HARMONY – IMI Big Data for Better Outcomes for Hematologic Malignancies

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Sacyl

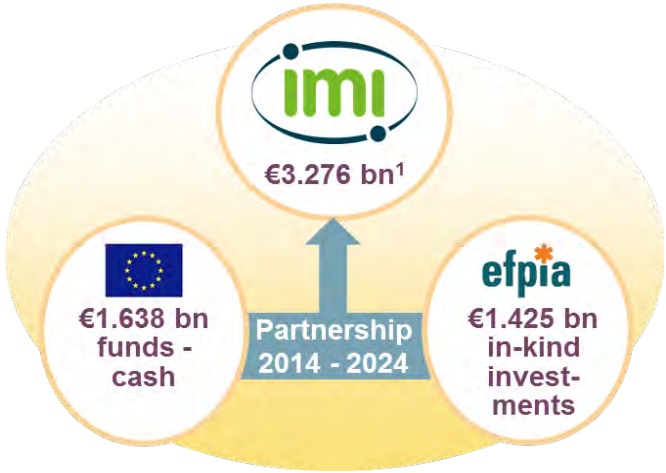
Hematología HOSPITAL UNIVERSITARIO SALAMANCA

HARMONY

IMI: Largest EU Public Private Partnership for Health R&D

- 1:1 funding, joint decision making
- All EU funds go to SMEs, academia, patient organisations
- Pharmaceutical industry matches contribution **in-kind**
- 3.400 M€ in IMI-2
- IMI-2 not limited to pharmaceutical industry (NGS, IT, medical devices, diagnostics)

IMI2



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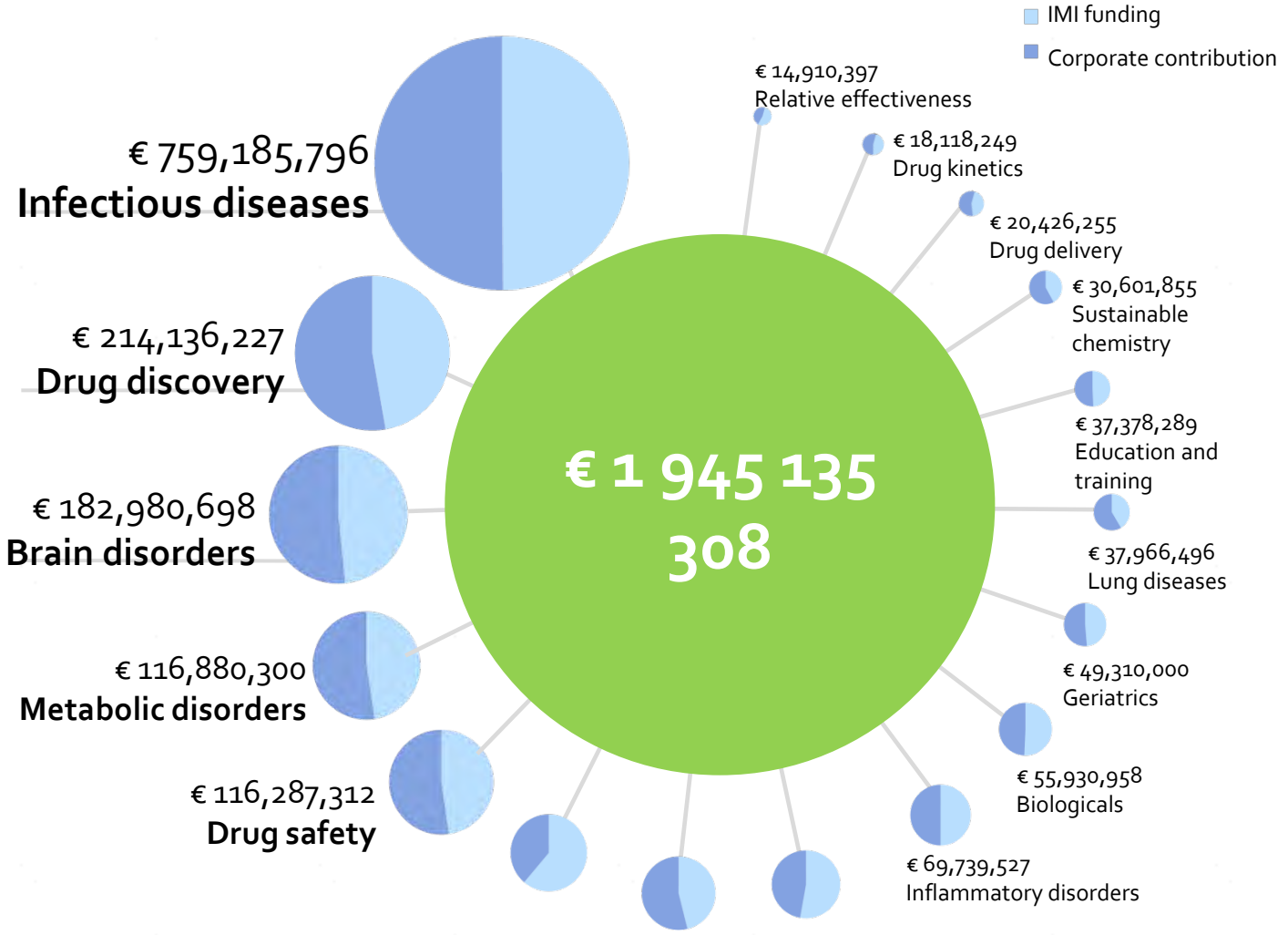
11 Calls for Proposals under IMI-1 spend €2 billion



Oncology?
Hematology?

IMI-1: 59 Projects Covering Wide Spectrum of Topics

HARMONY

imi innovative medicines initiative

efpia

IMI2 Scientific Program: Initial Five Big Themes

Therapeutic Areas and Cross-cutting Themes

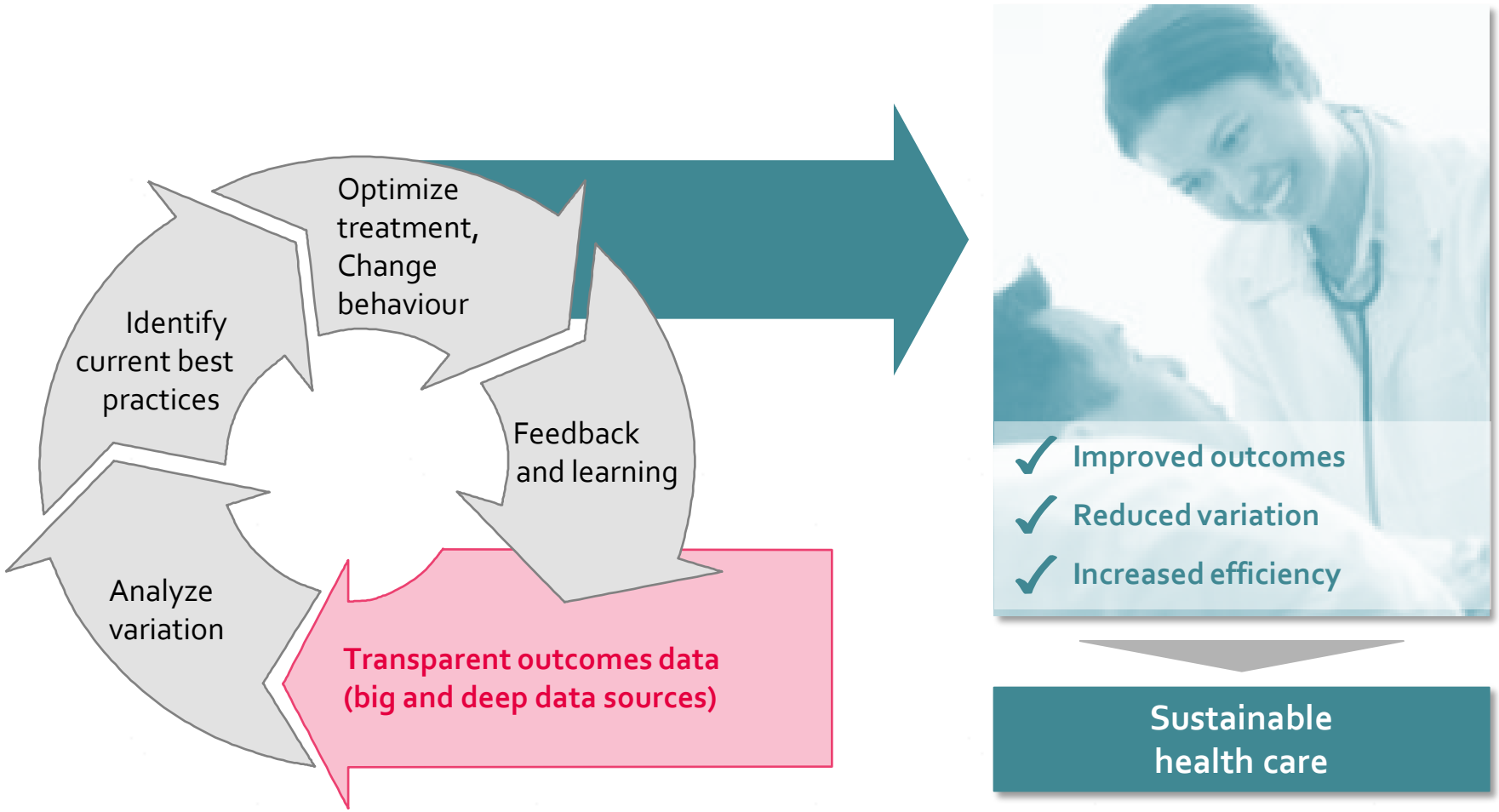
1. **Neuro-degeneration**
   prevention and treatment of dementia and other neurodegenerative diseases
2. **Prevention and treatment of immune mediated disease**
   Advance immunological understanding to deliver new medicines and better vaccines
3. **Metabolic disorders**
   prevention and early intervention type 2 diabetes, obesity, dislipidemia, hypertension and its complications
4. **Infection control**
   Address multidrug resistance and create incentives for renewed investment (antimicrobials, antivirals) and better vaccines
5. **Translational Safety**
   identification and development of point of care safety biomarkers and new system biology platforms to better predict toxicity and safety during early development

