Press release

The Hague, 11 December 2021

New AML and CLL research results from HARMONY to facilitate tailored treatment choices in subtypes of blood cancer

- **Big Data analyses have produced novel insights that may improve the prognostication of patients with Acute Myeloid Leukemia (AML) and Chronic Lymphocytic Leukemia (CLL)**
- **These results may be used to identify high-risk patients and to make better-informed treatment choices in the future**
- **The new data is presented at the 63nd Annual Meeting of the American Society of Hematology (ASH)**

The HARMONY Alliance presents new results that may allow physicians to more precisely determine the prognosis of patients with Acute Myeloid Leukemia (AML) and Chronic Lymphocytic Leukemia (CLL) in the future. The researchers based their conclusions on anonymized data from thousands of patients comprised in the HARMONY Big Data Platform. The results are presented at the 63nd American Society of Hematology Annual Meeting & Exposition (ASH). The ASH annual meeting will also feature an inspiring Special-Interest session about the role of Real-World Data collection in Hematologic Malignancies.

Does RAD21 Co-Mutation Have a Role in DNMT3A Mutated AML? Results of Harmony Alliance AML Database

(608 Azibeiro Melchor et al | Program: Oral and Poster Abstracts | Type: Oral | Session: 617. Acute Myeloid Leukemias: Biomarkers, Molecular Markers and Minimal Residual Disease in Diagnosis and Prognosis: Further unraveling the genetic background of AML | Hematology Disease Topics & Pathways: Genomics, Adults, AML, Bioinformatics, Clinical Research, Health Outcomes Research, Diseases, Myeloid Malignancies, Biological Processes, Genomic Profiling, Technology and Procedures, Study Population || Monday, December 13, 2021: 10:45 AM)

LINK: https://ash.confex.com/ash/2021/webprogram/Paper150766.html

Raúl Azibeiro Melchor of Hospital Clínico Universitario de Salamanca (CAUSA/IBSAL): *"Many genetic mutations are known to be involved in the development or course of AML, either alone or in combination. The clinical relevance of these mutations is usually unclear, especially when it comes to rare mutations and combinations of mutations. We studied gene-gene interactions in ~3600 patients with AML. We discovered that a mutation in the RAD21 gene has a positive effect on outcome in a particular group of patients. These results provide insight into the molecular landscape of AML. In the long term, the results may be used to improve prognostication and inform treatment choices in patients with AML."*

Harmony Alliance provides a machine learning researching tool to predict the risk of relapse after first remission in AML patients treated without allogeneic hematopoietic stem cell transplantation (alloHSCT)

(4041 Sobas et al | Program: Oral and Poster Abstracts | Session: 903. Health Services Research—Myeloid Malignancies: Poster III | Hematology Disease Topics & Pathways: AML, Clinical Research, Clinically Relevant, Patient-Reported Outcomes, Diseases, Registries, Myeloid Malignancies, Technology and Procedures, Machine Learning || Monday, December 13, 2021, 6:00 PM-8:00 PM)
LINK: https://ash.confex.com/ash/2021/webprogram/Paper149521.html

Marta Sobas of Medical University of Wroclaw, Poland: *"The decision to perform stem cell transplantation in AML patients who achieved the first complete remission is based on the risk-benefit ratio. Patients with a low to intermediate risk of relapse are not classical candidates for stem cell transplantation. However, the current method to predict the risk of relapse in these patients is not as precise as we would like. Therefore, we have developed a machine learning tool to more accurately predict the risk of relapse in these particular patients. We used data from 842 patients with AML to develop the tool. Based on patient characteristics such as age, gender, molecular genetic mutations, and cytogenetic abnormalities, the tool graphically provides the probability of Relapse-Free Survival over time. The tool is still a prototype, but ultimately, it should allow clinicians to carefully weigh the risks and benefits in this group of patients."*

Impact of Gender on Molecular AML Subclasses – a HARMONY Alliance Study

(3438 Matteuzzi et al | Program: Oral and Poster Abstracts | Session: 617. Acute Myeloid Leukemias: Biomarkers, Molecular Markers and Minimal Residual Disease in Diagnosis and Prognosis: Poster III Hematology Disease Topics & Pathways: Genomics, Adults, AML, Diseases, Myeloid Malignancies, Biological Processes, Study Population || Monday, December 13, 2021, 6:00 PM-8:00 PM)
LINK: https://ash.confex.com/ash/2021/webprogram/Paper152215.html

