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Review Article

Current Aspects of Non Hodgkin Lymphoma (NHL) In Bangladesh: A Mini Review

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Abstract:

Approximately 90% of all lymphomas are classified as non-Hodgkin lymphoma (NHL), a subtype of lymphoma originating in other parts of the immune system outside the lymph nodes. Adult NHL may be classified as either B-cell lymphoma, T-cell lymphoma, or natural killer cell lymphoma, according to the World Health Organization's (WHO) categorization system. According to the statistics, about one and a half million new people are diagnosed with cancer in a year in Bangladesh, among which more than seven thousand people are affected by various blood cancers. Non-Hodgkin and Hodgkin lymphoma, leukaemia, and myeloma belong to blood cancers. Treatment also varies depending on the disease's type and stage or risk. The paper aims to express the current condition of NHL & the treatment approach for this disease by analysing the literature and data of Bangladesh.

Keywords: NHL, Cancer, Lymphomas, Globocan, Bangladesh, etc.

Introduction

The annual global economic burden of USD 1.16 trillion due to cancer is the second biggest cause of death worldwide. There are around 1.5 million cancer patients in Bangladesh, with 150,000 deaths annually, as reported by the World Health Organization (WHO). According to the data presented in the paper, two hundred thousand individuals are diagnosed with cancer each year [3]. However, there are no population-based statistics on the prevalence of cancer, making it difficult to establish an accurate count of the number of persons who have cancer in the nation. Current hospital-based cervical cancer screening strategies have relatively low uptake. Dhaka also serves as the hub for the country's medical institutions. It is anticipated that by 2030, the annual rate of new cases will have increased by roughly 77%. Extrapolating from regional data (India) and a single hospital, the WHO's estimates are based on projected increases in cancer incidence and mortality. These rates may not accurately reflect the actual cancer situation [1]. Many instances go unreported owing to a lack of knowledge, education, misunderstandings, and poverty among communities, as well as weak health systems and lousy governance; therefore, the numbers are likely to be low. In addition, the high expense of treatment, the absence of oncologists, and the inadequate infrastructure have resulted in cancer care and management systems that fall short of worldwide standards [2].

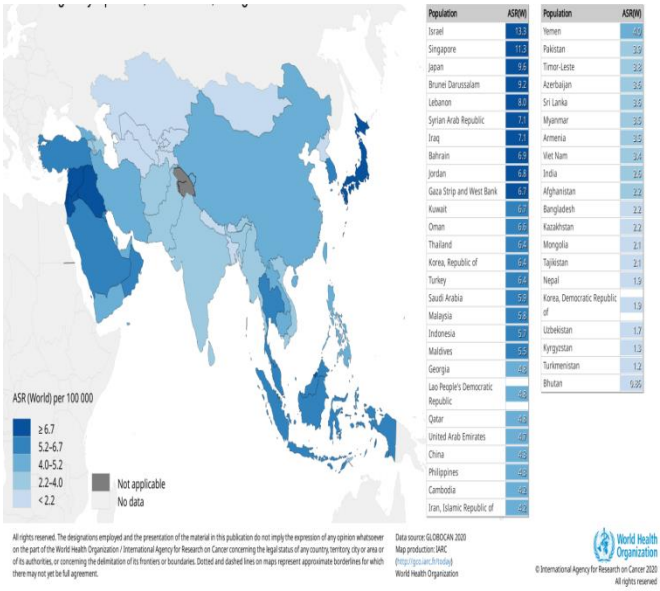

Figure 1: Estimated age-standardized incidence rates

(World) in 2020, NHL.(Globocan 2020)

Non-Hodgkin lymphomas (NHL) are a diverse category of lymphoproliferative tumours with a higher propensity for metastasis outside of lymph nodes and less predictable behaviour than Hodgkin's lymphomas. In most instances, nodal and extranodal sites are involved; however, about a quarter of NHL cases originate in extranodal areas [5]. In affluent nations, diffuse large B-cell lymphoma (about 30%) and follicular lymphoma (approximately 20%) are the most prevalent subtypes of NHL [6]. Other subtypes of NHL are far less common, occurring in less than 10% of cases. After prostate, breast, lung, colon, and bladder cancers, NHL is the sixth leading cause of cancer mortality in the United States [7]. Squamous cell carcinoma is the most frequent oral cancer. However, oropharyngeal lymphomas are also quite prevalent [4]. In this review, we try to express the current condition of NHL & the treatment approach to this disease.

