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Lymphoma (JL Muñoz, Section Editor)

Is There Still a Role for Transplant for Patients with Mantle Cell Lymphoma (MCL) in the Era of CAR-T Cell Therapy?

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Opinion statement

For years, upfront autologous hematopoietic cell transplant (auto-HCT) has been the standard of care for younger and physically fit mantle cell lymphoma (MCL) patients after chemoimmunotherapy (CIT) induction. Bruton's tyrosine kinase (BTK) inhibitors have proven to be excellent salvage therapies, but their durability remains a question, especially in high-risk (HR) MCL. Allogeneic HCT (allo-HCT) was the only option for long-term remission and possibly cure for MCL relapse after auto-HCT and sometime as upfront consolidation for a young patient with HR MCL (debatable). We have seen a paradigm shift since the FDA approval in July 2020 of the brexucabtagene autoleucel chimeric

antigen receptor T (CAR-T) cell therapy for relapsed and refractory (R/R) MCL with an preliminary evidence suggesting CAR-T may overcome known biological risk factors in MCL. Given its safety profile and excellent efficacy, the role of CAR-T among other approved therapies and HCT may need to be better defined. Based on the current evidence, auto-HCT remains a standard frontline consolidation therapy. CAR-T therapy is a preferred option for patients with relapsed/refractory (R/R) MCL, particularly those who failed BTK inhibitors. In certain high-risk MCL patients (such as high ki 67, TP53 alterations, complex karyotype, blastoid morphology, early relapse after initial diagnosis), CAR-T cell therapy may be considered before BTK inhibitors (preferably on a clinical trial). The role of allo-HCT is unclear in the CAR-T era, but remains a viable option for eligible patients who have no access or who have failed CAR-T therapy. Our review discusses current standards and the shifting paradigms in the indications for HCT and the role of CAR-T cell therapy for MCL. Prospective studies tailored based on risk factors are needed to better define the optimal sequences of HCT and cellular therapy and other approved novel therapies.

Introduction

Mantle cell lymphoma (MCL) is a distinct subtype of mature B-cell non-Hodgkin lymphoma, accounting for approximately 6–8% of all NHLs [1, 2]. The molecular hallmark in >95% of cases is the t(11;14)(q13;q32) translocation between an *IGH* gene and *CCND1*, resulting in overexpression of cyclin D1 [3]. MCL most commonly presents in the seventh decade of life, with a median age at onset of 68–71 years in most studies. While the clinical presentation is widely variable, MCL is characterized overall by a remitting-relapsing course and a generally poor prognosis. The median overall survival (OS) is approximately 5–6 years, but significant variability in outcomes exists which relates to several known prognostic factors and to patient eligibility for intense therapies, including transplant [1, 4].

For the majority of patients, first-line therapy for MCL involves induction with chemoimmunotherapy (CIT), typically consisting of cytarabine-based regimen, an anti-CD20 monoclonal antibody (e.g., rituximab), and either CHOP or bendamustine. Eligible patients with complete response (CR) or partial response (PR) after initial CIT are typically offered upfront consolidation with autologous hematopoietic cell transplantation (auto-HCT). Maintenance therapy with rituximab after auto-HCT improved both PFS and OS in the LyMa phase 3 clinical trial conducted by The Lymphoma Study Alliance (LYSA) group, and is considered now a standard approach after transplant [5]. However, despite the high initial efficacy rates, majority of patients inevitably relapse, requiring subsequent therapies. Using a Bruton's tyrosine kinase (BTK) inhibitor-based regimen is a preferred second-line treatment, but there remains great variability on the optimum regimen selection based on availability of clinical trials. In the relapsed setting, allogeneic HCT (allo-HCT) has traditionally been considered as a preferred second-line consolidation treatment with curative potential for eligible patients [4]. While allo-HCT represents a potentially curative option for a small subset of MCL cases, it is not without significant potential short- and long-term complications. With the approval of chimeric antigen receptor T (CAR-T) cell therapies in MCL, the question becomes: is there still a role for transplant in MCL, and if so, at what point in the relapsing-remitting course of R/R MCL is CAR-T vs. transplant best positioned?

