

A Step towards Personalised Cancer Treatment in Lower Middle-income Countries (LMICS): Molecular Tumour Boards

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ABSTRACT

Tumour boards are meetings where physicians from various disciplines treating cancer patients meet to recommend evidence-based or the best possible treatment plan. These meetings have evolved with time and now, in every part of the world; site-specific multi-disciplinary tumour boards are established. These meetings are considered pivotal for improving patient outcomes. The advances in molecular and genetic knowledge and technique and their integration in treatment options have paved the way for multiple therapeutic options. However, the adoption of personalised treatment choices is associated with a huge financial burden, especially in low and middle-income countries (LMICS). A molecular tumour board can help to identify and suggest the most appropriate plan of management.

Key Words: Molecular, Genetics, Personalised, Challenges.

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With a continuously evolving oncology field, it is impossible for the cancer-care provider to be updated in all disciplines. This challenge can be mitigated, to a large extent, by the establishment of multidisciplinary tumour board meetings and providing a comprehensive management plan for patients. In the recent past, connecting all related disciplines has been swift and has transitioned from general to site-specific multidisciplinary tumour boards.

The recent developments in molecular pathology and translational science have opened new avenues for cancer prevention, early detection, diagnosis and treatment, and have been termed as precision oncology. Just as the knowledge of HER2-amplification in breast cancer, mutations in estimated glomerular filtration rate (EGFR) and anaplastic lymphoma kinase (ALK) genes in patients with non-small cell lung cancer (NSCLC) is mandatory to prescribe appropriate targeted therapies, it is equally important to know the tumour mutational burden (TMB), the status of mismatch repair proteins (MMR), *b-raf* mutations, breast cancer (BRCA) gene mutation and neurotrophic tyrosine receptor kinase (NTRK) fusion in several cancers to guide the treatment.

Comprehensive genomic profile (CGP) combines immunohistochemistry, transcriptomics, and gene sequencing to allow to choose not only the druggable molecular alterations, but also the driver mutations, and the mechanisms of resistance. Alternatively, the results may direct the oncologist and the patients to an ongoing clinical trial. These tests also help in establishing diagnosis and communicating prognosis. This information at the genetic and molecular level helps an oncologist to provide personalised cancer management. Pursuing the concept of personalised treatment in the modern era can be further enhanced with the establishment of a molecular tumour board (MTB). With constantly increasing opportunities for precision oncology and closing the gap between diagnosis and matched targeted therapies, the importance of the role of MTBs is ever-growing.¹⁻⁴

MTB is a relatively new and evolving concept in the literature.⁵⁻⁷ In order to establish an MTB, a medical oncologist, surgeon, radiation oncologist, pathologist, radiologist, geneticist and genetic counsellor, clinical pharmacist, molecular pathologist, and bioinformatician are considered the core members.⁶

MTB can enhance the quality of patient care and the institution's reputation in several ways. The selection of patients, optimum time to do CGP in the course of illness, and the turnaround time of the molecular results have been under debate.⁸ Patients discussed in the MTB usually have exhausted multiple lines of treatment, and no guideline-based treatment is available. Additionally, a heterogeneous group of rare tumours, such as sarcoma, is frequently discussed. More recently, with the advent of immune checkpoint inhibitors and other tissue

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agnostic tyrosine kinase inhibitors, common tumours such as lung and colo-rectal cancers and other diverse tumour types are also discussed. Rare cancer collectively represents 1/4th of all tumour types, and in the absence of standard-of-care treatments, especially at relapse, the cases could be discussed in MTB. For many physicians, the optimum time to ask for the Next-generation sequencing (NGS) would be at the time of diagnosis for patients with rare cancers, and at the time of relapse for patients not responding to standard-of-care systemic therapies. MTB should also discuss the pre-analytical aspects of the outcomes, such as selection of tissue, informed consent in the case of a germline mutation, and the management plan, especially in the case of false-negative results. It is also important to keep in mind the turnaround time of almost 4-6 weeks before the results could be discussed further in MTB. Finally, the impact of the results should be kept in mind. Targeted therapies and expanding are expensive. For example, in one series of 191 patients, 69% underwent molecular testing using NGS, of whom 34.5% were identified to have actionable mutations.⁹

The leading cancer centres have initiated MTBs, intending to provide precision care. A recently published systematic review reported 6303 cases from 40 centres discussed in MTB from all around the world, highlighting its adaptation.¹⁰ MTB may also pave the way for more research. One example is to study the correlation between gene alterations and radiological features, the so-called 'radio genomics'.^{11,12} Furthermore, MTB may help institutions to develop collaboration to increase clinical trial participation. The Global Alliance for Genomics and Health has published literature emphasising the importance of sharing genomic data sets and stressing the need of a globally harmonised, more effective data sharing culture. Furthermore, MTB can be used for quality care. A survey on global practices for sequencing cancer samples found wide variation in procedures, with bioinformatics pipelines employing different mutation calling/variant annotation algorithms.¹³ Siu *et al.* reviewed key molecular profiling and big data initiatives in cancer care, including the current data with challenges and potential solutions. MTB can facilitate the interpretation of cancer genomics and thus, optimal MTB functioning.¹⁴

On the one hand, MTB helps to guide precision treatment, which may improve the efficacy of treatment, reduce undesired toxicity, and save the cost; on the other, setting up the core facilities for the MTB, such as NGS may be expensive, especially in resource-constrained settings and countries, such as the LMICs. Furthermore, the cost of adaptation and procurement of personalised treatment may also be a major hurdle. The treatment of cancer is already expensive, especially for the pay-out-of-pocket payers. A data study of Surveillance, Epidemiology and End-Results Program (SEER) data 2.7 times more chances of bankruptcy as compared to non-cancer patients, in one of the best health systems in the world. The same statistic was quoted for the younger population who are at a greater risk of bankruptcy.¹⁵ Seventy-nine percent of cancer patients were reported to be suffering from a moderate to catastrophic financial burden during the treatment, also leading to a greater risk of

death as compared to non-cancer patients.¹⁶ A new term, "financial toxicity" has emerged, underscoring the need for judicious use of the technology.

Setting up MTB in LMICs should be carefully considered. The cost of setting up the NGS, the interpretation by the bio-informatician, and the discussion with geneticist, can be reduced by establishing MTBs in centre of excellence and allowing cancer centres the access through teleconferencing. This would not only curtail the cost, save the travelling time, but will also provide the expert advice and a second opinion from the experienced oncologists in academic institutions and centres of excellence. Secondly, the general oncologist should receive awareness and education about the importance of CGP in different patients and indications for referring patients to MTB. Thirdly, the addition of a financial counsellor to the MTD may help to identify possible sources of funding. Finally, patients may be directed to ongoing clinical trials, or alternatively, clinical trials may be initiated, and the patients could be recruited.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

AMH: Concept designing, drafting, final approval, agreement to be accountable for all aspects of the work.

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