**A notable Impact of Rituximab in Managing Follicular Lymphoma:A Case Report and Review of Management Strategies.**

**Abstract:**

**Aim**

This case report aims to re-emphasize the renewed hope for distressed patients with follicular lymphoma. It highlights the tremendous positive impact of rituximab-based immunochemotherapy in a patient treated at Redeemers Health Village, a multi-specialty tertiary academic hospital located in the Southwestern region of Nigeria while also reviewing the management strategies.

**Presentation of case**

This report describes the case of a 45-year-old Uber driver who was diagnosed with stage IVB follicular lymphoma (FL). The patient was categorized as high-risk according to the Follicular Lymphoma International Prognostic Index (FLIPI) at Redeemers Health Village, a multi-specialty tertiary academic hospital in Western Nigeria. The patient underwent a complete treatment course of rituximab combined with chemotherapy. This treatment resulted in significant clinical improvement, transforming the patient from one with a high tumour burden to one full of vigour and vitality.

**Discussion**:

Until recently, the treatment for FL has been quite challenging. The three-year event-free survival (EFS) and overall survival (OS) rates with CHOP regimen were previously as low as 30% and 35% to 40%, respectively. However, the outlook significantly improved after the introduction and approval of rituximab for use alongside CHOP in 1997 and 2006, resulting in EFS and OS rates 95% and 70% respectively. Although rituximab-based therapy has only recently become widely available, its inclusion in routine treatment regimens has provided renewed hope and improved overall survival for our patients. Similarly, while exploring other anti-CD20 targeted therapies, Obinutuzumab has emerged as an effective alternative monoclonal antibody that shows promise. In those with transformed FL (DLBCL), relapsed or refractory FL (grade 1 to 3A), innovative therapies, such as bispecific T-cell engager (BiTE) therapy (e.g., Mosunetuzumab and Glofitamab), and chimeric antigen receptor T-cell therapy (e.g., Tisagenlecleucel, and Axicabtagene ciloleucel), are expected to enhance patients’ outlooks, and provided reassurance that regaining a pre-morbid state of health is possible.

**Conclusion**

Managing non-Hodgkin lymphoma (NHL), including follicular lymphoma, has historically posed significant challenges. The availability of rituximab has notably improved treatment outcomes for NHL overall. Exploring other anti-CD 20 alternatives such as Obinutuzumab, along with innovative therapies like bispecific T-cell engager (BiTE) therapy and chimeric antigen receptor T-cell (CAR T-cell) therapy, will further enhance the prospects for these patients. The possibility of regaining their pre-morbid state of health is increasingly reassuring.

Keywords: Lymphadenopathy, Chromosomal translocation, FLIPI, Rituximab, Tumour regression, overall survival.

**Introduction**

Follicular lymphoma (FL) is characterized by the uncontrolled growth of malignant germinal center B cells (GCBs). These cancerous cells coexist with non-malignant cells, including T cells, follicular dendritic cells, and macrophages. In follicular lymphoma, the primary cell types are centrocytes and centroblasts, which typically exhibits a follicular growth pattern. [1] Therefore, FL is subclassified according to the cytological grade based on the proportion of centroblasts.[1, 2] Notably, FL designated as grade 1-2 or grade 3A are positive for the BCL2 rearrangement (BCL2R) in 85% of cases, FL grade 3B is most often negative for BCL2R, and more closely related to diffuse large B-cell lymphoma.[3,4] Follicular Lymphoma is the second most common form of NHL accounting for about 20 to 30% of all non-Hodgkin lymphoma (NHL).[5] It is typically found in the United State and Europe but rare in the rest of the world. Follicular lymphoma is a slow growing tumour with no gender preponderance, it increases with age, and its median age at diagnosis is 64. [3,5,6,7,]. Many aetiological factors have been linked to the development of follicular lymphoma including viruses, Epstein-Barr virus (EBV), Human T cell Lymphotropic virus type 1 (HTLV-1), Human herpes virus-8 (HHV-8), Hepatitis B virus (HBV) and Hepatitis C virus (HCV), Chemicals, immunodeficiency states, immunosuppressants, autoimmune disease, and chromosomal translocation. [5,8] The hallmark of FL developing in 80-85% of cases is in the genetic change in the chromosomal translocation involving t (14:18) ;(q32; q21) in the pro B cells or pre-B cells in the bone marrow, and this translocation, results in the B-cell lymphoma 2 (BCL2) gene being placed under the control of the immunoglobulin heavy-chain enhancer (IgH), specifically the Eµ. [9, 5,17,18, 20] This leads to the continuous overexpression of the BCL2 protein.[3] This overexpression allows B cells to escape the usual apoptotic program that occurs in the germinal center. FL as in most tumours, exhibit recurring genetic alterations, including gains (1q, 2p, 8q, 12q & 18q), losses (1p, 6q, 10q & 13q), and mutation in the genome JAK (Janus associated Kinase) signal, BCR (B-cell receptor) pathways, MYD88 (Myeloid differentiation primary response 88), and NOTCH (Neurogenic locus homolog) pathway; this phenomenon provided a growth advantage to the cancer cells. [5,10]

