

HARMONY



ALLIANCE



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HARMONY

#BigDataforBloodCancer

Lars Bullinger
Charité Universitätsmedizin Berlin

HARMONY



ALLIANCE

Public-Private Partnership for Big Data in Hematology
Accelerating better treatment of blood cancer patients



Community of approx.
400 professionals

Over
100
organizations



from
18
countries



14
key targeted
blood cancers



Big Data
analytic services



Big Data Platform with
>70.000 anonymized
patient records identified



Research, Delphi and
Multi-stakeholder projects

Funded by



Innovative Medicines
Initiative

Support from



European Union's
Horizon 2020 Research
and Innovation
Programme



European Federation of
Pharmaceutical
Industries and
Associations

Part of



IMI Big Data for
Better Outcomes
(BD4BO)

About HARMONY



The first and largest
Public-Private Partnership in
Hematology



Budget
40 million Euro



5-year project
from January 2017
until Dec 2021

Focus on **Big Data** in



Acute
Lymphoblastic
Leukemia



Acute
Myeloid
Leukemia



Childhood
Hematologic
Malignancies



Chronic
Lymphocytic
Leukemia



Multiple
Myeloma



Non-Hodgkin
Lymphoma



Myelodysplastic
Syndromes



Community of
multi-stakeholder organizations representing
18 European countries



53
Partners

Patient Cluster with
**7 European Patient
Organizations**



43
Associated
Members



About HARMONY PLUS



Part of the largest
Public-Private
Partnership in
Hematology

Community of

39
Partners

8
Associated Partners

Will create the availability of a
historical control arm as a new model
of supporting HMs' CT design



Focus on **Big Data** in



Myeloproliferative
Disorders



Chronic Myeloid
Leukemia



Polycythaemia
Vera



Essential
Thrombocythemia



Myelofibrosis



Hodgkin's
Lymphoma



Waldenström
Macroglobulinaemia



and other
rare blood
cancers



Budget
11,8 million Euro

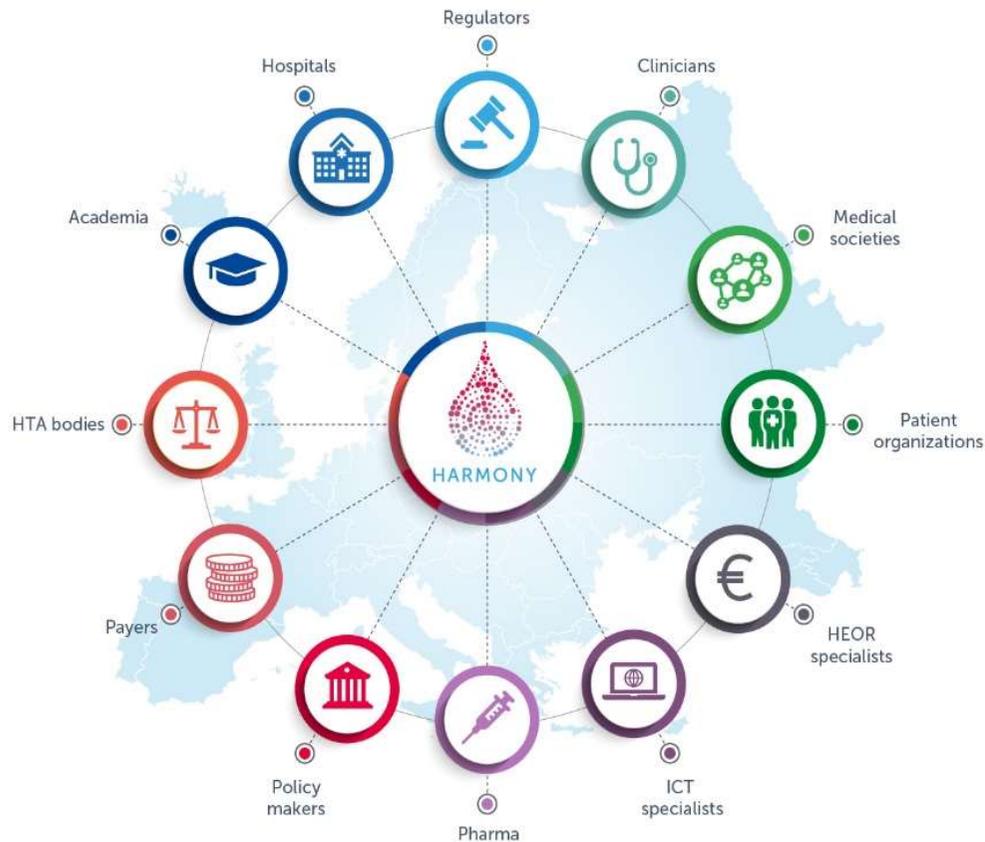
Will build additional modules that
will enable data driven decisions for
payers and regulators, based on
Artificial Intelligence techniques



3-year project
from October 2020 until Oct 2023

Will pursue more collaborations
with other big data projects
worldwide

HARMONY – Uniting the European hematological community



Building a high-quality Big Data platform on hematologic malignancies



Harmonization of outcome measures and endpoint definitions for HMs at European level



