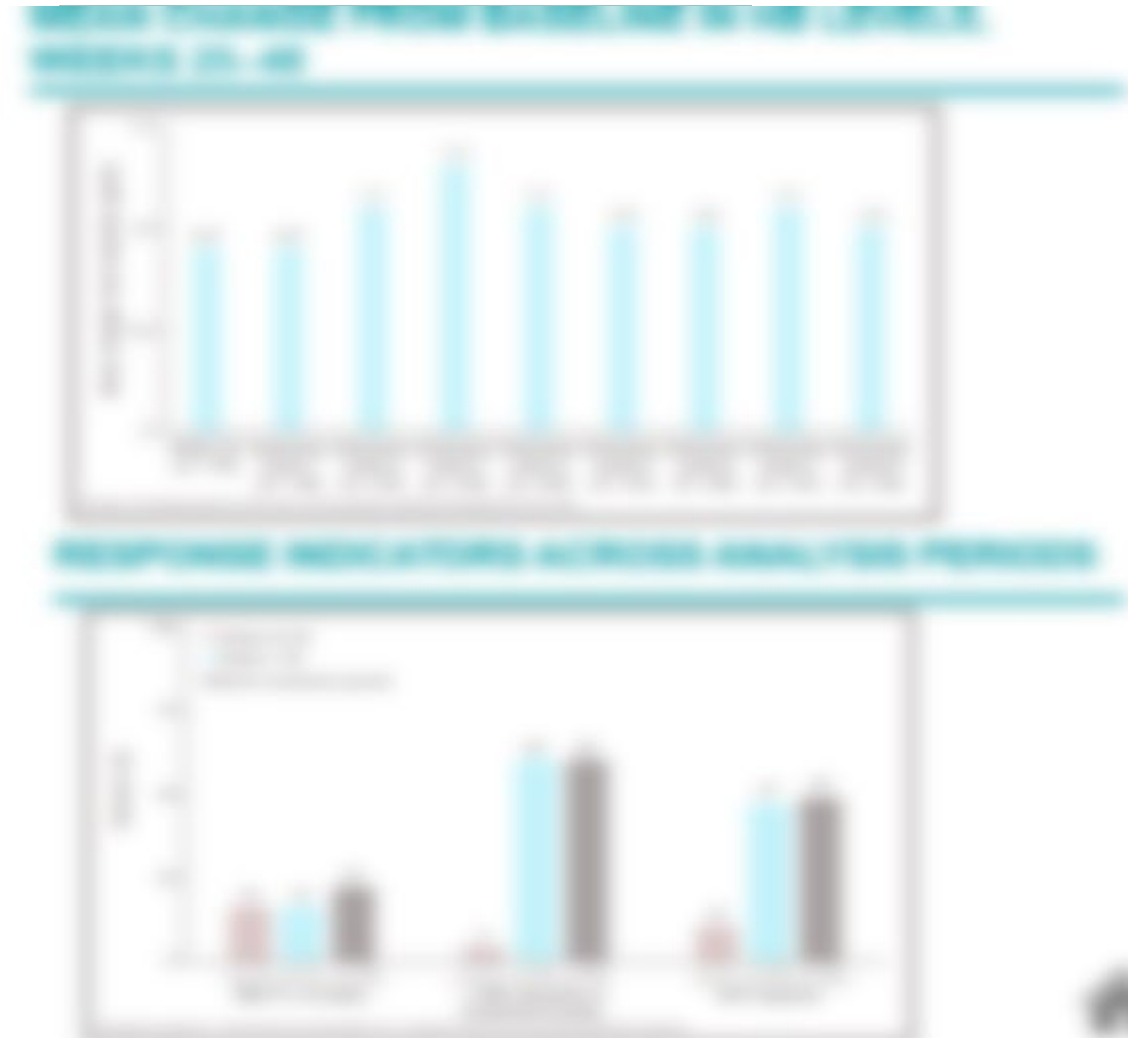
Subcutaneous epcoritamab + R-CHOP for first-line treatment of patients with high-risk diffuse large B-cell lymphoma: Phase 1/2 update

