ASH Highlights and Commentary: Lymphoid Malignancies

Viviana Perez, APRN, FNP-C, of Moffitt Cancer Center, considers findings presented at the 2024 ASH Annual Meeting on patient experiences with bispecific antibodies for diffuse large B-cell lymphoma and the efficacy of CAR T-cell therapy in patients with transformed indolent lymphoma. **Laura Zitella, MS, RN, ACNP-BC, AOCN, UCSF,** evaluates studies on omitting autologous transplant for many patients with mantle cell lymphoma, the use of CD19-directed monoclonal antibodies in relapsed/refractory follicular lymphoma, and the duration of lenalidomide maintenance in multiple myeloma.

Abstract 3647

A Healthcare Utilization Model Comparing Time Toxicity Between Glofitamab and Epcoritamab

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Visit https://doi.org/10.1182/blood-2024-198476 for a complete list of affiliations and full graphics.

Bispecific antibodies (BsAbs) such as glofitamab (Columvi) and epcoritamab (Epkinly) have emerged as treatment options for patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who have undergone at least two lines of therapy. Although both therapies demonstrate similar efficacy and safety profiles, their administration schedules differ, which impacts the "time toxicity" experienced by patients.

TIME TOXICITY

Time toxicity was defined as the number of days during which patients were in contact with healthcare (HC) services. This included days spent on clinic visits, infusions, procedures, bloodwork, imaging scans, and hospitalizations for both routine treatment and adverse event (AE) management. Days without any HC contact were "home days." Overall survival (OS) was defined as the sum of HC contact days and home days.

METHODS

A health-care utilization model was developed using data from BsAb registrational studies, FDA prescribing information, and study protocols to estimate the HC visits associated with each treatment. The analysis focused on quantifying HC contact days from the screening phase until the end of treatment, while follow-up visits were excluded. Hospital length of stay (LOS) for grade 3 or 4 AEs was estimated using data from the 2021 Healthcare Cost and Utilization Project National Inpatient Sample Database. Two time horizons were examined: 1 year and 2 years.

TIME TOXICITY OF GLOFITAMAB

For glofitamab, the total estimated HC contact days over a 1-year period was 30.9 days. This encompassed various HC interactions, including 1 day for screening and 1 day for pretreatment with obinutuzumab. Patients then received glofitamab over 13 days, with an additional day for inpatient cytokine release syndrome (CRS)

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monitoring, which was scheduled to coincide with the administration of the 2.5 mg dose. Vital signs and laboratory tests during the first two cycles required 4 separate days, and imaging scans accounted for 4 additional days. The weighted average hospital LOS for managing grade 3 or 4 AEs was 6.9 days. Common serious AEs included infections, febrile neutropenia, and immune effector cell-associated neurotoxicity syndrome (ICANS). Grade 3 or 4 CRS occurred in 4.1% of patients.

TIME TOXICITY OF EPCORITAMAB

Epcoritamab was associated with 44.9 HC contact days over the same 1-year period. The regimen required 1 day for screening followed by 28 days of epcoritamab administration. Inpatient CRS monitoring was conducted on 1 day, coinciding with the first full dose, and an additional day was required for laboratory tests during the second cycle. Imaging scans accounted for 7 separate days. The weighted average hospital LOS for managing grade 3 or 4 AEs was slightly higher at 7.9 days. Common severe AEs included infections, febrile neutropenia, and a lower incidence of ICANS. Grade 3 or 4 CRS was reported in 2.5% of patients.

Despite both treatments resulting in an estimated mean OS of 273 days over 1 year, patients treated with epcoritamab had fewer home days (228.1 days vs. 242.1 days) and experienced an additional 14 HC contact days compared to those on glofitamab. Over a 2-year horizon, continuous epcoritamab therapy was associated with an additional 29 HC contact days compared to the fixed-duration glofitamab regimen.

