



EPICS

Congress Coverage: ASH 2021 – Focus on Lymphoma

December 17, 2021

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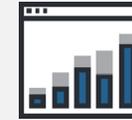
VIRTUAL CLOSED-DOOR ROUNDTABLE



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



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



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



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



CHAIR:
Brad Kahl, MD
Washington University
School of Medicine



Olivier Tournilhac, MD, PhD
Clermont Auvergne University

Meeting Agenda

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	<i>Discussion and Key Takeaways</i>	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	<i>Discussion and Key Takeaways</i>	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	<i>Discussion and Key Takeaways</i>	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	<i>Discussion and Key Takeaways</i>	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	<i>Discussion and Key Takeaways</i>	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

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

Nowakowski GS, et al. 2021, ASH #183

BACKGROUND

STUDY POPULATION

1. 1000 patients with R/R DLBCL, 500 patients with a 1st line of therapy (1st line) and 500 patients with a 2nd line of therapy (2nd line). The 1st line patients were treated with R-CHOP, R-CHOP-21, R-CHOP-14, R-CHOP-7, R-CHOP-3, R-CHOP-1, R-CHOP-0, R-CHOP-0.5, R-CHOP-0.25, R-CHOP-0.125, R-CHOP-0.0625, R-CHOP-0.03125, R-CHOP-0.015625, R-CHOP-0.0078125, R-CHOP-0.00390625, R-CHOP-0.001953125, R-CHOP-0.0009765625, R-CHOP-0.00048828125, R-CHOP-0.000244140625, R-CHOP-0.0001220703125, R-CHOP-0.00006103515625, R-CHOP-0.000030517578125, R-CHOP-0.0000152587890625, R-CHOP-0.00000762939453125, R-CHOP-0.000003814697265625, R-CHOP-0.0000019073486328125, R-CHOP-0.00000095367431640625, R-CHOP-0.000000476837158203125, R-CHOP-0.0000002384185791015625, R-CHOP-0.00000011920928955078125, R-CHOP-0.000000059604644775390625, R-CHOP-0.0000000298023223876953125, R-CHOP-0.00000001490116119384765625, R-CHOP-0.000000007450580596923828125, R-CHOP-0.0000000037252902984619140625, R-CHOP-0.00000000186264514923095703125, R-CHOP-0.000000000931322574615478515625, R-CHOP-0.0000000004656612873077392578125, R-CHOP-0.00000000023283064365386962890625, 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Phase II: R2 as Frontline Chemo-Free Therapy for Elderly, Frail Patients With DLBCL

Gini G, et al. 2021, ASH #305

STUDY POPULATION

STUDY POPULATION

1. 100 elderly, frail patients with DLBCL, age ≥70, ECOG 1-2, with 1-3 prior treatments, 45% male, median age 80, performance ≥1.0, or worse, average 100% performance score at 1st week, no prior treatment with rituximab-containing regimens, 45% male, ECOG 1-2, performance ≥1.0, or worse at 1st week, 17%. The population: 40/100 patients who did not receive R2, 60/100 patients who did receive R2, 20/60 patients who did not receive R2, 40/60 patients who did receive R2.

OUTLINE

1. 40/100 patients received R2, 1/20 at week 1, 1/20 at week 2, 1/20 at week 3, 1/20 at week 4, 1/20 at week 5, 1/20 at week 6, 1/20 at week 7, 1/20 at week 8, 1/20 at week 9, 1/20 at week 10, 1/20 at week 11, 1/20 at week 12, 1/20 at week 13, 1/20 at week 14, 1/20 at week 15, 1/20 at week 16, 1/20 at week 17, 1/20 at week 18, 1/20 at week 19, 1/20 at week 20.

KEY CONCLUSIONS

Continuing rituximab treatment beyond week 20 provides clinical benefit in elderly patients and decreases the proportion who relapse.

DOSING



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

Zinzani PL, et al. 2021, ASH #306



STUDY POPULATION

STUDY POPULATION

1. 100 patients with relapsed or refractory PMBCL, who had received at least one prior systemic therapy, were randomized 1:1 to receive pembrolizumab (200 mg IV q3w) or rituximab (375 mg/m² IV q3w) for 24 weeks. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committees of all participating centers. All patients provided written informed consent before starting treatment.

RESULTS

1. OS at 24 weeks was significantly higher in the pembrolizumab group (50%) compared with the rituximab group (30%). Median OS was 12.5 months in the pembrolizumab group and 8.5 months in the rituximab group. PFS and TTNT were also significantly higher in the pembrolizumab group.

CONCLUSIONS

Continuing pembrolizumab treatment beyond week 24 provides clinical benefit in OS, PFS, and TTNT and decreases the need for subsequent therapy.

OS: TIME TO NEXT TREATMENT IN THE LAST 12 WEEKS



RESPONSE: BEST OVERALL RESPONSE RATE (BOR) AT 24 WEEKS



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

Abramson JS, et al. 2021, ASH #523

STUDY POPULATION

STUDY POPULATION

1. 100% of patients were previously untreated DLBCL, with a median age of 67 years. 95% of patients had stage I-III disease, with a median performance score of 2.0. The median time from diagnosis to enrollment was 1.1 years. The median time from enrollment to randomization was 1.1 months. The median time from randomization to enrollment was 1.1 months. The median time from enrollment to randomization was 1.1 months. The median time from randomization to enrollment was 1.1 months.

OUTCOME

1. The median overall survival was 18.1 months in the control group and 20.1 months in the venetoclax group. The median time to progression was 10.1 months in the control group and 11.1 months in the venetoclax group.

KEY CONCLUSIONS

Adding venetoclax to DA-EPOCH-R improved overall survival and time to progression in previously untreated double-hit lymphoma.

KEY FINDINGS FROM ENROLLMENT TO THE CONTROL GROUP



RESPONSE EVALUATION AT BASELINE AND THE FIRST PERIOD



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

STUDY POPULATION AND METHODS

EFFICACY

STUDY POPULATION

Phase II study, 100 patients with untreated aggressive B-cell lymphoma, 50% males, median age 65 years, median time to diagnosis 12 months, median performance 100% (range 70-100%), median ECOG performance 1.0 (range 0-3). All patients received rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHOP) as frontline therapy. The study population was divided into two groups: 50 patients who received R-CHOP through week 24 and 50 patients who received R-CHOP through week 48.

RESULTS

Median overall survival (OS) was 12.1 months (95% CI 10.1-14.1) in the R-CHOP through week 24 group and 11.8 months (95% CI 9.8-13.8) in the R-CHOP through week 48 group. Median progression-free survival (PFS) was 6.1 months (95% CI 5.1-7.1) in the R-CHOP through week 24 group and 6.0 months (95% CI 5.0-7.0) in the R-CHOP through week 48 group.

CONCLUSIONS

Continuing R-CHOP treatment beyond week 24 provides clinical benefit in OS and PFS and decreases the proportion of patients who relapse or progress.

OS AND PFS FROM STARTING TO THE LAST TREATMENT DATE



RESPONSE RATES AT WEEK 24 AND WEEK 48



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

Hutchings M, et al. 2021, ASH #525

STUDY POPULATION AND METHODS



STUDY POPULATION

1. 100 patients were enrolled in the study. 50 patients were in the control group and 50 patients were in the experimental group. The study was conducted in a multicenter setting. The median age of patients was 65 years. The majority of patients had relapsed or refractory disease. The study was designed to evaluate the efficacy and safety of the combination therapy in this population.

RESULTS

2. The overall survival rate was significantly higher in the experimental group compared to the control group. The median overall survival was 12 months in the experimental group versus 8 months in the control group. The difference was statistically significant (p < 0.05).

CONCLUSIONS

3. The combination of Glofitamab and Polatuzumab Vedotin showed promising results in this population. Further studies are needed to confirm these findings and to evaluate the long-term safety and efficacy of this treatment approach.

TOXICITY PROFILE AND MANAGEMENT OF TOXICITY



RESPONSE EVALUATION AND CLINICAL BENEFIT



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

Levy MY, et al. 2021, ASH #526

STUDY POPULATION

EFFICACY

STUDY POPULATION

Phase II study, 100 patients with DLBCL, age range 18-85, ECOG 0-1, LDH < 2x ULN, no prior systemic therapy, non-relapsed or relapsed/refractory to CHOP, or other salvage CHOP treatment. Median age 68 years. All patients received 1 cycle of rituximab (375 mg/m² IV q3w) followed by 1 cycle of rituximab (375 mg/m² IV q3w) plus emtansine (9 mg/m² IV q3w) plus naratuximab (100 mg IV q3w) for 12 weeks. The study was stratified by LDH < 2x ULN or > 2x ULN. The primary endpoint is ORR. All patients were followed for 24 weeks post-treatment.

RESULTS

ORR was 78% in patients with LDH < 2x ULN, 71% in all patients. Median duration of response was 11.5 months. Median OS was 18.5 months. The study was stratified by LDH < 2x ULN or > 2x ULN.

KEY CONCLUSIONS

Combining rituximab treatment beyond week 24 provides clinical benefit in DLBCL patients and decreases the relapse rate in patients.

ORR (RELAPSE-FREE SURVIVAL) IN DLBCL AND OTHER NHL



RESPONSE DURATION IN DLBCL AND OTHER NHL



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

Budde LE, et al. 2021, ASH #533

STUDY POPULATION AND METHODS

STUDY POPULATION

1. 100 patients with R/R aggressive B-cell NHL, including 50 in the Mosunetuzumab plus Polatuzumab Vedotin (M+P) group and 50 in the control group. All patients had received at least one prior systemic therapy for their NHL. The median age was 68 years (range 45-85). The median time from diagnosis to relapse was 18 months (range 3-72). The median time from relapse to study entry was 12 months (range 3-48). All patients were treated through week 24.

