HEMATOLOGY, TRANSFUSION AND CELL THERAPY

www.htct.com.br

Speech Summary

01

DIFFUSE LARGE CELL LYMPHOMAS WITH RESTRICTED SOURCES

Suzana Krasniqi

Hematology Clinic, University Clinical Center of Kosovo, Prishtina

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 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.

https://doi.org/10.1016/j.htct.2025.103865

02

MISSION TO MARS: RADIATION RISKS FROM INTER-PLANETARY TRAVEL

Robert Peter Gale

Centre for Haematology, Department of Immunology and Inflammation, Imperial College of Science, Technology and Medicine, Sidney St, Sheffield

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

2531-1379/

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-tern 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.

https://doi.org/10.1016/j.htct.2025.103866

03

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

Rüdiger Hehlmann

Medizinische Fakultät Mannheim, Heidelberg University, Alemana

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.

https://doi.org/10.1016/j.htct.2025.103867

04

MDS DIAGNOSIS? STILL BY BONE MARROW EXAMINATION?

Moshe Mittelman

Tel-Aviv Sourasky Medical Center, Tel Aviv University, Israel

The Myelodysplastic Syndromes (MDS) are a heterogenous 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.

https://doi.org/10.1016/j.htct.2025.103868

05

HOW I TREAT PH+ ACUTE LYMPHOBLASTIC LEUKEMIA

Robin Foà

Emeritus Professor of Hematology, Sapienza University of Rome, Italy

The greatest improvements in the management of Acute Lymphoblastic Leukemia (ALL) have been witnessed in Ph +ALL patients. The advancements have stemmed from an always more precise genetic characterization at presentation, the use of tailored treatment, the precise monitoring of minima/Measurable Residual Disease (MRD) and, finally, by the inclusion of immunotherapy in the frontline treatment. Prior to the advent of Tyrosine Kinase Inhibitors (TKIs), Ph+ALL was the hematologic malignancy with the worse outcome. The frontline use of TKIs has changed the natural history of the disease. Since year 2000 in Italy all patients enrolled in the GIMEMA multicenter protocols have been treated in induction with a TKI alone (plus steroids) and no systemic chemotherapy. The subsequent advancement has been brought by the addition of the bispecific monoclonal antibody blinatumomab as consolidation, always in the absence of systemic chemotherapy. The results of the GIMEMA LAL2116 (D-ALBA) trial for patients of all ages showed high rates of molecular response following an induction/consolidation treatment with dasatinib and blinatumomab. At 53-months, survival rates of 75%–80% were recorded, with 50% of patients being managed only with a TKI and blinatumomab, without chemotherapy and transplant. Most MRD+ patients were allografted. IKZF-plus patients have a less favorable outcome and should be identified at diagnosis. When possible, they should undergo an allogeneic transplant. In the subsequent phase 3 GIMEMA ALL2820 trial, patients enrolled in the experimental arm and treated with ponatinib followed by blinatumomab showed even higher rates of molecular response, with estimated OS and DFS of 94.9% and 95.6% at 12-months. Of interest, the combination of dasatinib and ponatinib plus blinatumomab, in the absence of systemic chemotherapy, is associated with a marked host immune activation. The MDACC group also reported the effectiveness of ponatinib combined with blinatumomab, though the combination was associated with greater toxicity. For a review on the treatment of adult Ph+ALL see Chiaretti & Foà. The GIMEMA ALL2820 trial will conclusively show how many patients can be spared systemic chemotherapy and transplant. At the interim analysis, only 10% of patients enrolled in the ponatinib + blinatumomab arm have so far undergone a transplant. I have been asked to cover 'How I Treat Ph+ALL', which more appropriately should be 'How Should I Treat Ph+ LL' Based on the 25-year experience gathered through the GIMEMA trials, the optimal algorithm should be: i) Identify the presence of the BCR/ABL gene lesion within one week from diagnosis; ii) During this time treat patients with steroids; iii) Start induction with dasatinib or ponatinib plus steroids, with no systemic chemotherapy; iv) CNS prophylaxis should be carried out; v) MRD should be monitored molecularly at given timepoints; vi) After induction, all patients should be consolidated with multiple cycles of blinatumomab (up to 5 in our protocols); vii) TKI should not be stopped. Through this approach the large majority of patients – of all ages – will become molecularly negative. IKZF-plus patients should be identified on the diagnostic material. Transplant should be offered to patients with an unfavorable genetic profile and/or evidence of MRD. All patients should be closely monitored for MRD during the follow-up. The possibility of offering such a personalized frontline management to all patients – including the elderly – strongly relies on adequate and standardized laboratory facilities aimed at a broad diagnostic work-up and at an accurate monitoring of MRD, as well as an optimal and timely access to the different drugs. In the real life, this is often not possible. Patients should then undergo a TKI (plus steroid) induction associated with mild chemotherapy. Many such patients are offered an allogeneic transplant. The future of patients with Ph+ALL of all ages is looking always more favorable if all the pieces of the puzzle are in place. It is likely that with the advent of the subcutaneous formulation of blinatumomab the long-term outcome will look even better.

