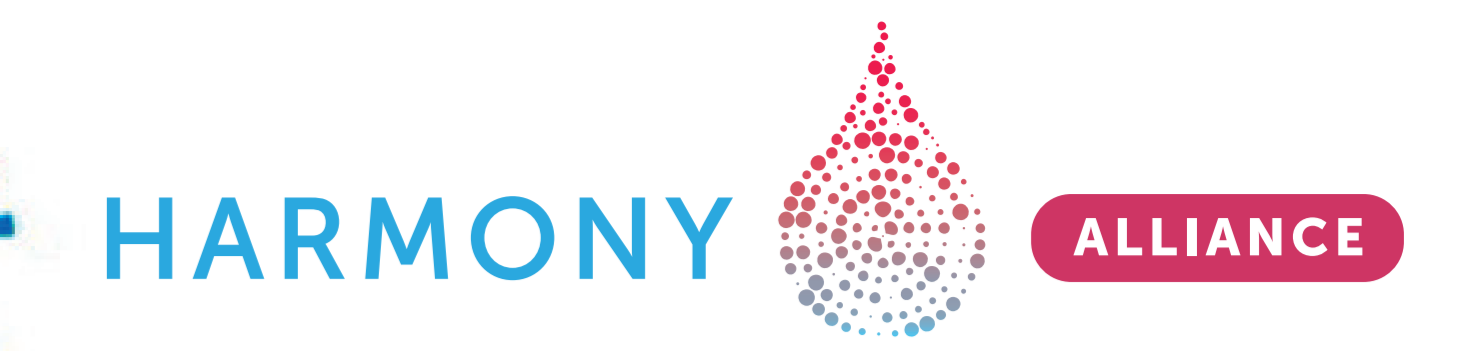


Pan-Stakeholder Core Outcome Set (COS) Definition for Hematological Malignancies within the framework of HARMONY and HARMONY PLUS projects

Katharina M Lang¹, Tamás Bereczky², Jan Geissler², Natacha Bolanos³, Kate Morgan⁴, Ananda Plate⁴, Ana Vallejo⁴, Sophie Wintrich⁵, Nick York⁶, Peter Loffelhardt⁷, Brian Huntly⁸, Pieter Sonneveld⁹, Mario Boccadoro¹⁰, Valeria Santini¹¹, Sarka Popisilova¹², Andreas Hochhaus¹³, Tiziano Barbui¹⁴, Peter Borchmann¹⁵, Christian Buske¹⁶, Yann Guillevic¹⁷, Frederico Calado¹⁸, Katy Harrison¹⁹, Dalia Dawoud¹⁹, Guillermo Sanz²⁰, Jesus Maria Hernandez Rivas²¹, Ellen De Waal²², Martje Barbus²³, Renate Schulze-Rath²⁴, Lars Bullinger¹

¹ Charité Universitätsmedizin Berlin, Germany ² LeukaNET, Germany ³ Lymphoma Coalition, Canada ⁴ Myeloma Patients Europe, Belgium ⁵ MDS UK Patient Support Group, UK ⁶ LeukemiaCare, UK ⁷ MPN Advocates Network, Switzerland ⁸ University of Cambridge, UK ⁹ Erasmus MC, The Netherlands ¹⁰ University of Turin, Italy ¹¹ University of Florence, Italy ¹² Masarykova Univerzita, Czech Republic ¹³ University Hospital Jena, Germany ¹⁴ University Bergamo, Italy ¹⁵ University Köln, Germany ¹⁶ Universitätsklinikum Ulm, Germany ¹⁷ BMS - Bristol Myers Squibb, Switzerland ¹⁸ Novartis, Switzerland ¹⁹ NICE, UK ²⁰ Hospital Universitario y Politécnico La Fe, Spain; Health Research Institute La Fe, Spain; CIBERONC, IS Carlos III, Spain ²¹ University of Salamanca, Spain ²² European Hematology Association, The Netherlands ²³ AbbVie, Germany ²⁴ Bayer AG, Germany



INTRODUCTION

Definition of a core outcome set (COS), which represents an agreed set of outcomes for each hematological malignancy (HM) may improve the interpretation and comparability of clinical trials, especially if a respective COS addresses the needs of all stakeholders including patients, clinicians, industry, as well as regulators/HTA bodies. In accordance, HARMONY – the Healthcare Alliance for Resourceful Medicine Offensive against Neoplasms in Hematology – and the follow up project HARMONY PLUS have made it its task to develop COS for HMs.