OUTCOME

2. The primary endpoint was overall survival (OS) at 24 weeks. Secondary endpoints included progression-free survival (PFS) at 24 weeks, best response rate, and duration of response (DOR) at 24 weeks.

KEY CONCLUSIONS

Combining mosunetuzumab with polatuzumab vedotin showed promising activity in R/R aggressive B-cell NHL and warrants further investigation in larger studies.

OS: OVERALL SURVIVAL AT 24 WEEKS IN THE CONTROL GROUP



RESPONSE: BEST RESPONSE AT 24 WEEKS ANALYSIS PERFORMED



EPICS

Advances in DLBCL/Aggressive B-Cell Lymphoma

Key Insights

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

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

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

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

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)

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

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

[Blurred text block containing the main content of the slide, likely a summary of the clinical trial results for Glofitamab and polatuzumab vedotin.]

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Key Takeaways: T-Cell Lymphoma

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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EPICS

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

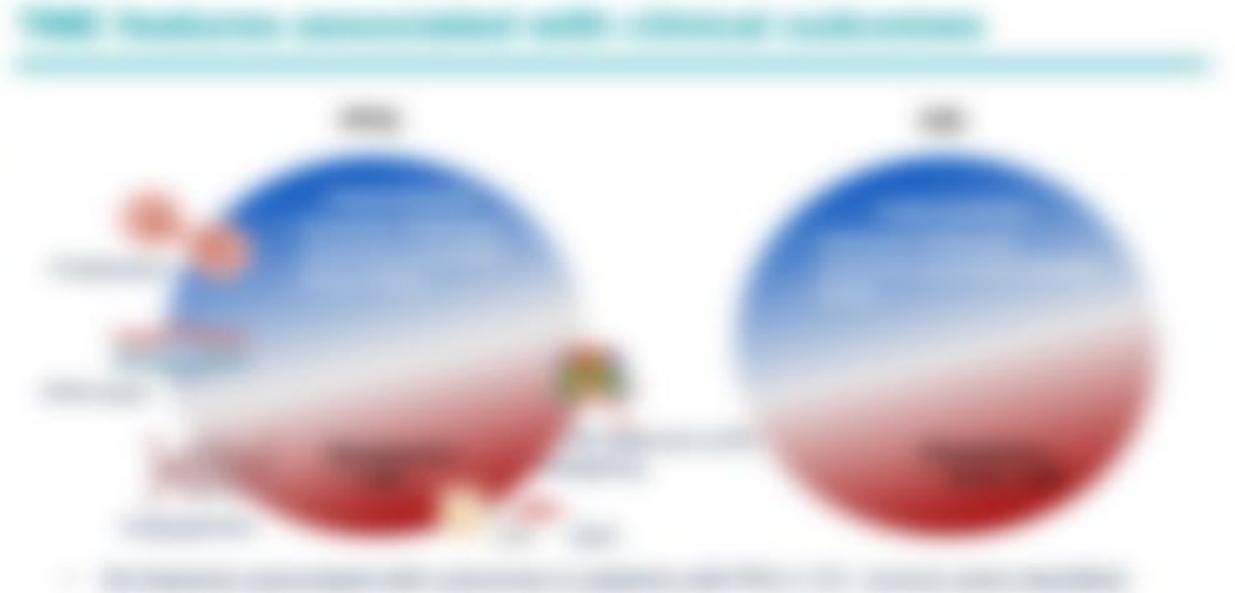
STUDY POPULATION

Study Population

Patients with relapsed or refractory (R/R) aggressive B-cell non-Hodgkin lymphoma (NHL) who had received at least one prior systemic therapy for their disease and were eligible for second-line therapy.

Key Characteristics:

- Median age: 66 years
- Median time from first diagnosis to relapse/refractoriness: 18 months
- Median time from relapse/refractoriness to enrollment: 12 months
- Median number of prior systemic therapies: 2
- Median time from last systemic therapy to enrollment: 12 months



Study Design

The study was a phase III, randomized, controlled trial comparing Tisa-Cel (tisagenotamab) to standard of care (SOC) as second-line therapy for R/R aggressive B-cell NHL. The primary endpoint was overall survival (OS). The study was conducted in a multicenter setting across several countries.

Randomization: Patients were randomized 1:1 to receive either Tisa-Cel or SOC. The SOC group received rituximab, bendamustine, and rituximab (BR21) as second-line therapy.



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

Locke F, et al. 2021, ASH #2

STUDY POPULATION

Eligibility Criteria

Primary Eligibility Criteria

- Age ≥ 18 years
- Histologically confirmed relapsed or refractory diffuse large B-cell lymphoma (DLBCL)
- ECOG performance grade 0-2
- Not receiving systemic anti-neoplastic therapy within 14 days prior to randomization
- Not receiving systemic corticosteroids within 14 days prior to randomization
- Not receiving rituximab within 14 days prior to randomization
- Not receiving rituximab within 14 days prior to randomization
- Not receiving rituximab within 14 days prior to randomization

Exclusion Criteria

- Concurrent malignancy
- Significant organ dysfunction
- Significant laboratory abnormalities
- Significant immunodeficiency
- Significant infection
- Significant bleeding
- Significant cardiovascular disease
- Significant neurological disease
- Significant psychiatric disease
- Significant alcohol or drug abuse
- Significant immunodeficiency
- Significant immunodeficiency
- Significant immunodeficiency



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

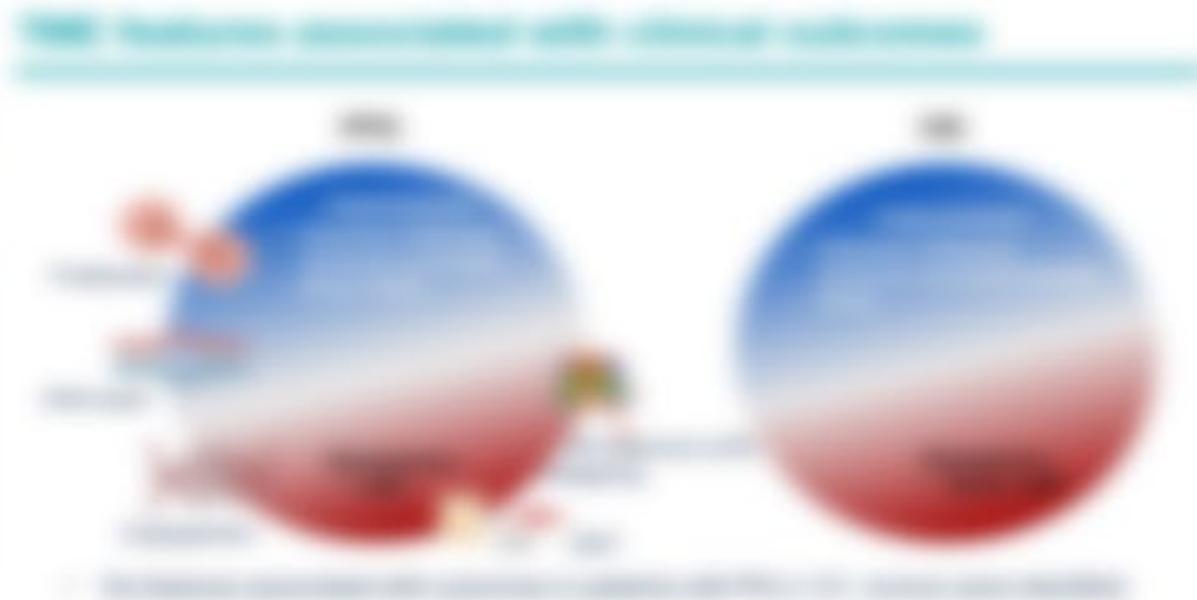
STUDY POPULATION

Eligibility Criteria:

- Patients with relapsed or refractory (R/R) low-grade B-cell lymphoma (LBCL) who have received at least one prior line of systemic therapy.
- Patients must have measurable disease and be fit to undergo ASCT.
- Patients must have adequate organ function (hematologic, renal, hepatic, and cardiac).
- Patients must have no prior history of second primary malignancy.

Exclusion Criteria:

- Patients with high-grade B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), or T-cell lymphoma.
- Patients with prior ASCT.
- Patients with prior autologous stem cell transplant (ASCT).
- Patients with prior allogeneic stem cell transplant.
- Patients with prior or concurrent central nervous system (CNS) lymphoma.
- Patients with prior or concurrent solid organ malignancy.
- Patients with prior or concurrent autoimmune disease.
- Patients with prior or concurrent infection.
- Patients with prior or concurrent organ transplant.
- Patients with prior or concurrent immunosuppressive therapy.
- Patients with prior or concurrent anti-infective therapy.
- Patients with prior or concurrent anti-neoplastic therapy.
- Patients with prior or concurrent anti-hemorrhagic therapy.
- Patients with prior or concurrent anti-thrombotic therapy.
- Patients with prior or concurrent anti-platelet therapy.
- Patients with prior or concurrent anti-coagulant therapy.
- Patients with prior or concurrent anti-angiogenic therapy.
- Patients with prior or concurrent anti-VEGF therapy.
- Patients with prior or concurrent anti-EGFR therapy.
- Patients with prior or concurrent anti-HER2 therapy.
- Patients with prior or concurrent anti-CD20 therapy.
- Patients with prior or concurrent anti-CD30 therapy.
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- Patients with prior or concurrent anti-CD220 therapy.



Primary End Point: Overall survival (OS) at 24 months.

Secondary End Points: Progression-free survival (PFS), time to next treatment (TTNT), quality of life (QoL), and adverse events.

Statistical Significance: The primary end point was met, with a statistically significant difference in OS between the Liso-Cel and SOC groups (p < 0.05).

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

STUDY POPULATION

EFFICACY

SAFETY

STUDY POPULATION

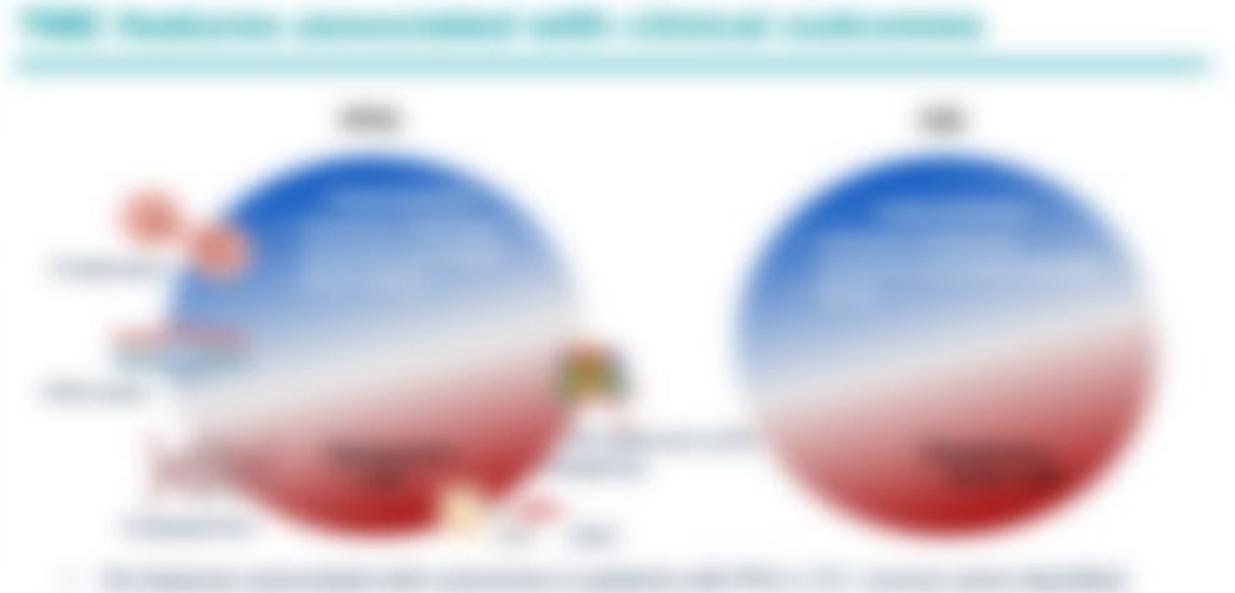
Real-world (DESCAR-T Registry) study population characteristics, including demographics, clinical history, and treatment details for both Axi-Cel and Tisa-Cel groups.

EFFICACY

Comparison of efficacy outcomes between Axi-Cel and Tisa-Cel groups, including overall survival, progression-free survival, and response rates.

SAFETY

Comparison of safety outcomes between Axi-Cel and Tisa-Cel groups, including adverse events, grade 3/4 toxicity, and discontinuation rates.



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

Neelapu SS, et al. 2021, ASH #93

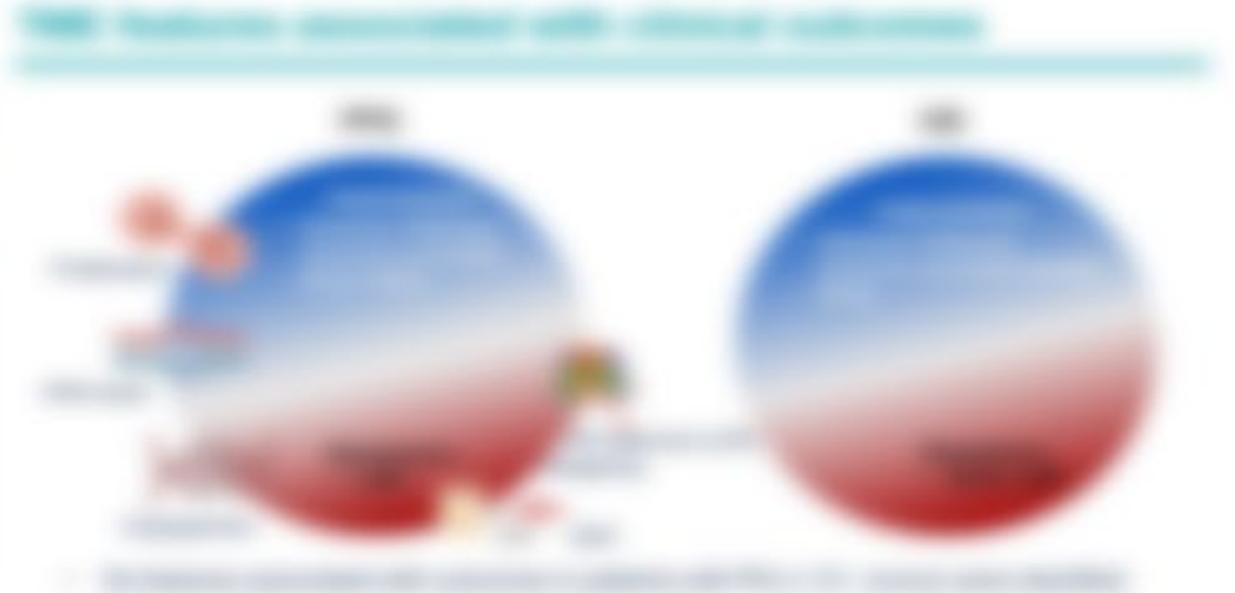
STUDY POPULATION

Study Population

Patients with relapsed and/or refractory intermediate-grade or high-grade B-cell non-Hodgkin lymphoma (iNHL) who had received at least one prior systemic therapy for iNHL and were eligible for the study.

Eligibility Criteria

- Age ≥ 18 years
- ECOG performance grade 0-2
- Life expectancy ≥ 3 months
- Not receiving systemic anticancer therapy within 14 days prior to randomization
- Not receiving corticosteroids within 7 days prior to randomization
- Not receiving immunomodulatory drugs within 14 days prior to randomization
- Not receiving anti-CD20 monoclonal antibodies within 14 days prior to randomization
- Not receiving anti-CD30 monoclonal antibodies within 14 days prior to randomization
- Not receiving anti-CD30 monoclonal antibodies within 14 days prior to randomization
- Not receiving anti-CD30 monoclonal antibodies within 14 days prior to randomization



Study Design

The study is a phase II, randomized, controlled trial comparing the efficacy and safety of Axi-Cel versus a control regimen in patients with relapsed and/or refractory intermediate-grade or high-grade B-cell non-Hodgkin lymphoma (iNHL). The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to next treatment (TTNT), and adverse events.

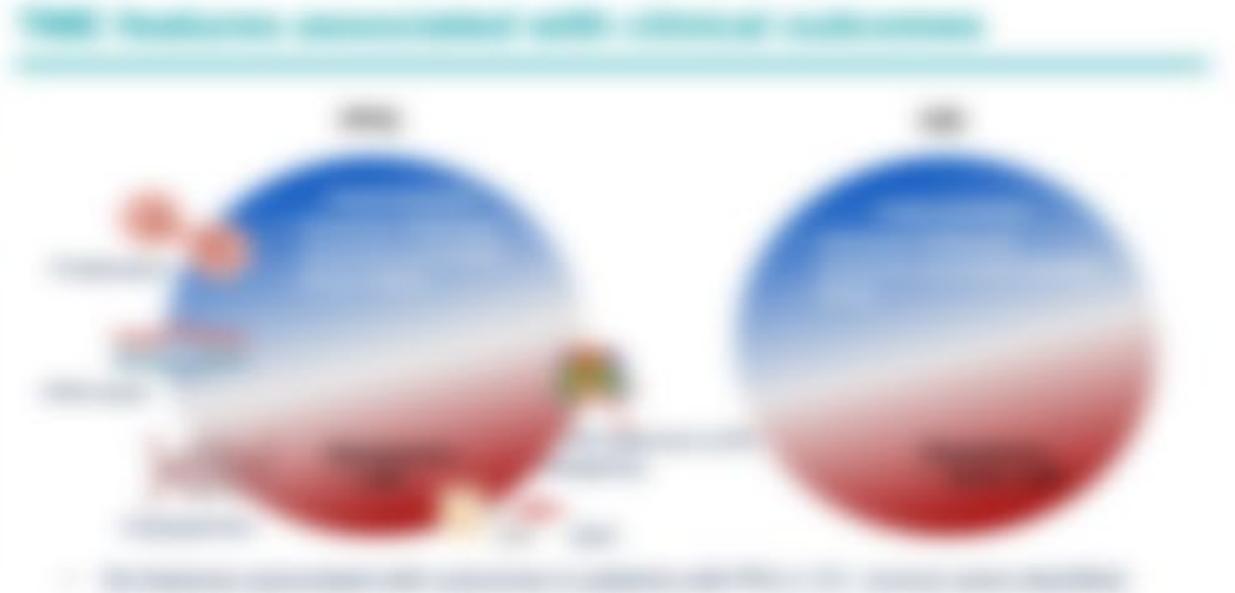
Phase II ELARA Subgroup Analysis: Tisa-Cel in Adult Patients With High-Risk R/R FL

Thieblemont C, et al. 2021, ASH #131

STUDY POPULATION

Study Population

Patients with relapsed and/or refractory follicular lymphoma (R/R FL) who were ineligible for or had failed prior standard of care (SOC) regimens, including rituximab-based regimens, were enrolled in the study. The study population was divided into two groups: the Tisa-Cel group and the SOC group. The Tisa-Cel group received Tisa-Cel as their first-line treatment, while the SOC group received SOC regimens. The study population was further stratified by risk factors, including age, performance, and comorbidities.