https://doi.org/10.1016/j.htct.2025.103869

06

WHICH IS THE BEST TREATMENT FOR AML WITH RESTRICTED RESOURCES

Mipsang Lama

Tata Medical Center, Katmandu Nepal

AML itself is one of the worst prognostic hematological malignancies which has to be managed timely, adequately and aggressively to get on top of it. Such, kind of patients will need intensive chemotherapy therapy (3+7, Flag IDA) followed by allogeneic SCT. That is why it is challenging to manage such cases in resource limited setting. Due to constant development of new drugs treatment of such patients with azacytidine and venetoclax have been lot easier. With these drugs we are being able to put patients in remission with less toxicities, and low cost as compared to intensive chemotherapy.

https://doi.org/10.1016/j.htct.2025.103870

07

UPDATES ON HODGKIN DISEASE

Valeh Huseynov

Baku Medical Plaza, Hematology Department, Azerbaijan

Hodgkin Lymphoma (HL) is a B-cell malignancy accounting for approximately 10% of all lymphoma cases and 5% of lymphoma-related mortalities. Incidence increases in younger adults and those above 55-years of age and has a bimodal distribution. Approximately 95% of all HL cases are diagnosed as classical Hodgkin Lymphoma (cHL) and 5% as Nodular

Lymphocyte Predominant B-cell Lymphoma (NLPBL). Nodular sclerosis, mixed cellularity, lymphocyte depletion, and lymphocyte–rich HL are subgroups of classical HL. Risk Stratification An accurate assessment of the stage of disease in patients with HL is critical for the selection of the appropriate therapy. Prognostic models that identify patients at low or high risk for recurrence, as well as the response to therapy as determined by Positron Emission Tomography (PET) scan, are used to optimize therapy. Risk–Adapted Therapy Initial therapy for HL patients is based on the histology of the disease, the anatomical stage and the presence of poor prognostic features. Patients with early–stage disease are typically treated with combined modality strategies utilizing abbreviated courses of combination chemotherapy followed by involved–field radiation therapy, whereas those with advanced stage disease receive a longer course of chemotherapy often without radiation therapy. However, newer agents including brentuximab vedotin and anti–PD–1 antibodies are now standardly incorporated into frontline therapy. Management of Relapsed/Refractory Disease High–Dose Chemotherapy (HDCT) followed by an Autologous Stem Cell Transplant (ASCT) is the standard of care for most patients who relapse following initial therapy. For patients who fail HDCT with ASCT, brentuximab vedotin, PD–1 blockade, non–myeloablative allogeneic transplant or participation in a clinical trial should be considered. The AETHERA study (NCT01100502) shows that Brentuximab Vedotin (BV) improves Progression-Free Survival (PFS) after ASCT in patients with Refractory or Relapsed HL (R/R HL). For patients who relapse after ASCT, BV, and anti-PD-1, monoclonal antibodies were considered incurable, and their outcome is rather dismal, with a median Overall Survival (OS) of 2-years. For Refractory or Relapsed cHL (R/R cHL) patients who have failed both ASCT and BV, Chimeric Antigen Receptor T-cell (CAR-T) therapy offers a new therapeutic option.

