Hematologic Malignancies: 2022 ASCO Annual Meeting Highlights for the Advanced Practitioner

P. Andrew Allred, MS, PA-C, of Banner MD Anderson Cancer Center, considers data on managing newly diagnosed MM and CAR T-cell therapy in MM. **Amy Pierre, MSN, ANP-BC,** of MSKCC and Flatiron Health, reviews findings on telemedicine inequities and real-world data on axicabtagene ciloleucel. **Meredith Beaton, MSN, RN,** of UCHealth, evaluates data on *FLT3*-mutated AML and TKI discontinuation in CML. **Pamela Lee, NP, MSN,** of UCSF Medical Center, analyzes results of a new BiTE therapy in DLBCL and CAR T-cell therapy in MCL. **Amber Koehler, PA-C,** of Mayo Clinic Cancer Center, reviews combination therapies for CLL.

Abstract LBA4

Early Transplant With Triplet Therapy May Delay Progression of Myeloma, but Individualized Approach Recommended

By Caroline Helwick

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In the phase III DETERMINATION trial, progression-free survival was significantly improved with triplet induction therapy and early transplantation in newly diagnosed patients with multiple myeloma, but overall survival at 5 years was similar to the nontransplant approach. The findings were presented at the Plenary Session of the 2022 ASCO Annual Meeting by Paul G. Richardson, MD, Clinical Program Leader and Director of Clinical Research at the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute and the RJ Corman Professor of Medicine at Harvard Medical School, Boston.

"The addition of transplant to novel agent triplet induction therapy using lenalidomide, bortezomib, and dexamethasone [RVd] followed by lenalidomide maintenance until disease progression resulted in a highly significant increase in progression-free survival, with an improvement in the median of over 21 months. Remarkably, despite this advantage, overall survival with follow-up that is now approaching a median of 7 years proved similar between the two arms," Dr. Richardson reported.

"Our results provide support for personalized treatment approaches," Dr. Richardson said. "Importantly, we also saw more toxicity and significant effects on quality of life with early transplant. Overall, these results suggest you may be able to selectively delay transplant to use it in a more tailored fashion, recognizing there is an impressive progression free–survival benefit, but to date there appears to be equal outcome in overall

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survival." He continued, "patients therefore have the option of keeping early transplant in reserve, particularly if they have a high-quality response to induction therapy and especially in the setting of MRD [measurable residual disease] negativity."

Primary Endpoint Met

After a median follow-up of 76.0 months, median progression-free survival was 67.5 months with RVd and autologous stem cell transplantation (ASCT), vs 46.2 months with RVd alone (hazard ratio [HR] = 1.53; $P < .0001$). At 5 years, overall survival was 80.7% vs 79.2%, respectively (HR = 1.10; $P = .99$).

Although response rates and quality of responses were similar between the arms, "interestingly and encouragingly," he added, MRD negativity was improved with transplantation. The advantages of RVd plus ASCT, however, came at the cost of more hematologic toxicity and nonhematologic side effects, as well as certain secondary cancers.

The lack of an overall survival benefit is probably associated with the many highly effective options now available after first-line therapy, Dr. Richardson suggested. After RVd alone, 28% of participants had ASCT as salvage therapy; other treatments included next-generation immunomodulatory drugs, proteasome inhibitors, and monoclonal antibodies.

By cytogenetic risk, median progression-free survival was 82.3 months with transplant vs 53.2 months without, respectively, for the standard-risk group. Importantly, for patients with high-risk cytogenetics, it was 55.5 vs 17.1 months, respectively. Patients with t(4;14) mutations derived more progression-free survival benefit from RVd plus ASCT than did those with del(17p), Dr. Richardson said. In addition, RVd plus ASCT yielded less progression-free survival benefit for Black participants, individuals with a body mass index greater than 25 kg/m^2, and those with a higher disease stage.

The DETERMINATION trial was conducted in parallel with the French IFM 2009 study. The two had the same design, but DETERMINATION evaluated continuous lenalidomide maintenance, whereas IFM 2009 limited lenalidomide maintenance to 1 year. IFM 2009 demonstrated significantly superior progression-free survival with early transplant, and after almost 8 years of median follow-up, overall survival also remained similar but with almost 80% of patients having undergone delayed ASCT, in contrast to the 28% reported in DETERMINATION.

The much longer progression-free survival for both arms in the DETERMINATION study vs IFM 2009 (which was 47 months with early transplant vs 35 months without) "suggests there is clearly a benefit to continuous maintenance," Dr. Richardson said. "This comparison was preplanned, and the difference seen in favor of the continuous approach was striking. Given the benefit seen in other phase III studies, we are able to confirm that the use of lenalidomide maintenance until disease progression is now a standard of care."

About DETERMINATION

The phase III DETERMINATION (Delayed vs Early Transplant With Revlimid Maintenance and Antimyeloma Triple Therapy) trial sought to determine whether first-line ASCT enhances the efficacy of triplet induction therapy or whether it can be kept in reserve for selected patients. The study's 722 adults (aged 18–65 years) with symptomatic newly diagnosed myeloma received one cycle of RVd and then were randomly assigned to receive two additional RVd cycles plus stem cell mobilization and either five more RVd cycles (the RVd-alone group) or high-dose melphalan plus ASCT followed by two additional RVd cycles (the transplantation group).

For maintenance, both groups received daily lenalidomide (10 mg/d in months 1–3 and thereafter 15 mg/d) until disease progression. The median duration of maintenance was 41.5 months after RVd plus ASCT and 36.4 months after RVd alone. The primary endpoint was progression-free survival.

Notably, approximately 19% of trial participants were Black, which is apparently the highest representation of this subset of patients in any phase III trial in myeloma. "That was incredibly gratifying to see," Dr. Richardson added.

MRD Negativity

MRD negativity is increasingly recognized as important for long-term outcomes in myeloma. It was more likely to be achieved for patients in the transplantation group, despite similar rates of complete responses between the two groups.

