IHI Impact Event
Blood Cancers

Leveraging big data and CAR-T therapies to improve outcomes for patients

KARROUM Oussama, PhD
IHI Scientific Officer
1 October 2025

innovative health initiative

innovative health initiative

Use the chat box

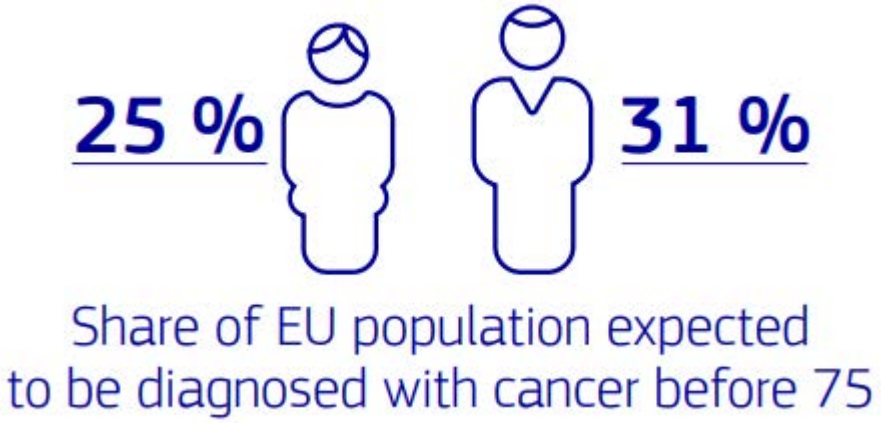
Ask questions and interact with the speakers *(bottom of your screen)*

The session is being **recorded.**
The recording will be posted on IHI's website and Youtube channel.

COCIR Advancing Healthcare · efpia · EuropaBio The European Association for Bioindustries · MedTech Europe from diagnosis to cure · Vaccines Europe · Co-funded by the European Union

Cancer in the EU

2,7 Million new cases / year



https://ecis.jrc.ec.europa.eu/

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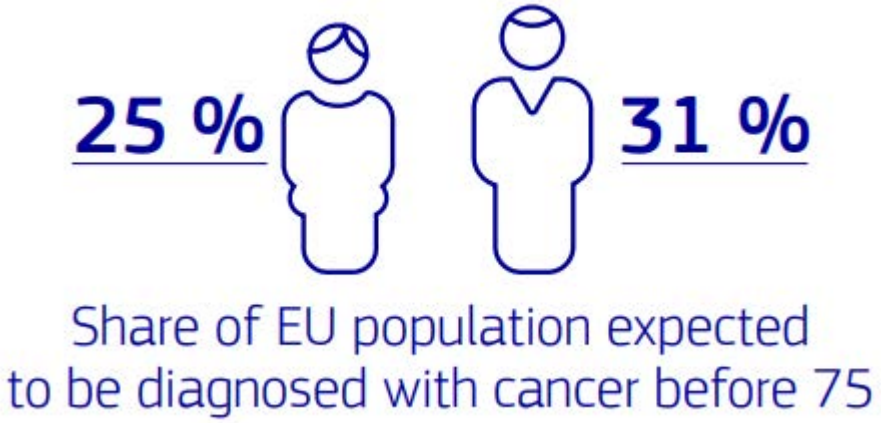
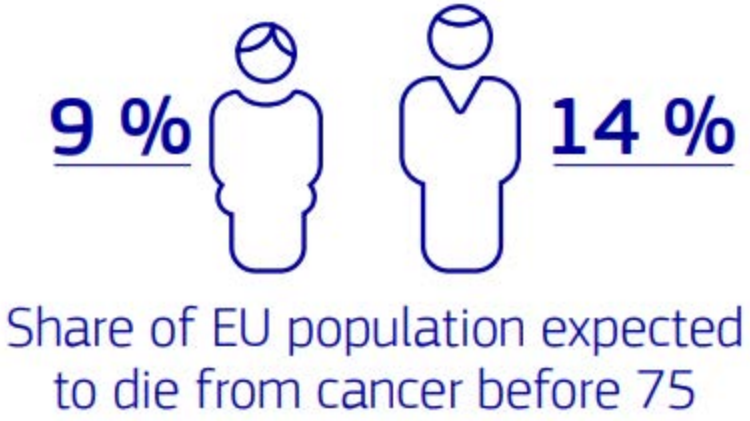


1,3 Million deaths / year



https://ecis.jrc.ec.europa.eu/

Blood Cancer in the EU

2,7 Million new cases / year

1,3 Million deaths / year

214 000 new cases / year

106 000 deaths / year

https://gco.iarc.fr/en

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IHI Cancer portfolio per Indication

14 Cancer Indications

Lung
- IMMUCAN
- PERSIST SEQ
- OPTIMA
- IMAGIO
- IDHERA
- GUIDE MRD

Breast
- IMMUCAN
- PERSIST SEQ
- OPTIMA
- ACCELERATE EU

Blood
- HARMONY
- HARMONY PLUS
- T2EVOLVE
- ITCCP4
- EASYGEN

Prostate
- PIONEER
- OPTIMA
- ILLUMINATE
- THERA4CARE
- BRECISE

Sarcoma
- IMAGIO
- THERA4CARE
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Brain
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Ovarian
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Colorectal
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Head & neck
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Oesophagus
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Blood Cancer Awareness Month

September is **Blood Cancer Awareness Month** to raise awareness about **leukemia, lymphoma, myeloma, and other blood cancers**

Focus of Today's Webinar

HARMONY

Big Data

HARMONY
Big data in Blood Cancer
HARMONY PLUS

innovative health initiative

Focus of Today's Webinar

T²EVOLVE

easygen

Big Data

HARMONY
Big data in Blood Cancer
HARMONY PLUS

T2EVOLVE
Support the development of engineered T-cells

CAR-Ts

EASYGEN
Advancing CAR-T cell therapy for Cancer in Europe

innovative health initiative

Focus on Specific Projects:

HARMONY

T2EVOLVE

EASYGEN

HARMONY

innovative health initiative

The HARMONY Alliance

Jesús María Hernández Rivas

University of Salamanca, Spain

HARMONY and HARMONY PLUS Coordinator

President of the HARMONY Alliance Foundation

Lars Bullinger

Charité University, Berlin, Germany

HARMONY and HARMONY PLUS WP2 Coordinator

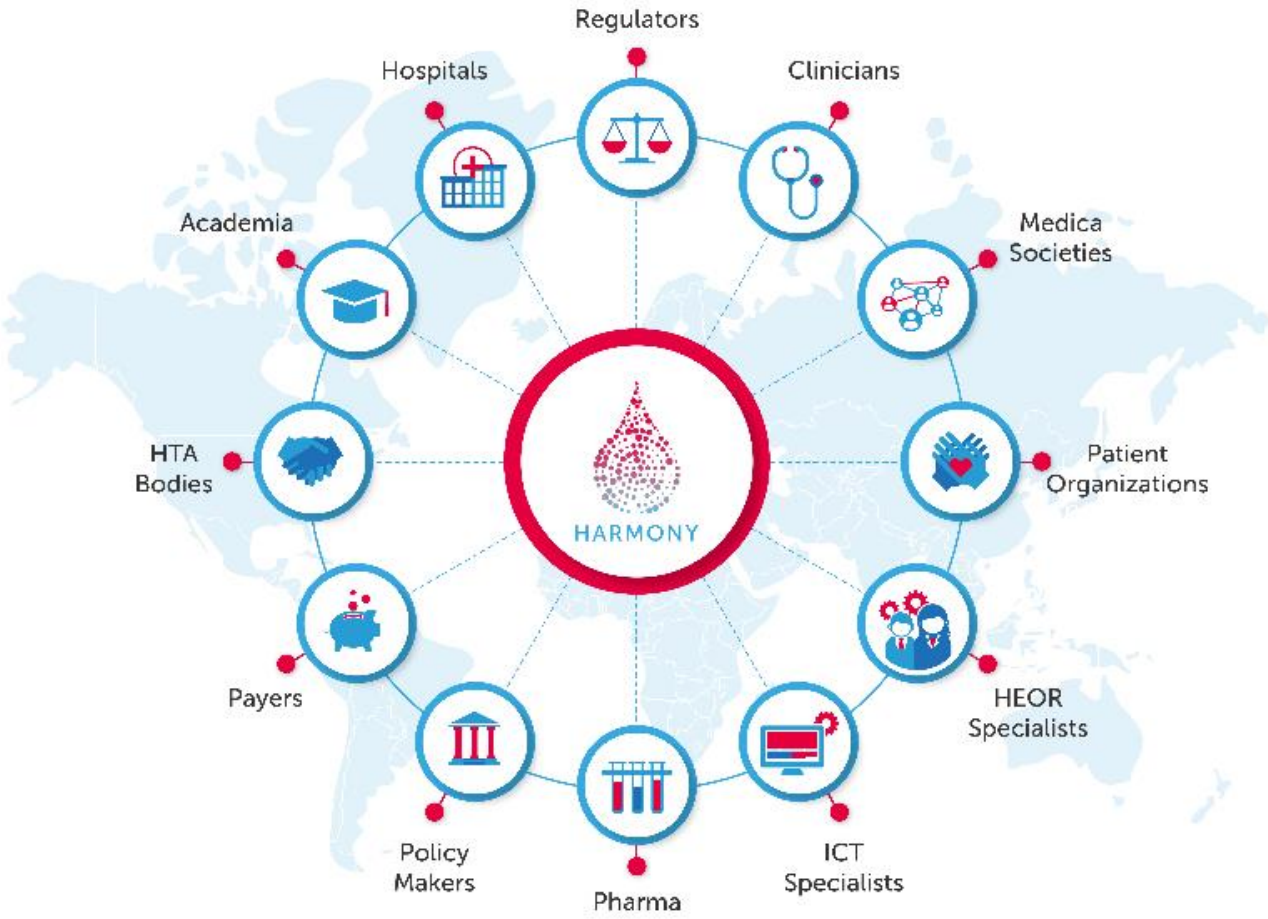
Board of Trustees Member – HARMONY Alliance Foundation


HARMONY
ALLIANCE
HARMONY and HARMONY PLUS
Key objectives
BIG DATA FOR BLOOD CANCER
innovative medicines initiative
efpia

About the HARMONY Alliance

European Public-Private Partnership for big data in hematology

- HARMONY (2017-2023) and HARMONY PLUS (2020-2024) were **IHI funded projects.**
- We built a **community with a wide representation of all stakeholder groups** in the field of blood cancers.
- Both projects had an interest in medicines intended for the **treatment of blood cancers.**
- Ultimate goal: to increase the application of omics data in clinical practices**, speed up drug development,** access pathways **for patients** and bench-to-bedside processes.



About the HARMONY Alliance

A 7-year-long history of European Public-Private collaboration

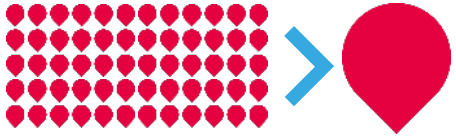
Community of approx.
500 professionals

> 140 Data Providers from 34 countries,
19 being European

9 European Patient Organizations, also involved in carrying out research

9 Pharma companies, providing in-cash and in-kind support, and data

Big Data Platform
with **165,000** records identified in all HMs Integrated Data Services



+100 Databases harmonized to OMOP common data model

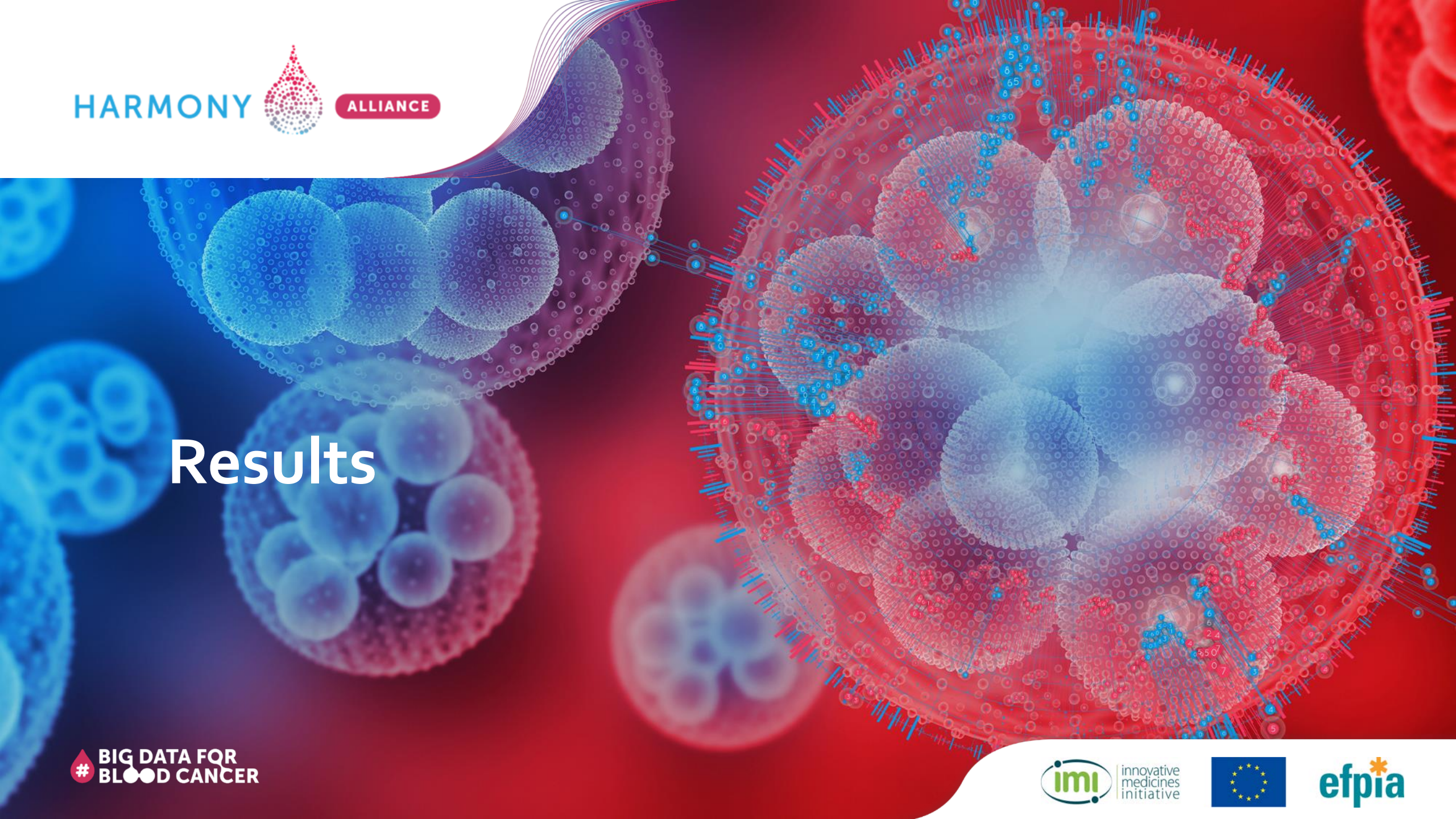
+30 Collaborative projects, comprising research ideas, definition of COS, and other multi-stakeholder activities

Robust Big Data Platform, GDPR-compliant data life cycle, and visualization tools

