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A SPECIAL MEETING REVIEW EDITION

Highlights in Large B-Cell Lymphoma and Follicular Lymphoma From the 66th ASH Annual Meeting and Exposition

A Review of Selected Presentations From ASH 2024
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Special Reporting on:

- Golcadomide + R-CHOP Has High MRD Negativity Across High-Risk, Untreated a-BCL
- Tafasitamab + Lenalidomide and Rituximab for R/R FL: Results From a Phase 3 Study (inMIND)
- Longer Follow-up of Golcadomide, a Cereblon E3 Ligase Modulator (CELMoD™) Agent, ± Rituximab in Patients With R/R DLBCL
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PLUS Meeting Abstract Summaries

With Expert Commentary by:

Grzegorz S. Nowakowski, MD
Professor of Medicine and Oncology
Enterprise Chair, Lymphoid Malignancy Group
Enterprise Deputy Director, Mayo Clinic Comprehensive Cancer Center for Clinical Research
Mayo Clinic
Rochester, Minnesota

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Golcadomide + R-CHOP Has High MRD Negativity Across High-Risk, Untreated a-BCL

Golcadomide is an investigational cereblon E3 ligase modulator (CELMoD) that binds to cereblon to induce targeted degradation of Ikaros/Aiolos, 2 transcription factors involved in the development of B-cell malignancy.[1,2] Degradation of Ikaros and Ailos by golcadomide induces direct antitumor activity and exerts immunomodulatory activity.

The open-label, phase 1b, dose escalation and expansion trial CC-220-DLBCL-001 is evaluating the safety and activity of golcadomide added to first-line rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in patients with aggressive B-cell lymphoma (a-BCL). As reported previously, golcadomide plus R-CHOP demonstrated preliminary activity in patients with high-risk disease, with a 1-year progression-free survival (PFS) rate of 86% and high rates of minimal residual disease (MRD) negativity.[3] At ASH 2024, Jason R. Westin, MD, and colleagues presented an updated analysis from the CC-220-DLBCL-001 trial evaluating the circulating tumor DNA (ctDNA) kinetics of golcadomide plus R-CHOP in different patient subgroups and the association between MRD and clinical outcomes (Figure 1).[4]

The study enrolled patients with previously untreated a-BCL with a measurable lesion of 1.5 cm or greater. Patients had an International Prognostic Index (IPI) score of 0 to 5 in part 1 (dose escalation) or 2 to 5 in part 2 (dose expansion). Patients in the dose escalation group received golcadomide at increasing dose levels on days 1 through 7 or days 1 through 10 plus R-CHOP-21 (R-CHOP in 21-day cycles). Patients in the dose expansion group were randomly assigned to golcadomide at 0.2 mg (n=35) or 0.4 mg (n=37) on days 1 through 7 plus R-CHOP-21. Treatment was continued for 6 cycles. Most patients (83%) had high-risk disease, defined as an IPI score of 3 to 5 or IPI score of 1 or 2 with at least 1 lesion with a maximum diameter of 7 cm or greater and/or a screening lactate dehydrogenase of at least 13 × upper limit of normal. Molecular high risk was defined as a high baseline ctDNA (≥$10^{2.5}$ hGE/mL) or genomically defined patient populations with poor outcomes.

After a median follow-up of 14.3 months, golcadomide 0.4 mg plus R-CHOP was associated with complete metabolic responses regardless of the cell of origin that were detected early in treatment. The median duration of response (DOR) was not reached overall (n=37) or in high-risk patients (n=31). The 12-month PFS rate was 85% overall and 86% in

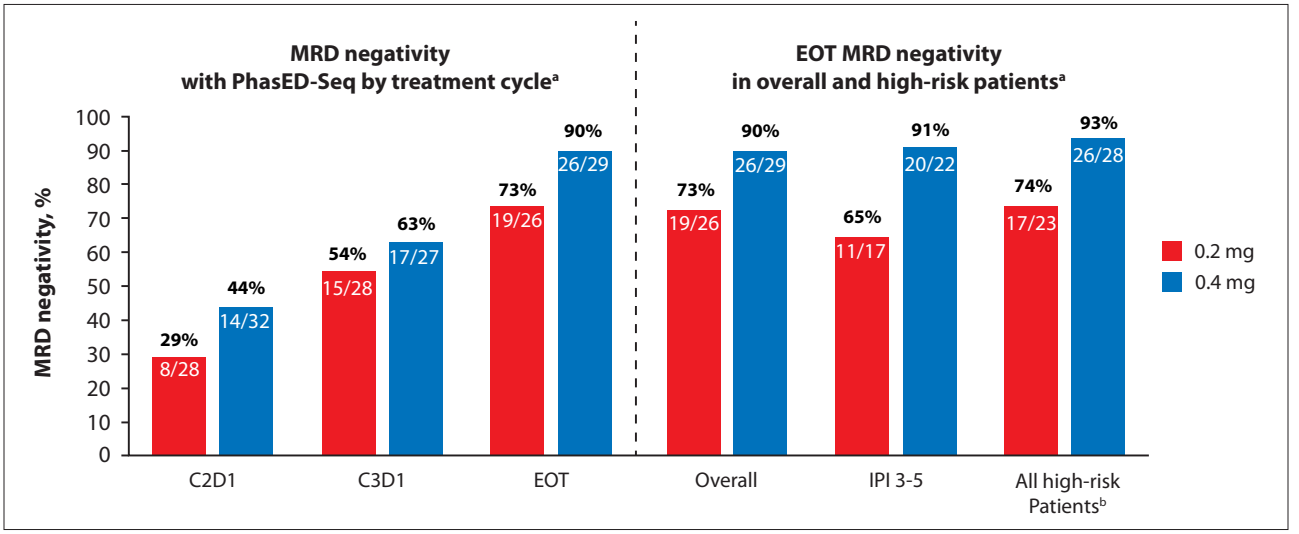

Figure 1. High MRD negativity with golcadomide + R-CHOP across high-risk, untreated aggressive B-cell lymphoma.

[a]Denominators represent the number of patients with available ctDNA.

[b]Combined high-risk population includes IPI 3-5 patients and IPI 1-2 with either elevated LDH or bulky disease.

C, cycle; ctDNA, circulating tumor DNA; D, day; EOT, end of treatment; IPI, International Prognostic Index; LDH, lactate dehydrogenase; MRD, minimal residual disease; PhasED-Seq, phased variant enrichment and detection sequencing; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Adapted from Amzallag et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 579.

ABSTRACT SUMMARY GOLSEEK-2: A Phase 2 Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Golcadomide in Combination With Rituximab in Participants With Newly Diagnosed Advanced FL

Jose C. Villasboas Bisneto, MD, presented the design of the randomized, open-label, phase 2 GOLSEEK-2 study evaluating golcadomide plus rituximab in patients with newly diagnosed advanced-stage FL (Abstract 4422.2). Approximately 90 patients with newly diagnosed grade 1 to 3a FL or classic stage II to IV FL will be randomly assigned 1:1:1 to rituximab plus golcadomide at 0.2 mg or 0.4 mg once daily on days 1 through 14 every 28 days for 12 cycles or investigator's choice of rituximab plus chemotherapy (R-CHOP or bendamustine plus rituximab). The primary endpoint is complete metabolic response during the golcadomide plus rituximab combination treatment period. Secondary endpoints include PFS, OS, ORR, DOR, 30-month CR rate, complete metabolic response rate at 6 months and 12 months, and safety outcomes.

high-risk patients, and the 12-month overall survival (OS) rate was 91% and 93%, respectively.