This case report aims at re-emphasising the rejuvenated vigour in a patient with a high tumour-burden arising from a follicular lymphoma, and highlighting the tremendous positive impact of rituximab-based chemoimmunotherapy in a patient treated at Redeemers Health Village, a multi- specialist tertiary academic hospital located in the Southwestern region of Nigeria, while also reviewing the Management Strategies.

**Presentation of Case**

A 45-year-old Uber driver, presented to the haematology clinic of the Redeemers Health Village with an 18-month history of generalized lymphadenopathy. The painless lymph node enlargement began with the preauricular nodes and subsequently extended to other groups of lymph nodes. He experienced intermittent fevers and significant weight loss, along with recurrent episodes of easy fatiguability. Patient reported no bleeding disorders, blood transfusion or exposure to obnoxious chemical substance.

On physical examination, the patient was chronically ill but without distress. There were no petechial lesions, and no oedema was observed in the extremities. He exhibited generalized painless lymphadenopathy involving the following node groups: Pre- and Post- auricular: 8x3cm, 8x2cm, 6x6cm, and 6x4cm. Cervical: 6x4cm, Submandibular: 4x4cm, Bilateral axillary (right: 10x11cm, left: 10x9 cm), Inguinal (right: 9x6cm, left: 9x6cm) and left popliteal: 4x4cm.

Chest and cardiovascular examinations revealed no abnormalities. Abdominal examination did not show any palpable organomegaly; however, multiple intra-abdominal masses were affirmed. The assessment of the central nervous system also revealed no remarkable findings.

The result of the lymph node biopsy conducted, shows a complete loss of the nodal architecture, which has been replaced by small, uniform lymphoid cells primarily organized in sheets, exhibiting indistinct, closely packed follicular patterns. The individual cells display oval, hyperchromatic nuclei with clumped chromatin, inconspicuous nucleoli, and scant amphophilic cytoplasm. Immunohistochemistry (IHC) revealed positive results for CD 20, CD45, and BCL2, while CD3, CD4, CD5, AE1/AE3 and CD23 were all negative.

The peripheral blood film showed marked lymphocytosis, with lymphoid cells pleomorphism. Majority of the cells were small, spherical, and with scant cytoplasm, while the nuclear chromatin appeared compact and coarse. A few smudged cells were observed. Also revealed were mild to moderate neutopaenia, adequate platelets number and a normocytic and normochromic red cells morphology. [fig 1]

Bone marrow aspiration revealed lymphoid infiltration with mild depression of erythropoiesis and myelopoiesis. The megakaryopoiesis were intact. [fig 2]

The patient tested negative for Hepatitis B surface antigen, Hepatitis C virus, and human immunodeficiency virus. A chest x-ray showed normal findings, C-reactive protein (CRP) level was 7mg/dL (reference range: 0 -10mg/dL) The results of the other biochemical and haematological parameters are summarized in Table 1.

Based on these findings, the patient was diagnosed with Follicular lymphoma, classified as Ann Arbor stage IV and categorized as high risk according to the Follicular lymphoma International Prognostic Index (FIPI). [15]

The patient was counselled about the nature of the disease, its prognosis, and the available treatment options, including the standard first-line treatment.[3] Based on the patient’s body surface area of 1.7m2, intravenous Rituximab (375mg/m2) was administered in combination with cyclophosphamide (650mg/m2), Adriamycin (50mg/m2), Vincristine (1.4mg/m2), ensuring that the Vincristine dose did not exceed 2mg per dose (R-CHOP). Additionally, Prednisolone (40mg/m2) was included in the regimen. This treatment was administered in a three-week cycle for a minimum of six (6) cycles and a maximum of eight (8) cycles.[14]

To prevent Tumour lysis Syndrome, a xanthine oxidase inhibitor, Allopurinol (150mg twice daily), was administered prior to the commencement of intravenous R-CHOP. Additionally, acetaminophen, and an antihistamine were given as premedication for rituximab on Day1.