https://doi.org/10.1016/j.htct.2025.103871

08

HISTORY OF BLOOD TRANSFUSION

Tanju Atamer

Istanbul University (Retired), Istanbul, Turkey

It is not easy to cover the history of transfusion in all its aspects. In the era when blood transfusion was first tried, the indications for blood transfusion were also very different: mental illness, gaining strength, rejuvenation, etc. Blood transfusion process has gone through many dangerous and difficult stages, from obtaining the blood to its safe application in peace, in war, and in the laboratory. This presentation focuses on some stages and developments in the application of blood transfusion. The main developments are summarized in Table 1. The main problems encountered in the history of transfusion can be summarized as follows:

- Blood clotting and preservation could be prevented by the use of 0.2% sodium citrate and dextrose.
- Severe transfusion reactions could mostly be prevented after the ABO blood groups were identified.
- Infection problems that could be partially controlled with antiseptic agents.

In this presentation, various obstacles encountered in the history of blood transfusion and developments regarding their solutions are presented.

Table 1 Important stages in the history of blood transfusion.

1628	William Harwey (GB)	Discovery of human blood circulatory system
1666	Richard Lower (Oxford)	Experiments of blood transfusion beetween animals
1667	Jean Denis (Paris)	Transfusion blood from animals to humans
1818	James Blundell (London)	First blood transfusion from one human to another
1854	J Bovell E Hodder (Toronto)	Cow's milk transfusions was first attempted
1901	Karl Landsteiner (Wienna)	Discovery of ABO blood groups (Nobel Prize in 1930)
1915	Richard Lenwinsohn (NY)	Developing 0.2% sodium citrate as anticoagulant
1921	Percy Oliver (London)	The first blood donor service is established
1932	in the SU and the USA	Cadaveric blood began to be used
1937	Bernard Fantus (Chicago)	The first blood bank
1940	Edwin Cohn (Boston)	A method for fractionation of plasma proteins
1951	Edwin Cohn (Boston)	Developping the first blood cell separator
1971		Hepatitis B surface antigen testing of donated bloods
1982	J Goldstein	Developing universal type O blood by enzyme treatment
1983	L. Montaignier (Paris)	Isolation of the virus that causes AIDS
From 1987 to 2008		A series of tests are developed to screen donated blood for infectious diseases
2010	Seifinejad A et al.	RBCs generated from human induced pluripotent SCs
2020	Ebrahimi M, et al.	Differentiation of human induced pluripotent stem cells into RBCs

SU, Soviet Union; USA, United States of America; RBCs, Red Blood Cells; SCs, Stem Cells.

https://doi.org/10.1016/j.htct.2025.103872

09

TREATMENT FOR HODGKIN'S LYMPHOMAS IN COUNTRIES WITH LIMITED RESOURCES

Khalid Halahleh

King Hussein Cancer Center, Amman, Jordania

The incidence and long-term clinical outcome of Hodgkin Lymphoma (HL) vary according to different patient, disease-related factors and geographic location. There have been

dramatic changes in the staging and treatment of Hodgkin's Lymphoma (HL) over the last two decades. 75%–80% of patients with classical HL can achieve long-term remission with contemporary risk-adapted frontline therapy in high income countries. However, 25%–30% of patients with advanced-stage disease experience relapse or have primary refractory disease. For patients with Relapsed/Refractory HL (rrHL), salvage therapy followed by Stem Cell Transplantation (SCT) is the current standard of care. Despite the significant improvement in the diagnosis, staging, the use of risk-adapted approach, introduction of novel agents (CPI, Bv) in frontline setting, the use of post-transplant consolidation maintenance therapy, 50% of patients still experience disease progression, with poor prognosis and shortened survival. Most of the real-world data regarding treatment pathways and clinical outcomes in relapsed refractory HL published from high income countries in Euro and North America. There is a limited data on clinical characteristics and clinical outcomes of HL in low-resourced countries. Very few studies published so far with limited number of patients, single-center experiences, poor data quality, or lack of comprehensive information on patients, treatment, or clinical outcomes. In my presentation, we will highlight the disease entity from diagnosis, staging to treatment options worldwide; the availability and the use of novel agents in frontline and in relapsed refractory setting, availability of stem cell transplantation procedures and compare the clinical outcomes of HL patients in both high- and low-resourced countries.