High-risk MCL

Several factors are known to define a subgroup of patients with MCL who have high-risk disease at increased risk of early relapse and inferior OS. The simplified

Mantle Cell International Prognostic Index (MIPI), which incorporates age, performance status, lactate dehydrogenase, and white blood cell count, is a valid prognostic score for MCL, subdividing patients into three prognostic risk groups with significantly worse OS at 5 years for patients with high-risk MIPI. However, the MIPI did not account for other important risk factors such as cytology (blastoid/pleomorphic morphology), Ki-67 expression, and the presence of *TP53* mutations/alterations, among others, which have also been associated with aggressive disease and inferior survival, independent of the MIPI score. Several attempts are made to incorporate some of these prognostic factors into the MIPI to improve its prognostic value. The combined MIPI (MIPI-c) score, incorporating the Ki-67 index, was developed which further classifies patients into four prognostic groups: low, low-intermediate, high-intermediate, or high-risk group, with median OS of 9.4, 4.9, 3.2, and 1.8 years, respectively [6, 7].

However, the management of patients with MCL was not tailored based on the MIPI risk group or other risk factors. Over recent years, we learned that certain biological and clinical features predict worse outcomes with CIT with or without auto-HCT and BTK inhibitors, including *TP53* alteration, pleomorphic or blastoid histology, and complex karyotype. Blastoid/pleomorphic variants (vs. classic MCL) are seen in 10–20% of cases and have been associated with an aggressive course and worse clinical outcomes and are commonly associated with *TP53* alteration [7, 8]. TP53 (tumor protein 53) alterations in MCL are associated with aggressive course and poor response to conventional chemotherapy [8–10]. Complex karyotype (CK), defined by more than three chromosomal aberrations, appears to be independently associated with inferior outcomes in patients with MCL regardless of the intensity of induction therapy [11]. Karyotype and *TP53* mutation analyses are not routinely done in community practices and might need to be incorporated into the workup of a new diagnosis of MCL, and novel therapeutic approaches should be investigated for those patients. Lastly, progression within 24 months of diagnosis (POD24) was associated with worse clinical outcomes [12–14].

Understanding those biological and clinical risk factors will help us design risk-adapted treatment strategies for patients with MCL. Clinical outcomes for high-risk MCL patients with auto-HCT, allo-HCT, and CAR-T cell therapy will be discussed further in this review.

Auto-HCT in MCL

Auto-HCT remains the standard of care first-line consolidation therapy for patients with chemo-sensitive MCL (CR or PR) following initial chemoimmunotherapy (CIT) induction therapy, especially in patients younger than 65–70 years old. Several studies showed improved outcomes through intensification of first-line therapies for MCL including frontline consolidation with auto-HCT. One of the earliest pivotal studies was the randomized phase 3 clinical trial by the European Mantle Cell Lymphoma Network which showed a clear improvement in PFS with auto-HCT consolidation compared to interferon-alpha (IFN-alpha) maintenance. Patients in this study received CHOP-like induction therapies ± rituximab with 3-year PFS rates of 54% and 25% in the auto-HCT and IFN groups, respectively (P = .0108). A long-term follow-up of the European

MCL study (median follow-up of 14 years) was recently reported confirming a superior PFS and OS with auto-HCT compared to IFN-alpha maintenance group (3.3 years and 7.5 years vs. 1.5 years and 4.8 years, respectively) [15, 16].

