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DIFFUSE LARGE B-CELL LYMPHOMA

Effective Practices for Meaningful Care Conversations in a Changing Landscape

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Diffuse Large B-Cell Lymphoma

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Introduction

Diffuse large B-cell lymphoma is the most common subtype of non-Hodgkin's lymphoma. It accounts for 30% of non-Hodgkin's lymphoma cases in the United States[1] and its incidence increases with age. This aggressive disease is considered treatable with chemotherapy; it can be cured in many patients who achieve complete remission with first-line treatment.[2]

The Association of Cancer Care Centers (ACCC), in partnership with The Leukemia & Lymphoma Society (LLS), has developed the educational initiative *Reframing the Conversation: Effective Practices for Diffuse Large B-Cell Lymphoma*. The initiative aims to improve care conversations between patients and providers to incorporate new therapy advancements, define expectations with patients about their treatment journey, and provide confidence about promising advancements in managing diffuse large B-cell lymphoma.

THE BASICS

30% of cases of non-Hodgkin's lymphoma in the United States are DLBCL.[1]

30,000 new cases of diffuse large b-cell lymphoma are diagnosed annually in the US.[2]

ACCC conducted a literature review along with focus group discussions with 9 participants, including oncologists and hematologists, oncology nurse and nurse practitioners, patient advocates, patients, and caregivers, to identify areas of need for more effective care conversation for patients with diffuse large B-cell lymphoma and their caregivers.

Diffuse Large B-Cell Lymphoma Landscape Analysis Highlights

Summary of Key Findings From the Analysis

Management of diffuse large B-cell lymphoma is complex, and it requires open communication among a multidisciplinary care team.

> The disease has a high rate of relapse, with up to 40% of patients experiencing relapse within the first 2 years after primary treatment.[2]

Treatment of patients with diffuse large B-cell lymphoma begins with a prognostic evaluation of the disease and assessment of the potential adverse events (AEs) of treatment. It should be followed by physical, physiological, cognitive, and socioeconomic evaluations of the patient. When considering treatment options, health care professionals should engage the patient to share expectations and goals related to disease control and quality of life.

Undoubtedly, the future of treatment for patients with newly diagnosed and relapsed/refractory (R/R) diffuse large B-cell lymphoma will look different over the next few years as many clinical trials are testing novel treatments. Data from these trials and real-world sources will help to inform treatment decisions, improve clinical outcomes, and preserve quality of

life for patients.

Recent Therapeutic Advancements

Newly Diagnosed

Since 2006, R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) has been the standard of care for frontline treatment of fit patients with diffuse large B-cell lymphoma.[3] In patients with high-risk large B-cell lymphoma subtypes, such as high-grade B-cell with translocations of MYC and BCL2 (commonly referred to as double-hit lymphoma), intensified chemoimmunotherapeutic regimens such as dose-adjusted R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) are used.[4]

In April 2023, the FDA approved polatuzumab vedotin-piiq (pola), an antibody-drug conjugate (ADC) to be used in combination with R-CHP (rituximab, cyclophosphamide, doxorubicin, prednisone) for patients who have untreated diffuse large B-cell lymphoma or high-risk large B-cell lymphoma, not otherwise specified, and an international prognostic index score of 2 or greater.[5,6] In the randomized trial, a greater percentage of patients who received pola plus R-CHP than patients who received R-CHOP attained 2-year progression-free survival (PFS) (76.7% vs 70%, respectively). No differences in overall survival were observed. Studies are ongoing to investigate whether bispecific antibodies and ADCs are beneficial in frontline therapy.[7]

Relapsed/Refractory Disease

Treatment for relapsed diffuse large B-cell lymphoma in the second and third line largely depends upon whether the patient is eligible for autologous transplant.