Biochemical and haematological parameters were monitored throughout the duration of the R-CHOP therapy. Due to the cardiotoxic effects of Adriamycin, electrocardiogram (ECG) reading was monitored periodically. The patient’s general condition before and after R-CHOP treatment is illustrated in Fig. 3 and Fig. 4, respectively.

**Table 1: Biochemical and Haematological parameters**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cycle of treatment** | **BIOCHEMICAL PROFILE** | | | | | | **LIVER FUNCTION TEST** | | | | | | **HAEMATOLOGY PARAMETERS** | | | | | |
| LDH  U/L | URIC ACID  µmol/L | CAL  mmol/L | PO4  mmol/L | CR-  µmol/L | UREA  µmol/L | T.BIL µmol/L | ALT U/L | AST  U/L | ALP  U/L | GGT  U/L | ALB  g/L | WBCX 109/l | NEUT% | LYMP% | HBg/dL | PCV  % | PLATELET  X 109/l |
| 1 | 355 | 382.1 | 2.3 | 1.2 | 70.1 | 5.1 | 8.13 | 16.6 | 27.7 | 84.1 | 46.2 | 47.9 | 47 | 2.6 | 96.2 | 11.9 | 34.1 | 158 |
| 2 | 167.2 | 187.7 | 5.04 | 0.88 | 87.4 | 2.5 | 6.57 | 27.1 | 18.9 | 72 | 73.8 | 45.1 | 19.6 | 3.2 | 96.2 | 10.9 | 31.5 | 174 |
| 3 | 262 | 247.6 | 3.41 | 1.38 | 86.5 | 3.06 | 4.01 | 14.3 | 20.9 | 73.7 | 49.9 | 48.9 | 7.37 | 15 | 81.9 | 10.7 | 30.8 | 250 |
| 4 | 312.6 | 274.9 | 1.89 | 1.04 | 88.1 | 2.1 | 6.18 | 16.9 | 12.9 | 62.9 | 36.3 | 48 | 3.62 | 8.7 | 84.9 | 11.4 | 33.2 | 164 |
| 5 | 617.9 | 274.9 | 2.34 | - | 100.2 | 3.5 | 6.36 | 13.8 | 14.1 | 70.9 | 43.3 | 47.7 | 4.24 | 21.8 | 75 | 12.1 | 36.2 | 198 |
| 6 | 617 | - | 2.46 | 0.22 | 87.1 | 2.2 | 5.8 | 17.5 | 23.9 | 66.1 | 69.2 | 46.2 | 3.1 | 8.8 | 83.4 | 11.1 | 35 | 166 |

Reference ranges: LDH [140 - 248 U/L], Calcium [2.2 - 2.265 mmol/L], Uric acid [214 -488µmol/L], P04 [0.8 -1.45 mmol/L], Cr- (59-104µmol/L), Urea (2.8-7.2 mmol/L) , ALT (7-45U/L), AST (8-35U/L), ALP (40-129U/L), T.BIL (2-21µmol/L), GGT (5-78IU/L), ALB (34-53g/L), WBC (2-8 X 109/l ), HB (12-18g/dL), PCV (39-54 %), Platelet (100 - 400)

Figure 1: Peripheral Blood Film Figure 2: Bone Marrow Aspiration

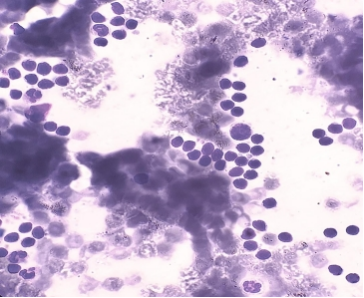
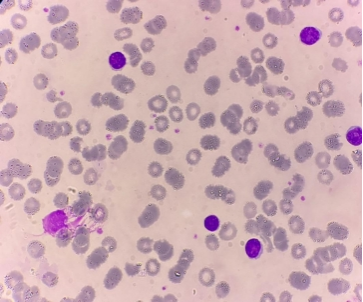
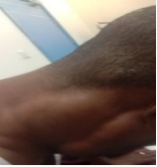
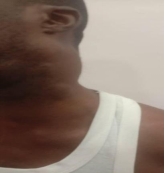


