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Original Article

Expert Consensus on Molecular Tumor Boards in Taiwan: Joint Position Paper by the Taiwan Oncology Society and the Taiwan Society of Pathology

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Abstract

Background: The Taiwan Oncology Society (TOS) and the Taiwan Society of Pathology (TSP) have collaborated to present a joint

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position paper on the molecular tumor boards (MTBs) within the medical institutions of Taiwan. **Materials and Methods:** To raise awareness of MTBs among health-care professionals, policymakers, and the public, a total of 20 experts from TOS and TSP formulated a joint consensus statement through a voting process. **Results:** The joint statement proposes key recommendations: (1) MTB discussions encompass diverse molecular analyses including next-generation sequencing (NGS), RNA sequencing, whole-exon sequencing, and whole-genomic sequencing addressing relevant genomic changes, tumor mutation burden, microsatellite instability, and specific biomarkers for certain cancers. (2) MTB meetings should involve multidisciplinary participants who receive regular updates on NGS-related clinical trials. (3) Prioritize discussing cases with unique clinical needs, gene alterations lacking treatments, untreatable neoplasms, or oncogenes unresponsive to targeted therapies. (4) Base MTB discussions on comprehensive patient data, including genetics, pathology, timing of specimen collection, and NGS outcomes. (5) MTBs offer treatment recommendations: standard therapies, off-label use, clinical trials, genetic counseling, and multidisciplinary reviews. (6) MTB effectiveness can be gauged by member composition, case reviews, treatment suggestions, and patient outcomes. Encourage government incentives for MTB engagement. **Conclusion:** The primary aim of this initiative is to promote the advancement of precision oncology in Taiwan.

Keywords: Molecular tumor board, next-generation sequencing, Taiwan Oncology Society, Taiwan Society of Pathology

Introduction

Next-generation sequencing (NGS) technology has become increasingly vital in clinical cancer diagnosis and treatment. It has enabled rapid and accurate detection of tumor-related genetic variants and has provided clinicians with numerous treatment options and insights into prognostic factors. However, according to the international criteria, such as the Joint Consensus Recommendation (JCR), the European Society for Medical Oncology (ESMO) Scale of Clinical Actionability for Molecular Targets (ESCAT), and the Oncology Knowledge Base (OncoKB), only a small subset of patients qualify for strong evidence base. For patients who are not qualify for the strong evidence of criteria, further interpretation and evaluation of the clinical relevance of NGS results and potential treatment options for each genetic variant should be completed. Although a growing number of molecular tumor boards (MTBs) have been established and such boards have increasingly been used for clinical cancer diagnosis and treatment internationally, a comprehensive MTB system has not yet been established in Taiwan, despite many Taiwanese hospitals and institutions having participated in international clinical trials. Establishing an MTB system is crucial because such boards can assist clinicians in effectively applying NGS technology, interpreting NGS results, and providing better treatment options and prognostic assessments, which can ultimately improve survival rates and the overall quality of life for patients with cancer. MTB teams can assist clinicians to more thoroughly understand NGS results and devise optimal treatment strategies. Consequently, establishing MTBs is crucial for advancing the development of precision medicine. NGS is likely to be covered by health insurance in the near future, which is likely to lead to an increased demand for MTBs.

Materials and Methods

Study design

The Taiwan Oncology Society and the Taiwan Society of Pathology (TSP) participated in a consensus development conference. The primary objective of this conference was to arrive at a consensus regarding the implementation and functioning of MTBs in Taiwan to advance the development of precision oncology. This study did not involve human participants, their data, or biological material. Therefore, following applicable ethical standards, including the 1964 Declaration of Helsinki and its later amendments or comparable ethical norms, this research did not require Institutional Review Board (IRB) approval. The conducted research was purely theoretical (or observational, analytical, etc.), without involving any human subjects, adhering to the ethical guidelines for studies exempt from IRB review.

Expert selection

A total of 20 experts participated in the conference. Among these experts, 8 were affiliated with the TSP and 12 were affiliated with the Taiwan Society of Oncology. The participants were selected on the basis of their expertise and experience in the fields of medical oncology, molecular pathology, and precision medicine.

Discussion process

The consensus was reached after a Delphi-like approach. The kick-off meeting was held by expert members formed the sections and the proposed detailed questions of each section. The first meetings were section based and the experts discussed and reached a consensus on the critical questions of each section that would be discussed in the second meeting. In the second meeting, the questions were presented and explained by the lead experts followed by a consensus voting from all the experts from the MTB consensus group.