Clausen M, et al. 2022, EHA P1214

STUDY POPULATION

> Pts with newly diagnosed DLBCL and IPI ≥ 3

Response Profile



Zanubrutinib combined with R-CHOP in the treatment of newly diagnosed non-GCB DLBCL with extranodal involvement: A prospective phase II study

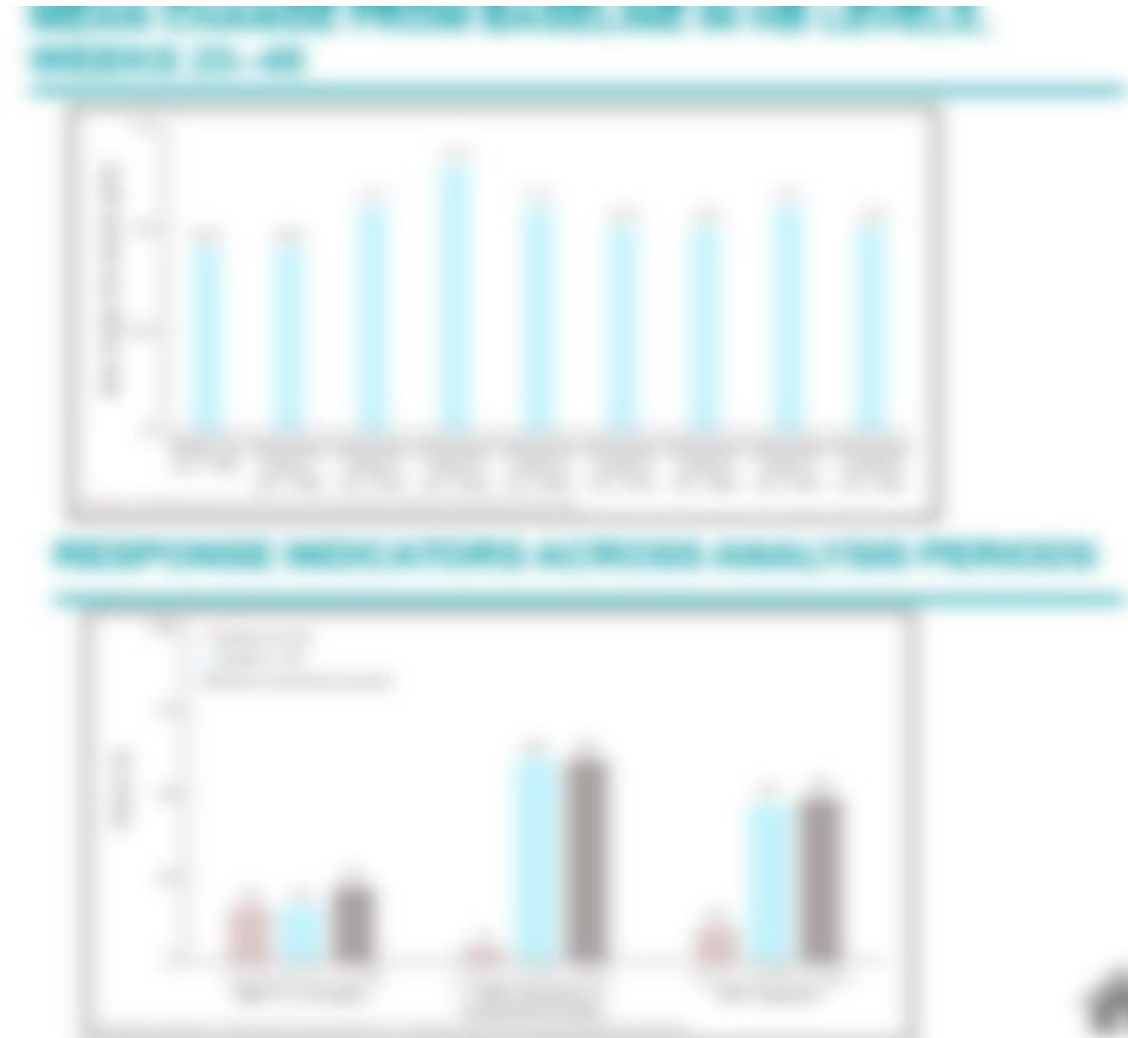
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Li C, et al. 2022, EHA P1185