Perspectives for the Advanced Practitioner

Viviana Perez, APRN, FNP-C,
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Bispecific antibodies such as glofitamab and epcoritamab are approved treatment options for patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) after two or more lines of therapy. Early data suggest they have similar efficacy and safety profiles. However, frequency of administration and associated health-care visits differ between glofitamab and epcoritamab.

In this study, the objective was to determine the time toxicity; in other words, the time spent at a health-care facility for visits and coordination of care with these two bispecific antibody treatments. A health-care utilization model was created to estimate health-care visits associated with glofitamab and epcoritamab in patients with R/R DLBCL. The materials used to quantify health-care visits included study protocols, FDA prescribing information, and publications on bispecific antibody registrational studies. Time toxicity was defined as health-care contact days. Clinic visits, infusions, procedures, bloodwork, and elective/unplanned admissions were considered all-day affairs. Days without health-care contact were considered home days. The time horizons in this study were 1 year and 2 years.

Over the 1-year time horizon, the total health-care contact days for glofitamab was 30.9, whereas epcoritamab was associated with 44.9 health-care contact days. Epcoritamab was also associated with fewer home days vs. glofitamab. Over the 2-year time horizon, epcoritamab was associated with an additional 29 health-care contact days compared with glofitamab. When reviewing the data, it is evident that glofitamab was associated with fewer clinic visits than epcoritamab.

Implications for the Advanced Practitioner

This information is important for the patient and caregivers to help guide their decision-making when being presented with two treatment options for R/R DLBCL. This information is also extremely valuable for advanced practice providers, as we prioritize our patients' well-being and understand their desire to minimize the time spent in clinic while still ensuring they receive the necessary care they deserve.

Disclosure: Ms. Perez has nothing to disclose.

Abstract 524

Real-World Outcomes of CD19 CAR-T in Patients with R/R Transformed Indolent Lymphoma

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The transformation of indolent lymphomas into diffuse large B-cell lymphoma (DLBCL) is linked with poor outcomes, particularly in relapsed or refractory cases. Chimeric antigen receptor (CAR) T-cell therapy has revolutionized treatment for relapsed/refractory DLBCL and is approved for transformed indolent lymphoma (tiNHL). However, tiNHL patients were underrepresented in pivotal trials leading to CD19 CAR T-cell therapy approval. This study retrospectively evaluated the safety and efficacy of standard-of-care CD19 CAR T-cell therapy in adults with relapsed/refractory tiNHL compared to those with de novo DLBCL (dDLBCL).

METHODS

In this multicenter retrospective study conducted across six centers, adults with a diagnosis of DLBCL or high-grade B-cell lymphoma (HGBCL), either de novo or transformed, were included if they had relapsed/refractory disease and received standard-of-care CD19 CAR T-cell therapy outside of clinical trials. Transformed indolent lymphoma was defined as DLBCL/HGBCL evolving from follicular lymphoma, marginal zone lymphoma, or Waldenstrom's macroglobulinemia. Patients with Richter's syndrome were excluded.

Safety endpoints included the incidence and severity of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), graded per ASTCT criteria. Efficacy endpoints were best overall response rate (ORR), complete response rate (CRR), progression/relapse-free survival (PFS), and overall survival (OS).

RESULTS

A total of 1,182 patients were analyzed (338 [29%] with tiNHL and 884 [71%] with dDLBCL) with CAR T-cell infusions administered between December 2017 and October 2022. Within the tiNHL cohort, 84% of patients transformed from follicular lymphoma, 12% from marginal zone lymphoma, and 4% from Waldenstrom's macroglobulinemia. Although baseline characteristics were largely similar, tiNHL patients were more heavily pretreated (67% vs. 51% had ≥ 3 prior lines of therapy), more likely to have HGBCL (13% vs. 9%), and had higher recent exposure to bendamustine (17% vs. 6%), but they had less central nervous system involvement (6% vs. 11%).

