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CLINICAL TRIAL LANDSCAPE OF T-CELL LYMPHOMAS IN ASIA-PACIFIC

CONTENTS

EPIDEMIOLOGY OVERVIEW

Background

T-cell lymphomas (TCLs) are types of non-Hodgkin's lymphoma (NHL) that affect T lymphocytes. About 10% of NHLs are TCLs, with this proportion reaching over 30% in certain Asian locations [1]. There are numerous subtypes of TCLs including Cutaneous T-cell lymphomas (CTCLs), Peripheral T-cell lymphomas (PTCLs), PTCL-not-otherwise specified (PTCL-NOS), Anaplastic large cell lymphoma (ALCL), angioimmunoblastic T-cell lymphoma (AITCL), NK-/ T-cell lymphoma (NKTCL) and adult T-cell leukemia (ATLL). In CTCLs, there is an abnormal accumulation of malignant T-cells in the skin leading to the potential development of rashes, plaques, and tumours [2]. PTCLs, an aggressive form of the disease, develop from mature-stage white blood cells called T-cells and natural killer (NK) cells and result when T-cells develop and grow abnormally [3]. The clinical performance and pathogenesis vary widely across the different TCLs leading to different therapeutic strategies although with some overlaps in their early stages. However, due to wide variations in pathogenesis and limited therapeutic strategies, there is often a poor prognosis and easy relapse observed in TCL patients [4].

Disease Prevalence

Among the TCLs, PTCL, is generally more common in Asia, with the subtypes NKTCL and ATLL touted as the most common in the region. The subtypes PTCL-NOS and ALCL are found mostly in North America and Europe, whereas the AITCL, is primarily observed in Europe [5].

As for CTCLs, the Asia region shows high rates of subtypes such as extranodal NK/T-cell lymphoma (ENKTL), hydroa vacciniforme-like lymphoma (HVL), subcutaneous panniculitis T-cell lymphoma (SPTCL), and adult T-cell leukemia/lymphoma [6], with a prevalence 15% higher compared with Western countries [7].

The overall annual age-adjusted incidence of CTCL is approximately six cases per one million and is twice as common in men as in women, with incidence increasing with age (average onset between 50 and 60 years [8]. CTCL represents ~ 80% of the TCL cases in South Korea and Japan, ~70% in the USA, and ~77% in Europe.

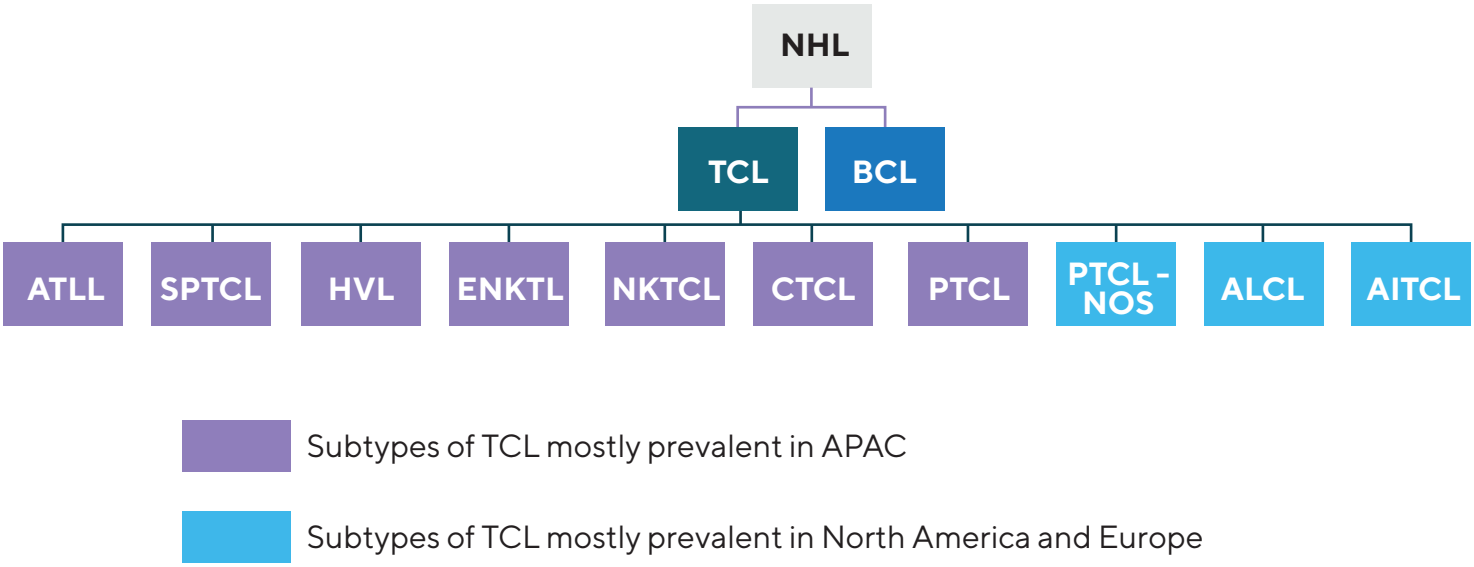
A higher incidence of PTCLs in Asian countries compared to Western countries is attributable to exposure to specific viruses, such as the Epstein-Barr virus (EBV) and the human T-cell leukemia virus-1 (HTLV-1). The proportion of T- and NK-cell lymphomas from NHL is particularly high in East Asia such as in China (33 %), Thailand and Japan (25% respectively), and South Korea (22 %). ENKTL makes up 48% and 29% of PTCL cases in China and South Korea respectively [9].