Figure 3: Before R-CHOP Therapy

A B C D



E F

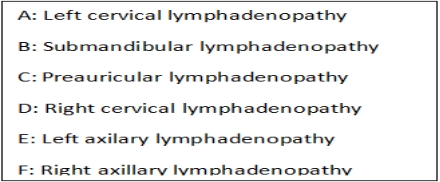
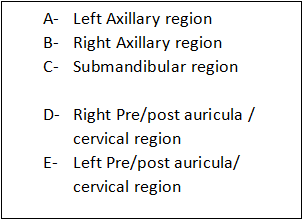
 

Figure 4: Post R-CHOP Therapy

A B C

D E

**Discussion**

Follicular lymphoma is a slow-growing tumour, and until recently, its treatment has posed a significant challenge. Traditionally, treatment relied heavily on a combination of cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP).[3] Before the introduction of rituximab, this treatment regimen had limited effectiveness, particularly for low-grade lymphomas. Some studies [11,13,14,15] have shown that the CHOP chemotherapy regimen achieved complete responses (CRs) in only 40% to 50% of the patients with this condition. Additionally, the three-years event-free survival (EFS) and overall survival (OS) rates were as low as 30% and 35% to 40% respectively. [13] The outlook for patients improved substantially following the introduction and approval of rituximab for use in 1997 and 2006 resulting in EFS and OS rates of 95% and 70% respectively. [11, 12, 13 14,15] Despite the long period history of rituximab and other targeted monoclonal antibodies in developed countries, these therapies have only recently become widely available but rarely affordable in developing nations. [16]

The management of follicular lymphoma depends on the stage of the disease and its progression. According to the Ann-Arbor classification, follicular lymphoma is categorized into four stages based on the extent of disease spread. Stages I and II indicate localized disease, while stages III and IV represent advanced disease. The treatment approach is tailored according to these stages. For asymptomatic patients with limited or localized disease, a watchful waiting strategy may be employed. Those with symptomatic localized disease might benefit from localised radiotherapy. For patients with advanced disease, treatment typically involves targeted therapies using rituximab, either as a standalone treatment or in combination with chemotherapy. Patients with poor performance status tend to benefit from non- chemotherapeutic targeted therapies such as anti-CD 20 (rituximab, Obinutuzumab), Bruton’s tyrosine kinase (BTK) inhibitors (Zanubrutinib), and B-cell lymphoma 2 (BCL-2) inhibitors (venetoclax) rather than from chemoimmunotherapy. [14, 15, 16]

The outcomes for patients with follicular lymphoma primarily depend on the lymphoma’s grade and the risk assessment determined by the Follicular Lymphoma International Prognostic Index (FLIPI). [15] The grading system evaluates the percentage of centroblasts present in the germinal center: low-grade FL indicates 0-5 centroblasts, intermediate-grade shows 6-15 centroblasts, and high-grade lymphoma contains more than 16 centroblasts. [3,4]

The FLIPI score is essential for risk stratification and takes into account several factors, including age over 60, elevated lactate dehydrogenase (LDH) levels, involvement of more than three lymph node areas, Ann Arbor stage III or IV, and a haemoglobin concentration of less than 12g/dL.[15] In the case presented, the patient was diagnosed with advanced follicular lymphoma classified as stage IVB and had a FLIPI score of 3. This score was attributed to elevated LDH levels, involvement of more than four lymph node areas, and a haemoglobin concentration below 12g/dL.

Considering these factors, the patient received detailed counselling about treatment options, treatment cycles, duration, and maintenance. Given the patient’s good performance status, a standard rituximab-containing regimen, R-CHOP, was administered along with all necessary precautions to prevent adverse reactions.

The bulky generalized lymphadenopathy significantly shrank, reaching nearly insignificant dimensions. This positive response was also reflected in the white cell count, which decreased from an initial 45 x 109/L (with a predominance of lymphocytosis) to 4.3 x 109/L by the end of the six cycles of therapy. Throughout treatment, both renal and liver function parameters remained within the reference ranges, and the patient’s haematocrit value increased from an initial 29% to 35%. These positive changes alongside the patient’s improved psychological well-being, contributed to an overall favourable clinical condition.