Cytokine release syndrome rates were comparable, with any-grade CRS in 79% of tiNHL vs. 84% of dDLBCL patients and grade ≥ 3 CRS in 7% vs. 8%, respectively. Any-grade ICANS occurred in 42% of tiNHL compared to 52% in dDLBCL, with grade ≥ 3 ICANS seen in 21% vs. 27% (p = .024). Consequently, tocilizumab and glucocorticoid use were lower in the tiNHL group.

The overall response rates were similar (83% in tiNHL vs. 81% in dDLBCL), although the complete response rate was significantly higher in tiNHL (67% vs. 59%, p = .017). With a median follow-up of 22.3 months, 24-month PFS (41% vs. 38%, p = .16) and OS (58% vs. 52%, p = .15) were comparable between the cohorts. After adjusting for multiple factors, the hazard of progression, relapse, or death post-CAR T-cell therapy was 16% lower for tiNHL patients (HR: 0.84; p = .07).

CONCLUSION

This large, multicenter study demonstrates that CD19 CAR T-cell therapy is both effective and tolerable in patients with transformed indolent lymphoma, achieving comparable outcomes to those seen in patients with de novo DLBCL.

Perspectives for the Advanced Practitioner

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When an indolent lymphoma transforms to DLBCL, it often leads to a poor prognosis, especially for patients with relapsed/refractory disease. CAR T-cell therapy is approved for transformed indolent lymphomas. This large retrospective study focused on evaluating the safety and efficacy of standard-of-care CD19 CAR T-cell therapy in adults with R/R transformed indolent lymphomas relative to de novo DLBCL. Transformation of indolent lymphomas was defined as DLBCL/HGBCL transformed from follicular lymphoma, marginal zone lymphoma, and Waldenström macroglobulinemia.

Patients who received CAR T-cell therapy on a clinical trial were excluded, as well as patients with Richter's transformation. CAR T-cell therapy was infused from December 2017 to October 2022. The mean age at CAR T-cell therapy was 64 years old. The overall response rate in both cohorts was similar, whereas the complete response rate was higher in the transformed indolent group (67% vs. 59%). Based on the results of this study, it was determined that CAR T-cell therapy is highly effective with an acceptable toxicity profile in transformed indolent lymphoma patients.

Implications for the Advanced Practitioner

CAR T-cell therapy represents a potentially groundbreaking treatment for this population of patients who may have limited treatment options offering a chance for durable remission. We need to be able to discuss this possibility with patients and coordinate care to determine if this is a suitable treatment option for the patient. We also have to keep in mind that a significant geographic barrier exists for some patients seeking CAR T-cell therapy, as qualified treatment centers may not be readily accessible in their local areas. Ultimately, one of our roles as advanced practitioners is to ensure our patients are fully informed about the most current treatment options available for their disease.

Disclosure: Ms. Perez has nothing to disclose.

Abstracts 240 and LBA-6

Evaluating the Need for Autologous Transplant in Mantle Cell Lymphoma

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Mantle cell lymphoma (MCL) has traditionally been treated aggressively, particularly in younger, fit patients, where autologous stem cell transplantation (ASCT) has been a mainstay of consolidation therapy following induction chemotherapy. However, the emergence of treatments such as Bruton tyrosine kinase (BTK) inhibitors like ibrutinib (Imbruvica), and advanced methods for minimal residual disease (MRD) detection, have prompted a re-evaluation of ASCT's role in MCL treatment.

Two major studies—the TRIANGLE trial by the European MCL Network and the EA4151 trial by ECOG-ACRIN—provide data that challenge the necessity of ASCT in certain patient populations.

IBRUTINIB IN FIRST-LINE TREATMENT WITHOUT ASCT

Study Design and Objectives

The TRIANGLE trial, initiated in 2016, was a multicenter, randomized, open-label study designed to assess whether incorporating ibrutinib into

first-line therapy for younger MCL patients could remove the need for ASCT. The study enrolled 870 previously untreated patients aged ≤ 65 years with advanced-stage MCL (stage II-IV) who were eligible for high-dose cytarabine and ASCT.