Notably, treatment assignment was not found to be important for this group, as they had favorable 5-year progression-free survival regardless of treatment assignment: 53.5% with RVd plus ASCT and 59.2% with RVd alone (HR = 0.91). For MRD-positive patients, RVd plus ASCT improved progression-free survival by 67% (HR = 1.67).

The finding is further evidence that sustained MRD negativity is a potentially valuable clinical endpoint. Treatment adaptation based on MRD status could be an alternative to the standard use of ASCT as well as maintenance until disease progression, according to the investigators.

More Toxicity

The advantages of the transplant arm came with the cost of significantly more grade ≥ 3 hematologic adverse events: 89.9% vs 60.5% ($P < .001$). Of note, after ASCT, 10 patients developed myelodysplastic syndrome and/or acute myeloid leukemia, compared with none in the RVd-alone arm ($P = .002$). Patients in the ASCT arm also had reductions from baseline in their quality of life, around the time of transplantation, but these decreases were reported to be transient and improved over time.

Recent trials and exploratory studies are "providing clues" that even newer approaches, such as quadruplet regimens that include monoclonal antibodies such as daratumumab or isatuximab have shown great promise and may produce even more "transformative" improvements than what has been shown in the DETERMINATION trial, Dr. Richardson noted.

The Advanced Practitioner Perspective

P. Andrew Allred, MS, PA-C
Banner MD Anderson Cancer Center

Autologous stem cell transplantation (auto-SCT) has been a mainstay of myeloma management since the 1990s and is currently considered standard of care in newly diagnosed myeloma patients under the age of 70 years old and without significant comorbidities. This is because data historically have suggested that compared with chemotherapy and steroids alone, auto-SCT performed early in the disease process improves event-free and overall survival. However, this paradigm is just beginning to shift due to new and credible data which all advanced practitioners providing myeloma care should not only be aware of, but also be able to discuss freely with patients and physician collaborators.

The results of the phase III DETERMINATION trial confirm the findings of the French IFM 2009 study that demonstrated that in the current era of multiple generations of novel anti-myeloma therapy, early auto-SCT significantly improves progression-free survival but no longer provides overall survival benefit.

DETERMINATION results also showed that the improvement in progression-free survival comes at the cost of increased toxicity and decreased quality of life, at least temporarily, for patients undergoing auto-SCT.

Nonetheless, auto-SCT in this setting can improve progression-free survival for 2 to 2.5 years if coupled with ongoing lenalidomide maintenance. Auto-SCT can also help myeloma patients achieve measurable residual disease (MRD) negativity when triplet therapy alone failed to do so. This is important because MRD negativity is thought to be correlated with better outcomes.

The authors of DETERMINATION encourage myeloma providers to be empowered with this information and therefore be better situated to recommend personalized approaches to each myeloma patient.

Disclosure: Mr. Allred has no conflicts of interest to disclose.

Abstract 6511

Use of Telemedicine for Cancer Care Increased During the COVID-19 Pandemic but Varied by Race, Socioeconomic Status, and Other Factors

By The ASCO Post Staff

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With the rapid acceleration of the spread of the COVID-19 virus in the United States in March 2020, telemedicine visits became more common for cancer care. However, in an evaluation of telemedicine inequities among patients with 21 common cancers, there were distinctly lower levels of telemedicine use by Black patients and those who were uninsured, lived in suburban or rural areas, and resided in a neighborhood with low socioeconomic status. The research was presented by Guadamuz et al at the 2022 ASCO Annual Meeting.

About the Study

The health records used in the study were from 26,788 patients who were age 18 years or older and who started first-line cancer treatment between March 2020 and November 2021 (with follow-up through March 2022) at community-based cancer centers. The investigators looked at differences in the number of telemedicine visits across race/ethnicity, insurance coverage, rural vs suburban vs urban residence, and neighborhood socioeconomic status. They found that 15.9% of patients in the study used telemedicine services within 90 days (about 3 months) after initiation of systemic cancer treatment.

The data for the study was derived from electronic records from Flatiron Health. Before March 2020, only a very small percentage of patients with cancer used telemedicine services, according to research published by Katz et al in *JAMA Oncology*.

Key Findings

Black patients were less likely to use telemedicine services than White patients (13.2% vs 15.6%, respectively) during the first 2 years or so of the COVID-19 pandemic. Telemedicine use was lower among patients without documented insurance than those with private insurance or Medicare (11.7% vs 16.4%). Patients in rural (9.8%) and suburban areas (12.9%) were less likely to use telemedicine services than patients in urban areas (17.7%). Patients living in the lowest socioeconomic status areas were less likely to use telemedicine than those in the highest areas (10.6% vs 23.6%).

"Our study provides the most recent and comprehensive evaluation of trends and inequities in telemedicine use across many sociodemographic characteristics. While telemedicine may expand access to specialty care, the proliferation of these services may widen cancer care disparities if vulnerable populations do not have equitable access," said lead study author Jenny S. Guadamuz, PhD, a quantitative scientist at Flatiron Health.

Next Steps

The study researchers emphasized that it will be important to evaluate whether the use of telemedicine is associated with quality care.

The researchers hope the lessons learned from this study are imparted to cancer care centers nationwide with the goals of:

- Ensuring that Centers for Medicare and Medicaid Services (CMS) policies that allowed the proliferation of telemedicine services are made permanent and not just tied to the COVID-19 public health emergency declaration.
- Improving access to health insurance—one of the greatest determinants of telemedicine use.
- Making sure that technologies are accessible for those with low tech literacy and limited English proficiency, which is distinct from health literacy.

The Advanced Practitioner Perspective

Amy Pierre, MSN, ANP-BC
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The COVID-19 pandemic has radically affected health-care delivery. Telemedicine usage increased as oncology centers across the country equipped their clinics with telemedicine services to provide continuity of care. But as new forms of oncology care emerge, it is important to consider who has access to them.