HARMONY

HARMONY ALLIANCE

Results



#BIG DATA FOR BLOOD CANCER

imi innovative medicines initiative

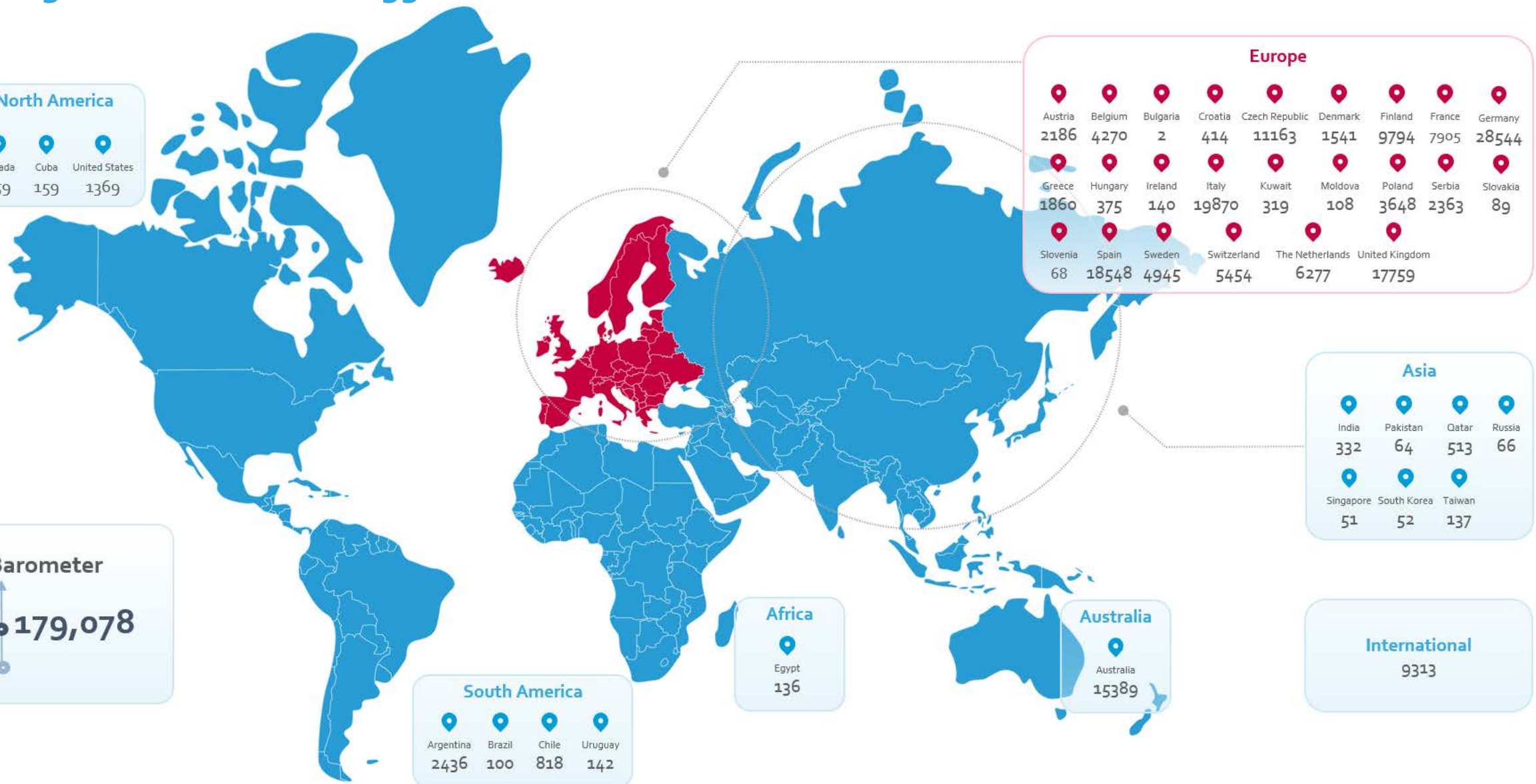
efpia

The HARMONY Alliance Network

+100 Organisations from across the world

The HARMONY Alliance Network

Joining forces to build the biggest database of Blood Cancers



The HARMONY Platform

A GDPR-compliant data transfer and processing environment

DATA ANONYMIZATION

Personal Data

Technical anonymization
suppression | generalization | perturbation

De-identification

Data access restrictions

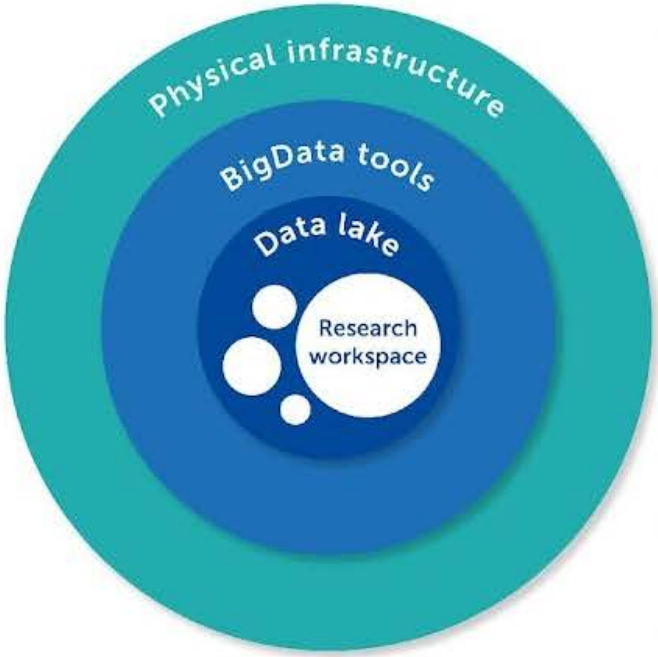
Organizational security
policies | processes | contracts

Anonymous data

TECHNICAL BARRIERS

Private Internet

Audit Trail



- Controlled entrance
- ISO 27001 certified
- First firewall layer

- Virtual private network
- Second firewall layer
- Named access
- Roles segregation

- Data governance
- Named access
- De facto anonymization

- Data governance
- Named access
- Specific fields only
- Limited in time

ORGANISATIONAL MEASURES

- Risk analysis
- Contracts and SOPs
- Training
- Project review and approval
- Trusted third party

GDPR AND LOCAL LEGISLATION COMPLIANT

The HARMONY Platform

The data journey in the HARMONY Platform

Mapping to OMOP

The HARMONY Platform uses OMOP data model, terminologies, vocabularies, and coding schemes to standardize the format of the data bases received

Anonymization

Data undergoes a double-step anonymisatio process and is checked by a TTP before entering the HARMONY Platform

Curation

Each dataset is checked for completeness and accuracy

Identification of data sources

The HARMONY Platform contains data from national registries, hospitals, study groups, universities, pharmaceutical companies…

Dissemination

We make sure sure that the results produced by our community not only reach the scientific community, but also the wider public.

Analytics

The HARMONY Platform counts with a team of analysts that support researchers implement state-of-the art analysis techniques.

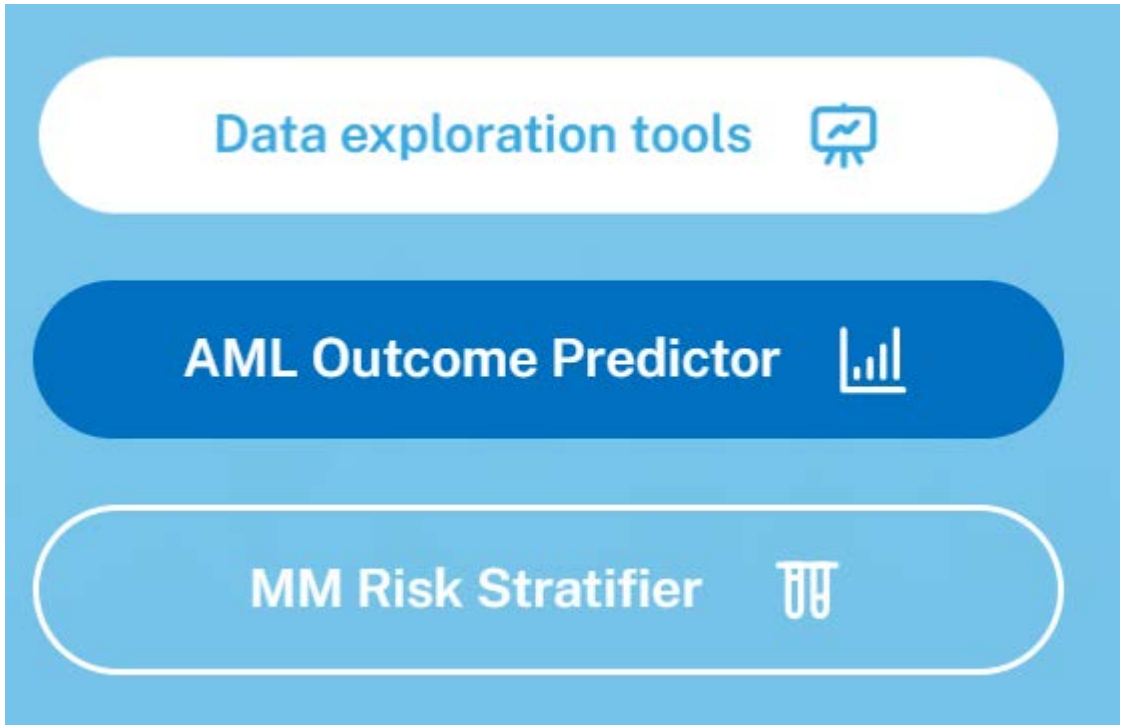
Visualization

We have developed visualization tools to support the generation of new research project ideas and assess their feasibility with the data that is currently available on the HARMONY Platform.

HARMONY

The Tools Developed

From data to decisions



- Tools freely accessible on the HARMONY platform website are designed to make datasets accessible and useful for **clinicians, researchers, patients and decision-makers.**

[Harmony Platform - Harmony Alliance Foundation]

Data visualization tools for Researchers

AML and ALL **Data Visualization Tools are publicly available** on the HARMONY Alliance website now

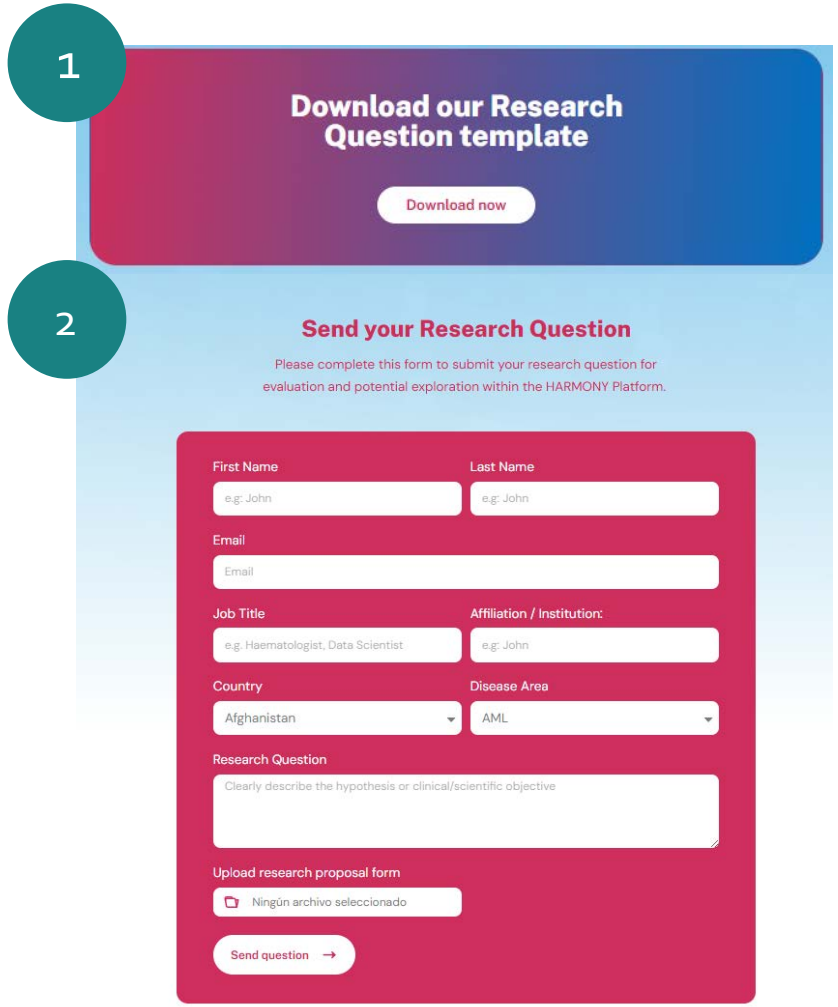
Researchers select specific parameters and instantly see how many cases are **available in the platform**.

This helps researchers **refine their study design**.

Submit your research question to the HARMONY Platform!

Leverage Europe's largest anonymised haematological malignancies data lake to advance your research and accelerate discovery.

- Access a uniquely large volume of real-world data that would be impossible to gather independently.
- Work with harmonised data optimised for advanced analytics and data science.
- Receive support for dissemination to increase the visibility and impact of your results.
- Join a collaborative environment that contributes to regulatory decision-making, clinical guidelines, and healthcare innovation.



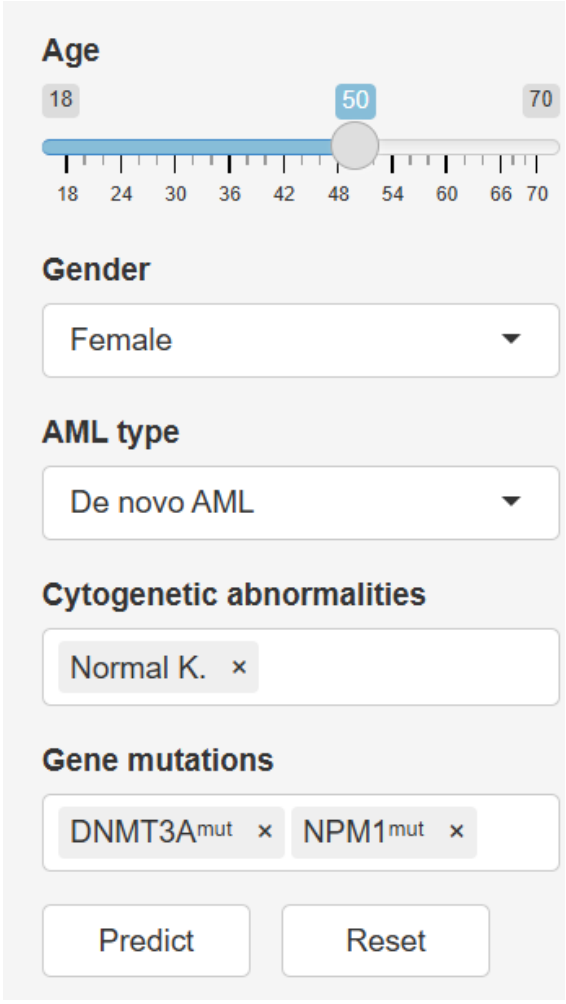
https://harmony-alliance.eu/join-us/#send-research-question

HARMONY

Tools to support decision-making for Physicians and Patients

Individualized prediction of outcomes in AML

Aim of this **online tool:** to create a more accurate risk prediction to easily visualize the likelihood of relapse for patients in complete remission and help **to determine in which patient a blood stem cell transplant (alloHSCT) is needed.**



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Age

18 50 70

18 24 30 36 42 48 54 60 66 70

Gender

Female

AML type

De novo AML

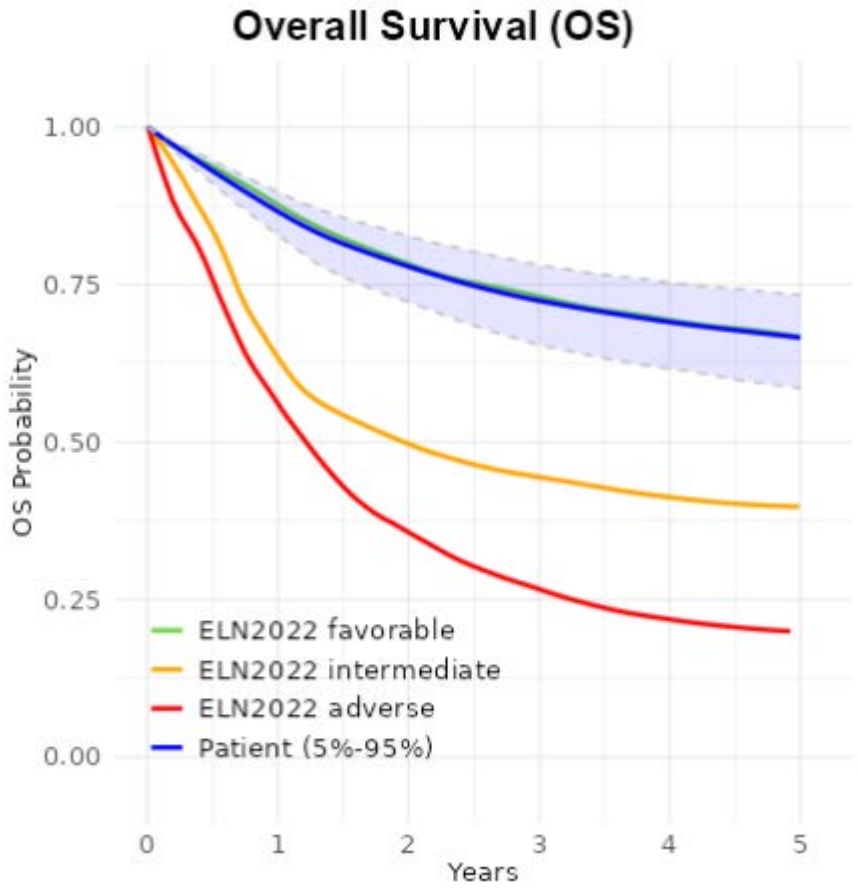
Cytogenetic abnormalities

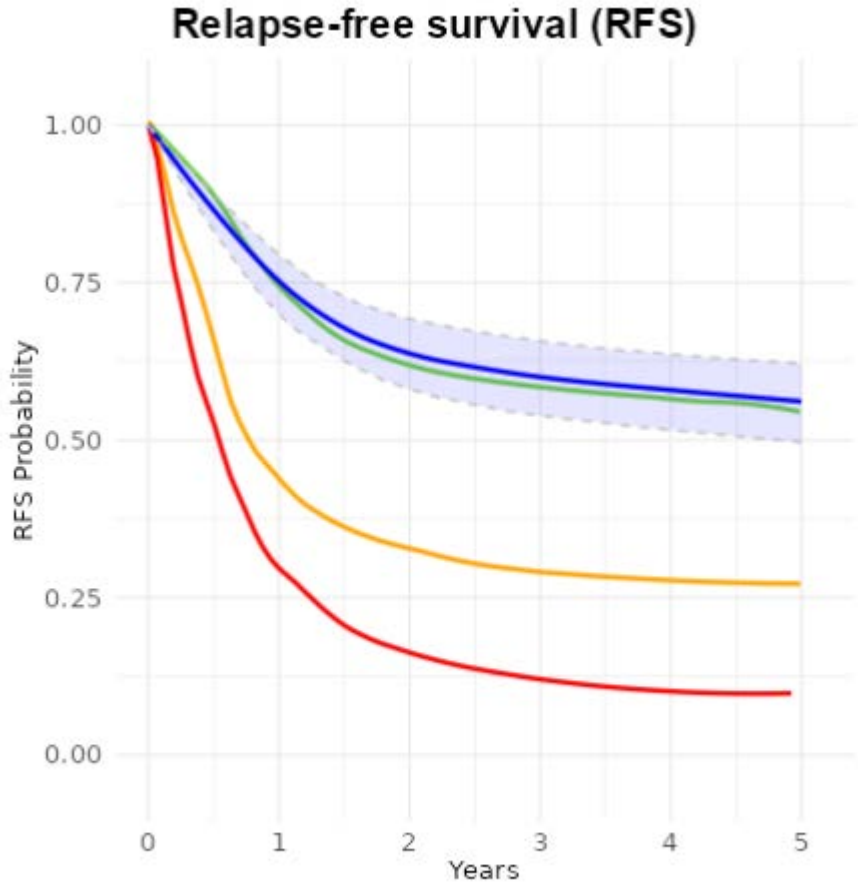
Normal K. ×

Gene mutations

DNMT3A^{mut} × NPM1^{mut} ×

Predict Reset

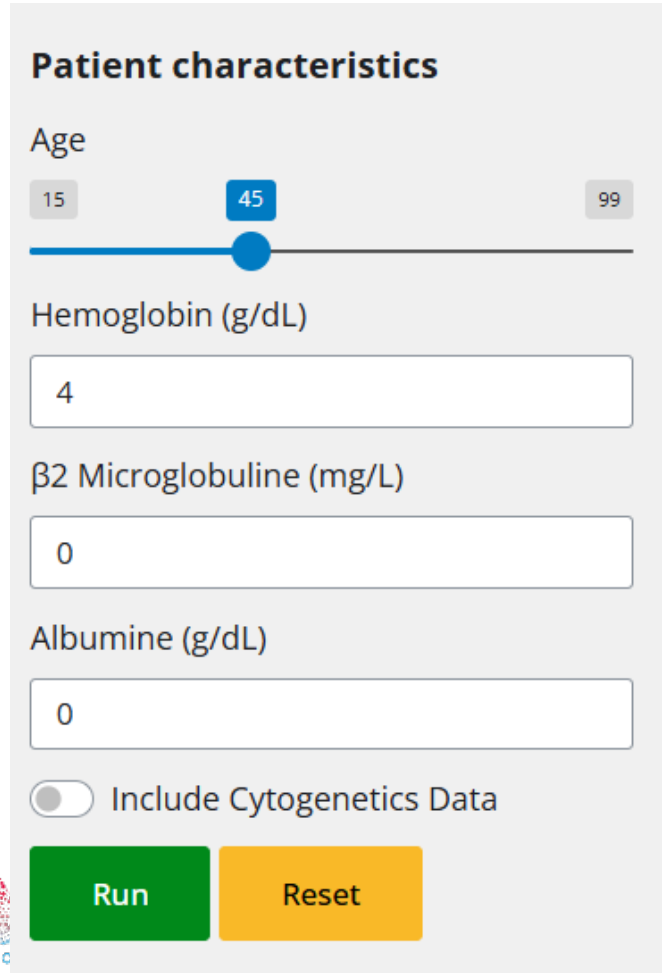




Tools for risk stratification for Physicians and Patients

Supports risk classification for patients with multiple myeloma

Aim of this **online tool:** to enable more refined risk stratification at diagnosis and may support treatment planning and study design in multiple myeloma.



Tools for risk stratification for Physicians and Patients

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Patient characteristics

Age

15 45 99

Hemoglobin (g/dL)

4

β2 Microglobuline (mg/L)

0

Albumine (g/dL)

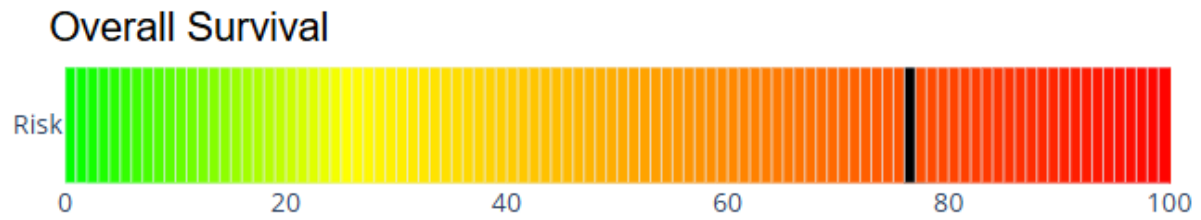
0

Include Cytogenetics Data

Run Reset

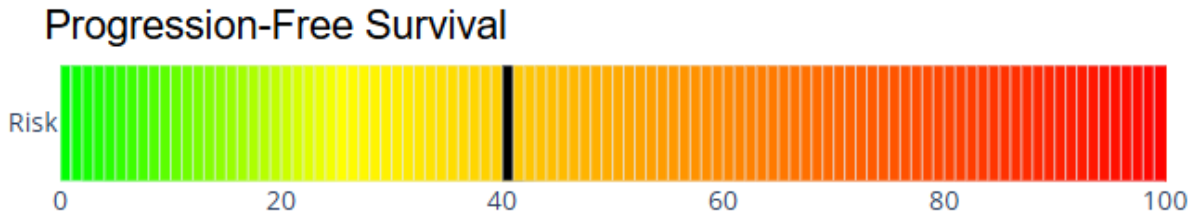
Overall Survival Prediction

This chart represents risk stratification for Overall Survival (OS) based on the Baseline Risk Model.



Progression-Free Survival Prediction

This chart represents risk stratification for Progression-Free Survival (PFS) based on the Baseline Risk Model.



Publications in high-impact journals

Leveraging substantial data collections has generated meaningful insights

Leukemia

Article | Open access | Published: 04 July 2024

ACUTE MYELOID LEUKEMIA

Rearrangements involving 11q23.3/*KMT2A* in adult AML: mutational landscape and prognostic implications – a HARMONY study

Alberto Hernández-Sánchez, Teresa González, Marta Sobas, Eric Sträng, Gastone Castellani, María Abáigar, Peter J. M. Valk, Ángela Villaverde Ramiro, Axel Benner, Klaus H. Metzeler, Raúl Azibeiro, Jesse M. Tettero, Joaquín Martínez-López, Marta Pratcorona, Javier Martínez Elicegui, Ken I. Mills, Christian Thiede, Guillermo Sanz, Konstanze Döhner, Michael Heuser, Torsten Haferlach, Amin T. Turki, Dirk Reinhardt, Renate Schulze-Rath, ... Lars Bullinger + Show authors

Leukemia **38**, 1929–1937 (2024) | Cite this article

blood

RESEARCH ARTICLE | NOVEMBER 6, 2024

Acute Promyelocytic Leukemia: Long-Term Outcomes from the HARMONY Project

Maria Teresa Voso, Luca Guarnera, Sören Lehmann, Konstanze Döhner, Hartmut Döhner, Uwe Platzbecker, Nigel H. Russell, Richard James Dillon, Ian Thomas, Gert J Ossenkoppele, Torsten Haferlach, Marco Vignetti, Edoardo La Sala, Alfonso Piciocchi, Paola Fazi, Ángela Villaverde Ramiro, Laura Tur Giménez, Carmelo Gurnari, Lars Bullinger, Jesus M. Hernandez

HARMONY

Leukemia

Article | Published: 05 August 2024

Transfusion independence after lenalidomide discontinuation in patients with del(5q) myelodysplastic neoplasm: a HARMONY Alliance study

Elena Crisà, Elvira Mora, Ulrich Germing, Cecile Bally, Maria Diez Campelo, Mikko Myllymäki, Martin Jädersten, Rami Komrokji, Uwe Platzbecker, Detlef Haase, Wolf-Karsten Hofmann, Najla H. Al Ali, Daniela Barraco, Juan José Bargay, Teresa Bernal, Felix López Cadenas, Anna Calvisi, Isabella Capodanno, Marco Cerrano, Rosanna Ciancia, Monica Crugnola, Andrea Kündgen, Carlo Finelli, Claudio Fozza, ... Valeria Santini + Show authors

Leukemia **38**, 2259–2265 (2024) | Cite this article

haematologica

Open access journal of the Ferrata-Storti Foundation, a non-profit organization

Outcomes with intensive treatment for acute myeloid leukemia: an analysis of two decades of data from the HARMONY Alliance

Marta Anna Sobas, Amin T. Turki, Angela Villaverde Ramiro, Alberto Hernández-Sánchez, Javier Martinez Elicegui, Teresa González, Raúl Azibeiro Melchor, María Abáigar, Laura Tur, Daniele Dall'Olio, Eric Sträng, Jesse M. Tettero, Gastone Castellani, Axel Benner, Konstanze Döhner, Christian Thiede, Klaus H. Metzeler, Torsten Haferlach, Frederik Damm, Rosa Ayala, Joaquín Martínez-López, Ken I Mills, Jorge Sierra, Sören Lehmann, Matteo G. Della Porta, Jiri Mayer, Dirk Reinhardt, Rubén Villoria Medina, Renate Schulze-Rath, Martje Barbus, Jesús María Hernández-Rivas, Brian J.P Huntly, Gert Ossenkoppele, Hartmut Döhner, Lars Bullinger

Haematologica Early view Nov 7, 2024 https://doi.org/10.3324/haematol.2024.285805

HARMONY ALLIANCE

Impact

#BIG DATA FOR BLOOD CANCER

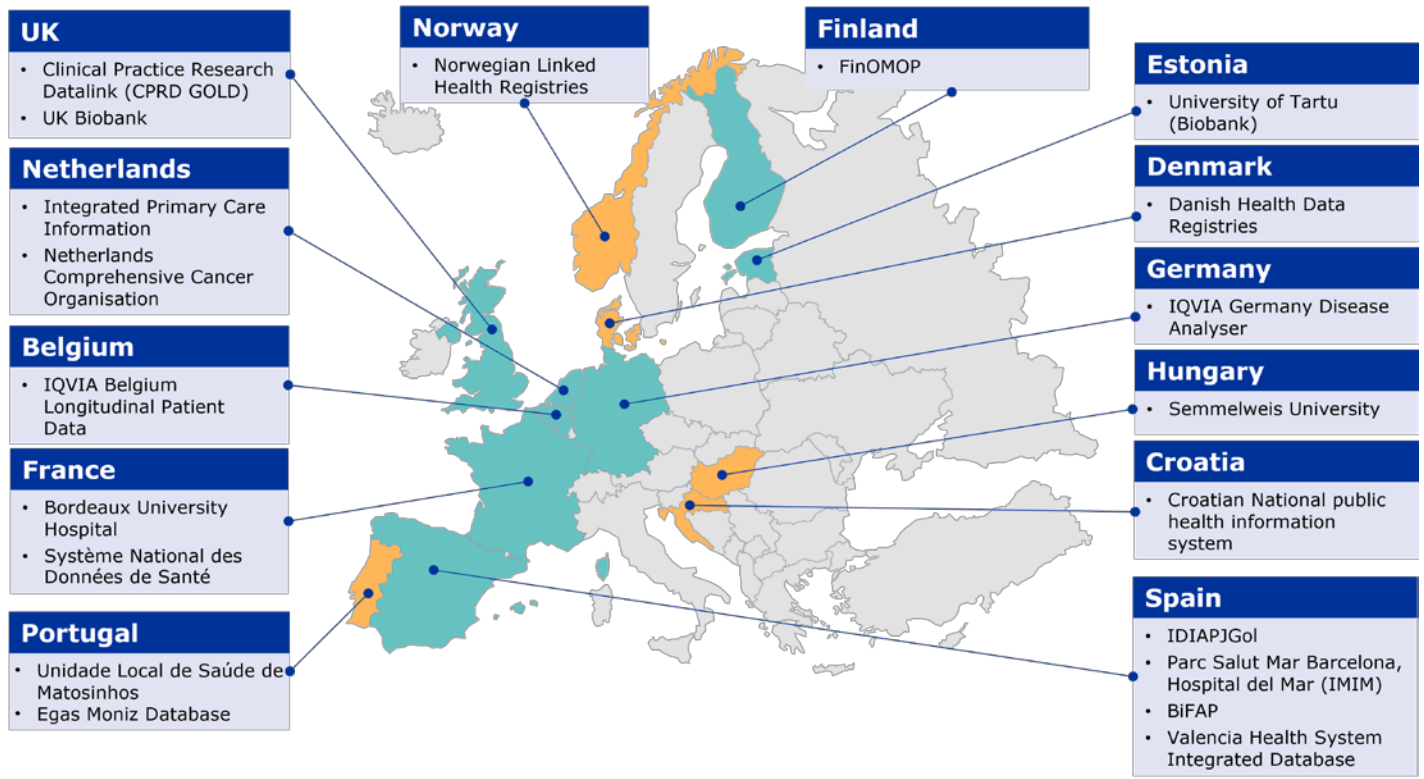
imi innovative medicines initiative

efpia

The HARMONY Platform

Onboarded as DARWIN EU® Data Partner

DARWIN EU® is a federated **network** of **data, expertise** and **services** that supports better decision-making by generating reliable **evidence from real world healthcare data**



DARWIN EU Data Partner network in 2023, composed of 20 European Data Sources

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

DARWIN EU

FEDERATED NETWORK PRINCIPLES

- Data stays **local**
- **Use of the OMOP Common Data Model** to perform studies in a timely manner and increase consistency of results

PARTICIPATION IN STUDIES

- After a study request has been made, the DARWIN EU® Coordination Centre will **assess feasibility.**
- **Selection** of appropriate Data Partners will be made **together with the EMA.**
- Selected Data Partners will receive an **invitation to participate in a specific study**, including all available information about the study, including study type as per the above classification.
- Invited **Data partners will be able to accept or decline participation**, subject to the corresponding local approvals.

