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Original Article

Implementation of Precision Oncology in Clinical Practice: Results of a National Survey for Health Care Professionals

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Abstract

Background: Two main aspects lead the implementation of precision oncology into clinical practice: the adoption of extended genome sequencing technologies and the institution of the Molecular Tumor Boards (MTBs). CIPOMO (Italian Association of Heads of Oncology Department) promoted a national survey across top health care professionals to gain an understanding of the current state of precision oncology in Italy.

Methods: Nineteen questions were sent via the SurveyMonkey platform to 169 heads of oncology departments. Their answers were collected in February 2022.

Results: Overall, 129 directors participated; 113 sets of answers were analyzed. Nineteen regions out of 21 participated as a representative sample of the Italian health care system. The use of next-generation sequencing (NGS) is unevenly distributed; informed consent and clinical reports are managed differently, as the integration of medical, biologic, and informatics domains in a patient-centered workflow is inconsistent. A heterogeneous MTB environment emerged. A total of 33.6% of the responding professionals did not have access to MTBs while 76% of those who have did not refer cases.

Conclusions: NGS technologies and MTBs are not homogeneously implemented in Italy. This fact potentially jeopardizes equal access chances to innovative therapies for patients. This survey was carried out as part of an organizational research project, pursuing a bottom–up approach to identify the needs and possible solutions to optimize the process. These results could be a starting point for clinicians, scientific societies, and health care institutions to outline the best practices and offer shared recommendations for precision oncology implementation in current clinical practice.

Key words: precision oncology implementation; national survey; healthcare delivery; healthcare management research; molecular tumor boards; healthcare innovation implementation.

Implications for Practice

The findings of this national survey underline the need of producing evidences and shared recommendations on how to best manage the implementation of precision oncology to guarantee uniform care chances in heterogeneous health care systems. To date, the efforts carried out in various centers have resulted in a different offer of services, potentially jeopardizing the equal access possibility to innovative therapies for patients. The information acquired with this work will be the starting point to draft national consensus statements on NGS use and MTB activity, which will be shared with other scientific societies and health care authorities.

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Introduction

Precision oncology (PO) is a revolutionary and highly penetrating innovation in medicine. PO is not a new paradigm, since it has been adopted to select patients who may benefit the most from personalized treatment, avoiding toxicity for those with low chance of response and limiting skyrocketing drug related expenditures. Although over 75% of US physicians use information on genomic tests or tumor molecular profiling acquired through a sequencing platform for diagnosis, prognostic assessment, and refining treatment selection even in routine oncological care,[1] the final impact of this model on health care system organizations is still uncertain. Although the availability of genomic testing is expanding worldwide, the incorporation of PO in clinical practice seems to be slower and more complex. PO is founded on both the application of extended genome sequencing technologies, mainly NGS (next-generation sequencing), and the activity of Molecular Tumor Boards (MTBs), multidisciplinary groups with focus on the interpretation of biomarker analysis for clinical purposes.[2,3] The implementation of these 2 elements is strictly bonded and involves professional, technological, managerial, and ethical aspects. Most likely, due to this intrinsic complexity consistent differences among health care systems worldwide are still present.[4]

The Italian national health care system is a highly decentralized, region-based system that provides coverage for authorized health services to all the residents of the country. Regions are in charge of designing the architecture and the governance of their local health care systems, establishing levels of coverage and reimbursement of services and determining patient access to benefits. The high level of autonomy granted to the regions is designed to respond effectively to residents' health care needs given different (socioeconomic, demographic, and geographical) contexts, and to make them accountable for their performance in achieving nationally set objectives in terms of quantity and quality of services to guarantee to all citizens. However, regional autonomy can also lead to fragmentation in the national framework, and the implementation of PO is one clear example. Molecular investigations are currently performed free of charge as part of the ordinary diagnostic process, managed according to guidelines. However, a pricing for extended sequencing has not yet been defined within the approved essential levels of assistance.