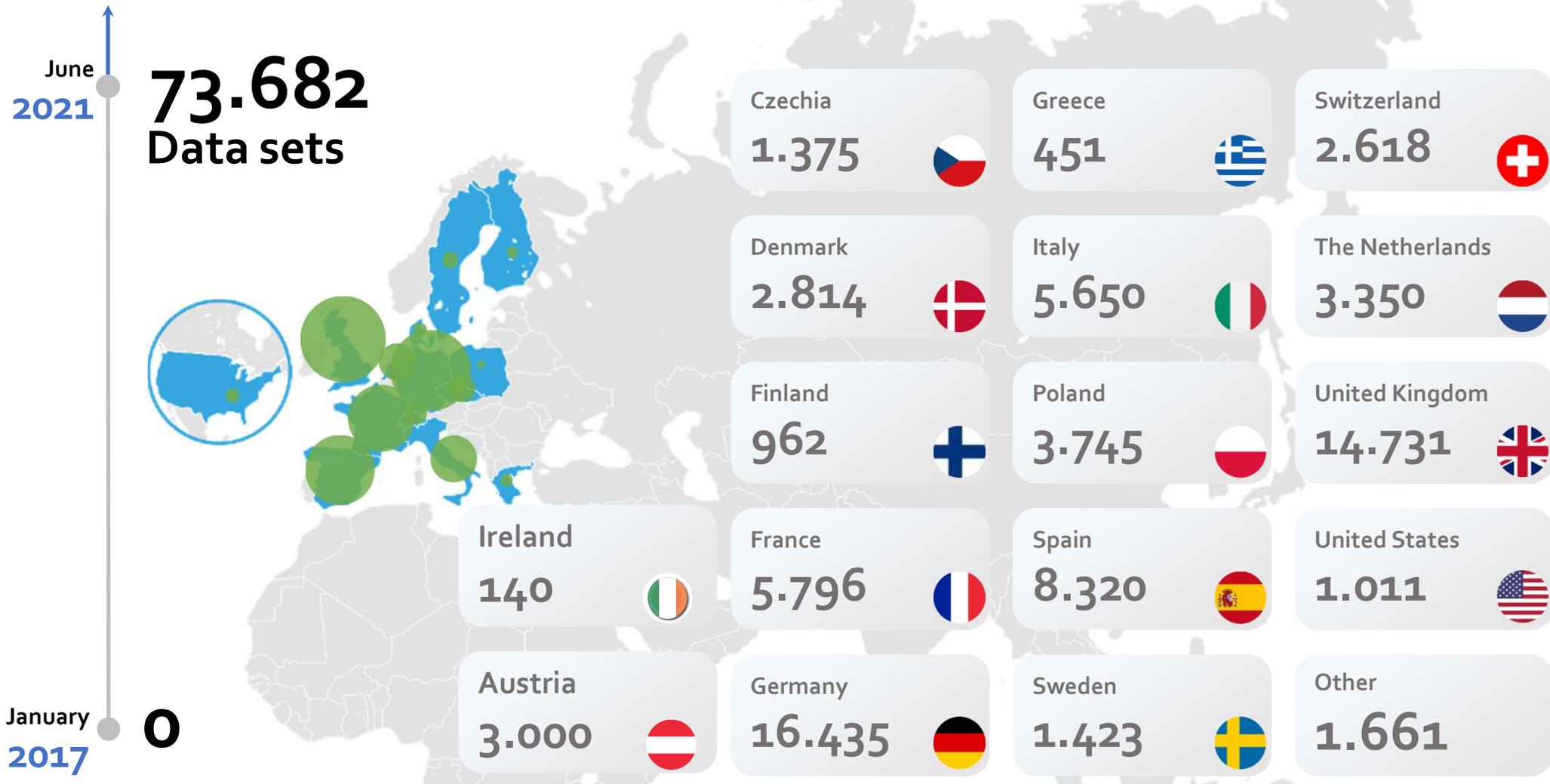
Speed up drug development, access pathways, and bench-to-bedside process



Increase the application of omics data in clinical practice

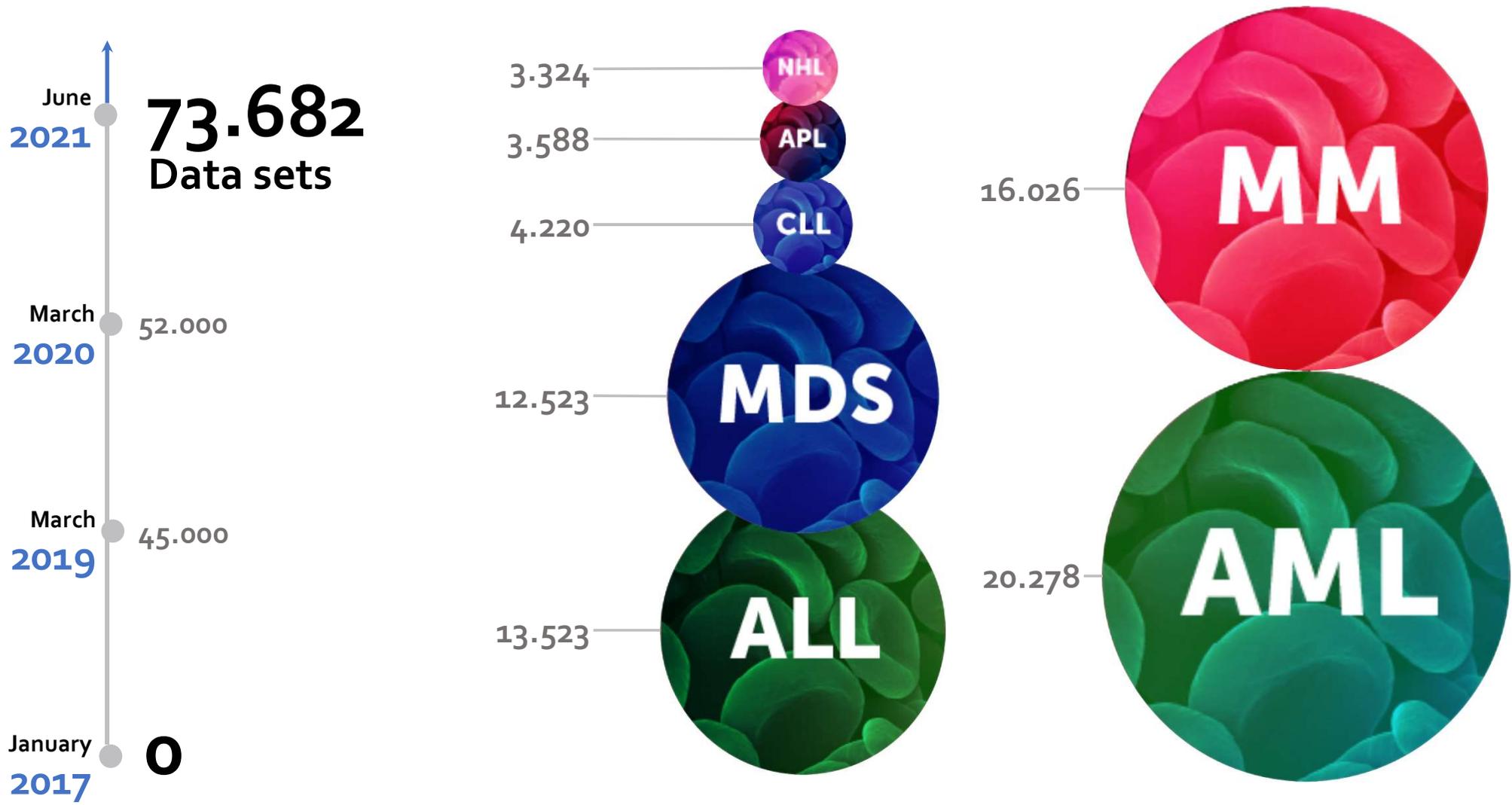
Data barometer HARMONY Big Data Platform