In China, the ENKTL is a common subtype that accounts for about half of PTCL cases, or about 10% to 15% of all lymphomas, much higher than in North America and Europe [10].

In Australia, PTCL accounts for approximately 7% of all NHL cases, equating to about 440 Australians diagnosed each year, most frequently affecting men aged over 60 years [11].

In India, the age-adjusted incidence rates for NHL in men and women in India are 2.9 per 100,000 and 1.5 per 100,000 respectively, with TCLs accounting for 10-15% of cases. PTCL-NOS, lymphoblastic lymphoma and ALCL are the three common subtypes of T-cell NHL observed in the country [12].

Figure 1. Classification of NHL subtypes and relative prevalence in APAC and Western location [13]



STANDARD OF CARE

The treatment of patients with TCL is challenging. Novel therapeutic strategies are urgently warranted to improve the therapeutic effects for this difficult to treat cancer type. For patients with mature T-cell and NK-cell neoplasms, a well-defined consensus on primary therapy is not yet established for those newly diagnosed and refractory patients.

Hence, anthracycline-containing chemotherapies such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CHOP-like regimens are being relied upon as the main treatment choice for the newly diagnosed patients, despite not having satisfactory outcomes.

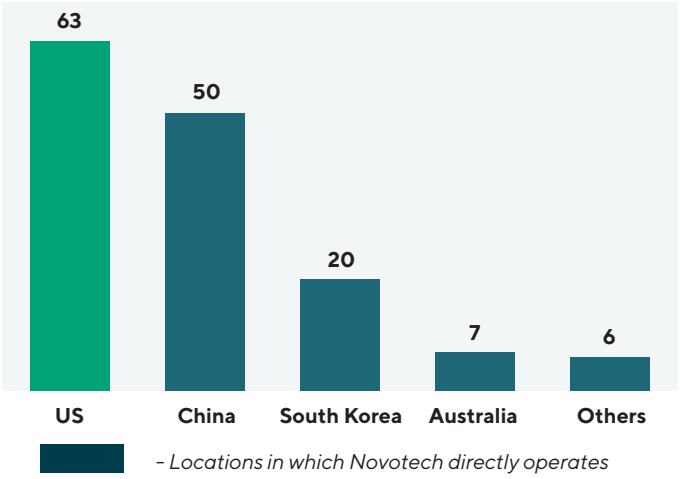
Likewise, non-anthracycline-based chemotherapies which incorporate the non-P-glycoprotein-dependent drugs, methotrexate, ifosfamide, and L-asparaginase are commonly used for ENKTL patients. However, for patients who do not respond to primary therapy, there seems to be institutional variations among the next appropriate treatment choices, and hence the types of clinical trials conducted at each institution may vary accordingly.

Despite the variable drug regimens used, the survival outcome has been reported as extremely poor for PTCL and T-cell and NK/T-cell lymphoma patients showing relapse after first-line treatment, in previous retrospective studies [14].

CLINICAL TRIAL LANDSCAPE

Biopharma companies have initiated about 200 clinical trials in T-cell lymphomas since 2018, with a majority involving the Asia Pacific region. Clinical trials in Asia-Pacific predominantly involve China, South Korea and Australia with fewer competing trials compared to the US, but also involve sites in Singapore, Taiwan, New Zealand and Thailand as well (figure 2).

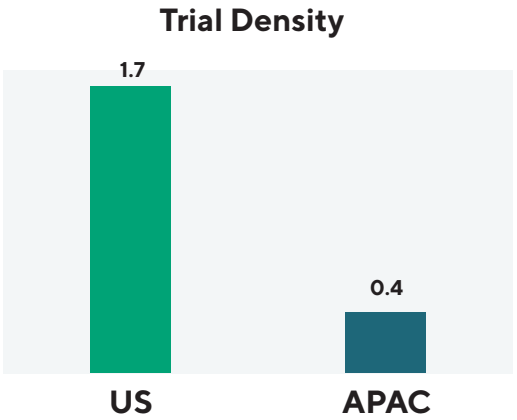
Figure 2: Top countries in Asia-Pacific in relation to the number of studies in T-cell lymphomas initiated by Biopharma companies since 2018 [15].