Differentiating Enablers for all themes

Towards early and effective patient access to innovative prevention and treatment solutions (MAPPs):

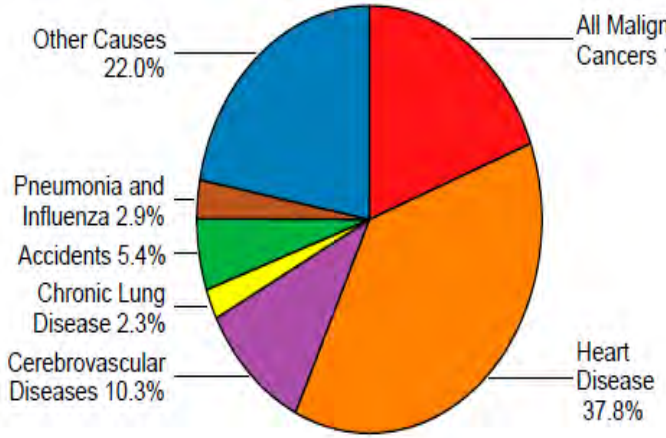
- Target validation based on human biology
- Stratified medicine, precision medicine
- Innovation in clinical trials
- Data generation and interpretation (knowledge management)
- Prevention, disease interception, patient adherence (incl. societal acceptance of vaccines)
- Effect on medical practice and outcomes (health/disease management)
- Regulatory framework (including pharmacovigilance)
- Patient access

Within IMI2, big data is a key topic as it holds significant potential to improve outcomes and drive healthcare efficiency

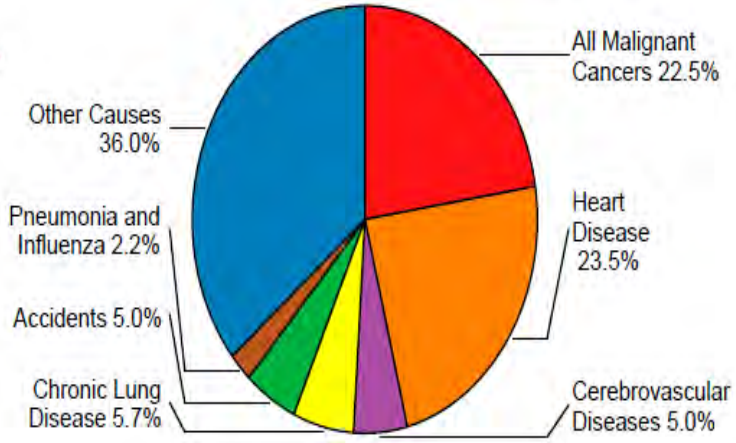


Leading Causes of Death in US, 1975 vs 2013

(% of All Causes of Death)