The HARMONY Platform

Added value to each stakeholder group

Patients

- Access to Quality of Life data and possibility to send their own research questions
- Identification of prognostic factors
- Patient engagement process
- Consents & anonymisation

Clinicians and researchers

- Research questions, study design
- High-tier publications
- Improving clinical outcomes

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Pharma

- Evidence generation when submitting dossiers to HTA agencies
- Generation of historic or synthetic arms for single arm trials/external comparison
- Contextualization of Randomized Clinical Trials-based evidence package with real-world evidence

Regulators and HTAs

- Critical appraisal of company submissions
- Proper definition of the PICO parameters and the place in therapy
- To explore real-life treatment sequencing over time
- Research and validation of surrogate endpoints
- Support development of external controls to inform decision making

HARMONY

The HARMONY Platform

Added value to each stakeholder group

Patients

- Access to Quality of Life data and possibility to send their own research questions
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All stakeholders

- Submit research proposals
- Become a member of a dedicated research group that includes skilled data scientists
- Contribute to scientific publications under the umbrella of the HARMON Alliance
- Contribute to improving outcomes for individuals with blood cancer

Clinicians and researchers

- Research questions, study design
- High-tier publications
- utcomes

Phar

- Evidence generation whe HTA agencies
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HARMONY ALLIANCE

Uniting the hematology community

Working to produce results that improve the lives of patients with Blood Cancers

After project end, a foundation was created to sustain project results and continue the work

HARMONY
ALLIANCE FOUNDATION

Check our website!

HARMONY
ALLIANCE FOUNDATION

Mission

Enabling data | Fostering collaboration | Transforming patient care

We imagine a future where open data sharing and scientific collaboration deliver personalised treatments and cures for patients with haematological malignancies.

Vision

We empower the haematology community to share and harness data, advancing research, and driving innovation to improve the lives of patients worldwide.

HARMONY
ALLIANCE FOUNDATION

Join us in creating the next generation of care for blood cancer patients

www.harmony-alliance.eu
www.bigdataforbloodcancer.eu

@HarmonynetEU
#bigdataforbloodcancer

HARMONY Alliance Foundation

office@harmony-alliance.eu

HARMONY
ALLIANCE FOUNDATION

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- www.harmony-alliance.eu

Focus on Specific Projects:

HARMONY

T2EVOLVE

EASYGEN

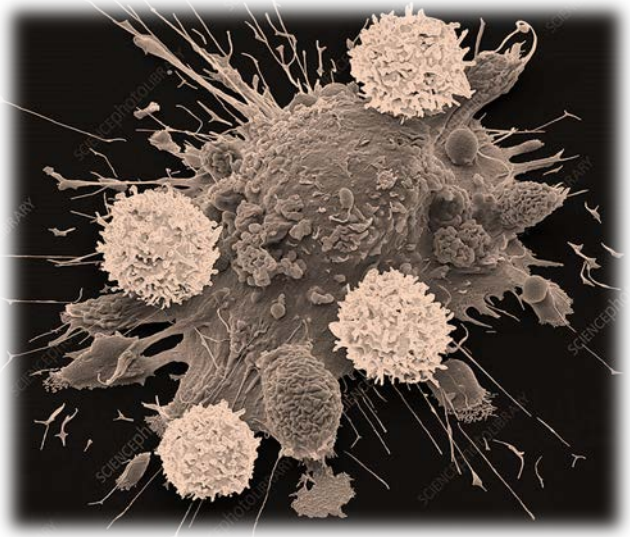
Accelerating Development and Improving Access to CAR and TCR engineered T cell therapy in Europe

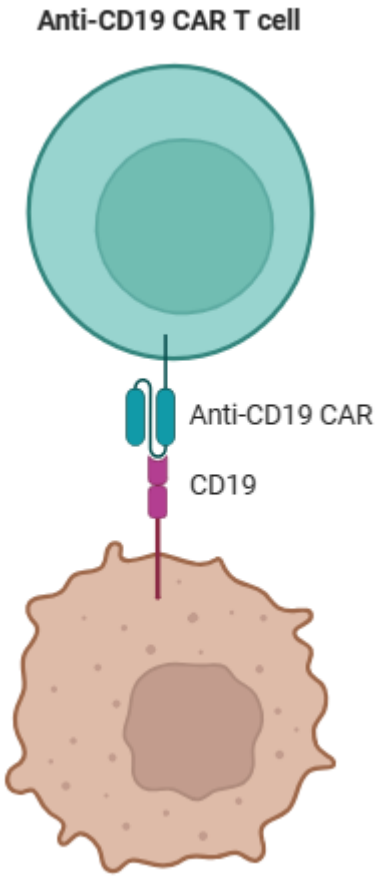
Prof. Dr. Michael Hudecek – University Hospital Würzburg, Germany

Project Coordinator

This project received funding from the innovative Medicines initiative 2 Joint Undertaking (JU) under grant agreement No 945393. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programe and EFPIA. More information can be found at: https://www.imi.europa.eu/

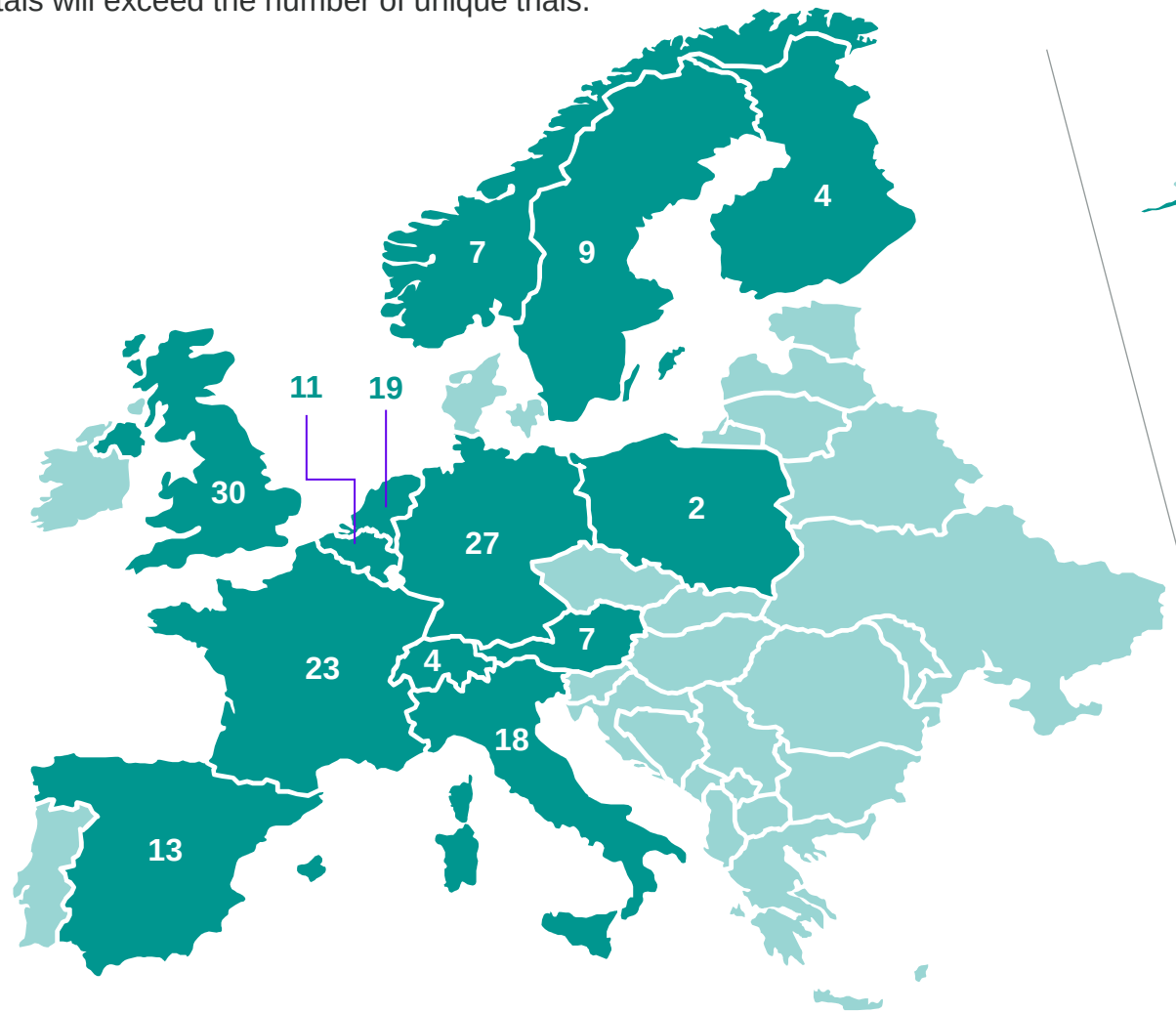
„CAR T-cell therapy is the next big thing“



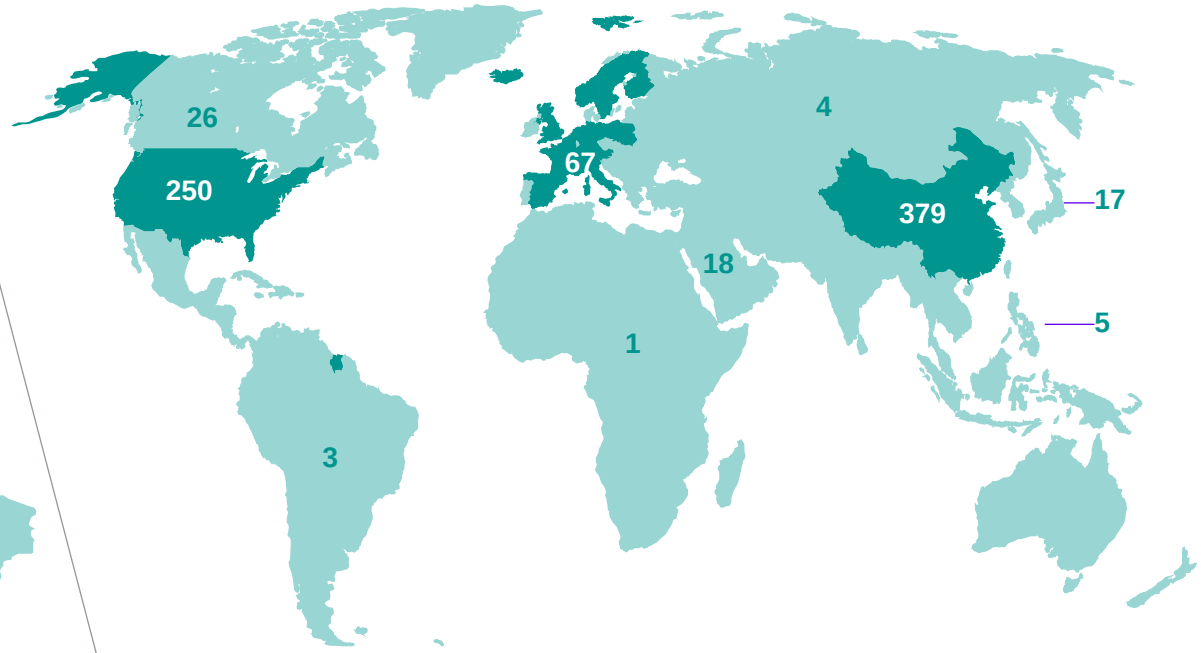


Global CAR T-Cell Therapy Race

Totals reflect **multi-country trials counted in each country** they run in, so regional totals will exceed the number of unique trials.



Clinical Trials Worldwide



Region	Studies started by end 2019	Studies started by end 2020
Europa	50	67
China	**278**	**379**
USA	**187**	**250**

Official kick-off of T2EVOLVE in January 2021, after receiving funding from IMI

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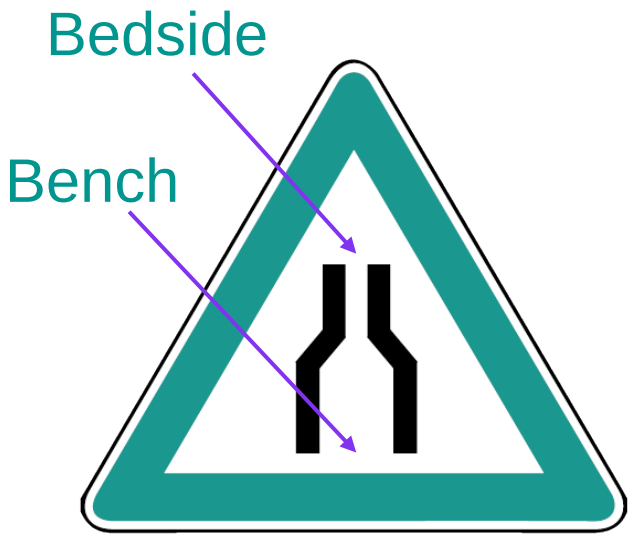
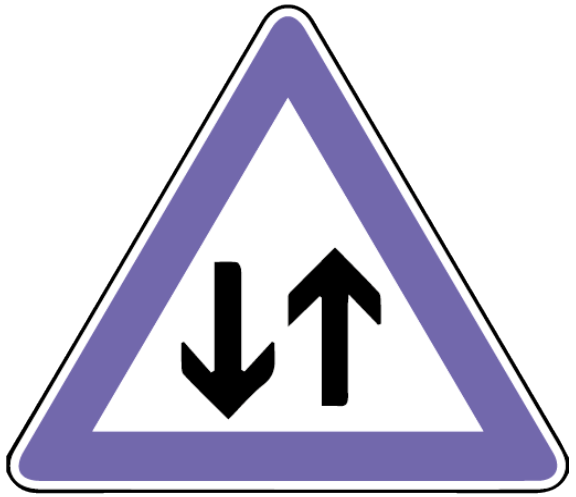
The Challenge (Why T2EVOLVE?)

Cancer patients need faster, safer access to engineered T-cell therapies



Approach: Set standards in pre-clinical & clinical development

Goal: Self-sustaining cycle of bench-to-bedside and back learning



Present

Future

Breaking through the bench-to-bedside bottleneck

T2EVOLVE Vision in 2019: A New Therapy Comes To Patients In Record Time

In December 2025, scientists in Germany discuss **preclinical model results** for a new engineered T-cell therapy that shrinks tumors and eliminates breast cancer cells. The concept was developed during the T2EVOLVE project.

The next day, they meet with the head of their preclinical development team and she agreed to perform **preclinical efficacy and safety studies**, using **T2EVOLVE standards and models**. The results will inform what lymphodepletion regimen would be optimal, what analytical monitoring will be necessary and how the GMP manufacturing should be conducted.

The T2EVOLVE network built up expertise in Europe for engineered T-cell therapy development, allowing the company to perform preclinical testing and validation, and **plan clinical development in Europe**.