Search and Selection Criteria

Using the phrases "lymphoma," "NHL," "Bangladesh," "therapy," "epidemiology," and "incidence," we searched PubMed, Google Scholar, and the references of pertinent papers. Due to the lack of studies from Bangladesh, we only considered primary articles, reviews, and case reports on fewer than 30 cases published in English after January 1, 1995. We also looked through the International Agency for Cancer Research's website and their databases "Globocan," "Cancer Incidence in Five Continents," "Survcan," and other books and journals on cancer in Bangladesh.

Current Status of NHL in Bangladesh

Lymphomas originate in the lymphoreticular system and are the third most frequent tumour seen in the head and neck area. Hodgkin disease and non-Hodgkin lymphoma are the two main types of malignant lymphomas (NHL). Nearly five percent of all head and neck cancers are NHL, and its wide variety of symptoms and physical manifestations is reminiscent of Hodgkin's disease. Head and neck lymphomas may be either Hodgkin's or non-Hodgkin's, and although both types can affect lymph nodes, NHL patients more often have the extranodal disease. Waldeyer's ring (the tonsils, throat, and base of the tongue), the salivary glands, the orbit, the paranasal sinuses, and the thyroid glands are examples of extranodal sites of involvement. While there are a few other ways to put NHL into categories, the WHO classification for lymphoid neoplasms is the most often used [4].

Table 1: Incidence, mortality and prevalence by Globocan 2020

Incidence, Mortality and Prevalence by cancer site

	New cases				Deaths				5-year prevalence (all ages)	
Cancer	Number	Rank	(%)	Cum.risk	Number	Rank	(%)	Cum.risk	Number	Prop. (per 100 000)
Oesophagus	21 745	1	13.9	1.69	20 319	1	18.6	1.58	23 372	14.19
Lip, oral cavity	13 985	2	8.9	1.12	8 137	3	7.5	0.68	29 536	17.93
Breast	13 028	3	8.3	1.83	6 783	4	6.2	1.03	31 232	38.35
Lung	12 999	4	8.3	1.18	12 003	2	11.0	1.08	13 915	8.45
Cervix uteri	8 268	5	5.3	1.16	4 971	7	4.6	0.76	18 132	22.27
Stomach	7 599	6	4.8	0.61	6 642	5	6.1	0.55	10 235	6.21
Hypopharynx	7 476	7	4.8	0.63	3 151	9	2.9	0.29	9 542	5.79
Gallbladder	7 252	8	4.6	0.55	5 742	6	5.3	0.43	9 399	5.71
Larynx	5 270	9	3.4	0.46	3 219	8	3.0	0.31	11 457	6.96
Oropharynx	3 852	10	2.5	0.31	2 377	11	2.2	0.20	7 711	4.68
Non-Hodgkin lymphoma	3 327	11	2.1	0.24	1 998	14	1.8	0.15	7 692	4.67
Liver	3 261	12	2.1	0.25	3 139	10	2.9	0.25	3 560	2.16
Ovary	3 122	13	2.0	0.43	2 096	13	1.9	0.34	7 044	8.65
Leukaemia	2 812	14	1.8	0.16	2 132	12	2.0	0.13	6 912	4.20
Colon	2 753	15	1.8	0.21	1 772	15	1.6	0.13	5 408	3.28
Rectum	2 530	16	1.6	0.18	1 467	16	1.3	0.10	5 185	3.15
Prostate	2 441	17	1.6	0.39	1 289	18	1.2	0.18	4 578	5.50
Bladder	1 719	18	1.1	0.15	920	21	0.84	0.08	3 786	2.30
Thyroid	1 526	19	0.97	0.10	359	26	0.33	0.04	3 935	2.39
Kidney	1 519	20	0.97	0.12	969	20	0.89	0.08	3 220	1.96
Pancreas	1 448	21	0.92	0.12	1 404	17	1.3	0.11	1 379	0.84
Brain, central nervous system	1 284	22	0.82	0.09	1 144	19	1.0	0.08	2 898	1.76
Corpus uteri	1 049	23	0.67	0.18	376	25	0.34	0.07	2 563	3.15
Salivary glands	882	24	0.56	0.07	591	24	0.54	0.05	2 233	1.36
Nasopharynx	872	25	0.56	0.07	670	23	0.61	0.05	2 107	1.28
Multiple myeloma	805	26	0.51	0.07	728	22	0.67	0.06	1 590	0.97
Penis	640	27	0.41	0.09	246	28	0.23	0.04	1 618	1.94
Hodgkin lymphoma	548	28	0.35	0.03	213	29	0.20	0.01	1 473	0.89
Melanoma of skin	457	29	0.29	0.04	278	27	0.26	0.02	1 078	0.65
Testis	439	30	0.28	0.04	107	33	0.10	0.01	1 331	1.60
Anus	381	31	0.24	0.03	196	30	0.18	0.02	777	0.47
Vulva	264	32	0.17	0.05	136	31	0.12	0.02	690	0.85
Vagina	262	33	0.17	0.05	125	32	0.11	0.02	576	0.71
Mesothelioma	11	34	0.01	0.00	9	34	0.01	0.00	10	0.01
Kaposi sarcoma	0	35	0	0	0	35	0	0	0	0
All cancer sites	156 775	-	-	11.45	108 990	-	-	8.41	270 866	164.5