In the National Plan of Recovery and Resilience, adopted according to the European Community Recovery Plan, the Italian Parliament approved a law to empower the development of precision medicine in Italy. The institution of MTBs within the regional oncology networks and the identification of specialized centers for the execution of profiling tests with NGS are the main issues to be addressed. Thus, tasks, reimbursement criteria, and regulations for MTB activity as well as for NGS genomic profiling will be defined nationally. Thus far in Italy, the Veneto region has been a forerunner on this topic. In 2019, an official document stating the aims and composition of a regional MTB was enacted, with a top–down approach. Several other regions followed this example, instituting MTBs mainly at the regional level.

A different experience has been running in the Hub & Spoke hospital network of the Friuli Centrale Local Health Authority (ASUFC), Northeast Italy, as part of a project called "Precision Oncology Pathways." The aim of the project is to integrate PO practices into clinical routine according to local peculiarities, following a bottom–up approach. This work has been designed as an organizational research project, managed in partnership with SDA Bocconi School of Management (Milan) and the Italian Association of Heads of Oncology Department (CIPOMO), involving all Local Health Authorities of Friuli Venezia Giulia Region, and 3 other Health Authorities from Northern Italy. The direct comparison among the regulatory provisions of the different regions and the study of documents on the topic (guidelines and recommendations) revealed a confusing and heterogeneous approach to PO nationwide.

To obtain a clearer picture of the state of PO in Italy, CIPOMO promoted a national survey for investigating the implementation of NGS technologies and the establishment of MTB, recording the state of the art and the personal point of view of participants on both subjects. Here, the results of this survey are reported.

Materials and Methods

A 19-question survey was created with the SurveyMonkey platform ("Individual Advantage" version) and was emailed to 169 heads of medical oncology departments, affiliated with CIPOMO. The answers were collected from February 10, 2022 to February 28, 2022. During this period, 3 reminder emails were sent by CIPOMO's secretary to encourage further responses.

The questions were developed after a literature review (scientific and institutional documents) and semi-structured interviews with different professionals: oncologists, pathologists, molecular biologists, and geneticists. The interviews were carried out in the context of the organizational research project promoted by ASUFC and included professionals from 2 institutes for research and treatment, 2 local health authorities of Friuli Venezia Giulia, and 3 extraregional local health authorities from Emilia-Romagna, Lombardia, and Veneto.

After a first round of interviews, the main topics, the questions, and the multiple-choice answers were selected by GF, MCB, and GP. The survey was designed with a "quick skip logic" to make responders skip to specific queries based on their answers to previous close-ended questions.

The results, downloaded directly from SurveyMonkey platform in Excel format, were analyzed both as question summaries and individual responses. The results were reported as percentages of the responders answering the specific question.

Results

Overall, 129 heads of medical oncology departments participated in this survey. A total of 113 sets of answers were analyzed, with a total of 100 complete responders.

In Which Region Do You Work? In Which Kind of Center Do You Work?

Nineteen regions out of 21 (including 2 autonomous provinces) were represented in the survey, a proxy of more than 98.5% of the Italian population, from different institutions including health authorities (45.1%), public hospitals (36.3%), public university hospitals (10.6%), scientific institutes for research (3.5%), and private professionals (0.9%).

Knowledge of PO-Related Guidelines

The survey investigated the diffusion of knowledge regarding recommendations published by the Italian Association of Medical Oncology (AIOM) on PO and MTB,[5] and by the European Society of Medical Oncology (ESMO) on NGS.[6]

Do You Know AIOM or ESMO Recommendations on PO?

A total of 101 participants answered: 65.4% claimed to know both, 23.8% and 2.0% reported to knowing only the AIOM or the ESMO guidelines, respectively, while 8.9% knew neither of them.

NGS Technology: Diffusion, Implementation, and Implications in Clinical Practice

The availability and diffusion of extended sequencing is one of the main topics in PO: its use is spreading from research to clinical practice allowing for broader diagnostic analysis but bringing issues related to the handling of molecular information and communication to patients.[7,8]

What Is the Approach to Molecular Diagnosis Adopted in Your Center?