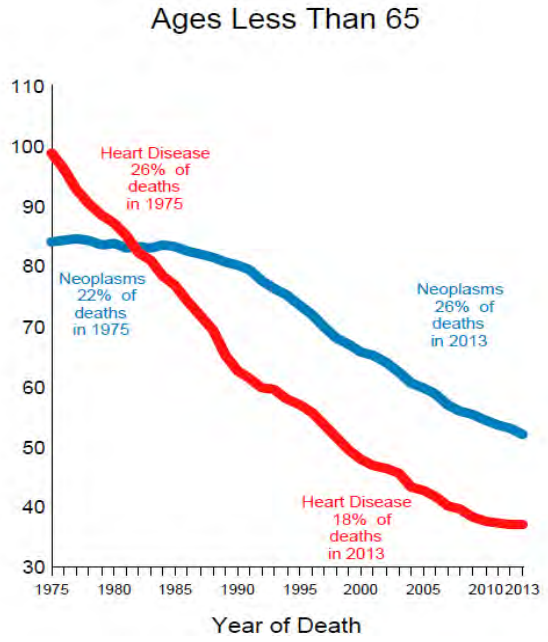


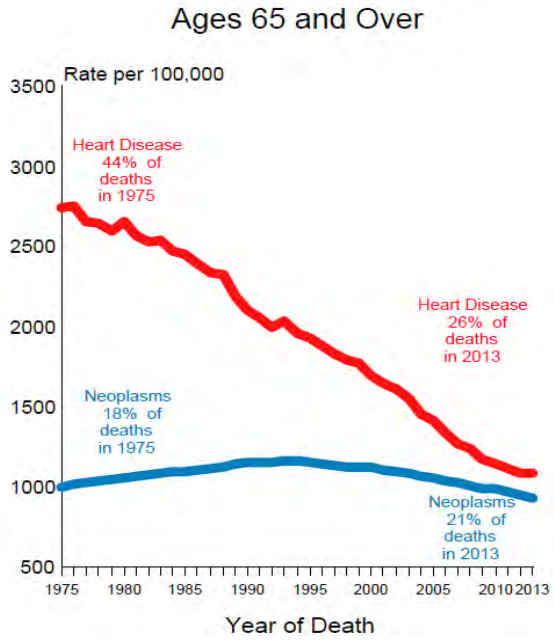
1975



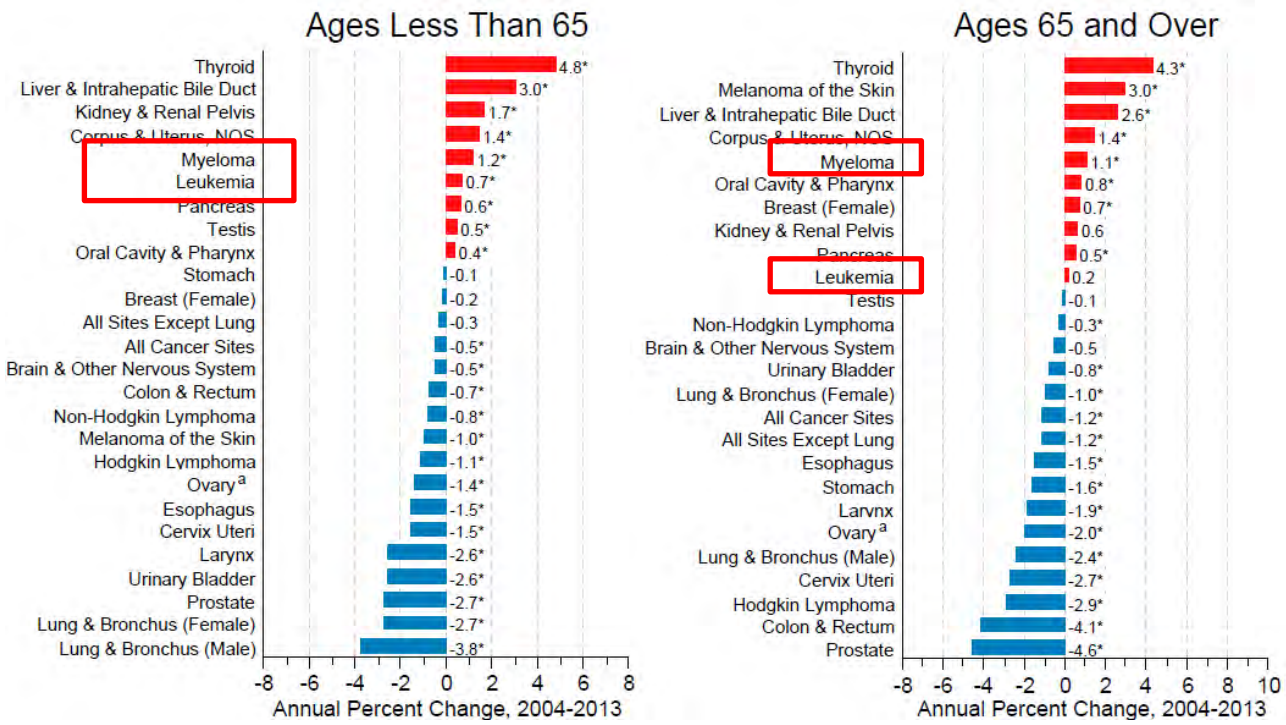
2013

Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention





Trends in SEER incidence rates and Life Lost



Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention

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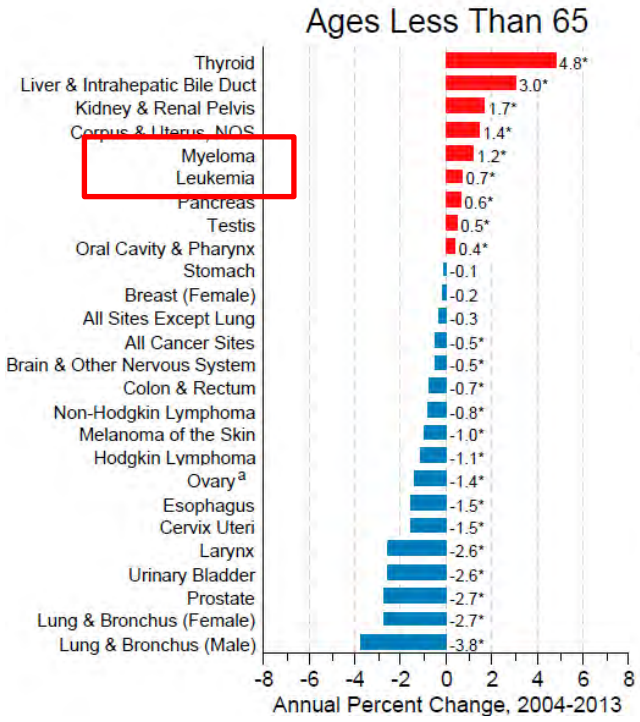
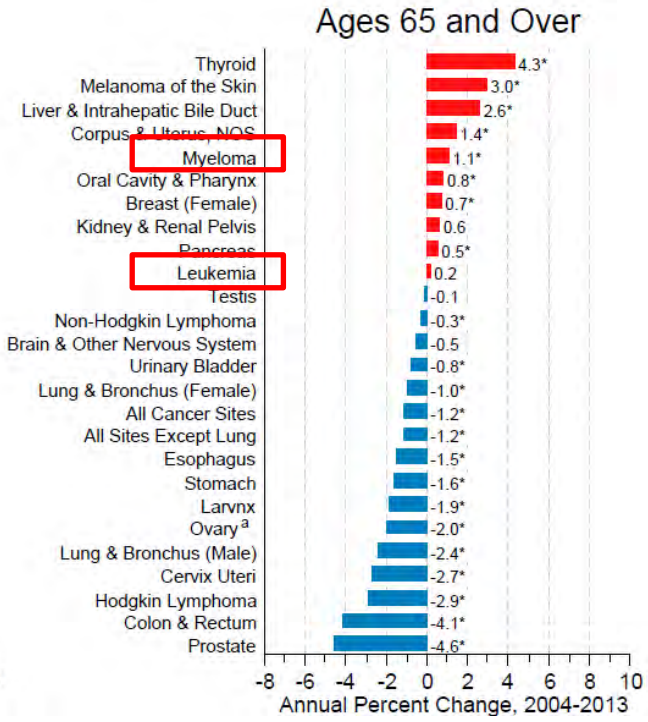
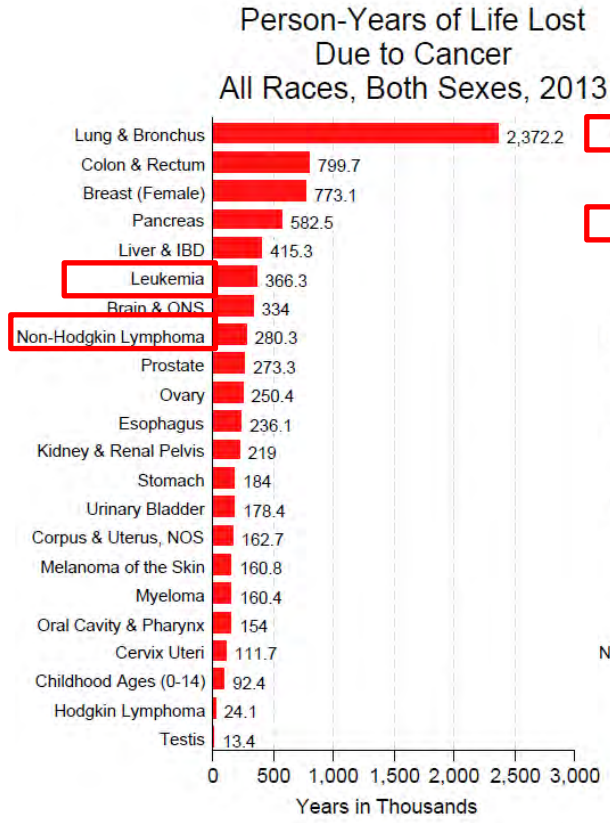
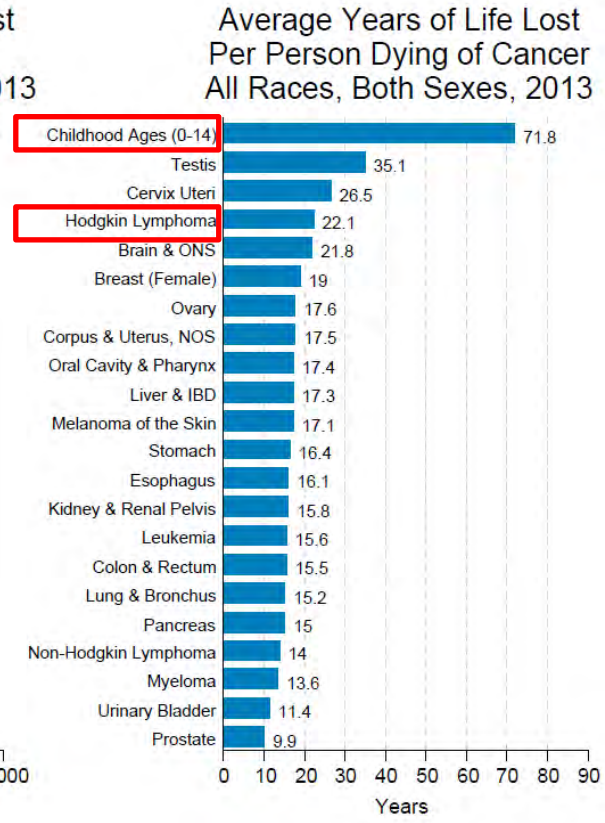