There was a considerable gender difference in the prevalence of haematological malignancies (HM), with 3468 men (69.2%) and 1545 females (30.8%) sampled from a survey of 5013 cases collected from eleven tertiary institutions. 3.38 out of every 100 people diagnosed with a haematological malignancy were younger than 20 (6.7%). The most common HM in Bangladesh was AML (28.3%), with a median age of 35 years; the median age for NHL was 48 years [8].

Table 2: Cases of hematological malignancies in Bangladesh from 2008 -2012

HM types	Cases	Distribution (%)
AML	**1417**	**28.3**
CML	**912**	**18.2**
ALL	**706**	**14.1**
CLL	**183**	**3.7**
NHL	**846**	**16.9**

HL	**196**	**3.9**
MM	**528**	**10.5**
MDS	**225**	**4.5**
Total	**5013**	**100**

From September 2018 through October 2019, the duration of this research, we collected data on 1100 haematological neoplasm (HN) instances. The lymphoid neoplasm was the most prevalent haematological malignancy, accounting for 60.0% of the total cases. This was followed by the myeloid neoplasm, which accounted for 40% of the real cases. The overall median age of 55 was present at the time of diagnosis for all haematological cancers. In this study, we identified HL at a frequency of 5.6% and NHL at a rate that included DLBCL at 5.5%, FL at 1.8%, MCL at 0.9%, MZL at 0.9%, PEL at 0.9%, PMBCL at 0.9% [11].

Cancer Registry in Bangladesh

A cancer registry is a database that stores information on cancer patients and their treatment. The primary function of a cancer registry is cancer registration, which is the systematic, ongoing collection of data on the types, prevalence, and treatment outcomes of cancer in all of its forms, as well as the demographics and lifestyles of those who have been diagnosed with it. In the United States, cancer registration is the cornerstone approach to systematically collecting data on cancer incidence and types, cancer site, disease stage at diagnosis, treatments received, and therapy and clinical management results. 14 Cancer registries are an invaluable tool for clinical and epidemiological studies because they include information on the disease's prevalence in the general population [9]. The obtained information may be used for various purposes, including but not limited to statistical analyses, unique research, reporting obligations, and program evaluations by the medical staff, hospital management, and other healthcare professionals. A sophisticated health information system would thus include cancer registration. When gathering data to arrange strategies to reduce cancer rates, the cancer registry is a cost-effective and efficient option. There has been a significant increase in cancer registries, with over 250 population-based cancer registries now active in more than 60 countries. More and more clinical and epidemiological studies are using these registries' growing maturity [10]. There are two significant types of cancer registries: a) Hospital-based registries and b) Population-based registries.

Hospital-based registries

Two types of hospital registers exist individual hospital registries and group registries. All cancer cases diagnosed and treated at a hospital are recorded in a cancer registry. Clinical treatment and institutional management are at the heart of the hospital-based cancer registry [12].

Population-based registries

Population-based registries focus on epidemiology and public health by documenting all new cases in a specified population (often a geographical region such as a state). There are two types of population-based registries: those that record all malignancies and those that focus on one specific location, age range, or both [12].

