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.

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CLASSIFICATION OF MPN

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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.

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

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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".

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

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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.