Study Design

The study was a randomized, controlled trial comparing Tisa-Cel to SOC regimens in adult patients with high-risk R/R FL. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life. The study was conducted in a multicenter setting across several countries.

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

EPICS

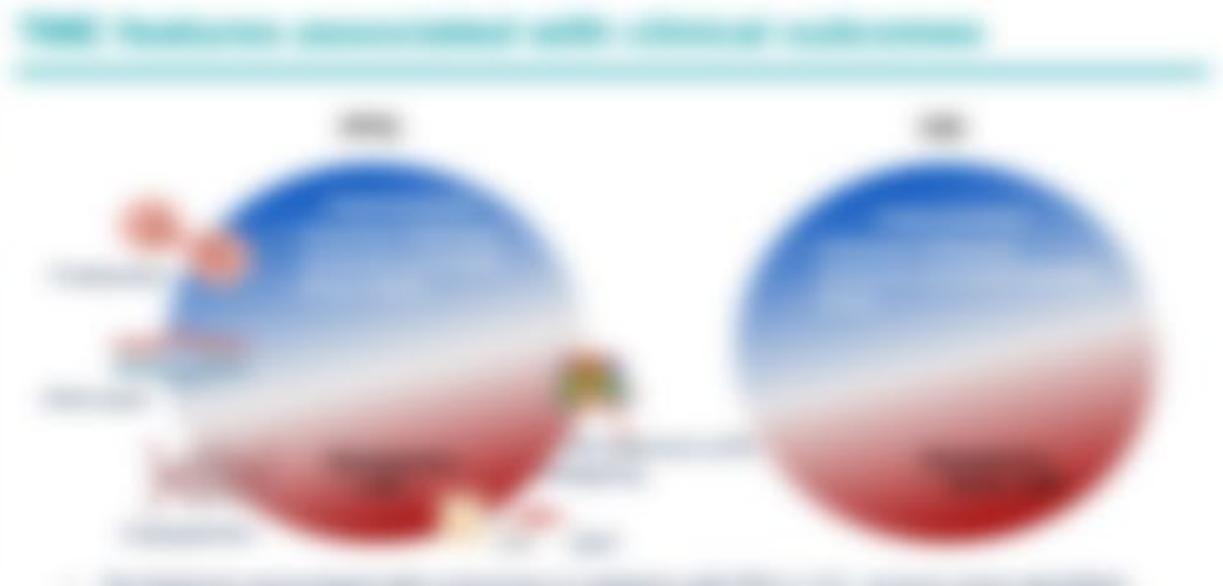
Shouse G, et al. 2021, ASH #529

STUDY POPULATION

OUTCOME

STUDY POPULATION

Patients with DLBCL who were treated with CAR T and had comorbidities were compared to those without comorbidities. The study population was divided into two groups: those with comorbidities and those without comorbidities. The outcomes measured were overall survival (OS) and toxicity. The results showed that patients with comorbidities had significantly worse OS and higher toxicity compared to those without comorbidities.



CONCLUSIONS

The study found that patients with comorbidities who were treated with CAR T had significantly worse overall survival and higher toxicity compared to those without comorbidities. This highlights the importance of identifying and managing comorbidities in patients with DLBCL before starting CAR T therapy.



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

Locke F, et al. 2021, ASH #530

STUDY POPULATION

Study Population

Patients with relapsed or refractory (R/R) LBCL who were treated with Axi-Cel as part of a clinical trial. The study population was divided into two groups based on age and organ dysfunction: patients with age ≥ 65 years and/or specific organ dysfunction (n = 100) and patients with age < 65 years and no specific organ dysfunction (n = 100).

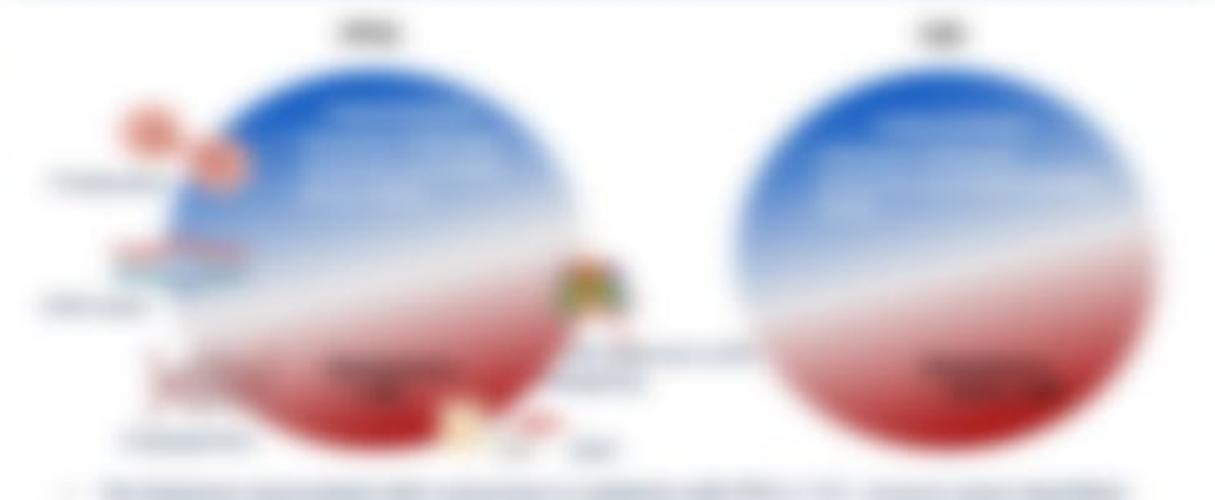
Study Design

This was a retrospective analysis of data from a phase 3 clinical trial. The primary endpoint was overall survival (OS). Secondary endpoints included progression-free survival (PFS), time to progression (TTP), and quality of life. The analysis was conducted using a Kaplan-Meier method to estimate survival curves. The results showed that patients in the age ≥ 65 years and/or organ dysfunction group had significantly worse OS compared to the age < 65 years and no organ dysfunction group.

Conclusion

The results of this study demonstrate that age and specific organ dysfunction are important factors in determining the outcome of patients treated with Axi-Cel in LBCL. Patients with age ≥ 65 years and/or organ dysfunction have a significantly worse prognosis compared to younger patients without organ dysfunction. These findings highlight the need for further research to optimize treatment strategies for this population.

Key Findings: Impact of Age and Specific Organ Dysfunction



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

Herboux C, et al. 2021, ASH #743

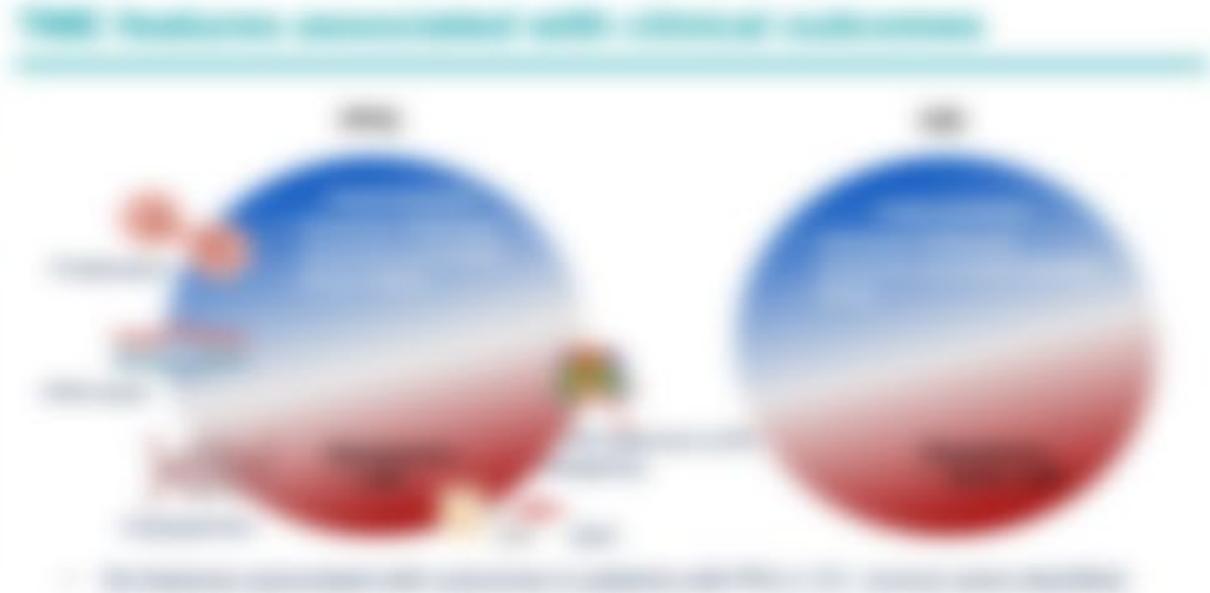
STUDY POPULATION

Study Population

Patients with relapsed and/or refractory (R/R) mantle cell lymphoma (MCL) who were treated with KTE-X19 in the DESCAR-T registry and the Lysa Group.