This retrospective study utilizing real-world data is the largest study conducted to understand the inequities that exist in telemedicine usage during the COVID-19 pandemic. By analyzing over 800 sites providing oncology care, it was found that Black patients, uninsured patients, patients residing in rural or suburban areas, and those of lower socioeconomic status were less likely to utilize telemedicine services during the pandemic. This inequity in telemedicine access and usage was not due to baseline differences in patients, as this study adjusted for clinical characteristics such as age, gender, performance stage, and stage of disease. Among all factors contributing to this inequity in telemedicine usage, socioeconomic status had the greatest impact. And despite telemedicine usage expanding, the inequity in usage did not improve but rather, persisted.

As an advanced practitioner, it is always encouraging to see new forms of care delivery such as telemedicine. But this excitement comes with caution, because as we cast a wider net in reaching patients, there could also be a widening gap in health-care access for a subset of patients who have been historically marginalized.

Telemedicine usage is likely to remain even after we reach an endemic stage of the pandemic. Therefore, it is important to consider those patients who are not appearing on our telemedicine platform, as they are the patients who need our assistance now more than ever.

Disclosure: Ms. Pierre has served as a consultant for BMS and on the advisory board for Pfizer, and owns stock in Roche.

Abstract 7007

FLT3 Inhibitor Crenolanib in Combination With Chemotherapy for Newly Diagnosed Patients With *FLT3*-Mutant AML

By The ASCO Post Staff

Visit https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.16_suppl.7007 to read the full abstract and view author disclosures.

Eunice Wang, MD, Chief of Leukemia at Roswell Park Comprehensive Cancer Center, and colleagues presented the long-term results of a phase II clinical trial combining crenolanib, a second-generation FLT3 inhibitor, with standard intensive chemotherapy for the treatment of adults with newly diagnosed *FLT3*-mutant acute myeloid leukemia (AML) at the 2022 ASCO Annual Meeting.

In this multicenter clinical trial, 44 patients with newly diagnosed *FLT3*-mutant AML received standard front-line induction chemotherapy with cytarabine for 7 days and daunorubicin or idarubicin for 3 days. Starting on day 9, crenolanib, which is an active inhibitor of *FLT3*-ITD, TKD, and variant AML mutations, was administered three times per day until 3 days before the next chemotherapy treatment. Most patients (75%) had *FLT3*-ITD mutations, eight patients (18%) had TKD mutations, and three patients (7%) had both ITD and TKD mutations.

After one treatment cycle, 73% of patients experienced clinical responses, and 86% of patients responded to treatment after two cycles. Better responses were noted in younger patients (≤ 60 years) and those with *FLT3*-ITD mutations.

The most common treatment-related adverse events were diarrhea, nausea, and febrile neutropenia, and six patients required crenolanib dose reduction during treatment. Approximately 15% of patients experienced disease relapse, but mutational analysis in these patients showed clearance of multiple *FLT3* mutations and no new *FLT3* clones.

"Our results were highly promising, with more than 80% of patients who received the crenolanib chemotherapy combination achieving clinical responses after treatment, and more than half still alive after almost 4 years," said Dr. Wang, principal investigator of the clinical trial and senior author

of the study. "We believe that addition of this next-generation FLT3 inhibitor to conventional chemotherapy could significantly improve outcomes and become the new standard of care for patients with *FLT3*-mutant AML."

A larger, phase III clinical trial randomly assigning patients with newly diagnosed *FLT3*-mutant AML to receive either crenolanib or midostaurin is underway at 31 sites and currently enrolling patients.

The Advanced Practitioner Perspective

Meredith Beaton, MSN, RN
UCHealth Blood Disorders and Cell Therapies Center - Anschutz Medical Campus

Mutations in the FLT3 receptor are the most common genetic mutation in AML and are seen in approximately one third of newly diagnosed AML patients. *FLT3* mutations are associated with increased relapse and poor overall survival.

In the past 5 years, type I FLT3 inhibitors such as gilteritinib (Xospata) and midostaurin (Rydapt) have been incorporated into standard-of-care therapy when treating patients with *FLT3*-mutated AML with specific activity against *FLT3*-ITD and -TKD mutations. Crenolanib is a second-generation type I FLT3 inhibitor that has shown promise when used in combination with standard 7+3 induction and consolidation chemotherapy. In particular, crenolanib is more specific than the first-generation FLT3 inhibitor midostaurin and appears to be effective against *FLT3*-ITD and -TKD mutations that develop resistance to midostaurin.

Long-term outcomes of this phase II clinical trial with crenolanib and standard 7+3 induction and consolidation in adults with *FLT3*-mutated AML demonstrated high response rates (composite complete remission: 86%) with cumulative incidence of relapse of 15% and mutational analysis demonstrating clearance of multiple *FLT3* variant mutations and no new FLT3 clones.

This phase II trial is particularly important for advanced practitioners, as crenolanib appears to be a more targeted FLT3 therapy that is better tolerated than other FLT3 inhibitors. The most common side effects were diarrhea (66%), nausea (57%), and febrile neutropenia (52%). Additionally, for patients at risk of QTc prolongation for whom midostaurin may not be a viable option, crenolanib showed no QTc prolongation in this study. Lastly, crenolanib may be an alternative for patients with midostaurin resistance.

While this trial seems promising so far, we look forward to the results of the ongoing phase III head-to-head comparison of midostaurin and crenolanib in conjunction with standard chemotherapy when used in both front-line and relapsed *FLT3*-mutated AML.

Disclosure: Ms. Beaton has no conflicts of interest to disclose.

Abstract 7050

Treatment-Free Remission in Patients With Chronic Myeloid Leukemia After Discontinuing Tyrosine Kinase Inhibitors

By JADPRO Staff

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Tyrosine kinase inhibitor (TKI) discontinuation in patients with chronic myeloid leukemia (CML) is increasingly considered. Researchers at the 2022 ASCO Annual Meeting presented results on outcomes of patients with CML who discontinued TKIs and determined the factors associated with differences in the rates of treatment-free remission (TFR).