MRD negativity was observed starting at day 1 of cycle 2. At the end of treatment with golcadomide 0.4 mg plus R-CHOP, the rate of MRD negativity was 90% overall (26/29), 91% in patients with an IPI score of 3 to 5 (20/22), 93% in all high-risk patients (26/28), 87% in patients with high ctDNA at baseline (13/15), and 80% in patients at high genomic risk (4/5). Rates of MRD negativity in some high-risk subgroups were higher with golcadomide 0.4 mg than with golcadomide 0.2 mg, supporting use of the higher dose in ongoing trials. The randomized, phase 3 GOLSEEK-1 trial is comparing golcadomide 0.4 mg plus R-CHOP vs placebo plus R-CHOP in patients with previously untreated LBCL with an IPI score of 1 or 2 and high risk or IPI score of 3 to 5 (NCT06356129).

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4. Amzallag A, Basavanhally T, Westin JR, et al. Golcadomide + R-CHOP has high minimal residual disease (MRD) negativity across high-risk, untreated aggressive B-cell lymphoma (a-BCL). Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 579.

In this phase 2 study, the addition of golcadomide to R-CHOP resulted in a high level of MRD negativity, including in patients with the high-risk disease, defined clinically and by baseline MRD levels. These are promising results that provide a great foundation for the currently ongoing randomized phase 3 study of golcadomide plus R-CHOP vs R-CHOP alone, which could potentially be practice changing.
—Grzegorz S. Nowakowski, MD

Tafasitamab + Lenalidomide and Rituximab for R/R FL: Results From a Phase 3 Study (inMIND)

Tafasitamab is a CD19-targeted monoclonal antibody that has direct cytotoxic effects and immune-modifying effects. In the single-arm, phase 2 L-MIND trial, tafasitamab demonstrated activity in combination with lenalidomide in patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL), with a complete response (CR) rate of 43% (34/80) in patients ineligible for autologous stem cell transplant.[1] These findings led to the 2020 US Food and Drug Administration (FDA) approval of tafasitamab plus lenalidomide in patients with R/R DLBCL not eligible for autologous stem cell transplant.[2]

The double-blind, placebo-controlled, international, multicenter, phase 3 inMIND trial is evaluating tafasitamab plus lenalidomide and rituximab (R^2) in patients with R/R follicular lymphoma (FL) or marginal zone lymphoma.[3] The trial was open to patients with grade 1 to 3A FL or marginal zone lymphoma who had received at least 1 prior line of therapy

including an anti-CD20 monoclonal antibody but had not received R². Patients were randomly assigned to receive tafasitamab 12 mg/kg or placebo intravenously (IV) for 12 cycles (weekly in cycles 1-3 then every 2 weeks in cycles 4-12) plus lenalidomide 20 mg/day on days 1 through 21 for 12 cycles and rituximab 375 mg/m² IV for 5 cycles (weekly in cycle 1 then every 4 weeks in cycles 2-5). Patients with FL were stratified based on whether they had disease progression within 24 months of their initial diagnosis (POD24), refractoriness to prior anti-CD20 therapy, and the number of prior lines of therapy (1 vs ≥2).

At ASH 2024, Laurie H. Sehn, MD, MPH, presented results from the 548 enrolled patients with FL assigned to tafasitamab plus R² (n=273) or placebo plus R² (n=275) (Figure 2). The median age overall was 64.0 years (range, 31-88 years); the median time since initial FL diagnosis was 5.3 years (range, 0-34 years), 25.2% of patients had grade 3A FL, and 52.4% had a Follicular Lymphoma International Prognostic Index (FLIPI) score of 3 to 5. Patients had received a median of 1 prior line of therapy (range, 1-10), 31.6% had POD24, and 42.5% were refractory to a prior anti-CD20 therapy.

The primary endpoint, PFS by investigator assessment, was significantly longer with tafasitamab plus R² vs placebo plus R² (median PFS, 22.4 vs 13.9 months; hazard ratio [HR], 0.43; *P*<.0001); this PFS benefit was maintained in the independent review committee analysis, in which the median PFS was not reached vs 16.0 months (HR, 0.41; *P*<.0001). The PFS benefit with the addition of tafasitamab was maintained whether patients had POD24, whether they were refractory to a prior anti-CD20 therapy, and whether they had received 1 or multiple lines of prior therapy.

Tafasitamab plus R² was also associated with significant improvements over placebo plus R² in the positron emission tomography–complete response (PET-CR) rate (49.4% vs 39.8%; odds ratio [OR], 1.5; nominal *P*=.0286), overall response rate (ORR) (83.5% vs 72.4%; OR, 2.0; nominal *P*=.0014), median DOR (21.2 vs 13.6 months; HR, 0.47; *P*<.0001), and median time to next treatment (not reached vs 28.8 months; HR, 0.45; *P*<.0001). After a median follow-up of 15.3 months, there was no significant difference in OS between arms but the futility threshold was not reached and a positive trend in the tafasitamab-containing arm was observed (HR, 0.59; 95% CI, 0.31-1.13).

The most frequent grade 3 or 4 treatment-emergent adverse events (TEAEs) in the tafasitamab plus R² and placebo plus R² arms, respectively, were neutropenia (39.8% vs 37.5%),

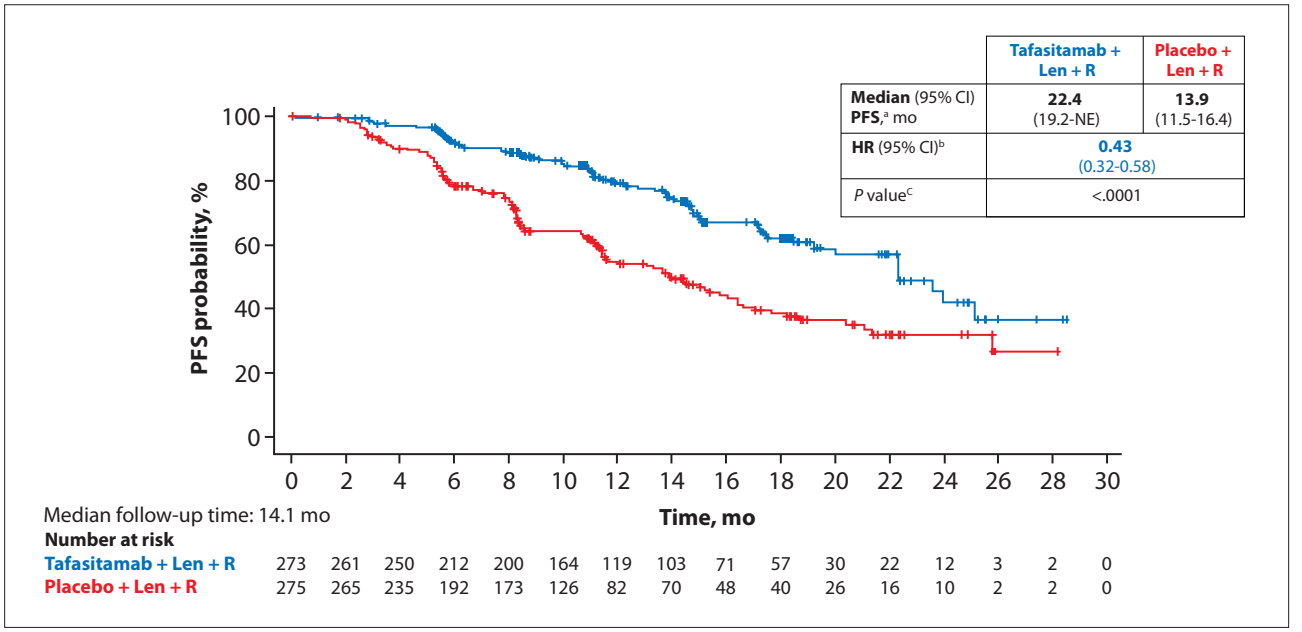

Figure 2. PFS with tafasitamab + lenalidomide and rituximab for R/R FL in the phase 3 inMIND study.
[a]Estimated using Kaplan-Meier method.
[b]Estimated using a stratified Cox proportional hazard model.
[c]Stratified log-rank test with a 2-sided significance level of 5%.
HR, hazard ratio; ITT, intent-to-treat; Len, lenalidomide; mo, months; NE, not evaluable; PFS, progression-free survival; R, rituximab.

Adapted from Sehn et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract LBA-1.

ABSTRACT SUMMARY GOLSEEK-1: A Phase 3, Double-Blind, Randomized Study Comparing the Efficacy and Safety of Golcadomide + R-CHOP vs R-CHOP in Patients with Previously Untreated, High-Risk LBCL

Marc Hoffman, MD, presented the study design for the randomized, double-blind, phase 3 GOLSEEK-1 trial evaluating the addition of golcadomide to R-CHOP in patients with previously untreated high-risk LBCL (Abstract 1742.2). The trial aims to enroll approximately 850 patients with DLBCL-NOS, high-grade B-cell lymphoma with *MYC* and *BCL2* rearrangements or NOS, T-cell/histiocyte-rich LBCL, or Epstein-Barr virus–positive DLBCL. Patients can have an IPI score of 1 or 2 if considered high risk, or an IPI score of 3 or greater, and must have measurable disease. Patients will be randomly assigned to receive golcadomide or placebo administered orally once daily for 7 consecutive days for 6 cycles, plus R-CHOP in 21-day cycles. The primary endpoint is investigator-assessed PFS in untreated high-risk LBCL; secondary endpoints include PFS in untreated non–high-grade BCL, event-free survival in untreated high-risk LBCL, independently assessed complete metabolic response rate, undetectable MRD, and OS.

pneumonia (8.4% vs 5.1%), thrombocytopenia (6.2% vs 7.4%), neutrophil count reduction (5.8% vs 6.6%), and anemia (4.4% vs 5.9%). Rates of dose interruptions or delays were similar between groups at 74% and 70%, respectively, as were rates of study treatment discontinuation, at 11% and 7%, respectively. Rates of lenalidomide discontinuation owing to TEAEs were similar with tafasitamab and placebo (14% vs 11%) as were rates of lenalidomide dose reduction, with median relative dose intensity of 86% and 87%, respectively. Fatal adverse events (AEs) included COVID-19 (n=2), COVID-19 pneumonia (n=2), sepsis (n=2), gastric adenocarcinoma (n=1), large intestine carcinoid tumor (n=1), bronchopulmonary aspergillosis (n=1), cardiac failure (n=1), pneumonia (n=1), and an unexplained death (n=1).

Investigators concluded that the study validated the approach of combining an anti-CD19 antibody with an anti-CD20 antibody in the treatment of FL. They noted that tafasitamab plus R^2 can be administered in academic or community settings and could be a potential new standard of care for patients with R/R FL.

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3. Sehn LH, Luminari S, Scholz CS, et al. Tafasitamab plus lenalidomide and rituximab for relapsed or refractory follicular lymphoma: results from a phase 3 study (inMIND). Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract LBA-1.

The inMIND study is important for 2 reasons: (1) the addition of tafasitamab to lenalidomide and rituximab improved PFS in patients with R/R FL with relatively little added toxicity; and (2) this study serves as the first proof that adding 2 monoclonal antibodies in FL can improve clinical outcomes. These results will likely lead to the approval of this regimen by regulatory agencies, making it another option for treatment of patients with R/R FL. —Grzegorz S. Nowakowski, MD

Longer Follow-up of Golcadomide, a Cereblon E3 Ligase Modulator (CELMoD™) Agent, ± Rituximab in Patients With R/R DLBCL

The first clinical trial of golcadomide was a multicenter, open-label, phase 1/2 dose-escalation and expansion study (CC-99282-NHL-001) in which golcadomide was administered as monotherapy or with rituximab in patients with R/R DLBCL or FL. This 2-part multicenter study enrolled patients with R/R DLBCL or FL after at least 2 lines of therapy or with DLBCL after at least 1 line of therapy who were unfit for transplant. Following the dose-escalation phase, patients in the dose-expansion phase received golcadomide at 0.2 mg or 0.4 mg alone or with rituximab in intermittent schedules. The total duration of golcadomide

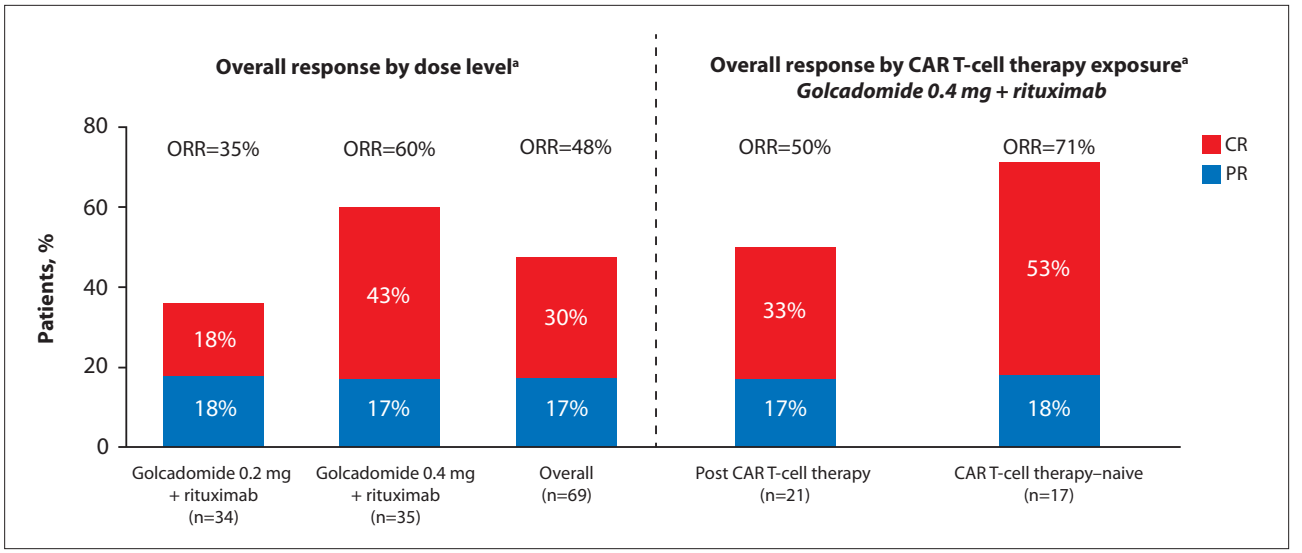

Figure 3. Longer follow-up of golcadomide ± rituximab in patients with R/R diffuse large B-cell lymphoma: overall response.

[a]Efficacy-evaluable population consisting of patients who completed ≥1 cycle of golcadomide (taking ≥75% of assigned doses) and having baseline and ≥1 postbaseline tumor assessments.

CAR, chimeric antigen receptor; CR, complete response; ORR, overall response rate; PR, partial response; R/R, relapsed or refractory.

Adapted from Michot et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 869.

treatment was up to 2 years.

At ASH 2024, Jean-Marie Michot, MD, presented a study update that focused on Cohort C, which enrolled 77 patients with R/R DLBCL who were randomly assigned to golcadomide 0.2 mg plus rituximab (n=39) or golcadomide 0.4 mg plus rituximab (n=38) (Figure 3).[1] Patients had received a median of 4 prior lines of therapy (range, 1-11); 55% had received prior chimeric antigen receptor (CAR) T-cell therapy and 27% had received a bispecific antibody.

After a median follow-up of 10.2 months, 20% of patients remained on treatment and 78% had discontinued treatment, primarily owing to progressive disease (56%). The most frequent treatment-related AE was neutropenia, with an incidence of 49% (46% grade 3/4) with golcadomide 0.2 mg plus rituximab and 76% (74% grade 3/4) with golcadomide 0.4 mg plus rituximab. Neutropenia was considered by investigators to be as expected and related to Ikaros degradation and was managed with granulocyte colony-stimulating factor (G-CSF) and/or dose interruptions. Nonhematologic treatment-related AEs were infrequent.

Golcadomide plus rituximab was associated with an ORR of 48% (30% CR) overall, 35% (18% CR) with golcadomide 0.2 mg plus rituximab, and 60% (43% CR) with golcadomide 0.4 mg plus rituximab. In subgroup analyses, golcadomide 0.4 mg plus rituximab was associated with an ORR of 50% (33% CR) in patients previously treated with CAR T-cell therapy and 71% (53% CR) in CAR T-cell therapy–naive patients. Responses were also observed regardless of cell of origin and use of prior therapies.

The median DOR was 8.34 months (range, 1.5-26.7 months); responses exceeding 12 months occurred in 8 patients. Reductions

ABSTRACT SUMMARY Fixed-Duration Epcoritamab + Lenalidomide in Patients With R/R DLBCL: Updated Results From Arm 1 of the EPCORE NHL-5 Trial

Ronit Gurion and colleagues presented an update from Arm 1 of the phase 1b/2 EPCORE NHL-5 trial evaluating epcoritamab plus lenalidomide in 40 patients with R/R DLBCL (Abstract 3110). After a median follow-up of 11.5 months, the ORR in 37 evaluable patients was 67.6%, including CR in 51.4%. Median DOR was not reached. CRs were observed across subgroups including patients receiving second-line therapy (56.3%; n=16), patients who had received prior CAR T-cell therapy (50%; n=10), and across cell of origin. Safety outcomes were consistent with prior reports (Mazza. *Blood*. 2023;142[suppl 1]:438.). The most common grade 3 or 4 TEAEs were neutropenia (60%), anemia (20%), thrombocytopenia (17.5%), and CRS (10%). The overall incidence of CRS was 65%; all events resolved, with a median time to resolution of 2 days. Use of dexamethasone vs prednisone for CRS prophylaxis was associated with lower rates of CRS and lower peak interleukin-6 levels. One fatal TEAE considered related to epcoritamab was a case of COVID-19 pneumonia.

Golcadomide shows enhanced antiproliferative and apoptotic activity in preclinical models of DLBCL, and this study proves that this is indeed happening in the clinical setting as well. Combination of golcadomide with rituximab resulted in high and durable response rates in patients with R/R DLBCL, even those relapsing after CAR T-cell therapy. It not only makes this combination therapy a viable option for patients with R/R DLBCL, including those relapsing after CAR T-cell therapy, but also builds the new backbone, which can be then improved.

—Grzegorz S. Nowakowski, MD

in ctDNA were observed starting at day 15 of cycle 1 and included cases of MRD negativity. Reductions in ctDNA during cycles 1 and 2 correlated with responses to treatment.

Investigators concluded that golcadomide plus rituximab was associated with predictable and manageable safety consistent with prior reports with golcadomide monotherapy, and that the combination of golcadomide and rituximab showed promising efficacy in patients with heavily pretreated R/R DLBCL, supporting the ongoing development of the regimen.

Reference

1. Michot JM, Morschhauser F, Ferrari S, et al. Longer follow-up of golcadomide, a cereblon E3 ligase modulator (CELMoD™) agent, ± rituximab in patients with R/R DLBCL. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 869.

Three-Year Update From the EPCORE NHL-1 Trial: Epcoritamab Leads to Deep and Durable Responses in R/R LBCL

Epcoritamab is a CD3 × CD20 bispecific antibody that received FDA approval in 2023 for use in adults with R/R DLBCL and high-grade B-cell lymphoma after 2 or more lines of systemic therapy.[1] The approval followed results of the open-label, multicenter, single-arm EPCORE NHL-1 trial, in which epcoritamab demonstrated an ORR of 63.1% (40.1% CR), a 2-year PFS rate of 27.8%, and a 2-year OS rate of 44.6% in this population.[2] At ASH 2024, Julie M. Vose, MD, MBA, presented a 3-year update from the EPCORE NHL-1 trial in patients with R/R LBCL (Table 1).[3]

The trial enrolled patients with R/R CD20-positive LBCL who had received at least 2 prior lines of systemic therapy, including an anti-CD20 monoclonal antibody. Patients received epcoritamab subcutaneously at 48 mg until progressive disease or unacceptable toxicity. Of the 157 enrolled patients (median age, 64 years [range, 20-83 years]; median of 3 prior lines of therapy [range, 2-11]), 61% had primary refractory disease, 75% were refractory to at least 2 consecutive prior lines of therapy, and 39% had received prior CAR T-cell therapy.

After a median follow-up of 37.1

Table 1. Deep and Durable Responses With Epcoritamab in R/R LBCL in the EPCORE NHL-1 Trial: 3-Year Update[a,b]

Response	LBCL (n=157)	DLBCL transformed from FL (n=32)
ORR, n (%)	92 (59)	16 (50)
CR	65 (41)	14 (44)
PR	27 (17)	2 (6)
Median (95% CI) DOR, mo	20.8 (13.0-32.0)	NR (10.6-NR)
36-month estimate, %	39	55

[a]For patients in the DLBCL + HGBCL subgroup (n=148): ORR/CR=57%/41%; median (95% CI) DOR=20.8 (13.0-32.0) mo; 36-month estimate=38%.
[b]For patients in the DLBCL subgroup (n=139): ORR/CR=58%/42%; median (95% CI) DOR=20.8 (13.4-32.0) mo; 36-month estimate=38%.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; mo, months; NR, not reached; ORR, overall response rate; PR, partial response; R/R, relapsed or refractory.

Adapted from Vose et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 4480.

months, 12% of patients were still on treatment. The ORR was 59% overall (92/157), with a CR rate of 41%, and 50% in patients with DLBCL transformed from FL (16/32), with a CR rate of 44%. The median DOR was 20.8 months overall and not reached in patients with DLBCL transformed from FL (3-year DOR rate, 39% and 55%, respectively). The median duration of complete response (DOCR) was 36.1 months overall.

The median PFS was 4.2 months overall. Among patients with a CR, the median PFS was 37.3 months and the 3-year PFS rate was 53%. The median OS was 18.5 months overall and not reached among patients with a CR. At 3 years, 75% of patients with a CR had not started a new antilymphoma therapy. Fifteen patients with a CR paused epcoritamab for more than 6 weeks, primarily owing to AEs (8/10 owing to COVID-19); all patients maintained a CR at their next imaging assessment. Among 119 patients evaluable for MRD, 45% attained MRD negativity at any point and 98% of evaluable patients (40/41) were MRD-negative at day 1 of cycle 13.

The most common TEAEs were cytokine release syndrome (CRS) (51%; 3% grade 3), fatigue (25%), and pyrexia (25%). Investigators noted that the incidence and severity of CRS, immune effector cell–associated neurotoxicity syndrome (ICANS), and serious infections were similar to prior reports. Of the patients receiving epcoritamab for at least 2 years, 73% did not develop a grade 3 or higher infection after 2 years.

Investigators concluded that the efficacy and safety findings support treatment until progression and suggest long-term disease-free survival in these patients.

> The most important clinical question in R/R LBCL is whether patients can be cured. In other words, can we achieve CR that is durable? Epcoritamab results in significant response rates that appear to be durable, and this study is proof that patients with R/R LBCL who achieve CR can have very durable responses: at 3 years, the majority of the patients are maintaining CR, which is very promising.
>
> —Grzegorz S. Nowakowski, MD

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3. Vose JM, Cheah CY, Clausen MR, et al. 3-year update from the EPCORE NHL-1 trial: epcoritamab leads to deep and durable responses in relapsed or refractory large B-cell lymphoma. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 4480.