Growing T2EVOLVE Innovation Ecosystem

45

The T2EVOLVE Innovation Ecosystem

+10 Roundtable Discussion
+5 Panel discussions

Organized and hosted for major events like ***ESGCT***, ***EBMT***, **EHA**, ***ISCT***

+5 Science Plus Cafe' Events

Involving ***patient stakeholders, physicians and experts*** *in the field*


Molecular Therapy
Review

Optimizing CAR-T treatment: A T²EVOLVE guide to raw and starting material selection

Sergio Navarro, Carole Moukheiber, Susana Inogés Sancho, Marta Ruiz Guillén, Ascensión López-Díaz de Cerio, Carmen Sanges, Toshimitsu Tanaka, Sylvain Arnould, Javier Briones, Harry Dolstra, Michael Hudecek, Rashmi Choadhary, Inga Schapitz, Manel Juan, Nina Worel, Delphine Ammar, Maik Luu, Mirko Müller, Bernd Schroeder, Hélène Negre, and Paul Franz

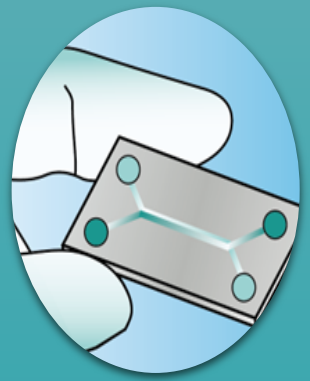
4 Joint Workshops Events

Evolving in ***guides***, *recommendations*, ***white papers,*** *and joint working groups*

46

T2EVOLVE - Key Action Areas

Patient Information



Preclinical methods

Analytical methods

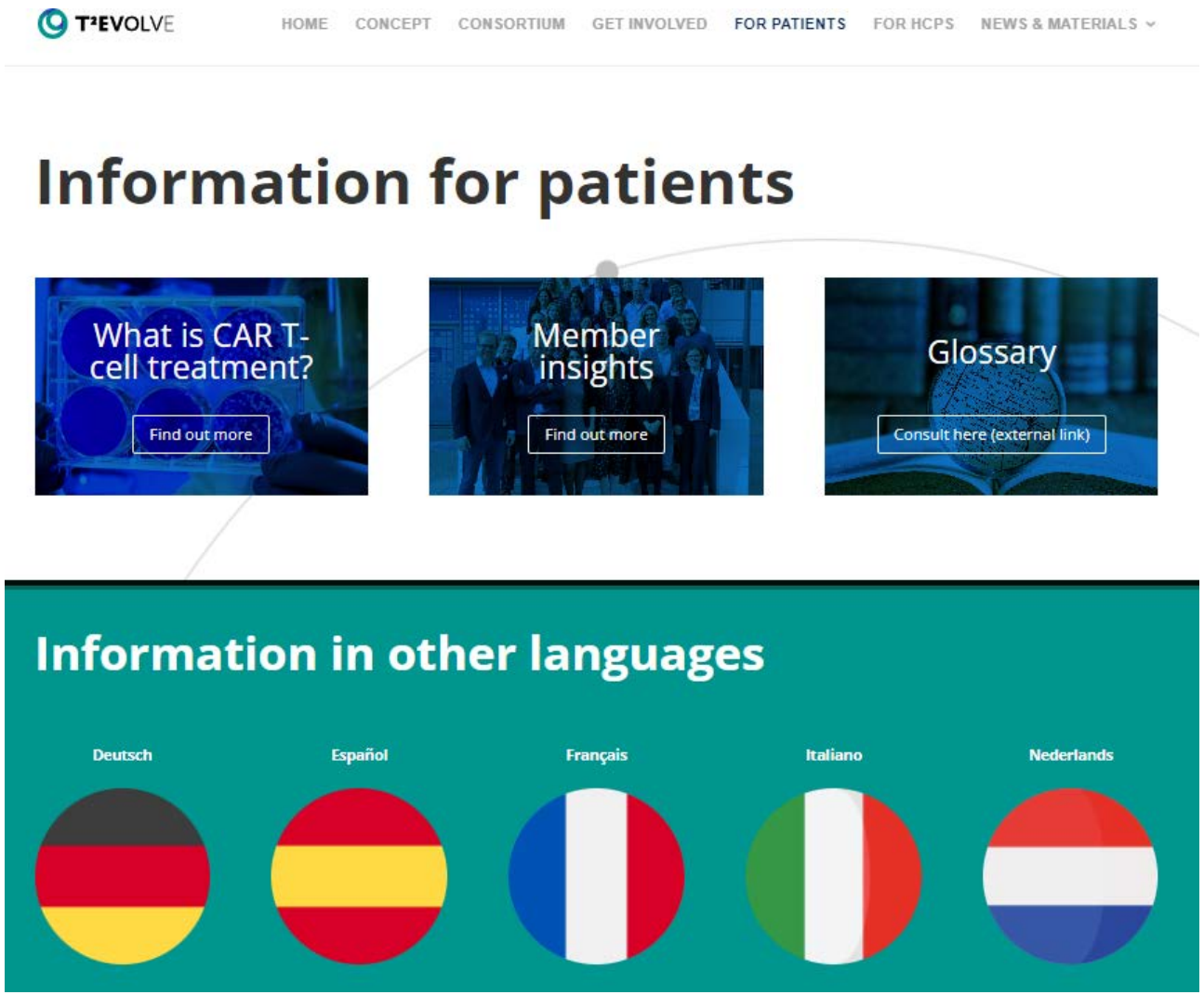
Harmonized registries

Regulatory framework

Patient Access

From science to society: faster, safer, fairer access to cell therapies.

T2EVOLVE Patient Engagement



- The **T2EVOLVE Patient Hub** is designed to support patients through **open access** educational materials.
- **Patient-centered Informed Consent Forms**: T2EVOLVE is improving CAR-T informed consent through clearer, patient-friendly forms. The work is ongoing, with two clinical trials ready to pilot their use.
- **A T2EVOLVE survey** of *389 CAR-T patients* across 10 countries showed overall good Quality of Life, but persistent physical, social, and cognitive issues. Anxiety about relapse and long-term effects, and more financial strain for younger patients, highlighting the need for tailored follow-up care.

Is T2EVOLVE Achieving its Vision?
Concrete Outcomes and Clinical Impact

University Hospital Würzburg

LION-1 :
Anti-ROR1 CAR T
Hematologic: MCL, CLL
Solid: ACC, TNBC, OvC

LION-2:
Anti-ROR2 CAR T
Hematologic: MM
Solid: Renal, BrC, Glioblastoma

Hospital Clinic Barcelona

CARTD-BG-1:
ARI0003 (anti CD19, anti BCMA)
NHL
B-Cell Lymphoma

9 Phase I/II clinical trial submissions during the project!

Ospedale Bambin Gesu'

GD2CAR02:
anti-GD2
NB, Pediatric CNS tumor

CD19.CAR
In B-ALL, autoimmune deseases

CD7.CAR
T-ALL, LL

Ospedale San Raffaele

Anti-CDH17
liver metastasis from colorectal cancer

Hospital Santpau Barcelona

HSP-CAR30
Anti-CD30
HL, NHL

CD62L+ CAR19
Anti CD19
DLBL, ML, FL

T2EVOLVE Preclinical models utilized for regulatory submission!
T2EVOLVE SOPs for Cell Count and Viability adopted!

…new therapies to **PATIENTS** in record time…

Is T2EVOLVE Achieving It`s Vision?
T2EVOLVE ecosystem enabled faster clinical progression

T-CURX

- **SIGBLAST**
  AML Clinical Trial
  Phase I/II
- **2025 Kytopen tech-access**
  Deal to strengthen non-viral CAR-T manufacturing in Europe

Janssen

- **CARTITUDE -5 in NDMM Phase III**
  CARTITUDE – 6 in NDMM Phase III
  Cilta-cel LTFU Phase IV
- **First European CAR-T production facilities at Tech Lane Science Park (Ghent, BE)**

BMS

- **Ide-cel in MM Phase III**
  Ide.-cel in R/R MM Phase III
- **First European CAR-T production facilities: cell-therapy plant (Leiden, NL)**

T2EVOLVE facilitates academic–industry collaboration, early scientific exchange and technology access

T2EVOLVE Regulatory Innovation

EMA Early dialogue

Enabled the consortium to recognize the regulatory significance of its work on **predictive preclinical models, analytical standards, and GMP guidance** for engineered T-cell therapies.

Parent-child

T2EVOLVE introduced the **parent–child approach in Europe**:

A "parent dossier" defines standardized **platform elements** (preclinical models, analytical methods, GMP protocols). "Child dossiers" for individual products then **reference and build upon** this validated parent framework.

Platform Technology Approach

Follow-up recommendations on the parent-child approach, the **Platform Technology approach** for cell-based therapies, includes a clear definition of **prior knowledge, data extrapolation**, and platform technology.

Currently under submission.

Policy Briefs

First example of a **European consortium** positioning itself with a **unified voice** in the regulatory policy space, highlighting the need to preserve **CAT's specialized expertise** to ensure Europe's leadership in ATMP development.

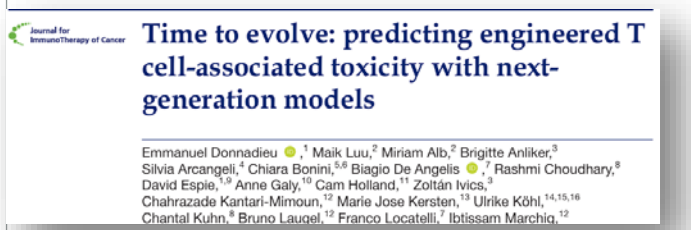
Paper will be published shortly.

CAR-T Access

CAR-T Access roadmap completed. White paper submitted and accepted.

Active engagement in the **CAR-T Vision** steering committee.

Advanced HTA models are ongoing in synergy with multiple other initiatives (e.g. **ASCERTAIN**)


Journal for ImmunoTherapy of Cancer

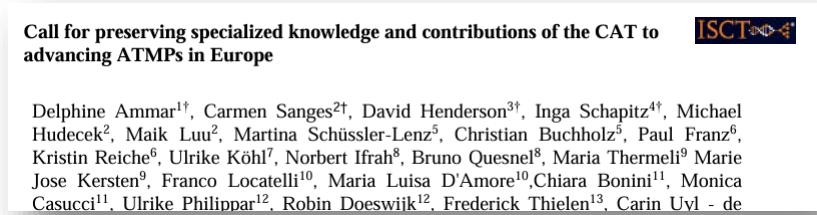
Time to evolve: predicting engineered T cell-associated toxicity with next-generation models

Emmanuel Donnadieu, Maik Luu, Miriam Alb, Brigitte Anliker, Silvia Arcangeli, Chiara Bonini, Biagio De Angelis, Rashmi Choudhary, David Espie, Anne Galy, Cam Holland, Zoltán Ivics, Chahrazade Kantari-Mimoun, Marie Jose Kersten, Ulrike Köhl, Chantal Kuhn, Bruno Laugel, Franco Locatelli, Ibtissam Marchiq


frontiers | Frontiers in Immunology

Accelerating development of engineered T cell therapies in the EU: current regulatory framework for studying multiple product versions and T2EVOLVE recommendations

Delphine Ammar, Inga Schapitz, Maik Luu, Michael Hudecek, Miriam Meyer, Timmothy Taps


Call for preserving specialized knowledge and contributions of the CAT to advancing ATMPs in Europe

ISCT

Delphine Ammar[1†], Carmen Sanges[2†], David Henderson[3†], Inga Schapitz[4†], Michael Hudecek[2], Maik Luu[2], Martina Schüssler-Lenz[5], Christian Buchholz[5], Paul Franz[6], Kristin Reiche[6], Ulrike Köhl[7], Norbert Ifrah[8], Bruno Quesnel[8], Maria Thermeli[9] Marie Jose Kersten[9], Franco Locatelli[10], Maria Luisa D'Amore[10],Chiara Bonini[11], Monica Casucci[11], Ulrike Philippar[12], Robin Doeswijk[12], Frederick Thielen[13], Carin Uyl - de

T2EVOLVE Achievements in a bite

New Standards – *Preclinical models*, *analytical assays*, and ***CAR-T Core Data Set*** consolidated, forming a reference for regulators and developers.

Regulatory Engagement – Active dialogue with EMA and national agencies on platform technologies and product monitoring.

Patient & Clinician Voice – Two large EU surveys completed; created a patient–Health Care Providers hub and piloted improved informed consent forms. Innovative HTA assessments (joint with ASCERTAIN)

Collaboration in Action – >**300 stakeholders** engaged; **10+ joint publications**;

10 joint workshops and **roundtables** with other EU projects.

👉 **Impact so far:** Built a trusted ecosystem and common language across science, clinics, regulators, and patients.

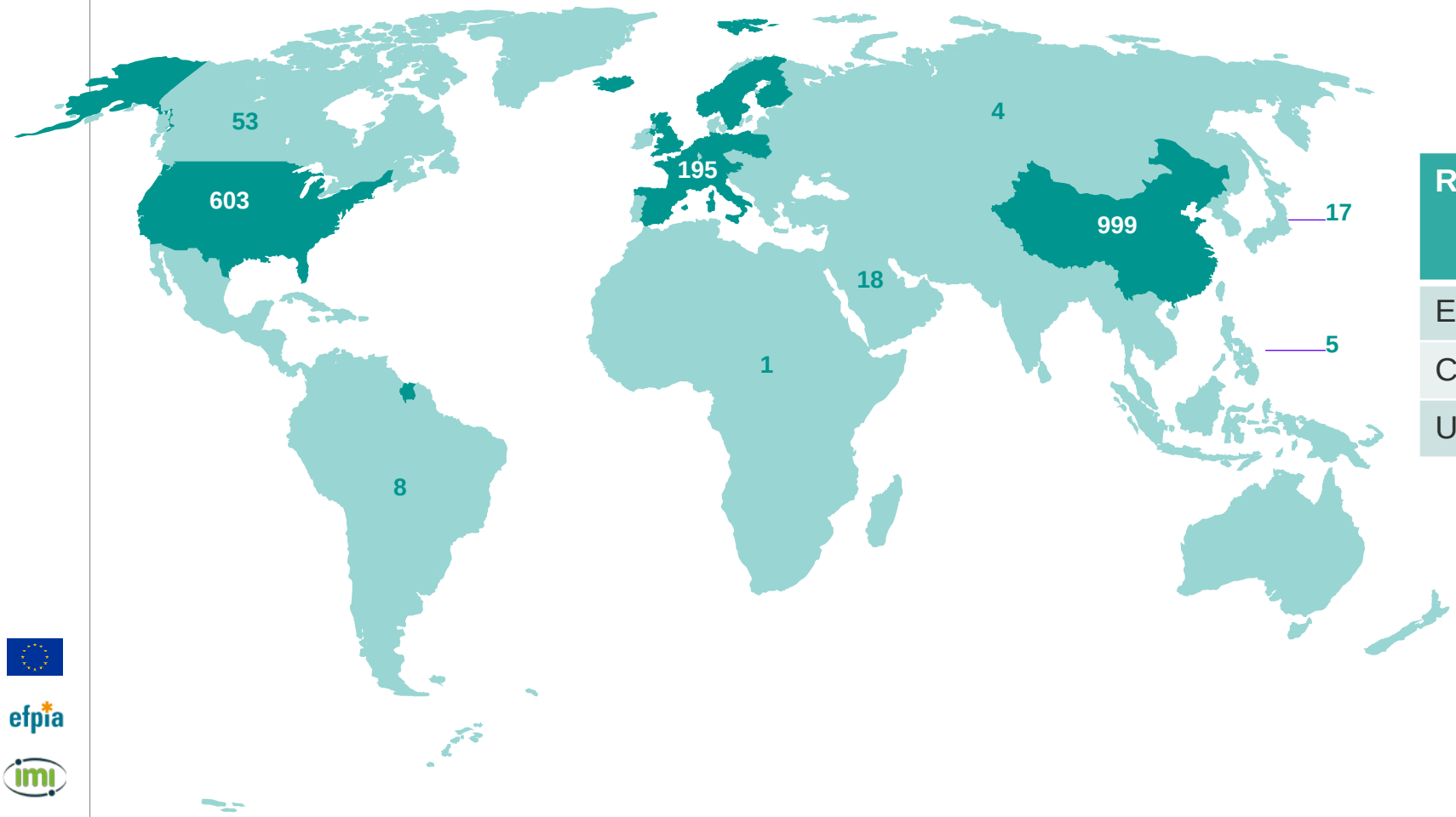
👉 **Sustainable Community:** By joining forces with initiatives like **GoCART** and **EuroGCT**, we have ensured that results are not just published but used in practice.

Beyond Science: T2EVOLVE Economic and Societal Impact

Key impacts	Concrete examples
Safer and more effective T cell therapies	**5 models were processed - 3 preclinical models obtained regulatory acceptance (INSERM, IDIBAPS and OPBG). An additional 2 are under evaluation.**
Increased industrial competitiveness	**3 new manufacturing sites from T2EVOLVE partners Jansenn, Bayer and BMS. Several SMEs and CDMOs are using T2EVOLVE recommendations on Raw and Starting Materials across Europe.**
Increased access to engineered T cell therapy	**9 new products developed. IDIBAPS and OPBG** are advancing products for adult ALL and pediatric solid tumors, already **granted EMA PRIME designation.** **Parent-child approach white paper, Policy brief and Access roadmap paper (accepted)**
Increased HCP and public awareness	Extensive dissemination and outreach activities through more than **20 conference events, 30 publications, more than 5,000 t2evolve website visits and +1,000 LinkedIn followers.**
Combining of public and private funds and contributions	**Joint work between public and private project** partners has led to synergistic outcomes, with **12 of 30 publications resulting from such collaborations. More to come after project closure.**
Opportunity to compare data generated from standardised analytical methods	**Evaluation of Immunomonitoring methods across Europe**, and developed optimized Standard Operating Procedures (SOPs). **SOPs tested at 10 different sites**, and are being validated across T2EVOLVE and Europe. The SOPs describe critical steps for cell count and CAR T detection, independently of instruments used.