https://doi.org/10.1016/j.htct.2025.103873

10

CLASSIFICATION OF MPN

Haifa Kathrin Al-Ali

University Hospital Halle (Saale), Halle, Germany

The 2022 updated 5th edition of the World Health Organization Classification of myeloproliferative neoplasms and mastocytosis focused on changes in the rationale behind the classification, combined morphologic, immunophenotypic, molecular, and cytogenetic data that help to refine diagnostic criteria and emphasize therapeutically and/or prognostically actionable biomarkers. While a genetic basis for defining diseases is sought where possible, the classification strives to keep practical applicability in perspective. In addition, a new International Consensus Classification (ICC) has been introduced for myeloid neoplasms and acute leukemia. In the context of MPN, the classical subtypes of MPN remained unchanged; however, the experts made an effort to refine the diagnostic criteria to allow a distinction between subtypes. With refinement of the diagnostic criteria, the hope is that clinicians will be able to distinguish between specific subtypes with greater accuracy and present a more definitive and holistic management for patients from diagnosis through disease monitoring.

https://doi.org/10.1016/j.htct.2025.103874

11

PREDİCTİON OF THE RİSK OF LEUKEMİA DEVELOPMENT İN AGED HEALTHY POPULATİON: IMPLEMENTATİON İN THE PUBLİC HEALTH SYSTEM

Francesco Frassoni [a,b], Roberto Tedone [b], Emanuela Marcenaro [c], Giorgio Piastra [a], Davide Guerr [b]

[a] *Department of Clinical and Biological Sciences, University of Torino, Torino, Italy*
[b] *Dedalus Italia S.p.A., Florença, Italy*
[c] *Department of Experimental Medicine (DIMES), University of Genoa, Genoa, Italy*

In the last 10-years, several scientific reports have provided evidence of the accumulation of somatic mutations in Hematopoietic Stem and Progenitor Cells (HSPC) in subjects aged > 50yrs. This phenomenon is defined as Clonal Hematopoiesis of Indeterminate Potential (CHIP). As discovered and developed by Abelson et.al. (Nature. 2018) these mutations are detectable many years before the clinical onset of Acute Myeloid Leukemia (AML) and are potentially linked to its subsequent evolution. It is important to underline that the correlation between mutations and the development of AML does not represent an early diagnosis but only an increased risk of developing AML. The risk depends on many factors: type of mutations, how many cells carry the mutation, and combination of mutations. A risk score has been established (NEJM 2023); according to this study few subjects with CHIP are going to develop AML. Of note: the studies that document these correlations were retrospective. It might be relevant to emphasize that "early diagnosis of AML" does not seem to have, given the dynamics of cellular proliferation, concrete advantages. The identification early in advances of a constellation of mutations and their combinations possibly associated with the risk of developing AML could instead be very effective, if there were drugs targeting specific mutations. From a precision, personalized and participatory medicine perspective, these studies have led us to launch a prospective project on a healthy population of individuals between 50 and 80-years old. We reasoned that this type of screenings based on complex landscapes of genetic mutations will become more and more present in the evolving scenario of predictive medicine. Thus, the company Dedalus Italia S.p.A. designed the model and the software for implementing these screening studies in the Health Services. The project' name is "SInISA"*. The experimentation is carried out in the territory of the Regional-Health-Service (ASL5) of Eastern Liguria (Italy), with the aim of verifying and evaluating both the organizational model and the technological infrastructure to support it, with the ambition of initially sequencing the DNA with a panel of about 90 genes. The first step was to identify subjects with higher probability of bearing mutations. The first screening element will be the RDW parameter. Subjects with RDW > 15 have higher probability of bearing mutations in blood cells. It was calculated that to identify individuals with RDW > 15 it is necessary start from a population of approx. 12000 subjects This study is based on the free and voluntary participation of

citizens. Therefore, this approach opens the doors to the so-called "participatory medicine" which is, and will be, an essential element for the development of these new paths for the management of citizens' health. The objectives are therefore: 1) To verify the correlation of RDW > 15 and presence of mutation in a prospective study; 2) To define an organizational model that can be the basis of future screening processes, in the adult/elderly population; 3) To design and implement an integrated technological platform capable of supporting the screening campaign, managing the information and process peculiarities of genetic studies, automating the identification of the target, the sequence of controls and the interactions with the sequencing structures, activating in a logic of continuity of care and follow-up pathways. * "SInISA" is funded under the POR-FESR Liguria 2021–2027 Action 1.1.1 and is carried out by Dedalus Italia S.p.A., lead company, Leonardo S.p.A, Genartis S.r.l., Rulex Innovation Labs S.r.l., CherryChain S.r.l., VIS S.r.l., University of Genoa with Department of Experimental Medicine and the SRV Center".