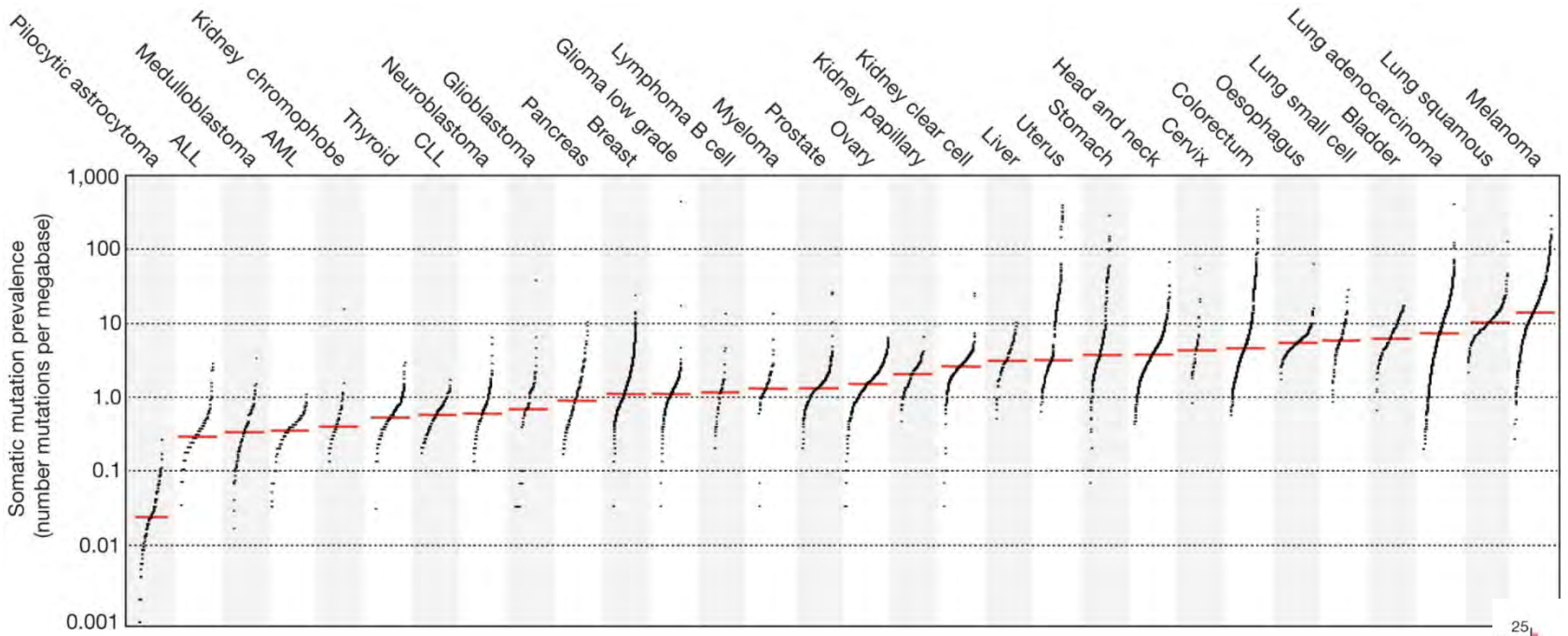






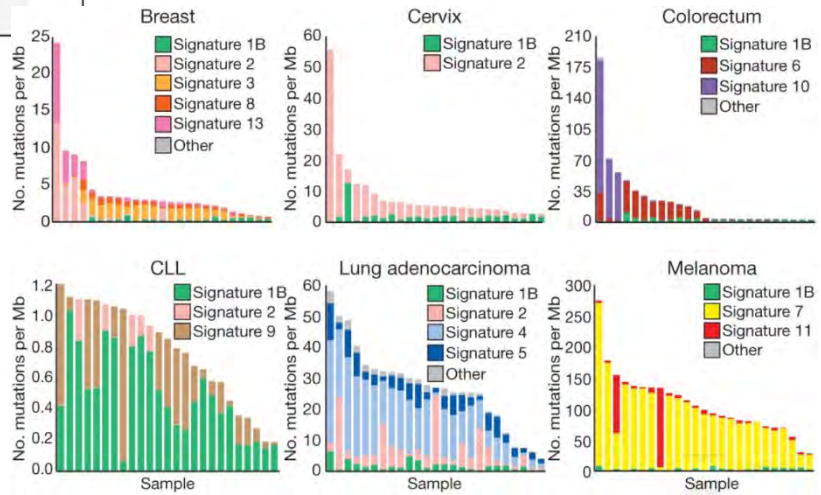
Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention

Genetic Signatures in Cancer



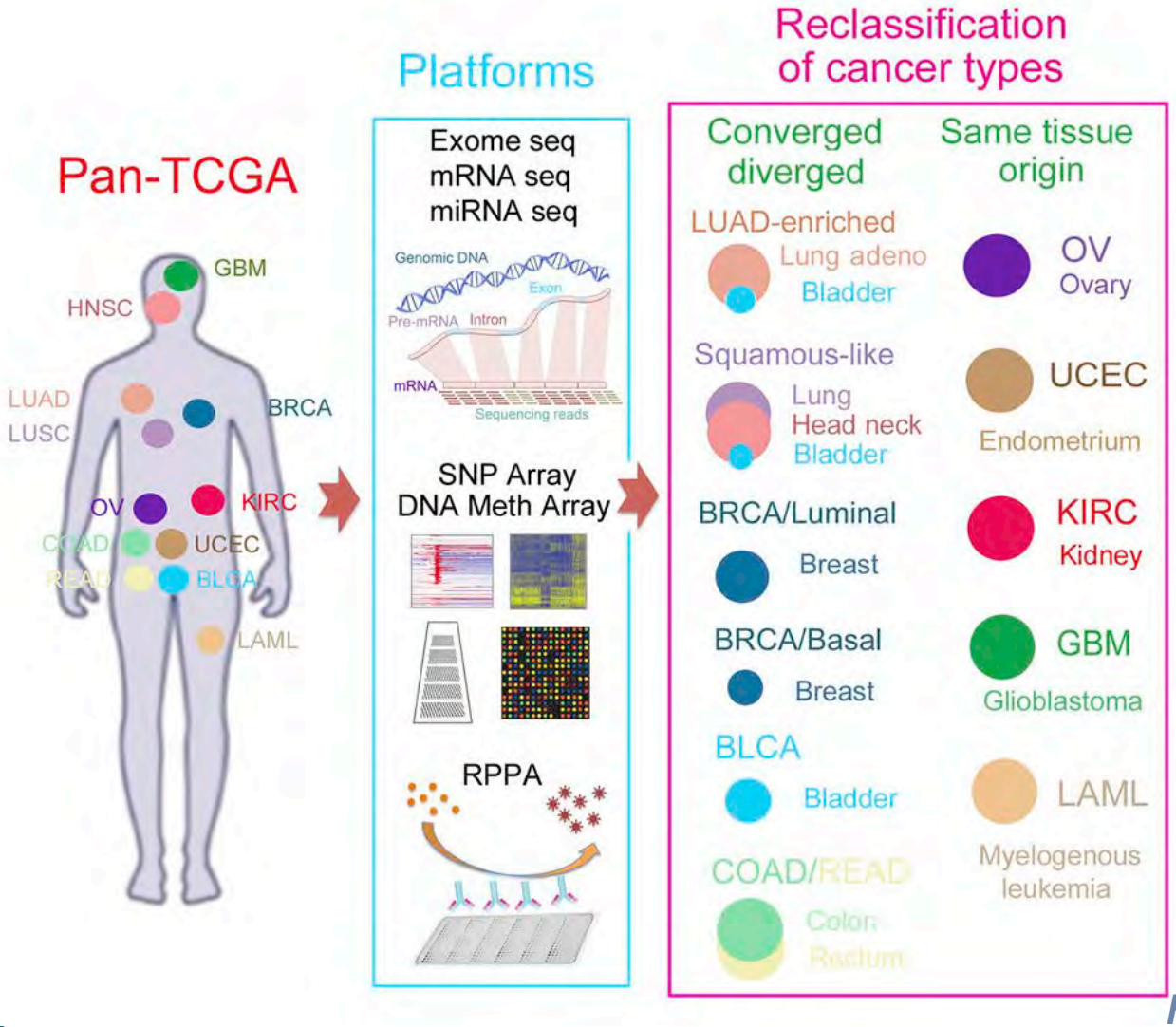
4.938.362 mutations in 7.042 patients with cancer