Fixed-Duration Epcoritamab + R-CHOP Induces High Complete Response Rates in Patients With Previously Untreated DLBCL With High-Risk Features: Long-Term Results From the EPCORE NHL-2 Trial

There is a need for more effective therapies for patients with DLBCL, particularly for those with high-risk features, as no new regimens have demonstrated an OS improvement over first-line R-CHOP. The combination of epcoritamab plus R-CHOP in patients with newly diagnosed DLBCL was evaluated in Arm 1 of the EPCORE NHL-2 trial. At ASH 2024, Lorenzo Falchi, MD, presented long-term results from this cohort, with a median follow-up of 27.4 months (Figure 4).[1]

EPCORE NHL-2 Arm 1 enrolled 47 patients with newly diagnosed CD20-positive DLBCL considered high risk, with an IPI score of 3 or greater, to receive epcoritamab 48 mg subcutaneously weekly in cycles 1 through 4, every 3 weeks in cycles 5 through 6, and every 4 weeks thereafter for up to 1 year, plus R-CHOP. The median age of enrolled patients was 64 years (range, 19-82 years); 53% had an IPI score of 4 or 5 at screening, 21% had double-hit or triple-hit lymphoma, and 34% had bulky disease (>10 cm).

The CR rate with epcoritamab plus R-CHOP in the efficacy-evaluable population (n=46) was 87% overall, 91% in patients who completed 6 cycles of R-CHOP with epcoritamab (n=44), 83% in

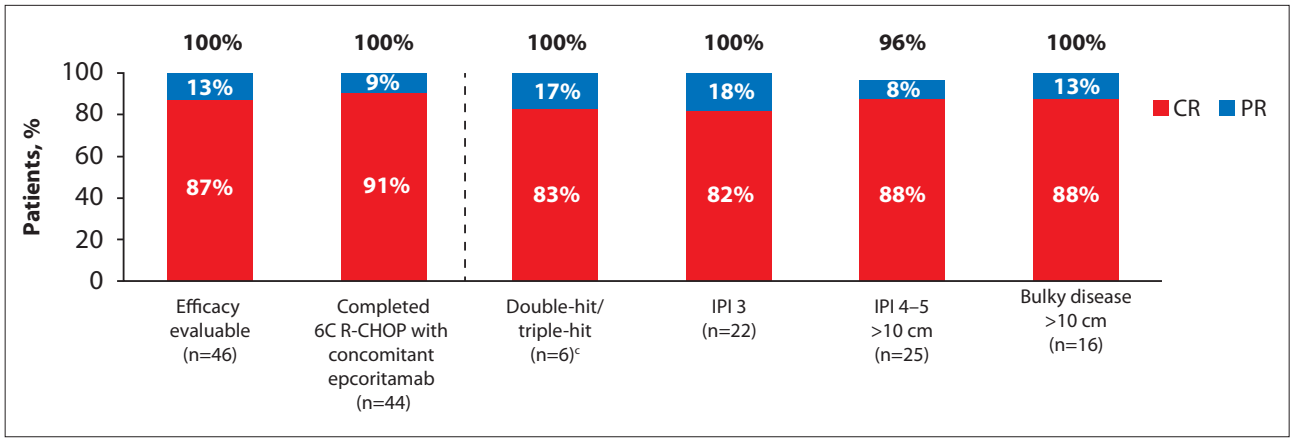

Figure 4. CR rates with fixed-duration epcoritamab + R-CHOP in patients with previously untreated DLBCL with high-risk features: long-term results from the EPCORE NHL-2 trial.[a,b]

[a]Median follow-up: 27.4 mo.

[b]Response rates based on modified response-evaluable population, defined as patients with ≥1 target lesion at baseline and who had ≥1 postbaseline response evaluation or died within 60 days of first trial treatment.

[c]Double-hit/triple-hit status by central laboratory testing was not evaluable in 19 patients.

6C, cycle 6; CR, complete response; DLBCL, diffuse large B-cell lymphoma; IPI, International Prognostic Index; mo, months; PR, partial response; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Adapted from Falchi et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 581.

patients with double-hit or triple-hit lymphoma (n=6), 82% in patients with an IPI score of 3 (n=22), 88% in patients with an IPI score of 4 or 5 (n=25), and 88% in patients with bulky disease (n=16). CRs were durable, as they were sustained in 94% of patients (30/32) who completed treatment.

MRD negativity was attained in 91% of evaluable patients (30/33); MRD negativity was attained by day 1 of cycle 3 in 83% of patients (25/30), including 5 of 6 patients with double-hit or triple-hit lymphoma.

After a median follow-up of 21.1 months, the median DOCR had not been reached; at 21 months, 83% of CRs were sustained. After 21 months, the PFS rate was 82%. After a median follow-up of 27.4 months, most patients were alive; the 24-month OS rate was 87% overall and 83% in the patients with double-hit or triple-hit lymphoma.

The most frequent grade 3 or 4 TEAEs were neutropenia (66%) and anemia (32%). Febrile neutropenia occurred in 5 patients. G-CSF was administered to 36% of patients. There were 2 grade 5 TEAEs of COVID-19 and septic shock. CRS developed in 60% of patients overall but was primarily grade 1 or 2, with 4% developing grade 3 events. ICANS developed in 2 patients (4%) and was grade 1 or 2. All cases of CRS and ICANS resolved after a median time of 2 days and 2.5 days, respectively.

Investigators concluded that epcoritamab plus R-CHOP demonstrated high rates of durable CRs in patients with high-risk DLBCL, including in patients with double-hit or triple-hit lymphoma, and demonstrated a manageable safety profile.

ABSTRACT SUMMARY Fixed-Duration Epcoritamab in Combination With Bendamustine + Rituximab for First-Line Treatment of FL: Initial Results From EPCORE NHL-2 Arm 3

Joshua Brody, MD, presented initial results from Arm 3 of the ongoing phase 1b/2 EPCORE NHL-2 trial evaluating fixed-duration epcoritamab plus bendamustine plus rituximab as first-line treatment for patients with FL (Abstract 1627). A total of 25 patients with grade 1 to 3A CD20-positive FL received epcoritamab plus bendamustine plus rituximab for 6 cycles followed by epcoritamab monotherapy. Epcoritamab was initially administered with step-up dosing, with up to 48 mg given weekly in cycles 1 through 3, every 2 weeks in cycles 4 through 9, and every 4 weeks thereafter for up to 2 years. The regimen was associated with a CR rate of 96%. The estimated 30-month PFS and OS rates were 93% and 96%, respectively. The most common TEAE was COVID-19 (72%) followed by CRS (68%), nausea (64%), fatigue (52%), and injection site reaction (52%). All CRS events were grade 1 or 2 and resolved. Immunophenotypic analysis showed sustained reductions in peripheral CD4+ T cells.

The regimen is being evaluated in an ongoing phase 3 trial in patients with previously untreated DLBCL (NCT05578976).

Reference

1. Falchi L, Offner F, de Vos S, et al. Fixed-duration epcoritamab + R-CHOP induces high complete response rates in patients with previously untreated diffuse large B-cell lymphoma with high-risk features: long-term results from the EPCORE NHL-2 trial. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 581.

We are currently witnessing the development of a new wave of phase 3 studies in LBCL using combinations of different agents with R-CHOP compared with R-CHOP alone. These studies are based on phase 2 studies like this one, which showed that the addition of epcoritamab to R-CHOP results in high CR rates, excellent PFS, and duration of CRs. These results are promising and provide a great foundation for the ongoing phase 3 study, which could be practice changing.

—Grzegorz S. Nowakowski, MD

Five-Year Analysis of the POLARIX Study: Prolonged Follow-up Confirms Positive Impact of Polatuzumab Vedotin + Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (Pola-R-CHP) on Outcomes

The antibody-drug conjugate polatuzumab vedotin received approval for use in patients with previously untreated DLBCL, not otherwise specified (NOS), or high-grade B-cell lymphoma who have an IPI score of 2 or greater, in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) based on the POLARIX trial, in which polatuzumab vedotin plus R-CHP (Pola-R-CHP) was associated with a significant improvement in PFS over R-CHOP in patients with previously treated intermediate-risk or high-risk DLBCL.[1,2]

At ASH 2024, Gilles Salles, MD, PhD, presented 5-year outcomes from the POLARIX study, which enrolled 879 patients with previously untreated DLBCL and randomly assigned them to Pola-R-CHP (n=440) or R-CHOP (n=439) for 6 cycles, followed by rituximab for 2 cycles (Figure 5).[3]

After a median follow-up of 54.9 months, Pola-R-CHP demonstrated a sustained improvement in PFS over R-CHOP, with 5-year PFS rates of 64.9% and 59.1%, respectively (HR, 0.77; 95% CI, 0.62-0.97). The 5-year disease-free survival rates were 71.8% and 66.5%, respectively (HR, 0.75; 95% CI, 0.57-1.00). Subsequent therapies were required by 38.3% of patients on the Pola-R-CHP arm vs 61.7% of patients on the R-CHOP arm, reflecting a 23.4% reduction in the need for subsequent therapies.

