

Updated Pan-Stakeholder Core Outcome Set (COS) Definition for Hematological Malignancies in the framework of the EU project HARMONY

Healthcare Alliance for Resourceful Medicine Offensive against Neoplasms in Hematology

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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.

HARMONY – the Healthcare Alliance for Resourceful Medicine Offensive against Neoplasms in Hematology – and the follow up project HARMONY PLUS developed COS for different HMs.

Additionally, COS for cross-entity therapies - such as advanced therapy medicinal products (ATMPs) - were also defined, particularly the use of chimeric antigen receptor (CAR) - T cells.

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

METHOD

Traditional Delphi survey, 2 iterative survey rounds, predefined consensus criteria, final consensus meeting

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

METHOD

Delphi „Hackathon“, 2 iterative survey rounds on virtual meetings, predefined consensus criteria, final consensus meeting, and final expert panel meeting

HARMONY PLUS – expert panel discussion – COS definition for overarching therapies – CARTs

METHOD

Expert panel meeting, experts in field of use of CARTs

DELPHI SURVEYS

Towards Core Outcome Sets for Blood Cancers

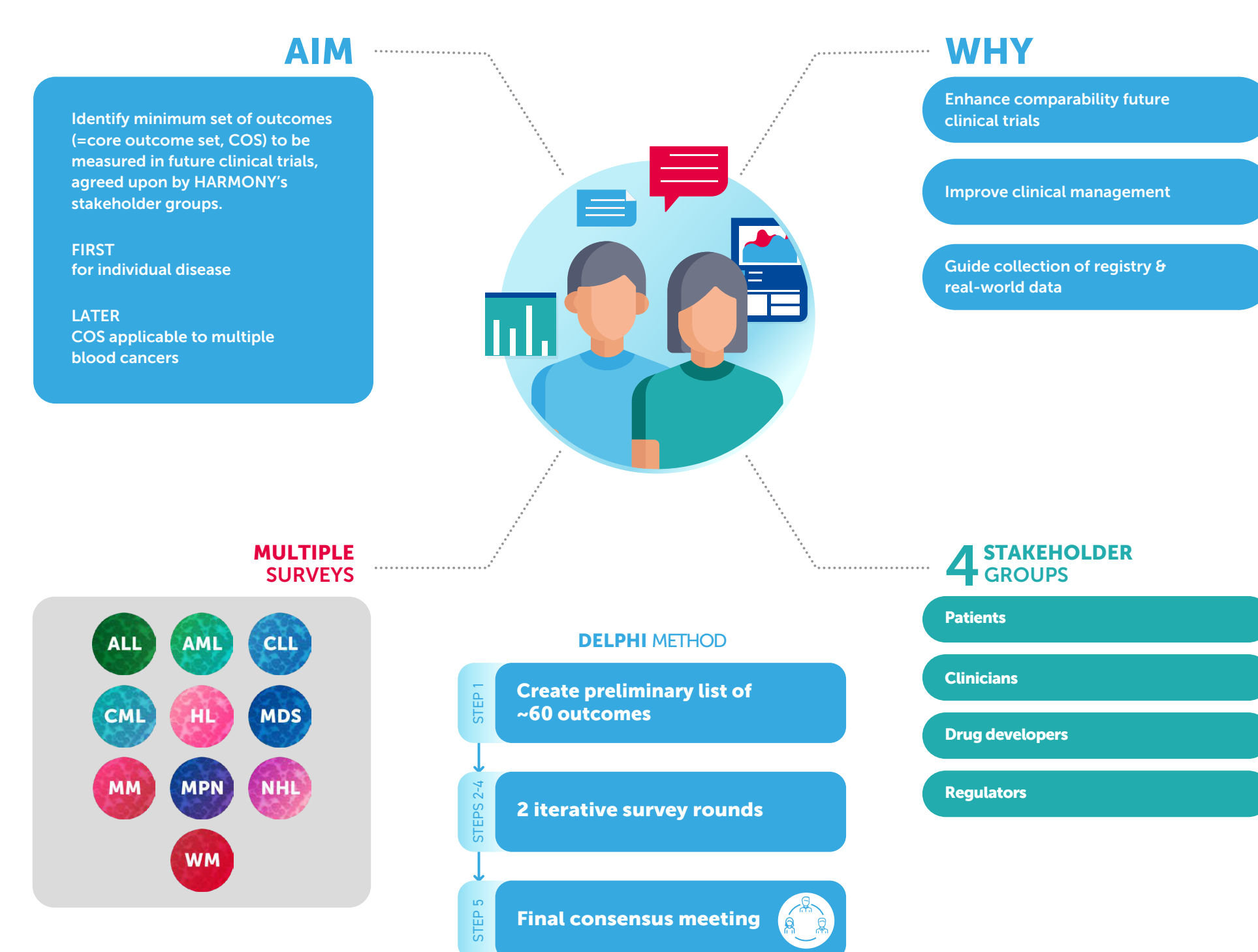


Figure 1: Infographic of the HARMONY Alliance Delphi Survey method

HARMONY RESULTS

Participation 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%)

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	pain, pathological fractures

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 transfusion 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

HARMONY PLUS RESULTS

Participation Delphi surveys 161 persons participated in total including

- 20 patients/patient advocates (12%),
- 93 clinicians (58%),
- 39 EFPIA/industry members (24%), and 9 regulators/ members of HTA bodies (6%)

COS for CML

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

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

COS for CART cell therapy

domain	outcome
type of event	response *, clinical relapse, OS
time to event	PFS, TTR
toxicity	AEs SAEs, hem tox, non-hem tox, neurotoxicity
PRO	pain, nausea, fatigue, psychosocial fct, physical fct
Use of resources	cost of treatment, ICU admissions

* overarching term that combines complete and partial response

HARMONY PLUS RESULTS

Participation expert panel 13 experts participated including

- 3 patients/patient advocates,
- 3 clinicians,
- 2 EFPIA/industry members,
- and 5 regulators/members of HTA bodies

additional patient-important

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
clinical parameters	infections
use of healthcare resources	cost of treatment

DISCUSSION

→ COS as a starting and discussion point for future study design

→ early patient involvement to make the important patient voice heard

The HARMONY Alliance is a Public-Private Partnership for Big Data in Hematology including over 120 organizations such as European medical associations, hospitals, research institutes, patient organizations, pharmaceutical and IT companies. Funded by the Innovative Health Initiative (IHI, formerly known as IMI) of the European Commission: HARMONY (116026 / January 2017 - June 2023) and HARMONY PLUS (945406 / October 2020 - March 2024). 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 165,000 anonymized patient records, making it one of the largest databases of its kind.