Editorial

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The molecular tumor board: a tool for the governance of precision oncology in the real world

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Abstract

Clinical oncology is going through a period of profound change. Targeted therapy, and more recently immunotherapy, have revolutionized the natural history and outcomes of many solid tumors. Clinical oncology is now indissoluble from molecular oncology, a rapidly evolving field. This profound transformation is the rationale for molecular tumor board (MTB) implementation. MTBs represent a resource for the development of precision oncology and clinical practice implementation is a complex and important challenge for the future of clinical and molecular oncology. Economic sustainability of genomic tests, access to drugs or clinical trials according to the MTB recommendation, and expanded use of existing anticancer drugs are required for MTBs to become a useful tool for the governance of precision oncology in the real world. This is an ongoing process, with establishment of MTBs the first step. Continuing to work in collaboration with scientific societies, MTBs are poised to become a homogeneous and well-structured reality that can make the care pathway of the patient with cancer more efficient, with the ultimate goal to offer personalized therapy based on the most advanced scientific knowledge.

Keywords

Molecular profiling, molecular tumor board, mutational oncology, precision oncology

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Introduction

Clinical oncology is going through a period of profound change. Targeted therapy, and more recently immunotherapy, have revolutionized the natural history and outcomes of many patients with solid tumors. Clinical oncology is indissoluble from molecular oncology, a rapidly evolving field.[1] Next-generation sequencing (NGS) launched the era of genomic profiling tests, with several examples of successful congruence between "actionable" tumor alterations with candidate drugs, and making these genetic aberrations "druggable."[2]

In addition to a tumor's morphologic and histologic factors, its genomic makeup may offer great clinical opportunities, leading to more precise patient selection, in which specific molecular alterations present in the tumor become the target of individualized treatment, thus using the new model of mutational oncology to consolidate the well-known concept of treatment personalization in oncology.[3]

This model can now further modify the oncologic therapeutic scenario. The therapeutic choice can be guided by driver mutations and the agnostic biomarkers represent the novel frontier of precision oncology.[4] Actionable agnostic targets become predictive biomarkers for agnostic drugs, active regardless of tumor location and histology.[4] Basket

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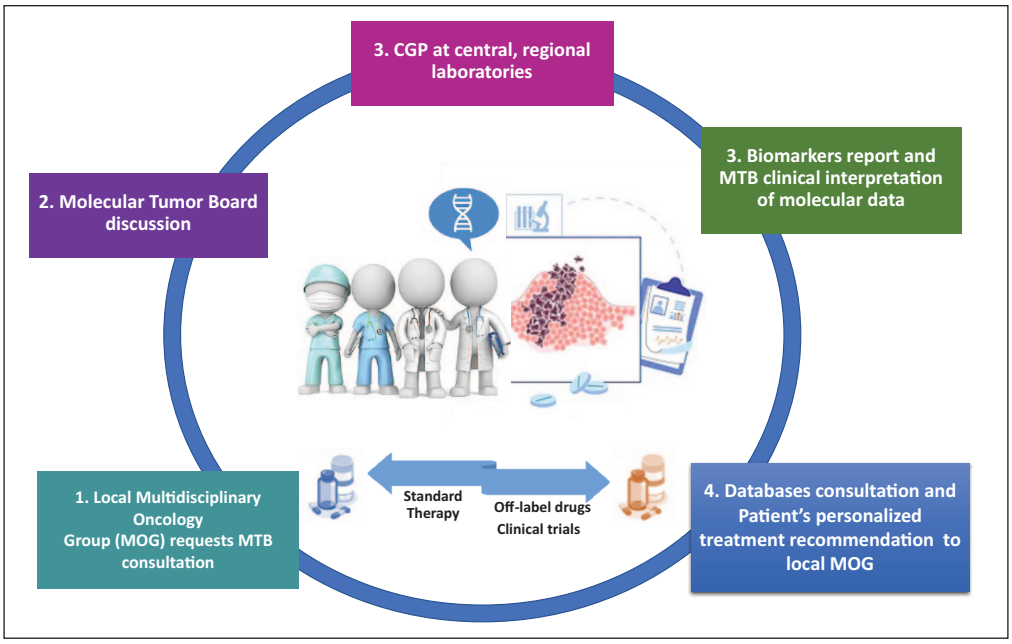

