Cancerworld

Molecular tumour boards: translating data into tailored therapeutics

Manuela Maria Campanelli / 6 April 2023

Developments in molecular diagnostics are allowing us to capture an extraordinarily detailed picture of the genomic and other molecular changes that characterise a given tumour specimen. But making best use of the information at our disposal is proving quite a challenge. How do we deal with the ever-increasing amount of genomic data generated by new techniques such as next generation sequencing? How do we use to best effect the growing number of therapies targeted at specific genes or proteins? How do we match treatments to the oncogenic mutations identified? In short, how do we transform data into information and information into knowledge that can benefit patients?

As the use of next generation sequencing spread to the clinic, it soon became clear that the task of interpreting a tumour's genomic profile and identifying the therapies most likely to be effective against the specific set of genetic alterations would be too much for any single specialist. A solution was needed that would enable expertise from many fields to brought to bear.

The solution found was to develop multidisciplinary molecular tumour boards, which, as Vichitra Behel of the Department of Medical Oncology at Mumbai's Tata Memorial Hospital, and colleagues, write in *JCO Global Oncology*, were created in response to the complexity associated with the delivery of targeted therapies.

A tried and tested approach

The concept of involving specialists from different cancer disciplines in discussing the diagnosis and treatment options for individual patients and making recommendations for their management is not new.

It was Europe's professional cancer societies that first felt the need for such a collective consultation to respond to the rapid development of treatment regimens involving multiple disciplines. In a narrative review of virtual molecular tumour boards, Vittorio Gebbia, of the Medical Oncology Unit of the University of Palermo, says the concept "was first introduced in the UK in 1990s, gaining more strength with the radical reform of the UK's cancer services to ensure patients with cancer high and uniform standard of care, no matter where they might live."

Small multidisciplinary groups, often with no more than four clinicians – usually a medical oncologist, a surgeon, a radiation oncologist and a pathologist – started to form, driven by the concept that care is better when based on a collective decision. This marked the emergence of 'multidisciplinary teams', which currently operate worldwide to optimise the management of patients with cancer.

It is thanks to these initiatives, together with an increasing awareness about the benefits that sharing experiences among experts can have on the quality of patient care, that the collegial discussion of cancer cases has slowly caught on.

Molecular tumour boards – next generation multidisciplinarity

The concept of molecular tumour boards, by contrast, emerged more recently, in response to the 'omics' revolution. They are typically bigger than a multidisciplinary team, and include figures from a wide variety of disciplines, which may include molecular biologist, geneticist, anatomy-pathologist, clinical epidemiologist, bioethicist, clinical pharmacist, hospital pharmacist, and last but not least bioinformaticians and biostatisticians and a data manager – essential in dealing with the huge amount of data.

Molecular tumour boards are now considered an essential component of contemporary cancer care, with a proven impact on clinical management. In the case of patients managed at the Tata Memorial Hospital, Behel notes, "We observed that of the 339 cases discussed in our institution's MTB [molecular tumour board], a recommendation to modify the existing course of clinical management was made in 206 (60.7%) cases."

This indicates that they significantly help oncologists to identify patients who could potentially benefit from targeted therapies, which tend to have less severe side effects than cytotoxic cancer treatments. It also helps them identify the more effective therapy options, and can help patients access those options. But is there evidence that patients actually benefit?

Impact on outcomes

The existing literature looking to define the clinical utility of molecular tumour boards is mainly retrospective, observational, and underpowered for efficacy, but has been growing consistently in the past couple of years.

A systematic review, published in *JCO Precision Oncology*, concluded that molecular tumour boards appear to improve clinical outcomes for cancer patients. Two prospective trials pointed to an improvement in survival indices for patients with a wide variety of tumour types and in patients with non-small-cell lung cancer. A clinical trial conducted by the University of Kentucky Markey Cancer Center, in patients with advanced cancer, found that therapy directed by molecular tumour boards led to patients surviving longer without further tumour progression than had been the case with the therapy they had been prescribed immediately prior to the trial.

"The study suggests that the precision medicine expertise offered by an MTB can lead to better

outcomes even in patients with advanced cancer who have already received treatment," said Jill Kolesar, professor at University of Kentucky's College of Pharmacy and one of the study authors, who directs Markey's Precision Medicine Center and co-directs the molecular tumour board.