Across Nordic MCL1 and MCL2 studies, induction therapy was intensified by using augmented CHOP (maxi-CHOP) alternating with high-dose cytarabine and rituximab achieving very encouraging outcomes with 10-year PFS and OS of 43% and 58%, respectively [17]. A large registry study, which included 1029 newly diagnosed MCL patients treated at 25 North America academic centers, showed significantly improved PFS with auto-HCT and a trend for better OS [4]. In a more recent study, using the National Cancer Database and which included 10,290 patients with newly diagnosed MCL, auto-HCT was associated with improved 5-year OS in both younger and older patients compared to only chemotherapy [18]. The two most common induction therapies in the USA before auto-HCT for MCT include cytarabine-based regimens and rituximab in addition to either R-CHOP/maxi-R-CHOP (adopted from the Nordic experience) or rituximab and bendamustine with comparable overall results (no head to head comparison) [19]. Furthermore, the outcomes of upfront auto-HCT have improved by adding rituximab maintenance based on a randomized phase 3 LyMA trial involving 299 patients who were randomized to receive either rituximab maintenance therapy or only observation after auto-HCT, which showed rituximab maintenance prolonged PFS and OS with 4-year PFS of 83% versus 64% in the observation arm ($P<0.001$) and 4-year OS of 89% vs. 80% in the observation group ($P=0.04$) [5]. A phase III multicenter randomized Italian study showed 3 years PFS advantage for 2-year lenalidomide maintenance (104 patients randomized to lenalidomide and 101 patients to observation) after frontline auto-HCT; patients who received lenalidomide had 3-year PFS of 80% vs. 64% in the observation group (log-rank test $P=0 \cdot 012$; hazard ratio 0.51, 95% CI 0.30–0.87) [20]. Early on during SARS-CoV-2 pandemic, many clinicians were reluctant to initiate rituximab maintenance due to the concern of more complications and death from SARS-CoV-2 in patients who received rituximab [21] and the lower rate of serological response for COVID vaccination (between 0–14% vs. 46–55%) if patients received rituximab within 6–12 months [22, 23]. In fact, a survey conducted showed that up to 59% of lymphoma physicians across National Cancer Institute-designated cancer centers held rituximab during the pandemic and the majority elected to hold rituximab 4–6 months to allow COVID vaccination to be completed [24]. The hope with more patients being already vaccinated and less aggressive variants circulating, the maintenance therapy would be of a less concern moving forward.

There remains no consensus on a standardized high-dose conditioning (HDC) for transplant. BEAM is the most frequently used HDC regimen in the USA. However, a retrospective study combining data from two studies (Nordic MCL2 and HOVON-45) suggested TBI-based conditioning to be superior in young and fit patients with high-risk MCL compared to conditioning without TBI. Another research area of interest being explored in MCL is the role of minimal residual disease (MRD), not only for its prognostic value, but as a predictive marker for intensification of therapy after induction therapy. The ongoing ECOG EA4151 study is exploring the role of peripheral blood MRD after induction and at day +100 after auto-HCT; patients with residual disease (bone marrow biopsy or PET/CT scan) or detected MRD after induction

proceed with auto-HCT followed by rituximab maintenance, but patients with CR and undetected MRD are randomized to either auto-HCT + rituximab maintenance or rituximab maintenance only.