Present Treatment in Bangladesh

According to Globocan 2020 projections, around 1.9 million people worldwide were diagnosed with cancer in 2020. More than 1.2 million people have been affected by various blood cancers, including non-Hodgkin's and Hodgkin's lymphoma, leukaemia, and myeloma. According to the same statistics, about one and a half million new people are diagnosed with cancer in a year in Bangladesh, among which more than seven thousand people are affected by various blood cancers. Non-Hodgkin and Hodgkin lymphoma, leukaemia, and myeloma belong to blood cancers. Treatment also varies depending on the disease's type and stage or risk. Many blood cancers can be cured with good treatment. The condition is treated with oral medications, chemotherapy, targeted therapy, immunotherapy and, when applicable, radiation therapy. Drug efficacy is monitored through disease monitoring, and drug dosage may be changed if necessary. If the disease progresses, long-term treatment of the disease is possible through hematopoietic cell transplantation or bone marrow transplantation**.**

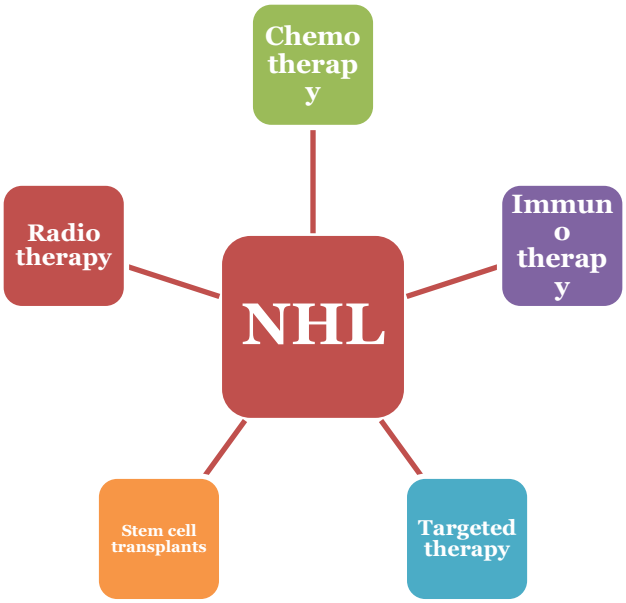

Figure 2: Available treatment in Bangladesh at present.

Chemotherapy

From a meta-analysis, 13 chemo-treatment protocols were examined for therapeutic efficacy and survival outcomes in patients with NHL. The statistical results regarding OS, CR, and relative ranking could serve as supportive information to optimize the treatment strategy based on individual disease conditions after direct evidence was extracted from 14 individual publications and both direct and indirect data were synthesized through network analysis. The aforementioned findings indicate that CNOP and VMP are the least effective treatment options. The third-generation chemotherapy regimen ProMACE-CytaBOM had better OS results; however, its superiority was not maintained in CR. R-HDS performed poorly in terms of OS. However, its CR performance was astounding. In addition, R-CHOP, the standard gold treatment for DLBCL according to the International Prognostic Index, ranked first in 3-year and 5-year overall survival, indicating its value in achieving a more excellent long-term prognosis than all other types of NHL, while I-CHOP was effective in short-term survival outcomes [20].

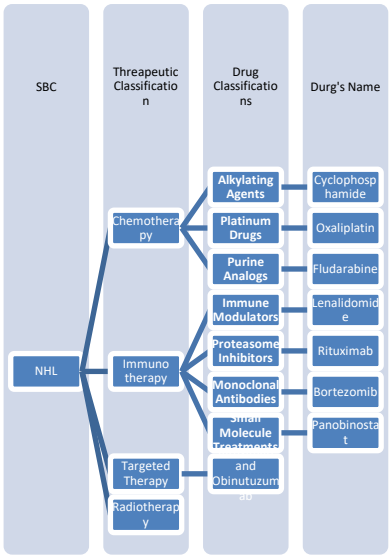

Figure 3: Recent available therapeutics for non-hodgkin's lymphoma (NHL). SBC = Solid Blood Cancer.

Immunotherapy

The cell surface antigens expressed by B-cells make them targets for specific monoclonal antibodies (MAB) classes. MAB was established in 1975. Anti-CD20, a monoclonal antibody (MAB) targeting a cell surface antigen [13], CD-20, of B-cell lymphoma, was the first immunotherapy to receive extensive study. This antigen is expressed uniformly among B-cells but is absent from precursor stem cells [14]. Whether used in the first line of treatment or as an R/R option, rituximab as a chimeric anti-CD20 is essential for the treatment of NHL. The Food and Drug Administration (FDA) approved it in 1997, and European regulators gave the green light to use it in a variety of settings in 1998, including as first-line therapy [15], second-line therapy, maintenance, or in combination with chemotherapy [16].