STUDY POPULATION

> Pts with newly diagnosed, non-GCB DLBCL with extranodal

Efficacy and Survival of Patients Completing Treatment



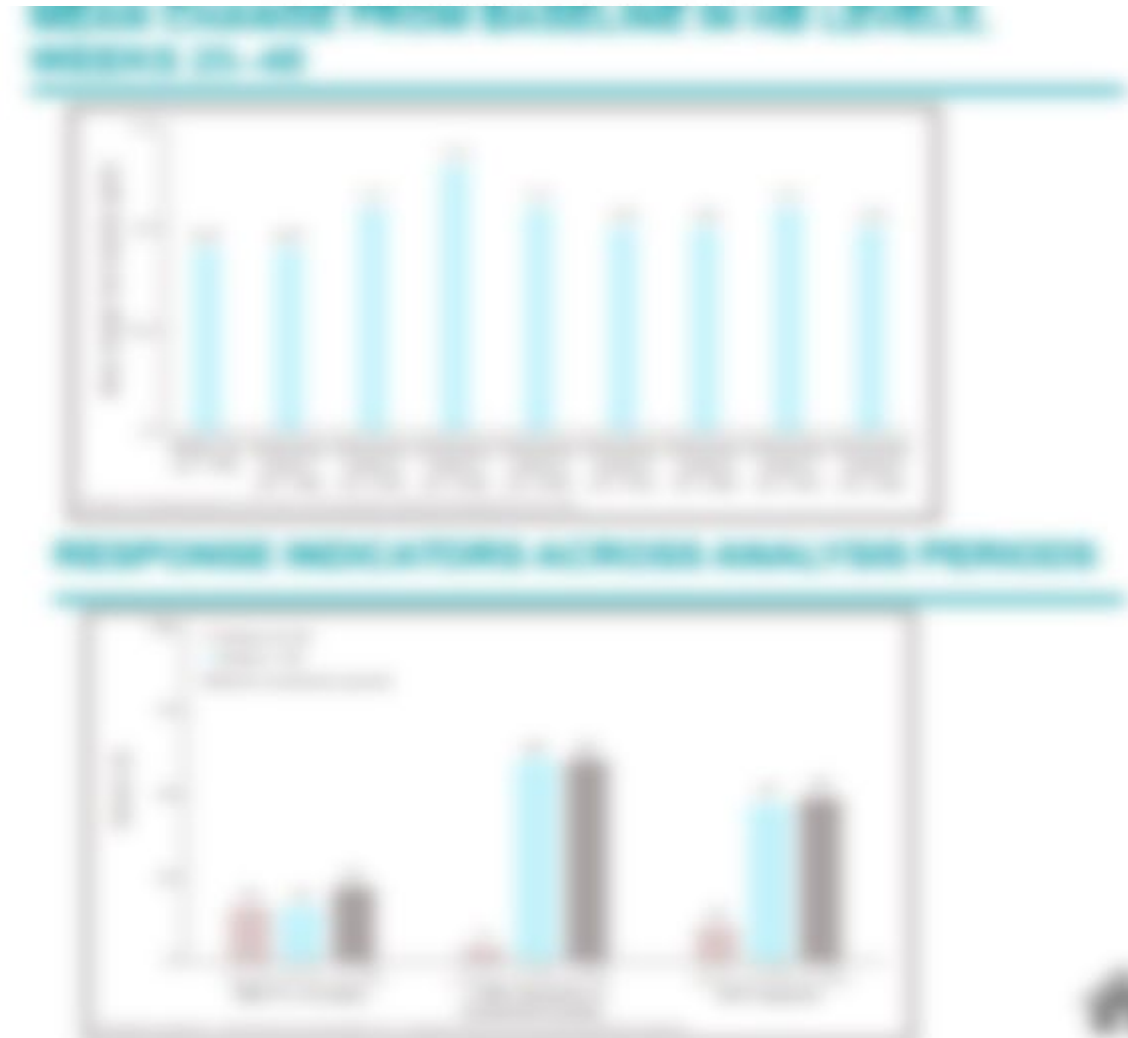
Zanubrutinib, lenalidomide plus R-CHOP (ZR²-CHOP) as the first-line treatment for non-GCB DLBCL