https://doi.org/10.1016/j.htct.2025.103875

12

VENETOCLAX-BASED VERSUS 7+3 INDUCTION THERAPY IN FIT YOUNGER ADULTS WITH NEWLY DIAGNOSED NON-CBF AML

Dmitrii Zhogolev, Nikita Pastukhov, Bella Aybova, Anna Smirnova, Ivan Moiseev, Sergey Bondarenko, Alexander Kulagin

RM Gorbacheva Research Institute, Pavlov University, St. Petersburg, Russian Federation

Objective: Venetoclax-based regimens have emerged as a standard therapeutic option for newly diagnosed Acute Myeloid Leukemia (AML) in patients deemed unfit for intensive chemotherapy. However, the efficacy of venetoclax in fit patients remains an area of ongoing investigation. Notably, in specific AML subsets, such as Core Binding Factor (CBF) AML, venetoclax-based therapy has demonstrated inferior outcomes compared to intensive chemotherapy. Despite these findings, direct comparative data between venetoclax-based therapies and intensive induction chemotherapy in fit patients with non-CBF AML remains limited. This study aims to evaluate and compare the clinical outcomes of fit younger adult patients with newly diagnosed non-CBF AML who underwent induction therapy with either venetoclax-based regimens or standard 7+3 chemotherapy. **Methodology:** This retrospective cohort study included patients assessed at RM Gorbacheva Research Institute for eligibility for Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) from June 2020 to August 2024. Eligible patients were adults with non-CBF AML who received either 7+3 induction chemotherapy or venetoclax in combination with a Hypomethylating Agent (HMA) or Low-Dose Cytarabine (LDAC). Exclusion criteria included age > 60-years and a Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) score > 2. To minimize confounding, pairwise propensity score matching was performed based on age, secondary AML status, and ELN 2022 risk classification. Remission in this study referred to Complete Remission (CR), CR with partial or incomplete hematologic recovery, and a morphological leukemia-free state according to the ELN response criteria. Patients who failed to achieve remission after two induction cycles were categorized as refractory. Overall Survival (OS) was defined as the time from start of treatment to death from any cause. Event-Free Survival (EFS) included refractoriness, relapse, or death, with censoring at the last follow-up. Relapse was defined as the reappearance of ≥5% blasts in bone marrow or peripheral blood, or extramedullary disease. Non-Relapse Mortality (NRM) was defined as death in remission. Survival analysis was conducted using the Kaplan-Meier method and log-rank test. Cumulative incidences of relapse and NRM were assessed using competing risk models with Gray's test. Statistical analyses were performed using R (version 4.4.2). The study adhered to the Declaration of Helsinki and Good Clinical Practice guidelines and was approved by the Pavlov University Ethical Committee. **Results:** A total of 112 patients met the inclusion criteria, with 64.3% (n = 72) receiving 7+3 induction and 35.7% (n = 40) treated with venetoclax plus HMA/LDAC. After propensity score matching, each treatment arm included 26 patients. Baseline characteristics of the matched cohort are summarized in Table 1. Remission rates were 73.1% (n = 19) in the 7+3 group and 61.5% (n = 16) in the venetoclax group. Refractory disease was documented in 11.5% (n = 3) and 34.6% (n = 9), respectively. Induction-related mortality occurred in 15.4% (n = 4) of the 7+3 group and 3.8% (n = 1) of the venetoclax group (p = 0.08) (Fig. 1). The median follow-up for surviving patients was 25.5 months (range: 2.5–37.9). Two-year OS rates were 33.8% (95% CI: 19.6–58.4) for the 7+3 group and 31.6% (95% CI: 15.1–66.2) for the venetoclax group (p = 0.7). Two-year EFS was 30.8% (95% CI: 17.3–54.8) and 31% (95% CI: 16.1–59.8), respectively (p = 0.8) (Fig. 2). Cumulative relapse incidence was 29% (95% CI: 11–50) in the 7+3 group and 49% (95% CI: 19–74) in the venetoclax group (p = 0.28). NRM was significantly higher in the 7+3 group at 38% (95% CI: 18–58) compared to 5.3% (95% CI: 0.3–22) in the venetoclax group (p = 0.039) (Fig. 3). The cumulative incidence of allo-HSCT was 46% (95% CI: 26–64) and 55% (95% CI: 30–75) for 7+3 and venetoclax groups, respectively (p = 0.15). **Conclusion:** In this propensity-matched analysis of fit younger adults with non-CBF AML, venetoclax-based induction therapy demonstrated comparable overall and event-free survival to standard 7+3 chemotherapy. While venetoclax-treated patients exhibited a numerically higher relapse incidence, this difference did not reach statistical significance. Conversely, those receiving 7+3 experienced significantly greater non-relapse mortality.