Consensus item generation

The expert panel conducted an extensive literature search and review to identify relevant topics and emerging concerns regarding MTBs. This review process yielded a preliminary draft of consensus items. These items were focused on key aspects of MTB implementation and operation. The consensus items were then peer-reviewed and revised through mutual verification.

Voting procedures and panel discussion

The experts individually and anonymously rated their agreement with each consensus item using Slido software.

To ensure the integrity and accuracy of the voting process, an external impartial, third-party staff member judged the validity of the vote and tallied the final number of votes. The results of this voting phase were analyzed. If a consensus item garnered agreement from over 50% of the participating experts, it was considered to pass and was recorded. By contrast, if an item garnered agreement from <50% of the experts, it was discussed further.

Consensus statement generation

The consensus items selected through voting were organized into the following categories: MTB objectives, molecular analyses to be included in MTB discussions, implementation of MTB meetings, selection criteria for MTB participants, essential patient information for MTB discussions, topics to be discussed during MTB meetings, and management strategies for MTBs. These consolidated consensus items served as the foundation for the implementation and operation of MTBs in Taiwan.

Results

Molecular tumor board objectives

Because of advances in genomic sequencing and analysis, MTBs have been increasingly adopted in medical institutions, which have improved the understanding of the molecular drivers of cancer. MTBs composed of a multidisciplinary team play a pivotal role in aiding in the selection of molecular-guided treatments for patients with cancer who have received an NGS report and have not responded to standard-of-care therapies.[1] By analyzing the molecular profile of a patient's tumor, MTBs can provide recommendations for targeted therapies or clinical trials that are suitable for the specific molecular alterations present in the patient's cancer. Through joint consensus, MTBs can assist physicians in making treatment decisions for solid tumors, including both common and rare malignancies. When an institution has an MTB, a group of experts collectively reviews a patient's molecular profile, which leads to the development of more personalized treatment plans that consider the unique molecular characteristics of the patient's tumor. Although evidence indicates that a hospital having an MTBs are beneficial for patients with advanced cancer. However, it's important to note that much of this evidence comes from retrospective or prospective non-comparative studies, which may yield less robust findings compared to randomized control trials.[2] In addition, the actual benefits of MTB may vary depending on several factors, including a country's health-care system, reimbursement policies, and drug availability. For example, in countries with universal health care, MTBs might be more accessible to patients, whereas in countries with privatized health-care systems, access to MTBs may be limited by insurance coverage or be considered an out-of-pocket expense. Reimbursement policies may also play a role in determining MTB accessibility and influence which drugs are recommended by the board. If certain medications are not covered by insurance, patients might be unable to access them, even if the MTB recommended their use. Furthermore, drug availability may influence the efficacy of MTBs. If specific drugs are unavailable in a particular region, MTBs might be unable to recommend them as a treatment option. This might limit the benefits of MTBs for patients living in areas with limited access to certain drugs. Concerted efforts from all involved parties are required to address the aforementioned problems and to ensure the comprehensiveness and effectiveness of MTBs in Taiwan [Table 1].

Table 1: Consensus: Molecular tumor board objectives

Item	Statement	Agreement rate
1-1	The accessibility of NGS for patients with cancer is foundational to the development of personalized therapy. MTBs can aid in recommending molecular-guided treatment for patients with NGS reports who have not responded to standard care	100% (16/16)
1-2	MTBs have the potential to guide treatment decisions for many types of solid tumors, including those of both common and rare cancers. An MTB's treatment suggestions can complement the discussions held within a multidisciplinary team specialized for a given cancer type	100% (16/16)
1-3	Evidence indicates that MTBs are beneficial for patients with advanced cancer; however, this evidence has primarily been obtained from retrospective or prospective noncomparative studies. The actual benefits MTBs can provide to such patients may vary according to factors such as health-care systems, reimbursement policies, and drug availability	100% (16/16)

MTBs: Molecular tumor boards, NGS: Next-generation sequencing

Molecular analyses to be discussed by molecular tumor boards

The testing tools that may be discussed in MTBs can vary with the individual patient's tumor and the treatment goals. Advances in NGS technology have led to the development of numerous molecular testing tools. These tools include targeted gene panels and comprehensive genomic profiling. Targeted gene panels are used in genetic testing to identify specific mutations within defined regions of cancer-related genes, which are commonly referred to as "hotspots." Using such panels enables the prediction of responses to particular molecular targeted therapies. CGP enables simultaneous analysis of multiple genes. It is often considered the preferred method for genetic testing because it provides a comprehensive understanding of genetic changes, including known and novel mutations in cancer genes. The sensitivity and specificity of CGP enable the detection of low-frequency mutations, making it a valuable tool for developing personalized treatment plans for patients with cancer. Other molecular testing tools include whole-exon sequencing (WES), whole-genomic sequencing (WGS), and RNA sequencing (RNAseq). WES can be used to capture and sequence exonic regions, which enables efficient analysis of genetic variations within protein-coding regions. Therefore,

