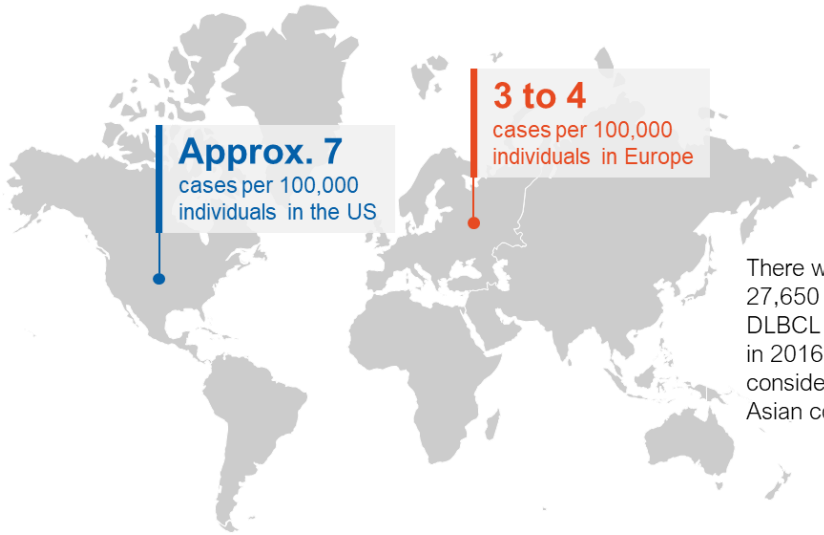
Diffuse Large B-cell Lymphoma

While there are many different sub-types of non-Hodgkin lymphoma (NHL), each are unique in how they present in patients and how they should be treated. Diffuse large B-cell lymphoma (DLBCL) is an aggressive (fast-growing), complex and difficult- to-treat form of NHL. NHL refers to a group of cancers of the lymphatic system that develop from the lymphocytes, a type of white blood cell involved in the body's immune system. In people with NHL, normal lymphocytes change and grow uncontrollably, displacing healthy white blood cells and weakening the body's ability to fight infection[1,2]. DLBCL is cancer of the B-lymphocytes (B-cells).

DLBCL is the most common subtype of NHL, accounting for up to

40% of all NHL cases globally[3]



There were an estimated 27,650 newly diagnosed DLBCL patients in the US in 2016. The incidence is considerably lower in East Asian countries.

Outlook

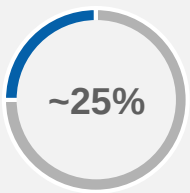
of patients with DLBCL achieve and maintain complete remission after first-line therapy[4].

However,

of patients relapse after receiving first-line treatment[5].

Out of those diagnosed with DLBCL,

of patients have refractory disease[5].



of r/r DLBCL patients are eligible for auto stem cell transplant[4].

If left untreated, r/r DLBCL has a life expectancy of 3 to 4 months[5].

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Diagnosis

Although DLBCL does occur in children, the incidence increases with age; approximately half of DLBCL patients are over 60 years of age at the time of diagnosis[6]. The general symptoms of DLBCL often resemble those caused by infection, such as swollen lymph nodes, fever, fatigue, weight loss and recurring night sweats[6,7]. The first symptom is often rapid swelling of the lymph nodes in areas including the neck, armpit or groin that may or may not be painful.

Physicians use a variety of tests to diagnose the presence of DLBCL cells, as well as to determine the subtype and stage of the disease. Staging determines how much lymphoma is present, where it is located and whether it has remained within the lymphatic system or spread to other parts of the body. Although the majority of DLBCL cases occur in the lymph nodes, the disease involves organs other than the lymph nodes about 40% of the time[18].

Treatment

The subtype and stage of disease can affect both prognosis and treatment choices[6]. Because it is a particularly aggressive type of cancer, DLBCL must be addressed quickly. It is important for patients to discuss all treatment options with their doctors to develop a plan that will help them reach their treatment goals.

Initial treatment typically consists of chemotherapy plus a monoclonal antibody, rituximab, and is often curative[9]. However, roughly one-third of patients relapse after receiving first-line treatment[5]. The mainstay of secondary therapy is second-line ("salvage") chemotherapy followed by high dose chemotherapy (HDT) and autologous stem cell transplant (ASCT); however, many patients cannot proceed to ASCT because of lack of response to salvage chemotherapy, or are ineligible due to poor health status[5,10,11]. Of those patients who are able to undergo ASCT, many ultimately face disease relapse. Options are limited and survival rates are low for patients who are ineligible for ASCT or for whom salvage chemotherapy and ASCT have failed[12].