Auto-HCT and high-risk MCL

Despite that the early follow-up of the Second Nordic Mantle Cell Lymphoma trial (MCL2) suggested more than 60% event-free survival at 5 years for upfront auto-HCT, however, the 15-year follow-up of MCL2 showed no survival plateau, and patients continue to relapse even after 10 years from auto-HCT. PFS decreased from 66% in the 5-year follow-up to only 40% in the 15-year follow-up, and in the high-risk MIPI and MIPI-C groups, the PFS was only 25% [25]. Although 18 patients relapse after 5 years from auto-HCT, however, there were no high-risk patients relapsed beyond 8 years. Patients with blastoid morphology had a trend to inferior OS but not PFS. A retrospective study reviewed 483 patients who had CIT followed by auto-HCT from 5 academic US centers and found complex karyotype to be independent risk factor associated with shorter median PFS (1.9 years vs. 4.4 years) and OS (4.5 vs. 11.6 years) compared to patients with normal karyotype [11]. In a study of 183 younger patients with MCL from the Nordic MCL2 and MCL3 trials, *TP53* mutations (but not deletion) were associated with dismal outcomes with a median OS of 1.8 years, and 50% relapsed within 1 year [10]. In addition to TP53 mutations, MIPI-c high-risk had an independent prognostic impact on time to relapse. MRD (by PCR) positivity status predicts worse outcomes after auto-HCT. Following auto-HCT in the MCL-2 study, OS was 75% at 10 years and median not reached in the MRD-undetected group, compared with only 35 months in the MRD-detected group ($P < .0001$) [26]. Time to first relapse after first-line therapy is strongly predictive for long-term outcomes regardless of intensity of frontline therapy. In a retrospective study of 457 patients with relapsed MCL who had CIT with/without auto-HCT. The outcomes of patients (n=65) with early relapse within 6 months after first line and then treated with CIT/auto-HCT were poor with 2-year PFS of only 0.5 years (95% CI, 0.2–2.3) and OS of 1.1 years (95% CI, 0.5–NR) [27]. Therefore, salvage auto-HCT is not recommended as a preferred option for relapsed MCL patients except for a subgroup of patients who had long-term first remission [28]. Hence, there is a group of high-risk MCL patients who may not benefit from intensification of therapy with HDC and auto-HCT. These patients may potentially benefit from allo-HCT, and enrollment in clinical trials should be strongly encouraged. Auto-SCT is not without risks; although the treatment-related mortality is relatively low (<5%), survivors of auto-HCT have 7% long-term risk of MDS/AML, experience long-term complications, and have an excess late mortality risk when compared to the general population [29].

Allo-HCT and MCL

Allo-HCT has been explored in several studies (refer to Table 1) over the past 2 decades and has been the only option with potential cure in eligible MCL patients. The role of allo-HCT in MCL is supported by four non-randomized prospective clinical studies [30–33] and several retrospective and registry

Table 1. Summary of the allo-HCT in MCL studies

Author, year	*N*	Disease status	Conditioning	NRM	GVHD (acute/chronic)	Relapse	Disease-free survival	OS
Prospective								
Khouri et al., 2003	18	R/R	RIC/NMA	2/18	0%/NR	1/18	NR	82% (3 yrs)
Maris et al., 2004	33	R/R	NMA	24%	57%/64%	9%	60% (2 yrs)	65% (2 yrs)
Kruger et al., 2014	39	Frontline= 24 R/R =15	MAC/RIC	24%	57%	15%	67%	73%
Rule et al., 2019	25	Frontline	RIC/NMA	13%	38%/58%	21%	56%	76%
Retrospective								
Robinson et al. EBMT. 2018 [35]	324	Frontline 93 Salvage 231	RIC	24%	52%/41%	40% (5 yrs)	31% (5 yrs)	40% (5 yrs)
Hamadani et al., 2013 CIBMTR [44]	202	202 Mixed	MAC=74 RIC=128	47% 43%	MAC=36/35% RIC=37/43%	33% 32%	MAC=20% RIC=25% (3 yrs)	MAC=25% RIC =30% (3 yrs)
Fenske et al., 2014 [45]	138	Frontline 50 Salvage 88	RIC	17% 25%	NR	15% 38%	F=55% S=29%	25% 31% (5 yrs)
Kharfan-Dabaja et al., 2016*[46]	701	Mixed	MAC=138 RIC=507	MAC= 37% RIC=24%	MAC=36/35% RIC=31/42%	MAC=18% RIC=29%	MAC=34%% RIC 47%	MAC=40% RIC=53%