> "Expertise offered by an MTB can lead to better outcomes even in patients with advanced cancer who have already received treatment"

Molecular tumour boards can also promote cancer patients' enrolment in clinical trials. A good example is the one at the Institut Curie in Paris, which implemented a three-year molecular screening programme that detected actionable molecular alterations to guide patients in relevant clinical trials. The Institute's molecular tumour board "enabled the inclusion of 10% of patients into a clinical trial with matched therapy," wrote Clémence Basse, of the Department of Drug Development and Innovation at Institut Curie, and co-authors, in 2018.

In addition to translating the complexity of precision medicine into better outcomes, including better control or even cure, molecular tumour boards can also focus attention on family members, identifying germline mutations that could require further genetic testing and counselling for patients and their relatives. Additional advantages include reducing the impact of personal bias on treatment recommendations and helping patients feel more comfortable. The discussions can also play a valuable educational role, allowing team members to learn from one another

Work in progress

While molecular tumour boards are now widely recognised as part of best practice in cancer management, and are recommended by many statutory bodies worldwide, obstacles remain that hinder their full implementation. The relative lack of clear policies or of universally endorsed organisational criteria, the medico-legal challenges associated with team-based decisions, and poor development of guidelines and best practices, have favoured a heterogeneous and fragmented development of the molecular tumour board landscape.

Back in 2013, the perceived need to stipulate fundamental principles for the functioning of multidisciplinary teams prompted a wide array of European oncology organisations to draw up a policy statement within the framework of the European Partnership for Action Against Cancer (the first of three European Joint Actions on cancer). The policy statement identified five key areas for policy relating to multidisciplinary teams: precise care objectives, organisation, clinical assessment, patients' rights, and empowerment and policy support.

These experiences have raised awareness in the scientific world to the point that some countries are now defining in law some of the criteria, modalities and procedures required to set up molecular tumour boards. A case in point is Italy where, in February 2023, the Minister of Health approved by decree a document that defines a standard pathway for identifying specialist centres for genomic profiling with next generation sequencing, and to establish regional molecular tumour boards that will be coordinated by a single national centre.

The document also details procedures for quality control and updating of the regional molecular tumour boards; defines their composition, competencies, and timing; and specifies rules covering access to diagnostic tests and drugs.

In an effort to encourage a unified approach at a global level, a tool to measure the 'maturity' of molecular tumour boards in the categories of Access, Consultation, Technology and Evidence has been developed and tested on 20 boards, spanning the USA, Europe and Asia-Pacific, to identify areas that would benefit from standardisation. This 'validity testing' revealed that, "the average maturity score was 3.3 out of 5, with MTBs in academic institutions showing significantly higher overall maturity levels than in non-academic institutions," wrote Okan Ekinci, Global Head of Marketing & Innovation at Roche Information, and adjunct professor at University College of Dublin's School of Medicine, in a 2022 study he co-authored.

> "Only a small percentage of patients found to have actionable biomarkers actually receive innovative molecular drugs"

Another severe obstacle to maximising patient benefit from molecular tumour boards is that many patients cannot access the drugs that are indicated. Only a small percentage of patients found by next generation sequencing to have actionable biomarkers actually receive innovative molecular drugs.

There are different reasons for this. Trial eligibility restrictions sometimes exclude patients from enrolment in recommended studies; reimbursement may be not available for off-label therapies, and getting drugs under compassionate use can be time-consuming and complicated from a regulatory standpoint.

Global turnround time for molecular tumour board decisions, defined as the time necessary for genomic testing and for the board to consider and make its recommendations, also impacts on the possibilities for implementing the recommended treatments. The turnaround time needs to be reasonably fast in order to avoid patients' clinical conditions deteriorating. Holding board meetings virtually offers one option that could help speed things up. A system developed over four years at Georgetown University Medical Center, Washington DC, reduced turnaround time from data receipt to report delivery from 14 days to 4 days and nearly doubled the volume of cases handled each year.

Molecular tumour boards are evolving quickly, and technological innovation is helping speed up their turnaround times. Videoconferencing technology, boosted by the Covid-19 pandemic, has facilitated the transition from face-to-face tumour boards to virtual ones, allowing physicians to easily participate by just clicking a link. Although this process requires a secure web platform to ensure that patients' privacy is respected, it improves participants' attendance and reduces travel time for health professionals and others.

Virtual molecular tumour boards also facilitate interactions between centres, helping overcome geographical barriers and the restrictions of limited funds and resources. And yet to be defined is the role that artificial intelligence may play in improving clinical decision making. It is certainly a cutting-edge tool that, with the proviso that it draws only on safe and well-maintained databases, could in future help molecular tumour boards manage the ever increasing volume of relevant data.

Illustration by Sara Corsi