Table 2: Consensus: Molecular analyses to be discussed by molecular tumor boards

Item	Statement	Agreement rate
2-1	The topics related to testing to be discussed in MTBs included but not limited to: (1) NGS-based gene panel tests, (2) WES and WGS, and (3) RNAseq, which is capable of providing information regarding fusion and rearrangement	100% (16/16)
2-2	MTB discussions of molecular analyses should include but not limited to the following topics: (1) clinically relevant genomic alterations, including mutations (SNVs and indels), gene fusion, and CNVs (amplification and large-scale deletion), with MTBs being recommended to include allele frequency of mutations in discussions; (2) TMB, MSI, and other tumor type-specific biomarkers, such as HRD/LOH scores; (3) mutations with VUS, if possible, with discussions including information related to VUS obtained from new public databases; (4) druggable molecular alterations; and (5) alterations indicating drug resistance	100% (16/16)

MTBs: Molecular tumor boards, NGS: Next-generation sequencing, WES: Whole-exon sequencing, WGS: Whole-genomic sequencing, RNAseq: RNA sequencing, SNVs: Single-nucleotide variants, CNVs: Copy number variations, TMB: Tumor mutation burden, VUS: Variants of unknown significance, MSI: Microsatellite instability, HRD/LOH: Homologous recombination deficiency/loss of heterozygosity

WES is considered an acceptable choice in certain situations. WGS is a more extensive but also more expensive method. It is suitable for researching and diagnosing rare diseases.[3,4] If WGS becomes less expensive over time, then it may become more accessible and it may be more broadly used and have a broader range of applications. RNAseq is used for identifying gene fusions and rearrangements. Targeted RNA-based assays are the method of choice for rearranged during transfection (RET) and Neurotrophic Tyrosine Receptor Kinase (NTRK) fusion screening.[5,6] RNAseq can detect changes in gene expression that DNA sequencing alone cannot.

In addition to testing, molecular analyses of tumors play a pivotal role in clinical practice. Molecular analyses provide valuable insights into the underlying genetic modifications that drive tumor growth and can be used to identify treatment options. The discussion of molecular analyses encompasses several essential elements, including but not limited to: (1) clinically relevant genomic alterations: these alterations include single-nucleotide variants, indels, gene fusions, and copy number variations that hold clinical significance in the context of the specific cancer type. Determining the allele frequency of mutations is recommended because it indicates their prevalence within the tumor. (2) Tumor mutation burden (TMB), microsatellite instability (MSI), and other tumor type-specific biomarkers: TMB is broadly defined as the number of somatic mutations per megabase of genomic sequence.[7] It is used to quantify the overall genomic instability or mutational load within a tumor. A higher TMB is associated with a greater neoantigen burden, which activates T-lymphocytes and induces them to proliferate and kill cancer cells.[8] MSI can be used to detect errors in repetitive DNA sequences.[9] By analyzing specific microsatellite markers across the genome, experts can identify changes in the lengths of repetitive sequences between tumor DNA and normal DNA. These changes indicate the presence of MSI, which can be used as a diagnostic and prognostic tool for specific cancers, such as colorectal cancer and endometrial cancer. These biomarkers and other tumor type-specific markers, such as homologous recombination deficiency/loss of heterozygosity scores in the BRCA1/2 gene, offer essential information for decision-making regarding treatment involving poly (ADP-ribose) polymerase (PARP) inhibitors.[10] (3) Mutations with variants of unknown significance: these are mutations with unclear clinical significance. MTBs should discuss such mutations with consideration of data obtained from new public databases to gain insights into the potential implications of these mutations. (4) Druggable molecular alterations: MTBs should consider druggable molecular alterations for which targeted therapeutic options exist. These include mutations or alterations in genes that can be effectively targeted with specific drugs or therapies. (5) Resistance-associated genetic alterations: genetic alterations that indicate potential resistance to certain drugs or therapies should be discussed in MTBs. Such information is pivotal in shaping treatment decisions that will maximize treatment effectiveness. Discussions regarding resistance-associated genetic alterations can aid in elucidating molecular characteristics that can enable informed decision-making regarding treatment and thereby ensure optimal patient care [Table 2].

Implementation of molecular tumor board meetings

Medical centers are recommended to establish MTBs because MTBs offer numerous benefits. Because MTBs comprise specialists from various fields, these boards are able to provide a comprehensive and multidimensional perspective on individual patient cases. This collaboration among specialists ensures that the diagnoses and treatment plans developed by MTBs are carefully reviewed and optimized, leading to more favorable outcomes for patients.

The number of NGS tests performed per year or month is a crucial factor in determining whether an MTB should be established. The number of NGS tests performed at an institution can serve as an indicator of the prevalence and availability of genomic profiling in the clinical practice of the institution, and determination of the optimal threshold of the number of cases for an MTB to be required may be guided by benchmarks established within multidisciplinary teams. The operational intricacies of MTBs must also be discussed with relevant governmental authorities to ensure that the determination of the optimal threshold is well informed and accounts for context.

When hospitals lack their own MTB, they are suggested to refer patients requiring an MTB consultation to hospitals that

possess such multidisciplinary boards. By implementing such a referral system, the hospitals can ensure that their patients receive the benefits of a multidisciplinary approach to diagnosis and decision-making. Alternatively, hospitals without an MTB can send patient specimens to a medical center with an MTB for analysis. The MTB can then provide result reports to the satellite hospital, even when the patient does not require a formal referral. By establishing MTBs and facilitating referrals from satellite hospitals, health-care systems can enhance patient care and broaden access to specialized expertise, thereby bridging the gaps in expertise within individual medical facilities [Table 3].

Assembly of experts participating in molecular tumor boards

An MTB is an interdisciplinary team of experts who review and discuss complex molecular and genetic information related to patients with cancer. The composition of an MTB can be tailored to an institution's specific resources and requirements. The key members of an MTB typically include pathologists with expertise in molecular pathology and clinical oncologists (MTBs must include at least one medical oncologist). These members should propose treatment options based on available clinical evidence after completing a comprehensive discussion and reaching an agreement. Primary care physicians should also be involved in MTB discussions. Furthermore, to enhance patient management, the MTB should be supported by a dedicated case coordinator.[11] Other MTB members, such as pharmacists, can share their expertise on oncology drugs and medication considerations. Additional nonessential MTB members are introduced in the discussion section [Table 4].

Table 3: Consensus: Implementation of molecular tumor board meetings

Item	Statement	Agreement rate
3-1	Medical centers are recommended to establish MTBs	76% (12/16)
3-2	The number of NGS tests performed per year can be considered when medical centers determine whether they require an MTB	100% (16/16)
3-3	The frequency of MTB meetings might be once or twice a month, with the frequency being determined by the number of cases requiring review and the capacity of institutions	100% (16/16)
3-4	Patients requiring MTB consultations from satellite hospitals that do not have an MTB may be referred to a hospital with an established MTB	100% (16/16)

MTBs: Molecular tumor boards, NGS: Next-generation sequencing

Timing of case discussions in molecular tumor board meetings

MTB meetings are conducted after a patient's diagnosis has been established and relevant diagnostic tests, such as NGS tests, have been completed. NGS testing can be performed at several stages of the patient's cancer journey. The sequence is as follows: at diagnosis, before systemic therapy, after treatment failure, or after curative therapy.[12] However, the timing of NGS tests is mostly determined by the patient's condition. In addition, the optimal time point for an MTB meeting may differ with the institution and health-care setting. Nevertheless, MTB meetings are typically held in one of two primary scenarios.

In the first scenario, MTB meetings are held before treatment is initiated for a patient with cancer. Pretreatment MTB discussions are completed to provide treatment recommendations and therapeutic strategies tailored to the patient's specific tumor characteristics. In the second scenario, MTB meetings are held after a patient has received cancer treatment. The focus of such meeting is evaluating treatment responses, assessing treatment effectiveness, and discussing long-term follow-up plans. The MTB team reviews the patient's treatment outcomes by evaluating, for example, their treatment response, the extent of residual disease, and considerations for long-term follow-up. Posttreatment MTB discussions can also serve an educational purpose, providing the team with the opportunity to learn from the treatment outcomes and enhance their knowledge for future cases [Table 5].

Patient selection factor for molecular tumor board discussions

Although discussing all patients who have undergone NGS testing in MTB meetings would be ideal, it is not always feasible or necessary. Whether a patient's case is discussed in an MTB meeting is typically determined by several factors,

Table 4: Consensus: Assembly of experts participating in molecular tumor boards

Item	Statement	Agreement rate
4-1	Panel members should include the following Primary care physicians Clinical oncologists (at least one medical oncologist) Pathologists (experts in molecular pathology) Case managers Pharmacists	Primary care physicians (100%, 16/16), pathologists (100%, 16/16), clinical oncologists (94%, 15/16), case managers (69%, 9/16), pharmacists (56%, 9/16)
4-2	Treatment recommendations should be proposed by experienced oncologists (preferably medical oncologists) and be based on clinical evidence. They should be discussed and agreed upon by the MTB	100% (16/16)
4-3	MTBs should be supported by a specialized case coordinator to enhance patient care	100% (16/16)

MTBs: Molecular tumor boards

including institutional guidelines, available resources, and the complexity of the case. MTBs should discuss as many relevant cases as possible to ensure that patients can receive comprehensive and personalized treatment recommendations.

The focus of the present study was discussions of solid tumors in MTB meetings. Patients with solid tumors with refractory metastasis who have received genomic-guided therapy have a better progression-free survival (PFS) ratio and longer median PFS than patients who have not received such therapy.[13] The following are scenarios in which a case is suitable for MTB discussion but not limited to: (1) patients are harboring mutations or gene alterations lacking clinical applications, (2) patients have neoplasms for which no therapeutic approaches are available, (3) patients have "oncogene-addicted" tumors that are unresponsive to targeted therapies, and (4) cases are referred by treating physicians because of a clinical need.[11] The MTB's expertise in genomics and molecular profiling can provide valuable insights for cases involving solid tumors that can guide treatment decisions and lead to the identification of potential targeted therapies, clinical trials, or other personalized treatment options based on the molecular characteristics of the tumor [Table 6].

Patient information for MTB discussions

The effectiveness of MTB discussions is highly dependent on the extent and scope of the patient information available to the MTB. To improve the efficiency of such discussions, comprehensive patient information, including information regarding the patient's age, sex, date of diagnosis, primary tumor site, pathologic and clinical staging, and prior therapies, must be considered.[14] Such comprehensive patient information can serve as a foundation on which an MTB can analyze the case and discuss the most suitable treatment options [Supplementary Table 1].

Prior genetic information is crucial for MTB discussions. Such information includes previous genetic testing results, such as results obtained through polymerase chain reaction to assess mutational status (e.g. epidermal growth factor receptor mutations) or other relevant genetic alterations. However, MTB members should be discerning in determining the relevance and significance of prior genetic findings. In addition, gaining an understanding of the sequencing platforms employed in previous genetic testing can provide valuable insights into the reliability and comprehensiveness of the genetic information available for MTB discussions.

Prior pathology reports and immunohistochemistry (IHC) results are also valuable in MTB discussions. Prior pathology reports can provide crucial information regarding the tumor type, grade, and stage. Moreover, they provide information regarding the origin of the tumor and provide insights into its histological features. IHC tests can aid evaluations of the expression levels of specific proteins or biomarkers in tumor tissue, such as programmed death-ligand 1, which can enable assessment of the likelihood of an immunotherapy response.[15] By reviewing the prior data, MTBs can obtain a deeper understanding of the molecular characteristics of tumors; identify potential therapeutic targets; and evaluate a patient's eligibility for specific treatments, such as immunotherapies or targeted therapies [Table 7].

Table 5: Consensus: Timing of case discussions in molecular tumor board meetings

Item	Statement	Agreement rate
5-1	MTB discussions can be held either before or after treatment. Pretreatment discussions are focused on exploring potential therapeutic strategies and providing treatment recommendations	100% (16/16)
5-2	Posttreatment discussions are focused on evaluating treatment responses and enhancing knowledge for future cases	100% (16/16)

MTB: Molecular tumor board

Table 6: Consensus: Patient selection factor for molecular tumor board discussions

Item	Statement	Agreement rate
6-1	All patients who have undergone NGS testing should be discussed in MTBs	100% (16/16)
6-2	MTB discussions should focus on solid tumors	100% (16/16)
6-3	The cases that should be suggested for MTB discussion should include but not limited to (1) those involving patients harboring mutations or gene alterations lacking clinical applications, (2) those involving neoplasms for which no therapeutic approaches are available, (3) those involving "oncogene-addicted" tumors that are unresponsive to available targeted therapies, and (4) those referred by treating physicians because of a clinical need	100% (16/16)

MTBs: Molecular tumor boards, NGS: Next-generation sequencing

Table 7: Consensus: Patient information for molecular tumor board discussions

Item	Statement	Agreement rate
7-1	Patient information for MTB discussions includes age, sex, date of diagnosis, primary tumor site, pathologic and clinical staging, and prior therapies	100% (16/16)
7-2	Patient information for MTB discussions includes prior genetic information, such as mutational status (e.g., EGFR), obtained through techniques such as polymerase chain reaction and different sequencing platforms	100% (16/16)
7-3	Prior pathology reports and IHC results, including the expression status of PD-L1 and Her2, should be included	100% (16/16)

MTB: Molecular tumor board, EGFR: Epidermal growth factor receptor, IHC: Immunohistochemistry, PD-L1: Programmed death-ligand 1

Information from next-generation sequencing reports for molecular tumor board meetings

The discussions and treatment decisions of MTBs are guided by information provided in NGS reports. NGS reports provide

essential information, such as patient identifier information; laboratory information; dates of specimen collection and reporting; specimen type and identifier indication; tumor content and diagnosis; details regarding genetic alterations, including somatic mutations and structural rearrangements; and methodology descriptions and targeted gene lists.[16] NGS reports must be obtained from an accredited testing facility.