Note: Others include Singapore (2), Taiwan (2), New Zealand (1) and Thailand (1)

Due to its large population and lower volume of studies, the Asia-Pacific region has lower competing trial risk with a trial density about 4 times lower than the US (figure 3).

Figure 3. Comparison of the trial density* for industry-sponsored T-cell lymphoma clinical trials in the US and Asia-Pacific [15]



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

In addition, the 2020 trials in the Asia-Pacific region recruited twice faster than the US (1.5 and 0.7 patient per site per month respectively) (figure 5).

Figure 4. Comparison of median patient enrolment duration (in months) for T-cell lymphoma clinical trials, since 2018 in the US and Asia-Pacific. [15]

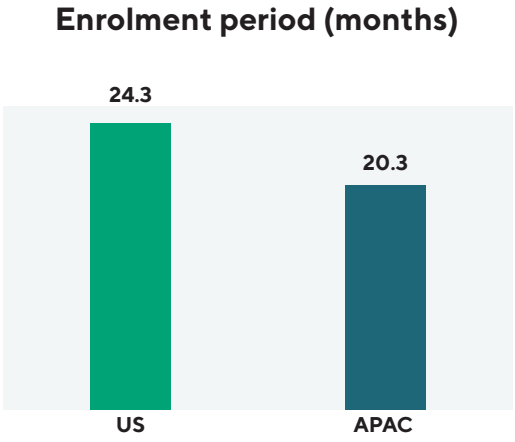
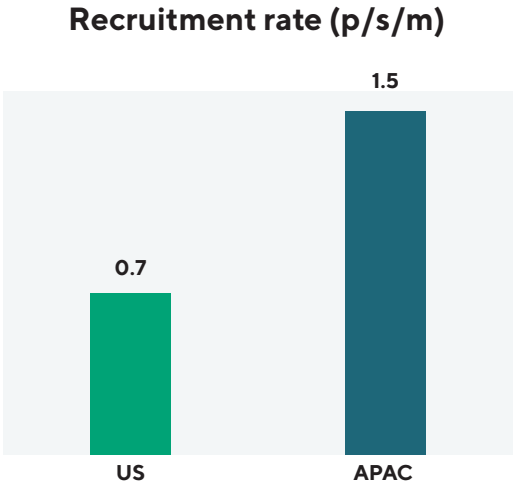


Figure 5. Comparison of median patient recruitment rate (in subjects per site per month) for 2020 T-cell lymphoma clinical trials, in the US and Asia-Pacific [15]



KEY OPINION LEADERS IN T-CELL LYMPHOMA

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Won Seok Kim is a Professor of Hematology and Oncology at the Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea. Dr.Kim specializes in malignant lymphoma and has published more than 130 articles in academic journals, such as *American Journal of Clinical Oncology, Annual Oncology, Cancer, Blood*.

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Dr. Yuankai Shi, professor at the Radiation Medicine and Molecular Nuclear Medicine, Peking Union Medical College has authored and co-authored multiple peer-reviewed scientific papers in addition to presenting works at many national and international conferences. He has been the principal investigator for over 100 oncology trials, and as study director and as study chair in a few others, with more than 50 publications under his belt.

Prof. Hui-qiang Huang
Sun Yat-sen University of Medical Sciences – CHINA

Prof.Hui-qiang Huang is currently the Deputy-Chief of the Department of Medical Oncology, Sun Yat-Sen University Cancer Center (SYSUCC). He focuses on basic research and clinical study on new therapeutic strategy for NK/T lymphoma and is actively involved in autologous hematopoietic progenitor cell transplantation for aggressive relapsed or refractory lymphomas. Dr. Huang has participated as Principal Investigator or participant in many global or national clinical trials. He has authored over 100 peer-reviewed articles including the New England Journal of Medicine, Nature Medicine and Lancet Oncology.

Prof. H. Miles Prince AM
University of Melbourne – AUSTRALIA

Professor H. Miles Prince AM is a Professor at both Melbourne and Monash universities. He manages all types of blood-related conditions including anaemia, blood clotting disorders and all blood-related cancers. He is also engaged in major stem cell research, mechanisms of the immune systems' control of blood and cancer growth. His research focuses on targeted treatments for blood diseases. Miles has been a principal investigator on 10 trials and has co-authored 14 publications.

Prof. KWONG Yok Lam
University of Hong Kong – HONG KONG

Professor Kwong is Chief of the Division of Haematology, Oncology and Bone Marrow Transplantation at the Department of Medicine, University of Hong Kong. He is specialized in haematology and hematopathology. His clinical work focuses on the management of haematological malignancies, with special interests in the treatment of leukemias, T-cell and natural killer cell lymphomas, which are neoplasms prevalent in Asian populations. Kwong and his team also pioneered the development and use of oral arsenic trioxide in the treatment of acute promyelocytic leukaemia and other blood cancers. He has been a principal investigator on 17 trials and has co-authored 25 publications.

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