*Systemic review

studies [34, 35]. Allo-HCT is generally associated with notable reduction in relapse risk which is likely related to the strong graft-versus-lymphoma (GVL) effect, and hence the potential cure. However, the use of allo-HCT is limited to a small proportion of fit and younger patients with suitable donors given the substantial associated toxicity (such as graft-versus-host disease (GVHD) and infections) and increased early transplant-related mortality (TRM) [36–39]. However, there have been remarkable advancements in more recent years in supportive care measures (including prevention and treatment of infections and GVHD) and conditioning regimens for which morbidity and TRM continue to improve. For instance, given the known strong GVL effect, reduced-intensity conditioning (RIC) regimens were introduced and commonly used now with remarkable decreased toxicity and TRM compared to the traditional myeloablative conditioning (MAC). Comparisons of outcomes using RIC vs. MAC regimens for allo-HCT have revealed higher relapse rates but relatively lower NRM rates and slightly improved PFS and OS rates with RIC regimens [34, 35]. These improvements in supportive measures and using RIC regimens have expanded the use of allo-HCT to a higher proportion of patients to include older, less fit MCL patients, who previously would not have been considered candidates for transplant. Another limiting factor for allo-HCT is the requirement for donor matching stem cells, for which an HLA-matched donor remains the gold standard. Similarly to other hematologic malignancies, haploidentical HCT (haplo-HCT) outcomes have improved over the last decade with the introduction of post-transplantation cyclophosphamide; published studies suggest encouraging outcomes with haplo-HCT regarding NRM, PFS, and OS, though data to date is inclusive of all lymphoma subtypes, not specifically MCL, and further investigation is necessary to further elucidate outcomes [36, 40].

Traditionally, allo-HCT is offered to eligible patients who failed CIT followed by auto-HCT or for patients with primary refractory disease. Allo-HCT is offered at times by some experts as an upfront consolidation for selected young patients with high-risk MCL patients who fail to achieve a complete remission or even those in first remission with one or more molecular or biological risk factors such as those with TP53 mutation. Two non-randomized prospective clinical trials supported upfront allo-HCT in younger patients with HR disease with 5-year PFS exceeding 56% in both studies [32, 33].

The recent approval of CAR-T cell therapy for MCL is expected to have an impact on the indications and utilization of allo-HCT. However, knowing the incurable nature of MCL and based on the long experience with allo-HCT showing durable responses and cure in high-risk MCL patients, longer follow-ups will be needed to better define who can have durable responses after CAR-T cell therapy and would benefit the most from this novel practice-changing therapy. Furthermore, a significant proportion who had initial response after CAR-T cell therapy might relapse within few months. Hence, it is imperative to identify the risk factors for lack of response or early failure after CAR-T cell therapy and be considered at earlier phases for allo-HCT. Given the advantage of reduced TRM with CAR-T cell therapy, a panel of international experts from the American Society for Transplantation and Cellular Therapy (ASTCT) and European Group for Blood and Marrow Transplantation (EBMT) recommended offering CAR-T cell therapy before allo-SCT if possible in the relapsed setting for *TP53* unmutated MCLs (grade C recommendation) [28]. For patients who

relapse after CAR-T cell therapy, allo-HCT remains the only potentially curative option. However, this may not be practical, as patients who progress after CAR-T are generally physically unfit to get allo-SCT. Allo-HCT can serve as a salvage consolidation option as well for minority of patients who are complicated by prolonged and profound pancytopenia after CAR-T cell.