Zhu H, et al. 2022, EHA P1219

STUDY POPULATION

> Pts with high-risk, non-GCB DLBCL and no prior therapy

ctDNA Clearance in a Patient With a TP53 Mutation



Initial safety run-in results of the phase III POLARGO trial: Polatuzumab vedotin plus rituximab, gemcitabine, and oxaliplatin in patients with relapsed/refractory diffuse large B-cell lymphoma

McMillan A, et al. 2022, EHA P1189

STUDY POPULATION

STUDY POPULATION

1. 100 patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) were enrolled in the study. The median age was 65 years (range 45-85). All patients had received at least one prior systemic therapy for DLBCL. The median time from diagnosis to study entry was 12 months (range 3-48). The majority of patients (70%) had relapsed disease, and 30% had refractory disease. The median number of prior systemic therapies was 2 (range 1-5). The majority of patients (80%) had stage III or IV disease. The median performance status was ECOG 1 (range 0-3). The majority of patients (70%) had a relapse within 12 months of their last systemic therapy. The majority of patients (80%) had a relapse within 24 months of their last systemic therapy. The majority of patients (90%) had a relapse within 36 months of their last systemic therapy. The majority of patients (95%) had a relapse within 48 months of their last systemic therapy. The majority of patients (98%) had a relapse within 60 months of their last systemic therapy.

STUDY DESIGN

1. This was a phase III, randomized, controlled trial. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL). The trial was conducted in a multicenter setting across several countries. The majority of patients were from Europe and North America. The trial was funded by AstraZeneca and Bristol Myers Squibb.

KEY FINDINGS

1. The study demonstrated that the combination of polatuzumab vedotin plus rituximab, gemcitabine, and oxaliplatin (Pola-R-GemOx) significantly improved OS compared to the control arm. The median OS was significantly longer in the Pola-R-GemOx group. The study also demonstrated that the combination of Pola-R-GemOx significantly improved PFS and TTNT compared to the control arm. The study also demonstrated that the combination of Pola-R-GemOx significantly improved QoL compared to the control arm. The study was well-tolerated, with no significant differences in adverse events between the two groups.

Peripheral Neuropathy With Pola-R-GemOx



A phase I/II study of golidocitinib, a selective JAK1 inhibitor, in refractory or relapsed peripheral T cell lymphoma

Kim W, et al. 2022, EHA S218

STUDY POPULATION

> Pts with R/R PTCL

Reduction in Tumor Burden



Duvelisib in patients with relapsed/refractory peripheral T-cell lymphoma from the phase 2 PRIMO trial: Updated expansion phase analysis

Zinzani P, et al. 2022, EHA P1172

STUDY POPULATION

> Pts with R/R PTCL

Reduction in Tumor Burden



Tislelizumab, a PD-1 inhibitor, for relapsed/refractory mature T- and NK-cell neoplasms: Results from a phase 2 study

Bachy E, et al. 2022, EHA P1239

STUDY POPULATION

> Pts with R/R ENKTL, PTCL, or CTCL

DOR in PTCL-NOS

Figure 1: DOR in PTCL-NOS



Figure 2: Response rate in PTCL-NOS



Preliminary analysis of the phase II study using tolinapant (ASTX660) monotherapy in 98 PTCL and 51 CTCL subjects with R/R disease

Michot J, et al. 2022, EHA S217

STUDY POPULATION

> Pts with R/R PTCL or CTCL and at least 2 prior systemic

Responses in Patients With PTCL



Zanubrutinib + obinutuzumab vs obinutuzumab monotherapy in patients with relapsed or refractory follicular lymphoma: Primary analysis of the phase 2 randomized ROSEWOOD trial

Zinzani P, et al. 2022, EHA S205

STUDY POPULATION

> Pts with R/R FL and at least 2 prior systemic therapies, including

Overall Survival

Overall Survival: Kaplan-Meier Plot of Overall Survival (OS) in the Intent-to-Treat Population (n=100)



Response: Bar Chart of Response Rates in the Intent-to-Treat Population (n=100)



Obinutuzumab plus chemotherapy demonstrates long-term benefit over rituximab plus chemotherapy in patients with previously untreated follicular lymphoma: Final analysis of the GALLIUM study