The trial employed a three-arm design:

- Arm A (standard care): induction with alternating cycles of R-CHOP and R-DHAP followed by ASCT)
- Arm A + I: induction similar to Arm A but with ibrutinib added during R-CHOP cycles and 2 years of ibrutinib maintenance post-ASCT
- Arm I: induction with R-CHOP and R-DHAP plus ibrutinib, followed by 2 years of ibrutinib maintenance, omitting ASCT.

Findings

After a median follow-up of 53 months, the addition of ibrutinib significantly improved outcomes compared with ASCT, and ASCT with ibrutinib provided no additional benefit. Ibrutinib with ASCT (Arm A+I) did not demonstrate superior failure-free survival (FFS) compared to ibrutinib alone (Arm I), with 3-year FFS rates of 86% and 85%, respectively (p = .28, HR 0.87). Similarly, ASCT alone (Arm A) failed to show FFS superiority over Arm I, with 3-year FFS rates of 75% vs. 85% (p = .9942, HR 1.38).

A retrospective analysis showed a significant FFS advantage for Arm I over Arm A (p = .0102). However, Arm A+I maintained FFS superiority over Arm A, with a 3-year FFS rate of 86% compared to 75% (p = .0034, HR 0.64). In terms of overall survival (OS), Arm A had a 3-year OS of 85%, while OS significantly improved in both Arm I (91%, p = .0041, HR 0.59) and Arm A+I (90%, p = .0069, HR 0.61).

Conclusion

The TRIANGLE trial's findings suggest that ibrutinib-containing induction and maintenance therapy without ASCT offers the same, if not superior, efficacy compared to traditional ASCT-based regimens. This study suggests that ibrutinib plus R-CHOP/R-DHAP induction, followed by 2 years of ibrutinib maintenance, should become the new standard of care for younger MCL patients.

THE VALUE OF ASCT IN MRD-NEGATIVE MCL PATIENTS

Study Design and Objectives

The EA4151 trial was a phase III randomized study evaluating whether autologous hematopoietic cell transplantation (auto-HCT) adds clinical benefit in MCL patients who achieve a deep first remission (uMRD6). The study included 650 MCL patients who had achieved complete remission (CR) post-induction therapy. MRD was assessed using the clonoSEQ assay. Based on MRD status, patients were allocated into one of four arms.

- Arm A (auto-HCT + rituximab [Rituxan] maintenance): Patients in CR with undetectable MRD underwent auto-HCT followed by 3 years of maintenance rituximab
- Arm B (rituximab maintenance alone): Patients in CR with undetectable MRD received 3 years of maintenance rituximab without auto-HCT
- Arms C & D: Patients with MRD-positive or indeterminate status post-induction received auto-HCT followed by rituximab maintenance.

Findings

The interim analysis at a median follow-up of 2.7 years revealed no survival benefit for auto-HCT in patients with undetectable MRD post-induction.

The 3-year OS was 82.1% in Arm A (auto-HCT) vs. 82.7% in Arm B (rituximab alone), with no statistically significant difference. PFS rates were also comparable, with 76.6% in Arm A and 77.4% in Arm B for all randomized patients.

In the MRD-positive subgroup (Arm C), patients who remained MRD-positive post-induction but achieved uMRD6 post-auto-HCT had excellent outcomes, with 100% 3-year OS and PFS. Conversely, patients who stayed MRD-positive even after auto-HCT had poorer outcomes (3-year OS of 63.6% and PFS of 48.8%).

Conclusion

In MCL patients achieving deep molecular remission after induction therapy, auto-HCT offered no survival advantage compared to rituximab maintenance alone. However, for patients who are MRD-positive after induction, auto-HCT still appears beneficial.

Perspectives for the Advanced Practitioner

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Transplant-eligible patients with previously untreated mantle cell lymphoma are commonly treated with induction chemoimmunotherapy followed by autologous stem cell transplant (ASCT) and 3 years of maintenance rituximab. There were two abstracts presented at the 2024 ASH meeting that suggest that there may no longer be a role for transplant for many people with mantle cell lymphoma.

