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CLINICAL TRIAL LANDSCAPE OF B-CELL LYMPHOMA IN ASIA-PACIFIC

CONTENTS

EPIDEMIOLOGY OVERVIEW

Background

B-cell non-Hodgkin lymphomas (BNHL) are clonal tumours of mature and immature B cells [1]. Among the mature BHNL, the subtype called the Diffuse large B-cell lymphoma (DLBCL) is the most common and the most aggressive form in adults. Other common subtypes include follicular lymphoma (FL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL, including mucosa-associated lymphoid tissue [MALT] lymphoma), chronic lymphocytic and small lymphocytic lymphoma (CLL/SLL), Waldenström's macroglobulinemia (WM or lymphoplasmacytic lymphoma) and Primary mediastinal large B-cell lymphoma (PMBCL). There is a notable ethnic and regional distribution difference among BNHL subtypes, most commonly due to genetic, lifestyle, and environmental factors [2].

Disease Prevalence

According to the 2020 GLOBOCAN data, 544,352 new cases of non-Hodgkin lymphoma (NHL) were diagnosed in 2020, comprising almost 3% of cancers worldwide [3]. Of these, DLBCL, FL and CLL/SLL were the three most common subtypes accounting for about 85% of all non-Hodgkin lymphomas (NHLs). In Asia, the subtype DLBCL constitutes 60%–70% of BNHL. The risk of developing DLBCL is also higher among patients with HIV/AIDS, which drives the number of DLBCL cases in geographies such as India where high infection rates of HIV/AIDS are prevalent [4].

According to China's National Cancer Centre, the subtype DLBCL represents approximately 50,000 new cases of cancer per year which is about 40 to 50% of all NHL cases in China. In addition, the subtype FL accounts for about 45% of NHL cases in the country and is seen as a disease of high morbidity and mortality [5]. In mainland China, DLBCL is seen as the most common aggressive subtype while FL is the most common indolent NHL [6].

In South Korea, between 2011 and 2015, out of a total of 27,866 newly diagnosed NHL cases, there were 19,500 BNHL patients. Among these, DLBCL was the most frequently diagnosed subtype comprising anywhere between 42 and 48%, with other common subtypes being FL and MZL [7]. Additionally, among the 7,737 new lymphoma patients who were enrolled in the 4th nationwide study from 31 institutes between 2015 and 2016, the relative frequency of NHL was close to 95%, among which the BNHL accounted for nearly 83%. The relative frequency of DLBCL, extranodal marginal zone lymphoma (MALT) and FL were about 42%, 20% and 8% respectively within the BNHL category [8].

In Singapore, there were 7,131 total incident cases of lymphomas from 1998 to 2012 according to the Singapore Cancer Registry. DLBCL was found to be the most common subtype, accounting for about 3 out of 10 lymphoma cases. Other common subtypes were FL, CLL/SLL and MZL [9].

In Malaysia, according to the International Agency for Research on Cancer's (IARC), of the estimated cancer incidence in 2012, NHL was the ninth most common cancer. DLBCL constituted about 46% of all NHL cases from a single medical centre, with similar trends from other single centre studies in the country [10].

In Taiwan, a total of 21,929 lymphoma cases were diagnosed between 2002 and 2012. Of these, the aggressive BCL constituted 52% (11,450 cases) and was consistently the most common lymphoma followed by indolent BCL which constituted 25% (5,535 cases) [11].

In Australia, DLBCL is the most common subtype of lymphoma, accounting for around 30% of all lymphoma cases and affecting around 2,000 Australians each year [12].

In New Zealand, DLBCL is one of the most common types of lymphoma representing about 30% of all lymphoma cases in the country [13].

In the Philippines, there were 4,140 new cases and 2,415 deaths due to NHL in 2020 [14].

In Hong Kong, as per Hong Kong's Cancer Registry, the number of patients diagnosed with DLBCL between 2000 and 2018 was 4088 [15].

In Thailand, DLBCL accounted for 67% of NHL cases in 2017 [16].

STANDARD OF CARE

Standard B cell lymphoma therapies include chemotherapy, immunotherapy, radiation therapy and targeted therapies. Other therapies, such as CAR T-cell therapy, are being considered for cancers unresponsive to other forms of treatment.

For patients with BNHL, common chemotherapy drug regimens used includes CHOP (Cyclophosphamide, Doxorubicin, Prednisone, Vincristine), BR (bendamustine and rituximab) and combinations using fludarabine and R-CVP (cyclophosphamide, prednisone, rituximab, and vincristine). Research shows that adding an anti-CD20 monoclonal antibody, such as rituximab or obinutuzumab, to CHOP is expected to work better than using CHOP alone.