Global CAR T-Cell Therapy Race in 2025

Clinical Trials Worldwide



Region	Studies by end 2019	Studies by end 2021	Studies by Q3 2025
Europa	50	90	195
China	**278**	**465**	**999**
USA	**187**	**305**	**603**

CAR-T Access in Europe: 2020 vs. 2025 (T2EVOLVE Vision)

2020 – Limited & Fragmented	2025 – with T2EVOLVE Contribution
Few CAR-T centers (mainly Germany, France, UK, Spain, Italy)	**Expanded** network of GMP & treatment centers across EU
Eastern & smaller EU states: **no access**	**Equitable** access roadmap to enable inclusion of all EU states
High costs, no harmonized reimbursement	**Improved affordability** through HTA & innovative models
Complex logistics: apheresis shipped to U.S.	**Point-of-care manufacturing** reduces delays & logistics
Long wait times due to limited global capacity	**≥6 GMP facilities** producing CAR-T in Europe
Fragmented regulation, national rules dominate	**Standardized** models, monitoring & GMP protocols adopted
Most trials & investments outside EU (U.S. & Asia)	EU regains competitiveness: **≥20 development programs**

T2EVOLVE Pillars for Long-Term Impact

Patient Education:

Comprehensive resources for patients and families.

Regulatory innovation and roadblocks to access:

Industry and academic common ground to move forward the field

Frontiers Innovation:

Workshops, pilot studies, and task forces for cutting-edge initiatives.

Clinical Translation and Correlative Research:

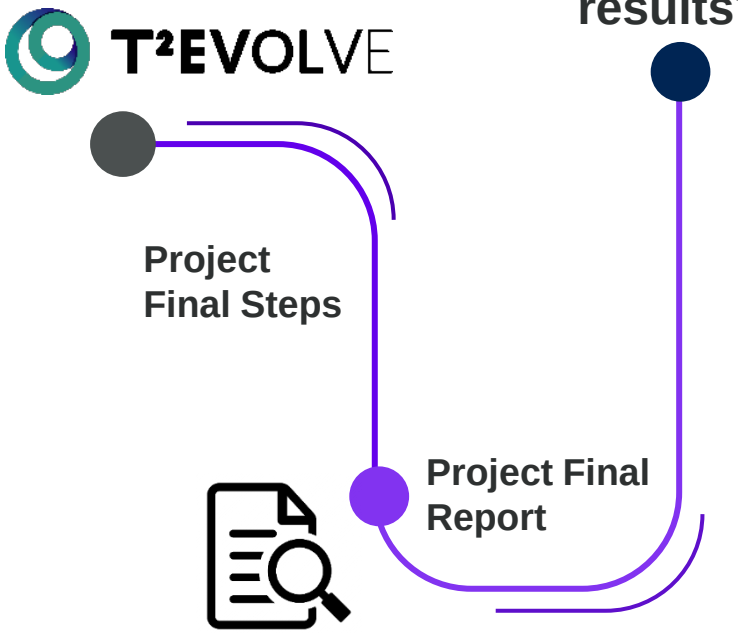
impact of harmonized and reusable data frameworks and methods.

Faster therapies, broader access

What Is In For The Future of an IMI Project?

December 2025

How to sustain the T2EVOLVE results?



Challenges After EU Project Funding Ends

- **Loss of Momentum** – No structure to continue collaborations
- **Limited Funding** – No direct continuation of EU funding
- **Dispersed Knowledge** – Risk of fragmentation of results
- **No Legal Entity** – Harder to apply for funding, form agreements, or engage with regulators

The T2EVOLVE story continued…

WE CAN MAKE IT!

T2EVOLVE Association - Turning Dialogue into Action

Roundtable discussions

Multistakeholder in person discussions on critical gaps in the field.

Key outcomes:

Reports

Position papers

White papers

Policy briefs

Science Plus Café

In depth expert online discussion on highly relevant gaps or solutions to specific problems in the field

Key Outcomes:

Publications

Collaborations

Technology Scan Events

Knowledge sharing

Showcase of innovative technologies

Key Outcomes:

Collaboration ideas

Accelerant Projects

Joint Workshops

Series of Joint Workshops:

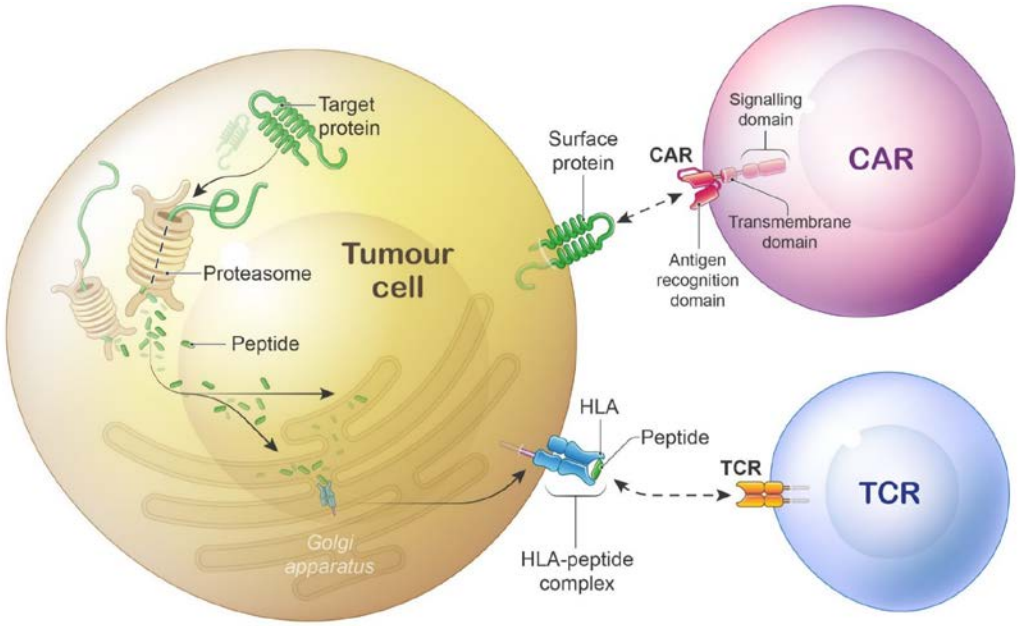
- Addressing common challenges
- Create awareness
- Knowledge sharing

Key Outcomes:

collective impact across the European landscape

From discussions to action: *dedicated working groups* will focus on achieving the **Key Outcomes**.

Looking ahead: Expanding to new T-cell modalities



Hematologic Malignancies

- Acute & Chronic B-Cell Leukemia
- B-Cell Lymphoma
- Multiple Myeloma
- T-Cell Leukemia & Lymphoma

Solid Tumors

- Neuroblastoma
- Melanoma
- Sarcoma
- Breast Cancer
- Lung Cancer
- Glioblastoma
- etc.

Autoimmune Diseases

- Systemic Lupus Erythematosus
- Myasthenia Gravis
- Etc.

Infectious Diseases

- Human Immuno-Deficiency Virus (HIV)
- Hepatitis B & C Virus
- Cytomegalovirus
- Aspergillus fumigatus

Cardiovascular Diseases

- Cardiac Fibrosis
- Cardiac Failure
- Myocardial Infarction
- Atherosclerosis
- Heart Transplant

Call to Action

The journey does not end with T2EVOLVE.

Join us in the T2EVOLVE Association to keep innovation alive and ensure that no patient is left behind.

T²EVOLVE

www.t2evolve.com

Leveraging Synergies Across Consortia

T²EVOLVE

Safety prediction

imSAVAR

CERTAINTY
A cellular immunotherapy virtual twin for personalised cancer treatment

Manufacturing innovation

AIDPATH

easygen

Patient Access and RWD

ASCERTAIN

JOIN 4 ATMP

IDERHA
integrating health data

Patient and HCP education

EURO GCT
European Consortium for Communicating Gene & Cell Therapy Information

Focus on Specific Projects:

HARMONY

T2EVOLVE

EASYGEN

easygen

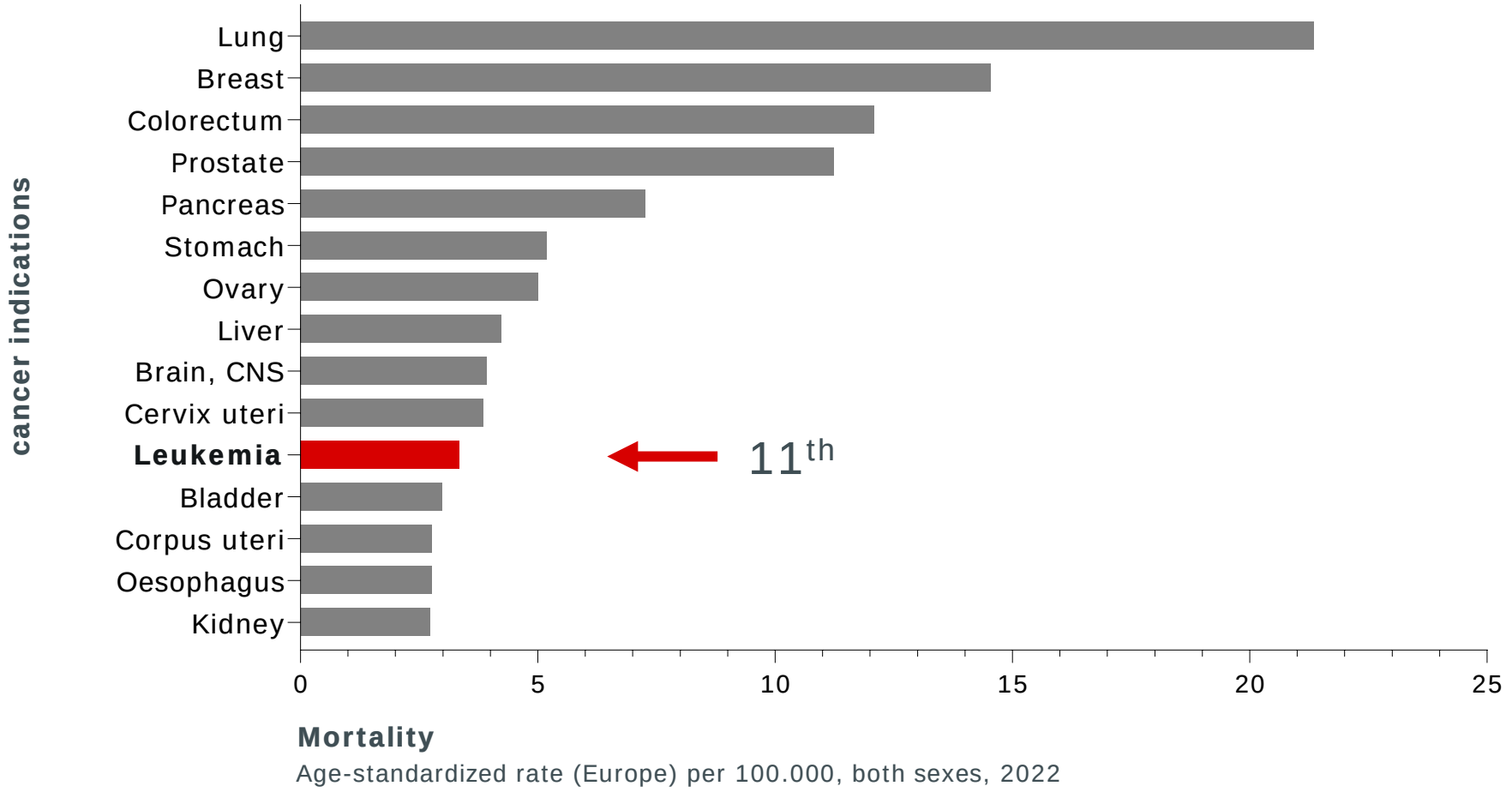
EASY workflow integration for **GEN**e therapy

How the EASYGEN consortium aims to transform CAR-T manufacturing

Dr. Sonja Steppan
Principal Investigator EASYGEN consortium
Fresenius SE & Co. KGaA

Bad Homburg, October 1 2025

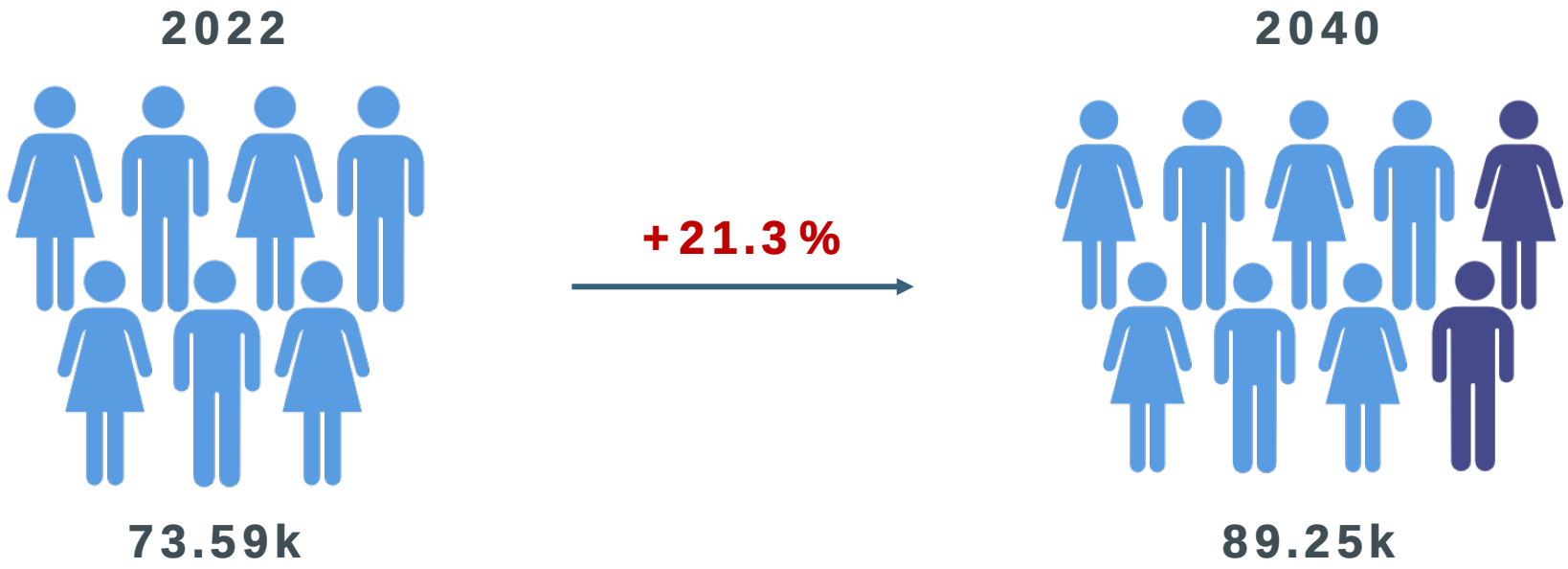
Leukemia is the 11th leading cause of cancer death across Europe



Source: Cancer TODAY | IARC https://gco.iarc.who.int/today (Sept 2025)

Leukemia incidence surges: 2022–2040 data reveal over 21% rise across Europe

Leukemia



= 10.000 patients

Increase due to demographic change

27 EU countries, both sexes, all ages

Source: ECIS - European Cancer Information System (Sept 2025)

Multiple myeloma incidence projected to rise by almost 23% in Europe by 2040

Multiple myeloma

Source: ECIS - European Cancer Information System (Sept 2025)

The CAR-T revolution – A new way to treat cancer
Available for patients with no therapeutic options left

nature reviews drug discovery

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nature > nature reviews drug discovery > news in brief > article

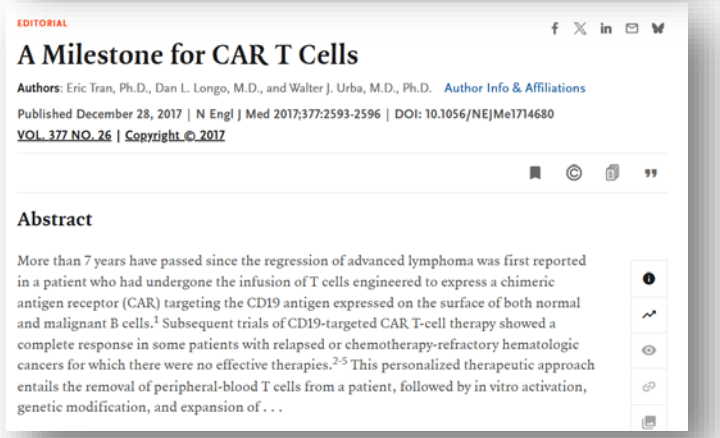
News in Brief | Published: 29 September 2017