Understanding the purpose of NGS tests is crucial because such tests provide comprehensive genomic information regarding cancers that encompass several key dimensions, such as prognostic information (e.g. the likelihood of recurrence and overall survival rates), drug discoveries related to specific genetic alterations, diagnoses for patients with cancer of unknown primary tumor, detection of minimal residual disease in the cancer-free state through liquid biopsy, and discovery of resistance-associated genes. This information is critical and informs treatment choices.[17] Specimens for NGS testing may be obtained from metastatic lesions or primary tumors, depending on the clinical situation.[18] Previously resected or currently recurrent samples may also be selected. In addition, blood or tissue samples or both may be obtained.[19] To ensure that the information considered in MTB meetings is relevant and current, the most recent NGS reports should be used.[20] MTBs should remain aware of the limitations associated with NGS sampling and NGS platforms [Table 8].[21]

Key topics for discussion in molecular tumor board meetings

Several key topics should be addressed during MTB discussions focused on clinically significant genetic alterations. First, MTBs should provide recommendations for treatment options within the following six categories: (1) standard therapy, (2) off-label therapy, (3) clinical trials, (4) germline testing and genetic counseling, (5) subspecialty reviews by multidisciplinary tumor boards, and (6) advice for classifying tumors of unknown origin.[22]

In the panel discussion, all experts realized and agreed the importance of germline mutation and may occur in some cancer patients. Therefore, relevant family history and pedigree will be needed in such cases. However, we need more qualified genetic counselors to provide more comprehensive health care for these patients. Many genetic counselors in Taiwan specialize in rare diseases and may have limited experience with adult cancer patients. Therefore, the urgent need of more qualified genetic counselors will be the next step.

Second, identified genetic alterations should be classified on the basis of their clinical significance and the level of evidence supporting their potential for actionability. Variants for which evidence is strong and significant should be briefly discussed during MTB meetings, whereas variants for which evidence is lacking should be discussed in detail during meetings. Standardized frameworks or knowledge databases such as ESMO Scale for Clinical Actionability of molecular Targets (ESCAT), OncoKB, and JCR are sources that have been peer-reviewed and constantly updated that could be referenced to. These frameworks enable clinicians to evaluate the clinical significance and actionability of genetic alterations in cancer.[23,24]

Finally, MTBs in Taiwan can collect real-world evidence that is specific to the Taiwanese population. By tracking patient outcomes, collaborating with national cancer registries, participating in collaborative networks, and leveraging data integration and analysis, MTBs in Taiwan can obtain evidence that can improve patient care, inform health-care policies, and guide research efforts, which can ultimately lead to more favorable treatment outcomes and the implementation of personalized approaches to cancer management [Table 9].

Table 8: Consensus: Information from next-generation sequencing reports for molecular tumor board meetings

Item	Statement	Agreement rate
8-1	The content suggestions for NGS reports include (1) patient identifiers, (2) laboratory information, (3) the date of specimen collection and reporting, (4) the specimen type and identifier, (5) the tumor content and diagnosis, (6) the genetic analysis results, and (7) a methodology description and targeted gene list	100% (16/16)
8-2	The purposes of NGS testing are (1) prognostic assessment, (2) identification of new drugs related to genetic alterations, (3) obtaining a diagnosis for patients with CUP, (4) detection of minimal residual disease under cancer-free status, and (5) identification of drug resistance-related genes	100% (16/16)
8-3	Information regarding the samples used for NGS testing, such as whether the samples were obtained from (1) metastatic lesions or primary tumors, (2) previously resected or currently recurrent samples, and (3) blood or tissue, or both blood and tissue, should be provided. Most recent results are preferred	100% (16/16)
8-4	MTB members should remain aware of the limitations associated with sampling and with the NGS platform used for testing	100% (16/16)

MTB: Molecular tumor board, NGS: Next-generation sequencing, CUP: Cancer of unknown primary tumor