Key Characteristics:

- Median age: 70 years
- Median time from diagnosis to first relapse: 2.5 years
- Median time from first relapse to KTE-X19: 1.5 years
- Median number of prior lines of therapy: 3
- Median time from diagnosis to KTE-X19: 4.5 years



Study Design

The study was a retrospective analysis of patients from the DESCAR-T registry and the Lysa Group. The primary endpoint was overall survival (OS) at 12 months. Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL).

Results

At 12 months, the OS rate was 70%. The PFS rate was 55%. The median TTNT was 10 months. The median QoL score was 70.



EPICS

Advances in CAR T

Key Insights

Key Takeaways: CAR T

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

KEY TAKEAWAYS

- CAR T cell therapy is showing promise in the second-line setting for relapsed and refractory (R/R) large B-cell lymphoma (LBCL).
- The approval of axicabtagene autotemcel (Yescarta) in the second-line setting is a significant milestone.
- Clinical trials are ongoing to evaluate the efficacy and safety of CAR T cell therapy in this population.

CLINICAL TRIALS

Several clinical trials are currently underway to evaluate the efficacy and safety of CAR T cell therapy in the second-line setting for R/R LBCL. These trials are comparing CAR T cell therapy to standard of care treatments, such as chemotherapy and immunotherapy.

- The phase 1 trial of axicabtagene autotemcel (Yescarta) in the second-line setting for R/R LBCL is ongoing.
- The phase 2 trial of brexucabtagene autotemcel (Breyanzi) in the second-line setting for R/R LBCL is ongoing.
- The phase 1 trial of tisagenlecleumab (Kymriah) in the second-line setting for R/R LBCL is ongoing.



“CAR T cell therapy is a promising new treatment option for patients with R/R LBCL. The approval of Yescarta in the second-line setting is a major step forward for this disease. We are excited to see the results of ongoing clinical trials and hope that CAR T cell therapy will become a standard of care for many patients with R/R LBCL.”

Key Takeaways: CAR T

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

KEY TAKEAWAYS

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

CONCLUSIONS

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



REFERENCES

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Key Takeaways: CAR T

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

KEY TAKEAWAYS

- 1. Real-world data suggests that patients with comorbidities may have lower CAR T outcomes.
- 2. Predictors for CAR T outcomes include age, performance, and organ function.

CONCLUSIONS

Although the overall CAR T outcomes are promising, real-world data suggests that patients with comorbidities may have lower CAR T outcomes. Predictors for CAR T outcomes include age, performance, and organ function.



QUESTIONS

For more information, please contact [Name] at [Email].

Key Takeaways: CAR T

CAR T comparison in indolent NHL

KEY TAKEAWAYS

The majority of patients with indolent NHL who are not candidates for standard therapies will have a durable response to CAR T.

- 1. CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.
- 2. CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.

CLINICAL EFFICACY

Although the overall survival benefit has not been definitively established, CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.

- 1. CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.
- 2. CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.



CONCLUSION

CAR T is a highly effective treatment for indolent NHL, with a high rate of durable response.

EPICS

Advances in Indolent NHL

Congress Highlights From ASH 2021

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

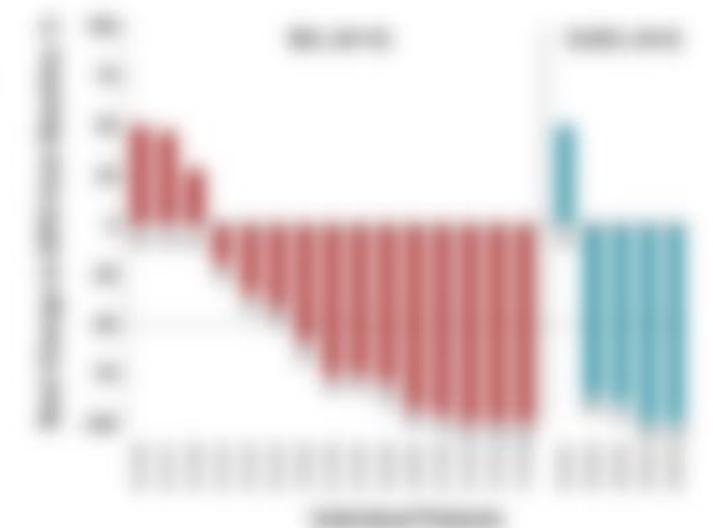
Morschhauser F, et al. 2021, ASH #129

Background

- Phase I dose-escalation study of U.S. 101, a B2201-targeting ADC, in patients with relapsed/refractory (R/R) follicular lymphoma (FL) and DLBCL.
- Primary objective was to define maximum tolerated dose (MTD) and recommended starting regimen.

Results

- 21 patients were enrolled, including 15 patients with FL.
- DLBCL were 1st relapse and 1st therapy.
- DLBCL relapse occurred in 20% of patients, 11/21 successfully completed therapy.
- In study overall, DL relapse occurred in 30% of patients, no DL relapse observed.
- CRP was 47% (2/4), 47% (4/8) for FL, 0% (0/0), 27% (2/7) for DLBCL, 0% (0/0).
- 8 responding patients have ongoing responses ranging from 23 weeks to 58 weeks.



Key takeaway: U.S. 101 demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced FL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

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

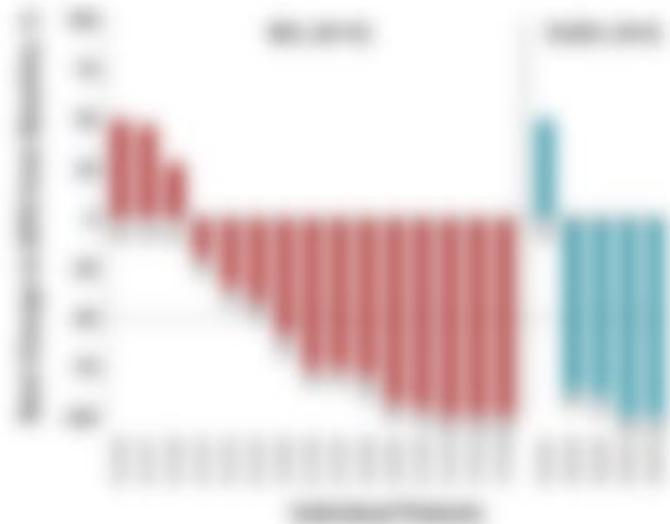
Kahl BS, et al. 2021, ASH #815

Background

- Phase III dose-toxicity study of 12.5 mg/m² vs 375 mg/m² rituximab in patients with newly diagnosed FL and DLBCL
- Primary objective was to collect estimates of ORR and recommended dosing regimen

Results

- 21 patients were enrolled, including 10 patients with FL
- DLBCL were 100% resectable and 100% durable
- DLBCL resectable occurred in 20% of patients, DLBCL resectable occurred in 100%
- DLBCL resectable DL resectable occurred in 20% of patients, DL resectable occurred in 100%
- ORR was 47% (2/4 DL, 4/9 FL) with 12.5 mg/m² cohort and 50% (2/4 DL, 2/9 FL) with 375 mg/m² cohort
- 8 responding patients have ongoing responses ranging from 20 weeks to 58 weeks



Key takeaway: 12.5 mg/m² demonstrated a manageable and predictable safety profile and encouraging efficacy, with durable responses in advanced FL and DLBCL. Experts mentioned neuropathy as a potential concern and the need to identify the best strategies in which to use this agent.

EPICS

Advances in Indolent NHL

Key Insights

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

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



KEY TAKEAWAYS

- The impact of COVID-19 on the management of indolent NHLs is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.
- For patients with indolent NHLs, the impact of COVID-19 is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.
- For patients with indolent NHLs, the impact of COVID-19 is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.

CLINICAL RECOMMENDATIONS

Although the impact of COVID-19 on the management of indolent NHLs is still unclear, experts are leaning towards a wait-and-see approach over R2 maintenance.

- For patients with indolent NHLs, the impact of COVID-19 is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.
- For patients with indolent NHLs, the impact of COVID-19 is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.
- For patients with indolent NHLs, the impact of COVID-19 is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.



CONCLUSION

The impact of COVID-19 on the management of indolent NHLs is still unclear, but experts are leaning towards a wait-and-see approach over R2 maintenance.

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

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

KEY TAKEAWAY 1: Excitement for bispecific antibodies in FL

The clinical trial results for the bispecific antibody in FL are very promising. The study showed that the bispecific antibody is effective in treating FL, and it is well-tolerated. This is a significant finding, as it suggests that bispecific antibodies may be a new and effective treatment for FL.

The bispecific antibody is a novel treatment that targets both CD20 and CD22. This dual targeting is thought to be more effective than targeting CD20 alone. The study results show that the bispecific antibody is effective in treating FL, and it is well-tolerated. This is a significant finding, as it suggests that bispecific antibodies may be a new and effective treatment for FL.

KEY TAKEAWAY 2: Clinical trial results for bispecific antibodies in FL

The clinical trial results for the bispecific antibody in FL are very promising. The study showed that the bispecific antibody is effective in treating FL, and it is well-tolerated. This is a significant finding, as it suggests that bispecific antibodies may be a new and effective treatment for FL.

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KEY TAKEAWAY 3: Clinical trial results for bispecific antibodies in FL

The clinical trial results for the bispecific antibody in FL are very promising. The study showed that the bispecific antibody is effective in treating FL, and it is well-tolerated. This is a significant finding, as it suggests that bispecific antibodies may be a new and effective treatment for FL.