FDA approves first CAR T therapy

Asher Mullard

Nature Reviews Drug Discovery **16**, 669 (2017) | Cite this article

8280 Accesses | **202** Citations | **57** Altmetric | Metrics



EDITORIAL

A Milestone for CAR T Cells

Authors: Eric Tran, Ph.D., Dan L. Longo, M.D., and Walter J. Urba, M.D., Ph.D. Author Info & Affiliations

Published December 28, 2017 | N Engl J Med 2017;377:2593-2596 | DOI: 10.1056/NEJMe1714680

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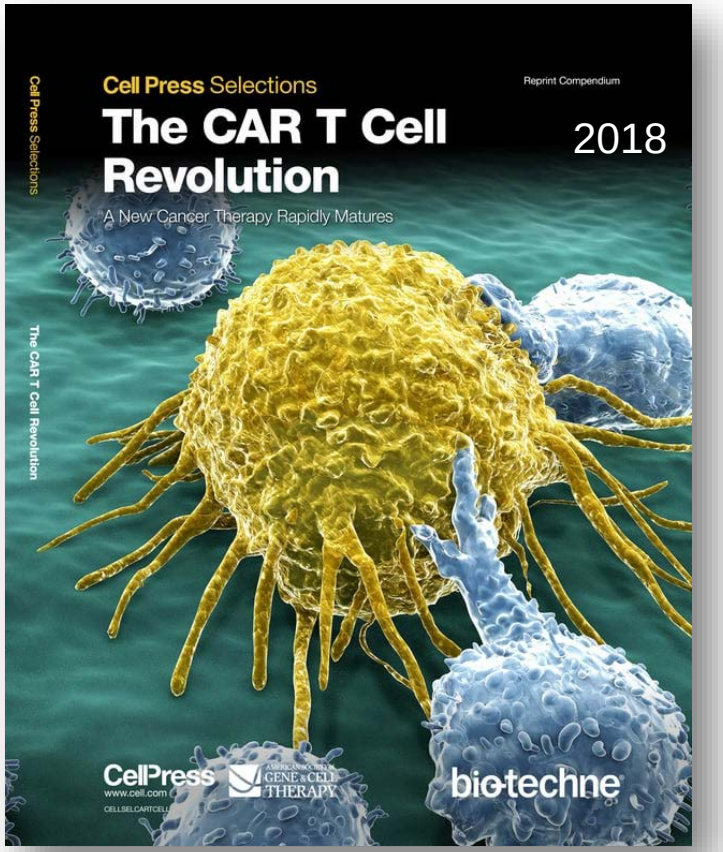
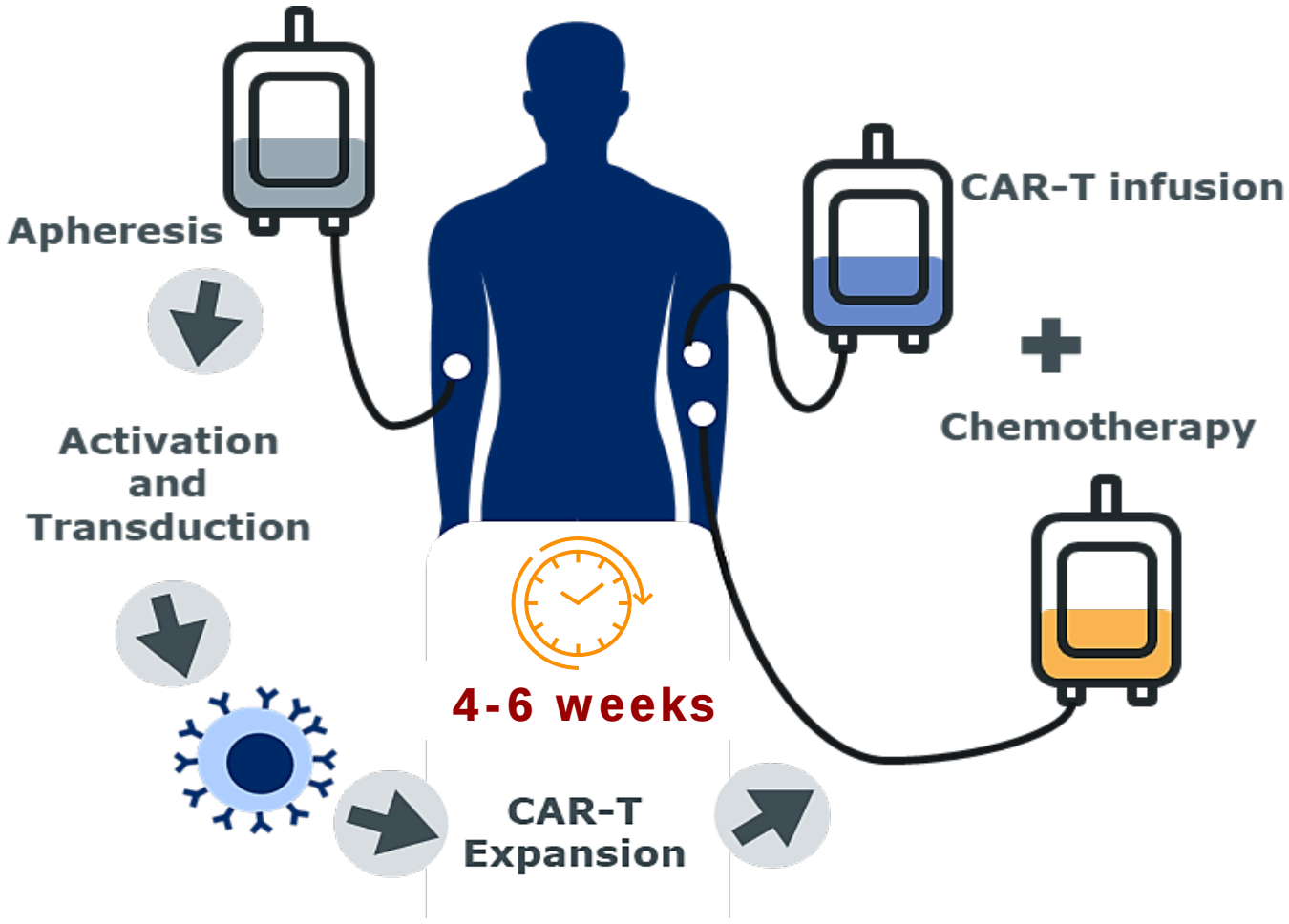
Abstract

More than 7 years have passed since the regression of advanced lymphoma was first reported in a patient who had undergone the infusion of T cells engineered to express a chimeric antigen receptor (CAR) targeting the CD19 antigen expressed on the surface of both normal and malignant B cells.[1] Subsequent trials of CD19-targeted CAR T-cell therapy showed a complete response in some patients with relapsed or chemotherapy-refractory hematologic cancers for which there were no effective therapies.[2-5] This personalized therapeutic approach entails the removal of peripheral-blood T cells from a patient, followed by in vitro activation, genetic modification, and expansion of . . .



CAR-T manufacturing process in a nutshell

Current process



CAR-T therapy landscape
Seven approved CAR-T products as of Sept 2025

Brand product	Company
KYMRIAH®	**Novartis** Basel, CH
YESCARTA®	**Gilead Sciences / Kite Pharma** Foster City, CA, US
TECARTUS™	**Gilead Sciences / Kite Pharma** Foster City, CA, US
Breyanzi®	**Bristol Myers Squibb** New York, NY, US
CARVYKTI™	**Johnson & Johnson / Legend Biotech** New Brunswick, NJ, US / Somerset, NJ, US
Abecma®	**Bristol Myers Squibb / 2seventy Bio** New York, NY, US / Cambridge, MA, US
AUCATZYL®	**Autolus** London, UK

Multiple myeloma: CAR-T delivers 3× better responses, expanding options beyond standard care

Standard of care therapy

Corticosteroids

Immuno-modulatory drugs

Anti-CD38 monoclonal antibodies

22 %
Complete response

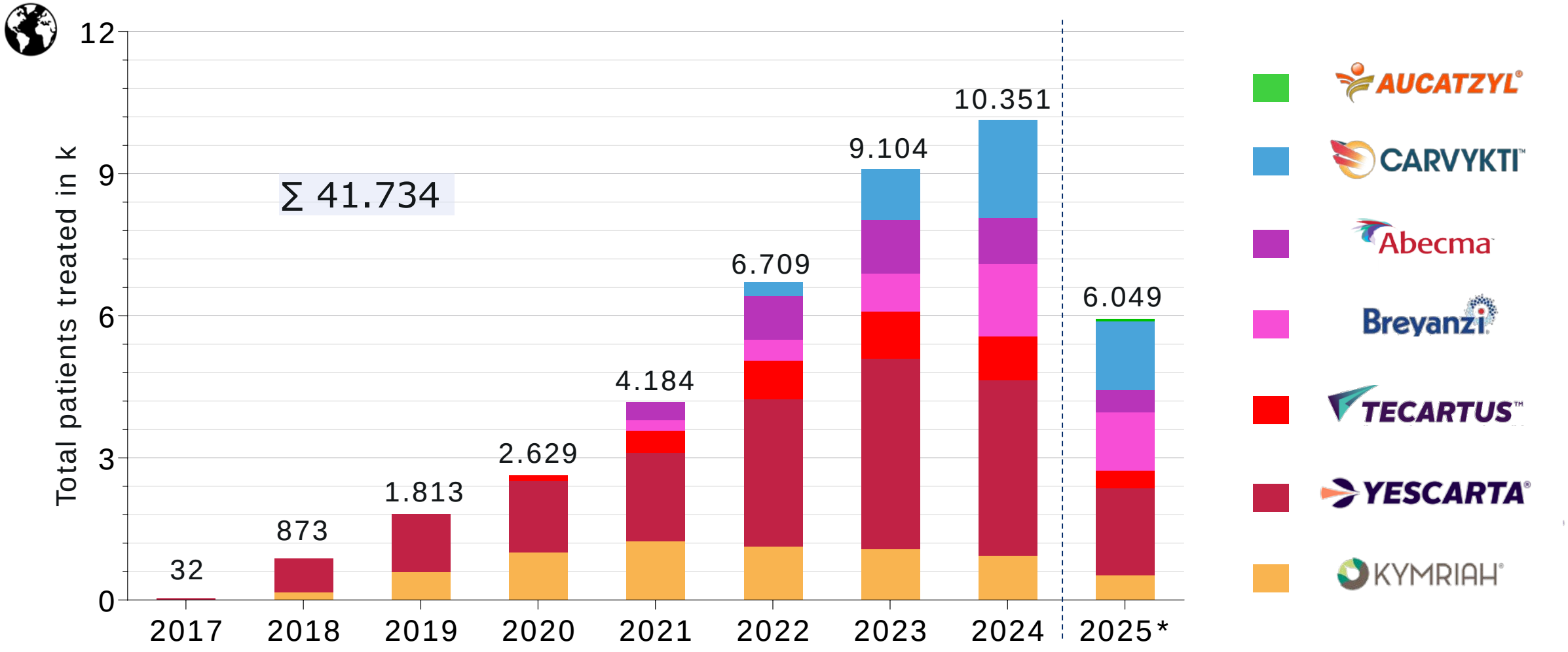
Carvykti CARTITUDE-4 trial

73 %
Complete response

Phase 3, randomized, open-label trial, 419 patients (208 to receive Carvykti and 211 to receive standard care)

Source: San-Miguel et al., N. Engl. J. Med., 2023 (CARTITUDE-4 trial)

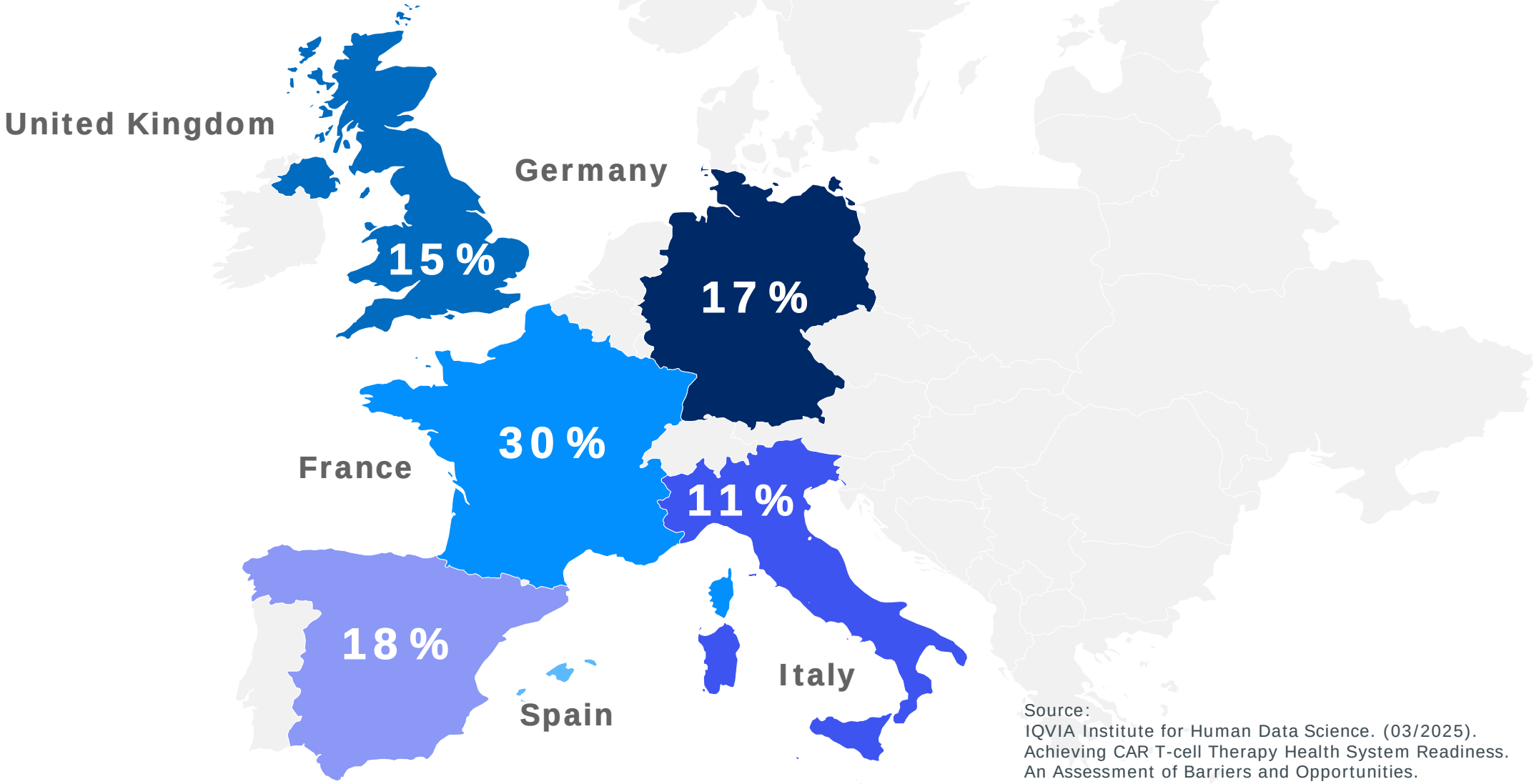
CAR-T's access gap: ~42k treated worldwide leaving millions behind



Source: Oribiotech Patient Access Tracker (Sept 2025)

*Q3&4 missing

Only ~18% of eligible European patients receive CAR-T therapy



Source:
IQVIA Institute for Human Data Science. (03/2025). Achieving CAR T-cell Therapy Health System Readiness. An Assessment of Barriers and Opportunities.