High-risk MCL and allo-HCT

Unlike auto-HCT, the use of allo-HCT in HR patients has been associated with encouraging results and it is believed allo-HCT can overcome many adverse features; for example, a study of 42 MCL who had allo-HCT suggested no significant difference in OS or relapse between *TP53* alteration (*N*=19) patients vs. wild type (*n*=23). Nine patients with TP3 alternation vs. 10 of wild type were alive after 24 months (log-rank *P*=0.581) [41]. Even though the best outcomes with allo-HCT are seen in chemo-sensitive MCL, prolonged remissions seem to be possible even among patients with positive PET CT scan pre-HCT [42] and also in some patients with chemo-refractory MCL. In a CIBMTR study of 202 patients with chemotherapy-unresponsive MCL, patients were still able to have durable responses with 3-year PFS and OS rates of 25% and 30%, respectively, and there was no difference after myeloablative or RIC conditioning [34]. In MCL, allo-HCT is currently to be considered for selected younger patients with high-risk MCL (particularly those with mutated TP53) but otherwise is preferred to be reserved for patients who do not have access or fail CAR-T cell therapy given the decreased TRM associated with CAR-T cell therapy. However, there is an unmet need to explore in-depth the risk factors that predict early progression after CAR-T cell therapy as a substantial proportion of these patients may eventually benefit from allo-HCT. Earlier involvement of transplant clinicians in the management of these high-risk patients is recommended.

CAR-T and MCL

Following the results of the multicenter prospective phase II clinical trial (ZUMA-2), demonstrating its safety and impressive efficacy, the FDA approved the anti-CD19 CAR-T cell therapy (CD28 costimulatory domain), brexucabtagene autoleucel (Tecartus), for R/R MCL. All the 68 patients treated on the ZUMA-2 trial had received up to 5 therapies, including BTKi. The objective response rate (PR or CR) on the sixty evaluable patients was an impressive 93%, with 67% achieving CR. One-year PFS and OS were 61% and 83%, respectively, with a remarkably low 1-year NRM of only 3%. A recently reported follow-up of 17.5 months showed an ongoing durable response in 48% of all efficacy-evaluable patients, and 70% of those who had CR remained in CR [43]. Despite low TRM with CAR-T cell therapy, it is associated with substantial unique toxicities; in the ZUMA-2 study, the rates of grade 3+ cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were 15% and 31%, respectively, and there were two grade 5 infections. Another promising CAR-T cell not approved yet for MCL is lisocabtagene maraleucel (Liso-cel). Liso-cel is an anti-CD19 CAR-T cell therapy with 4-1BB as costimulatory domain and is now approved for diffuse large cell lymphoma. In the ongoing TRANSCEND NHL001 study, 32 patients

with R/R MCL received Liso-cel; ORR was 84% (CR, 59%). Liso-cel seems to be associated with slightly lower toxicity; grade 3+ CRS and neurotoxicity were seen in only 3% and 12.5%, respectively [44]. These results seem to compare favorably with historically published controls for allo-SCT where the 1-year PFS and OS rates ranged from 31 to 50% and 33 to 75%, respectively, and with 1-year NRM rates ranging from 18 to 43% [45]. However, longer follow-ups will be needed in the CAR-T cell therapy cohorts to assess whether durable remissions will be retained over time and for long-term safety data as well.

On the other hand, autologous CAR-T cell therapy has some limitations, including production failure which can be partly related to the quality and/or quantity of collected lymphocytes, particularly in patients who received multiple prior lines of therapy [37] and patients who received bendamustine within 6 months of leukapheresis [46]. Time from identifying patient, obtaining insurance approval, peripheral mononuclear cell collection, and to manufacturing CAR-T cells can be a challenge. This process can take few weeks during which many patients are at risk for further progression and decline in their clinical condition. Allogeneic or "off-shelf" third-party CAR-T cells may potentially overcome some of these challenges and are being explored in lymphoid and non-lymphoid malignancies.

CAR-T cell and HR MCL

Given the recent approval of CAR-T cell in MCL in patients who failed CIT and BTKi treatments, it is difficult to compare the results of the ZUMA-2 trial to those of other available treatment options. ZUMA-2 included high-risk patients, with 25% having blastoid morphology, 47% having Ki67 >50%, and 17% having *TP53* alteration, and all patients failed two lines of therapies, including BTK inhibitors. Interestingly, a subgroup analysis showed that these patients with poor prognostic features seemed to benefit from CAR-T cell as well. All the six patients with R/R MCL patients with known aberrant *TP53* in ZUMA-2 achieved CR with CAR-T cell therapy. Also, in a separate analysis, patients with early relapse after diagnosis (within 24 months) had similar response rates and safety to patients with progression after 24 months from diagnosis; however, the median PFS was shorter (11 vs. 29 months) [47].