At diagnosis, 47.8% of the participants prescribed molecular analysis on single-gene testing, 41,6% used single gene and/or NGS depending on the molecular alterations of interest, and only 10.6% reported using NGS routinely for the majority of patients (Fig. 1a).

Where Is NGS Technology Located?

Among those using NGS, 81.4% have the technology available in-house or within the regional network. Only 18.6% refer to private services.

When Using NGS Technology, Which Panels Are Chosen?

Among the responders who used NGS, 49.2% used tumor-specific panels, 30.5% had a unique pantumor panel, and the remaining 20.3% declared not knowing which type of panel was used in their laboratory (Fig. 1b).

When a Pantumor Panel Is Chosen, What Is Its Extension?

Considering that tumor-specific panels are likely to include a limited number of biomarkers, the focus was on the pantumor panels' extension: 77.8% of the centers use a panel containing up to 50 biomarkers (38.9% even smaller 20 genes panel), whereas only 3 centers (16.7% of the responders to this question) have panels exceeding 50 genes (Fig. 1c).

In Your Opinion, What Would Be the Most Appropriate Diagnostic Approach Today?

In total 41.6% of the directors believe that a small panel with the biomarkers identified by international guidelines should be used. The 30.7% would choose a single-gene approach for routine diagnostics, followed by extended NGS in subsequent phases, whereas the 27.7% use extended NGS panels upfront (Fig. 1d). In summary, 72.3% of responders judged it more appropriate to focus only on biomarkers indicated by guidelines at diagnosis, with both single-gene testing and NGS. In contrast, less than 30% of participants supported the use of extended sequencing at diagnosis. Among them, a cluster of responders linked to research institutes was not identified.

According to You, Which Information Should an NGS Report Contain?

The opinion on the structure of the NGS report also varies across responders: 58.2% support a report including all