Table 9: Consensus: Key topics for discussion in molecular tumor board meetings

Item	Statement	Agreement rate
9-1	MTBs should provide recommendations for prioritizing standard therapies, off-label drug use, and clinical trial participation	100% (16/16)
9-2	Clinically significant genetic alterations should be classified on the basis of the level of evidence for actionability using frameworks such as ESCAT, OncoKB, and JCR	100% (16/16)
9-3	MTBs can gather real-world evidence for analysis	100% (16/16)

MTBs: Molecular tumor boards, JCR: Joint Consensus Recommendation, ESCAT: ESMO Scale of Clinical Actionability for Molecular Targets, OncoKB: Oncology Knowledge Base

Future expectation for molecular tumor boards

The effectiveness of MTBs can be evaluated on the basis of several parameters, including (1) their composition; (2) the frequency of MTB meetings; (3) the frequency with which an MTB reviews cases; (4) the frequency with which an MTB recommends treatments, such as clinical trials, off-label or compassionate use, approved drug treatment, and early access programs; (5) the frequency of and reasons for an MTB not offering treatment recommendations; and (6) the outcomes of patients who received MTB-guided treatment. Considering these parameters can enable assessment of the proficiency of an MTB, its accessibility, its workload, its impact on treatment options, reasons for noncompliance, and the efficacy of MTB-guided treatments.

MTB teams should connect and regularly obtain up-to-date information regarding clinical trials involving genomic sequencing. By regularly obtaining updates on relevant clinical trials, MTBs can provide patients with current information regarding their trial options and can obtain information regarding novel therapies and investigational interventions.[25] Although the Taiwanese government established a clinical trial website, the data on the website are incomplete. The current author proposes that the government be encouraged to improve the quality of the information on this website. Doing so would ensure that patients receive the most recent and relevant treatment recommendations.

To encourage MTB participation and acknowledge the invaluable contributions of MTB participants, governmental organizations or other relevant entities can offer financial incentives or honorific awards to MTB members. Such incentives would serve as a form of recognition and demonstrate appreciation for MTB members' time, effort, and expertise. These financial incentives could include grants or stipends awarded to support the members' MTB activities. Honorific awards, such as certificates or public acknowledgments, can be offered to highlight MTB members' contributions to improving personalized cancer care and research [Table 10].

Table 10: Consensus: Future expectation for molecular tumor boards

Item	Statement	Agreement rate
10-1	Health providers might maintain records of parameters for evaluating MTB performance, including (1) MTB composition, (2) frequency of MTB meetings, (3) the frequency with which cases are reviewed by an MTB, (4) the frequency with which MTB-recommended treatments (e.g., clinical trials, off-label or compassionate use, approved drug treatments, and early access programs) are received, (5) frequency of and reasons for not receiving MTB-recommend treatments, and (6) outcomes of patients who received MTB-recommended treatments	100% (16/16)
10-2	MTB teams should obtain up-to-date information on clinical trials involving genomic sequencing	100% (16/16)
10-3	To encourage MTB participation, governmental organizations should offer financial incentives or honorific awards to MTB members	100% (16/16)

MTB: Molecular tumor board

Discussion

NGS has emerged as an essential tool for treating patients with advanced solid tumors. The current joint consensus statement presents a cohesive set of clinical agreements developed to guide NGS testing in patients with advanced solid tumors in Taiwan. These agreements include several vital focuses that can advance precision oncology, namely, comprehensive molecular analyses, multidisciplinary participation, case selection, patient information, treatment recommendations, performance evaluation, and governmental support.

A detailed explanation for the consensus items of this study for which agreement did not exceed 50% is provided in the following. For the types of experts who should participate in MTBs, geneticists, molecular biologists, bioinformaticians, and laboratory principal investigators were considered valuable but not necessary in all cases. Such experts can offer valuable insights during molecular and genetic data interpretation, identification of potential hereditary factors, and informed selection of targeted therapies and can provide crucial contributions to ongoing research efforts. However, these experts may have been considered unnecessary because of competing demands for human resources within organizations or budgetary constraints, which may affect the recruitment of specialized personnel; data privacy and security concerns resulting from an absence of raw data; and data sharing restrictions. In addition, because the time allocated to each case in MTB discussions varies with the case complexity and available information, the experts of this study did not recommend the implementation of fixed time limits. Time must be sufficient to complete comprehensive discussions and determine optimal outcomes, and therefore, flexibility based on case specifics was determined to be preferable to standardized time constraints.