Notably, venetoclax-based therapy was associated with a lower induction-related mortality and a higher rate of refractory disease, underscoring the distinct response dynamics of these regimens. These findings highlight the nuanced risk-benefit profiles of venetoclax and intensive chemotherapy, warranting further prospective validation to optimize patient selection and treatment strategies in fit AML patients.

Table 1 Baseline characteristics of the matched cohort.

	7+3 n = 26	Ven+HMA/LDAC n = 26	p.overall
Age at diagnosis, median (range)	46.5 (21–59)	47 (27–60)	0.56
Gender, n (%)			0.26
Male	8 (30.8)	13 (50)	
Female	18 (69.2)	13 (50)	
ELN 2022 risk, n (%)			1.00
Favorable	3 (11.5)	3 (11.5)	
Intermediate	10 (38.5)	10 (38.5)	
Adverse	13 (50)	13 (50)	
Secondary AML, n (%)			1.00
No	20 (76.9)	20 (76.9)	
Yes	6 (23.1)	6 (23.1)	
Midostaurin, n (%)			1.00
No	22 (84.6)	22 (84.6)	
Yes	4 (15.4)	4 (15.4)	

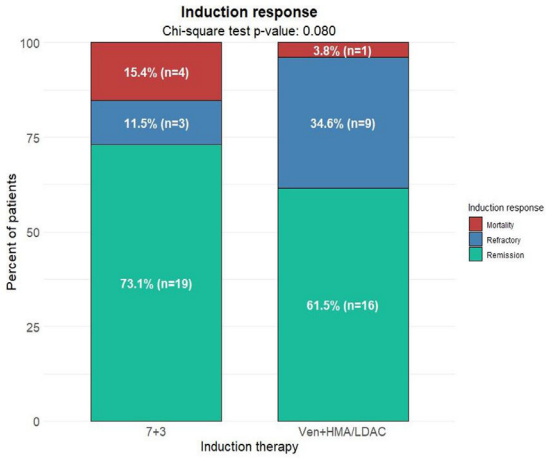

Figure 1 Comparison of induction response.

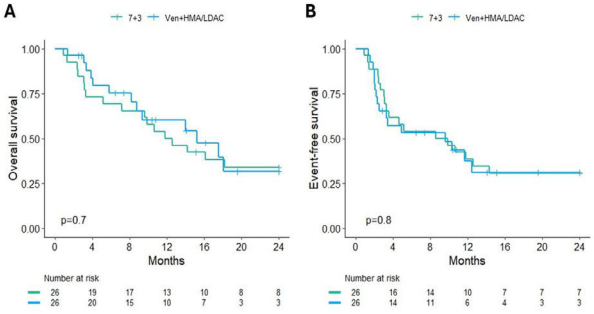

Figure 2 Comparisons of overall (A) and event-free survival (B).