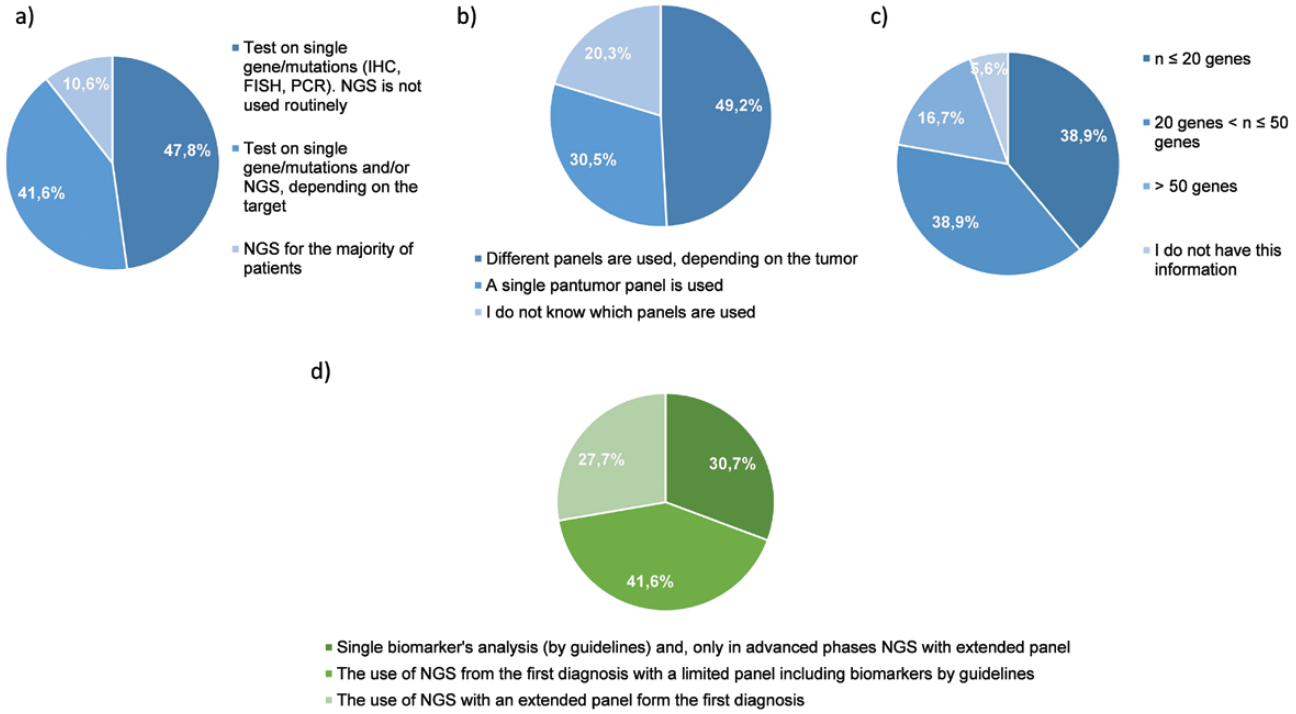

Figure 1. State of the art of molecular diagnostic strategies and use of next-generation sequencing (NGS) panels. (**a**) Current molecular diagnostic strategy; (**b**) type of NGS panels used; (**c**) pantumor panels' extension; and (**d**) responders' opinion on the most appropriate diagnostic strategy.

biomarkers analyzed, 18.2% think that only the biomarkers approved by guidelines should be presented, omitting all the others, whereas the 23.6% would prefer 2 different reports: a complete one for the clinician and a simplified one with selected data for patients.

In Your Center, Is an Informed Consent Submitted to Patients for Routine Clinical Practice?

Another point of heterogeneity is the use of informed consent for molecular diagnostics: 53.5% of respondents report that a consent is requested for all diagnostic analyses, 36.6% report that it is never requested for biomarker testing in clinical practice, and 9.9% submit a consent to patients only for NGS analysis.

Have NGS Analysis Specific Rates Been Defined in Your Regional Health Care System?

Regarding reimbursement aspects, the majority of responders (57.7%) did not know if their regional health care authorities defined specific fees for NGS analysis.

MTBs: Diffusion, Implementation, and Activity

Has an MTB Been Formed in Your Region/ Health Care Authority/Hospital? If So, at Which Institutional Level Is It Established?

According to the survey, there are MTBs in 13 out of 19 represented Italian regions, but one-third of the responders (33.6%) does not have access to MTB. The active MTBs are instituted to different levels, not only among, but also within regions (Fig. 2a, 2b).

If You Have Access to an MTB, Do You Refer Cases to It?

Among those who declare to have access to an MTB, only 23.9% refer cases for consultation, most of which are intraregional groups, whereas the large majority have not yet referred cases to MTBs (Fig. 2c). Interestingly, 43.7% report they never needed it, and 32.4% find that the current organization of MTBs in their context does not fit their needs.

To Your Knowledge, What Would Be the Most Suitable Level to Establish an MTB?

A total of 38.6% would prefer a regional MTB, 43.6% believed that an intraregional level would be more appropriate (33.7% in the Hub&Spoke network, 7.9% as a single Hub center, and 2.0% as single Spoke center), and 17.8% considered that the coexistence of a local MTB for current activity and a coordinating regional MTB could be the best solution (Fig. 2d).

Does a Database for the Cases Discussed in MTB Exists?

Recording MTB clinical activities is fundamental; nevertheless, 31.3% of the responders do not know if there is a database for MTB's discussions, 26.9% say that it does not exist, 22.4% have a local database, 14.9% have a regional database, and only 4.5% use an online platform to keep track of MTB discussion data.

Which Cases Are Referred to MTB? Which Cases, in Your Opinion, Should Be Referred?