The 5-year OS rate was 82.3% with Pola-R-CHP and 79.5% with R-CHOP (HR, 0.85; 95% CI, 0.63-1.15). There were fewer deaths overall in the Pola-R-CHP arm than the R-CHOP arm (80 vs 92). However, most deaths (50% in the Pola-R-CHP arm and 55% in the R-CHOP arm) were owing to progressive disease. Lymphoma-unrelated deaths occurred at a similar rate between arms. Subset analyses suggested similar treatment effect with Pola-R-CHP across subgroups, including high-risk

ABSTRACT SUMMARY Real-World Effectiveness of Tafasitamab for the Treatment of R/R DLBCL in the United States

Kimberly Saverno, PhD, presented a study evaluating the real-world effectiveness of tafasitamab in 181 adults with R/R DLBCL in the United States (Abstract 2375). The population was 56% male and 64% White, and had a median age of 71 years when initiating tafasitamab; 72% were receiving tafasitamab in the second line. After a median follow-up of 14.7 months, 71% of patients had discontinued tafasitamab owing to disease progression (71%), toxicity (10%), patient or caregiver request (7%), CR (4%), or another reason (8%). The real-world ORR was 72%, including 23% CR. The median DOR was 9.6 months overall and 19.2 months among those with a CR. Median real-world PFS and OS were 11.3 months and 24.8 months, respectively. Factors associated with risk of progression in a multivariate analysis ($P<.05$) were use of tafasitamab in later lines vs second-line, bulky disease, Ann Arbor stage III to IV, and increasing National Cancer Institute Charlson Comorbidity Index scores.

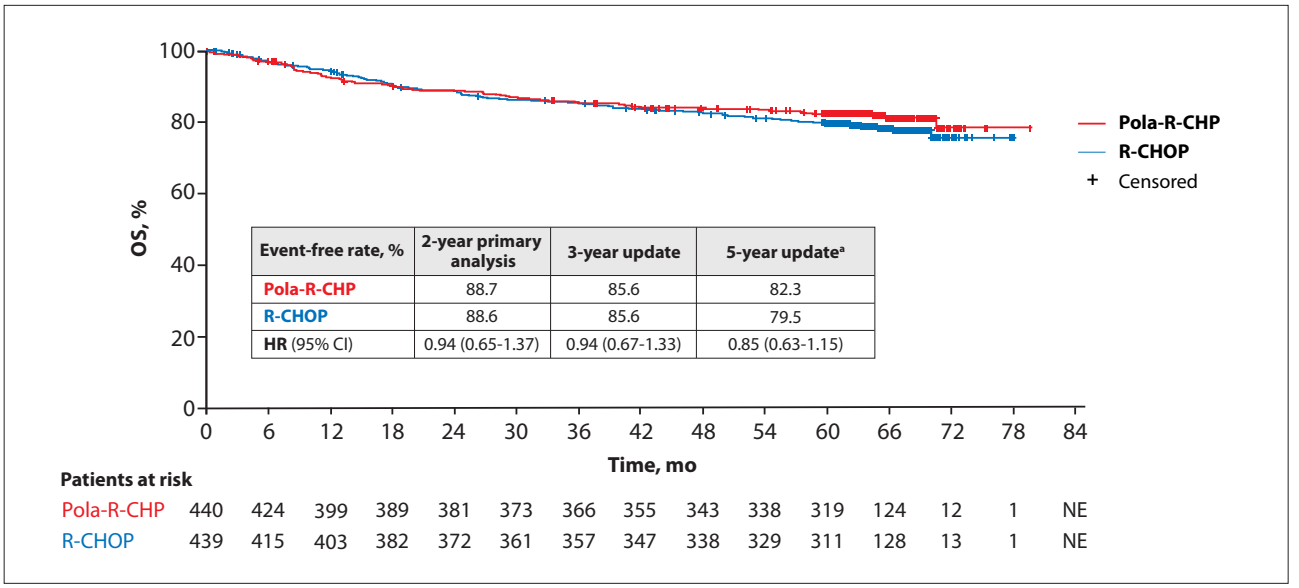

Figure 5. Five-year OS with Pola-R-CHP in the POLARIX study.

[a]Data cutoff: July 5, 2024.

HR, hazard ratio; mo, months; NE, not evaluable; OS, overall survival; Pola-R-CHP, polatuzumab vedotin + rituximab, cyclophosphamide, doxorubicin, and prednisone; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Adapted from Salles et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 469.

subgroups, although investigators cautioned that these analyses are exploratory and underpowered.

An expanded population cohort that added 121 patients from a Chinese extension study showed similar outcomes as the initial global population. A competing risk analysis in the expanded population found a lower cumulative incidence of lymphoma-related deaths with Pola-R-CHP vs R-CHOP at 5 years (9.02% vs 12.05%).

Safety profiles were comparable between arms, as previously reported. The incidence of new serious AEs in long-term follow-up was 1.8% with Pola-R-CHP and 2.2% with R-CHOP. The expanded population showed less than a 5% difference between Pola-R-CHP and R-CHOP in rates of hematologic toxicities and infections. The most frequent grade 3 or higher AEs reported with Pola-R-CHP and R-CHOP were neutropenia (43.6% vs 41.2%), infection (15.2% vs 13.3%), and anemia (11.3% vs 9.8%). Secondary malignancies occurred in 1.0% and 2.4% of patients, respectively.

Investigators concluded that the 5-year data confirm Pola-R-CHP as a standard of care for patients with previously untreated intermediate- or high-risk DLBCL.

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1. U.S. Food & Drug Administration. FDA approves polatuzumab vedotin-piiq for previously untreated diffuse large B-cell lymphoma, not otherwise specified, and high-grade B-cell lymphoma. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-polatuzumab-vedotin-piiq-previously-untreated-diffuse-large-b-cell-lymphoma-not. Accessed January 27, 2025.
2. Tilly H, Morschhauser F, Sehn LH, et al. Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma. *N Engl J Med*. 2022;386(4):351-363.
3. Salles G, Morschhauser F, Sehn LH, et al. Five-year analysis of the POLARIX study: prolonged follow-up confirms positive impact of polatuzumab vedotin + rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) on outcomes. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 469.

This is a very important update to the POLARIX study, which initially showed no difference in OS, a modest improvement in PFS, and event-free survival. This led to the lingering question of whether there would be any change in OS results in the longer follow-up. Although this has not been shown, the difference in PFS appears to be maintained at 5 years. So, a sustained benefit in PFS did not translate into OS. Clinically, this means that, although Pola-R-CHP remains an option, it is not necessarily a new standard of care.