The similarity in efficacy and functionality between rituximab and the chimeric anti-CD20 biosimilar rixathon was observed in NHL; the only significant differences were observed for the biosimilar concerning size and charge heterogeneity, as well as glycosylation pattern [17]. The FDA approved anti-CD20 biosimilar Ruxience in 2020 for use in NHL, and its efficacy and safety were demonstrated in the Reflections B3281006 study, in which it was directly compared to rituximab in low tumour burden FL [18], with no discernible difference shown in terms of clinical benefits or safety profile [19].

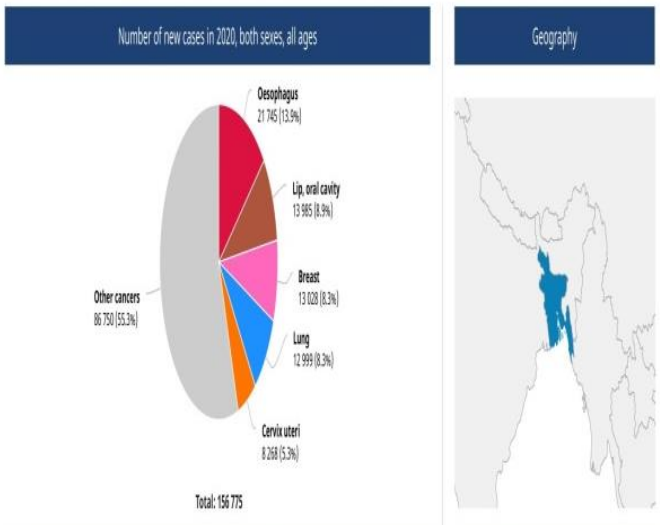

Figure 4: Number of cancer cases of Bangladesh in 2020.

Conclusion

The World Health Organization recommends one cancer centre for every one million people. In contrast, Bangladesh has just 20 or 22 service centres for its 17 crore people. Since it is a developing nation, Bangladesh is struggling with various issues related to health care. Cancer is the leading cause of death worldwide, taking more lives yearly than TB, HIV/AIDS, and malaria. It's important to note that haematological malignancies (HM) are not uncommon in the United States. All demographics, regardless of age or gender, are vulnerable. Cancers of the blood and immune system are often referred to as haematological malignancies. Both communicable and non-communicable diseases are a significant problem in Bangladesh, causing a double illness burden. Therefore, it will not be a simple task for Bangladesh to see a dramatic change in the cancer situation overnight. It is critical to have accurate information regarding the cancer burden in Bangladesh. Therefore, a disability-adjusted life year, years of life lost owing to early death in the population, years lost due to disability, and an overall health impact assessment (HIA) for cancer are all things that need to be determined. When policymakers in Bangladesh realize that cancer creates a significant burden on the country's health care system as well as a financial loss, they may develop an interest in these issues.

Abbreviations

HM: Hematological malignancies;
AML: Acute myeloid leukemia;
ATCL: primary mediastinal B cell lymphoma
ALL: Acute lymphoblastic leukemia;
CML: Chronic myeloid leukemia;
CLL: Chronic lymphocytic leukemia;
DLBCL: Diffuse large B cell lymphoma;
FL: Follicular lymphoma;
NHL: Non-Hodgkin lymphoma;
HL: Hodgkin's lymphoma;
MM: Multiple myeloma;
MCL: Mantle cell lymphoma;
MDS: Myelodysplastic syndromes;
MZL: Marzinal zone lymphoma;
PEL: Primary effusion lymphoma;
PMBCL: Primary mediastinal B cell lymphoma

Competing interests

The authors declare that they have no competing interests.