Overall, most responders would refer patients who run out of therapeutic options, those with rare or complex mutations

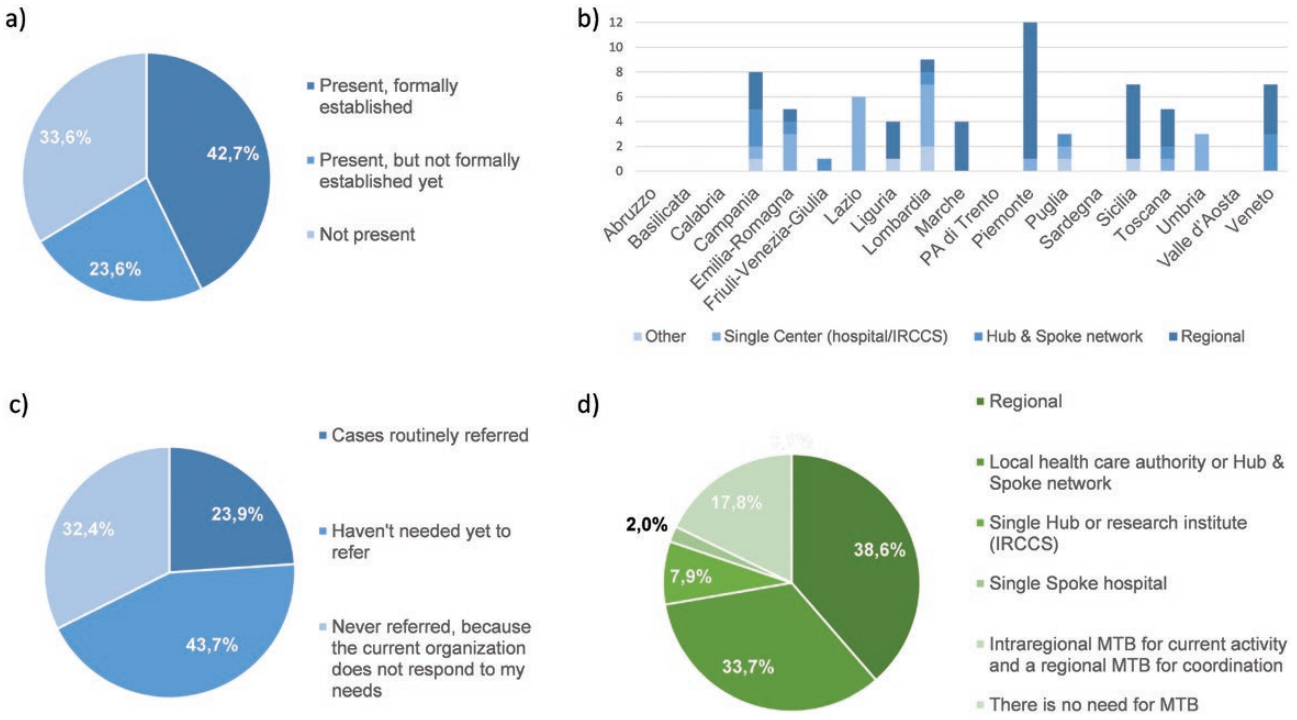

Figure 2. State of the art of Molecular Tumor Boards (MTBs) implementation. (**a**) Presence of MTB in the Italian territory; (**b**) MTB institution levels in different regions; (**c**) current cases' referral; and (**d**) opinion on the most appropriate level for MTB institution.

or those with rare or orphan tumors. However, responders believe that more attention should be given to referring patients to MTB when extended gene sequencing is required for research or when an off-label target drug could be prescribed. No additional characteristics were proposed by the participants (Fig. 3a).

Which Professionals Should Be Part of the Core Composition of an MTB?

All the participants were concordant with the presence of an oncologist (100%) and the majority considered it essential for an MTB: molecular biologists (96%), pathologists (92%), geneticists (76%), hospital pharmacists (60%), and case managers (57%). Other professionals indicated by less than half of responders are: hematologists (48%), bioinformatics (38%), patient representatives (33%), bioethicists (33%), research nurses (28%), pharmacologists (27%), surgeons (26%), radiologists (21%), oncology-expert nurses (20%), scientific directors (19%), epidemiologists (15%), coroners (10%), medical directors (10%), health care directors (9%), or others (2%) (Fig. 3b).