Targeted therapies (such as Bruton's tyrosine kinase inhibitors) target specific genes, proteins, or the tissue environment that contributes to cancer growth and survival.

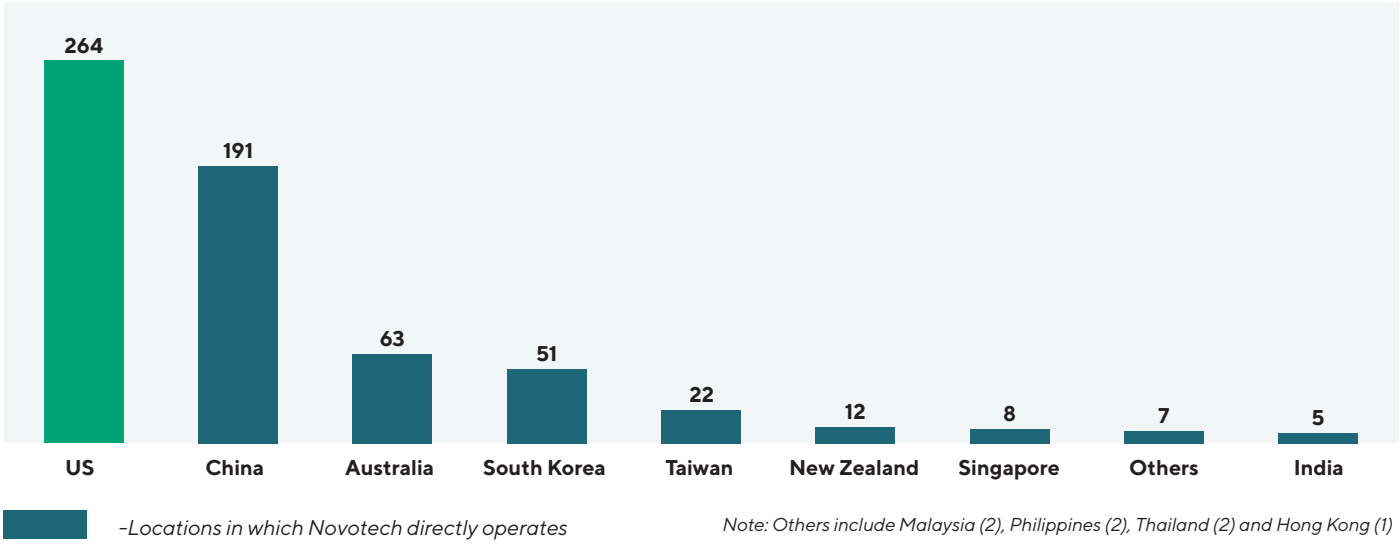
Furthermore, depending on individual patient needs, doctors may combine radiation treatment with other therapies, such as targeted therapy and chemotherapy, to prevent the growth of new cancer cells.

Other innovative treatments like CART-cell therapy such as Axicabtagene ciloleucel (Yescarta) and Tisagenlecleucel (Kymriah), have been made available to treat aggressive subtypes like DLBCL. Further CAR T-cell therapies are in development and being studied in clinical trials [17].

CLINICAL TRIAL LANDSCAPE

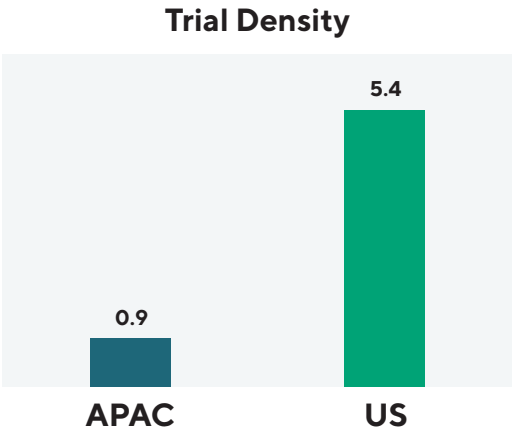
Biopharma companies have initiated around 550 clinical trials in BCL since 2018, over half of which involved sites in the Asia-Pacific region. Clinical trials in Asia-Pacific predominantly involve China, Australia, South Korea, Taiwan, and New Zealand due to fewer competing trials compared to the US, while also involving sites in Singapore, India, Malaysia, the Philippines, Thailand, and Hong Kong. (figure 1).

Figure 1: Top locations in the Asia-Pacific vs US based on the number of studies in B-cell lymphomas initiated by Biopharma companies since 2018 [18].



Due to its large population and lower volume of studies, the Asia-Pacific region has lower competing trial risk with a trial density of about six times lower than the US (figure 2).