Townsend W, et al. 2022, EHA S206

STUDY POPULATION

> Pts with previously untreated FL

PFS per Investigators (primary endpoint)



Primary results from the phase 3 SHINE study of ibrutinib in combination with bendamustine-rituximab (BR) and R maintenance as a first-line treatment for older patients with mantle-cell lymphoma

Wang M, et al. 2022, EHA S209

STUDY POPULATION

> Pts with previously untreated MCL

PFS (primary endpoint)



Acalabrutinib in patients with relapsed/refractory (R/R) marginal zone lymphoma (MZL): Results of a phase 2, multicenter, open-label trial

Strati P, et al. 2022, EHA P1129

STUDY POPULATION

> Pts with MZL and at least 1 prior therapy, including 1 anti-CD20

Reduction in Tumor Burden



Zanubrutinib in older patients with relapsed/refractory marginal zone lymphoma: Subgroup analysis of the MAGNOLIA study

Opat S, et al. 2022, EHA P1162

STUDY POPULATION

> Pts with R/R MZL and at least 1 CD20-directed regimen

Reduction in Tumor Burden



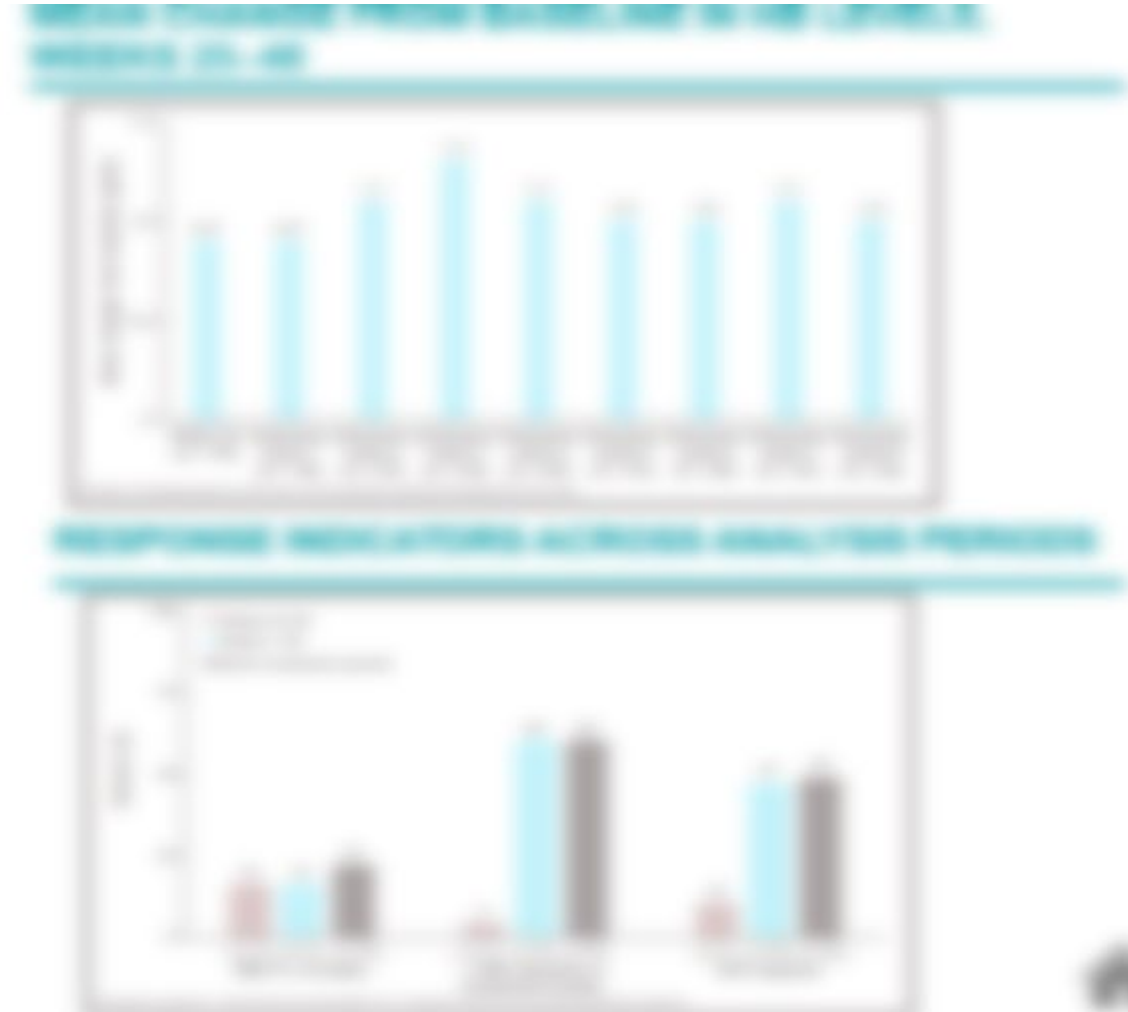
ASPEN: Long-term follow-up results of a phase 3 randomized trial of zanubrutinib vs ibrutinib in patients with Waldenström macroglobulinemia