Discussion

PO is one of the most relevant innovative areas of cancer care, and it is of paramount importance to guarantee its quick translation to bedside, both through a homogeneous use of sequencing technology and an appropriate introduction of MTB activity within the current care pathways (still histology based). In fact, studies have documented that the adoption of evidence into practice is not always straightforward.[9-11] Waiting for new national rules that uniquely define these activities, this survey gives a picture of PO state of the art within Italian National Health Service system. More than 100 professionals, belonging to almost all the Italian regions (North, Center, South, and Islands) responded, giving a precise portrait of the current state of the art of PO implementation at a national level, and a very heterogeneous environment emerged.

Awareness of the latest key contents of the main scientific recommendations on PO and its impact on clinical practice could be improved through educational interventions by dedicated groups.

Beyond on-label drug prescriptions, the result of deep tumor molecular profiling may facilitate clinical trial enrollment and help identify investigational drug opportunities in individual patients. When the chance for an off-label prescription is identified, the cost of the therapy is covered through dedicated processes and funds by law.

Single-gene analysis techniques are still widely used but more than half of the responders rely totally or partially on NGS technology for diagnosis: the majority analyze only the biomarkers indicated by guidelines and others use this tool more extensively for most patients. The large majority of participants judged it more appropriate to focus on biomarkers indicated by scientific guidelines at diagnosis, regardless of the technology used, rather than using extended panels upfront. NGS is routinely used in several laboratories and this aspect leads to 2 questions: are all structures able to guarantee the high-quality standards required to use this technology? Which model has the best cost-effectiveness ratio: a more diffuse or a more centralized one? According to European recommendations,[6] NGS analyses are currently appropriate for selected cancer types. In the future, they may be offered upfront for different pathologies, forcing a redefinition of the existing diagnostic paths with non-negligible effects. In this research, the aim was to understand the general approach without discerning between cancer types to presume the tendency for future use of this technology and the role of MTB in the diagnostic pathway.

The findings about NGS application and its impact on the organization underline the need for clear, shared indication.

This survey confirms the heterogeneity of the molecular diagnostic environment in Italy.[12] The user's choice of NGS panels varies in type (tumor-specific vs. pantumor panels) and extension, from less than 20 biomarkers to extended panels including more than 50 genes. The number and the type of the analyzed biomarkers impact the management of information (data analysis and communication) and consequently the medical report. To date, there are no consistent indications from scientific societies on which information has to be collected and how these should be reported when using non-specific sequencing. The survey also shows that the oncology director's opinion is divided on report's content and structure. Further considerations should be made about the