Figure. Challenges of critical implementation of the molecular tumor board in clinical practice.

and umbrella trials have been developed and represent a possible way to accelerate drug development. However, possibly due to strict eligibility criteria, low patient enrollment characterizes these trials and other elements are needed to facilitate the implementation of the precision oncology strategy in the clinic.[5] Indeed, the number of patients with cancer, potential candidates for a molecular profile evaluation, has significantly increased over the years, and at the same time, the number of molecular biomarkers under study as potential therapeutic targets has also increased.[6] The complexity in the interpretation is also increasing. Adequately translating and interpreting the complex genetic and molecular features of the neoplasm into information that clinicians can use to propose the most appropriate and individualized treatment is critical.

This profound transformation is the rationale for molecular tumor board (MTB) implementation.

Molecular tumor board: opportunity for a new therapeutic landscape

MTBs are groups created with the aim to discuss the complexity of clinical cases collectively, to understand the complex genetic and molecular results of profiling tests, and to propose the most appropriate therapeutic strategy based on the active drugs available. MTBs are by definition multidisciplinary and guarantee the involvement of different professionals based on their specific skills and expertise.[7]

MTBs can facilitate clinical trial enrollment or off-label treatments through online database consultation. MTBs may be helpful in selecting the most appropriate biological sample for the molecular analysis, for example, histologic sample or liquid biopsy, and the molecular profiling technologies and molecular test to use.[7] Liquid biopsy with the use of genomic profiling assays provides the opportunity to monitor several actionable mutations.[8] In current clinical practice, liquid biopsy is used for the identification of driver mutations in circulating tumor DNA, with the first clinical applications in non-small cell lung cancer. This is an active field of research and other solid tumors, together with other blood derivatives, are emerging as useful clinical tools.[9]

The MTB is particularly important for some patients: for example, patients with rare or complex molecular alterations, patients with tumors carrying alteration without targeted drugs approved in clinical practice, patients with oncogene-addicted neoplasms not responsive to the molecular drugs available, or patients with rare neoplasms without recognized therapeutic approaches.[7]

Published real-world experiences of MTBs suggest that patients treated with the MTB-recommended regimen according to their tumor molecular alterations showed better outcome in terms of progression-free or overall survival compared to patients treated according to physician choice.[5] Further investigations and randomized controlled trials are needed to determine whether this approach is consistently more effective.

Whereas MTBs represent a resource for the development of precision oncology, clinical practice implementation is a complex and challenging goal for clinical and molecular oncology (Figure).

MTBs: real-world challenges for the governance of precision oncology

Economic sustainability of genomic tests, access to drugs or clinical trials according to the MTB recommendation,

and expanded use of existing anticancer drugs are required in order for MTBs to become a useful tool for the governance of precision oncology.[4,10] This is an ongoing process in which the establishment of MTBs is the first step. Integrated scientific and clinical skills must follow the complex and rapid evolution of cancer genetics and the availability of novel or investigational anticancer therapies. Development of an efficient network system that overcomes heterogeneity in selection criteria of patients, molecular profiling technologies or molecular tests proposed, and choice of medical therapies across different institutions will be a new challenge.[11] It is also important to work for the transparent and efficient accreditation of qualified laboratories performing molecular tests, especially NGS-based assays, and to ensure adequate training for all the professionals involved.[12,13]

Continuing work in this direction and collaboration of scientific societies will enable the MTB to become a homogeneous and well-structured reality that can make the care pathway of the patient with cancer more efficient, with the ultimate goal to offer personalized therapy based on the most advanced scientific knowledge.

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