HARMONY – COS definition for AML, NHL, MM, MDS, CLL

METHOD

Traditional Delphi survey, 2 iterative survey rounds with predefined consensus criteria, final consensus meeting
→ definition of a COS for each HM

DELPHI SURVEYS

Towards Core Outcome Sets for Blood Cancers

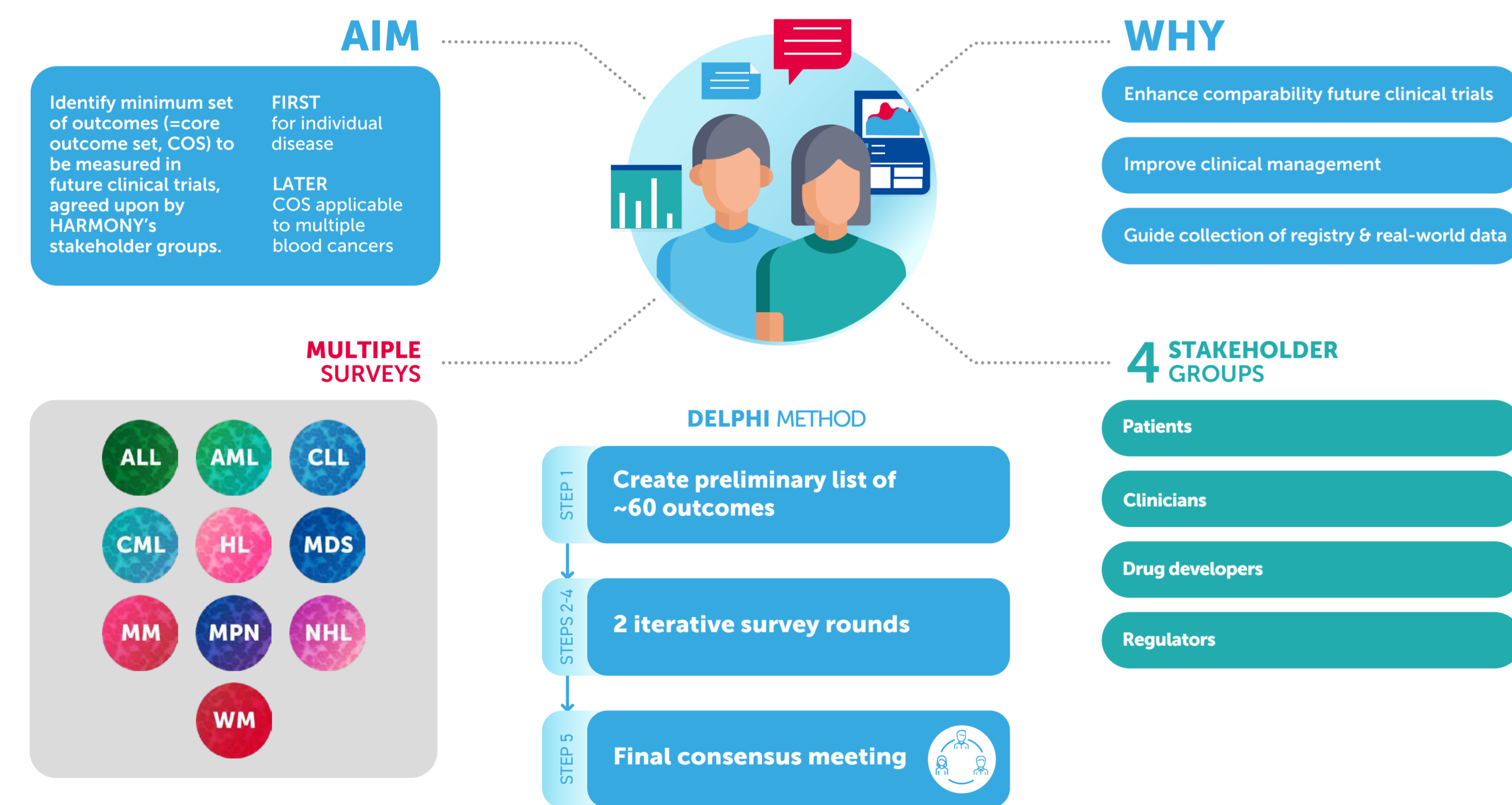


Figure 1: Infographic of the HARMONY Alliance Delphi Survey method

HARMONY PLUS – COS definition for CML, HL, MPN, WM

METHOD

Delphi „Hackathons“, 2 iterative survey rounds as virtual meetings with predefined consensus criteria, final consensus meeting and final expert panel meeting
→ definition of a COS for each HM
→ additional important PROs for CML

RESULTS IN HARMONY

A total of 365 individuals participated including 177 patients/patient advocates (48%), 126 clinicians (35%), 46 EFPIA/industry members (13%) and 16 regulators/members of HTA bodies (4%)