https://cancergenome.nih.gov/



Alexandrov et al. Nature, 2013

Next Generation Sequencing studies allow a new reclassification of Cancer

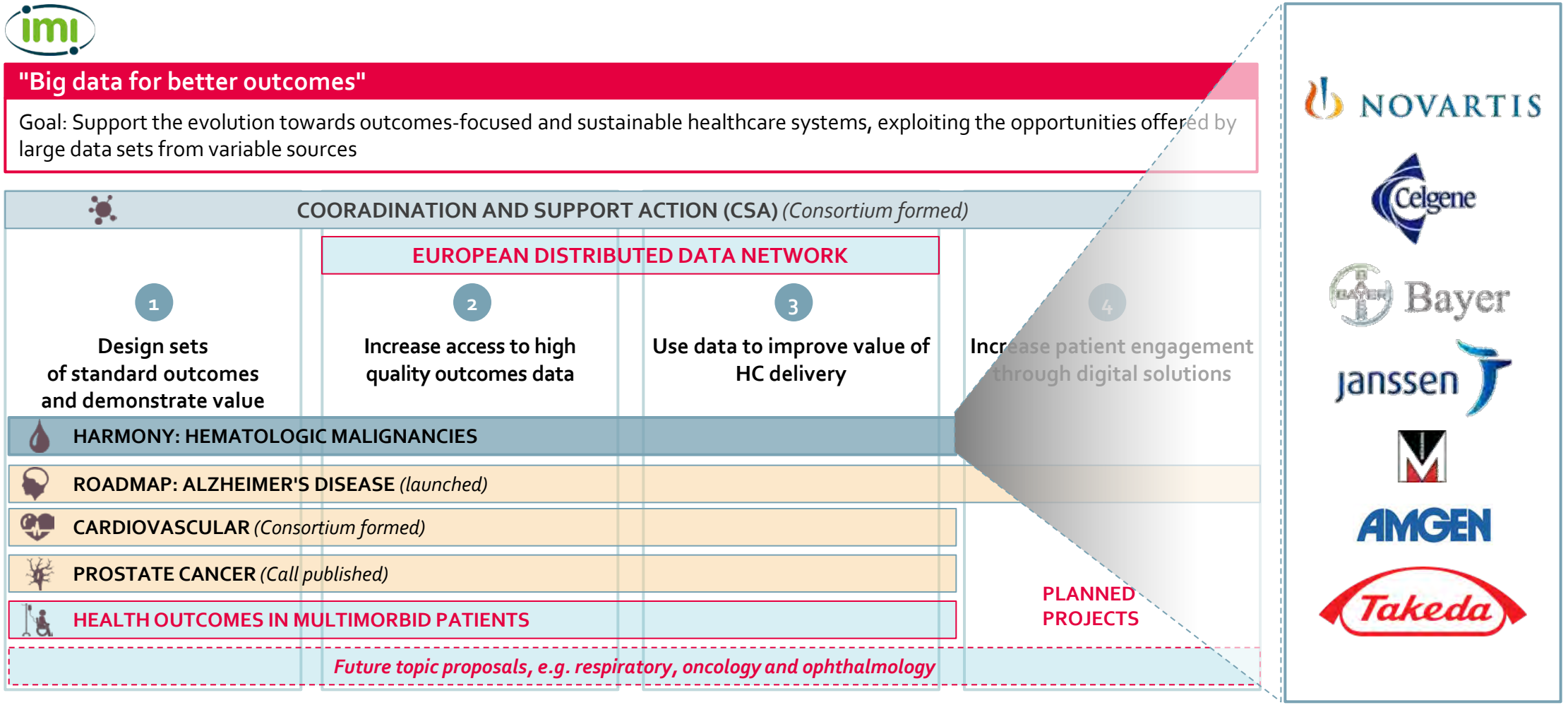


Hoadley et al. Cell, 2014

HM as examples of targeted therapy

			Survival
CML	TKI	Imatinib, Nilotinib, Dasatinib	>90%
APL	TT	ATRA, ATO	90%
B-NHL	Mo Ab	Rituximab	>70%
MM	Proteasome inh / IMIds	Bortezomib, Lenalidomide	>5 y
CLL	BTKInh	Ibrutinib	TBA
B-ALL	MoAb	Blinatumomab	TBA

HARMONY is currently the largest program under the IMI "Big Data for Better Outcomes" umbrella



Our journey so far
Significant milestones … but not always easy

Topic Text Development
April – July 2015

HM Webinar Launch
October 2015

Independent Evaluation, Phase I
February 2016

Madrid F2F HARMONY
April 2016

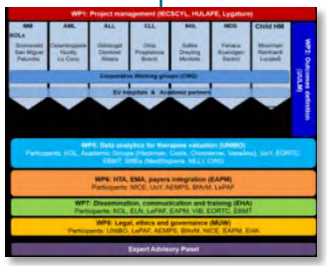
Independent Evaluation, Phase II
July 2016

Kick Off
Jan 2017

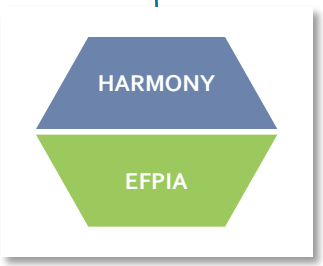
2015: FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC
2016: JAN | FEB | MAR | APR | MAY | JUN | JUL | AUG | SEP | OCT | NOV | DEC
2017: JAN

Original Idea
Feb 2015

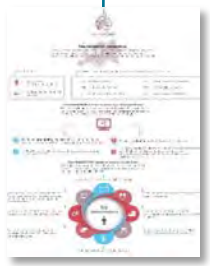
Topic Text Call Launch
September 2015



HARMONY Proposal
January 2016



Leadership Kick Off meeting
March 2016



Submission Deadline
June 14 2016

Negotiation Phase
July-November 2016

CA & DoA
December 2016

HARMONY Kick Off, Salamanca, January 16th-17th 2017

HARMONY

150 Participants

18 Countries

>45 Partners

>40 Associated Members & Observers

Participation of key stakeholders

NICE

EBN Foundation

LeukaNET

+ leading European KOLs highly engaged, with defined projects & seeking collaboration with Pharma

Press coverage internationally and in Spain

PR Newswire

EHA

La Vanguardia

Interviews with leadership

"Combining data available from clinical trials as well as real world patients allows us to do more advanced analyses on possible treatment options that could be effective for individual patient or categories of patients"