Figure 2. Comparison of the trial density* for industry-sponsored B-cell lymphoma clinical trials in the US and the Asia-Pacific (APAC) [18]



Trial density is the number of recruiting sites for industry-initiated trials per million urban population

DLBCL trials running in the Asia-Pacific region show median recruitment durations about 20% shorter than trials in the US (figure 3) for the period 2018-2021. In addition, DLBCL studies ongoing in the Asia-Pacific region show twice faster patient recruitment rate than the US (0.4 and 0.2 patient per site, per month respectively) (figure 4).

Figure 3. Comparison of the median patient enrolment duration (in months) for DLBCL clinical trials in the US and the Asia-Pacific, 2018-2021 [18]

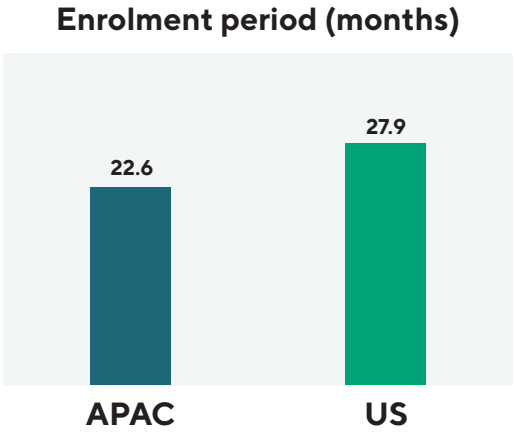
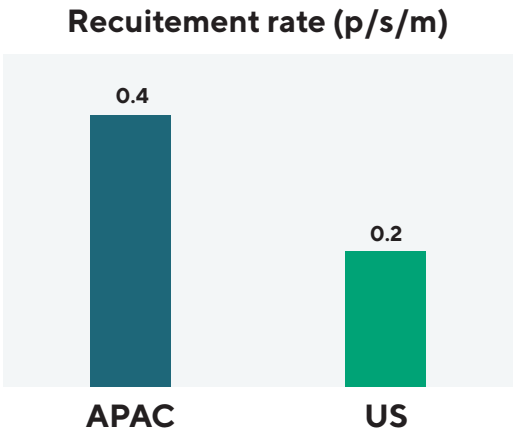


Figure 4. Comparison of median patient recruitment rate (in subjects, per site per month) for DLBCL clinical trials in the US and the Asia-Pacific, 2018-2021 [18]



KEY OPINION LEADERS IN B-CELL LYMPHOMA

Prof. Jun Zhu
Peking University Cancer Hospital and Institute – CHINA

Professor Zhu practices in the Lymphoma Department of Peking University Cancer Hospital. He was a Principal Investigator in 54 trials, and a Study Chair in 3 of them with sponsors such BeiGene Ltd and Pfizer Inc among others. Dr. Zhu has 4 publications under his name. In 2020, Dr. Zhu was named the first Principal Investigator of a BeiGene sponsored China study, for the US approved lymphoma treatment Brukinsa.

A/Prof. Michael Dickinson
Peter McCallum Cancer Centre – AUSTRALIA

Dr. Dickinson is a Clinical Haematologist and internationally recognized specialist in aggressive Lymphoma. He is the co-author of over 40 publications including in British Journal of Haematology and was involved in 15 early and late phase clinical studies in Haematological cancers for GSK, Epizyme, Novartis, Roche, and Celgene.

Prof. Ho S Lee
Kosin University Gospel Hospital – SOUTH KOREA

Dr Ho S Lee is a Professor of the Department of Internal Medicine, Koson University College of Medicine, South Korea. Lee was a Principal Investigator in 6 cancer trials including BCLs with sponsors such as Millennium Pharmaceuticals Inc, Biogen Inc and Celltrion Inc. His speciality areas include multiple myeloma, malignant lymphoma, acute and chronic leukemias. He has more than 80 co-authored publications.

Prof. Ching-Liang Ho
National Defense Medical Center – TAIWAN

Dr Ching-Liang Ho is the Vice President and Professor, Department of Medicine, National Defense Medical College, Taiwan. He was a Principal Investigator for 15 trials of various cancers including lymphomas with sponsors such as Golden Biotechnology Corp, Arcus Biosciences Inc and AbbVie Inc to name a few and has participated in about 20 publications.

Prof. Wei-Li Zhao
Shanghai Jiao Tong University School of Medicine - CHINA

Dr Zhao Wei-Li is the Professor of Hematology, Ruijin Hospital, School of Medicine. Her focus areas include clinical and basic research of haematological malignancies, especially the molecular mechanism and targeted therapy of malignant lymphoma. She has published over 70 articles in leading hematology journals like Cancer Cell and Cancer Genetics. She has been a Principal Investigator in more than 30 trials with sponsors such as Shanghai Sunway Biotech Co Ltd, Pfizer Inc, Biogen Inc and Eternity Bioscience Inc to name a few.

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