

Speech Summary

01

DIFFUSE LARGE CELL LYMPHOMAS WITH RESTRICTED SOURCES

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Context: Non-Hodgkin Lymphoma (NHL) encompasses a range of blood cancers originating in the lymphatic system, with Diffuse Large B-Cell Lymphoma (DLBCL) being the most prevalent type. In Kosovo, a country with limited healthcare resources, managing NHL remains a significant challenge. In 2024, Kosovo reported 60 cases of lymphoma, of which 53 were classified as NHL, and 24 of those were identified as DLBCL. The healthcare system faces numerous obstacles, particularly in providing specialized treatments such as Bone Marrow Transplantation (BMT), which is not available domestically. These limitations impact the diagnosis, management, and outcomes for DLBCL patients. **Aim:** This study aims to explore the prevalence of DLBCL among NHL cases in Kosovo, identify the healthcare challenges posed by limited resources, and highlight the critical issue of the unavailability of bone marrow transplantation as part of lymphoma treatment. **Methods:** Data from the Kosovo National Cancer Registry for 2024 shows that out of 60 lymphoma cases, 53 were NHL, and 24 were DLBCL. This retrospective study assesses the diagnostic, treatment, and follow-up data of these patients, focusing on challenges in managing DLBCL, especially the lack of bone marrow transplant services. **Discussion:** Kosovo's healthcare infrastructure is underdeveloped in terms of both diagnostic tools and treatment options for cancers like DLBCL. Early diagnosis, which is crucial for the successful treatment of DLBCL, is often delayed due to the lack of advanced imaging and molecular diagnostic techniques. Furthermore, chemotherapy regimens – standard treatments for DLBCL – are often delayed because of limited access to essential drugs, inadequate oncology training, and logistical issues in the healthcare system. A major issue is the absence of Bone Marrow Transplantation (BMT) services in Kosovo. BMT, a critical treatment for certain aggressive cases

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of DLBCL, is not available within the country, forcing patients to seek treatment abroad. This process is expensive, and many patients face financial barriers to accessing this life-saving procedure. For those who cannot afford treatment outside Kosovo, the lack of BMT options often leads to poorer outcomes, particularly for patients with relapsed or refractory DLBCL. Additionally, limited access to second-line treatments such as immunotherapy and targeted therapies exacerbates the situation. The healthcare system struggles with a shortage of specialized medical personnel and advanced cancer care facilities. The lack of access to BMT and modern therapies limits the treatment options available for patients who fail to respond to first-line chemotherapy, resulting in a worse prognosis. **Conclusion:** Kosovo faces significant challenges in managing Diffuse Large B-Cell Lymphoma due to limited healthcare resources, particularly the unavailability of bone marrow transplantation. This limitation forces many patients to seek treatment abroad, which is not feasible for everyone due to financial constraints. Improving the country's healthcare infrastructure, ensuring access to bone marrow transplantation, and strengthening the oncology workforce are essential steps toward improving patient outcomes. Additionally, international partnerships and funding are crucial in bridging these gaps and enhancing cancer care in Kosovo.

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02

MISSION TO MARS: RADIATION RISKS FROM INTER-PLANETARY TRAVEL

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Exploration and innovation are 2 hallmarks of human endeavor. Human travel to the moon was accomplished in 1969 by the US. There are now plans to return to the moon

