

**Objective Introduction:** The natural course of hepatitis B virus (HBV) infection is determined by the interaction between viral replication and the host's immune response. HBV persists in the body of all infected patients, even those with evidence of serological recovery. Therefore, individuals with a history of HBV infection receiving immunosuppressive therapy are at risk for HBV reactivation. HBV reactivation can result in increased serum aminotransferase levels, fulminant liver failure, and/or death. HBV reactivation has been described in patients receiving chemotherapy for various hematological and solid tumors. We present our patient with a diagnosis of chronic lymphocytic leukemia (CLL) who was spontaneously reactivated during follow-up without treatment. **Case report:** A female patient, who had been followed up with the diagnosis of chronic lymphocytic leukemia for 13 years without treatment, presented in August 2022 with complaints of loss of appetite, weight loss, and jaundice in the eye. It was learned in her history that she had not received chemotherapy or radiotherapy before, had no known disease, and did not use any medication. On physical examination, sclera icteric, multiple lymph nodes with a size of 1 cm in the cervical region and splenomegaly were detected. The patient's Rai stage 2, CLL-IPI score of 3, 17p(-), mutation in the IGHV gene was detected. Detection of leukocyte count 157,000/mm<sup>3</sup>, lymphocyte count 149.660/mm<sup>3</sup>, hemoglobin 13.5 g/dL, platelet count 117.000/mm<sup>3</sup>, alanine aminotransferase (ALT) 2045 U/L, aspartate aminotransferase (AST) 2252 U/L, total bilirubin 10.72 mg/dL, direct bilirubin 9.62 mg/dL, protrombin time 18.7 sec, active partial thromboplastin time 30 sec. While IgG was normal, IgA and M were low. HBsAg positive, anti-HBs negative, anti-HBc IgM negative, anti-HBcIgG positive, HBV-DNA 28,000,000 IU/mL were determined to explain liver dysfunction. One year ago, HBsAg was negative, anti-HBs negative, anti-HBc-IgM negative, while anti-HBc-IgG was positive. The patient was accepted as HBV reactivation and tenofovir disoproxil was started. In the first month of treatment, AST-ALT and bilirubin values returned to normal limits. In the 3rd month of the treatment, HBsAg and HBV-DNA became negative and anti-HBs became positive. The patient was followed up without treatment for CLL. Long-term use of tenofovir disoproxil was planned, despite the possibility of spontaneous HBV reactivation again. **Methodology detected:** Detection of leukocyte count 157,000/mm<sup>3</sup>, lymphocyte count 149.660/mm<sup>3</sup>, hemoglobin 13.5 g/dL, platelet count 117.000/mm<sup>3</sup>, alanine aminotransferase (ALT) 2045 U/L, aspartate aminotransferase (AST) 2252 U/L, total bilirubin 10.72 mg/dL, direct bilirubin 9.62 mg/dL, protrombin time 18.7 sec, active partial thromboplastin time 30 sec. While IgG was normal, IgA and M were low. HBsAg positive, anti-HBs negative, anti-HBc IgM negative, anti-HBcIgG positive, HBV-DNA 28,000,000 IU/mL were determined to explain liver dysfunction. One year ago, HBsAg was negative, anti-HBs negative, anti-HBc-IgM negative, while anti-HBc-IgG was positive. The patient was accepted as HBV reactivation and tenofovir disoproxil was started. In the first month of treatment, AST-ALT and bilirubin values returned to normal limits. In the 3rd month of the treatment, HBsAg and HBV-DNA became negative and anti-HBs became positive. The patient was followed up without

treatment for CLL. Long-term use of tenofovir disoproxil was planned, despite the possibility of spontaneous HBV reactivation again. **Results:** determined to explain liver dysfunction. One year ago, HBsAg was negative, anti-HBs negative, anti-HBc-IgM negative, while anti-HBc-IgG was positive. The patient was accepted as HBV reactivation and tenofovir disoproxil was started. In the first month of treatment, AST-ALT and bilirubin values returned to normal limits. In the 3rd month of the treatment, HBsAg and HBV-DNA became negative and anti-HBs became positive. The patient was followed up without treatment for CLL. Long-term use of tenofovir disoproxil was planned, despite the possibility of spontaneous HBV reactivation again. **Conclusion:** tenofovir disoproxil was planned, despite the possibility of spontaneous HBV reactivation again. **Discussion:** HBsAg positive individuals are at greater risk for HBV reactivation compared to HBsAg negative individuals. It has been reported that HBV reactivation rate is up to 70% in HBsAg-positive individuals receiving standard chemotherapy. For those with cured infection (defined as HBsAg-negative, anti-HBc-positive, HBV DNA-negative), reactivation ranged from 0.3% to 9.0%.