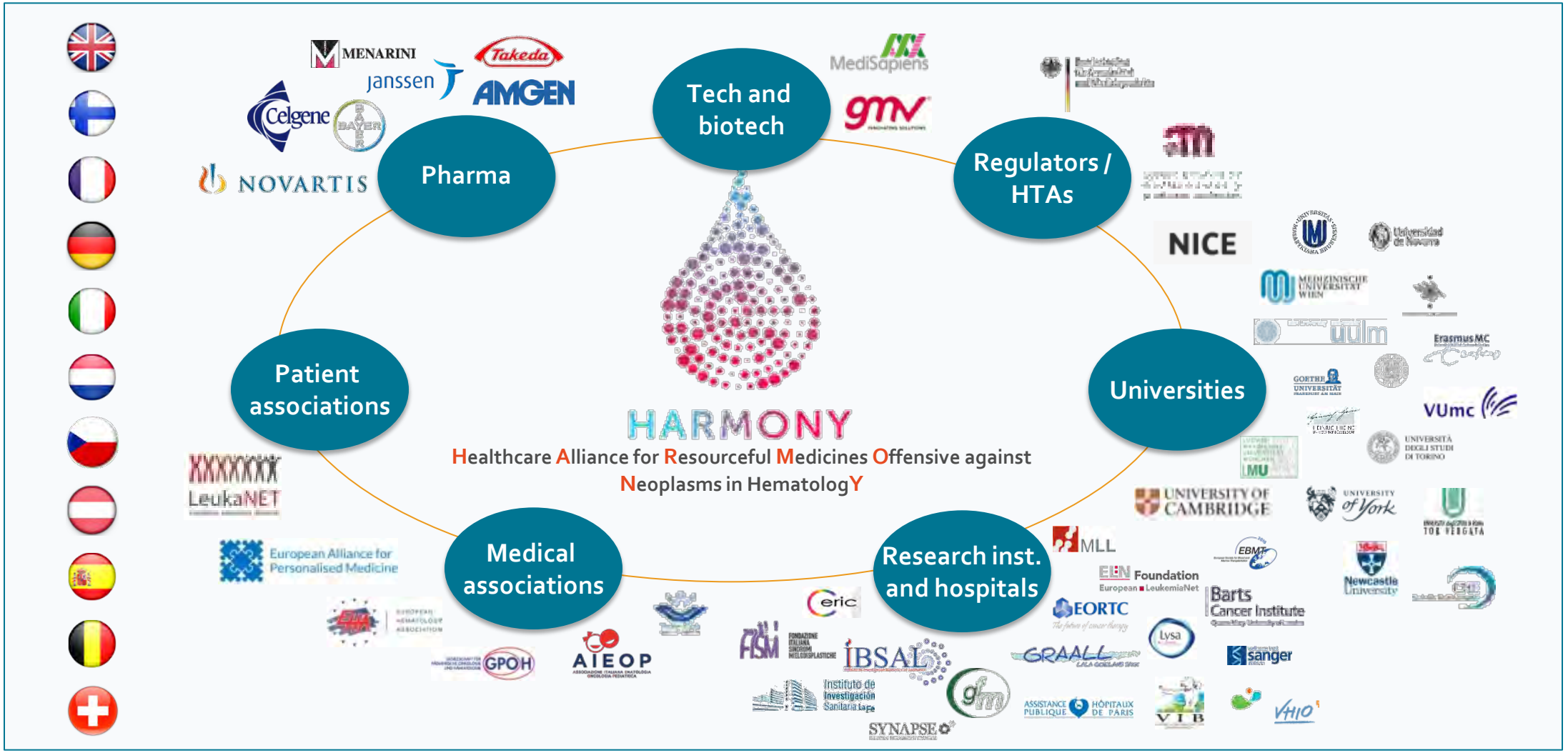
Jesús M. Hernández Rivas (Project Coordinator)

"Big Data doesn't mean collecting only large quantities. The quality of the data is much more important. Therefore HARMONY is open to associate partners that can provide high quality data"

Guillermo Sanz (Project Co-Coordinator)

HARMONY: public-private partnership

51 partners, including 44 public partners, from 11 different European countries



HARMONY Executive Committee

Jesús M. Hernández
Project Coordinator

Patricia van Dijck
Project Leader

Guillermo Sanz
Project Co-Chair

Pam Bacon
Project Co-Leader

HARMONY aims to meet major unmet needs in HMs

HARMONY

Healthcare **A**lliance for **R**esourceful **M**edicines **O**ffensive against **N**eoplasms in Hematolog**Y**

Need for harmonization of outcome measures and endpoint definitions for HMs at European level

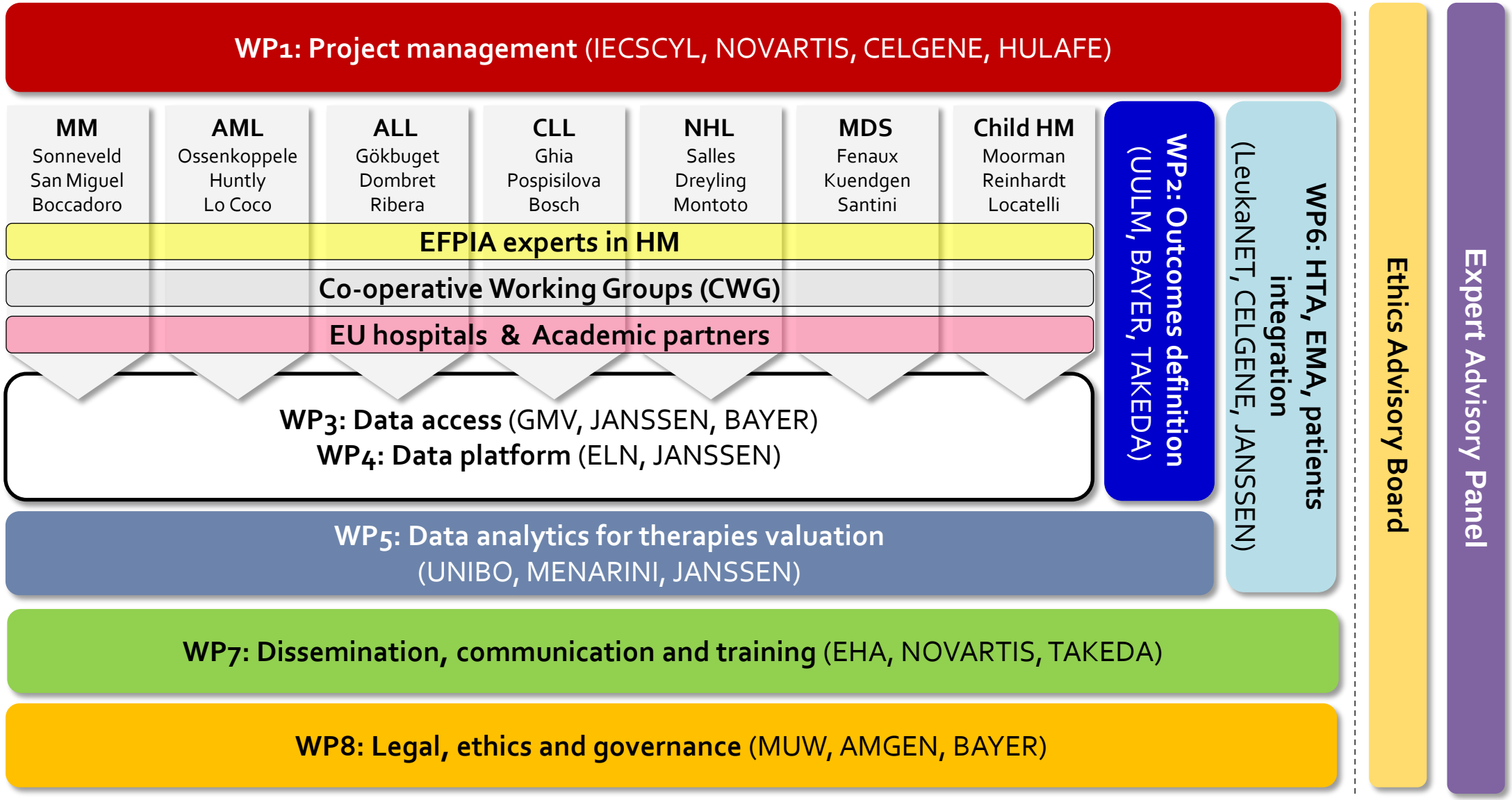
Increasing omics data available, but limited **application** in clinical practice

Need for speeding up drug development, access pathways and **"bench-to-bedside"** process