Dimopoulos M, et al. 2022, EHA P1161

STUDY POPULATION

> Pts with WM requiring therapy

Responses Over Time in MYD88^{MUT} (primary endpoint)



Long term outcomes of IFCG regimen for first line treatment of patients with CLL with mutated IGHV and without del(17P)/TP53 mutation

Jain N, et al. 2022, EHA S149

STUDY POPULATION

> Pts with previously untreated CLL and mutated *IGHV*; no del(17p)

PFS and OS

STUDY POPULATION

1. 100 patients with previously untreated CLL, with mutated *IGHV*, without del(17p) or TP53 mutation, were randomized to either the IFCG regimen (n=50) or the standard of care (SOC) regimen (n=50). The median age was 70 years (range 55-84). All patients were treated with rituximab, flutamide, and cyclophosphamide (FCR) as first-line therapy. The SOC regimen consisted of FCR followed by ibrutinib. The IFCG regimen consisted of FCR followed by ibrutinib and venetoclax. The primary endpoint was overall survival (OS) at 5 years. Secondary endpoints included progression-free survival (PFS), time to treatment failure (TTF), and quality of life (QoL).

RESULTS

1. At 5 years, OS was significantly higher in the IFCG group (75%) compared to the SOC group (60%). PFS was also significantly higher in the IFCG group (85%) compared to the SOC group (75%). TTF was significantly higher in the IFCG group (90%) compared to the SOC group (80%). QoL was significantly higher in the IFCG group (85%) compared to the SOC group (75%).

CONCLUSIONS

The IFCG regimen significantly improved OS, PFS, TTF, and QoL compared to the SOC regimen in patients with previously untreated CLL, with mutated *IGHV*, without del(17p) or TP53 mutation.



Patient-reported outcomes from a phase 3 randomized study of zanubrutinib versus bendamustine plus rituximab in patients with treatment-naïve CLL/SLL

Ghia P, et al. 2022, EHA P662

STUDY POPULATION

> Pts with treatment-naive CLL/SLL (SEQUOIA trial)

Improvement in QOL at Week 24



Acalabrutinib ± obinutuzumab vs obinutuzumab + chlorambucil in treatment-naive chronic lymphocytic leukemia: 5-year follow-up of ELEVATE-TN

Sharman J, et al. 2022, EHA P666

STUDY POPULATION

> Pts with treatment-naive CLL

PFS per Investigators



Acalabrutinib vs rituximab plus idelalisib or bendamustine in relapsed/refractory chronic lymphocytic leukemia: ASCEND results at ~4 years of follow-up

Ghia P, et al. 2022, EHA P668

STUDY POPULATION

> Pts with R/R CLL

PFS (primary endpoint)

100



Venetoclax-obinutuzumab for previously untreated chronic lymphocytic leukemia: 5-year results of the randomized CLL14 study

Al-Sawaf O, et al. 2022, EHA S148

STUDY POPULATION

> Pts with previously untreated CLL and coexisting medical

PFS (primary endpoint)

Figure 1: Overall survival (OS) in the CLL14 study



Figure 2: Response rates in the CLL14 study



The combination of ibrutinib plus venetoclax results in a high rate of MRD negativity in previously untreated CLL: The results of the planned interim analysis of the phase III NCRI FLAIR trial