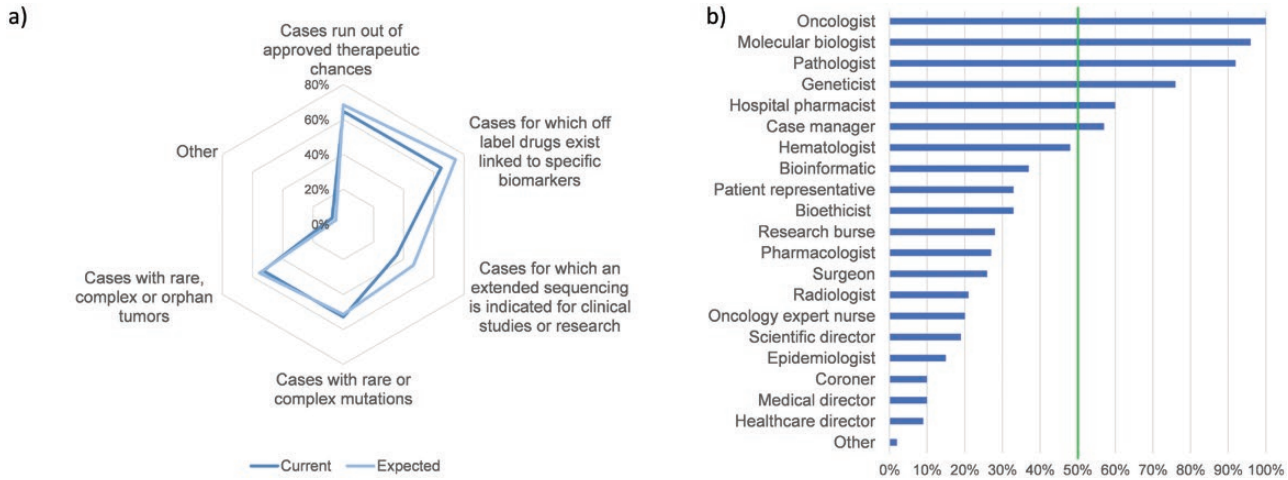

Figure 3. Oncology directors' opinion on Molecular Tumor Board (MTB) activity and composition (**a**) current and expected cases referral to MTB; and (**b**) opinion on the professional composition of MTB.

management of the information, including which resources and how much is needed to analyze and interpret the data, and what impact could redundant information have on patient treatment and on health care organizations?

Moreover, the use of informed consent is not consistent. It is important for clinical practice pathways not only to be lean but also to have tools that guarantee both patients and clinicians when dealing with genetic information with possible hereditary implications. This topic has legal consequences and should be carefully evaluated with the support of coroners.

NGS implementation in clinical practice presents important issues that must be considered and regulated to guarantee homogeneous access, quality of the data, economical sustainability, and legal guarantees for patients and health care authorities.

The uneven geographical distribution of MTBs and their different levels of implementation might generate disparities in the opportunities for patients to access targeted therapies or clinical trials. At the time of this survey's submission, 7 regional MTBs have been established, but coexisting intra-regional groups are also reported. Single center or network MTBs are reported in other regions. It is interesting to highlight that the large majority of directors with access to MTBs have not yet referred cases, showing how MTB implementation works is still in progress.

Additionally, most of the responders believe that MTBs should be established at a local level rather than at a regional level and that MTB composition should be limited to few key professionals (namely: oncologists, molecular biologists, pathologists, geneticists, hospital pharmacists, and case managers). These aspects underline the need for restricted MTBs focused on clinical activities rather than coordination or policy matters. Indeed, other professionals could be involved on demand to solve specific issues and support the core team.

Recording MTB clinical activities is fundamental for evaluating their impact on patients' pathways and outcomes. A homogeneous collection of data is important for pooling and comparing information on the PO approach, and local and even regional databases are unlikely to meet this aspect. Platform-based databases could be a more appropriate tool but their use could be complicated by privacy matters between professionals and private authorities.[13]

Conclusions

The "big bang" of PO is revolutionizing classical oncological workflows, but the implementation of this subject is still magmatic. There are no right or wrong approaches, but a shared method to face this new challenge is needed. Starting from the information acquired with this survey, in the context of a structured organizational research project, CIPOMO will formulate consensus statements on NGS use and MTB activity in Italy to share with other scientific societies. This work, carried out with a bottom–up approach, contributes to the implementation of PO in clinical practice, aiming to facilitate this innovation to the patient's bedside.

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Conflict of Interest

Gianpiero Fasola reported honoraria for lectures from AstraZeneca and support for attending meetings from Bristol-Myers Squibb, Merck Sharp & Dohme, Ipsen, and Roche; Giacomo Pelizzari C/A MSD, Boehringer Ingelheim, Astra Zeneca; Other (support for attending meetings) Eli-Lilly (participation on data safety monitoring board), Amgen; reported consulting fees from MSD, Boehringer Ingelheim, and AstraZeneca; support for attending meetings from Eli Lilly; and participation on data safety monitoring board for Amgen; Bruno Daniele reported honoraria for lectures from Eisai, Ipsen, Lilly, Bayer, MSD, Roche, Amgen, Merck Serono, and AstraZeneca; support for attending meetings from AstraZeneca, Sanofi, Celgene, and BMS; and participation on a Data Safety Monitoring Board for Sanofi; Cinzia Ortega reported honoraria for lectures from Janssen and Pfizer; support for attending meetings from Janssen and Pfizer; and participation on data safety monitoring boards for MSD, Pfizer, BMS, and Astellas. Giuseppe Aprile reported consulting fees from Astellas, Amgen, and Incyte; and payment or honoraria for lectures from Astellas, Amgen, AstraZeneca, BMS, Eli-Lilly, Italfarmaco, Novartis, and Seagen. The other authors indicated no financial relationships.