Total participation HARMONY Delphi surveys

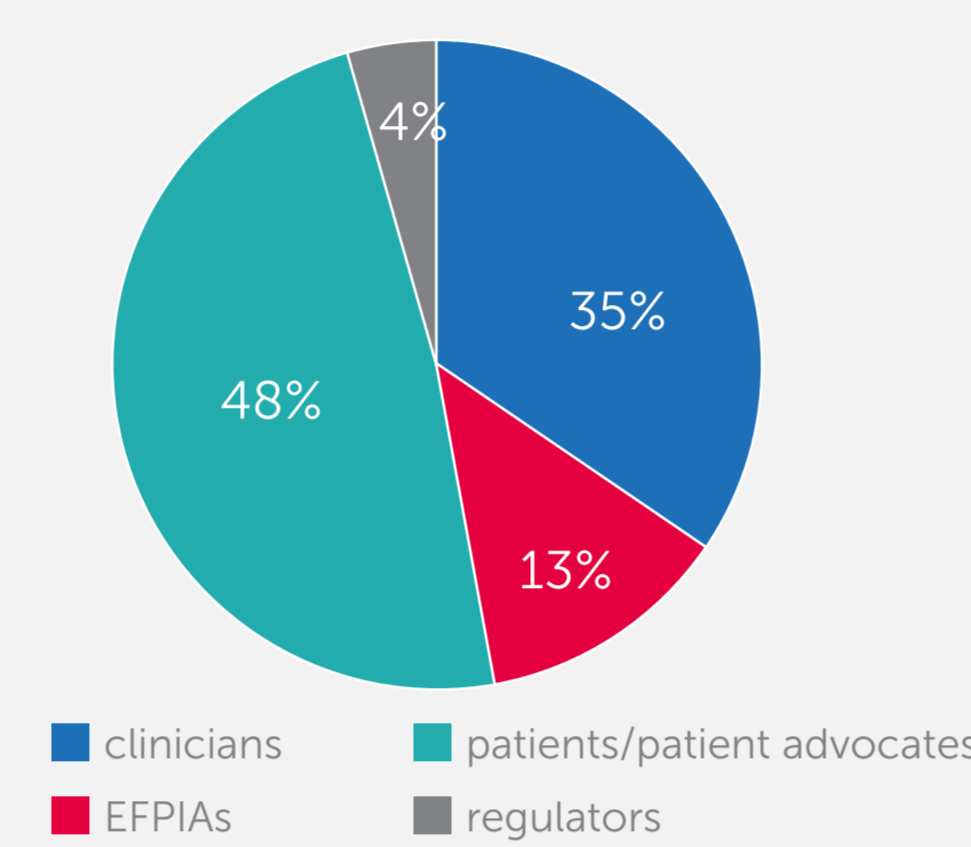


Figure 2: Total participation for HARMONY Delphi surveys

RESULTS

COS for AML

domain	outcome
type of event	OS, CR, CR+MRD neg, clin relapse, PD
time to event	PFS, EFS, DOR
toxicity	SAEs, discount of treatment
PRO	physical fct

COS for NHL

domain	outcome
type of event	OS
time to event	PFS
toxicity	AEs SAEs, cardiovascular tox, tol-rel outcomes
PRO	sensory neuropathy, pain, dyspnoea

COS for MM

domain	outcome
type of event	CR, clinical relapse, PD, OS
time to event	PFS, PFS2, DOR
MRD	mol MRD
toxicity	AEs SAEs, discontinuation of treatment
PRO	sensory neuropathy, pain, dyspnoea

COS for MDS

domain	outcome
type of event	OS, clinical relapse
time to event	PFS, DOR, time to AML, time to HR-MDS
clinical paramter	blood tranfusion dependence, transfusion independence
toxicity	AEs SAEs
PRO	GQI, dyspnoea, independent living

COS for CLL

domain	outcome
type of event	CR, SD, clinical relapse, PD, OS
time to event	PFS, EFS, DOR, TTP, TTNT, time to transformation, TFI
toxicity	AEs SAEs, medical adherence, SPM
use of resources	EU admission, ICU admissions