Methods

Data from 284 patients with CML treated with TKIs at the investigators' institution between October 1999 and February 2017 and who subsequently discontinued therapy were reviewed. Major molecular response (MMR) was defined as a BCR-ABL1/ABL1 transcripts ratio ≤ 0.1% as determined by real time (RT)-PCR, MR^4 as a ratio ≤ 0.01% IS, and $MR^{4.5}$ as a ratio ≤ 0.0032%. Treatment-free remission failure was defined as the loss of MMR on any single test. Treatment-free remission rates were analyzed according to duration and depth of response , and a multivariate analysis was conducted for factors associated with loss of MMR.

Results

199 patients (70%) had electively discontinued their TKI, while 70 patients (24%) stopped therapy because of adverse events. 92 patients (32%) had switched ≥ 1 TKI prior to discontinuation due to drug intolerance or resistance. The median time from the initiation of front-line TKI to discontinuation was 117 months. The median duration of MR^4 and $MR^{4.5}$ before TKI discontinuation was 74 months and 64 months, respectively. At a median follow-up of 36 months after TKI discontinuation, 53 patients (19%) lost MMR, translating into a 5-year TFR rate of 79%. 50 patients (94%) resumed TKI therapy and, among 47 evaluable patients, all but one patient regained MMR, with 41 patients (88%) achieving $MR^{4.5}$. The estimated 5-year TFR rates were 91%, 76%, and 70% in patients achieving $MR^{4.5}$ for ≥ 6 years, between 5 and 6 years, and < 5 years, respectively. The estimated 5-year TFR rates were higher with MR^4 and $MR^{4.5}$ ≥ 5 years, compared with MR^4 < 5 years (87% vs. 92% vs. 64%). Patients who remained on their front-line TKI at the time of discontinuation had a 5-year TFR rate of 82%, compared with 75% and 72% among patients who switched to a second-line TKI or beyond because of intolerance or resistance, respectively. Treatment-free remission rates did not vary according to the type of frontline TKI used. By multivariate analysis, only durations in MR^4 or $MR^{4.5}$ ≥ 5 years before stopping treatment were associated with a lower risk of loss of MMR, with hazard ratios of 0.37 and 0.20, respectively.

The impact of the frequency of molecular monitoring on the success rate of TFR was also evaluated. The estimated 5-year TFR rate was 79% for patients monitored monthly compared with 85% for patients monitored every 6 to 8 weeks following discontinuation.

Conclusions

The study findings suggest that achieving MR^4 for ≥ 5 years was associated with a very high probability of maintaining TFR, and that less frequent molecular monitoring could be more cost effective without any negative impact on outcomes.

The Advanced Practitioner Perspective

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Since the advent of tyrosine kinase inhibitors (TKIs), chronic myeloid leukemia (CML) has become a disease in which patients can enjoy a nearly normal life expectancy. The five TKIs used in clinical practice include imatinib (Gleevec), nilotinib (Tasigna), dasatinib (Sprycel), bosutinib (Bosulif), and ponatinib (Iclusig), with each having a distinct safety profile and indication given a patient's comorbidities. Despite excellent outcomes of each TKI, more than half of patients will fail first-line therapy due to resistance or intolerance. In general, the most common side effects of all TKIs are cytopenias, diarrhea, fatigue, rash, and liver damage. While some of these side effects can be mitigated by dose reduction or intermittent drug interruption, many patients continue to experience low-level side effects resulting in decreased quality of life.

This study of patient outcomes after TKI discontinuation is critical for advanced practitioners (APs), since APs are often managing these therapies for patients. Tyrosine kinase inhibitors are currently recommended as indefinite therapy for the treatment of CML. Based on this study, it appears that patients who were maintained on their TKI therapy longer (~5 years) with major molecular response (MMR) to their front-line or subsequent therapy had a very high probability of maintaining a 5-year treatment-free response after discontinuation of their TKI.

Additionally, of those patients who discontinued therapy, lost MMR, and were subsequently restarted on a TKI, there was a high probability of regaining MMR. Implications for APs managing TKIs are vast, including the ability to discontinue therapy for patients with MMR after 5 years, with the potential for molecular monitoring every 6 to 8 weeks. The potential for patients to experience higher quality of life due to decreased side effects after discontinuation of therapy cannot be overstated and should play a role in how APs determine the duration of therapy and monitoring for CML patients.

Disclosure: Ms. Beaton has no conflicts of interest to disclose.

Abstract 7500

New Data Show Benefit of Glofitamab for the Treatment of R/R DLBCL

By JADPRO Staff

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Glofitamab, an investigational CD20xCD3 T-cell engaging bispecific antibody, yields durable complete remission in heavily pretreated patients with diffuse large B-cell lymphoma (DLBCL). Results of the phase II NP30179 study were presented at the 2022 ASCO Annual Meeting.

Diffuse large B-cell lymphoma is an aggressive form of lymphoma, where as many as 40% of patients will relapse, at which point treatment options are limited and survival is shortened. In a phase I/II study, escalating glofitamab doses were highly active and well tolerated in patients with relapsed/refractory B-cell lymphomas, with obinutuzumab pretreatment and cycle 1 step-up dosing providing effective cytokine release syndrome (CRS) mitigation.

Study Design

All patients had DLBCL and had received ≥ 2 prior regimens, including ≥ 1 anti-CD20 antibody and ≥ 1 anthracycline. Intravenous obinutuzumab pretreatment 1,000 mg was given 7 days before the first glofitamab dose. Intravenous glofitamab was then given as step-up doses on day 1 (2.5 mg) and day 8 (10 mg) of cycle 1 and at the target dose (30 mg) on day 1 of cycles 2 to 12 (21-day cycles). The primary endpoint was complete response (CR) rate. Cytokine release syndrome was assessed using American Society for Transplantation and Cellular Therapy (ASTCT) criteria.

Pivotal Results

107 patients received ≥ 1 dose of study treatment. Median prior therapies was 3; 59% had ≥ 3 prior therapies and 35% had received prior CAR T cells. Most patients were refractory to a prior CD20 antibody-containing regimen (85%) and to their most recent regimen (85%). Many were refractory to their initial therapy (59%) and to prior CAR T-cell therapy (32%).