For statement 3-1, while it is recommended that medical centers establish MTBs for comprehensive cancer care, the practicality of having every medical center equipped with an MTB can be challenging due to resource limitations. For statement 4-1, the reason why case managers and pharmacists are not universally recommended for inclusion in MTB is because some experts believe that it may not be necessary at the current stage. Concerning case managers, some hospitals may already have dedicated case managers for different cancer types, leading to concerns about potential redundancy in functionality if specialized case managers were added to MTBs. In the case of pharmacists, it might be due to limited experience with MTBs in Taiwan, and some experts believe that more time is needed to assess the actual impact of their involvement.

Although we do not have national certificates for genetic counselors in Taiwan, our government has authorized the Taiwan Human Genetics Society and the Taiwan Association of

Genetic Counseling to certificate qualified genetic counselors. The small number of genetic counselors in Taiwan may be due to the reason of a few rare disease cases per year. Therefore, we are not limited to education programs in Taiwan but lack of working positions after they graduate as a certificated genetic counselor. If more health-care providers pay attention to the MTB, the more career opportunities will be.

Oftentimes, the recommended treatment of the MTB is not reimbursed by the National Health Insurance in Taiwan and these targeted treatments may elicit onerous financial stress. Supportive roles such as social workers could be considered part of the members to be involved in the treatment assessment during or after the MTB discussion.

In the current version, due to a lack of in-depth discussion on the specifics of molecular analysis for specific cancer types during the consensus-forming process in Table 2, it is anticipated that the next version of consensus will focus specifically on discussing molecular testing for particular cancer types. This will involve providing more recommendations and relevant details about which molecular tests should be conducted.

The multi-omics approach is broadening cancer research from traditional gene expression to encompass the epigenome, transcriptome, proteome, and metabolome. Although in its early stages, the potential for clinical application in this field is immense, offering the prospect of a more comprehensive understanding and personalized cancer treatments in the near future.

Conclusion

The consensuses of this study are paramount because they represent the first step toward Taiwan developing a standardized MTB system. However, because evidence regarding MTBs in Taiwan is lacking, the recommendations of this study were proposed on the basis of expert opinions. In future, the consensuses of this study can be further developed using concrete evidence. This report can serve as an invaluable guide offering practical insights into the application of precision oncology in routine patient care in Taiwan and can facilitate cancer research in clinical research centers.

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Conflicts of interest

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Supplementary Material

Supplementary Table 1: Molecular tumor board report

Molecular Tumor Board Report
Date (DD-MM-YYYY): _ _ _ _ _ _ _ _

Writer	
Confirmer	
Participants	
Patient information	
Subject ID	
Sex	☐ Male ☐ Female
Age	
Type of cancer	
Stage	
Sample information	
Type of sample	☐ Tumor tissue primary ☐ Tumor tissue metastasis ☐ Plasma sample for circulating tumor DNA ☐ Tumor tissue and germline ☐ Others
Platform	
Tumor cellularity (tissue)/tumor fraction (liquid)	
Quality of concern	☐ Aged tissue ☐ Low tumor cellularity ☐ Others ☐ NA
Time of NGS	☐ At diagnosis ☐ Before systemic therapy ☐ After the failure of standard therapies ☐ After curative therapy
Actionable genetic alterations	
Actionable genetic alterations	☐ Yes ☐ No
Number of actionable genetic alterations	☐ 1 ☐ 2 ☐ ≥3 ☐ No
Treatment recommendation	☐ Standard treatment ☐ Off-label treatment ☐ Clinical trial (trial #:) ☐ Others (palliative care, radiotherapy, etc.)
Evidence of treatment recommendation (refer to the table below)	
Discussion	
Follow-up	

Reference for evidence of treatment recommendation

OncoKB		ESCAT	
Level 1	FDA-recognized biomarker to an FDA-approved drug	Tier I	Alteration-drug match is associated with improved outcome in clinical trials
Level 2A	Standard biomarker to an FDA-approved drug in this indication	Tier II	Alteration-drug match is associated with antitumor activity, but magnitude of benefit is unknown
Level 2B	Standard biomarker to an FDA-approved drug in another indication	Tier III	Alteration-drug match suspected to improve outcome based on clinical trial data in other tumor types or with similar molecular alteration
Level 3A	Clinical evidence supports biomarker to be predictive for a drug efficacy in this indication	Tier IV	Preclinical evidence of actionability
Level 3B	Clinical evidence supports biomarker to be predictive for a drug efficacy in this indication	Tier V	Alteration-drug match is associated with objective response, but without clinically meaningful benefit
Level 4	Biological evidence supports biomarker to be predictive for a drug efficacy	Tier X	Lack of evidence for actionability

ESCAT: ESMO Scale of Clinical Actionability for Molecular Targets, NGS: Next-generation sequencing, OncoKB: Oncology Knowledge Base, FDA: U.S. Food and Drug Administration