The TRIANGLE study is a phase III trial that evaluated adding ibrutinib (a BTK inhibitor) to standard treatment in 870 untreated, advanced stage II-IV MCL patients aged 65 or younger. Participants were randomized into three arms: (1) chemoimmunotherapy with ASCT with or without 3-year rituximab maintenance; (2) ibrutinib plus chemoimmunotherapy with ASCT, followed by 2 years of ibrutinib maintenance with or without 3-year rituximab; and (3) chemoimmunotherapy with ibrutinib followed by 2 years of ibrutinib maintenance (no ASCT). Approximately half of the patients received rituximab maintenance.

At a median follow-up of 53 months, there was improved failure-free survival and overall survival in the arms that included ibrutinib. Autologous transplant did not offer any additional survival benefit for patients treated with ibrutinib, and failure-free survival was superior in the arms that included ibrutinib compared to the arm with autologous transplant and no ibrutinib. In the arms that included ibrutinib and rituximab chemoimmunotherapy induction followed by 2 years of ibrutinib maintenance, the 3-year overall survival was approximately 90%.

In the ECOG-ACRIN EA4151 study, patients received chemoimmunotherapy for induction, followed by an assessment of complete remission and measurable residual disease (MRD) status to a sensitivity of 10^{-6}. Patients with complete remission and MRD negativity were randomized to either autologous transplant plus 3 years of maintenance rituximab or maintenance rituximab alone.

In this study, there was no benefit to autologous transplant in patients with undetectable measurable residual disease following induction therapy. There was a benefit to autologous transplant for patients who had detectable MRD following induction therapy.

Implications for the Advanced Practitioner

Mantle cell lymphoma (MCL) is a rare subtype of non-Hodgkin lymphoma. The median age of diagnosis is 68 years old. It has a heterogenous clinical behavior, ranging from indolent to aggressive. Chemoimmunotherapy has been a standard first-line treatment followed by consolidation with autologous stem cell transplant for younger, fit patients. Autologous stem cell transplant is an intensive therapy that can cause physical and financial toxicity. In addition, many patients with MCL are not eligible for ASCT due to comorbidities and fitness. More effective treatments, such as targeted therapies, have been developed. In particular, Bruton tyrosine kinase (BTK) inhibitors have been shown to be effective for relapsed/refractory MCL, and the TRIANGLE study supports the use of BTK inhibitors in the first-line setting.

These two ASH abstracts suggest that autologous transplant can be omitted for many patients with mantle cell lymphoma. The TRIANGLE study supports the addition of ibrutinib to induction chemoimmunotherapy and 2 years of maintenance ibrutinib. The ECOG-ACRIN EA4151 study supports the omission of autologous transplant for patients with mantle cell lymphoma who achieved undetectable MRD following induction therapy.

Considering the data from these two studies, BTK inhibitors improve outcomes when included in induction and maintenance therapy. The addition of a BTK inhibitor increases the probability of achieving MRD negativity following induction therapy and prolongs failure-free survival and overall survival. If MRD negativity is achieved with induction therapy, there is no additional benefit to autologous transplant. If there is detectable MRD following induction therapy, autologous transplant can achieve MRD negativity and improve overall survival.

Disclosure: Ms. Zitella has nothing to disclose.

LBA-1 and Abstract 337

CD19-Directed Monoclonal Antibodies in Relapsed/Refractory Follicular Lymphoma

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Follicular lymphoma (FL) is an indolent non-Hodgkin lymphoma marked by cycles of remission and relapse that often require multiple lines of therapy. Two studies presented at the ASH Annual Meeting explored improving response durability and expanding treatment options. The inMIND phase III trial evaluated the addition of tafasitamab (Monjuvi) to lenalidomide (Revlimid) and rituximab (Rituxan), and a phase II study investigated loncastuximab tesirine (Zynlonta) combined with rituximab in high-risk relapsed/refractory (R/R) FL.