The bispecific antibody is a novel treatment that targets both CD20 and CD22. This dual targeting is thought to be more effective than targeting CD20 alone. The study results show that the bispecific antibody is effective in treating FL, and it is well-tolerated. This is a significant finding, as it suggests that bispecific antibodies may be a new and effective treatment for FL.

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

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

KEY TAKEAWAY 1: Clinical trial results

The clinical trial results for bispecific antibodies in FL are promising, showing improved overall survival compared to standard of care. The data suggests that these novel therapies may offer a significant advantage for patients with relapsed or refractory disease.

- In a phase II study, patients receiving the bispecific antibody demonstrated a higher rate of complete response (CR) and a longer median overall survival (OS) compared to the control group.
- The safety profile of the bispecific antibody was manageable, with most adverse events being grade 1 or 2, consistent with the known toxicity of the individual components.

KEY TAKEAWAY 2: Mechanism of action

Bispecific antibodies work by simultaneously binding to CD20 on B cells and CD3 on T cells, recruiting T cells to kill CD20+ B cells. This mechanism is particularly effective in relapsed or refractory disease.

- The bispecific antibody acts as a bridge between CD20-expressing B cells and CD3-expressing T cells, facilitating T cell-mediated cytotoxicity against the tumor cells.
- This approach is designed to overcome the limitations of monospecific antibodies, which may not be able to recruit sufficient T cells for effective tumor killing.



CONCLUSION

The clinical trial results and the mechanism of action of bispecific antibodies in FL are highly encouraging. These therapies represent a significant advancement in the treatment of relapsed or refractory indolent NHL, offering improved survival outcomes and a manageable safety profile.

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



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

EMERGING THERAPIES

The emerging therapies for indolent NHLs are promising, but nothing yet practice changing. These include:

- CD20-targeted therapies (e.g., rituximab, obinutuzumab)
- BTK inhibitors (e.g., ibrutinib, acaliquimat)
- PI3K inhibitors (e.g., idelalisib, tucuzalisib)
- Venetoclax (BCL-2 inhibitor)
- CAR T-cell therapy (e.g., axicamab)

CLINICAL TRIALS

Several clinical trials are ongoing, evaluating the efficacy and safety of these emerging therapies in combination with standard of care. These include:

- CD20-targeted therapies in combination with BTK inhibitors
- BTK inhibitors in combination with PI3K inhibitors
- Venetoclax in combination with BTK inhibitors
- CAR T-cell therapy in combination with CD20-targeted therapies



CONCLUSIONS

Emerging therapies for indolent NHLs show promise, but nothing yet practice changing. These include:

- CD20-targeted therapies
- BTK inhibitors
- PI3K inhibitors
- Venetoclax
- CAR T-cell therapy

Compared with rituximab



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

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

EMERGING THERAPIES

The following emerging therapies are being studied in clinical trials and may offer new treatment options for patients with indolent NHL. However, these therapies are not yet approved for routine clinical use and their long-term efficacy and safety are still being evaluated.

- **CD20-targeted CAR T cells:** These are a type of immunotherapy that uses genetically modified T cells to target and kill CD20-positive cancer cells. They have shown promising results in early-stage trials for relapsed and refractory indolent NHL.
- **Novel BTK inhibitors:** Bruton's tyrosine kinase (BTK) is a key signaling molecule in the B cell receptor pathway. New BTK inhibitors are being developed to improve upon the efficacy and safety of ibrutinib, which is currently used for relapsed and refractory indolent NHL.

CLINICAL TRIALS

Several clinical trials are currently underway to evaluate the efficacy and safety of these emerging therapies in patients with indolent NHL. These trials are providing valuable information about the potential of these new treatments and may lead to improved outcomes for patients in the future.

- **Phase I/II trial of CD20-targeted CAR T cells:** This trial is evaluating the safety and efficacy of CD20-targeted CAR T cells in patients with relapsed and refractory indolent NHL.
- **Phase III trial of novel BTK inhibitor:** This trial is comparing the efficacy and safety of a novel BTK inhibitor to ibrutinib in patients with relapsed and refractory indolent NHL.



CONCLUSION

While there is much promise for emerging therapies in the treatment of indolent NHL, it is important to note that these treatments are still in the early stages of development. Patients should discuss the potential benefits and risks of these therapies with their healthcare provider and consider participating in clinical trials if appropriate.

EPICS

Advances in CLL

Congress Highlights From ASH 2021

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

Dauids MS, et al. 2021, ASH #640

EPICS

STUDY POPULATION

EFFICACY

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

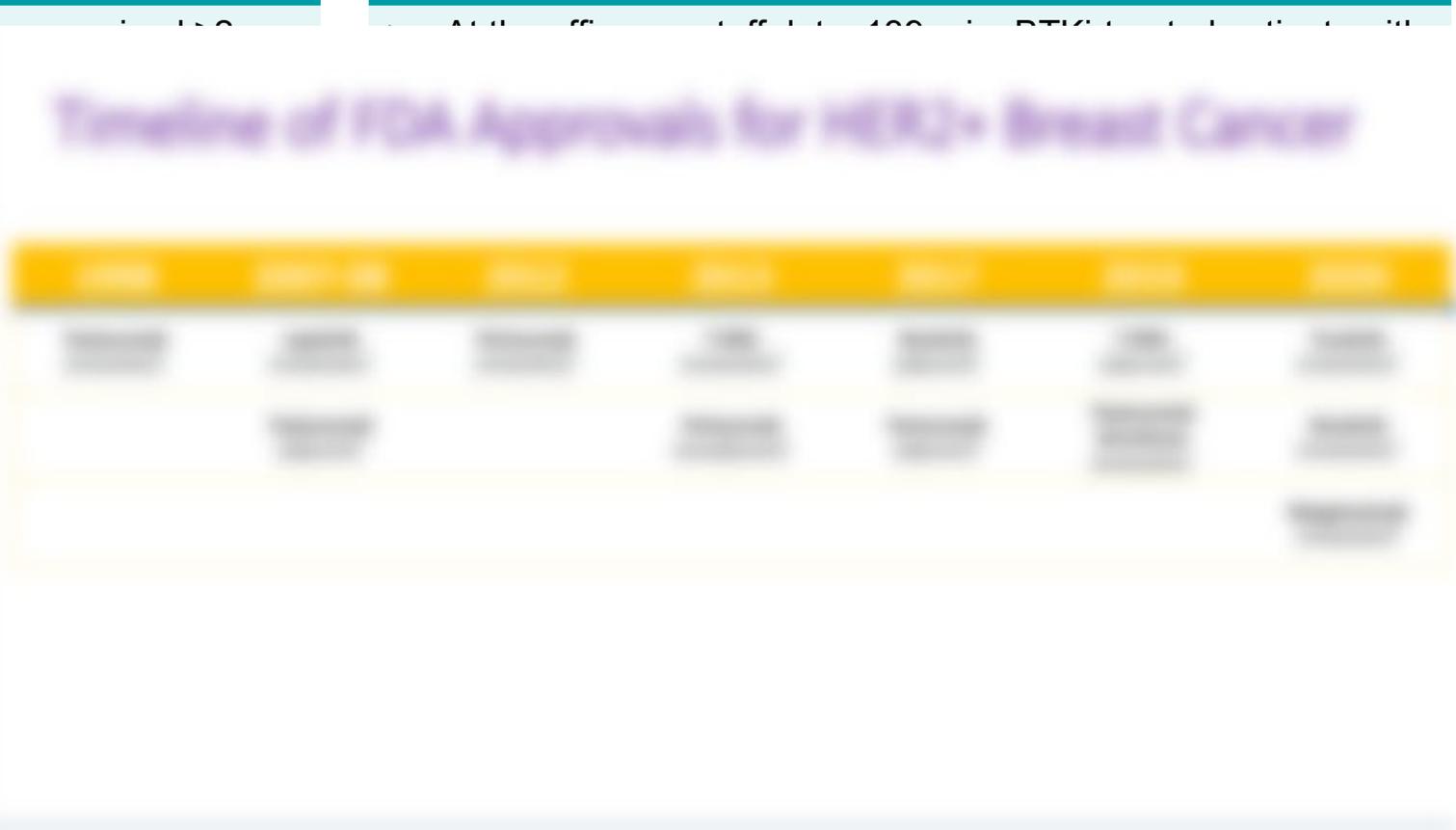


Mato AR, et al. 2021, ASH #391

STUDY POPULATION

Phase I/II BRUIN study design and results. The study was a phase I/II trial of pirtobrutinib in previously treated CLL/SLL. The study was conducted in two parts: a phase I dose-finding study and a phase II efficacy study. The phase I study included 15 patients, and the phase II study included 100 patients. 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 results of the study showed that pirtobrutinib was well-tolerated and had a promising efficacy profile in this patient 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