—Grzegorz S. Nowakowski, MD

Fixed-Duration Epcoritamab + R^2 Drives Deep and Durable Responses in Patients With R/R FL: 2-Year Follow-up From Arm 2 of the EPCORE NHL-2 Trial

Lenalidomide plus rituximab (R^2) is a commonly used regimen in patients with R/R FL based on results from the phase 3 AUGMENT trial, which demonstrated an improvement in PFS with the addition of lenalidomide to rituximab in patients with recurrent indolent lymphoma.[1] Epcoritamab is a CD3 × CD20 bispecific antibody that received FDA approval in 2024 for adults with R/R FL after 2 or more lines of systemic therapy following results of the open-label, multicenter, single-arm EPCORE NHL-1 trial, in which epcoritamab demonstrated an ORR of 82.0% (62.5% CR) and a manageable safety profile.[2,3]

At ASH 2024, Lorenzo Falchi, MD, presented a 2-year follow-up from Arm 2 of the EPCORE NHL-2 trial evaluating fixed-duration epcoritamab plus R^2 in patients with R/R FL (Table 2).[4] The trial enrolled 111 patients with R/R CD20-positive FL (grade 1-3A, stage II-IV) who had previously received treatment including an anti-CD20 antibody. Patients received subcutaneous epcoritamab via a 2-step (0.16 and 0.8 mg) step-up dosing regimen in cycle 1 and at 48 mg doses either once weekly in cycles 1 through 3, every 2 weeks in cycles 4 through 9, and every 4 weeks starting in cycle 10 (Arm 2a) or weekly in cycles 1 through 2 and every 4 weeks starting in cycle 3 (Arm 2b) for up to 2 years, plus rituximab 375 mg/m^2 IV weekly for 1 cycle then every 2 weeks in subsequent cycles and lenalidomide at 20 mg/day on days 1 through 21 of each cycle.

The trial enrolled 111 patients (median age, 65 years; range, 30-80 years), including 61% with stage IV disease, 59% with a FLIPI score of 3 to 5, and 50% with POD24 after any first-line treatment. Patients had received a median of 1 prior line of therapy (range, 1-7). After a median follow-up of 25.3 months, 48% of patients had discontinued treatment, 37% had completed treatment per protocol, and 15% were still on treatment.

The ORR with epcoritamab plus R^2 was 96% (87% CR) and 88% of patients attained MRD negativity at any point. The CR rate was 92% in patients receiving second-line therapy, 79% in patients with POD24 after first-line chemoimmunotherapy, 90% in primary refractory patients, and 82% in double-refractory patients.

Rates of MRD negativity in high-risk subgroups included 87% in patients with POD24 to first-line chemoimmunotherapy (26/30), 89% in patients with primary refractory disease (25/28), and 85% in double-refractory patients (23/27). Responses were durable, with the median DOR and DOCR not reached after a median follow-up of 21 months. At 21 months, 86% of CRs and 78% of all responses were maintained. Responses were durable across high-risk subgroups.

After a median follow-up of 22.3 months, median PFS was not reached overall (21-month PFS rate, 80%), 27.6 months in patients with POD24 after first-line chemoimmunotherapy (21-month PFS rate, 75%), 27.6 months in primary refractory patients (21-month PFS rate, 78%), 23.7 months in double-refractory patients

Table 2. Responses With Fixed-Duration Epcoritamab + R^2 in Patients With R/R FL: 2-Year Follow-up From Arm 2 of the EPCORE NHL-2 Trial

Best response[a], n (%) (n=111)	
OR	107 (96)
CR	97 (87)
PR	10 (9)
Progressive disease	2 (2)
MRD negativity, n/n (%)	
MRD negativity at any time[b]	66/75 (88)
MRD-negative and CR[c]	63/68 (93)
MRD negativity in high-risk subgroups[d]	
POD24 (1L CIT)	26/30 (87)
Primary refractory	25/28 (89)
Double refractory	23/27 (85)

[a]Two patients were not evaluable for response.
[b]MRD-negative at any time point with an assay cutoff of 10^{-6} (PBMC assay; clonoSEQ).
[c]One patient became MRD-positive at a subsequent assessment (C5D1); patient later experienced radiographic PD.
[d]Patients could be counted in ≥1 high-risk subgroup.
1L, first-line; C, cycle; CIT, chemoimmunotherapy; CR, complete response; D, day; FL, follicular lymphoma; MRD, minimal residual disease; OR, overall response; PBMC, peripheral blood mononuclear assay; PD, progressive disease; POD24, disease progression within 24 months of initial diagnosis; PR, partial response; R/R, relapsed or refractory.

Adapted from Falchi et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 342.

(21-month PFS rate, 71%), and not reached in patients with 1 prior line of therapy (21-month PFS rate, 83%). MRD negativity was associated with higher PFS. After a median follow-up of 24.7 months, 85% of patients had not initiated a next line of therapy.

After a median follow-up of 25.3 months, median OS was not reached overall or in key subgroups reported; 24-month OS rates were 90% overall, 88% in primary refractory patients, 86% in double-refractory patients, and 84% in patients with POD24 after first-line chemoimmunotherapy.

The most frequent grade 3 or higher TEAE was neutropenia (53%). Investigators noted that rates of neutropenia were consistent with prior reports of R².[1] G-CSF was administered to 51% of patients, including as prophylaxis to 26%. Febrile neutropenia occurred in 3 patients. The trial was conducted during the COVID-19 pandemic; as a result, there were 5 fatal cases of COVID-19; no other fatal TEAEs occurred.

CRS occurred in 51% of patients but was primarily grade 1 or 2; 2% of patients developed grade 3 CRS. No clinical CRS occurred, and CRS did not lead to any discontinuations of epcoritamab. One patient developed a grade 1 ICANS event that resolved in 7 days without treatment.

Investigators concluded that the results support the ongoing phase 3 EPCORE FL-1 trial comparing epcoritamab plus R² vs R² in patients with R/R FL (NCT05409066).

> R² is an important backbone in the treatment of patients with R/R FL. A way to improve outcomes with R² is adding other agents like epcoritamab, which has excellent activity in R/R FL. This study proved that addition of epcoritamab to R² is feasible and is associated with deep and durable responses. Ongoing randomized studies will answer if this will indeed change the standard of care. —Grzegorz S. Nowakowski, MD

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3. Linton KM, Vitolo U, Jurczak W, et al. Epcoritamab monotherapy in patients with relapsed or refractory follicular lymphoma (EPCORE NHL-1): a phase 2 cohort of a single-arm, multicentre study. *Lancet Haematol*. 2024;11(8):e593-e605.
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Golcadomide ± Rituximab Demonstrates Durable Efficacy and Is Well Tolerated in Patients With R/R FL: Updated Results From the Phase 1/2 CC-99282-NHL-001 Study

The phase 1/2 CC-99282-NHL-001 study is evaluating golcadomide as a single agent and in combination with rituximab in patients with R/R DLBCL or FL.[1] The study included patients with R/R DLBCL or FL after at least 2 lines of therapy or with DLBCL after at least 1 line of therapy and unfit for transplant. Patients received golcadomide monotherapy at a range of doses in the dose-escalation phase and received golcadomide with or without rituximab at 0.2 mg or 0.4 mg on days 1 through 14 every 28 days in the dose-expansion phase.

At ASH 2024, Julio C. Chavez presented results from 58 patients with stage III or IV FL who received golcadomide monotherapy in the dose-escalation phase (n=12) or who received golcadomide 0.2 mg plus rituximab (n=22) or golcadomide 0.4 mg plus rituximab (n=36) in the dose-expansion phase (Figure 6).[1] Patients had received a median of 3 prior lines of therapy (range, 1-12), including 21% with prior T-cell–directed therapy and 32% with prior lenalidomide.

After a median follow-up of 30 months, the best ORR was 67% (42% CR) with single-agent golcadomide, 72% (36% CR) with golcadomide 0.2 mg plus rituximab, and 92% (68% CR) with golcadomide 0.4 mg plus rituximab. In subset analyses, responses were observed in patients previously treated with lenalidomide (ORR 100%; 63% CR) and in patients previously treated with CAR T-cell therapies (ORR 87%; 50% CR); no patients with a response had developed progressive disease at the time of data analysis.