Specific outputs for Pharmaceutical companies

- **facilitate drug development pipelines, accelerate the "bench-to-bedside"** process in drug development by identifying appropriate targets/disease cohorts
- provide the **evidence base for large co-operative studies** to identify the most appropriate patient cohorts for future trial designs
- create a **holistic and timely approach for innovative clinical practice** by involving all **stakeholders** across the spectrum, from basic researchers to policy makers, in each stage of the project
- **facilitate reimbursement decisions**, by providing solid data and tools obtained across EU member states
- enable **broader and improved collaboration between the diagnostic test developers**, who are focusing on efforts for targeting early drug development, and the pharmaceutical companies

HARMONY: 8 Work Packages across 7 diseases



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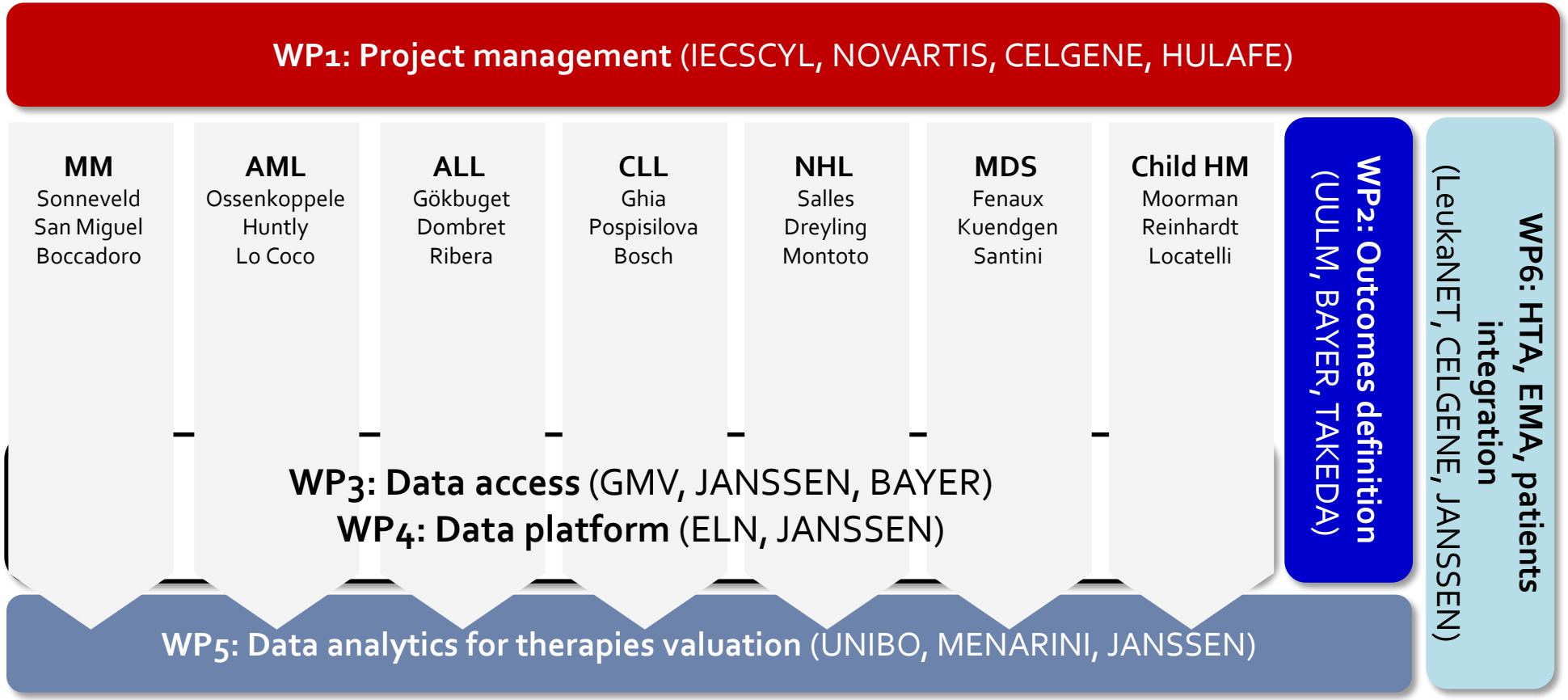

Specific questions by disease
Involvement of KOL + Working Groups
OMICs + Clinical Data

What makes HARMONY different from other projects?

1 Big Data

Data Quality Supervision (WP leaders WP1, 2, 3, 5)

Data Custodians

MM | AML | ALL | CLL | NHL | MDS | Child HM

KOLs

EFPIA Companies

Working Cooperative Groups (WCG)

Associated Members and Other sources

Clinical data	7000	7500	4000	5600	5500	6000	8000
Immunofluorescence	4000	1500	3750	2000	3000		5000
Cytogenetics	5000	4500	3750	4000	1000	4000	4000
"Omics"	2800	2800	1200	1700	1600	1500	3000

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What makes HARMONY different from other projects?

1. Big Data
2. **Stakeholders involved** (patients, regulators, HTA, policy makers)

Dedicated WP6 to HTA, EMA, patients alignment & optimisation

- Constitution of a **Policy Health Stakeholder Feedback Forum** (PHSFF)
- Development of a **Clinical Value Framework**
- Development of set of **outcomes relevant for decision-makers**
- **Health literacy**: communication strategy for transfer and adoption of project results
- **Patients perspective** incorporated – link with EUPATI

What makes HARMONY different from other projects?

1. **Big Data**
2. **Stakeholders involved** (patients, regulators, HTA, policy makers)
3. **Associated members** & variable budget

20 countries, 65+ members, 6.4 M€ budget

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AML Proof-of-Principle Study

Objectives:

1. **Identification of additional gene-gene interactions and impact on outcome**

   & validation and further refinement of novel genomic classification

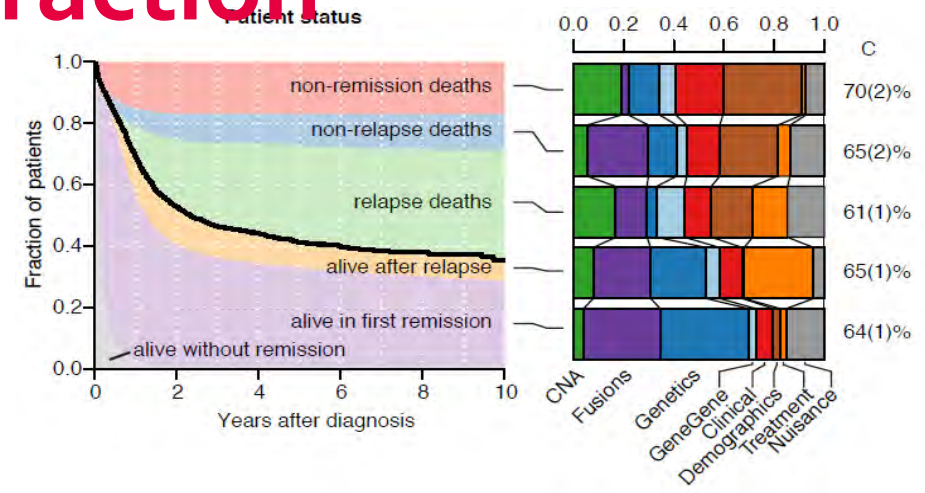
2. **Evaluate the impact of "intensive therapy" on "overlap cases", i.e. aggressive MDS cases (RAEB II) that are treated like AML**

3. Evaluate genomic information with regard on chemotherapy side effects, infectious complications, etc.
4. Determine impact on allogeneic transplantation

