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Policy Perspective

Building a Healthcare Alliance for Resourceful Medicine Offensive Against Neoplasms in Hematology Added Value Framework for Hematologic Malignancies: A Comparative Analysis of Existing Tools



Francesco Cerisoli, PhD, Farzad Ali, MSc, Tamás Bereczky, MA, PhD, Natacha Bolaños, BS, Lars Bullinger, MD, Sujith Dhanasiri, MPhil, MSc, James Gallagher, PhD, Sonia García Pérez, MSc, Jan Geissler, MiBA, Yann Guillevic, DEA, Kathryn Harrison, PhD, Anastasia Naoum, MSc, Carla Portulano, PhD, Ana E. Rodríguez Vicente, PhD, Renate Schulze-Rath, MD, MSc, Gabriela Yumi Gómez, MD, Guillermo Sanz, MD, PhD, Jesús María Hernández Rivas, MD, PhD

ABSTRACT

Objectives: The Innovative Medicines Initiative-funded, multistakeholders project Healthcare Alliance for Resourceful Medicine Offensive Against Neoplasms in Hematology (HARMONY) created a task force involving patient organizations, medical associations, pharmaceutical companies, and health technology assessment/regulator agencies' representatives to evaluate the suitability of previously established value frameworks (VFs) for assessing the clinical and societal impact of new interventions for hematologic malignancies (HMs).

Methods: Since the HARMONY stakeholders identified the inclusion of patients' points of view on evaluating VFs as a priority, surveys were conducted with the patient organizations active in HMs and part of the HARMONY network, together with key opinion leaders, pharmaceutical companies, and regulators, to establish which outcomes were important for each HM. Next, to evaluate VFs against the sources of information taken into account (randomized clinical trials, registries, real-world data), structured questionnaires were created and filled by HARMONY health professionals to specify preferred data sources per malignancy. Finally, a framework evaluation module was built to analyze existing clinical VFs (American Society of Clinical Oncology, European Society of Medical Oncology, Magnitude of Clinical Benefit Scale, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, Institute for Clinical and Economic Review, National Comprehensive Cancer Network Evidence Blocks, and patient-perspective VF).

Results: The comparative analysis describes challenges and opportunities for the use of each framework in the context of HMs and drafts possible lines of action for creating or integrating a more specific, patient-focused clinical VF for HMs.

Conclusions: None of the frameworks meets the HARMONY goals for a tool that applies to HMs and assesses in a transparent, reproducible, and systematic way the therapeutic value of innovative health technologies versus available alternatives, taking a patient-centered approach and using real-world evidence.

Keywords: clinical value framework, hematology, Healthcare Alliance for Resourceful Medicine Offensive Against Neoplasms in hematology, patient-reported outcomes.

VALUE HEALTH. 2022; 25(10):1760–1767

Introduction

In 2012, costs associated with hematologic malignancies (HMs) in the European Union (EU) reached €12 billion accounting for 8% of total EU cancer costs (€143 billion). This consisted of direct healthcare costs of €7.3 billion, productivity losses of €3.6 billion, and informal care costs of €1 billion.¹ It is evident that HMs are not only a major economic burden but also a major source of mortality and morbidity, with approximately 44 000 new cases in Europe per year.²

Of note, in 2020, there were 311 594 deaths because of leukemia worldwide.³ In the same year, leukemia mortality ranged from 5 cases per 100 000 inhabitants in Malta to 17.7 in Cyprus, with the EU27 average at 9.1.⁴