Hillmen P, et al. 2022, EHA S145

STUDY POPULATION

> Pts with previously untreated CLL requiring therapy

MRD Negativity at 2 Years



Fixed-duration ibrutinib + venetoclax for first-line treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma: 3-year follow-up from the phase 2 CAPTIVATE study FD cohort

Moreno C, et al. 2022, EHA P669

STUDY POPULATION

> Pts with previously untreated CLL/SLL requiring therapy

Best Response to Ibrutinib-Venetoclax

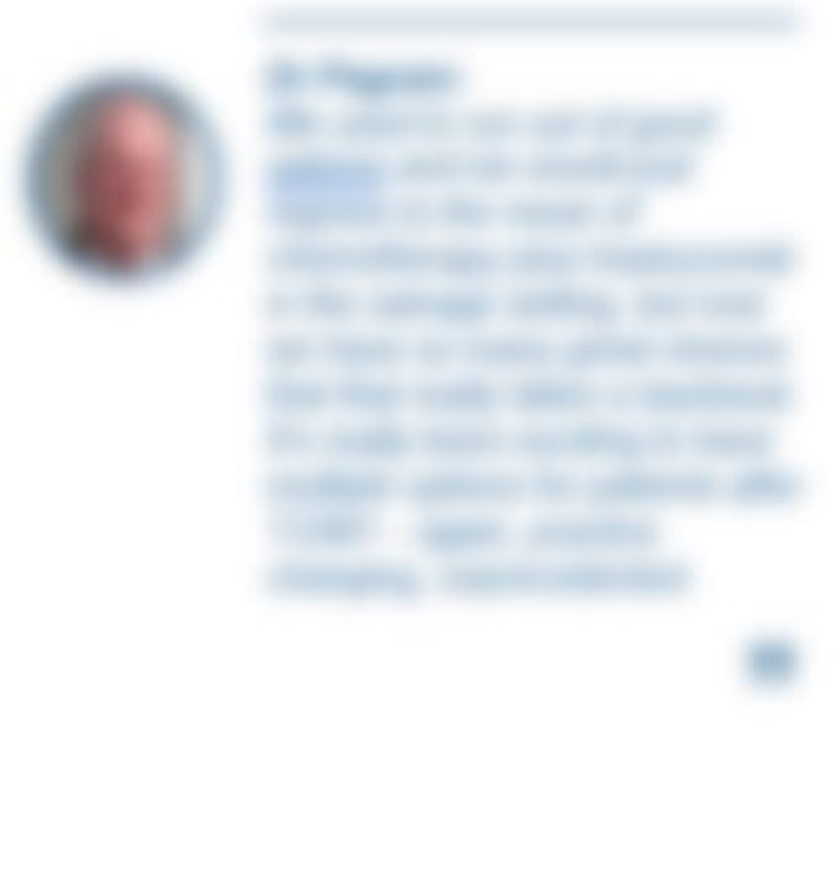


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Key Insights

Expert opinion is that the most impactful data in DLBCL at EHA 2022 came from trials of bispecific antibodies and next-generation BTK inhibitors

- > Epcoritamab + R-CHOP in first-line, high-risk DLBCL (#P1214)



- > Glofitamab in relapsed/refractory DLBCL (#S220)
 - These data are seen by the experts as impressive and good enough for approval as a single agent

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The experts are enthusiastic about the number of new classes of agents for patients with T-cell lymphoma (TCL)
> One of the experts pointed out that the previous generation of agents approved for relapsed/refractory TCL had response rates of ~30%: in



Follicular Lymphoma (FL)

> The experts think the ROSEWOOD trial of zanubrutinib-obinutuzumab vs obinutuzumab in relapsed/refractory FL was unexpectedly positive,



Mantle Cell Lymphoma (MCL)

> Expert opinion is that the SHINE study adding ibrutinib or placebo to BR and rituximab maintenance in patients with previously untreated MCL



Expert opinion is that for patients with CLL and mutated *IGHV*, approaches with chemotherapy such as IFCG (ibrutinib, fludarabine,

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Role of Fixed-Duration and MRD-Guided Strategies in CLL

Expert opinion is that fixed-duration combination regimens will play a part in the treatment of CLL patients, although it may be possible

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