by number of data sets identified per country



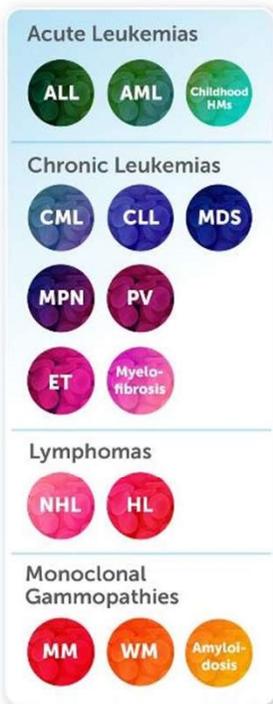
Data barometer HARMONY Big Data Platform

by number of data sets **identified** per blood cancer



Core elements of the HARMONY Architecture

FOCUS BLOOD CANCERS



DATA PROVIDERS

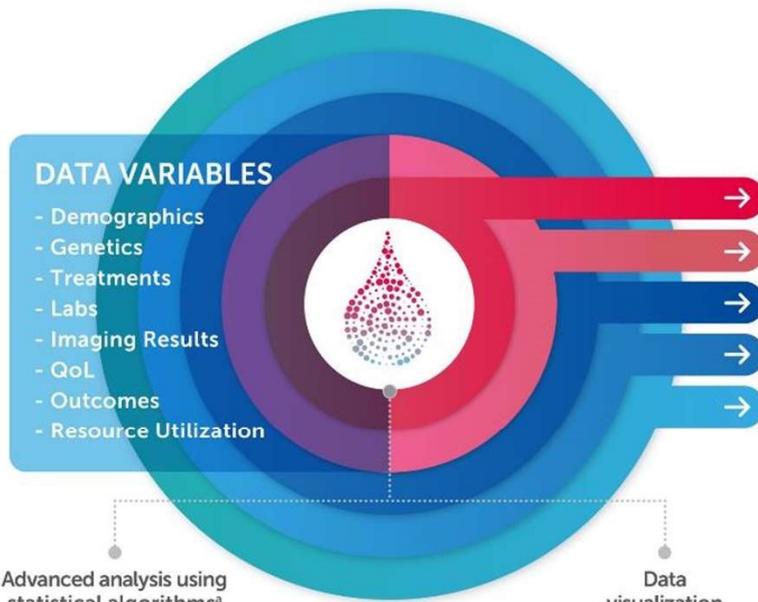
Partners and Associated members

- DATA SOURCES
- Hospitals
 - Interventional and non-interventional trials
 - Biobanks
 - Pharma

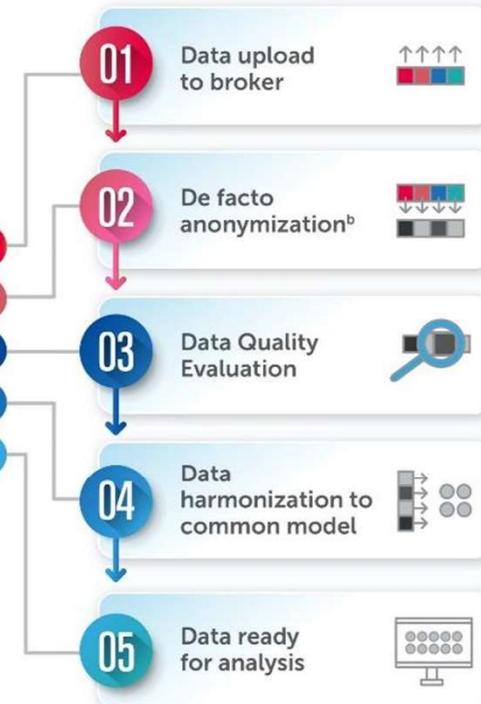
FULL PROJECT RESEARCH

HARMONY BIG DATA PLATFORM

DATA PROCESSING



BIG DATA PLATFORM ANALYTICS

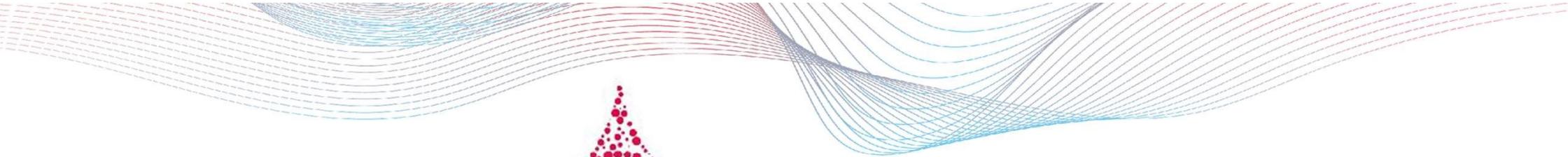


CURRENT AND UPCOMING PROJECTS

- Project Research publications
- New Research Projects
- Harmonization of Outcomes
- Guidelines
- Speed up drug development
- Increase application of omics data in clinical practice
- Additional safety signals
- Patient journey and disease knowledge

^a Only data essential to the analysis are accessible (to a limited group of users during a specific time span)