The most frequent grade 3 or 4 toxicity was neutropenia, reported in 83% of patients receiving golcadomide monotherapy, 55% of patients receiving golcadomide 0.2 mg plus rituximab, and

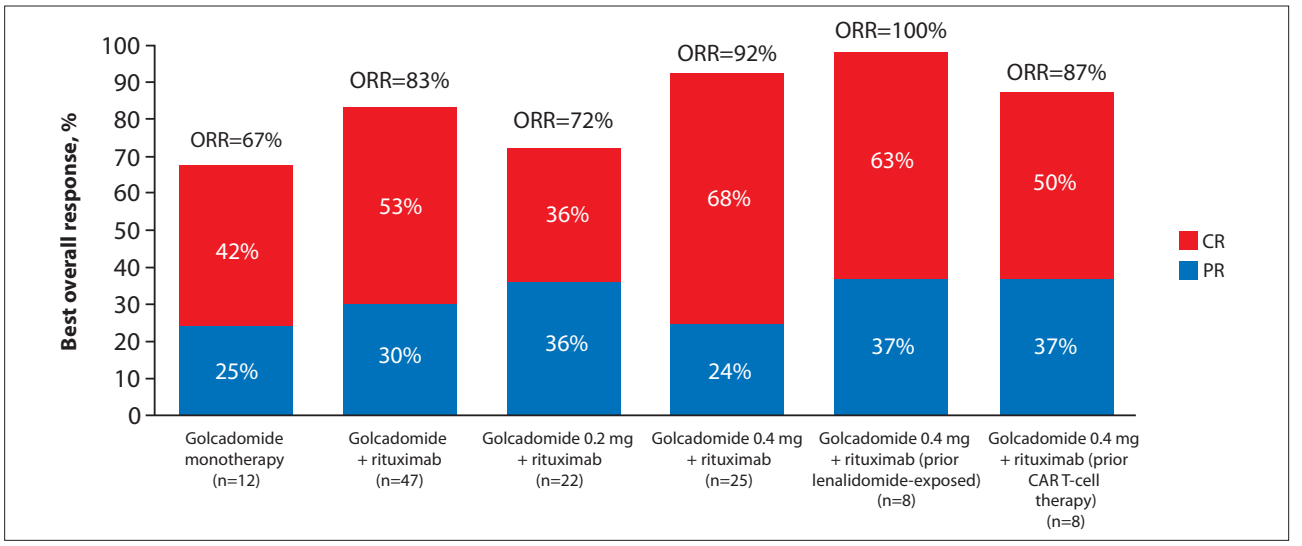

Figure 6. Durable efficacy with golcadomide ± rituximab in patients with R/R FL: updated results from the phase 1/2 CC-99282-NHL-001 study.[a]

[a]Efficacy-evaluable population.

CAR, chimeric antigen receptor; CR, complete response; FL, follicular lymphoma; ORR, overall response rate; PR, partial response; R/R, relapsed or refractory.

Adapted from Chavez et al. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 3018.

44% of patients receiving golcadomide 0.4 mg plus rituximab. Rates of febrile neutropenia were 17%, 5%, and 9%, respectively. Investigators noted that neutropenia was managed using G-CSF and/or dose interruptions. Nonhematologic AEs were primarily low grade and manageable.

Investigators concluded that golcadomide plus rituximab was an effective, safe, and well-tolerated combination in patients with R/R FL. The trial is ongoing and continues to enroll patients with R/R DLBCL and FL to receive golcadomide as monotherapy or in combination with rituximab.

Reference

1. Chavez JC, Fleury Perini G, et al. Golcadomide (GOLCA) ± rituximab demonstrates durable efficacy and is well tolerated in patients with relapsed/refractory follicular lymphoma (R/R FL): updated results from the phase 1/2 CC-99282-NHL-001 study. Presented at: 66th ASH Annual Meeting and Exposition; December 7-10, 2024; San Diego, California, USA. Abstract 3018.

ABSTRACT SUMMARY Deciphering the Mechanism of Action of the Novel CELMoD, Golcadomide, During Germinal Center B-Cell Immune Response and in a Preclinical Mouse Model of FL

Caroline Huber and colleagues presented results of preclinical studies investigating the mechanism of action of golcadomide (Abstract 955). The researchers developed an engineered human CRBN mouse model that allowed in vivo use of golcadomide in mice. They found that golcadomide strongly activates the T-cell immune response and induces B-cell depletion in lymphoid tissues. In a preclinical model of FL, golcadomide alone did not sufficiently affect the germinal center/memory B-cell continuum, thus leaving behind residual cells. However, golcadomide in combination with anti-CD20 exerted B-cell–depleting activity on all subsets, including memory B cells that are less sensitive to anti-CD20 alone. Restoration of immune surveillance through major histocompatibility complex class II upregulation on naive and memory-like B cells was a proposed mechanism of this synergistic activity.

In addition to the efficacy of rituximab and golcadomide combination in aggressive lymphomas, we see that this combination is quite active in FL. This study provides evidence that golcadomide can impact the immune microenvironment and synergize with the antibodies.

—Grzegorz S. Nowakowski, MD

NOTES

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GLOBAL STUDY

GOLSEEK-1:

A Phase 3 Trial of a Potential First-in-Class Oral CELMoD™ Agent, Golcadomide, for Previously Untreated High-Risk LBCL NCT06356129

GOLSEEK-1 is a randomized, double-blind, placebo-controlled, phase 3 registrational study of people with previously untreated high-risk LBCL comparing the efficacy and safety of:

Golcadomide + R-CHOP vs **placebo + R-CHOP**

GOLSEEK-1 is open to people with high-risk LBCL with IPI Score 1 or 2 with LDH >1.3 x ULN and/or bulky disease (single lesion of ≥7 cm) OR IPI ≥3. People with IPI 1-2 disease with high-risk features comprise a newly recognized subgroup with poor prognosis.[1]

Scan for complete study details

Key Eligibility Criteria*

Inclusion Criteria

- Age 18-80 years
- ECOG PS 0-2
- Histologically confirmed diagnosis of de novo, previously untreated LBCL, including:
  - Diffuse large B-cell lymphoma (DLBCL), not otherwise specified (including GCB and ABC subtypes)
  - High-grade B-cell lymphoma with MYC and BCL2 rearrangements
  - High-grade B-cell lymphoma, not otherwise specified
  - T-cell/histiocyte/rich large B-cell lymphoma (THRLBCL)
  - Epstein-Barr virus + DLBCL
- **High-risk LBCL: IPI Score 1 or 2 with LDH >1.3 x ULN and/or bulky disease (single lesion of ≥7 cm)** OR **IPI ≥3**
- Ann Arbor Stage II-IV disease
- Measurable disease per Lugano classification

Exclusion Criteria

- Any other subtype of lymphoma

Endpoints

- Primary: PFS by investigator
- Select Secondary: PFS by investigator non-HGBL, EFS by investigator, CMR at end of treatment by IRAC, OS, MRD negativity rate, DoR, QoL, safety

*Other protocol-defined Inclusion/Exclusion criteria apply.

Abbreviations: ABC=activated B-cell; **BCL2**=B-cell lymphoma 2; **CELMoD**=cereblon E3 ligase modulator; **CMR**=complete metabolic response; **DoR**=duration of response; **ECOG**=Eastern Cooperative Oncology Group; **EFS**=event-free survival; **GCB**=germinal center B-cell; **HGBL**=high-grade B-cell lymphoma; **IPI**=International Prognostic Index; **IRAC**=Independent Response Adjudication Committee; **LBCL**=large B-cell lymphoma; **LDH**=lactate dehydrogenase; **MRD**=minimal residual disease; **MYC**=myelocytomatosis oncogene; **OS**=overall survival; **PFS**=progression-free survival; **PS**=performance status; **QoL**=quality of life; **R-CHOP**=rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; **ULN**=upper limit of normal.

Reference: 1. Maurer MJ, Khurana A, Farooq U, et al. The presence of bulky disease and/or very high LDH defines a high-risk subset of IPI 1-2 for eligibility in clinical trials of newly diagnosed aggressive B-cell lymphoma. Abstract presented at: 65th Annual Meeting and Exposition of the American Society of Hematology; December 9-12, 2023; San Diego, CA. Abstract 4512.

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