in the Artemis mission in the next few years and then to travel to Mars. For perspective the direct distance to the Moon is 383,000 km whilst a mission to Mars could vary between 55–400, 000, 000 km. and could take about 3-years for a return trip. Besides the technical challenges of a journey to Mars there are important medical challenges including: (1) Space radiation; (2) Micro-gravity; (3) A hostile, closed environment; (4) Isolation and confinement; and (5) Distance from Earth. Radiation is an important hazard for human inter-planetary space flight. There are potential health consequences, immediate and long-term. The immediate potential risks are: (1) Acute radiation syndromes; and (2) Neuro-ocular disturbances whereas the long-term consequences include: (1) Cancer; (2) Cardio-vascular disease; (3) Cataracts; and (4) Degenerative diseases. Sources of radiation on a journey to Mars include: (1) Trapped charged particles and high energy electrons (Van Allen belts); (2) Galactic cosmic rays; and (3) Solar events (charged particles & UV). Galactic cosmic rays include: (1) High energy/high charge ions; (2) High energy protons; (3) Secondary protons; (4) Neutrons; and (5) Fragments produced by interactions with the spacecraft shielding and human tissues. Solar particle events include: (1) Solar winds; (2) Coronal mass ejections; and (3) Low to medium energy protons. The Earth's magnetosphere protects us from much of this radiation, but this protection is lost on a journey to Mars. The Artemis-1 mission which recently circumnavigated the Moon is providing data on radiation exposure. Our normal background radiation dose on Earth is about 2.4 mSv/year whereas journey to Mar could expose astronauts to 300–600 mSv over 3-years. Concernedly, damage to DNA produced by heavy charged ions encountered in space is different and probably more dangerous than our exposure to ionizing radiations on Earth. Several mitigation measures have been developed including: (1) Spacecraft shielding; (2) Crew shielding; (3) Spacecraft positioning; (4) Mission planning; (5) Radiation storm shelters; (5) Limited spacewalks; (6) Crew selection and others. My conclusions are: (1) Radiation is an important hazard of inter-planetary travel; (2) There are immediate and long-term consequences of high radiation exposures; (3) Interventions are needed to reduce radiation risk; (4) There are important knowledge gaps regarding long-term adverse events; and (5) We need to train a new generation of physicians to deal with these challenges.

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03

THE HISTORY OF CHRONIC MYELOID LEUKEMIA (CML): FROM ARSENIC TO TYROSINE KINASE INHIBITORS (TKI)

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It took 20-years from the first description of CML in 1845 to the report by Lissauer in 1865, of an effective treatment with arsenic. After another 38-years the beneficial effect of splenic

irradiation was described in 1903, and after 50 more years the palliative efficacy of the alkylating agent busulfan (Galton, 1953). Several other agents were found effective (dibromomannitol, hydroxyurea), and in 1979 first reports on the efficacy of bone marrow transplantation were published. After more than 100-years of trial and error, the observation in 1960 of the Philadelphia (Ph)-chromosome, a translocation between chromosomes 9 and 22, marked the first step to understanding the pathophysiology of CML and to a rational and causative treatment approach. The breakpoint on chromosome 9 occurred in the gene encoding the ABL-oncogene. Most of ABL was translocated to chromosome 22 next to a region called Breakpoint Cluster Region (BCR). The detection of a BCR:ABL fusion RNA in CML (R. Gale contributed), prompted transfection experiments to mice which developed CML-like phenotypes (Daley et al, Heisterkamp and Groffen, 1990). Since the ABL-oncoprotein is a tyrosine kinase deregulated by juxtaposition next to BCR, the search for an inhibitor of BCR-ABL was the logical next step. The choice of imatinib as the first BCR-ABL-TKI was fortuitous and led to a profound change of CML treatment. Other TKI followed, but none-prolonged survival of CML compared to imatinib. Still, progression to blast crisis occurred in 6%–7% of imatinib-treated cases, but CML-specific survival increased to more than 90% and survival of CML-patients diagnosed and treated in the chronic phase of CML approached that of the general population.

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04

MDS DIAGNOSIS? STILL BY BONE MARROW EXAMINATION?

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The Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal Bone Marrow (BM) stem cell myeloid neoplasms, characterized by BM dysplasia, macrocytic anemia or cytopenia with a tendency for leukemic transformation. The suspicion of MDS is raised by a typical but not specific clinical picture and routine laboratory findings, but the gold standard for the diagnosis of MDS is still BM examination with the presence of uni- or multi-lineage dysplasia and blast percentage, together with exclusion of other reasons. Cytogenetics is also a part of the diagnostic process. Flow cytometry and genetics are helpful but are not always mandatory for the diagnosis of MDS. We will summarize the current steps in the diagnostic approach for a patient suspected of having MDS. I will also describe new concepts that use non-invasive diagnostic technologies, especially digital methods as well as peripheral blood genetics. The hope is that one day these will mature, be introduced into clinical practice, and perhaps in many cases even replace the invasive BM biopsy.

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