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The Imperious Need for Molecular Tumor Boards in Portugal

A Necessidade Imperiosa de Consulta de Grupo Multidisciplinar de Oncologia Molecular em Portugal

João MARTINS GAMA [1], Rui CAETANO OLIVEIRA [1,2,3]
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The evolution of technology and advances in knowledge have made precision oncology a reality.[1] The core idea of precision oncology stems primarily from the molecular basis of disease, in which neoplastic lesions are driven by molecular events. The identification of these events enables a precise classification and the development of targeted therapies.[2]

Although it seems like a simple premise, in which the use of sequencing would allow us to provide more detailed answers, reality has proven to be more complex. Initial deoxyribonucleic acid (DNA)-based approaches have expanded to encompass ribonucleic acid (RNA) analysis, epigenetics and other aspects, such as the use of liquid biopsies and minimal residual disease assessment. For example, circulating tumor DNA (ctDNA) enables the detection of resistance mutations in lung cancer, while minimal disease assays in colon cancer have shown prognostic value guiding adjuvant therapy decisions. This fast-paced evolution makes precision oncology a complex and challenging field of study. Despite the promise of targeted therapies, only about half of patients will have an actionable genetic target.[3] To make things even more complex, most tumors will have more than one genetic driver, and tumors under the selective pressure of treatments usually exhibit adaptive responses and acquire resistance. Prospective oncology trials, like the MOSCATO-01, demonstrated that molecularly guided approaches improve progression free survival.[4] Similarly, the WINTER trial demonstrated that integrating RNA-based profiling increased the number of patients who could benefit from tailored therapies.[5]

In recent years, several drugs adjusted to specific molecular alterations have been granted approval. Some genetic changes are validated in specific tumor scenarios, while others are approved in a 'pan-cancer' context. Tumor-agnostic therapies, such as pembrolizumab for microsatellite instability-high tumors and larotrectinib for NTRK fusions, have demonstrated high response rates across diverse tumor types.

This reality has validated the use of molecular pathology methodologies and initiatives that aim for universal access to genomic profiling to guide personalized cancer treatments, such as the French Genomic Medicine Initiative and the British NHS Genomic Medicine Service.[6,7]

The increase in information about each patient and greater access to therapies result in extreme pressure for clinicians, who are expected to attend to an ever-increasing number of patients in a shorter period. The pressure does not allow sufficient time to thoroughly analyze the genetic results, thereby reducing the opportunities that may arise from that information, especially in clinical trials involving off-label therapies.

Precision oncology teams have been established worldwide, including in Portugal, where genetic testing is often performed in external institutions, with the ensuing common communication gaps. As patients are often referred to institutions within the healthcare system, the clinical information may become fragmented or misinterpreted, ultimately compromising optimal patient care. Clinical decision-making in these patients requires integrating information and expertise from multiple specialties, including the types of tests performed, the genetic alterations identified, whether the reported genes are actionable, and whether appropriate clinical trials are available and accessible.

Molecular tumor boards (MTBs) may be the solution to this situation.[8] These teams bring together experts in oncology, pathology, genomics, bioinformatics, and pharmacology to review patient information and identify more effective care options.

One way to alleviate this clinical burden would be to create a multi-institutional MTB, combining healthcare

1. Centro de Anatomia Patológica Germano de Sousa. Coimbra. Portugal.
2. Biophysics Institute. Faculdade de Medicina. Universidade de Coimbra. Coimbra. Portugal.
3. Area of Environment Genetics and Oncobiology. Coimbra Institute for Clinical and Biomedical Research (iCBR). Faculdade de Medicina. Universidade de Coimbra. Coimbra. Portugal.
✉ **Autor correspondente:** Rui Caetano Oliveira. ruipedrocoliveira@hotmail.com
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professionals from referral and reference centers. The development of national or regional molecular tumor boards composed of recognized experts could serve as a specialized workforce dedicated to the assessment of cases, thereby reducing the burden currently placed on MTBs operating solely within academic centers, leading to reduced costs.[9]

Virtual meeting platforms are widely accessible, enabling real-time discussions and decision-making, as well as the immediate sharing of genomic data, imaging studies, and pathology slides, the latter now made possible through digitization. The multidisciplinary and multi-institutional MTB can also serve as an educational tool, particularly in raising awareness of key genomic alterations and report interpretation in smaller medical centers and community oncology practices that lack this expertise. The presence of professionals from these institutions at meetings would be extremely valuable, in contrast to the current reality where they refer the patient to the academic center for a decision, and it returns with a treatment option that is often adopted passively.

The shift from local solutions adopted by academic centers to a nationwide solution would be advantageous from multiple perspectives. Nevertheless, establishing molecular tumor boards in Portugal would require, at least, approval from medical societies, regulation, and the development of an effective collaborative framework.

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CONFLICTS OF INTEREST

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