Total participation HARMONY Plus Delphi surveys

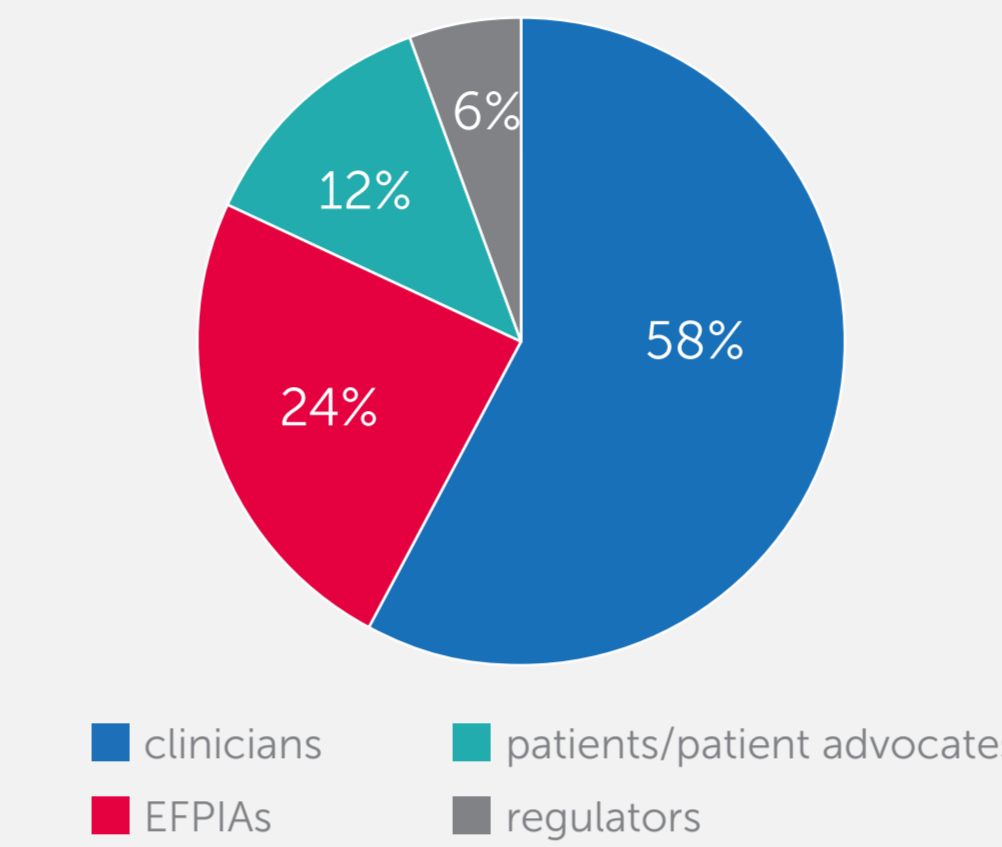


Figure 3: Total participation for HARMONY PLUS Delphi surveys

RESULTS IN HARMONY PLUS

A total of 161 individuals participated including 20 patients/patient advocates (12%), 93 clinicians (58%), 39 EFPIA/industry members (24%), and 9 regulators/members of HTA bodies (6%)

RESULTS

COS for CML

domain	outcome
type of event	OS, CR, MMR*
time to event	PFS, EFS, DOR, TTP

* Positive events such as e.g. the achievement of a major molecular remission should be rather termed "milestones".

COS for MPN

domain	outcome
type of event	OS
time to event	PFS, TTP, time to transformation
toxicity	AEs SAEs, hem tox
PRO	Pain, bleeding
clinical parameters	transfusion independence

COS for WM

domain	outcome
type of event	OS, CR, PR, VGPR
time to event	PFS
toxicity	AEs SAEs, discontinuation of treatment

COS for HL

domain	outcome
type of event	OS, CR, PR
time to event	PFS
toxicity	AEs SAEs, hem tox

Patient-important COS

domain	outcome
toxicity	discontinuation of treatment, AEs/SAEs, hema tox
PROs	physical fct, role fct, psychosoc fct, anxiety, depression, infertility, hair loss, nausea, constipation, diarrhea
use of healthcare resources	cost of treatment

DISCUSSION

- Through the adapted Delphi method, some lessons learned could already be addressed: drop out rate was significantly lower (9% vs 46%, respectively) and duration much shorter (3 months vs 18 months, respectively)
- Challenge in recruitment (particularly for acute diseases)
- Challenge meeting all needs of different stakeholders.
- Needs change during the course of the disease.
- Current COS as a starting point for discussion for further COS refinements that will have to take into account e.g. (i) age; (ii) disease stage; and (iii) novel treatment developments to name only few.