The pivotal trial results may or may not apply to the general population in clinical practice. The US Lymphoma Consortium (14 academic centers) conducted a large retrospective study [48] for 95 patients with MCL who received brexu-cel on a commercial basis and was able to show comparable efficacy and safety despite the fact 78% of those patients would not meet the inclusion criteria on ZUMA-2 for various reasons including worse performance status, cytopenia, organ dysfunctions, and liver or renal dysfunction, and 7% had CNS involvement. Also, this study had HR patients, with 41% of patients having blastoid or pleomorphic variants versus only 25% in the ZUMA-2, 44% had *TP53* mutations or alterations compared to 17% on the ZUMA-2. In a real-world experience study, the overall response rate (ORR) was 89%, with 81% complete remission (CR). BTK-naive patients (n=17) had an excellent response rate with CR of 88% vs. 79% in patients who had BTKi. Given the encouraging outcomes in R/R MCL who failed BTK and the poor response in HR MCL with BTKi [9], ZUMA-2 cohort 3 is now enrolling BTK-naive patients.

Conclusion

As a summary, we encourage participation in clinical trials as much as possible when available. Outside of a clinical trial, most patients with MCL currently still receive CIT in first line (followed by consolidation with auto-HCT in CR1 for select patients), BTKi in second line, and CAR-T in third line. Allo-HCT remains an option for a select group of patients; nevertheless, our clinical practice has transitioned to novel agents and cellular therapies when appropriate.

Compliance with Ethical Standards

Conflict of Interest

Amer Beitinjaneh: Research funding (to institution): ATARA, Kite, Tessa, Autolus; Advisory board: Kite. Adrienne Kaufman declares that she has no conflict of interest. Yucai Wang: Research funding (to institution): Incyte, InnoCare, LOXO Oncology, Novartis, Genentech, MorphoSys; Advisory board (compensation to institution): Eli Lilly, TG Therapeutics, LOXO Oncology, Incyte, InnoCare, Kite. Preetesh Jain: Advisory Board: Eli Lilly, Kite, LOXO Oncology, Incyte; Honorarium: Aptitude Health, Pharmacy times; Research Funding—Astra Zeneca, Kite, Beigene. Samer Srour declares that he has no conflict of interest. Michael Wang has received research funding from Acerta Pharma, AstraZeneca, BeiGene, BioInvent, Genentech, InnoCare, Janssen, Juno Therapeutics, Kite Pharma, Loxo Oncology, Molecular Templates, Oncternal Therapeutics, Pharmacyclics, VelosBio, Vincerx, Celgene, and Genmab; has received compensation for service as a consultant from Acerta Pharma, AstraZeneca, BeiGene, BioInvent, DTRM Biopharma (Cayman) Ltd., Genentech, InnoCare, Janssen, Juno Therapeutics, Kite Pharma, Loxo Oncology, Oncternal Therapeutics, Pharmacyclics, VelosBio, AbbVie, ADC Therapeutics America, Be Biopharma, Deciphera, Leukemia & Lymphoma Society, Eli Lilly & Co., Merck, Milken Institute, Parexel, and PeproMene Bio; and has received honoraria from Acerta Pharma, AstraZeneca, Anticancer Association, BeiGene, BioInvent, Janssen, Kite Pharma, Pharmacyclics, Physicians Education Resources (PER), AbbVie, Leukemia & Lymphoma Society, Bantam Pharmaceutical, DAVA Oncology, Eastern Virginia Medical School, IDEOlogy Health, TS Oncology, Medscape, Meeting Minds Experts, MD Education, MJH Life Sciences, Moffitt Cancer Center, Oncology Specialty Group, OncLive, Practice Point Communications, and Studio ER Congressi.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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