Assuming no relapse occurs, the remission-induction phase is expected to transition to eight weekly maintenance doses of rituximab (375mg/m2). In the event of relapse or refractoriness, intravenous rituximab monotherapy at 375mg/m2 weekly for four to eight weeks would be the recommended intervention. [14, 15]

The introduction of rituximab into traditional treatment regimens has significantly improved progression-free survival, overall survival, and outlook for patients with follicular lymphoma.[15] It is essential to emphasize that while FL is not curable, life expectancy has improved to more than 10 years following rituximab-based therapy. Similarly, while exploring other anti-CD20 targeted therapies, Obinutuzumab has emerged as an effective alternative monoclonal antibody that shows promise. In those with transformed FL (DLBCL), relapsed or refractory FL (grade 1 to 3A), innovative therapies, such as bispecific T-cell engager (BiTE) therapy (e.g., Mosunetuzumab and Glofitamab) and chimeric antigen receptor T-cell therapy (e.g., Tisagenlecleucel, and Axicabtagene ciloleucel), are expected to enhance patients’ outlooks, and provided reassurance that regaining a pre-morbid state of health is possible. [16, 17, 19, 21, 22]

It is crucial to emphasize the financial burden, and the emotional and psychological challenges faced by this patient, as well as by many others with similar malignancies. Patients with malignancy often have to deal with the weight of their illness alongside significant financial struggles, especially in developing countries. Most individuals with malignancy, similar to the case discussed, must finance their own treatment due to the absence of supportive government policies that could help subsidize the high cost of care. For instance, the average cost of rituximab in Nigeria is approximately 350,000 Naira, which translate to approximately $224 at the current exchange rate of 1,562.5 Naira to a Dollar. Considering that the country’s monthly minimum wage is 70,000 naira (about $45) and the high unemployment rate, it becomes exceedingly difficult for cancer patients to afford their treatment without government assistance. Despite these challenges, the patient found a renewed sense of hope, energy, and optimism during and after the administration of rituximab-based therapy,

**Conclusion**

Managing non-Hodgkin lymphoma (NHL), including follicular lymphoma, has historically presented significant challenges. The availability of rituximab has notably improved treatment outcomes for NHL overall. Exploring other anti-CD 20 alternatives such as Obinutuzumab, along with innovative therapies like bispecific T-cell engager (BiTE) therapy and chimeric antigen receptor T-cell (CAR T-cell) therapy, will further enhance the prospects for these patients. The potential to regain their pre-morbid state of health is increasingly encouraging. [16, 17, 19, 21, 22]

**Limitation**

This case report is limited by nonavailability of positron emission tomography (PET) scan; an imaging study that enabled the determination of tumour response to treatment. As the time of this case report, a repeated evaluation of the bone marrow has not been carried out, however, this does not negate the positive outcome so far recorded in this patient.

**Recommendations**

In developing countries like Nigeria, the cost of treating haematological malignancies, as well as other types of cancer is substantial, and many affected patients belong to low socio-economic groups. Given this reality, along with the high mortality associated with the unaffordability of treatment, we strongly recommend that the government subsidize rituximab, other cancer agents, and the full spectrum of cancer patient management through their respective health ministries.