- In accordance, involvement of all stakeholder groups, especially patient involvement is crucial to better develop with meaningful COS.

OS = overall survival, CR = complete remission, MRD = minimal residual disease, neg = negative, clin relapse = clinical relapse, PD = progressive disease, PFS = progression-free survival, EFS = event-free survival, DOR = duration of response, PRO = patient reported outcomes, SAEs = severe adverse events, discount of treatment = discontinuation of treatment, fct = function, AEs = adverse events, tox = toxicity, tol-rel outcomes = tolerability-related outcomes, MRD = molecular minimal residual disease, HR-MDS = high-risk-MDS, GQI = good quality of life interval, TTP = time to progression, TTNT = time to next treatment, TFI = treatment free interval, SPM = secondary primary malignancy, EU = emergency unit, ICU = intensive care unit, MMR = minimal molecular response, hema tox = hematological toxicity, VGPR = very good partial response

The HARMONY Alliance is a Public-Private Partnership for Big Data in Hematology including over 100 organizations such as European medical associations, hospitals, research institutes, patient organizations, pharmaceutical and IT companies.

Funded by IMI (per 2020: Innovative Health Initiative, IHI) of the European Commission: HARMONY (January 2017-June 2023) and HARMONY PLUS (October 2020-September 2023). Using Big Data analytics to accelerate the development of more effective treatments for blood cancer patients. Data are stored in the HARMONY Big Data Platform, which has already identified over 150,000 anonymized patient records, making it one of the largest databases of its kind.

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