The ultimate goal of treatment for r/r DLBCL is for patients to attain durable complete remission or complete response, meaning there are no signs of cancer detectable in the patient. Other measurements of response to treatment include a partial response and the duration of response (the time between initial response to a therapy and further disease progression).

While the prognosis for r/r DLBCL patients has historically been poor, innovative approaches such as immunocellular therapy have the potential to change outcomes for patients and the way this cancer is treated.

Disease Burden

Quality of Life

Both the disease and its treatment can have a significant impact on a patient's quality of life. Compared to healthy people, patients with DLBCL experience reduced health status and physical functioning, and higher rates of anxiety and depression; even long after therapy is completed, patients may continue to feel anxious about the future of their health. Besides these problems, patients are often faced with other pre- or post-transplantation physical problems such as neutropenia (having an unusually low number of white blood cells), infection, bleeding, fatigue, nausea-vomiting, dehydration, diarrhea and mucositis (inflammation and ulceration of the mucous membranes lining the digestive tract)[13,14].

Economic Burden

The direct and indirect costs of r/r DLBCL are substantial. Beyond treatment, overall healthcare resource use is high, including inpatient, ER, and with physician office visits and supportive care[15]. The economic burden is even greater for patients with r/r disease, who face significant costs for second-line procedures[16]. Indirect costs are also higher in this group as a result of impaired productivity, including absenteeism and short-term disability days[17].

References

1. American Society of Clinical Oncology. Lymphoma – Non-Hodgkin. http://www.cancer.net/cancer-types/lymphoma-non-hodgkin. Accessed October 2017.
2. Friedberg JW (2011) Relapsed/refractory diffuse large B-cell lymphoma. *Hematology Am Soc Hematol Educ Program* 2011 498-505. Accessed October 2017.
3. Raut, L., Chakrabarti, P. "Management of relapsed-refractory diffuse large B cell lymphoma." *South Asian J Can*, 2014 Jan-Mar; 3(1): 66-70
4. Leukemia & Lymphoma Society. Non-Hodgkin lymphoma (NHL). https://www.lls.org/lymphoma/non-hodgkin-lymphoma?src1=20045&src2=. Accessed October 2017.
5. World Health Organization. Diffuse large B-cell lymphoma. Review of cancer medicines on the WHO list of essential medicines. Available at: http://www.who.int/selection_medicines/committees/expert/20/applications/DiffuseLargeBCellLymphoma.pdf. Accessed October 2017.
6. Lymphoma Research Foundation. Diffuse Large B-Cell Lymphoma (DLBCL). http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300153. Accessed October 2017.
7. American Cancer Society. Non-Hodgkin Lymphoma: Early detection, diagnosis, and staging. Available at: https://www.cancer.org/cancer/non-hodgkin-lymphoma/detection-diagnosis-staging.html. Accessed October 2017.
8. Leukemia & Lymphoma Society. Lymphoma - Non-Hodgkin: Subtypes. http://www.cancer.net/cancer-types/lymphoma-non-hodgkin/subtypes. Accessed October 2017.
9. American Cancer Society. Treating B-Cell Non-Hodgkin Lymphoma. Available at: https://www.cancer.org/cancer/non-hodgkin-lymphoma/treating/b-cell-lymphoma.html. Accessed October 2017.
10. Gisselbrecht C, Glass B, Mounier N, Singh Gill D, Linch DC et al. (2010) Salvage regimens with autologous transplantation for relapsed large B-cell lymphoma in the rituximab era. *J Clin Oncol* 28 (27): 4184-4190.
11. Gisselbrecht C, Schmitz N, Mounier N, Singh Gill D, Linch DC et al. (2012) Rituximab maintenance therapy after autologous stem-cell transplantation in patients with relapsed CD20(+) diffuse large B-cell lymphoma: final analysis of the collaborative trial in relapsed aggressive lymphoma. J Clin Oncol 30 (36): 4462-4469.
12. Crump M, Neelapu S, Farooq U, Van Den Neste E, Kuruvilla J et al. (2017) Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. Blood. E-pub ahead of print August 03. doi: https://doi.org/10.1182/blood-2017-03-769620.
13. Oerlemans S et al., 2014.
14. Ovayolu O et al. *Pak J Med Sci* 2013;29(3):803-808.
15. Galaznik et al. 2017. https://learningcenter.ehaweb.org/eha/2017/22nd/182419/aaron.galaznik.economic.impact.and.healthcare.utilization.in.patients.with.html/. Accessed October 2017.
16. Purdum et al. 2017. http://abstracts.asco.org/199/AbstView_199_186101.html. Accessed October 2017.
17. Yu JS et al. Leuk Lymphoma 2016;57(11): 2636-2643. Accessed October 2017.

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