Nonetheless, there is a rapid development of new therapies in oncology and especially in HMs, which can transform the cancer treatment landscape. In 2020, the European Medicines Agency approved several hemato-oncology drugs, including treatments for multiple myeloma (MM) and mantle cell lymphoma.⁵ Chimeric antigen receptor-T cell treatments have been developed for HMs

and, if implemented widely, could save or improve the lives of 7700 patients in the EU diagnosed per year.⁶ Of importance, there were >1300 patients treated with commercial Chimeric antigen receptor-T cells in Europe by January 2021, according to the European Society for Blood and Marrow Transplantation.⁷ Moreover, there is a growing utilization in healthcare decision making of real-world data (RWD), meaning data collected in a non-randomized controlled trial setting, such as patient registries, electronic health records, or mobile health.^{8,9} The European Medicines Agency and relevant stakeholders acknowledge RWD and clinical evidence derived from RWD analysis, known as real-world evidence (RWE),¹⁰ as the way forward for healthcare decision making particularly in situations where randomized clinical trials (RCTs) are not feasible such as rare conditions including HMs.¹¹ Although RCTs remain the golden standard for assessing the comparative efficacy and safety of a treatment, the narrow and very specific inclusion and exclusion criteria greatly restrict the heterogeneity of patients, thus reducing the generalizability of the trial results to the real-world patient populations. It is estimated that, in the case of MM, >40% of real-world patients do not meet the criteria to participate to RCTs,¹² thus putting into question how relevant trial data are when making treatment decisions in the real world for patients not represented in the trial. Moreover, although efficacy and safety are without doubts crucial information, treatment decisions are not only based on those parameters but also treatment feasibility, cost, and other patient-relevant outcomes, such as quality of life (QoL), and impact of comorbidities that are not taken into account in RCTs.¹³ Furthermore, RWE allows for a higher reporting numbers of toxicity, adverse effects, and discontinuation because of toxicity of novel agents thanks to less stringent rules of reporting thresholds and higher heterogeneity of patients compared with the RCTs.¹⁴ Finally, RWE provides timely results for important clinical questions, allowing hematologists and other health professional to adapt in real time and optimize patient care.¹⁵

Value assessment tools are one of the many instruments policy makers, payers, and clinicians use to make informed decisions about treatment options and optimizing resource allocation in healthcare settings.¹⁶ Nevertheless, to date, no comprehensive clinical value framework (VF) for HMs has been developed and validated. The existing clinical VFs are not specifically designed for HMs, and their focus is mainly on clinical outcomes such as overall survival (OS) and its surrogates or cost considerations. Furthermore, most of these frameworks have been developed with little to no patient involvement, and their current versions do not allow for the use of registry data or RWE.

The Healthcare Alliance for Resourceful Medicine Offensive Against Neoplasms in Hematology (HARMONY)¹⁷ was established in January 2017 and is a public-private partnership for collecting, harmonizing, sharing, and mining big data in hematology. It comprises 53 partners and 41 associated members from 17 European countries, including 9 pharmaceutical companies and 7 patient umbrella organizations. This alliance aims to establish a database and mine big data in hematology, which will lead to improved therapies for patients and more effective treatment strategies. HARMONY is funded through the Innovative Medicines Initiative, Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. Funding is received from the Innovative Medicines Initiative 2 Joint Undertaking and is listed under HARMONY grant agreement number 116026. This Joint Undertaking receives support from the EU Horizon 2020 Research and Innovation Program and the European Federation of Pharmaceutical Industries and Associations. The HARMONY big data platform includes different types of data, such as symptom

diagnoses, biochemistry and physical examinations, information on treatment, survival, and QoL. These data are being collected by pharmaceutical companies, biobanks, hospitals, interventional, and noninterventional trials. The data are received in the same format as the source and then undergo a complex conversion to standardize and semantically homogenize all data sources. Then, all these data are being translated into meaningful data-driven analysis that informs treatment decisions. Currently, data collected cover 7 main HMs: acute lymphoblastic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia (CLL), MM, myelodysplastic syndromes (MDSs), non-Hodgkin lymphoma, and pediatric HMs.¹⁸ One of HARMONY's goals is to quantify therapeutic value of innovative technologies for HMs. This will be done by addressing the limitations of currently available non-validated tools and by developing a HARMONY added VF (HAVF), which will assess, in a transparent, reproducible, and systematic way, the therapeutic/clinical value of innovative health technologies compared with available alternatives. Specifically for HMs, the HAVF will help identify therapies providing high clinical benefit and patient/societal value that should be made rapidly available across countries.

HARMONY has the unique characteristic of being a multi-stakeholder project that comprised patient organizations, medical associations, pharmaceutical companies, and health technology assessment/regulator agencies' representatives. Lead and collaborating partners of this task force include the European Hematology Association, the National Institute for Clinical Care Excellence, Bundesinstitut für Arzneimittel und Medizinprodukte, University of York, Agencia Española de Medicamentos y Productos Sanitarios, Celgene-Bristol Myers Squibb, Janssen, Pfizer, Menarini, Charité Universitätsmedizin Berlin, Bayer AG, LeukaNET, Instituto de Estudios de Ciencias de la Salud de Castilla y León – Instituto de Investigación Biomédica de Salamanca, and Hospital Universitari i Politècnic la Fe, Valencia. The inclusion of all these stakeholders reflects HARMONY's ambition to develop tools that not only can be adopted by clinicians and patients but also be of interest for regulators, payers, and health technology assessment bodies.

The objective of this task force was to evaluate the suitability of previously established VFs for assessing the clinical and societal impact of new interventions for HMs.

Methods

The outcomes to be included in the HAVF were determined using the HARMONY lists of outcomes¹⁹ that were generated by multistakeholder groups specifically set up for the development of core outcome sets (COS) for the different HMs. COS were developed by a multistakeholder consensus-based Delphi methodology,²⁰ following COMET²¹ recommendations from the international COS-STAD study.²² Stakeholders included health service users, health service practitioners, researchers, regulators, drug developer, patients, and patient advocates. Participants of all stakeholder groups were recruited from members of different HARMONY work packages and were also integrated by participants outside the HARMONY network.

The outcomes list was created in a threefold process: literature research in the COMET database, followed by semistructured interviews of clinical public and private key opinion leaders to assess the initial selection and supplement with additional outcomes. The patients' perspective was included consulting the patient community including advocacy groups, in addition to a specific literature research for patient-reported outcomes. HARMONY includes 9 patient umbrella organizations (CLL Advocates

Network, CML Advocates Network, Lymphoma Coalition, Acute Leukemia Advocates Network, LeukaNET, Childhood Cancer International Europe, MDS Alliance, Myeloma Patients Europe, and MPN Advocates Network) represented by a hub organization that is also a full consortium member (LeukaNET). All patient organizations involved represent the local and regional disease-specific patient groups working in the respective disease areas.

By combining these 2 data sources, we collated an extensive list of outcomes to be considered in a range of existing clinical VFs. The most important outcomes included clinical outcomes, safety outcomes, risk profile characteristics, patient-reported outcomes/QoL, and resources use. A detailed list can be found in [Appendix Table 1](#) in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2022.04.1729>.

Having selected the outcomes, we explored the type of data sources that should be considered by each of the clinical VFs. A questionnaire was designed to identify which sources of data (RCTs, single-arm trials, and RWE) should be considered by clinical VFs. The questionnaire was distributed to the clinicians coordinating the different HARMONY projects addressing acute lymphoblastic leukemia, acute myeloid leukemia, CLL, MDS, MM, and lymphomas. Each project leader replied to the survey on behalf of its group.

After the health professionals' survey results and the list of outcomes compiled, we built a framework evaluation module whose elements are reflected in the column "protocol elements" in [Table 1](#): such elements were defined by the task force to address the main aspects that should be taken in consideration by clinical VFs, with no reference to a specific theoretical framework.

Results

Results of the review exercise are summarized in [Table 1](#).

Six frameworks were selected, based on the following parameters: the theoretical principles for the framework should be freely accessible, and the framework should address or be applicable in malignant settings and have been already in use or developed in a European or US context. All frameworks put strong attention on classical clinical outcomes such as OS or progression-free survival (PFS), given that the primary clinical objective is to decrease or delay mortality. Additional general considerations for each framework are reported below.

American Society of Clinical Oncology

The American Society of Clinical Oncology (ASCO) framework addresses value through a limited number of classic clinical outcomes. It does not consider RWE and only marginally takes in consideration QoL, without indicating specific, validated QoL measurement tools for HMs. Patient perspective seems to be of minor significance for this framework, whereas cost-related aspects are taken in account.²³

European Society for Medical Oncology Magnitude of Clinical Benefit Scale

The European Society for Medical Oncology (ESMO) developed the ESMO Magnitude of Clinical Benefit Scale to assess the magnitude of clinical benefit for cancer medicines. Although ESMO Magnitude of Clinical Benefit Scale does consider some patient outcomes, namely QoL and palliation of symptoms, it does not regard individual patient disease characteristics such as regimen burden.²⁴

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

The German Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [IQWiG]) adapted the efficiency frontier approach, which serves as a framework for evaluating cost-effectiveness and indirectly for pricing and reimbursement decisions. The IQWiG takes into consideration many patient-centered outcomes and can even consider wider medical costs, if a societal perspective is applied.²⁵

Institute for Clinical and Economic Review

The Institute for Clinical and Economic Review (ICER) states that the goal of the ICER VF is to "help the US evolve toward a health care system that provides fair pricing, fair access, and a sustainable platform for future innovation."²⁶

Patient input is encouraged; nevertheless, the focus is on clinical and cost-effectiveness recommendations on medical interventions from a US healthcare systems perspective.

National Comprehensive Cancer Network Evidence Blocks

The National Comprehensive Cancer Network (NCCN) Evidence Blocks (EBs) aim to "provide the health care provider and the patient information to make informed choices when selecting systemic therapies based on measures related to treatment, supporting data, and cost." The NCCN EB do not regard any patient-centered outcomes, including QoL.²⁷

Faster Cures Patient-Perspective VF

The patient-perspective VF was developed as a tool to assess the patient-centered value of healthcare services by considering factors that matter to the patients and weight them against patient preferences, such as complexity of regimens or nonmedical costs for patient's family.²⁸

Discussion

Based on the assessment described earlier, the existing frameworks, although carefully developed and implemented in a variety of countries, may not address the needs identified by this task force.

Data Sources

Most evaluation frameworks to date prefer to base their recommendations on a range of evidence levels from RCTs to expert opinions. In theory, the ICER and IQWiG frameworks adopt a comprehensive approach, where the expert panel reviews all relevant data, including meta-analyses, systematic literature reviews, cohort and observational studies generating RWD, and expert opinions. Nevertheless, in practice, ICER has been more focused on pricing aspects and IQWiG have not been open to considering RWD or endpoints that might be of importance to patients such as PFS. A focus on RWD is fundamental in building the HAVF, given that HARMONY builds a big data database containing large amounts of RWD of HMs, including clinical, genetic, and molecular data on patients and diseases from clinical trials and registries in different countries. The inclusion of RWE as evidence for decision making is a must for the HAVF.

Outcomes

The primary clinical objective of any intervention in malignant diseases is to decrease or delay mortality. All the VFs assessed take

Table 1. VF evaluation—the purpose and data sources.

Protocol element	ASCO	ESMO MCBS	ICER	IQWiG	NCCN EB	PPVF
Purpose						
Stated purpose	Patient-physician drug treatment decisions	Patient care and treatment decisions	Clinical and cost-effectiveness evaluations of new medicines	Cost-benefit of new drugs	Efficacy, safety, quality, and affordability of therapeutic regimes	Patient-centered value assessments
Approach	Scores	Scores	Scores	Scores	Scores	Scores
Treatment used as comparator	SoC	SoC	Active comparators are prioritized where available	ACT, which can be other drug or nondrug treatment (when available) Watchful wait, palliative care preferred over “doing nothing”	Not applicable	- No treatment - Watchful waiting or active surveillance/monitoring - Palliative and end-of-life care The comparator approach from PPVF broadens the standard clinical trials approach and narrows to the real-world practice.
Data sources						
Study types	RCT and expert opinion	RCTs, meta-analysis, RWE, expert opinion	Meta-analyses, systematic reviews, RCTs, patient surveys, RWE including cohort studies, case-control studies and long-term disease and drug registries. Expert opinion can also be used.	Company-submitted early benefit assessment dossier, including costs. For clinical efficacy in the dossier, relevance is given to RCTs (complying with CONSORT statement) and non-RCTs (complying with TREND statement), Observational and epidemiology studies (complying with STROBE statement), patient-reported outcomes (complying with STROBE statement) expert opinion	Published data, panel members' clinical experience, case reports	RCTs, observational studies (clinical registries or electronic medical records) RWE, clinical guidelines, drug/device label information, plan design information, cost estimates (from transparency organizations or estimates from literature)
Treatment setting	Advanced; potentially curable	Across treatment pathway	- Population level - Modified frameworks for serious, ultrarare disorders (< 10 000 patients) - High-impact single or short-term therapies.	Reference is the German current SoC for the indication at the moment of submission	Any	Distinction between chronic and acute

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Table 1. Continued

Protocol element	ASCO	ESMO MCBS	ICER	IQWiG	NCCN EB	PPVF
Outcomes						
Clinical outcomes	OS, PFS, RR, symptom palliation, time off treatment	In addition to standard outcomes, proxy outcomes, eg, PFS 2, EFS, MRD status	OS, PFS, and other therapeutic duration-based outcomes (the most important benefits and harms are those that are important to patients and their families/caregivers)	Mortality and other patient-relevant endpoints are considered for morbidity and HRQoL; surrogate endpoints if validated	Any	All clinical outcomes which show improvement
Effectiveness/efficacy	Tail of the curve	N/A	RCTs prioritized but other sources are considered	Improvement of state of health, shortening of illness duration, extension of lifespan, reduction of side effects, improvement of quality of life are the criteria considered to derive a patient benefit	N/A (The methodology applied by NCCN EB is proprietary and not known)	Significant improvement in endpoints from a broad evidence-level resources
Complexity/burden of regimen	N/A	Disease specific/setting specific	Can be considered in an "other benefits/disadvantages" domain	N/A	N/A	Dosing/treatment schedule and length, site of care, administration route, invasiveness of procedure
Side effects/complications	Clinically meaningful toxicity of each regimen	Breakdown by grade level	Can be considered as part of outcome measures	Reduction of side effects, and symptoms is part of the patient benefit assessment	N/A	Frequency, severity, duration of AEs, discontinuation of treatment
PRO—HR QoL	QoL, palliation of symptoms	QoL, palliation of symptoms	Included in cost-effectiveness model	HRQoL, PROs can be used to record HRQoL or other patient-relevant benefit dimensions (eg, symptoms) as reported by CONSORT-PRO extension or ISOQOL	No	PCOs, functional/cognitive status, palliation of symptoms, symptom-free intervals
Wider patient considerations	N/A	Should be considered	Patient input is encouraged	Patient satisfaction can be included, if health-related aspects are shown	No	Yes, the whole framework is patient focused

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Table 1. Continued

Protocol element	ASCO	ESMO MCBS	ICER	IQWiG	NCCN EB	PPVF
Caregiver considerations	N/A	Should be considered	Can be considered in an “other benefits/disadvantages” domain	Can be taken into account	No	“Patient & Family Costs” domain. Whereas traditional VF primarily focus on the cost to the healthcare system, the PPVF primarily focuses on costs to the patient and family
Economic considerations						
Medical costs	DAC and patient co-pay based on the treatment costs per month	N/A	Standard cost per QALY evaluation. Price threshold \$100-\$150 000 per QALY	<ul style="list-style-type: none"> • Direct medical costs • Indirect nonmedical costs • Indirect costs (also incurred by caregivers in societal perspective) • Transfer payments 	Overall therapy cost (acquisition, administration, inpatient vs outpatient care, supportive care, infusions, toxicity monitoring, antiemetics and growth factors, and hospitalization)	No QALYs, PCOs are considered
Wider medical costs	N/A	N/A	Wider healthcare costs are excluded from base case analysis	Included if the societal perspective is adopted	N/A	Medical OoP costs and nonmedical costs

ACT indicates appropriate comparator therapy; AE, adverse effect; ASCO, American Society of Clinical Oncology; CONSORT, Consolidated Standards of Reporting Trials; DAC, drug acquisition cost; EFS, event-free survival; ESMO, European Society for Medical Oncology; HRQoL, health-related quality of life; ICER, Institute for Clinical and Economic Review; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen; ISOQOL, International Society of Quality of Life Research; MCBS, Magnitude of Clinical Benefit Scale; MRD, minimal residual disease; NCCN EB, National Comprehensive Cancer Network Evidence Blocks; N/A, not applicable (not found in the original publication); OoP, out-of-pocket; OS, overall survival; PCO, patient-centered outcome; PFS, progression-free survival; PPVF, patient-perspective value framework; PRO, patient-reported outcome; QALY, quality-adjusted life-year; QoL, quality of life; RCT, randomized clinical trial; RR, response rate; RWE, real-world evidence; SoC, standard of care; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; TREND, Transparent Reporting of Evaluations with Nonrandomized Designs; VF, value framework.

into consideration clinical outcomes, such as OS or PFS. The HAVF aims to put more attention on the appropriate assessment of value of patient-reported outcomes and to include RWD for further decisions. Despite the fact that these VFs claim to be patient centered, ASCO, NCCN, and ESMO frameworks do not regard individual patient disease characteristics such as burden of the regimen.

The NCCN EB do not take any patient-centered outcomes into consideration, not even QoL or palliation of symptoms.²⁷ The ESMO and ASCO clinical evaluation frameworks include in its evaluations QoL and palliation of symptoms, but wider patient and caregiver costs are not regarded. The ASCO task force acknowledges that some patient relative values are not taken into account in their clinical VF, such as “convenience of receiving therapy, the avoidance of interrupting the flow of activities of daily living, and the impact of a treatment on QoL and the ability to achieve personal and professional goals.”²³

Economic Considerations

The NCCN EB are not currently published in the NCCN Guidelines for Patients and are available on subscription only and intended for use in the United States only.²⁷ Although the NCCN

EB are rather comprehensive when it comes to defining the value of treatment options, the focus on affordability and treatment cost poses a challenge. Some of these aspects may become completely irrelevant as treatment options are weighed for geographic settings other than the United States. Even then, Mitchell et al²⁹ conclude that there are discrepancies as regards the affordability score (and the related cost factors) within the United States. “The NCCN AR [affordability] rankings and observed real-world costs from the health insurance plan perspective are inconsistent,” state Cohen et al,³⁰ and they suggest that the framework be revised accordingly.

VFs evaluated tend to deprioritize the impact of HMs on patient caregivers and the wider societal level. Although potentially captured as a scenario analysis in some cases, it is excluded from the base case evaluation, and therefore, its relevance and impact are diminished.³⁰

Findings of this article are aligned with previous work by the American Society of Hematology, which assessed the suitability of ASCO and ESMO VFs in 2016. The authors suggested that both VFs were challenging to apply to therapies for HMs and especially for innovative treatment approaches.³¹ The 2016 study concluded that the 2 frameworks “do not seem to measure the same construct of clinical benefit” and “may not fully capture all

relevant dimensions of value.” The authors recommended that the definition of value should be further evaluated and explored and a multistakeholder approach should be reached regarding the context and definition of value.³²

This HARMONY task force has implemented the American Society of Hematology recommendations by including different stakeholders in this project and by implementing the proposed multiple criteria decision analysis³² to define the concept of “value” and in designing the methodology of this VF.

Limitations

There are some limitations to this study. First, the stakeholders involved in this project are limited to HARMONY members or associated members. Although the stakeholders involved represent different healthcare players (patients, pharmaceutical companies, payers, and health professionals), their representation is still restricted to the HARMONY stakeholders and does not necessarily reflect the true healthcare environment. Moreover, there are few (bio) statistician or health economics professionals in this task force, which further limits the proper representation of the healthcare parties.

Second, the multistakeholder decision analysis approach adopted to develop the framework evaluation module used was not implemented fully. The framework evaluation module was developed in collaboration with all parties, but the outcomes were based mainly on the patients’ input, whereas the data sources to be considered by clinical VFs were identified mainly on clinicians’ input.

In addition, the qualitative data obtained via nonstructured interviews were not coded systematically.

Finally, consolidated definition of “value” was not easily identified by the involved stakeholders. The different concepts of “value” for each of the parties involved allow room for various perceptions, and its definition remains a precondition for the creation of a unified clinical VF.

Conclusions

Even though the current VFs are used, despite narrow scope and multiple limitation, as tool for decisions makings, there is much room for improvement. The overall conclusion of this reviewing exercise is that available frameworks do not meet the HARMONY ambitions for a tool that applies to HMs and assess in a transparent, reproducible, and systematic way the therapeutic/clinical value of innovative health technologies compared with available alternatives.

Considering that a VF involves different stakeholders, there is a different definition of “value” per stakeholder. A patient’s relative value does not necessarily match the clinician’s or payer’s definition of value. Therefore, the first, clear next step for the creation of a HAVF is to find a cross-stakeholder agreement on the definition of “value,” which remains elusive and is therefore subject to different interpretations.

The current set of stakeholders must be involved in this first step, but an additional, external expert contribution has to be explored, in the areas of RWE, interpretation of patient preferences, health economics, and pricing and reimbursement decisions across Europe.

The second step, after a solid consensus is reached on the right definition of “value,” should focus on the de novo design of an HAVF that uses as base the outcomes identified by this task force (Appendix Table 1 in Supplemental Materials found at <https://doi.org/10.1016/j.jval.2022.04.1729>), with the indispensable support of professionals from the aforementioned expert areas.

Finally, following the design of the HAVF, a proper validation of the newly developed tool should be implemented, through field testings conducted leveraging the vast HARMONY network.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.jval.2022.04.1729>.

Article and Author Information

Accepted for Publication: April 15, 2022

Published Online: May 17, 2022

doi: <https://doi.org/10.1016/j.jval.2022.04.1729>

Author Affiliations: European Hematology Association, The Hague, The Netherlands (Cerisoli, Naoum); Patient Health Impact, Pfizer, Montreal, Quebec, Canada (Ali); Patvocates GmbH, Munich, Bayern, Germany (Bereczky, Geissler); Regional Management Europe, Lymphoma Coalition, Madrid, Spain (Bolaños); Charité – Universitätsmedizin Berlin, Freie Universität Berlin and Humboldt, Berlin, Germany (Bullinger); Global Medical Affairs, Celgene International – A Bristol Myers Squibb Company, Boudry, Switzerland (Dhanasiri, Guillevic); Pfizer Inc, New York, NY, USA (Gallagher); Department of Medicines for Human Use, Spanish Agency of Medicines and Medical Devices (AEMPS), Madrid, Spain (Pérez); Science Policy and Research Programme, National Institute for Health and Care Excellence (NICE), Manchester, England, UK (Harrison); Menarini Ricerche SpA, Florence, Italy (Portulano); Departamento de Medicina, Universidad de Salamanca, Salamanca, Spain (Vicente); Medical Affairs & Pharmacovigilance, Pharmaceuticals, Bayer AG, Berlin, Germany (Schulze-Rath); Agencia Española de Medicamentos y Productos Sanitarios (AEMPS), Madrid, Spain (Gómez); CIBERONC, Instituto de Salud Carlos III, Madrid, Spain (Sanz); Hospital Universitari i Politècnic la Fe, Valencia, Spain (Sanz); Servicio de Hematología, Instituto de Investigación Biomédica de Salamanca (IBSAL), Departamento de Medicina, Hospital Universitario de Salamanca, Universidad de Salamanca, Salamanca, Spain (Rivas).

Correspondence: Jesús María Hernández Rivas, MD, PhD, Servicio de Hematología, Instituto de Investigación Biomédica de Salamanca (IBSAL), Departamento de Medicina, Hospital Universitario de Salamanca, Universidad de Salamanca, Paseo de San Vicente s/n, 37007 Salamanca, Spain Email: jmhr@usal.es

Author Contributions: *Concept and design:* Cerisoli, Ali, Bereczky, Bolaños, Geissler, Guillevic, Harrison, Sanz, Hernández Rivas

Acquisition of data: Cerisoli, Bereczky, Bolaños, Bullinger, Dhanasiri, Gallagher, García Pérez, Geissler, Guillevic, Harrison, Portulano, Rodríguez Vicente, Schulze-Rath, Yumi Gómez

Analysis and interpretation of data: Cerisoli, Ali, Bereczky, Bolaños, Bullinger, Dhanasiri, Gallagher, García Pérez, Guillevic, Naoum, Portulano, Schulze-Rath, Yumi Gómez, Sanz, Hernández Rivas

Drafting of the manuscript: Cerisoli, Naoum, Rodríguez Vicente, Hernández Rivas

Critical revision of the paper for important intellectual content: Ali, Bereczky, Bolaños, Bullinger, Dhanasiri, Gallagher, García Pérez, Geissler, Guillevic, Harrison, Naoum, Portulano, Rodríguez Vicente, Schulze-Rath, Yumi Gómez, Sanz, Hernández Rivas

Administrative, technical, or logistic support: Cerisoli, Naoum

Conflict of Interest Disclosures: Mr Ali is employed by and reported stock ownership in Pfizer Inc. Dr Bullinger and Mr Geissler reported receiving grants from the European Union Innovative Medicines Initiative HARMONY during the conduct of the study. Dr Bullinger reported receiving grants from Bayer and Jazz Pharmaceuticals outside the submitted work and reported receiving personal fees from AbbVie, Amgen, Astellas, Bristol Myers Squibb, Celgene, Daiichi Sankyo, Janssen, Jazz Pharmaceuticals, Novartis, Pfizer, Sanofi, and Seattle Genetics outside the submitted work. Messrs Dhanasiri and Guillevic are employed by Bristol Myers Squibb. Dr Gallagher is employed by Pfizer Inc. Mr Geissler reported receiving grants from Incyte, Takeda, Novartis, Pfizer, Bristol Myers Squibb, Servier, UCB, Bayer, Roche, Sobi, Alnylam, Boehringer-Ingelheim, Janssen, Daiichi Sankyo, and Gilead outside the submitted work. Dr Portulano reported

receiving personal fees from Menarini Ricerche outside the submitted work. Dr Schulze-Rath is employed by Bayer AG. Mr Sanz reported receiving personal fees from and serving as a member of the board of directors or advisory committees for AbbVie outside the submitted work; reported receiving personal fees from Amgen and Astellas outside the submitted work; reported receiving grants and personal fees from and serving as a member of the board of directors or advisory committees for Celgene/Bristol Myers Squibb, Janssen-Cilag, and Roche outside the submitted work; reported receiving grants from and serving as a member of the board of directors or advisory committees for Novartis outside the submitted work; and reported serving as a member of the board of directors or advisory committees for Takeda outside the submitted work. No other disclosures were reported.

Funding/Support: This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement no. 116026. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation program and EFPIA.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Acknowledgment: This analysis has been performed by the HARMONY work package 6 task force on clinical value framework (task 6.3). The authors thank the other components of the task force who participated in the general discussion leading to the definition of the current task: Ellen de Waal, Norbert Benda, John Butler-Ransohoff, David Chandiwana, Hélène Chevrou-Séverac, Frederik Damm, Piero Fantacci, Kalitsa Filoussi, Maren Gaudig, Sebastian Gonzalez, Pall Jonsson, Andrea Manca, Luca Tofani, and Kyriaki Tzogani. The communication reflects the author's view and that neither IMI nor the European Union, EFPIA or any Associated Partners are responsible for any use that may be made of the information contained therein.

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