Eichhorst B, et al. 2021, ASH #71

EPICS

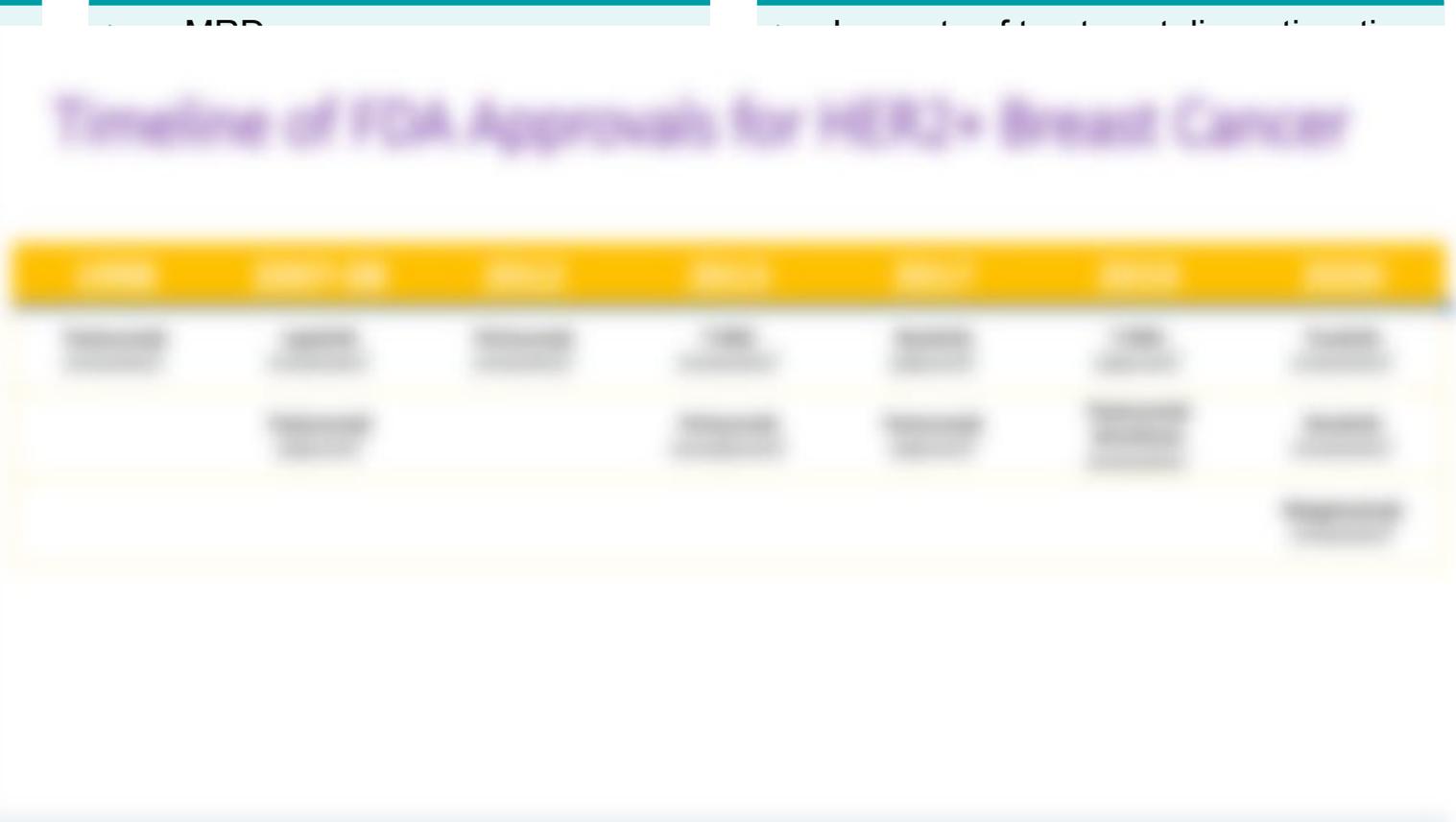
STUDY POPULATION AND METHODS

EFFICACY

SAFETY

STUDY POPULATION AND METHODS

The study population consisted of fit patients with CLL who were previously untreated or had received one prior line of therapy. The study was a randomized, controlled trial comparing the combination of venetoclax with rituximab, flutamide, and cyclophosphamide (RVe) to the standard of care combination of flutamide, cyclophosphamide, and rituximab (FCR). The primary endpoint was overall survival. Secondary endpoints included progression-free survival, time to next treatment, and quality of life. The study was conducted in a multicenter setting across several countries. The results of the study showed that the RVe combination significantly improved overall survival compared to FCR in fit patients with CLL.



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

STUDY POPULATION

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

Study Population

- 177 patients (100%) were enrolled in the study
- Median age: 74 years
- 100% were ≥ 65 years old
- 100% were ≥ 70 years old
- 100% were ≥ 75 years old
- 100% were ≥ 80 years old
- 100% were ≥ 85 years old
- 100% were ≥ 90 years old
- 100% were ≥ 95 years old
- 100% were ≥ 100 years old

PFS RATE

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2017	2018	2019	2020	2021	2022
HER2+ Breast Cancer		1	2	3	4	5



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

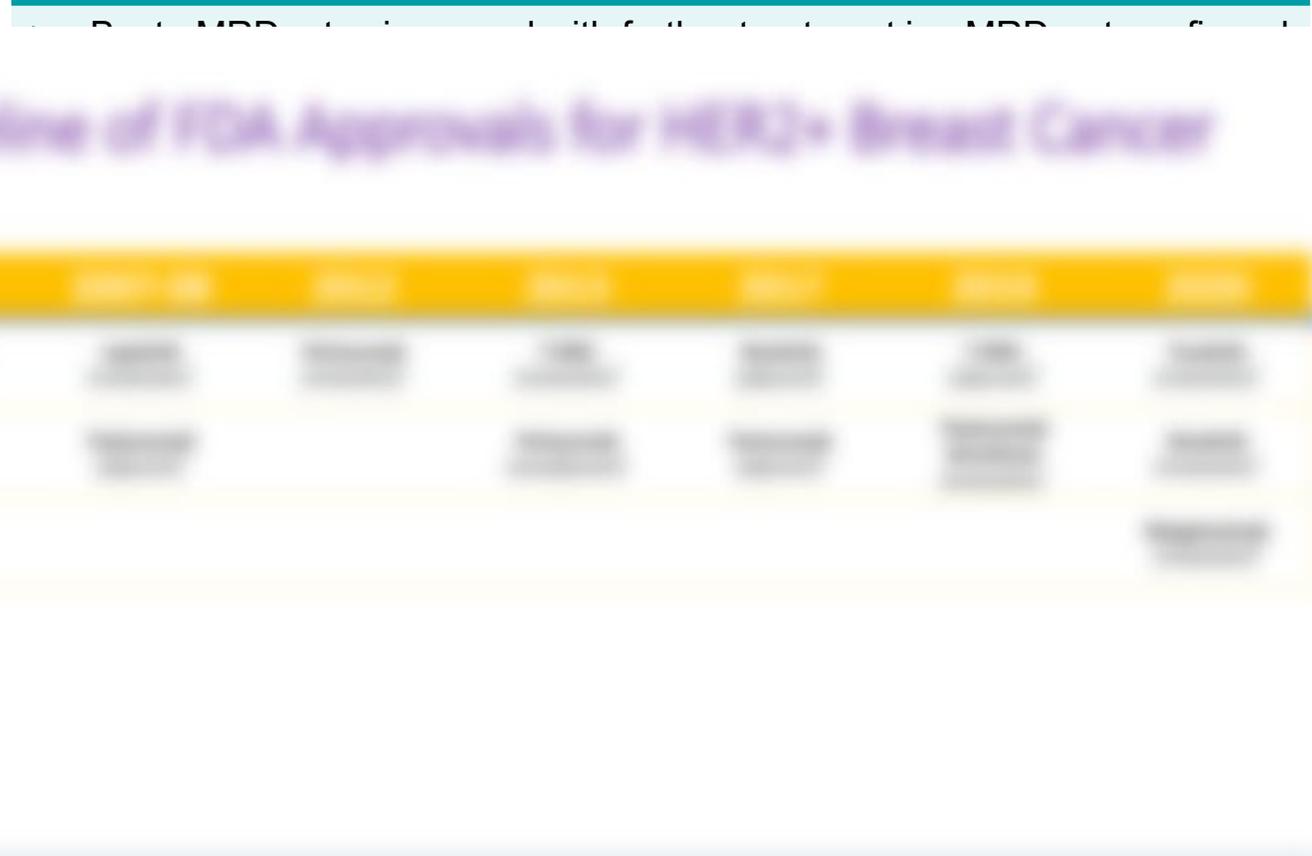
Ghia P, et al. 2021, ASH #68

STUDY POPULATION AND METHODS

Study Population

- 1000 patients (500 in each arm) were randomized to receive either ibrutinib plus venetoclax (n=500) or ibrutinib plus rituximab (n=500) as first-line therapy.
- All patients had a confirmed diagnosis of CLL and were eligible for the study if they had not received prior systemic anticancer therapy.
- The study population was stratified by age (≤65 vs >65 years), performance status (ECOG 0 vs 1-2), and prior therapy (naïve vs non-naïve).
- The primary endpoint was overall survival (OS) at 2 years.
- Secondary endpoints included progression-free survival (PFS), time to next treatment (TTNT), and quality of life.

3-YEAR PFS RATES AND uMRD



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

STUDY POPULATION

Study Population

Phase II, randomized, controlled, open-label, parallel-group study comparing ibrutinib plus venetoclax (IV) to flutamide, cyclophosphamide, and rituximab (FCR) in untreated fit patients with intermediate-risk CLL. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to next treatment (TTNT), and quality of life (QoL).

- 100 patients were randomized to IV (n=50) or FCR (n=50).
- The IV group received ibrutinib 420 mg daily and venetoclax 100 mg daily on days 1-28 of a 28-day cycle.
- The FCR group received flutamide 100 mg bid, cyclophosphamide 100 mg bid, and rituximab 375 mg/m² on days 1, 8, 15, and 22.
- The study is ongoing, and preliminary results are being presented.