> About 50% of patients with R/R diffuse large B-cell lymphoma are considered ineligible for salvage therapy and stem cell transplant.[8]

Patients ineligible for transplant are further considered either appropriate or inappropriate for receiving chimeric antigen receptor (CAR) T-cell therapy. Importantly, it is recommended that patients with progression or relapse of diffuse large B-cell lymphoma within 12 months of first-line treatment undergo CAR T-cell therapy regardless of transplant eligibility.[9]

The standard of care for patients with relapsed diffuse large B-cell lymphoma who demonstrate sensitivity to second-line salvage chemotherapy historically has been consolidative high-dose chemotherapy (HDCT) followed by autologous stem cell transplant (ASCT) (eg, with R-ICE [rituximab, ifosfamide, carboplatin, etoposide]). However, results of the ZUMA-1 and TRANSFORM studies showed that CAR T-cell therapy improved PFS compared with autologous stem cell transplant (ASCT), and the outcomes of ZUMA-1 have shown a definitive overall survival advantage with use of CAR T-cell therapy involving axicabtagene ciloleucel (axi-cel).

> Notably, only 30-50% of patients who were intended to undergo high-dose chemotherapy (HDCT) and ASCT actually received the transplant in these studies, often due to failure to respond to salvage chemoimmunotherapy.

For patients with diffuse large B-cell lymphoma who experience relapse more than 12 months after frontline therapy, salvage chemoimmunotherapy followed by consolidative HDCT-ASCT remains the standard of care in transplant-eligible patients. For those who do not have primary, refractory diffuse large B-cell lymphoma or who have a late relapse, ASCT remains standard of care if the disease is sensitive to chemotherapy.

> Only 30-50% of patients who intend to go for ASCT ultimately are able to receive an ASCT.

For patients with relapsed diffuse large B-cell lymphoma who are ineligible for transplant in the second line, several options may be considered. Transplant-ineligible patients with relapsed diffuse large B-cell lymphoma who are eligible for CAR T-cell therapy should be considered for treatment with lisocabtagene maraleucel (liso-cel), which is approved in this setting. Alternatively, the tafasitamab-lenalidomide regimen is approved for patients with R/R diffuse large B-cell lymphoma who are ineligible for transplant.[10] Approval was based on outcomes of the L-MIND study, which showed a median PFS of 12 months in patients with R/R diffuse large B-cell lymphoma who were treated with 1 to 3 prior lines of therapy. Based on results of the GO29365 study, the FDA approved pola plus bendamustine and rituximab to treat patients with R/R diffuse large B-cell lymphoma for whom 2 or more lines of therapy have failed.[11] Recently, the FDA approved 2 CD20-CD3 bispecific antibodies, epcoritamab and glofitamab, as treatment for R/R diffuse large B-cell lymphoma after failure of 2 or more lines of therapy.

In addition to newly approved treatments, cancer vaccines are providing preliminary success when used in combination with immunotherapeutics in clinical trials.[12] More trials are necessary before this treatment is approved for use in broader patient populations. Clinical trials should always be considered when treating patients with relapsed diffuse large B-cell lymphoma. In addition to testing new therapies, investigators working on ongoing studies are using genomic profiling and novel methods for detecting disease relapse (precision medicine) to improve outcomes for patients.

Insights in Patient and Provider Perspectives

In September 2023, ACCC held focus groups in partnership with LLS to explore how cancer programs may reframe the conversation between patients and providers. One focus group was held with members of the multidisciplinary cancer care team, and 2 focus groups were held with patients and patient advocates.

There were 4 key categories examined through focus group discussions, including:

- INVOLVING MULTIDISCIPLINARY CARE TEAMS
- COMMUNICATING THE DIAGNOSIS
- DISCUSSING TREATMENT OPTIONS
- MONITORING TREATMENT AND PROVIDING PSYCHOSOCIAL SUPPORT

MULTIDISCIPLINARY CARE TEAMS

Focus group participants identified the need for a comprehensive lymphoma care team to ensure adequate biopsy sampling, ancillary testing, and treatment planning. Regardless of where care is received (eg, large tertiary care centers vs smaller cancer programs), effective communication across the care team is necessary to prevent misinformation or conflicting medical advice.