^b Data anonymization process is ISO 27001 certified



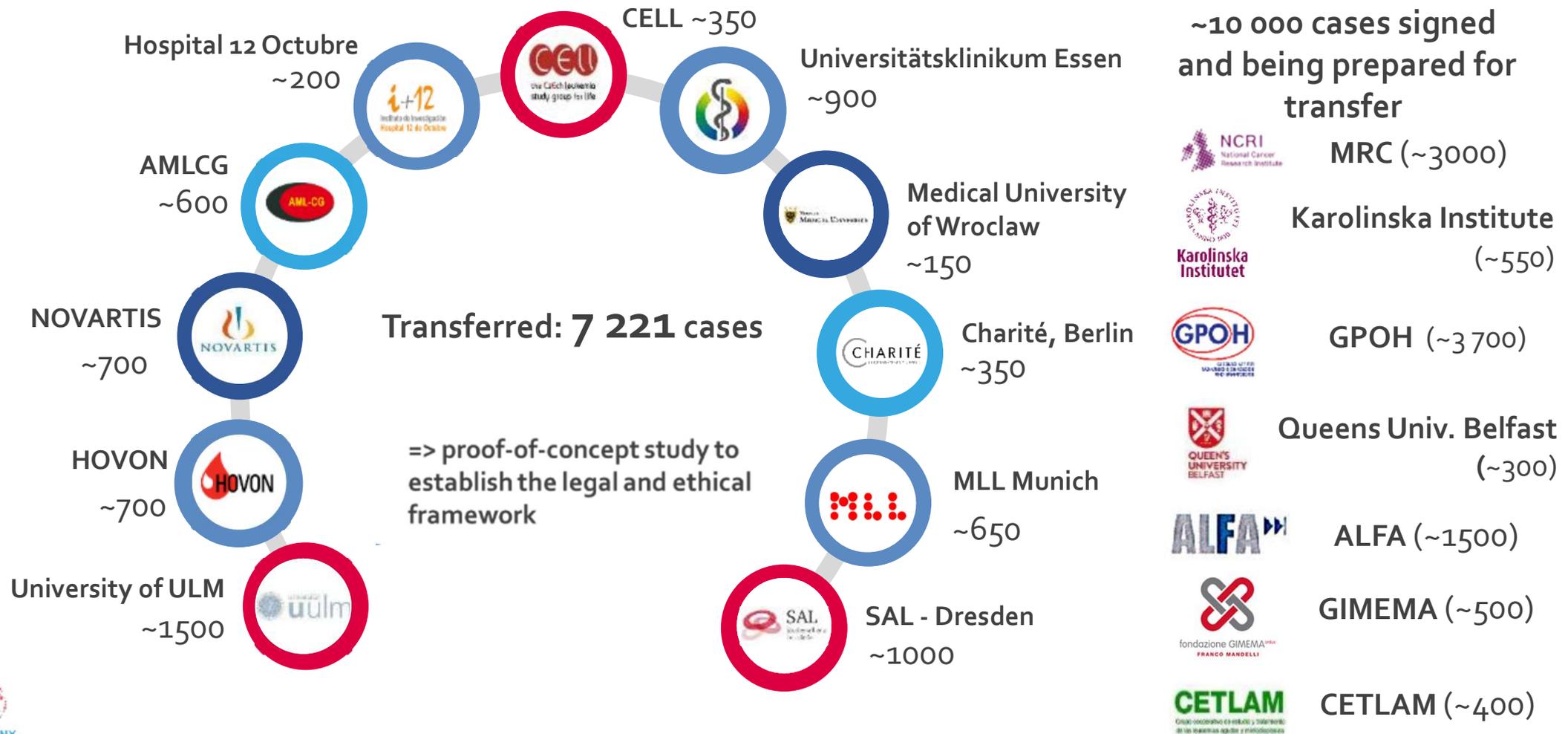
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HARMONY Case: Acute Myeloid Leukemia (AML)

AML Pilot Study: Gene-gene interactions influence treatment outcomes

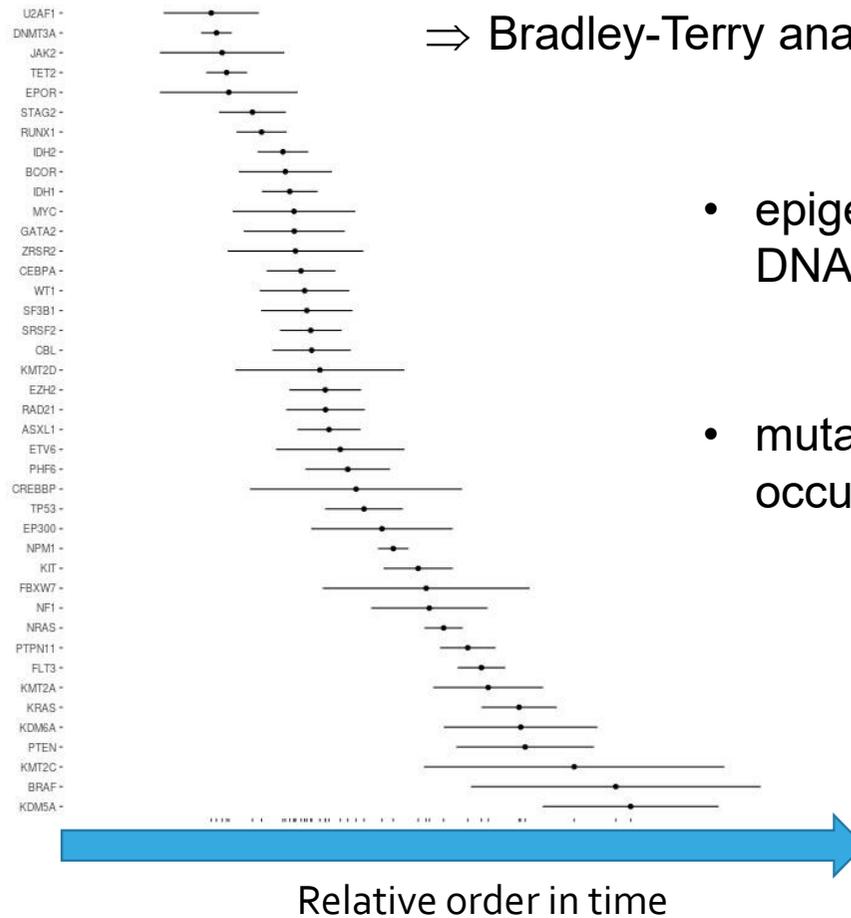


AML - Data granularity

- Data Dictionary has to be completed in order to finalise and sign the legal agreements.
- Data Dictionary is assessed by the **Data Quality Supervision Committee**.
- **Data granularity**
 - Demographic data
 - Diagnostic information
 - Omics data (NGS)
 - Treatment information (treatments received, response to the therapy, OS, DFS, follow-up including MRD data, etc.)
 - Quality of Life (QoL) data
- Data sets include treatment with new agents (e.g. midostaurin)