After a median follow-up of 9 months (0.1–16), overall response rate (ORR) and CR rates were 50.0% and 35.2%, respectively. Complete response rates were consistent in patients with and without prior CAR T-cell therapy (32% vs. 37%). Median time to CR was 42 days. The majority of CRs (33/38; 87%) were ongoing at data cut. An estimated 84% of complete responders and 61% of responders remained in response at 9 months. At data cut, the projected 12-month overall survival rate was 48%, and 92% of complete responders were alive. These results are consistent with earlier phase I data in 100 patients treated with target glofitamab doses ≥ 10 mg.

Cytokine release syndrome occurred in 68% of patients, was primarily associated with the initial doses, and was mostly grade 1 (51%) or grade 2 (12%); grade 3 (3%) and grade 4 (2%) events were uncommon. All but 2 CRS events were resolved at data cut. Glofitamab-related neurologic adverse events potentially consistent with immune effector cell-associated neurotoxicity syndrome occurred in 3 patients (all grade 1–2). Glofitamab-related adverse events leading to discontinuation were uncommon (3 patients, 3%).

The Advanced Practitioner Perspective

Pamela Lee, NP, MSN
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As CAR T-cell therapy becomes the standard of care for relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) patients, this study reminds us that there are other advances in immuno-oncology advanced practitioners should consider, specifically bispecific T-cell engager (BiTE) therapies such as glofitamab.

BiTE therapies offer a dual-pronged approach to treating cancers, unlike traditional antibody drugs that treat a specific antigen. They engage two disease targets, thus amplifying the effects of cancer treatment. In this case, glofitamab targets CD3 and CD20, two common DLBCL markers.

In this trial of 107 patients with a median of three prior lines of treatment, glofitamab was shown as a viable option with a manageable treatment regimen and favorable complete response (CR) and overall response. The schedule is enticing. After the first cycle, patients receive glofitamab once every 21 days, which is less time-intensive than other R/R therapy options.

The study results are remarkable. At the median 9 month follow-up, similar CR rates were found in those who had and had not received prior CAR T-cell therapy, at 32% and 37% respectively, thus raising the question if glofitamab should be considered prior to recommending someone for CAR T-cell therapy. Moreover, an estimated 84% of those who reached CR and 61% of responders were still alive at the 9-month mark.

Finally, the safety profile is reassuring, with cytokine release syndrome occurring primarily in cycle 1 and usually grade 1. Neurotoxicity-related events were very rare, and this study had no fatalities, affirming the safety for even the most risk-averse patients. Glofitamab appears to be a promising immunotherapy consideration for the R/R DLBCL patients.

Disclosure: Ms. Lee has no conflicts of interest to disclose.

Abstract 7518

Brexucabtagene Autoleucel in Relapsed or Refractory Mantle Cell Lymphoma: 3-Year Follow-up of ZUMA-2 Trial

By JADPRO Staff

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In an analysis presented at the 2022 ASCO Annual Meeting, Michael Wang, MD, and colleagues provided data from the 3-year follow-up of the pivotal ZUMA-2 trial of the chimeric antigen receptor (CAR) T-cell therapy brexucabtagene autoleucel in patients with relapsed or refractory mantle cell lymphoma.

Study Details

In the trial, 74 patients with a range of one to five prior therapies, including a BTK inhibitor, were enrolled and leukapheresed. Brexucabtagene autoleucel was successfully manufactured for 71, and 68 received a single infusion of 2×10^6 CAR T cells/kg.

Key Findings

During a median follow-up of 35.6 months, the objective response rate among all 68 treated patients was 91%, with complete response in 68%. Median duration of response was 28.2 months. A total of 25 patients converted to complete response after initial partial response or stable disease. At data cutoff, responses (all complete responses) were ongoing in 37% of treated patients. Median progression-free survival was 25.8 months, and median overall survival was 46.6 months.

Post hoc analyses indicated that objective response rates and ongoing response rates were consistent among prespecified subgroups by prior BTK inhibitor exposure or high-risk characteristics. For example, responses were ongoing at data cutoff in 41% of patients with prior ibrutinib exposure and in 44% with prior acalabrutinib exposure; in 33% to 44% of patients with Ki-67 proliferation index values of < 30% to ≥ 50%; and in 27% of those with disease progression < 24 months after initial diagnosis.

A total of 37 patients received prior bendamustine and 31 did not. Objective response was observed in 84% vs. 100% and responses persisted at data cutoff in 29% vs. 48%. An exploratory analysis showed that patients who received bendamustine within 6 months of apheresis had lower peak CAR T-cell levels after infusion than those with bendamustine treatment at > 6 months prior to apheresis or patients who did not receive bendamustine.

Late-onset toxicities were uncommon, with only 3% of treatment-emergent adverse events of interest occurring during long-term follow-up.

The authors concluded, "These data, representing the longest follow-up of CAR T-cell therapy in patients with mantle cell lymphoma to date, suggest that brexucabtagene autoleucel induced durable long-term responses with manageable safety in patients with R/R mantle cell lymphoma and may also benefit those with high-risk characteristics."

The Advanced Practitioner Perspective

Pamela Lee, NP, MSN
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CAR T-cell therapy is quickly becoming the standard treatment for many relapsed/refractory malignant hematology patients. This trial provides both validation and hope that this therapy can and will be a cure for patients previously thought incurable, such as those with mantle cell lymphoma.

As the longest follow-up trial of CAR T-cell therapy, the ZUMA-2 trial proves that these patients can obtain the coveted complete response (CR). Out of 68 patients who received CAR T-cell therapy, 68% of them achieved a sustained CR at the median 35.6-month follow-up mark regardless of their BTK inhibitor use and high-risk disease status. Moreover, bendamustine seemed to put these patients at a disadvantage, raising questions of when CAR T-cell therapy should be introduced for these patients.

This study substantiates the promise of immuno-oncology. It is imperative for advanced practitioners to consider this therapy, as it offers this lymphoma subpopulation a chance of a cure that was previously unattainable. Advanced practitioners will need to educate patients on the CAR T-cell process and potential risks of the therapy, including cytokine release syndrome, neurotoxicity, and prolonged immunosuppression. This study fortunately showed late-onset CAR T-cell therapy–related toxicities are rare.