No economies of scale: lentiviral, centralized CAR-T manufacturing + complex logistics = high price

Approval 2018-2020

KYMRIAH® 266.438k €

YESCARTA® 281.609k €

TECARTUS™ 282.714k €

Approval 2021-2022

Abecma™ 351.351k €

Breyanzi® 281.609k €

CARVYKTI™ 286.326k €

Source: Gemeinsamer Bundesausschuss (Sept 2025)

Why EASYGEN matters: demand up, access down (1/2)

14,900

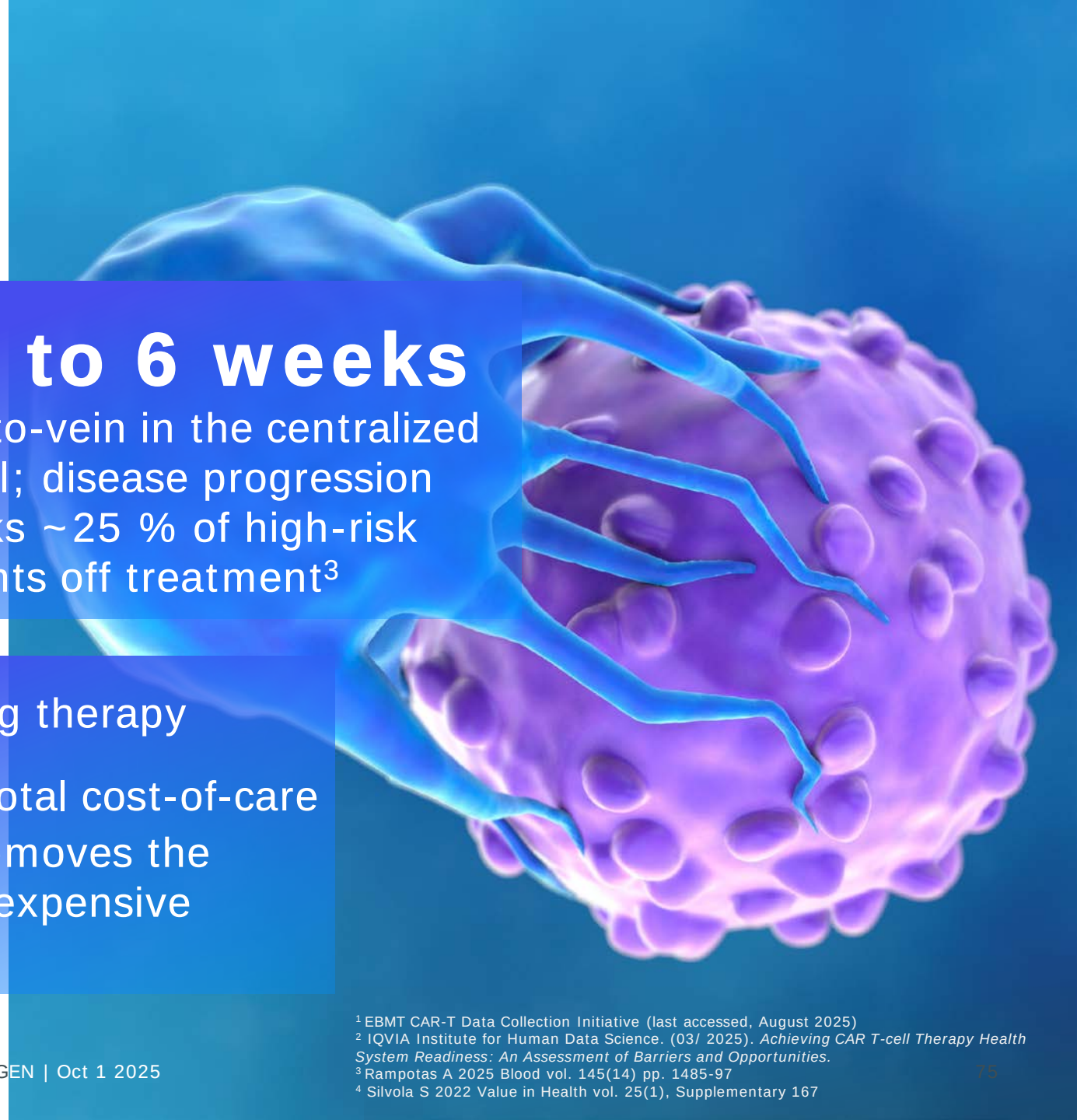
CAR-T treatments logged in EBMT (Aug 2025)[1] – still < 20% of eligible EU patients[2]

Up to 6 weeks

vein-to-vein in the centralized model; disease progression knocks ~25 % of high-risk patients off treatment[3]

Logistics & bridging therapy

≈ **30 %** of total cost-of-care – decentralizing removes the longest and most expensive steps[4]



[1] EBMT CAR-T Data Collection Initiative (last accessed, August 2025)
[2] IQVIA Institute for Human Data Science. (03/ 2025). *Achieving CAR T-cell Therapy Health System Readiness: An Assessment of Barriers and Opportunities.*
[3] Rampotas A 2025 Blood vol. 145(14) pp. 1485-97
[4] Silvola S 2022 Value in Health vol. 25(1), Supplementary 167

Why EASYGEN matters: demand up, access down (2/2)

>1,450 CAR-T assets
in clinical trials globally, pipeline growth will out-strip current viral plant capacity[4]

IHI Call 7 focus

Improve affordability ✓
workforce load ✓
and patient reach ✓
EASYGEN ticks all three boxes

[4] Beacon Intelligence Database (last accessed, September 2025)

CAR-T today: labor-heavy, non-scalable, expensive, bureaucratic - blocking timely access

Current process

centralized

1 Leukapheresis <4 h

2 Formulation/ aliquoting and freezing <3 h

1-2 days

3 Washing and T cell enrichment <6 h

4 T cell activation 1-2 days

5 Genetic modification (viral transduction) 1-2 days

Ex-vivo CAR-T expansion 6 7-14 days

7 Washing and concentration <2 h

8 Formulation/ aliquoting and freezing <3 h

9 Quality control & release testing 7-14 days

1-2 days

10 Re-infusion into patient <1 h

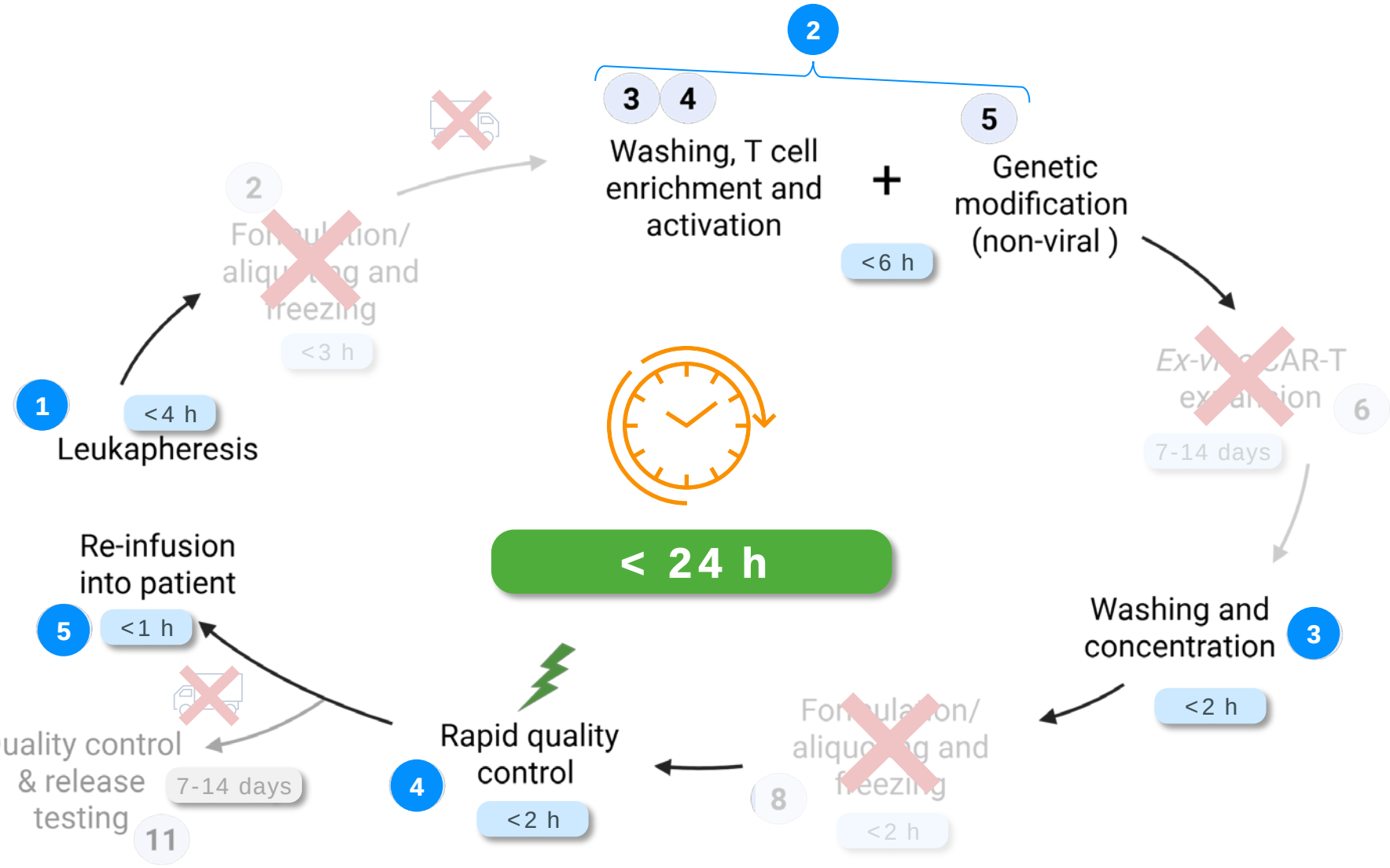
Up to 6 weeks

Sources: FDA – Considerations for the development of CAR T cell products (Sept 2025)
EMA – Assessment Reports (Sept 2025)

EASYGEN streamlines CAR-T manufacturing: decentralized, virus-free, designed for hospitals

easygen

decentralized



A cross-functional force ready to tackle the toughest challenges in CAR-T manufacturing

EASYGEN

brings together

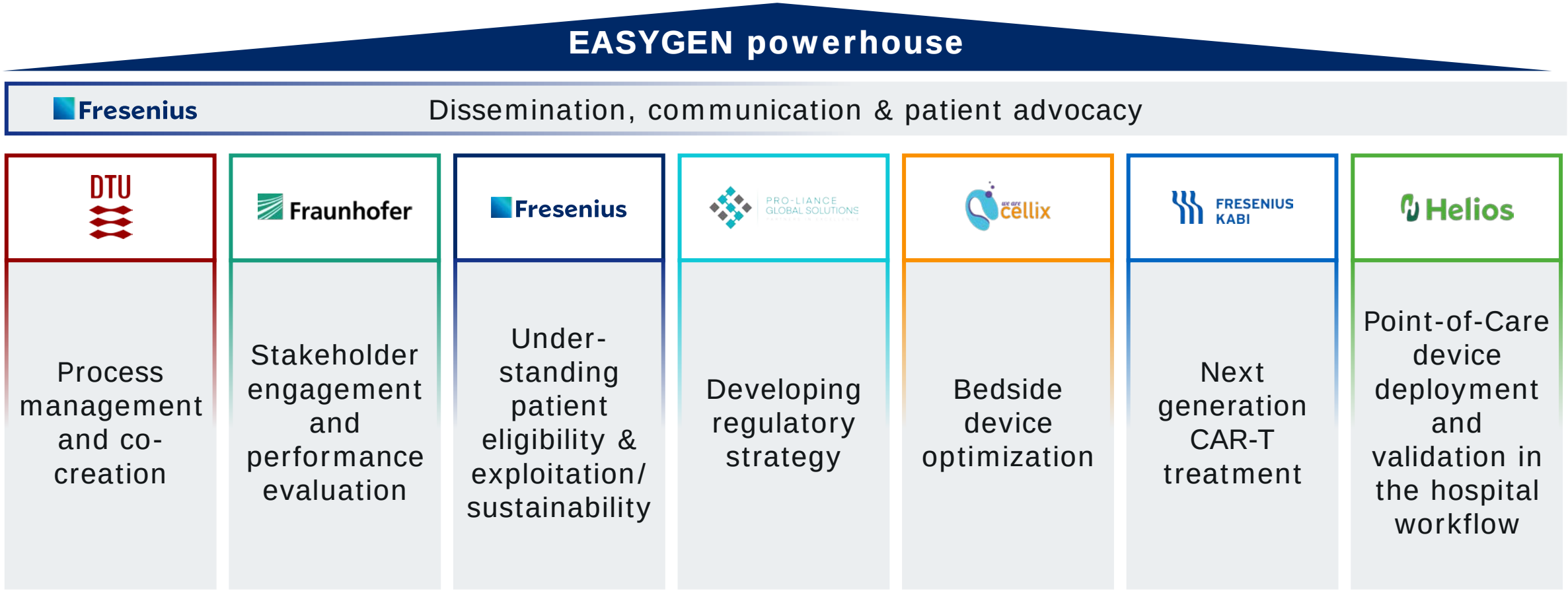
18 partners

across

8 countries

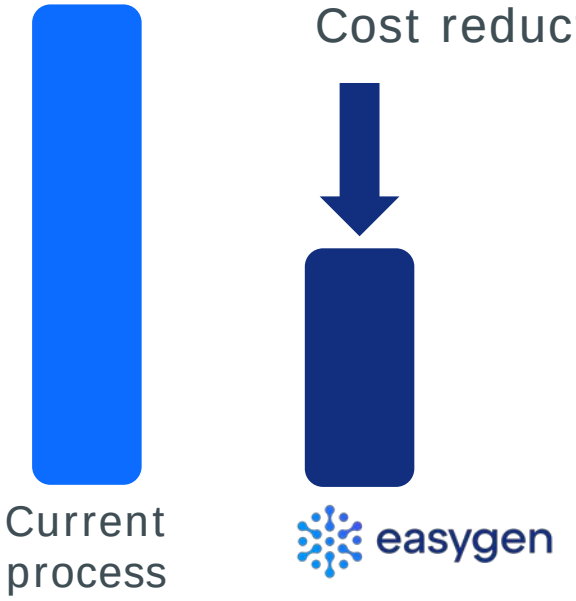
to enable decentralized CAR-T manufacturing

Workflow to enable hospital-integrated, decentralized CAR-T manufacturing

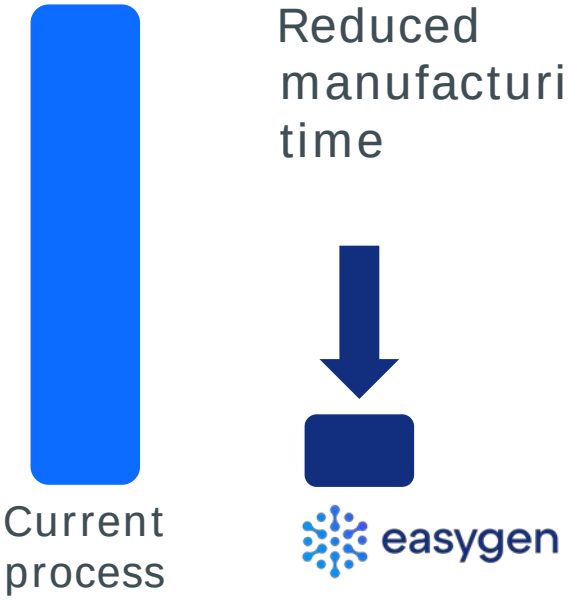


Potential EASYGEN impact: cost-effective democratization of cancer immunotherapy

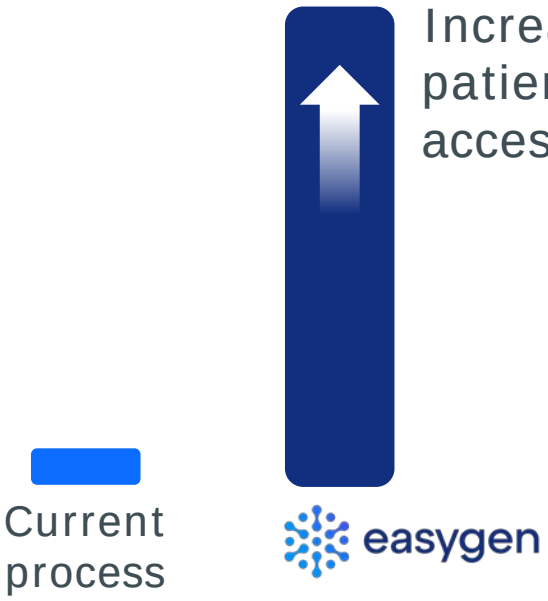
Production cost



Manufacturing time



Patient access



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activate the cure for childhood cancer

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OPTIMA

PROTECT trial radiation against esophagel cancer

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IHI Impact Events on Cancer

- **Passed Impact event on Cancer**
  - Watch it to learn how IHI and IMI projects are tackling cancer.

PIONEER	OPTIMA	IMAGIO	GUIDEMRD
Prostate Cancer	Optimal treatment through AI	Interventional Oncology	Liquid Biopsy

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Q&A

COCIR Advancing Healthcare

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