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**Reference**

1. Pinter-Brown CL. Follicular Lymphoma Management Overview. Medscape. 2024. [https://emedicine.mescape.com/article/203268-overview#a1](file:///C:\Users\drami\Desktop\Impact%20of%20Rituximab%20on%20the%20Quality%20of%20Life%20of%20Follicular%20Lymphoma%20Patient%202.docx#a1)
2. Kaseb H, Ali AM, Gasalberti PD, Koshy N. Follicular Lymphoma. 2024 SatPearls Publishing. Available at [www.ncbi.nlm.nih.gov.](http://www.ncbi.nlm.nih.gov.) accessed 12/3/2025
3. Kridel R, Sehn HL, Gascoyne DR. Pathogenesis of follicular lymphoma. J Clin Invest. 2012;122(10):3424-3431. dol:10.1172/JC163186.
4. Zhou T, Pittaluga S, Jaffe SE. Molecular insights into the pathogenesis of follicular lymphoma. Annals of Lymphoma. 2021;5. Available at aol.amegroups.org
5. (Carreras J. The pathobiology of follicular lymphoma. Journal of clinical and experimental hematopathology. 2023;63(3), 152-163.
6. Lackraj T, Goswami R, Kridel R. Pathogenesis of follicullar lymphoma.Best Pract Res Clin Haematol. 2018;31(1):2-14. dol: 10.1016/j.beha.2017.10.006
7. Lymphoma Research Foundation [https://lymphoma.org/understanding-lymphoma/aboutlymphoma/nhl/follicular-lymphoma/.](https://lymphoma.org/understanding-lymphoma/aboutlymphoma/nhl/follicular-lymphoma/)
8. Zallio F, Limberti G, Ladetto M. Infections and Follicular Lymphoma: is there a Link? Mediterr J Hematol Infect Dis. 2017;9(1): e2017035. dol:10.4080/MJHID.2017.035. available at pmc.ncbi.nlm.nih.gov (accessed 12/3/2025)
9. [Stefano Luminari](https://pubmed.ncbi.nlm.nih.gov/?term=%22Luminari%20S%22%5BAuthor%5D) , [Monica Bellei](https://pubmed.ncbi.nlm.nih.gov/?term=%22Bellei%20M%22%5BAuthor%5D) , [Irene Biasoli](https://pubmed.ncbi.nlm.nih.gov/?term=%22Biasoli%20I%22%5BAuthor%5D) , [Massimo Federico](https://pubmed.ncbi.nlm.nih.gov/?term=%22Federico%20M%22%5BAuthor%5D) . Follicular lymphoma - treatment and prognostic factors.Rev Bras Hematol Hemoter. 2012;34(1):54–59. doi: [10.5581/1516-8484.20120015](https://doi.org/10.5581/1516-8484.20120015)
10. Lopez C, Mozas P, Lopez-Guillermo A, Bea S. Molecular Pathogenesis of Follicular Lymphoma: Genetics to Clinical Practice. Hemato 2022;3(4), 595-614
11. Selewski DT, Shah GV, Mody RJ, Rajdev PA, Mukherji SK. Rituximab (Rituxan). AJNR Am J Neuroradiol. 2010;31(7):1178-1180. dol:10.3174/a/jnr. A2142. Available at pmc.ncbi.nlm.nih.gov
12. Storz U. rituximab: How approval history is reflected by a corresponding patent filing strategy. mAbs. 2014; 6(4): 820-837. Available at https://doi.org/10.4161/mabs.29105
13. Mohammed R. How the discovery of rituximab impacted the treatment of B-cell non-Hodgkin’s lymphoma. Available at <https://www.rcpath.org>
14. Hanif N, Anwer F. Rituximab. StatPearls Publishing, 2024. Available at [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)
15. Johnston A, Salles G. Prognostic Systems for Lymphomas. Hematology/Oncology Clinics of North America. 2008;22(5):839-861. <https://doi.org/10.1016/j.hoc.2008.07.12>
16. Chen JC, ChoiYM, Heyman MB. Targeted Therapy in Follicular Lymphoma: Towards a Chemotherapy-Free Approach. Cancer. 2023; 15:4483. <https://doi.org/10.3390/cancers> 15184483
17. Bal E, Kumar R, Hadigol M, Holms BA,Hilton KL, Loh WJ et al. Super-Enhancer Hypermutation Alters Oncogene Expression in B-cell Lymphoma. Nature. 2022; 607(7920):808-815. doi:10.1038/s41586-022-04906-8
18. Ong J, Stevens S, Roeder, GR, Eckhardt LA. 3’IgH enhancer elements shift synergistic interaction during B cell development. J Immunol.1998;160(10):4896-903
19. Coornert B, Carpenter I, Beyaert R. A20: Central Gatekeeper in Inflammation and Immunity. Journal of Biological Chemistry. 2009; 284(13):8217-8221. <https://doi.org/10.1074/jbc.R800032200>
20. Ariizumi K, Wang Z, Tucker WP. Immunoglobulin heavy chain enhancer is located near or in an initiation zone of chromosomal DNA replication. Proc Natl Acad Sci. 1993;90(8):3695-9. doi:10.1073/pnas.90.8.3695. Available at https://pubmed.ncbi.nih.gov/8475117/#
21. Abdultalib AS, Brudno NJ. CAR T-Cell Therapies: Trends and Indications. The ASCO Post. August 10, 2023. Available at <https://ascopost.com/issues/august-10-2023/car-t-cell-therapies-trends-and-indication/>
22. Shen D. Bispecific T-Cell Engagers for Cancer Immunotherapy. GenScript, Available at https://www.genscript.com/learning-center/bispecific-t-cell-engers-for-cancer-immunotherapy.html