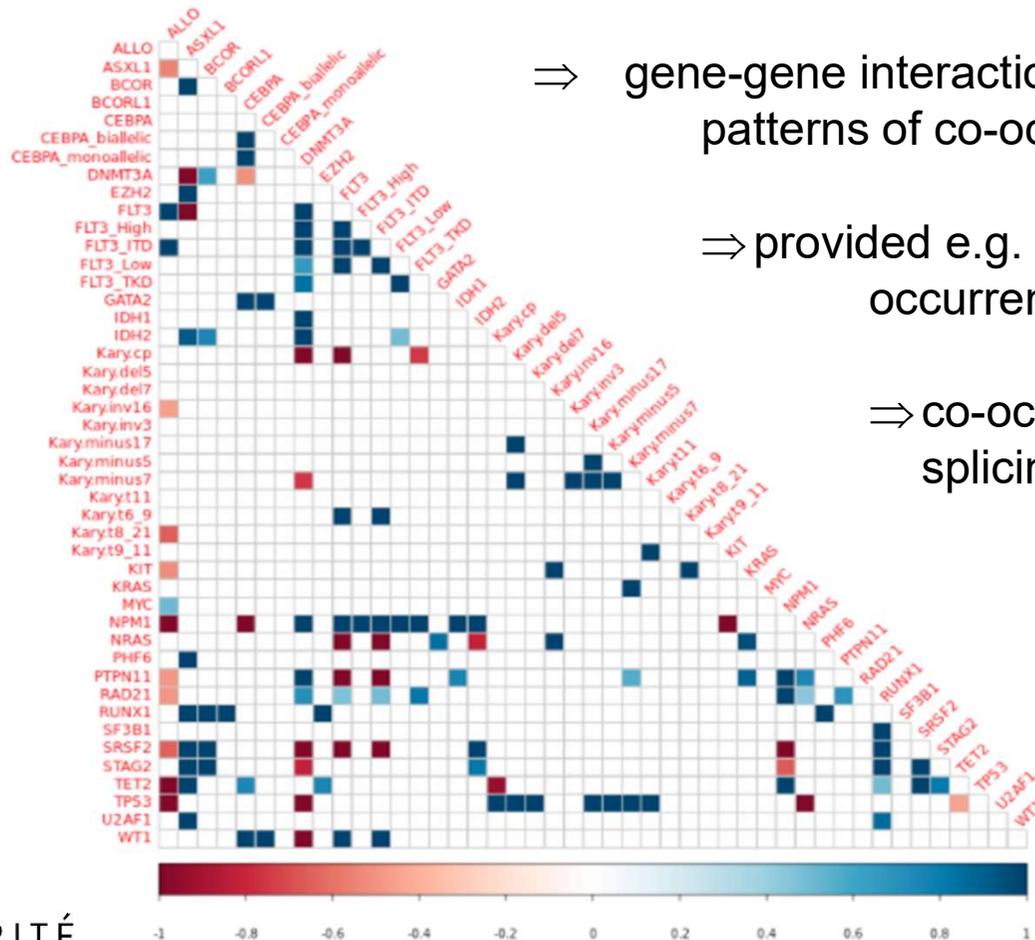
Disease group:
A: DEMOGRAPHIC DATA
Demographics
Medical History
Total Type A Percentage
B: DIAGNOSIS DATA
WHO/FAB Classification
Symptoms
Physical exam
Blood Count and Chemistry
Prognostic Score
PB and BM Cytology
Histology
Flow Cytometry
Karyotype + FISH
M.Biology
Imaging tests
Total Type B Percentage
C: OMICS DATA
Omics
Total Type C Percentage
D: TREATMENT DATA
Treatment and Response to Treatment
First line:
Second line:
Third line:
MRD by Flow Cytometry OR Molecular Biology
Treatment adverse effects
Treatment LATE adverse effects (e.g. infertility, puberty, growth retardation)
Transplantation details (including Relapse/GvHD data)
Survival data (follow-up data)
Total Type D Percentage
E: QoL DATA
QoL
Total Type E Percentage

Model of clonal evolution



- epigenetic driver mutations in genes affecting DNA methylation are very early events (e.g. *DNMT3A*, *TET2*, *IDH1/IDH2*)
- mutations in histone modifying enzymes occur later (e.g. *KMT2D*, *EZH2*, *ASXL1*, *EP300*)

Gene–gene interactions



⇒ gene-gene interaction analysis confirmed known patterns of co-occurrence and mutual exclusivity