EFFICACY



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

STUDY POPULATION AND METHODS

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

Study Population: Patients with relapsed/refractory (R/R) CLL who have undetectable minimal residual disease (uMRD) at baseline.

Study Design: Phase II, randomized, controlled trial.

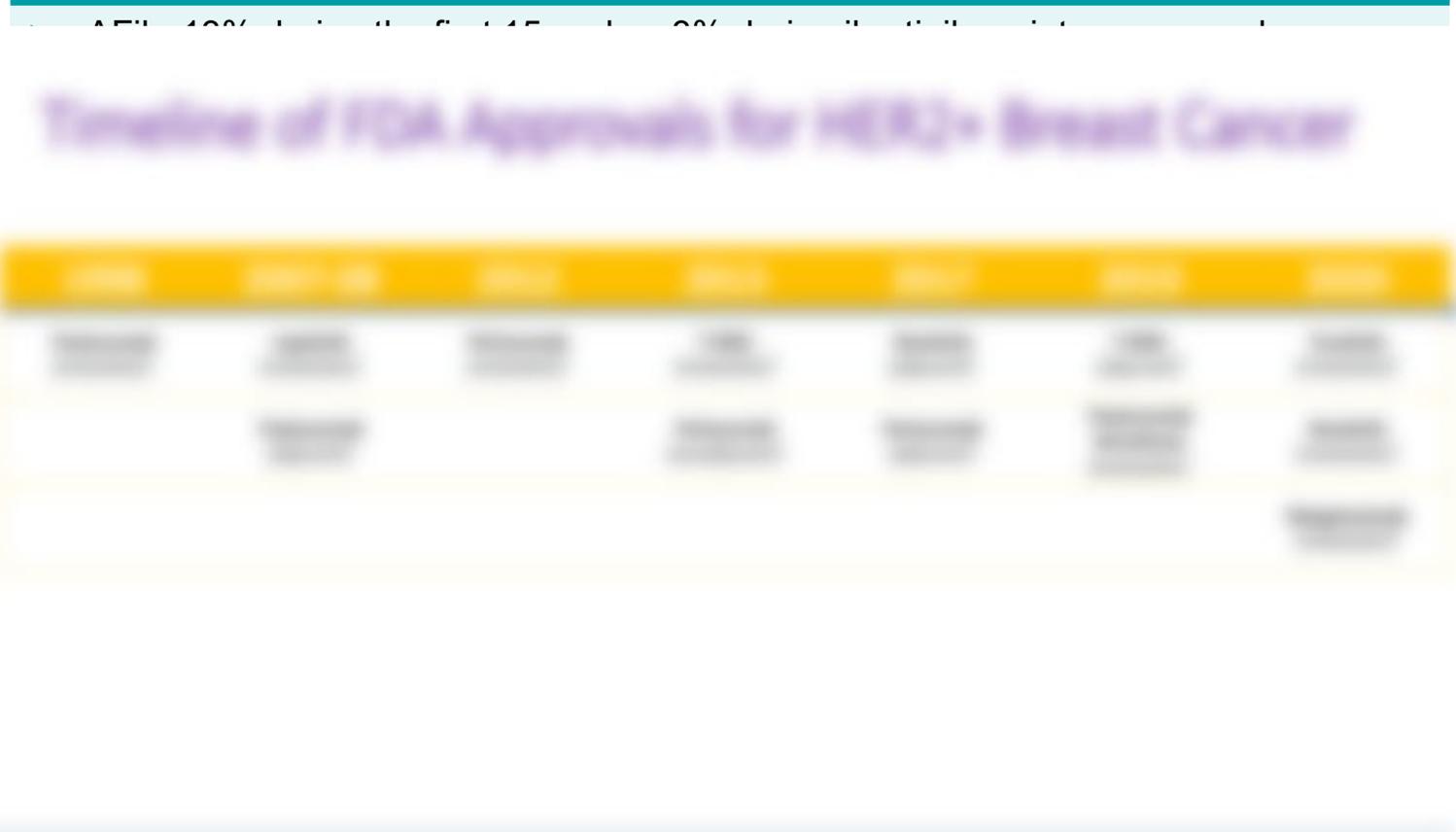
Interventions: Venetoclax + Ibrutinib (V+I) vs. Ibrutinib + Placebo (I+P).

Primary Endpoint: Overall survival (OS).

Secondary Endpoints: Progression-free survival (PFS), time to next treatment (TTNT), quality of life (QoL), and adverse events (AE).

Statistical Analysis: Intention-to-treat (ITT) analysis.

SAFETY



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

Roeker LE, et al. 2021, ASH #395

STUDY POPULATION AND METHODS

[This section contains a list of bullet points detailing the study population and methods, which are currently blurred in the image.]

EFFICACY



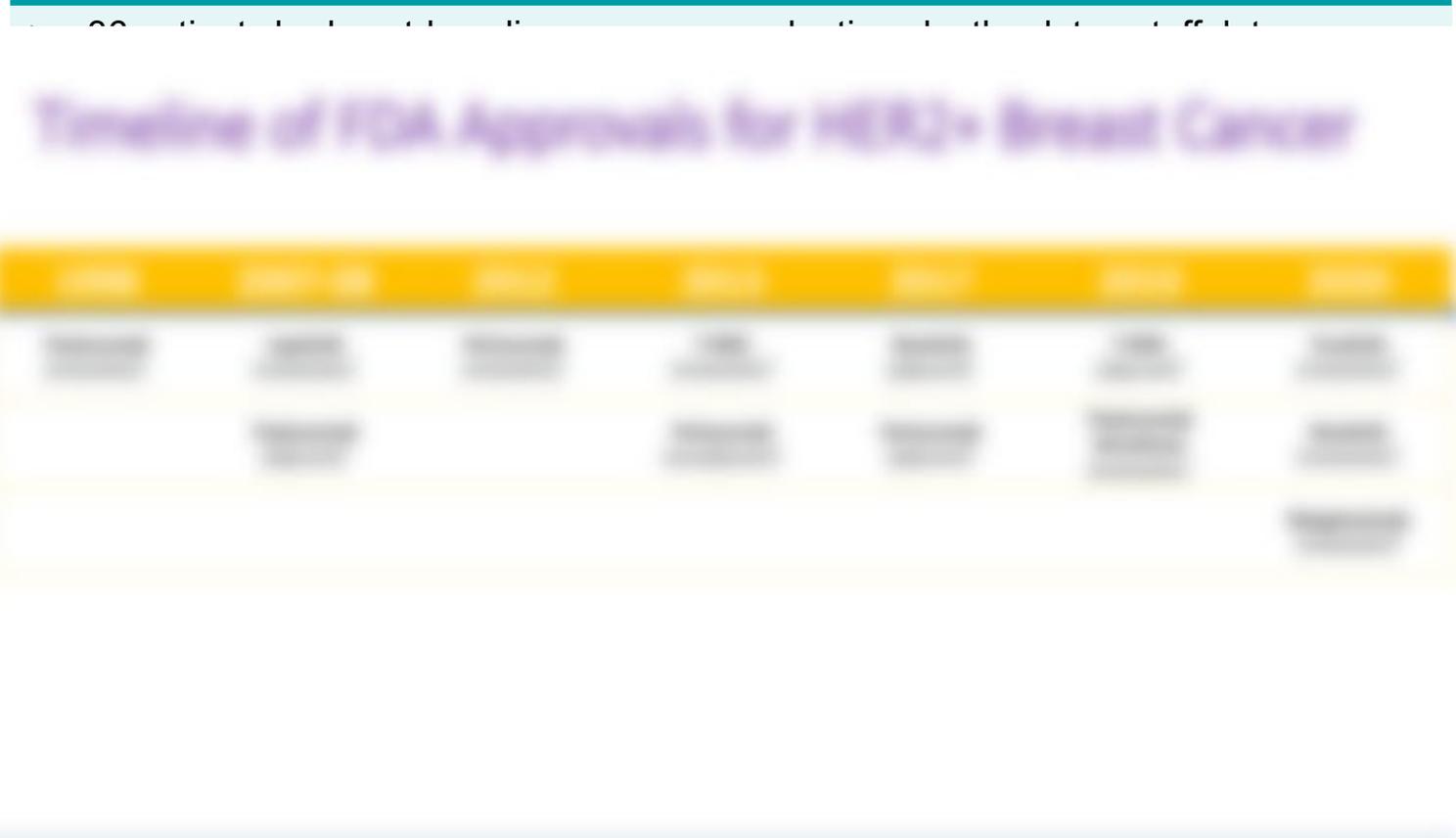
Phase III SEQUOIA Arm D: Early Results of Zanubrutinib Plus Venetoclax in Patients With Treatment-Naive CLL/SLL With Del(17p)

Tedeschi A, et al. 2021, ASH #67

STUDY POPULATION AND ARM D DESIGN

The study population included patients with treatment-naive CLL/SLL with Del(17p) who were ineligible for or had not received a BTK inhibitor. The study design is a phase III, randomized, controlled trial comparing the combination of zanubrutinib plus venetoclax to the combination of venetoclax plus a BTK inhibitor (ibrutinib or acalabrutinib). The primary endpoint is overall survival. Secondary endpoints include progression-free survival, time to next treatment, and quality of life. The study is currently ongoing and results are expected to be published in the near future.

EFFICACY



EPICS

Advances in CLL

Key Insights

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)

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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)

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Key Takeaways: CLL

Data on the non-covalent BTKi pirtobrutinib are very promising

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“



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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

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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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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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