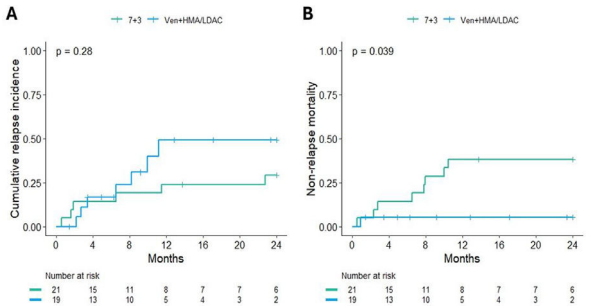

Figure 3 Comparisons of cumulative relapse incidence (A) and non-relapse mortality (B).

https://doi.org/10.1016/j.htct.2025.103876

13

PREDICTORS OF RESPONSE TO RUXOLITINIB THERAPY IN PATIENTS WITH MYELOFIBROSIS

Irina Turtanova [a], Maria Barabanshchikova [b], Elena Morozova [b], Tatiana Gindina [b], Tatiana Shneyder [a], Natalia Dorofeeva [a], Roman Vaschenkov [a], Nadezhda Medvedeva [a], Alexander Kulagin [b]

[a] *Municipal Clinical Hospital, Saint Petersburg, Russian Federation*
[b] *RM Gorbacheva Scientific Research Institute of Pediatric Hematology and Transplantation; Academician IP Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russian Federation*

Presentation Type: Oral. **Abstract Category:** Adult Hematology Abstract Categories -> Myeloproliferative Neoplasms. **Objective:** Since the introduction of targeted therapy for myelofibrosis and the incorporation of ruxolitinib into clinical practice, overall survival rates have significantly improved. Despite initial effectiveness, most patients eventually lose their response, and after stopping treatment, they have poor Overall Survival rates (OS). Currently, response criteria that can predict a response or indicate treatment failure are not well studied in patients receiving ruxolitinib. **Aim:** To analyze therapy with ruxolitinib and identify early predictors of response or treatment failure **Methodology:** The study included 225 patients (79 men and 145 women). The median age at the start of ruxolitinib therapy was 60 years (range 27–84).

- 149 patients (65%) were diagnosed with primary myelofibrosis;
- 55 patients (25%) had post-polycythemia vera myelofibrosis;
- 16 patients (7%) had post-thrombocythemia myelofibrosis;
- 8 patients (3%) were diagnosed with essential thrombocythemia.

For 169 patients (75%), the time to ruxolitinib therapy initiation was more than two years. According to the DIPSS prognostic scale, 88 patients (39%) were in the intermediate-1 risk

group, 110 patients (49%) were in the intermediate-2 risk group, and 26 patients (12%) were in the high-risk group. Most patients (82%) had the JAK2V617F mutation, 13% had a mutation in the CALR gene, 2% had a mutation in the MPL gene, and 4 patients were triple negative. 121 patients (54%) had a normal karyotype, and 51 patients (23%) had an unfavorable karyotype. An enlarged spleen size of more than 10 cm upon palpation was observed in 108 patients. **Results:** The median duration of ruxolitinib therapy was 22 months (range 7–123). In 91% of cases, the therapeutic dose of the drug was 30 mg per day or more, and in 9% it was less due to the presence of thrombocytopenia.

- Disease stabilization was recorded in 7 patients (35%);
- Clinical improvement was observed in 86 patients (38%);
- Disease progression was noted in 60 patients (27%).

In 75% of cases, a reduction in spleen size compared to baseline was achieved, and in 80 patients (40%), some reduction in disease symptoms was observed. In 70% of cases, there was no need for blood transfusion therapy. Ruxolitinib therapy led to an increase in the proportion of patients with low and intermediate-1 risk (53% vs. 39%). At the time of the current analysis, 184 patients (82%) were alive, and 40 patients (18%) had died. Overall survival rates were 72% in the intermediate-1 risk group, 60% in the intermediate-2 group, and 48% in the high-risk group ($p < 0.0001$). To build a predictive model of the response to therapy, a new RR6 calculator was used. The low-risk group included 46 patients (overall survival – 86%), the intermediate-risk group – 60 patients (overall survival – 83%), and the high-risk group – 59 patients (overall survival – 55%) ($p < 0.0015$). **Conclusion:** Ruxolitinib is the standard of care for patients with myelofibrosis. The RR6 prognostic model can be applied to patients with myelofibrosis after 6 months of ruxolitinib treatment to identify risk groups with an unfavourable course and those requiring a change in treatment strategy.

https://doi.org/10.1016/j.htct.2025.103877