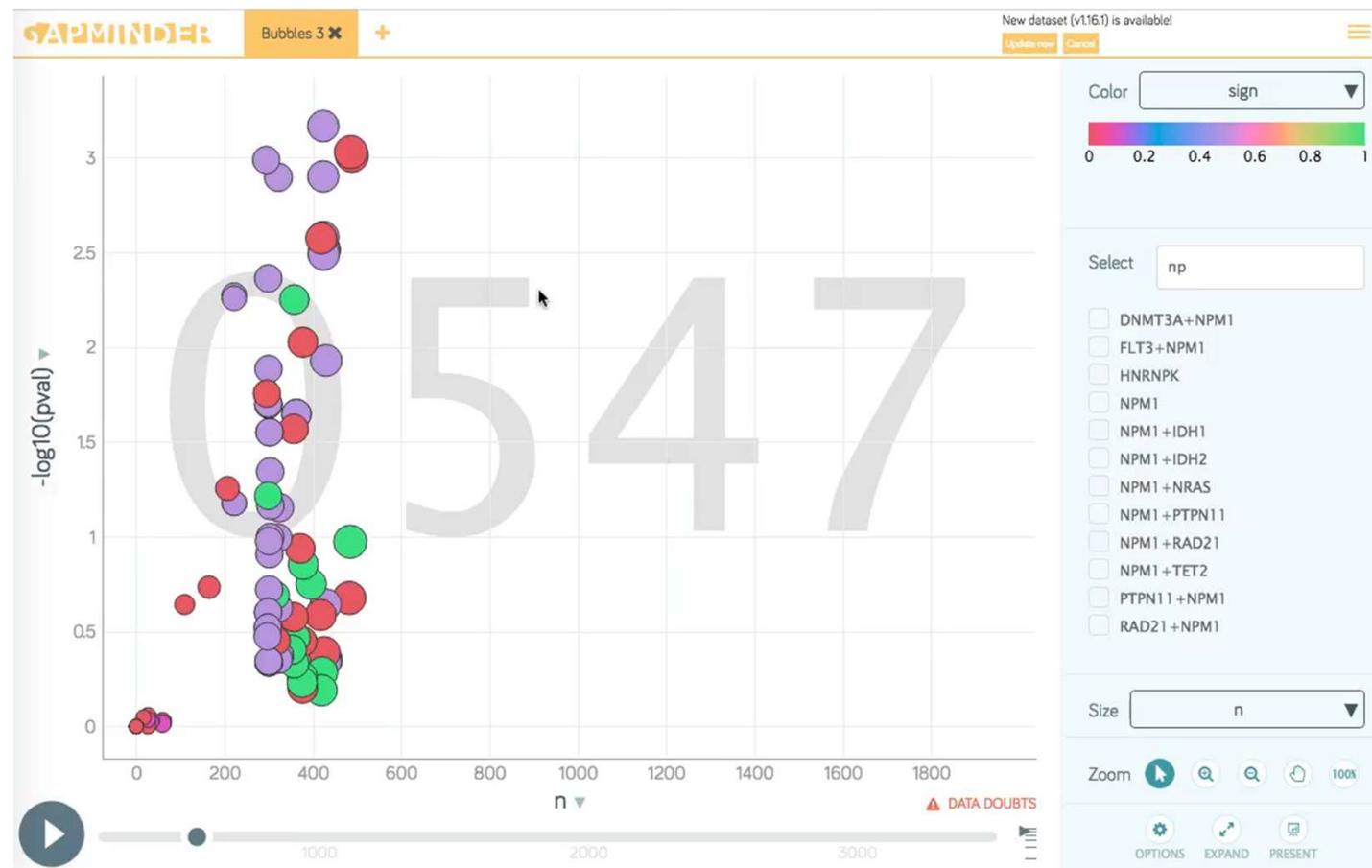
⇒ provided e.g. additional evidence for the co-occurrence of *EZH2* mutations with *RUNX1*

⇒ co-occurrence of *RUNX1* with “aberrant splicing” (*SRSF2*, *SF3B1*, and *STAG2*)

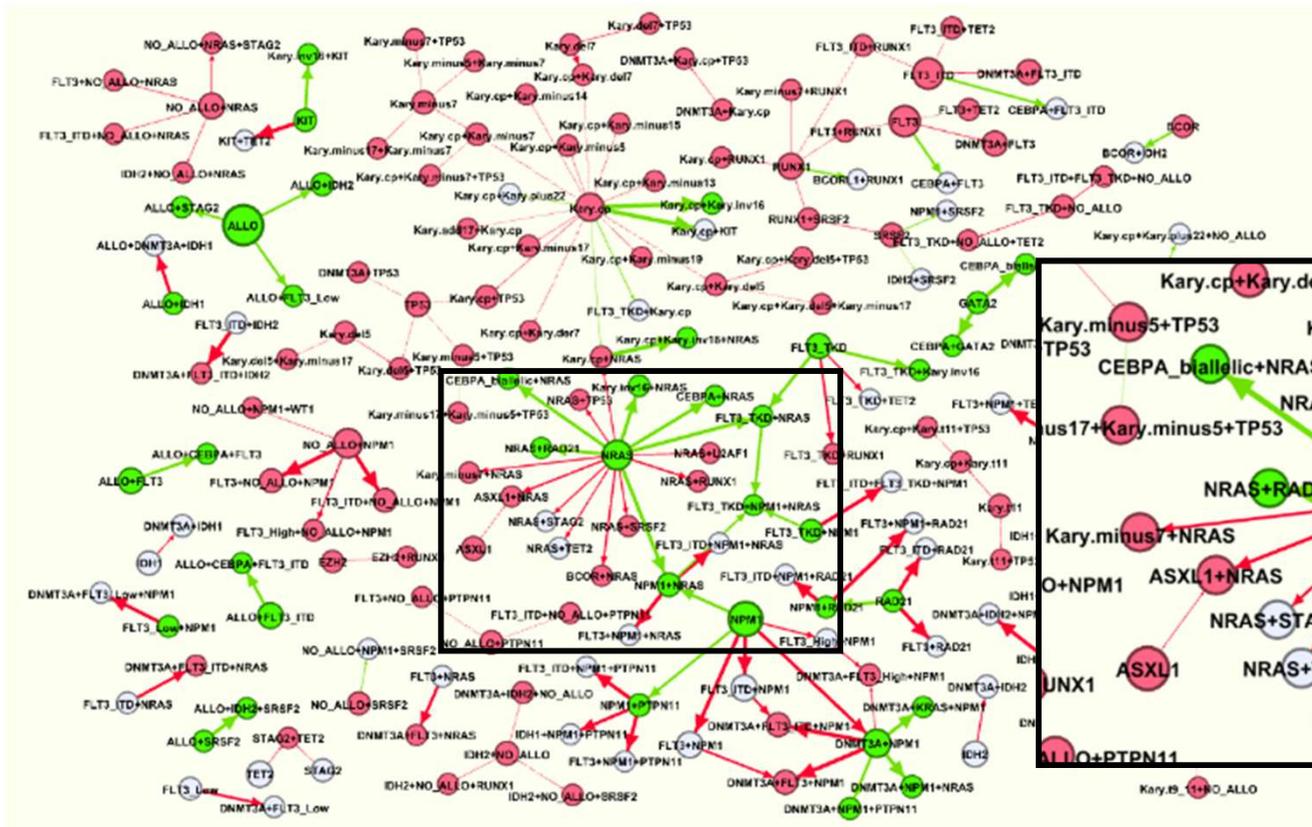
Only relationships with a p-value ≤ 0.05 are presented:

- blue color: co-occurrence
- red color: mutual exclusivity

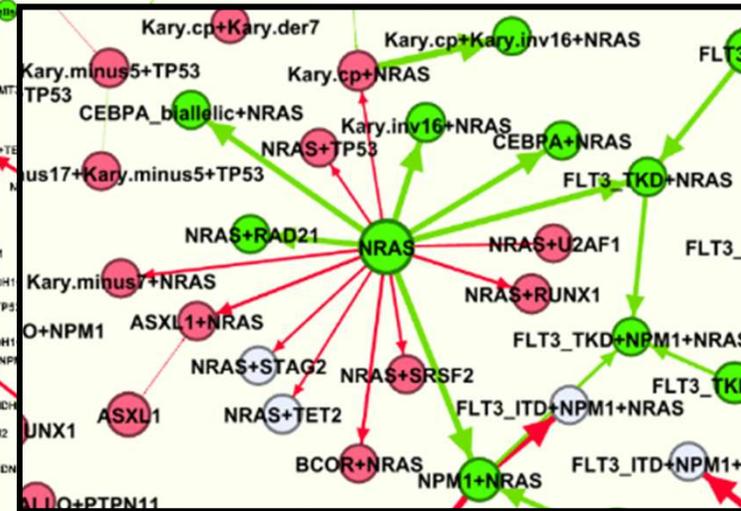
Clinical impact of gene-gene interactions



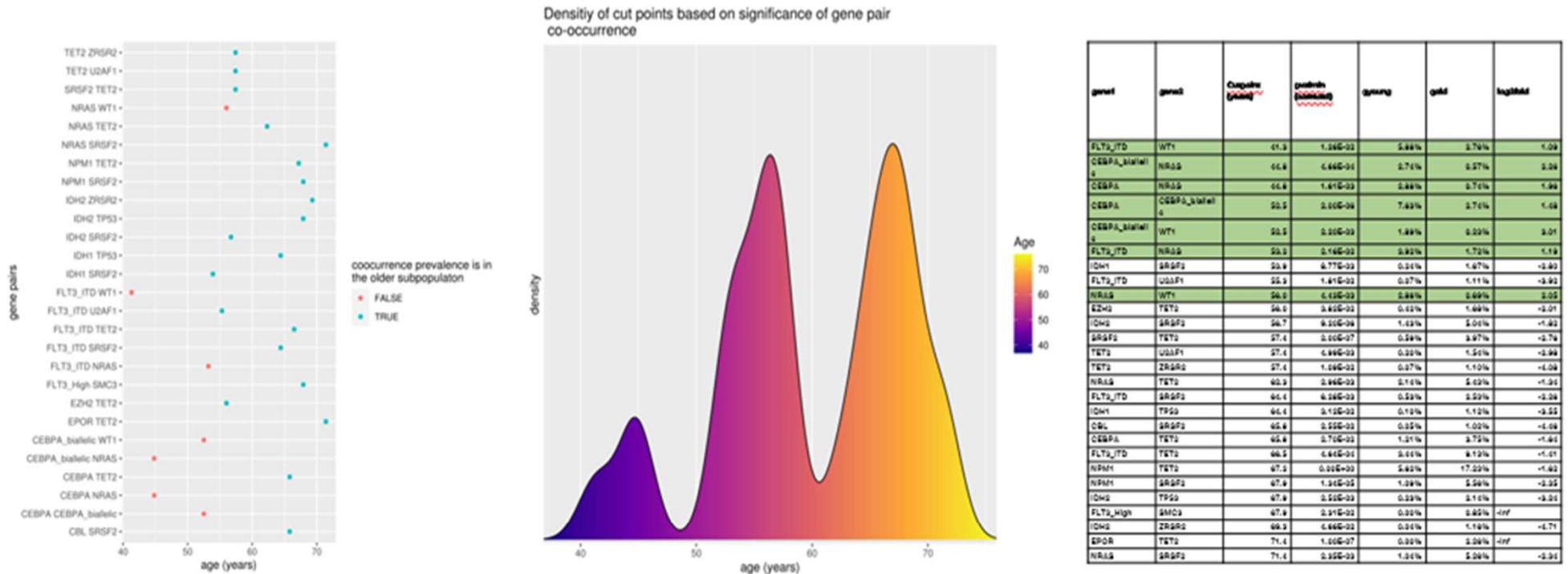
Gene-gene interactions – clinical implications



⇒ Interactive tools to explore gene-gene interactions



Classification based on of gene interactions



The age cutpoints are defined for the minimum p value of a χ^2 test on gene mutation co-occurrences for the split populations. The p values are corrected according to the asymptotic formula of Miller and Siegmund (see, e.g. Lausen and Schumacher 1994). Shown: only significant gene pairs.