Author Contributions

Conception/design: G.F., M.C.B., V.D.T. Provision of study material or patients: L.C. Collection and/or assembly of data: G.F., M.C.B., B.D., M.G., C.O., R.R.S., L.C., G.A. Data analysis and interpretation: G.F., M.C.B., G.P., F.G., C.P., V.D.T., G.A. Manuscript writing: G.F., M.C.B., G.P., F.G., C.P., V.D.T., G.A. Final approval of manuscript: All authors.

Data Availability

The data that support the findings of this study are available on request from the corresponding author.

References

1. Pritchard D, Goodman C, Nadauld LD. Clinical utility of genomic testing in cancer care. *JCO Precis Oncol*. 2022;6:e2100349-e2100353. https://doi.org/10.1200/PO.21.00349.
2. Schwartzberg L, Kim ES, Liu D, et al. Precision oncology: who, how, what, when, and when not? *Am Soc Clin Oncol Educ book Am Soc Clin Oncol Annu Meet*. 2017;37:160-169. https://doi.org/10.1200/EDBK_174176.
3. Incorvaia L, Russo A, Cinieri S. The molecular tumor board: a tool for the governance of precision oncology in the real world. Tumori. 2022;108(4):288-290. https://doi.org/10.1177/03008916211062266.
4. Horgan D, Curigliano G, Rieß O, et al. Identifying the steps required to effectively implement next-generation sequencing in oncology at

a national level in Europe. *J Pers Med*. 2022;12(1):72-98. https://doi.org/10.3390/jpm12010072.
5. AIOM: Raccomandazioni AIOM "Tumor Board Molecolare." 2020. https://www.aiom.it/raccomandazioni-2020-tumor-board-molecolare/. Last visited: February 10, 2023.
6. Mosele F, Remon J, Mateo J, et al. Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group. *Ann Oncol Off J Eur Soc Med Oncol*. 2020;31(11):1491-1505. https://doi.org/10.1016/j.annonc.2020.07.014.
7. De Maglio G, Pasello G, Dono M, et al. The storm of NGS in NSCLC diagnostic-therapeutic pathway: How to sun the real clinical practice. *Crit Rev Oncol Hematol*. 2022;169:103561-103570. https://doi.org/10.1016/j.critrevonc.2021.103561.
8. Bunnik EM, Dondorp WJ, Bredenoord AL, de Wert G, Cornel MCet al. Mainstreaming informed consent for genomic sequencing: a call for action. *Eur J Cancer*. 2021;148:405-410. https://doi.org/10.1016/j.ejca.2021.02.029.
9. Fasola G, Barducci MC, Beretta G. Impact of innovation in oncology: more questions than answers. *Tumori*. 2021;107(6):478–482. https://doi.org/10.1177/03008916211027646.
10. Check DK, Zullig LL, Davis MM, et al. Improvement science and implementation science in cancer care: identifying areas of synergy and opportunities for further integration. *J Gen Intern Med*. 2020;36(1):186–195. https://doi.org/10.1007/s11606-020-06138-w.
11. Sullivan R, Pramesh CS, Booth CM. Cancer patients need better care, not just more technology. *Nature*. 2017;549(7672):325-328. https://doi.org/10.1038/549325a.
12. Marchetti A, Barbareschi M, Barberis M, et al. Real-world data on NGS diagnostics: a survey from the Italian Society of Pathology (SIAPeC) NGS Network. *Pathologica*. 2021;113(4):262-271. https://doi.org/10.32074/1591-951X-324.
13. Warner JL, Prasad I, Bennett M, et al. SMART cancer navigator: a framework for implementing ASCO workshop recommendations to enable precision cancer medicine. *JCO Precis Oncol*. 2018;2018:PO.17.00292. https://doi.org/10.1200/PO.17.00292.