Disclosure: Ms. Lee has no conflicts of interest to disclose.

Abstract 7519

Fixed-Duration Ibrutinib/Venetoclax Continues to Show Durable Response in Previously Untreated Patients With CLL

By JADPRO Staff

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The 3-year follow-up results for the phase II CAPTIVATE study show that fixed duration of ibrutinib and venetoclax continues to provide durable responses with no new safety signals in previously untreated patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

William G. Wierda, MD, PhD, of The Ohio State University, Columbus, and colleagues presented their update at the 2022 ASCO Annual Meeting. The authors commented, "Fixed duration ibrutinib and venetoclax continues to provide deep, durable responses and clinically meaningful progression-free survival, including in patients with high-risk disease features, representing an all-oral, once-daily, chemotherapy-free fixed duration regimen for previously untreated patients with CLL/SLL."

Study Findings

The trial enrolled a total of 159 patients, aged 70 and older, with previously untreated CLL. Participants received 3 cycles of ibrutinib followed by 12 cycles of ibrutinib plus venetoclax. Undetectable measurable residual disease (MRD) was measured by flow cytometry. Ibrutinib-related serious adverse events reported more than 30 days after the last doses were collected.

Among the patients enrolled, there were those with high-risk features of del(17p) or *TP53* mutation (17%), unmutated *IGHV* (56%), and complex karyotype (19%). 147 (92%) and 149 (94%) patients completed treatment with ibrutinib and venetoclax, respectively.

The median time on study was 39 months. The objective response rate was 96%. The rate of complete response rose from 55% to 57%, and 93% of these individuals had responses lasting at least 12 months after study treatment.

78% of evaluable patients maintained their undetectable MRD status through 12 months after treatment. Overall survival and progression-free survival rates at 36 months were 98% and 88%, respectively, with similar rates seen in patients with high-risk features. A total of 12 patients were retreated in January 2022 with single-agent ibrutinib. Seven experienced a partial response, and two had stable disease.

The Advanced Practitioner Perspective

Amber Koehler, PA-C
Mayo Clinic Cancer Center

One current area of interest in chronic lymphocytic leukemia (CLL) is the use of combination therapies, particularly the combination of Bruton tyrosine kinase (BTK) inhibitors and BCL2 inhibitors with or without a monoclonal anti-CD20 antibody. BTK inhibitors have been approved in the front-line setting for several years, and have historically been given as an indefinite therapy, which has several implications in terms of cost, drug-drug interactions, and ongoing potential for adverse events over time.

The fixed duration cohort of ibrutinib (Imbruvica) and venetoclax (Venclexta) from the phase II CAPTIVATE study demonstrates high overall response rates with a 3-year PFS of 88%. Importantly, both PFS and overall survival were not significantly different in subgroup analyses of higher-risk patient groups, such as those with deletion 17p or *TP53* disruption, or those with unmutated *IGHV,* compared with the entire cohort.

Side effects were consistent with known adverse event profiles of both ibrutinib and venetoclax and were manageable; 92% and 94% of individuals completed treatment with ibrutinib and venetoclax, respectively.

In this cohort of the CAPTIVATE study, the disease debulking that occurs from the 3-month lead-in with ibrutinib prior to initiation of venetoclax results in a decreased risk of tumor lysis syndrome (TLS). Decreased risk for TLS results in a greater number of patients who can be monitored in the outpatient setting with adequate oral hydration during the weekly venetoclax dose escalation, as opposed to requiring hospitalization for inpatient monitoring. Coupled with being an all-oral, chemotherapy-free regimen, fixed duration ibrutinib plus venetoclax has several logistical benefits and represents an effective treatment option for patients with CLL, including those with high-risk features.

Disclosure: Ms. Koehler has served on advisory boards for AbbVie, AstraZeneca, and Pharmacyclics.

Abstract 7539

5-Year Follow-Up of ELEVATE-TN: Obinutuzumab-Based Regimens for CLL

By JADPRO Staff

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A 5-year follow-up of the ELEVATE-TN trial showed that acalabrutinib and obinutuzumab are still superior to obinutuzumab and chlorambucil in treatment-niave chronic lymphocytic leukemia (CLL). Jeff Porter Sharman, MD, of US Oncology Network, Woodlands, Texas, and colleagues presented these results at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting.

The 5-year follow-up study randomly assigned patients to receive acalabrutinib plus obinutuzumab, acalabrutinib monotherapy, or obinutuzumab plus chlorambucil. Patients whose disease progressed on obinutuzumab/chlorambucil treatment could cross over to acalabrutinib monotherapy.

Study Findings

The study included 535 patients: 179 received acalabrutinib/obinutuzumab, 179 received acalabrutinib monotherapy, and 177 received obinutuzumab/chlorambucil. The median age of patients was 70.

The median progression-free survival was not reached for acalabrutinib/obinutuzumab or acalabrutinib at 58.2 months of follow-up. The estimated 60-month progression-free survival rates were 84% for acalabrutinib/obinutuzumab, 72% for acalabrutinib monotherapy, and 21% for obinutuzumab/chlorambucil. The median overall survival was not reached in any treatment arm. However, the overall survival rate was significantly longer with acalabrutinib/obinutuzumab than with obinutuzumab/chlorambucil. The estimated 60-month overall survival rates were 90% with acalabrutinib/obinutuzumab, 84% with acalabrutinib monotherapy, and 82% with obinutuzumab/chlorambucil. The overall response rate was significantly higher with acalabrutinib/obinutuzumab and acalabrutinib monotherapy than with obinutuzumab/chlorambucil. The complete response/complete response with incomplete hematologic recovery rates were higher with acalabrutinib/

obinutuzumab (29%/3%) vs. obinutuzumab/chlorambucil (13%/1%).