Reference

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence, mortality and prevalence worldwide in 2012: GLOBOCAN 2012 v1.0. Lyon, France: International Agency for Research on Cancer.
2. Story HL, Love RR, Salim R, Roberto AJ, Krieger JL, Ginsburg OM. Improving outcomes from breast cancer in a low-income country: lessons from Bangladesh. Int J Breast Cancer. 2012.
3. Wasim BH, Mohammad AM. State of cancer care in Bangladesh. The Daily Star. 2022.
4. Singh R, Shaik S, Negi BS, Rajguru JP, Patil PB, Parihar AS, Sharma U. Non-Hodgkin's lymphoma: A review. J

Family Med Prim Care. 2020 Apr 30;9(4):1834-1840. http://doi.org/10.4103/jfmpc.jfmpc_1037_19
5. Bowzyk Al-Naeeb A, Ajithkumar T, Behan S, Hodson DJ. Non-Hodgkin lymphoma. BMJ. 2018; 362, 3204.
6. Ekstrom-Smedby K. Epidemiology and etiology of non-Hodgkin lymphoma-A review. Acta Oncol. 2006; 45: 258–71.
7. Kolokotronis A, Konstantinou N, Christakis I, Papadimitriou P, Matiakis A, Zaraboukas T, et al. Localized B-cell non-Hodgkin's lymphoma of oral cavity and maxillofacial region: A clinical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005; 99: 303–10.
8. Hossain MS, Iqbal MS, Khan MA, Rabbani MG, Khatun H, Munira S, Miah MM, Kabir AL, Islam N, Dipta TF, Rahman F, Mottalib A, Afrose S, Ara T, Biswas AR, Rahman M, Abedin AM, Rahman M, Yunus AB, Niessen LW, Sultana TA. Diagnosed hematological malignancies in Bangladesh - a retrospective analysis of over 5000 cases from 10 specialized hospitals. BMC Cancer. 2014; 14:438. http://doi.org/10.1186/1471-2407-14-438.
9. Jensen OM, Storm HH. Purposes and uses of cancer registration. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG (eds). Cancer registration: principles and methods. IARC scientific publication 95. Lyon: International Agency for Research on Cancer, 1991: 7-21.
10. Coleman M, Wahrendore J, Demaret E (eds). Directory of on-going research in cancer epidemiology. IARC scientific publication 117. Lyon: International Agency for Research on Cancer, 1992: 7-21.
11. Rahid S.M, Hafiza L,, Durba H, Shahjada. Hematological Malignancies Pattern among Bangladeshi Adult. Jour Med Sci Clin Res. 8(5), 2020.
12. Shariful A. Cancer Registry and Its Different Aspects. J Enam Med Col 2011; 1(2): 76-80.
13. Karmali R.Rituximab: A benchmark in the development of chemotherapy-free treatment strategies for follicular lymphomas. Ann onco, 2021, 29(2), 332-340, http://doi.org/10.1093/annonc/mdx768
14. Czuczman MS, Weaver R, Alkuzweny B, Berlfein J, Grillo-López AJ. Prolonged clinical and Molecular remission in patients with low-grade or Follicular Non-Hodgkin's Lymphoma treated With Rituximab plus CHOP chemotherapy: 9-Year Follow-Up. Jour Clin Onco, 2004, 22(23), 4711-4716, http://doi.org/10.1200/jco.2004.04.020
15. Fanale M, Younes A. Monoclonal Antibodies in the Treatment of Non-Hodgkin's Lymphoma, Adis Data Information BV. The University of Texas M.D. Anderson Cancer Center. 2007.
16. MH van Oers, Klasa R, Marcus RE. Rituximab maintenance improves clinical outcome of relapsed/resistant follicular non-Hodgkin lymphoma in patients both with and without rituximab during induction: Results of a prospective randomized phase 3 intergroup trial. Blood, 2006, 108(10), 3295-3301.
17. Visser J. Physicochemical and Functional Comparability Between the Proposed Biosimilar Rituximab GP2013 and Originator Rituximab. Bio Drugs, 2013, 27, 495-507.
18. Sharman J. A randomized, double-blind efficacy and safety study of PF-05280586 (a potential rituximab biosimilar) compared with rituximab reference product (Mabthera®) in subjects with previously untreated CD20-positive, low tumor burden follicular lymphoma (LTB-FL) Blood, 2018. 394, http://doi.org/10.1182/blood-2018-99-111248
19. Robak T. New anti-cd20 monoclonal antibodies for the treatment of b-cell lymphoid malignancies. BioDrugs: clinical immunotherapeutics, biopharmaceuticals and gene therapy, 2011, 25(1), 13-25, http://doi.org/10.2165/11539590-000000000-00000
20. Cai P, Hao J, Wang D, Xu J. Comparative efficacy of different chemotherapies for non-Hodgkin lymphoma: a network-meta analysis. Oncotarget. 2017 Aug 24;8(53):91238-91247. http://doi.org/10.18632/oncotarget.20437.