Summary – Overall Components

Genetic Drivers

NPM1, RUNX1/ASLX1, IDH2, CEPBA*bi*, TP53-CK

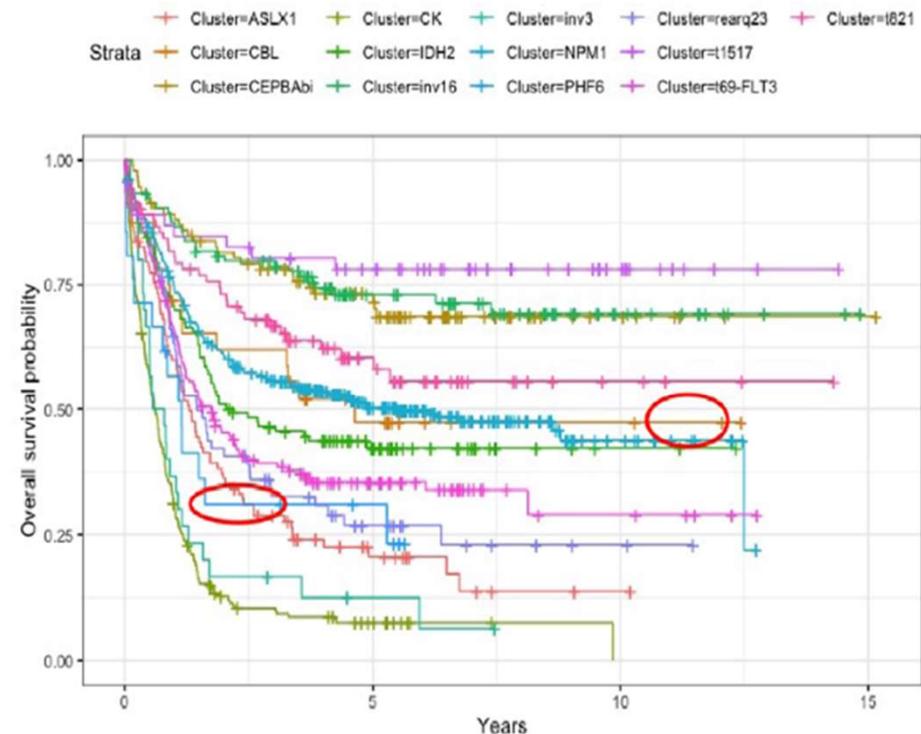
Gene Fusion Drivers

inv3, inv16, t821, t69-FLT3, rearq23, t1517

1. **NPM1** FLT3ITD FLT3TKD DNMT3A FLT3other WT1 PTPN11 KRAS NRAS IDH1 RAD21
2. **CKTP53** plus13 minus17abn17p abn3q
3. **ASXL1** TET2 SRSF2 EZH2 **RUNX1** STAG2 MLLpartialTD plus13 BCOR U2AF1
4. **IDH2** SRSF2 IDH2P140 ASXL1 IDH2P172
5. **CEPBA*bi*** del9q GATA2
6. **FLT3ITD t69 t1517** WT1 FLT3other
7. **IDH2** FLT3other
8. **t821** KIT minusY del9q KITexon17
9. **inv3** minus7 SF3B1
10. **Rearq23**
11. NRAS **inv16** KITexon8 KIT plus22

New Drivers Emerging from Bayesian Network Analysis:

**CBL
PHF6**



20 ongoing projects

The image displays a collection of 20 research project cards, each representing an ongoing project. The cards are arranged in a grid-like fashion, with some overlapping. Each card typically includes a small image, a title, a brief description, and logos for the programs involved (ALL, AML, CLL, COVID-19, MM, HARMONY, HARMONY PLUS, MPN).

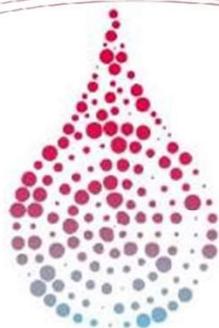
- ALL 1:** Use of Big Data to improve outcomes for patients with Acute Myeloid Leukemia. Programs: ALL, HARMONY.
- ALL 2:** Prognostic Value of IKZF1 Gene. Programs: ALL, HARMONY.
- ALL 3:** Exploring outcomes. Programs: ALL, HARMONY.
- ALL 4:** Using big data to confirm the link between MRD and survival in AML. Programs: ALL, HARMONY.
- AML 1:** Use of Big Data to revise treatment strategies in Acute Myeloid Leukemia. Programs: AML, HARMONY.
- AML 2:** Optimizing Leukemia Management. Programs: AML, HARMONY.
- AML 3:** Using big data to shed light on the clinical impact of genomic alterations in sAML/tAML. Programs: AML, HARMONY.
- AML 4:** Using big data to confirm the link between MRD and survival in AML. Programs: AML, HARMONY.
- CLL:** Harnessing big data to predict outcomes in Chronic Lymphocytic Leukemia. Programs: HARMONY.
- COVID-19:** Risks associated with COVID-19 in patients with hematological malignancies. Programs: COVID-19, HARMONY PLUS.
- MM 1:** Optimizing prognostication and personalizing treatment in Multiple Myeloma. Programs: MM, HARMONY.
- MM 2:** Contextualizing clinical trials by developing robust historical control arm cohort. Programs: HARMONY, MM.
- MPN:** Impact of Covid-19 on Myeloid Neoplasms. Program: MPN.
- MM 3:** Personalizing treatment in Multiple Myeloma. Programs: MM, HARMONY.

+2 projects recently approved in CLL and CML

+2 projects under review in AML and MDS



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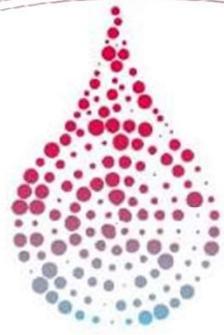
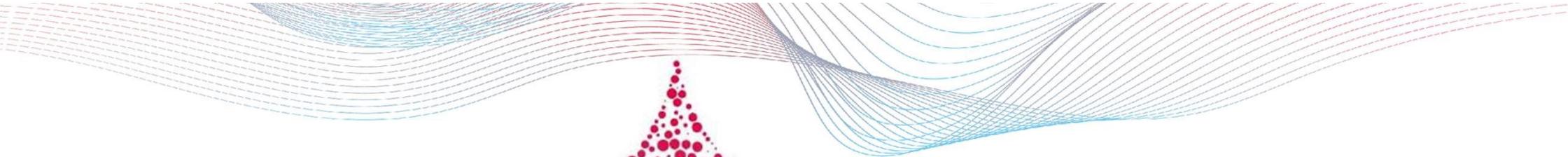


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Thank you



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innovative
medicines
initiative



efpia