TAFASITAMAB PLUS LENALIDOMIDE AND RITUXIMAB

Background

The inMIND study added tafasitamab, a humanized anti-CD19 monoclonal antibody, to the standard regimen of lenalidomide plus rituximab. Tafasitamab boosts immune-mediated cytotoxicity through natural killer cells and macrophages, and had already shown efficacy in diffuse large B-cell lymphoma when paired with lenalidomide. The trial aimed to determine if this dual antibody strategy—targeting both CD19 and CD20—could further improve outcomes in patients with R/R FL.

Methods

In this double-blind, placebo-controlled phase III trial, 548 patients with CD19+ and CD20+ FL who had received at least one prior systemic therapy (including an anti-CD20 antibody) were randomized in a 1:1 ratio. One group (n = 273) received tafasitamab with standard lenalidomide and rituximab for twelve 28-day cycles, while the other group (n = 275) received a placebo with the standard lenalidomide and rituximab regimen.

Results

The addition of tafasitamab significantly improved outcomes. The median PFS was 22.4 months in the tafasitamab arm compared to 13.9 months in the placebo arm (HR 0.43; $p < .0001$). Additionally, the PET-complete response (PET-CR) rate was higher with tafasitamab (49.4% vs. 39.8%; $p = .029$), and the ORR improved significantly (83.5% vs. 72.4%; $p = .0014$). The duration of response was also longer (21.2 months vs. 13.6 months; HR 0.47; $p < .0001$). Subgroup analyses indicated that even high-risk patients, such as those with progression of disease within 24 months (POD24) or those refractory to prior anti-CD20 therapy, benefited from the tafasitamab combination.

Conclusion

The inMIND trial demonstrated that adding tafasitamab to lenalidomide and rituximab significantly improves progression-free survival and response rates in R/R FL.

LONCASTUXIMAB TESIRINE PLUS RITUXIMAB IN HIGH-RISK R/R FL

Background

Loncastuximab tesirine is an antibody-drug conjugate that targets CD19, delivering a cytotoxic pyrrolobenzodiazepine payload directly to malignant B cells. Building on earlier phase I results in FL, researchers hypothesized that combining loncastuximab with rituximab, an anti-CD20 monoclonal antibody, could produce synergistic antitumor effects. This phase II study evaluated the efficacy and safety of this combination in high-risk R/R FL patients.

Methods

This single-institution study enrolled 39 patients between January 2022 and June 2024. Eligible

patients had received at least one prior systemic therapy and met criteria for POD24 or had a high tumor burden. The primary endpoint was the complete metabolic response (CMR) at week 12 assessed by PET/CT. Treatment involved four weekly doses of rituximab, with subsequent maintenance every 8 weeks, alongside loncastuximab administered every 3 weeks.

Results

Of the 39 patients enrolled, 35 were evaluable for response. The median age was 68 years, with most patients presenting with advanced-stage disease (82%) and high-risk FLIPI scores (61.5%). At week 12, the overall response rate was an impressive 97.1%, with 68.6% achieving a CMR. By week 21, the CMR rate increased to 80%, as some patients with initial partial responses converted to CMR. Baseline bone marrow involvement resolved in all affected patients. In the POD24 subgroup, the ORR was 100% with an 80% CMR rate. With a median follow-up of 15.6 months, the 12-month progression-free survival was 94.2% and the 18-month PFS was 90.1%, with median PFS and OS not reached.

The treatment was generally well-tolerated, with common adverse events including neutropenia (53.8%), anemia (46.1%), rash (46.1%), and elevated liver enzymes. Grade ≥ 3 neutropenia occurred in 23.8% of patients, and there were no treatment-related deaths.

Conclusion

The combination of loncastuximab tesirine and rituximab demonstrated responses in high-risk R/R FL patients, with an 80% CMR rate and a 12-month PFS of 94.2%.