Tommaso Matteuzzi, Alma Mater Studiorum - Università di Bologna, Italy: *"We searched for gender differences in mutational patterns in ~2800 AML patients, using a panel of 70 cytogenetic and genetic abnormalities. Data on the HARMONY Big Data Platform is harmonized, ensuring data comparability and allowing meaningful analyses of gender imbalances. We studied AML molecular subclasses with advanced clustering methods observing differences in mutational patterns between males and females. At ASH2021 will be discussed if and how this affects patient outcomes".*

Different prognostic impact of recurrent gene mutations in IGHV-mutated and IGHV-unmutated chronic lymphocytic leukemia: a retrospective, multi-center cohort study by ERIC, the European Research Initiative on CLL, in HARMONY

(2617 Mansouri et al: Program: Oral and Poster Abstracts | Session: 641. Chronic Lymphocytic Leukemias: Basic and Translational: Poster II Hematology Disease Topics & Pathways: Translational Research || Sunday, December 12, 2021, 6:00 PM-8:00 PM)
LINK: https://ash.confex.com/ash/2021/webprogram/Paper150648.html

Larry Mansouri, ERIC European Research Initiative on CLL/Karolinska Institutet, Sweden: "Two major subtypes of CLL are based on the mutational status of the immunoglobulin heavy variable genes (IGHV). We know that patients with mutated IGHV (M-CLL) tend to have a better prognosis than patients with unmutated IGHV (U-CLL). However, there is considerable clinical heterogeneity among M-CLL patients: some will never require treatment and others require therapeutic intervention at an early stage. Therefore, we have set out to further refine prognosis in this subgroup based on the pattern of other genomic aberrations. We discovered mutations within several genes (SF3B1, NOTCH1, XPO1 and NFKBIE) that constitute a high-risk profile in patients with M-CLL (i.e., short time to first treatment). We suggest incorporating the analysis of these gene mutations into clinical practice. This may help to identify patients with an unfavorable prognosis, with obvious implications for therapy choice."

ASH-HARMONY Special-Interest session: The role of Real World Data Collection in Hematologic Malignancies

Sunday, December 12, 2021, 4:30 p.m. - 6:00 p.m. EST | Georgia World Congress Center, B312-B314

There is an increasing interest in the role of Real-World Data (RWD) to accelerate research and speed-up drug development for more effective treatments of blood cancer patients. In an inspiring Special-Interest Session, representatives of ASH, the ASH Research Collaborative, the FDA, EHA and the HARMONY Alliance will address Challenges and Potential Solutions to Accelerate Research, Regulatory Perspective on Data sharing and RWD to generate RWE, Patients Viewpoint on Real World Data Sharing and Clinical Viewpoints on Real World Data for Research. Expert views are shared by scientific organizations, regulatory agencies, patient associations, the ASH Research Collaborative and the HARMONY Alliance.

#bigdataforbloodcancer: Accelerating Better and Faster Treatment for Patients with Hematologic Malignancies.

The HARMONY Alliance (HARMONY and HARMONY PLUS) is a public-private European Network of Excellence for Big Data in Hematology. Our mission is to unlock and spread valuable knowledge on hematologic malignancies (blood cancers) among a large number of stakeholders, with the goal to harness and mine Big Data to speed up the development of improved treatments for patients and more effective treatment strategies.

- HARMONY and HARMONY PLUS are funded through the Innovative Medicines Initiative (IMI), Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. Funding is received from the IMI 2 Joint Undertaking and is listed under grant agreement for HARMONY No. 116026 and grant agreement for HARMONY PLUS No. 945406. This Joint Undertaking receives support from the European Union's Horizon 2020 Research and Innovation Programme and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

- HARMONY: 53 Partners and 47 Associated Members, including 9 European Patient Organizations from 17 countries. Budget: 40 million | January 2017- June 2023

- HARMONY PLUS: 39 Partners from 10 countries. Budget 12 million. Period: October 2020 – October 2023

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www.harmony-alliance.eu | www.bigdataforbloodcancer.eu | @HARMONYnetEU

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