Treatment was ongoing in 65% of patients given acalabrutinib/obinutuzumab and 60% of patients given acalabrutinib. The most common reasons for treatment discontinuation were adverse events (17% [acalabrutinib/obinutuzumab], 16% [acalabrutinib monotherapy], 14% [obinutuzumab/chlorambucil]) and progressive disease (6%, 10%, 2%, respectively). Crossover from obinutuzumab/chlorambucil to acalabrutinib treatment occurred in 72 patients (41%). Of the 72 patients, 25% discontinued treatment with acalabrutinib.

The Advanced Practitioner Perspective

Amber Koehler, PA-C
Mayo Clinic Cancer Center

The choice of Bruton tyrosine kinase (BTK) inhibitor is a hot topic in chronic lymphocytic leukemia (CLL). The 5-year follow-up data from the ELEVATE-TN trial continues to demonstrate superiority of both acalabrutinib (Calquence) monotherapy and acalabrutinib plus obinutuzumab (Gazyva) compared with chlorambucil plus obinutuzumab as front-line treatment for CLL both in terms of overall response rate (ORR) and progression-free survival (PFS). Estimated 60-month PFS for patients with CLL treated with acalabrutinib and obinutuzumab in the front-line setting was 84% compared with 72% with acalabrutinib monotherapy; however, this study was not powered to detect a statistically significant difference between these two arms.

Side effects of acalabrutinib were similar to several prior studies, with the unique side effect of headache in approximately 40% of patients. Clinically, these headaches are usually manageable with hydration and caffeine, and typically resolve after the first several weeks. The most common adverse event of any grade in either the acalabrutinib or acalabrutinib plus obinutuzumab arm was bleeding, underscoring the importance of ensuring BTK inhibitors such as acalabrutinib are held before and after any planned procedures such as endoscopies or surgeries.

Another important observation is lower reported rates of hypertension and atrial fibrillation compared with previous studies with acalabrutinib's predecessor, the first-generation BTK inhibitor ibrutinib. Head-to-head data comparing acalabrutinib with ibrutinib in the relapsed setting is summarized in the ELEVATE-RR trial, the counterpart of ELEVATE-TN. Median PFS has not yet been reached with either the acalabrutinib plus obinutuzumab or acalabrutinib monotherapy arm at 5 years, indicating ongoing durable responses with acalabrutinib-based therapies in the front-line setting for patients with CLL.

Disclosure: Ms. Koehler has served on advisory boards for AbbVie, AstraZeneca, and Pharmacyclics.

Abstract 7571

Axicabtagene Ciloleucel in Real-World Study Is Effective Regardless of Race or Ethnicity

By JADPRO Staff

Visit https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.16_suppl.7571 to read the full abstract and view author disclosures.

Axicabtagene ciloleucel (axi-cel) showed favorable overall survival (OS), progression-free survival (PFS), and safety profile regardless of race and ethnicity in the real-world setting, according to findings presented at the 2022 ASCO Annual Meeting.

Study Details

Investigators examined outcomes by race and ethnicity among patients with large B-cell lymphoma (LBCL) who received axi-cel in the real-world setting. A total of 1,389 patients with LBCL were identified from a non-interventional safety study with patients receiving commercial axi-cel. Race (African American or Asian vs. White) and ethnicity (Hispanic vs. non-Hispanic) were self-reported. Patients who rescinded consent, enrolled in trials, had prior non–hematopoietic cell transplantation (HCT) cellular therapy, primary CNS lymphoma, unknown comorbidity, or data in query were excluded. The median follow-up was 12.7 months. Outcomes included overall response rate (ORR), complete response rate, duration of

response (DOR), PFS, OS, grade ≥ 3 cytokine release syndrome (CRS; Lee 2014 criteria), and immune effector cell-associated neurotoxicity syndrome (ICANS; ASTCT consensus grade).

Study Results

Among all patients, 1,127 (81%) were White, 70 (5%) African American, and 81 (6%) Asian. 152 patients (11%) were Hispanic, including 104 White, 2 Black, and 1 Asian Hispanic patients. African Americans compared with White patients were younger (median age 55.5 vs. 62.8 years), more likely to have pulmonary impairment (41% vs. 28%), and tended to have longer time from diagnosis (≥ 12 months 71% vs. 59%). Hispanic patients were younger (median age 58.5 vs. 62.6 years) than non-Hispanic patients.

Overall response rate was 74% (CR 57%, 12-month PFS and OS 48% and 63%) for White, 57% (CR 45%, 12-month PFS and OS 36% and 62%) for African American, 67% (CR 53%, 12-month PFS and OS 55% and 65%) for Asian, and 73% (CR 55%, 12-month PFS and OS 50% and 65%) for Hispanic patients. Grade ≥ 3 CRS and ICANS occurred in 7% and 18% of African American, 10% and 19% of Asian, and 8% and 27% of White patients, respectively. Hispanic patients had lower rates of grade ≥ 3 CRS and ICANS (4% and 15%) vs. non-Hispanic (9% and 27%). African American race was associated with inferior ORR (OR 0.40) and CR rate (OR 0.55) compared with White. Asian patients had favorable DOR compared to both White (HR 0.46) and African American (HR 0.39). No statistical differences were found in OS and PFS across races, nor in any efficacy outcome between Hispanic and non-Hispanic patients. Asian (OR 0.52 vs. White) and Hispanic patients (OR 0.51 vs. non-Hispanic) had lower risk of grade ≥ 3 ICANS.

The investigators commented, "Overall, axicel showed favorable OS, PFS, and safety profile regardless of race and ethnicity in the real-world setting. No notable differences in outcomes were observed for Hispanic or Asian patients." They added that lower response rates in African American patients noted in the study warrant further investigation, including any underrepresentation not explained by a lower incidence rate for LBCL (SEER), access to care, and disease burden.

The Advanced Practitioner Perspective

Amy Pierre, MSN, ANP-BC
Memorial Sloan Kettering Cancer Center and Flatiron Health

Chimeric antigen receptor (CAR) T-cell therapy has allowed patients to fight cancer with their own immune system. Access can only be obtained at certified cellular therapy centers and therefore is limited to those who are 1) eligible for the therapy 2) able to reach these certified centers. For those who have been able to obtain these therapies on clinical trial or as standard of care, it has been encouraging seeing such high response rates in patients who are heavily pretreated. However, it is unclear if these response rates and outcomes are equal across all patients.