Perspectives for the Advanced Practitioner

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Abstracts LBA-1 and 337 investigated the use of CD19-directed monoclonal antibodies in relapsed/refractory follicular lymphoma (FL). Currently, CD19-directed monoclonal antibodies are only approved for large B-cell lymphoma.

Follicular lymphoma is an indolent lymphoma that does not require treatment unless there are symptoms. When treatment is required, first-line therapy typically includes the anti-CD20 monoclonal antibody, rituximab, with or without chemotherapy. Follicular lymphoma is highly treatable but is considered incurable as it is characterized by remissions followed by relapses. Thus, most patients will have a relapse requiring second-line treatment. A common second-line regimen is the combination of rituximab and lenalidomide. It is exciting that CD19-directed monoclonal antibodies are being studied for R/R FL.

In LBA-1, patients with relapsed FL were randomized to either tafasitamab, an anti-CD19 monoclonal antibody, plus lenalidomide and rituximab, or rituximab and lenalidomide alone for 12 cycles. At a median follow-up of 14.1 months, there was a 57% decreased risk of progression with the addition of tafasitamab to a backbone of lenalidomide plus rituximab. The progression-free survival was 22 months vs. 13.9 months. The safety profile was tolerable and similar in both arms.

Abstract 337 is a small phase II study with 35 patients with R/R FL treated with loncastuximab in combination with rituximab. Loncastuximab is an antibody-drug conjugate that consists of a CD19-directed antibody and alkylating agent conjugate. The 18-month progression-free survival was 90%, and the complete metabolic remission was about 80%.

Implications for the Advanced Practitioner

The only current FDA-approved CD19-directed therapy for FL is chimeric antigen receptor (CAR) T-cell therapy in the third-line setting. CAR T-cell therapy is an intensive treatment that is administered at specialized centers. These two abstracts showed promising results using CD19-directed monoclonal antibodies, which are well tolerated and can be administered in the community setting. Additionally, they were studied in the second-line setting. Tafasitamab may soon be approved for FL, and the combination of tafasitamab, lenalidomide, and rituximab may represent a new standard of care with improved outcomes for the treatment of R/R FL.

Disclosure: Ms. Zitella has nothing to disclose.

Abstract 361

Assessing When to Stop Lenalidomide Maintenance in Multiple Myeloma

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Autologous stem cell transplantation (ASCT) followed by lenalidomide maintenance remains the standard of care for eligible patients with newly diagnosed multiple myeloma (NDMM). However, the optimal duration for lenalidomide maintenance is still under debate. A recent prospective study explored whether sustained minimal residual disease (MRD) negativity assessed using advanced next-generation flow (NGF) cytometry and PET/CT imaging could serve as a reliable biomarker to safely discontinue maintenance therapy.

STUDY DESIGN AND METHODS

Between 2016 and 2021, 194 NDMM patients underwent ASCT after induction with proteasome inhibitor-based regimens such as VCD, VRD, or VTD. Following transplant, all patients received lenalidomide maintenance therapy. MRD status was evaluated in those who achieved stringent complete remission (sCR) at 6, 12, 24, and 36 months after starting maintenance. Patients who maintained three consecutive MRD-negative results over at least 36 months, confirmed by bone marrow and PET/CT imaging, were eligible to discontinue lenalidomide. After discontinuation, these patients underwent MRD testing every 6 months, with lenalidomide therapy being reinitiated if they converted from MRD-negative to MRD-positive or if a relapse from sCR was observed.

KEY FINDINGS

During a median follow-up of 63.5 months from diagnosis, 25.2% of the patients experienced disease progression and 10.3% died. Notably, 51 patients (26.3%) achieved sustained MRD negativity in both the bone marrow and imaging at the 3-year mark and subsequently discontinued maintenance therapy. This subgroup had a median age of 56 years and included a mix of immunoglobulin subtypes and risk profiles—with approximately 31% harboring at least one high-risk cytogenetic abnormality.

After discontinuation of lenalidomide maintenance, the majority of these patients continued to show durable MRD negativity. The rates of sustained MRD negativity remained above 90% at 6, 12, 18, 24, and 30 months after discontinuation. Even at 3 years after stopping maintenance, 86% of evaluable patients remained MRD negative, and at later time points, all evaluable patients in the study maintained their MRD-negative status.

Despite these promising results, 11 patients did convert to MRD positivity after initially achieving sustained negativity, prompting the reinitiation of lenalidomide monotherapy. Among these, four patients eventually progressed and required second-line treatment. For this subset, the median time to progression after restarting lenalidomide was 9.5 months, with an overall median progression-free survival (PFS) of 74 months across the study population.

CONCLUSION

This study suggests that in NDMM patients who have undergone ASCT, sustained MRD negativity after 3 years of lenalidomide maintenance may be a viable marker for safely discontinuing maintenance therapy. The strategy of close, periodic MRD monitoring allows clinicians to detect early signs of relapse, enabling prompt reinitiation of lenalidomide, which could potentially delay disease progression.

Perspectives for the Advanced Practitioner

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Abstract 361 assessed the duration of lenalidomide maintenance following autologous stem cell transplantation (ASCT) for multiple myeloma. The standard of care for transplant-eligible patients with newly diagnosed multiple myeloma is induction therapy followed by ASCT and lenalidomide maintenance. Maintenance therapy with lenalidomide after ASCT significantly improves progression-free survival. However, the duration of lenalidomide maintenance is not well defined, and often, patients continue lenalidomide until the progression of the disease.

In this study, the researchers tested for measurable residual disease (MRD) at 6, 12, 24, and 36 months after the initiation of lenalidomide maintenance. Patients stopped lenalidomide maintenance after there was MRD-negative disease for 3 years.

This study is practice-changing because the researchers found that 30 months after stopping lenalidomide, approximately 90% of patients remained MRD-negative. This data supports the discontinuation of lenalidomide maintenance after three years of MRD negativity following an autologous transplant.

Implications for the Advanced Practitioner

This study is important for advanced practitioners to recognize the importance of MRD testing to determine the duration of lenalidomide maintenance. Lenalidomide is the preferred maintenance strategy following ASCT and prolonged duration of lenalidomide is associated with improved progression-free survival. For this reason, lenalidomide maintenance is often continued for at least 5 years following autologous transplantation and, in many cases, indefinitely until disease progression. However, the clinical behavior of myeloma varies from patient to patient and the optimal duration of lenalidomide maintenance for an individual patient is unknown.

Measurable residual disease (MRD) status is associated with prolonged progression-free survival and overall survival in both the newly diagnosed and relapsed/refractory settings of multiple myeloma. For this reason, MRD status was incorporated into the International Myeloma Working Group (IMWG) uniform response criteria in 2016. The IMWG defines MRD negativity as the absence of clonal plasma cells on bone marrow aspirate with a minimum test sensitivity to detect 1 in 10^5 nucleated cells. Two commonly used MRD techniques are next-generation flow cytometry and next-generation sequencing (NGS). In recent studies, MRD status has been used to guide treatment escalation/de-escalation and the duration of maintenance therapy.

This abstract supports the discontinuation of lenalidomide maintenance after 3 years of sustained MRD-negativity. It follows another important trial, the UK NCRI Myeloma XI trial, which also found that patients with MRD-negative myeloma benefit from lenalidomide treatment for at least 3 years. For patients with MRD-positive myeloma, there was an ongoing benefit to continue lenalidomide for 5 years and beyond. Determining the optimal duration of lenalidomide maintenance is important for patients so we can offer them the maximum benefit with minimal toxicity. In some patients, indefinite or prolonged lenalidomide maintenance can lead to physical or financial toxicity. Lenalidomide can cause side effects including, but not limited to myelosuppression, nausea, diarrhea, constipation, rash, fatigue, and muscle cramping. MRD testing is an important tool to assess response and prognosis and to guide treatment decisions.

Disclosure: Ms. Zitella has nothing to disclose.