Nurse navigators were recognized as a crucial component of care coordination, especially during the initial diagnostic process when ancillary tests may be required to tailor treatment plans. In addition to providing support during diagnosis, nurse navigators may also help patients retrieve outside medical records, allow access to assistance programs, and help coordinate appointments when patients require multimodal treatment. In some cancer programs, navigation tasks may be distributed across a team of nurses, social workers, and other members of the care team.

Other essential members of the care team include social workers, who can address psychosocial concerns and help patients with financial assistance programs or transportation coordination. Additionally, the treatment journey for patients with diffuse large B-cell lymphoma often may be lengthy and include treatments that affect the heart; therefore, members of the sections of cardio-oncology and integrative oncology may also provide essential services.

COMMUNICATING THE DIAGNOSIS

The ideal provider-patient conversation should begin with the provider asking how much detail that the patient would like to receive about their diagnosis.[13] This allows the provider to tailor the conversation and adjust the level of information so that the patient is not overwhelmed. Some patients who have a greater level of health literacy and knowledge about lymphoma may want to learn more about the specifics of their diagnosis, whereas others may prefer to receive a general overview.

Experts recommended the following measures to effectively communicate with patients during diagnosis:

- Recognize that patients have different levels of health literacy and awareness about lymphoma.
- Since patients are likely to experience strong emotions (eg, shock, fear), ask about their concerns and acknowledge these subjects during the initial visit. By building trust and rapport with the patient, providers can better explain the diagnosis, prognosis, and treatment options.
- Incorporate brochures, education materials, and resources like LLS support groups so that patients can learn more about their diagnosis and receive additional support.
- Let patients know that test results may become available on the patient portal before they have a chance to speak with their providers. Some patients may prefer to see their results, and others may prefer to wait and discuss them.

DISCUSSING TREATMENT OPTIONS

When treatment options are discussed with patients, providers should incorporate principles of shared decision-making (SDM) to align their treatment plans with patients' goals and preferences.[14] Providers should prepare patients for their treatment journey by explaining that it may be lengthy and include multiple modalities (eg, chemotherapy, radiotherapy).

Several patients shared stories about hearing conflicting recommendations from cancer providers. For example, one patient was told by a radiation oncologist that radiotherapy would be beneficial, but their medical oncologist did not think that the potential benefits outweighed the potential risks. This made the patient feel confused and frustrated. Patients found it comforting when their providers explained plans to adjust therapies if the initial treatment was not effective. By learning about additional treatment options (eg, transplant, bispecific antibodies, or CAR T-cell therapy), patients felt more hopeful about their long-term prognosis.

The participants offered the following recommendations for effectively communicating with patients when discussing treatment options:

Appreciate that in an ideal setting, the entire multidisciplinary treatment team would meet with the patient and recommend a coordinated multimodal treatment plan (eg, an integrated multidisciplinary clinic practice model for cancer care). If they cannot offer a group meeting, providers could hold a video conference that includes medical and radiation oncology professionals to discuss treatment recommendations with patients and caregivers.

Encourage patients to be very clear about their goals of treatment. Some patients may be able to voice this, yet others may need to consider the potential risks versus benefits of treatment to make certain decisions about their personal goals. Advocacy groups such as LLS offer resources that can help patients to learn more about treatment options and find support.

Prepare patients by being honest about the physical and emotional difficulties of the treatment journey.

> "A lot of times what lessens that fear is that there is a plan in place... Often doctors don't speak about all of the treatment options at the very beginning... But I think what's helpful is to know what can be done... if it does relapse, because fear of relapse is very real, with all cancer patients. So I think having that discussion at the beginning, is something that would actually help a patient understand the path, as well as be more positive, you know, for mental health reasons to know that there's options."
>
> **- Lizette Figueroa, MA** Senior Director, Education & Support, *The Leukemia & Lymphoma Society*

TREATMENT MONITORING AND PSYCHOSOCIAL SUPPORT

Some patients who start therapy may have difficulty in coordinating multiple appointments and traveling to receive care. Navigators, financial advocates, and social workers can address these issues by meeting with patients and proactively screening for psychosocial distress and barriers to access. Protocols and clinical pathways to monitor treatment should outline how symptoms should be evaluated and managed. Additionally, patients should be educated about treatment-related AEs and reminded about when and how to communicate symptoms or other concerns to their care teams.

Patients noted that they preferred access to 1 primary person when they had a question, experienced distress, or needed any form of assistance. A nurse navigator served this function for a majority of them throughout their entire cancer treatment journey. When a nurse navigator was not involved, patients often established a close rapport with an oncology nurse who became their trusted primary point of contact.

Additionally, it is critically important to check in with caregivers. Caregiver burden is often overlooked and not documented in the patient's chart. Caregivers may be at risk of emotional and mental exhaustion; it is important to make them aware of any resources that can address these issues to ensure they remain a valuable member of the patient's care team.

Participants also offered the following recommendations for effective communication during treatment monitoring:

For patients with technology proficiency, digital tools that include patient portals and secure messaging platforms can be effective ways to track adherence to oral therapies and monitor for treatment-related AEs. Telehealth visits can also be used as an effective way to evaluate how patients are doing and to monitor for AEs.

Remember to ask patients whether they would like to discuss any other concerns beyond their medical care. This may help patients feel more comfortable in bringing up any emotional distress they are experiencing.

Ask caregivers if they would like to learn about resources that can offer support.

Expert Insights on Effective Care Conversations

CANCER BUZZ spoke to Robin Atkins, RN, OCN, a symptom triage nurse at Virginia Oncology Associates in Norfolk, Virginia, about effective practices to support patients with diffuse large B-cell lymphoma throughout the care continuum. One of the most important factors of treatment planning is to engage the patient and caregiver to share their expectations and goals.

Key takeaways from Ms Atkins' experience appear below.

Listen for meaning when speaking with patients and caregivers who are undergoing treatment for diffuse large B-cell lymphoma.

"Hearing the meaning behind what they are saying and then incorporating that into the general care plan is a big thing that I try to do very consistently. It takes time, and it takes practice, but it is extremely effective in making the whole process patient centered."

Shared decision-making is a 2-way conversation. It is important to ensure that the patient and caregiver understand what has been discussed.

"I tend to say, 'What this means for you is…,' because that is what they really want to know. Effective communication includes that exchange of information where both parties are listening. But also, we concede with what the priorities are for the patient."

Office procedures must include the provisions of time and physical space to meet with the caregiver when care planning is happening.

"Caregivers being included in the care planning needs to be a priority for the facility. You need to have space and time for it. There needs to be face-to-face contact on some regular schedule."

Be authentic when building a relationship with patients and caregivers.

"Make yourself available, circle back to emotionally-based concerns at each follow-up, be astute to body language, opening the door for emotionally loaded conversations, helping patients set limits with caregivers, and providing information on how to reach you."

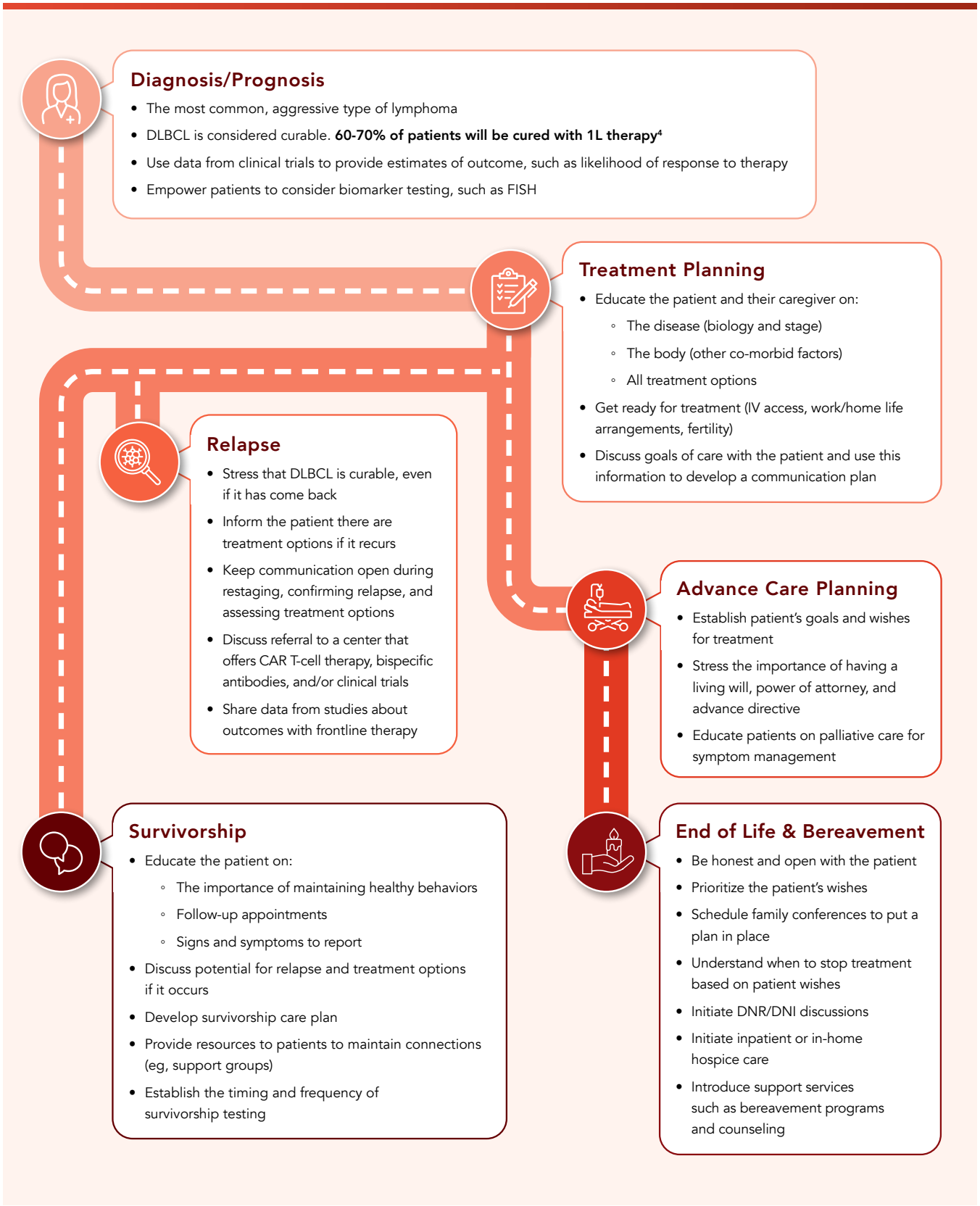
Continuity of care is very important.

"Patients don't like restating the story over and over. The care team needs to provide clinical visits with the same nurse and provider."

Communication Roadmap

With recent advancements in treatment options, it is important for providers to understand how these new therapies will be implemented in their practice setting and how they best may be integrated into practice. A communication roadmap was created as part of the educational initiative to support health care teams when having care discussions with patients and caregivers (**Figure 1**). It outlines the key steps and goals for conveying information clearly and efficiently.

Figure 1. Diffuse Large B-Cell Lymphoma Communication Roadmap



Conclusion

Diffuse large B-cell lymphoma is an aggressive disease. Recently approved treatments and those on the horizon provide new hope for patients with diffuse large B-cell lymphoma as therapeutic options become more targeted and personalized for their disease. All health care providers should be equipped to incorporate these new advancements, define expectations with their patients about their treatment journey, and communicate clearly for best outcomes.

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Acknowledgements

ACCC is grateful to the Advisory Committee, partner organizations, and others who graciously gave their knowledge and time to contribute to this publication.

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