This study examined the outcomes by race and ethnicity of 1,389 patients diagnosed with large B-cell lymphoma who received CAR T-cell therapy and found that African American patients had an increased length in time of diagnosis to receipt of CAR T-cell therapy and the lowest response rate compared with all other racial groups. However, African Americans had a lower rate of toxicity related to CAR T-cell therapy (high-grade cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome). Hispanic patients were younger and had lower rates of toxicity related to CAR T-cell therapy compared with non-Hispanic patients. Interestingly enough, despite these disparities, there was no statistical difference in overall survival or progression-free survival across different racial or ethnic groups.

One aspect of this study is that 5% of patients were African American, showing that there is clear inequity in the access to CAR T-cell therapy by race. As providers in oncology, it is important for us to understand why there are differing response rates across racial and ethnic groups: Is this a consequence of biological differences or a result of inequities stemming from a variety of complex socioeconomic factors? Further studies are warranted to understand existing modifiable risk factors that can be alleviated to allow optimal response rates and decreased toxicity for all patients at risk.

Disclosure: Ms. Pierre has served as a consultant for BMS and on the advisory board for Pfizer, and owns stock in Roche.

Abstract 8028

Ciltacabtagene Autoleucel in Relapsed or Refractory Multiple Myeloma: 2-Year Follow-up of CARTITUDE-1 Trial

By Matthew Stenger

Visit https://ascopubs.org/doi/abs/10.1200/JCO.2022.40.16_suppl.8028 to read the full abstract and view author disclosures.

In an analysis presented at the 2022 ASCO Annual Meeting, Thomas Martin, MD, and colleagues provided data from the 2-year follow-up of the pivotal CARTITUDE-1 trial of the anti–B-cell maturation agent (BCMA) chimeric antigen receptor (CAR) T-cell therapy ciltacabtagene autoleucel in relapsed or refractory multiple myeloma.

Study Details

Eligible patients had received three or more prior lines of therapy or were double-refractory to a proteasome inhibitor and immunomodulatory drug and had received a prior proteasome inhibitor, immunomodulatory drug, and anti-CD38 therapy. A total of 113 patients were enrolled and underwent apheresis and 111 underwent lymphodepletion; of these, 97 patients received a single dose of ciltacabtagene autoleucel in the target range of 0.5 to 1.0 × 10^6 CAR T cells/kg (median = 0.71 × 10^6 cells/kg). Treated patients had received a median of six prior lines of therapy. The current analysis occurred 2 years after treatment of the last treated patient enrolled.

Key Findings

Over a median follow-up of 27.7 months in 97 treated patients, the overall response rate was 97.9%, including stringent complete response in 82.5%. No complete responses other then stringent complete response were observed; rates were 12.4% for very good partial response and 3.1% for partial response. Responses deepened over follow-up; for example, the stringent complete response rate improved from 67% at the primary publication at median follow-up of 12 months to 82.5% in the current analysis. The median duration of response was not estimable.

Overall response rates were high across subgroups examined (95.1%–100%), including patients receiving three prior lines of therapy (100%) and those with high-risk cytogenetics (100%), high tumor burden (≥ 60% bone marrow plasma cells; 95.2%), or plasmacytomas (100%).

Median durations of response were shorter among patients with high-risk cytogenetics (22.2 months), International Staging System (ISS) stage III disease (23.1 months), high tumor burden (23.1 months in those with ≥ 60% bone marrow plasma cells), or plasmacytomas (12.9 months).

Median progression-free survival was not reached, with 27-month rates of 54.9% among all patients and 64.2% among those with stringent complete response. Median overall survival was not reached, with a 27-month rate of 70.4%. Patients with ISS stage III disease, high-risk cytogenetics, high tumor burden, and plasmacytomas had lower progression-free and overall survival rates.

Since the primary publication at a median follow-up of 12 months, no new cases of cytokine release syndrome were observed. One new case of parkinsonism was reported at day 914 after infusion (bringing the total to six cases observed among treated patients).

The investigators concluded, "At approximately 28 months median follow-up, patients treated with ciltacabtagene autoleucel maintained deep and durable responses, observed in both standard and high-risk subgroups. The risk/benefit profile of ciltacabtagene autoleucel remained favorable with longer follow-up."

The Advanced Practitioner Perspective

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Despite the ever-widening armamentarium of novel therapies, myeloma is still considered an incurable disease and invariably relapses or becomes refractory to treatment. Patients with relapsed/refractory myeloma have poor outcomes with median overall survival ranging from approximately 8 to 12 months. Recent US Food and Drug Administration (FDA) approvals of selinexor (Xpovio) and belantamab mafodotin (Blenrep) are certainly beneficial in this setting; however, the response rates were 25% and 38% and median progression-free survival was 15 months and 17 months, respectively.

Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the management of relapsed/refractory myeloma as it had done previously with various subtypes of lymphoma as well as acute lymphoblastic leukemia.

The 2-year follow-up of the CARTITUDE-1 trial continues to demonstrate unprecedented outcomes for relapsed/refractory myeloma treated with a single infusion of ciltacabtagene autoleucel (cilta-cel). Although study patients had received a median of six prior lines of therapy and many were triple-class refractory, impressively, the overall response rate improved to 97.9% between years 1 and 2, and 82.5% achieved a stringent complete remission. Median progression free and overall survival were not reached. No additional toxicities were noted in the updated data.

Advanced practitioners caring for myeloma patients can expect to be asked questions about cilta-cel, which is why knowing about the updated CARTITUDE-1 trial data is valuable. With the recent FDA approval of cilta-cel, this CAR T-cell therapy is not only available to myeloma patients on clinical trial, but also as a standard-of-care treatment. However, due to lentivirus shortages (an essential part of CAR T-cell manufacturing), availability is limited. As such, off-the-shelf options such as anti-BCMA bispecific antibodies are eagerly awaited in the myeloma community.

Disclosure: Mr. Allred has no conflicts of interest to disclose.