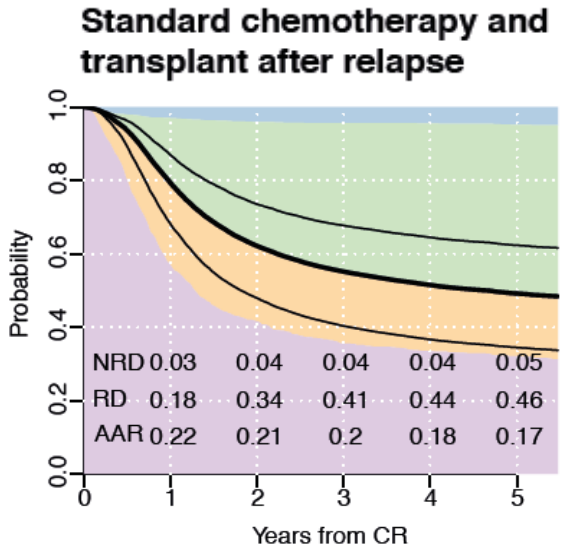
AML "Knowledge Database"
WP2 - WP5 interaction

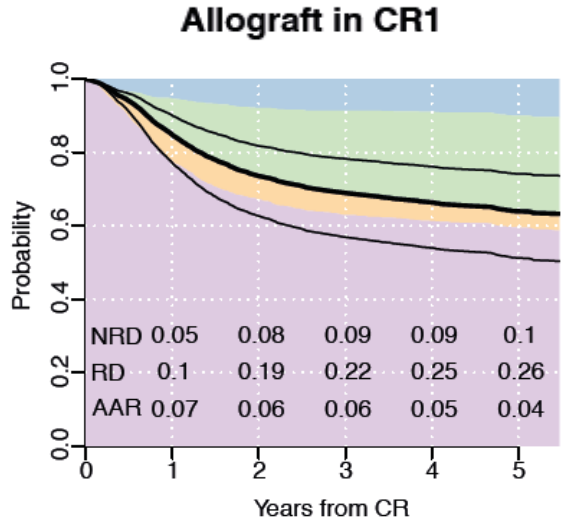
Prototype:

⇒ **Individual risk prediction depending on different treatment options**



49yr old male NK *NPM1*, *DNMT3A*, *IDH1*





Gerstung/Papaemmanuil et al. Nat Genet 2017

Projects in HARMONY

MDS → **Prognostic factors of treatment with hypomethylating agents (HMAs) in high-risk MDS**

Azacytidine or decitabine
Chemo or SCT
Mutational analysis
Several WCG

CLL → **Create novel prognostic/predictive scheme for improved risk stratification aimed at personalized medicine**

Mutational analysis
ERIC

Pediatrics → **What is the most efficient way to integrate risk factors to improve patient risk stratification?**

Several WCG including iBFM/AIEOP

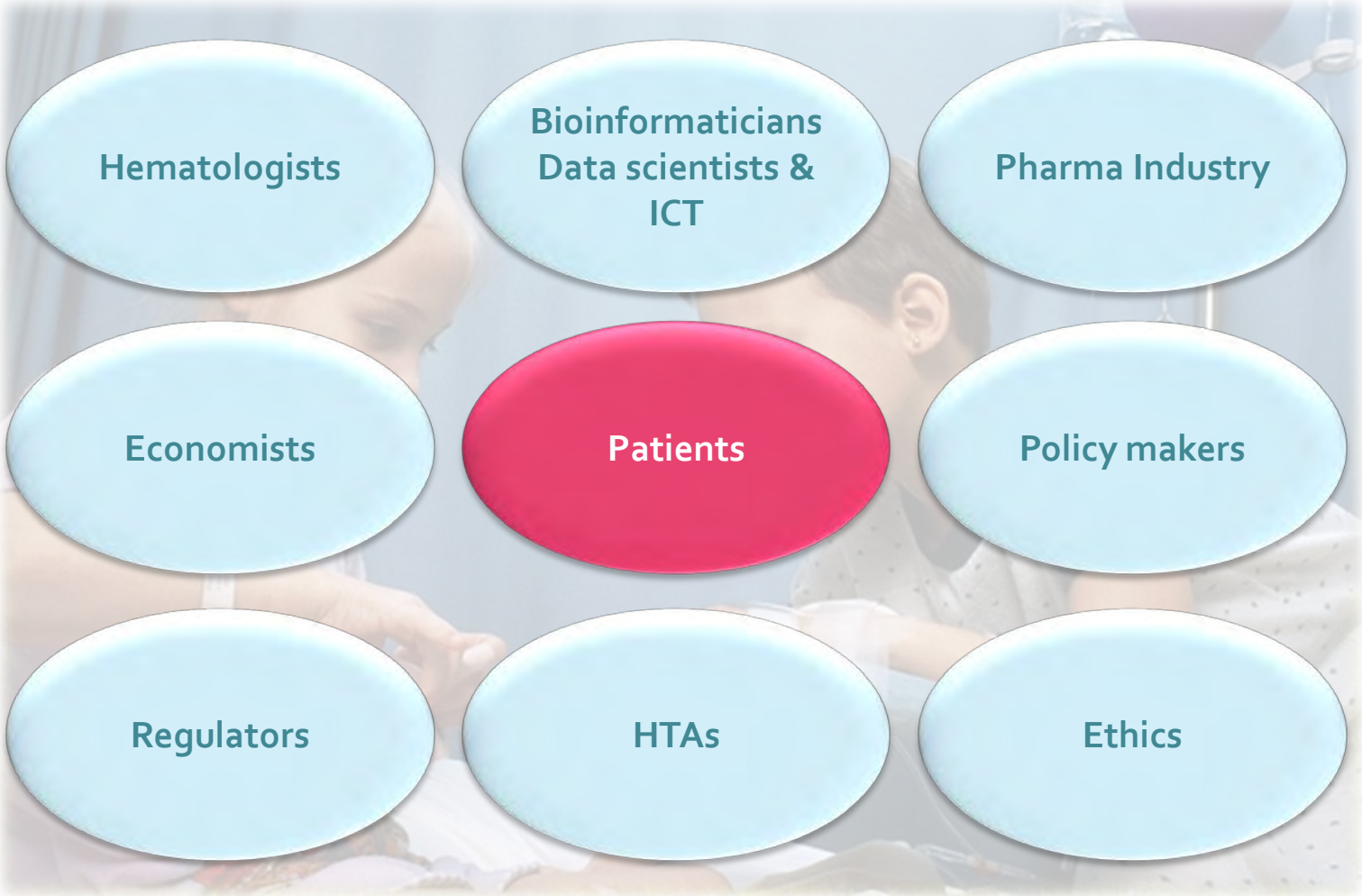
MM → **"Curable" Myeloma**

NHL → **T-Cell NHL**

Clinical characteristics
Mutational analysis

The patient is at the center of HARMONY:

Collaboration of all stakeholders needed to meet patients' needs



HARMONY Summary

1. **First IMI Project in Hematological Malignancies.**

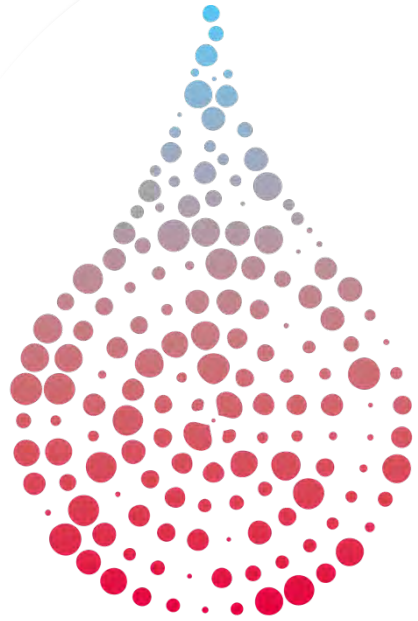
2. **A comprehensive Project** focused in Hematological Malignancies.

3. To integrate **Big Data Series** of patients **with high-quality data**.

4. **Stakeholders involvement:** Payers, HTAs, Regulators and Patients.

5. **Open project: Pharmaceutical companies,** Working Cooperative Groups and Hospitals are welcome.

HARMONY: Future Awareness Meetings



HARMONY

1. EHA, Madrid, 23 June 2017
2. HARMONY, Berlin, 23 October 2017
3. ASH, Atlanta, 10 December 2017

Healthcare **A**lliance for **R**esourceful **M**edicines **O**ffensive against **N**eoplasms in Hematolog**Y**

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HARMONY, Kick-Off Meeting, Salamanca, Jan, 2017