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#### ESTABLISHMENT OF EX VIVO DRUG SENSITIVITY SCREENING PLATFORM FOR LEUKAEMIA AND MULTIPLE MYELOMA USING A SOUTH AFRICAN PATIENT COHORT

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**Objective:** Our objective is to develop a functional precision medicine platform designed to directly identify tailored drug regimens that target individual patient cancer cells and give benefit to the same donors by supporting clinical decision-making. We demonstrate our *ex vivo* drug sensitivity screening platform for precision medicine using Leukaemia and Multiple Myeloma samples from a South African patient

cohort as proof of concept. **Methodology:** Through collaboration with Chris Hani Baragwanath and Donald Gordon Hospitals, Johannesburg, South Africa, we performed patient sample collections of n=80. Collected patient samples include Acute myeloid leukaemia (AML) (n=7), Chronic lymphocytic leukaemia (CLL) (n=4), Chronic myeloid leukaemia (CML) (n=30), Multiple Myeloma (n=40) and health donor (n=5). For each patient sample, peripheral blood mononuclear cell (PBMC) isolation was performed and cryopreserved in liquid nitrogen. **Results:** Our preliminary demographic analysis results show that we can group patients based on diagnosis, staging, exclusion and inclusion criteria. From our demographic analysis, we have also identified highly frequent chemotherapy drugs used in the cohort. Further, we can identify the most frequent chemotherapy drugs given as medication to the patient cohort. We then selected 30 drugs that are relevant for leukemia and multiple myeloma for Ex vivo drug sensitivity screening test. **Conclusion:** Using our results we will then select effective drugs for monotherapy and also drug combinations. Selected drug combinations will then be validated on patient samples using our ex vivo drug sensitivity test. These results will be analyzed using our statistical capabilities and developed as a packaged product of preclinical information for precision clinical trials. Thus, we are progressing our cutting-edge translational platform from technology readiness level (TRL4) to TRL6 on blood cancer.

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#### PP 04

##### IBRUTINIB RELATED NEUROPATHY: A CASE REPORT

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**Case report Introduction:** Chronic lymphocytic leukemia (CLL) is the most common leukemia seen in adulthood and mostly affects the older age group. The treatment of CLL has completely changed in recent years with the discovery of new agents. Today, ibrutinib, an oral inhibitor of the Bruton kinase signaling pathway, has become one of the commonly used agents in the treatment of CLL. Ibrutinib, a generally well tolerated agent, has manageable side effects. However, life-threatening side effects such as major bleeding, AF, and infections can be seen. Here, we present a case of CLL who developed peripheral sensorimotor neuropathy during ibrutinib treatment. **Case Report:** A 62-year-old female patient who was diagnosed with CLL 5 years before her admission was followed up in remission after R-FC chemotherapy. The patient, who received his last chemotherapy about 2 years ago, applied to the polyclinic with complaints of weakness and pallor for 2 weeks. Hepatosplenomegaly and diffuse (cervical, axillary, inguinal) lymphadenopathies were found in the outpatient clinic examination. In his abdominal

ultrasonography, the liver was 16 cm, and the spleen was 14 cm. There were paratracheal and mediastinal LAPs on thorax tomography. Bicytopenia was detected in whole blood examination. The patient was thought to have CLL recurrence and ibrutinib treatment was started at a dose of 420 mg/day. The patient presented with the complaint of weakness in the legs that started after ibrutinib treatment and continued to increase 3 weeks later. There was no significant finding in the patient's lumbar MR imaging. EMG examination of the patient revealed motor sensory axonal neuropathy. Ibrutinib was discontinued due to neuropathy thought to be related to ibrutinib. Neuropathy symptoms regressed in the patient's follow-up. After about 6 weeks, the patient's neuropathic symptoms regressed. Venetoclax treatment was started in the patient with persistent lymph nodes and B symptoms. The patient, whose neuropathic symptoms regressed, continues to be followed up. **Discussion:** With the introduction of new agents in the treatment of CLL, the chance of treatment in relapsed refractory patients has increased. In the treatment of CLL, standard R-FC (Rituximab-Fludarabine, Cyclophosphamide), and R-Bendamustine regimens were previously used as first-line therapy. Today, these treatments have been replaced by BTK inhibitors (Ibrutinib, Acalabrutinib), PI3K protein inhibitors (Idelalisib), BCL-2 inhibitors (Venetoclax) and CD-20 antibodies (Obinituzumab, Ofatumumab). The reason for this drastic change in the CLL treatment algorithm is that the newly discovered agents have less side-effect profiles, ease of use, and positive effects on mortality. Although these new treatments have less side effect profile, each newly reported side effect is very important for the follow-up of patients after treatment. Ibrutinib is a Bruton Tyrosine kinase inhibitor and is the first-line therapy for CLL. Among the side effects of ibrutinib, diarrhea, cough, nausea, HT, AF, major bleeding can be counted. It is mentioned in the literature that ibrutinib may cause neuropathy. In our case, motor neuropathy also developed, and symptoms regressed after discontinuation of the drug. The side effect of motor neuropathy should also be considered in patients given ibrutinib, and if this side effect develops, the treatment plan should be reconsidered.

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#### PP 05

##### RİCHTER SYNDROME TRANSFORMATION UNDER VENETOCLAX TREATMENT: A CASE REPORT OF A 51-YEAR-OLD FEMALE WITH CLL

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**Background:** Richter syndrome (RS) is typified by the emergence of an aggressive lymphoma in individuals who have been previously or simultaneously diagnosed with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma