European Journal of Cancer 222 (2025) 115433

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejcancer.com

Original research

A decalogue of Molecular Tumor Board (MTB) recommendations from the CAN.HEAL Consortium

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ARTICLE INFO

Keywords:
Cancer genomics
EU4Health
NGS assays
Personalized medicine
Precision oncology

ABSTRACT

Introduction: The CAN.HEAL consortium, comprising 47 cancer centers and academic institutions across 17 EU countries, has developed a set of recommendations for Molecular Tumor Boards (MTBs) to address the lack of standardized guidelines in personalized cancer medicine.
Methods: Over the past 2 years, through extensive collaboration and seven dedicated online meetings, CAN.HEAL experts developed consensus-based recommendations across 10 critical domains.
Results: The consortium agreed that MTBs' primary role is to perform molecular and clinical assessments for patients requiring care beyond standard treatment. Core MTB composition should include medical oncologists,

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https://doi.org/10.1016/j.ejca.2025.115433
Received 25 February 2025; Received in revised form 2 April 2025; Accepted 11 April 2025
Available online 14 April 2025

molecular biologists, pathologists, and bioinformaticians. Patient eligibility criteria should prioritize performance status, with flexibility for rare cases. Shared informed consent is crucial for sample collection, data use, and research. A two-tiered IT workflow, with minimal and maximal datasets, is recommended, along with a comprehensive decision support tool. These recommendations focus on genomic testing, acknowledging diversity of NGS assays and proposing general guidelines. MTB reports should be concise, with technical details provided in the molecular diagnostic report. Innovative approaches like the Drug Rediscovery Protocol support access to off-label therapies. Harmonized training for MTB members is essential to bridging knowledge gaps in this evolving field. Indicators are needed to assess MTB effectiveness over time. Expanding MTB benefits to underserved populations depends on creating a shared European MTB database.

Conclusion: Standardizing MTB practices represents a key step toward equitable access to personalized medicine and improved cancer care across Europe. Sustainable implementation requires coordinated EU efforts, and dynamic MTBs that continuously refine genomic-driven decisions within real-world contexts.

1. Introduction

Molecular Tumor Boards (MTBs) match patients' genomes with drugs, particularly when standard therapeutic options have been fully exploited. However, standardized guidelines and recommendations for this ethically complex approach remain insufficient.

To address this gap and promote equitable access to personalized medicine for all cancer patients, the CAN.HEAL consortium—comprising 47 cancer centers and academic institutions across 17 European Union (EU) countries–has worked to develop consensus criteria. Through extensive discussions and collaboration over the past 2 years, we have gained valuable insights into the diverse challenges and opportunities in this evolving field [1].

Although not all elements of a formal Delphi methodology were applied (e.g., anonymity was not maintained), key elements such as iteration, controlled feedback, and statistical stability of consensus were effectively achieved through seven online meetings.

The CAN.HEAL experts acknowledge the diversity of MTB formats [2,3]. These recommendations apply to real-world MTBs, such as institutional MTBs, which focus on the tumor-agnostic evaluation of patients who have failed standard therapies and do not follow a predefined study design or specific primary objective.

Table 1 provides a synopsis of MTB recommendations, while the text below elaborates on key considerations. Further details can be found on the CAN.HEAL website (*www.canheal.eu*) and in the CAN.HEAL Zenodo community (*https://zenodo.org/communities/canheal*).

1.1. MTB mission and goals

A broad consensus was reached that the primary mission of MTBs is to perform molecular and clinical assessments for cases beyond the standard of care (Table 1, Section 1). Cases with an available approved option (whether diagnostic, predictive, and/or therapeutic) may be better and more quickly assessed by multidisciplinary, institutional, and organ-specific disease management teams. While the MTB provides a therapeutic recommendation, the final therapeutic decision ultimately rests with the medical oncologist responsible for the patient's care. The oncologist is best positioned to determine potential conflicts between the suggested treatment and the patient's overall clinical condition.

1.2. MTB composition

A core MTB group (Table 1, Section 2) should always include at least one medical oncologist, a molecular biologist who has expertise in molecular profiling and reporting and is familiar with conventional scales of actionable alterations, as well as a pathologist and a bioinformatician with expertise in diagnostic pipelines and decision-support tools. The core group should involve additional specialists to discuss specific cases (see Table 1, Section 2, Highlights and Special Features). Two key MTB members with molecular and clinical expertise should be appointed to oversee the downstream clinical/molecular workflow to ensure efficient case presentation and workflow supervision.

1.3. MTB inclusion criteria

Given the broad scope of the MTB mission, four simple, widely inclusive patient eligibility criteria may suffice (Table 1, Section 3). A good performance status is a key prerequisite of paramount importance, as the patient's condition may rapidly deteriorate before an MTB recommendation can be implemented.

The CAN.HEAL experts acknowledge the need for even greater flexibility at accrual when evaluating young patients, patients with rare, unusual, or multiple cancers, or patients diagnosed with tumors characterized by distinct molecular features. In particular, the following cases may be considered by the MTB even if they do not meet all standard inclusion criteria:

- Patients with background information suggesting a special benefit from extended and/or comprehensive profiling for treatment selection, as outlined in the ESMO Guidelines [4];
- Patients with advanced/relapsed or metastatic cancers, where an early molecular assessment (before or during first-line treatment) could help define in advance the best second-line option;
- Patients with prior comprehensive genomic profiling indicating a potentially available non-standard treatment;
- Patients with cancers of unknown primary (CUP), where deep molecular profiling may aid in identifying the tumor's primary origin.

1.4. Informed consent

A shared informed consent template is a crucial initial step toward a patient-centric operational scenario (Table 1, Section 4). The information material and consent form should outline the following:

- The purpose of biological sample collection, processing, and storage;
- Authorization for the use of biological material and associated data, including personal and genetic information;
- Consent for future data use and reuse, including incidental and unexpected findings.

As legal frameworks for such extensive data usage continue to evolve, this approach is essential for collaborative multicenter MTB efforts.

1.5. Information technology (IT) workflow

As discussed in the Informed Consent section, MTBs need fully integrated data collection, recording, and annotation procedures. To effectively balance research and clinical goals, the CAN.HEAL consortium recommends the adoption of a two-tiered approach: a minimal dataset (for research purposes, structured according to EU standards) and a maximal (fully-fledged) dataset (for clinical recommendations). The minimal dataset should include patient demographics, medical

Table 1
A decalogue of MTB recommendations from the CAN.HEAL Consortium.

Section	Topic	Recommendations	Highlights and Special Features
Patients and setting			
1	MTB mission and goals	The primary MTB goal should be restricted to the collegial multidisciplinary assessment of cases ***beyond the current standards*** (diagnostic, prognostic, and predictive).	The psycho-social status of the patient must be given special attention. The medical oncologist ultimately decides on therapy application.
2	MTB composition	Core Team • Medical oncologist(s) - usually the physician(s) in charge • Pathologist • Molecular pathologist • Geneticist • Radiologist • Molecular biologist (wet lab) • Bioinformatician • Data manager/study coordinator • Secretary	Additional members: • Nuclear medicine expert • Hematologist • Surgeon • Radiotherapist • Hospital pharmacist • Bioethicist • Pharmacologist • Hospital and healthcare financial experts • Patient advocate(s)
3	MTB inclusion criteria	Standard criteria: • Performance status ECOG ≤ 2 • Progression following prior standard treatment for the specific tumor (typically, first-line treatment is out of scope, but with exceptions – see right) • No available standard therapy • Extended MTB-dedicated (see topic 10 below) informed consent	Special exceptions to the standard inclusion criteria: • Young adults, generally defined as diagnosed before age 40 • Rare histology with limited therapeutic options and/or unusual clinical history suggesting distinctive therapeutic implications • Miscellaneous special features (see text) • Cancers of unknown primary (CUP)
4	MTB informed consent	Template draft generated and available online, divided into four sections: • Purpose • Specimen collection and processing • Data collection and storage • Opt-in, opt-out, confidentiality/GDPR clauses	Clauses to be adapted to national and local regulations.
Tools			
5	MTB IT workflow	A Virtual MTB session platform with Decision-Support Tool (DST)-embedded logistics.Features: • Controlled data access • Session scheduling • WEB conferencing • Graphical web interface • Graphical timeline of the decision process • Annotation empowering field-specific knowledge • Customizable content • External data input • Dynamic fields • Adherence to a European Electronic Health Record Exchange Format • Link to external drug-matching databases • A clinical trial matching system • Reference to sources • A format for easy data export • Collection of MTB recommendations • Clinical outcome collection • Artificial intelligence (AI) and machine learning (ML) tools • Cybersecurity	• User-diversified granular privileges to protect privacy and preserve the legal accountability chain • Personal 2-factor user authentication (within federated and/or institutional systems). • Planning MTB attendance across locations • Professional video conferencing and recording software with robust, secure backup • Visualize and share content, including annotated clinical, pathological, and omic data • Participants visualize the discussion flow and key points in real time, fostering collaboration despite physical distance • Assisted, input-guided, multiple-choice compilation of database fields • Format compliant with different national standards and able to capture the nuances of individual cases • File upload capabilities (e.g., PDF, PNG, DOC, etc.) • Calculation of patient's age at sampling and similar dynamic fields • Link to databases like InterVar to implement guidelines by the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP). Additional databases: ClinVar, ClinGen, OncoKB, CiVIC. Embedding of the European Society for Clinical Oncology (ESCAT) scales • Clinical trial double-matching in a geographically-aware prioritization system to avoid attrition due to distance from the trial location • Reference to literature, databases, and guidelines to avoid the "black box" issue • Data export compatible with downstream analysis (e.g., JSON, CSV, etc.) • MTB recommendations organized to enhance definition consistency • Clinical outcome defined according to point 10 below • AI and Machine Learning (ML) generating automated worklists and personalized alerts for sequential MTB tasks • Prevention of accidental data loss (unintentional deletion, automatic backup, and versioning system)
6	MTB diagnostic assays	Targeted NGS should: • Include test genes and hotspots at least up to ESCAT Tier IIIA • Include test genes important to assign drugs being developed as 'nice to have' • Comply whenever possible with IVDR regulation (EU Regulation 2017/746) coming into force from May 2026 or undergo rigorous in-house validation	• Special needs (e.g., diagnostic sarcoma rearrangements and identification of CUP tissue of origin) may require special NGS approaches • The use of untargeted NGS (WES, WGS, RNAseq) may be helpful at MTB discretion • Common, non-actionable alterations may be instrumental in monitoring disease course and response to therapy
7	MTB diagnostic reporting	The MTB collegial report should contain information about: • Demographics (age, sex), performance status and diagnosis, geographical residence • Sample information: date of collection, type of specimen (biopsy, surgical tissue, aspirate, blood, etc.) and its anatomical origin,	The MTB collegial report should not contain a detailed molecular diagnostic report since this may be attached and listed in the annex sectionSince clinical trial knowledge base content suffers rapidly from obsolescence, extensive trial eligibility lists are not favoredAdditional MTB collegial report items may be applicable

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Table 1 (*continued*)

Section	Topic	Recommendations	Highlights and Special Features
		histology linked to a unique specimen identifier, tumor cell content/fraction, type of diagnostic assay(s) performed, biological macromolecule tested (e.g., DNA, RNA, both, else) • A short case presentation summarizing diagnostic, pathologic, and molecular evidence, including any technical difficulties/limitations (e.g., a difficult-to-biopsy tumor mass) • Actionable alteration(s) detected, level of evidence, recommended treatment(s), and their priority concerning the actionability scale used. Gene and transcript nomenclature should follow international standard codes (e.g., HUGO, RefSeq, NCBI, Ensembl). Type(s) of alteration with an associated legend (SNV, INDEL, CNV, translocation, etc.). The specific variants should be preferentially identified by multiple notations and coordinates (e.g., both nucleotide and amino acid positions for SNVs) for unambiguous identification; Variant allele frequency (VAF) and ploidy at the variant locus, if available; a table with reference database version and genome build • Technical details and reproducibility: tumor-only or paired tumor-normal testing (especially in case of genome-wide NGS), sequencing kit (including batch number, if available), analytical pipeline complete with version • Quality control and EQA certification • Therapeutic recommendation, including a succinct summary of clinical information and molecular profiling, is thoroughly motivated. • Availability of, and/or possibility to reimburse, the recommended drug and necessary actions, if any, to turn the recommendation into a specific patient treatment plan (e.g., availability of a clinical trial, expanded access program, etc.) • Date and signature, possibly in digital form, of the MTB lead and/or legal representatives and the key MTB members contributing to the specific recommendation • Annex list: recent and past NGS profiling reports, all to be attached to the MTB collegial report. A complete list of tested genes/biomarkers	• Insufficient testing adequacy and/or discrepancies; need to re-test • Incidental germline findings requiring genetic counseling
Actions			
8	Access to treatment	Drug access should be prioritized: enrolment in clinical trials remains the best option. If this is impossible, off-label treatment and compassionate use may be consideredShared cost approaches are the best MTB modelsExpanding MTBs across the EU will require a web platform infrastructure endorsed by Regulatory Agencies and may generate real-world evidence (RWE) data	Although conventional clinical trials remain the gold standard for approving new drugs/indications, RWE may provide crucial complementary information
9	Training and Education	Training: • Principles of molecular genomics • Latest biotechnological innovations • Genetic/genomic testing and interpretation of test results • Elements of bioinformatics and biostatistics • Online knowledgebases • Indications and application of targeted therapies • Ethics Education: • Inclusion of innovative, aligned topics in core curricula of medical specialist education • Development of advanced training courses for MTB members • Incorporation of the above into Continuing Medical Education (CME)	Organizational issues: • Improvement in communication skills • Insufficient cooperation • Conflicting priorities and responsibilities • Disparities in expertise among MTB members
10	Monitoring of the MTB function	Internal indicators (patient-specific): • Drugs administered, number and duration of previous therapy lines • Minimal information dataset (see section 05) • Number and type of tumor profiling assays (e.g., in the case of NGS: targeted, untargeted, genome-wide, etc.), with explicit mention of their level of regulatory approval (IVDR, in-house, licensed from commercial vendors but carried out in-house, outsourced, etc.). tDNA and ctDNA testing or other liquid biopsies should be noted • Turnaround time (from enrolment to MTB recommendation; molecular profiling and data interpretation separately considered) • Whether or not a germline alteration has been detected and its genomic coordinates • Whether or not genetic counseling has been requested and the downstream consequences for the patient and the family • Whether or not at least one actionable somatic alteration has been identified • Number and list of actionable alterations detected, along with the level of actionability • Number and list of the above not yet exploited in previous therapy lines at the time of MTB enrolment • Whether or not an MTB collegial report has been issued	External Indicators (helpful to build RWE): • Number of patients presented/discussed per year by tumor, age, sex, stage, etc. • Proportion of cases with germline alterations predisposing to cancer • Proportion of patients referred for genetic counseling • Gene profiling assays employed, preferences, utilization patterns, tDNA vs. ctDNA, etc. • Average turnaround time • Proportion of cases in which one or more actionable somatic mutations have been identified • Novel alterations (not yet identified) discovered through MTB profiling • Proportion of cases where a molecular report and an MTB collegial report have been issued • Proportion of cases where a specific therapeutic recommendation has been made • Implementation rate of treatments recommended by the MTB • Case distribution among treatment modalities recommended by the MTB • Proportion of cases with follow-up information

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Table 1 (*continued*)

Section	Topic	Recommendations	Highlights and Special Features
		• Whether or not a specific therapeutic recommendation has been made • Whether or not the specific recommendation resulted in actual treatment • Treatment modality (trial, off-label, compassionate use, expanded access, others) • Annotated clinical timeline listing post-MTB therapies, if any, and their duration • Patient-reported (self-assessed) experience as assessed by standard questionnaires • Costs incurred	• Clinical outcomes, e.g., objective tumor response according to RECIST 1.1 criteria, patient-specific and population metrics such as TTP, PFS, OS, and adverse events • Patient-reported outcomes • Economic impact and sustainability

history, disease-specific information, details on clinical specimens, omics profiling (e.g., genes tested/altered), medical imaging, immunohistochemistry, molecular test results, and clinical outcomes. Tests should be organized chronologically to allow retrospective reconstruction of the drug assignment process.

The maximal dataset may also include additional unstructured information, which can be best captured by Natural Language Processing.

Logistic procedures were mapped, and a large consensus was reached on developing a comprehensive digital framework provisionally defined by the EU Oncology Decision Support Tool (EU-OncDST) concept [5]. This tool aims to bridge gaps identified in existing OncDSTs, improve implementation and interoperability, and facilitate MTB operation at institutional, national, and European levels. Further details are available on the CAN.HEAL website (*www.canheal.eu*) and in the CAN.HEAL Zenodo community (*https://zenodo.org/communities/canheal*).

Building on previous approaches used by CAN.HEAL partner institutions, we envisage the development of a structured platform for virtual MTB consultation, incorporating the technical features outlined in Table 1, Section 5 (left and right, respectively). Several academic and commercial tools have been developed to manage a part or a superset of the tasks listed above. Notably, two relevant tools developed within national and European initiatives are the Molecular Tumor Board Portal (MTBP, Karolinska Institutet) [6] and the BALLETT-app (Jessa Hospital, affiliated with the CAN.HEAL project). A detailed, annotated list is provided in [5].

1.6. MTB diagnostic assays

Real-world MTBs adopt various structural and functional omics approaches; however, the CAN.HEAL consortium has chosen to focus its recommendations on genomic (mutational) testing, as it has the strongest evidence base. Both tumor tissue DNA (tDNA) and circulating cell-free tumor DNA (ctDNA) should be implemented in the MTB workflows. Nevertheless, integrating these approaches remains a major challenge and a focus for future research. While a large variety of hybrid-capture and amplicon-based next-generation sequencing (NGS) assays are currently available, most commercial and in-house NGS tests have not yet successfully cleared the In Vitro Diagnostic Medical Devices Regulation (IVDR/MDR) regulatory path. NGS tests used by many MTBs include both targeted (i.e., predefined NGS panels) and untargeted approaches (e.g., whole-exome and whole-genome sequencing as well as RNA sequencing [RNAseq]). New disruptive sequencing technologies are expected to hit the market in the near future. Rather than endorsing specific tests, the CAN.HEAL consortium provides general recommendations (Table 1, Section 6).

Specialized NGS panels (e.g., RNAseq or panels focusing on gene fusions) may be needed to profile specific cases, such as rare tumors, CUP, and sarcomas. These special-purpose panels should be shared across MTB networks to ensure diagnostic consistency. Additionally, NGS panels are also being developed in the context of the Pre-Commercial Procurement (PCP) by the OncNGS consortium (*www.oncngs.eu*) (Toungouz et al, currently under review). These panels focus on essential ("must-have") and desirable ("nice-to-have") features, offering a modular design that allows for a standard core panel with optional specialized modules to increase scalability and flexibility, making them highly adaptable for MTB applications.

1.7. MTB diagnostic reporting

The MTB collegial report, issued on institutional MTB letterhead, should include a header listing the MTB lead/head and all MTB members categorized by expertise (e.g., oncology, radiology, molecular biology, etc.) and should contain structured information (Table 1, Section 7).

There are several examples of MTB reports [7]. In some cases, the MTB collegial report is appended to a standard, detailed molecular diagnostic report. Such hybrid formats are not favored by the CAN.HEAL experts, who instead recommend keeping the two reports distinct. Technical details should be provided in a separate, independent molecular diagnostic report, mentioned in the annex section and included as an attachment, ensuring that the MTB collegial report remains concise and focused. For actionable variants, meta-knowledge bases have been proposed by the Variant Interpretation in Cancer Consortium (VICC, *https://cancervariants.org/*) to unify six annotation systems, including OncoKB [8]. The report should clearly state which scale was prioritized for annotation and provide a link to the corresponding database. To improve clinical implementation and minimize disparities in treatment recommendations, it is essential to establish standardized, harmonized processes for annotation, interpretation, and treatment-matching algorithms.

Regarding bioinformatic pipelines, the use of software virtualization techniques (e.g., Docker) is recommended, allowing different algorithm versions to be encapsulated in a virtual image.

Clinical trial knowledge base curation may be performed either manually (expert panel) or through automated methods (bot engine). Several companies currently offer these solutions; however, extensive trial eligibility lists are discouraged since clinical trial information becomes outdated rapidly. Conversely, trial selection should primarily rely on case-by-case expert MTB opinion.

Regarding germline alterations, the European Society for Medical Oncology Precision Medicine Working Group (ESMO PMWG) has provided a set of recommendations for following up on putative germline variants detected via tumor-only sequencing. Their recommendations prioritize a subset of tumor-detected variants for which germline follow-up is most likely to yield the highest number of actionable true germline variants [9].

1.8. Access to treatment

Access to treatment beyond standard indications, as well as issues related to funding/reimbursement, remains a significant challenge, regulated by varying national procedures and laws across the 27 EU countries. Within the CAN.HEAL consortium, most MTBs struggle to address these issues through:

- Enrolment in clinical trials, either locally or at different institutions, if the patient can travel;
- Off-label treatment if the institution can cover the cost;
- Compassionate use programs if pharmaceutical companies provide the drug free of charge.

The first option is strongly preferred because it guarantees proper regulatory oversight, informed consent processes, safety monitoring, high-quality data collection, and patient follow-up, while drug-related costs are typically covered by the sponsor.

Off-label prescription varies across Europe despite general principles and guidelines established by the European Medicines Agency (EMA) and national regulatory authorities. However, treatment decisions often rely on the oncologist's clinical judgment, expert consensus, and available evidence, leading to potential subjectivity. Additionally, cost-reimbursement issues may affect this opportunity differently across countries.

Compassionate use programs are part of corporate social responsibility efforts to tackle unmet medical needs, but they share the same limitations as off-label treatment.

The CAN.HEAL consortium emphasizes that steps must be taken to prevent the accumulation of case (and data) collections that, although often valuable, ultimately remain anecdotal and may lack sufficient scientific rigor and reproducibility.

An exemplary model is the Drug Rediscovery Protocol (DRUP), developed by a network of cancer hospitals in the Netherlands. The DRUP trial combines a basket-like design, parallel cohort recruitment, drug repurposing, and a shared-cost reimbursement model, where pharmaceutical companies initially provide the investigational drug free of charge. If clinical benefits are demonstrated, insurance companies step in to cover the costs [10]. The first 215 DRUP patients were reported in October 2019 [11], and similar trials have followed, including Magalit (Sweden), Impress (Norway), ProTarget (Denmark), and Finprove (Finland), as well as the EU4Health-funded PCM4EU [12] and the Horizon Europe Cancer Mission project PRIME-ROSE [13].

National regulatory agencies, pharmaceutical companies, and other stakeholders must be involved in expanding the DRUP model to a growing number of EU countries, offering all patients equal opportunities. To guarantee common rules and standards across countries, MTBs should operate with similar web platforms endorsed by regulatory agencies and generate real-world evidence (RWE) data. While conventional clinical trials undoubtedly remain the gold standard, RWE can provide rapid insights, inform future regulatory choices, and support evidence collection to assess the overall sustainability of precision oncology.

1.9. Training and education

Given their multidisciplinary nature, MTBs must establish robust training and education programs to facilitate knowledge sharing among members and the broader scientific, clinical, and healthcare communities. This approach is strongly supported by extensive evidence [14,15]. Europe should adopt harmonized training and education models similar to those implemented in the United States [16]. Coordinated efforts are essential to bridge knowledge gaps in this rapidly evolving field and ensure a standardized approach across the continent. Key training, education, and organizational aspects and related issues are detailed in Table 1, Section 9.

1.10. Monitoring of the MTB function

Objective indicators are required to assess MTB effectiveness and long-term impact. Many of these indicators align with CAN.HEAL's recommended items for inclusion in the MTB collegial report. They can be categorized as "internal" or "external". Internal indicators monitor the operational procedures, including the activity and performance of individual patients. External indicators track MTB-wide patient populations, providing valuable metrics for comparing different MTBs. Table 1, Section 10 outlines internal and external indicators.

A critical internal quality indicator is the attendance of key MTB members, which is essential to maintain high-quality standards. Similarly, multi-institutional MTBs operating under a hub-and-spoke model should monitor the proportion of cases presented by the hub institution versus individual spokes, ensuring balanced participation and avoiding hub dominance.

The most important external metrics assess the outcomes of MTB-recommended treatments, and these should be shared across MTB networks. While universally accepted criteria for evaluating real-world MTB treatment recommendations are lacking, a standardized annotation system could facilitate retrospective analysis of large datasets within MTB networks. Patient satisfaction and treatment costs are critical yet challenging metrics to monitor. A CAN.HEAL survey (to be published separately) found that only 18 % of MTBs track patient-reported outcomes, while 36 % assess economic impact. However, collecting and analyzing these data is crucial for securing funding and engaging key stakeholders. Ultimately, expanding MTB benefits to underserved patient populations depends on the ability to capture and evaluate these difficult but essential metrics.

A key CAN.HEAL recommendation is the establishment of a shared European MTB database/registry. To ensure privacy and security, data must be de-identified, fully GDPR (General Data Protection Regulation)-compliant, and stored securely. Subsequent data analysis should use federated approaches, with harmonized data formats as a prerequisite. Several initiatives have already contributed to this vision, including the MTBP of Cancer Core Europe, and numerous original publications and reviews have addressed this topic [2,3,6,17]. As outlined in Section 5 and in the EU-OncDST concept [5], integrating artificial intelligence and machine learning tools presents an opportunity to enhance these platforms. By aligning existing efforts, we can build a powerful resource to generate evidence, drive innovation, and improve patient care across Europe.

2. Conclusion

MTBs play a pivotal role in integrating molecular profiling into clinical decision-making. To address the lack of standardized MTB guidelines, the CAN.HEAL consortium has developed comprehensive recommendations covering key aspects such as patient eligibility, diagnostic workflows, IT infrastructure, treatment access, and training. However, despite notable advancements, major challenges persist in ensuring equitable access to precision oncology across Europe and sustaining these approaches over the long term.

Access to MTBs remains uneven across Europe, with clinical trial opportunities disproportionately concentrated in high-resource centres, primarily in urban areas. Without addressing the financial and logistical burdens of travel for patients existing disparities will only deepen. Implementing a "hub-and-spoke" network model may offer a viable solution [18]. Similarly, access to off-label treatment is currently dependent on contingent funding, favouring again larger institutions. A coordinated EU-wide effort is essential to establish sustainable financing and reimbursement models, ensuring broader and more equitable access to off-label therapies. Compassionate use programmes face similar constraints, underscoring the need for legislative reforms to integrate such programmes into a comprehensive precision oncology framework.

The CAN.HEAL recommendations mark a significant step toward a unified EU strategy for equitable and effective implementation of personalised cancer medicine. However, sustainability of precision oncology beyond standard indications requires constant collaboration among researchers, clinicians and policymakers. Long-term solutions must include innovative reimbursement models, public-private partnerships, and outcome-tracking registries. Most importantly, MTBs should be dynamic, self-correcting frameworks, not rigid authorities in

precision oncology. Their role is to challenge and refine recommendations, testing genomic-driven decisions against real-world outcomes and ethics. Without questioning their own assumptions, they risk becoming echo chambers. Instead, MTBs must remain open systems where every decision is provisional, ensuring precision oncology evolves toward a more equitable, evidence-based practice. Current and upcoming EU actions, such as the Joint Actions EUNetCCC and Personalised Cancer Medicine, will be key to further developing an MTB system aligned with the same principles and standards across Europe.

Ethics approval

Not required.

Authors' contributions

Conceptualization: GC, RDM, PG, VT, MKA, CLT; Writing original draft, review & editing: GC, RDM, PG, VT, MKA, CLT, GB, SB, ADN, CD, NF, MG, SI, MKO, LM, FN, MP, JS, AS, TS, MVDB, EVV, NVB, MZ, RDA, MB, LD; Formal analysis: GB, SB, ADN, CD, NF, MG, SI, MKO, LM, FN, MP, JS, AS, TS, EVV, NVB, MZ; Funding acquisition: MVDB, EVV, RDM;

Funding

This work is funded by the European Union (CAN.HEAL - grant number 101080009). Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HaDEA. Neither the European Union nor the granting authority can be held responsible for them. TS and MKO wish to acknowledge additional support by the Ministry of Health of the Republic of Poland.

CRediT authorship contribution statement

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Editorial assistance was provided by Raffaella Gatta, PhD, Valentina Attanasio, and Aashni Shah (Polistudium Srl, Milan, Italy). For TS and MK, project co-financed by the Polish Ministry of Science and Higher Education under the program called "International Co-Financed Projects"

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