Crowdsourcing Molecular Knowledge: A Practical and Affordable Approach to Create a Molecular Tumor Board

Bruno Murad[1] Auro Del Giglio[2] Andre M. Murad[1]

[1] Personal – Oncologia de Precisão e Personalizada, Belo Horizonte, MG, Brazil
[2] Faculdade de Medicina do ABC, Santo André, SP, Brazil

Address for correspondence Bruno Murad, MD, Rua Padre Rolim, 120 - Santa Efigênia, Belo Horizonte - MG, 30130-090, Brazil (e-mail: b.muradc@gmail.com).

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Abstract

Objective To evaluate the feasibility and effectiveness of implementing virtual molecular tumor boards (MTBs) through crowdsourcing molecular knowledge among Brazilian physicians to comprehensively discuss complex genomic information on cancer patients.

Materials and Methods We established a virtual group on WhatsApp (Meta Platforms, Inc.) consisting of medical oncologists, radiation therapists, oncogeneticists, radiologists, nuclear medicine personnel, oncologic surgeons, and pathologists from various institutions across Brazil.

Results From September 2022 to May 2024, the group discussed 22 cases, averaging 3.3 patients per month. The main primary cancer types discussed included breast cancer (6 cases), lung cancer (5 cases), and colorectal cancer (4 cases). The group suggested management options for all cases discussed.

Conclusion Crowdsourcing molecular knowledge through a virtual group of physicians has proven to be a feasible and effective solution for developing countries facing financial constraints to fund single institutional MTBs. This approach enabled comprehensive discussions on complex genomic information, providing valuable management options.

Keywords
- crowdsourcing
- precision oncology
- virtual collaboration
- low-resource settings
- cancer genomics

Introduction

The advent of precision medicine has revolutionized cancer treatment by tailoring therapies to individual patients based on the molecular characteristics of their tumors. The molecular somatic sequencing of tumors and germinative DNA through next-generation sequencing (NGS) has become a standard practice in cancer care.[1] The interpretation of the results of these tests is not always straightforward, requiring the expertise of several professionals, such as molecular biologists, pathologists, clinical oncologists, and geneticists. In most reference cancer centers, these professionals meet periodically at molecular tumor boards (MTBs), where clinical cases with complex genomic information are comprehensively discussed.[2] In developing countries such as Brazil, where most health institutions care for underserved patients in the Brazilian Unified Health System (Sistema Único de Saúde, SUS, in Portuguese), financial constraints limit simultaneous access to these professionals in an MTB. Therefore, the cases of some patients with complex genomic information do not undergo a multidisciplinary discussion due to the lack of an institutional MTB.

Materials and Methods

We initiated a crowdsourcing approach to molecular knowledge by assembling a group of Brazilian physicians from multiple cities and institutions into a virtual WhatsApp

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(Meta Platforms, Inc.) group. The group consisted of medical oncologists (n = 68), radiation therapists (n = 4), oncogeneticists/molecular biologists (n = 3), radiologists (n = 3), nuclear medicine personnel (n = 3), oncologic surgeons (n = 5), gynecologic oncologists (n = 3) and pathologists (n = 2). Most of the cases discussed were of breast cancer (6), followed by lung (5) and colorectal cancers (4) (►**Table 1**).

Patient confidentiality was safeguarded by prohibiting the sharing of identifiable information. Treating physicians were instructed to summarize cases using de-identified data only, and no patient names, initials, dates of birth, or hospital

Table 1 Cases discussed through a crowdsourced molecular tumor board

Case	Cancer type	Genomics data available	Previous treatment	Suggested management
1	Breast cancer	HR +; Her2 negative; BRCA wt; PIK3CA wt, NTRK; AKT1 wt; PDL1 wt	Ribociclib + fulvestrant	Capivasertib or everolimus + exemestane
2	Metastatic colon cancer	Negative for germline mutations; *MSH2* somatic mutation	N/A	Immunotherapy
3	Metastatic NSCLC (adenocarcinoma)	R337H; nonsense somatic mutation of *RB1* (VAF 56%); germline mutation (LP variant); PDL1: 20%; ERBB2: V659E mutation	N/A	Immunotherapy: anti-HER2 in case of disease progression
4	Metastatic high-grade Serous ovarian cancer	N/A	Chemotherapy	Deruxtecan or TDM-1 or pertuzumab + trastuzumab
5	Colon adenocarcinoma	Immunohistochemistry: absence of PMS2 expression; MSI-H status; MLH1 promoter hypermethylation	N/A	DNA methylation profiling for MLH1 and PMS2; anti-HER2 ADC or TDM-1
6	Metastatic breast cancer	ER+ (80%); PR+ (50%); HER2+ (IHQ 3 +)	N/A	Bone biopsy: tissue NGS
7	Invasive lobular breast cancer	ER 3%; PR 1%; HER2 1+	Doxorubicin + cyclophosphamide	Adjuvant treatment only after ctDNA
8	Malignant peritoneal mesothelioma	N/A	N/A	Somatic NGS: if no actionable mutations, start chemotherapy/anti-PD1 or nivolumab/ipilimumab
9	Stage-IV NSCLC (adenocarcinoma) brain metastases	Foundation (lung): mutations in *ATM*, *BRCA2* (V22 fs 4), *STKII* e *KRAS G12C*; foundation (breast): mutations in *BRCA2* (V22fs4 K437 fs22), *CBFB* loss exons 1–3, *ETV6* rearrangement, tp53 loss exon 2–11	Chemoimmunotherapy	First mutation (p.Val220Ilefs4) led to a frameshift: non-functional *BRCA2*; second mutation, K437fs22, rectified the reading frame of exon 11: functional *BRCA2*; sotorasib in case of disease progression
10	Stage -IV pancreatic adenocarcinoma	*KRAS G12D*	N/A	MRTX1133 RAS multi(on) triplex inhibitors or sotorasib/adagrasib
11	NSCLC (adenocarcinoma)	TARGET one: mutation in *EGFR* (NM_005228.5:c.2156 G > C, in exon18) liquid biopsy guardant: mutation in *EGFR*: G719A (0,9%).	Carboplatin + permetrexed > afatinib > carboplatin + paclitaxel + bevacizumab + atezolizumab > gemcitabine	Amivantamab + lasertinib with or without chemotherapy
12	Stage-IA invasive ductal breast cancer	ER 90%; PR 35%; HER2 3 +.	N/A	Neoadjuvant: dual HER2 blockade + adjuvant: trastuzumab
13	Locally-advanced gastro-esophageal junction adenocarcinoma	PD-L1 50 (DAKO); preserved expression of *PMS2* (EP51), *MLH1* (ES05), *MSH6* (EP49) e *MSH2* (FE11). *HER2* negative (IHC); no somatic sequencing	Chemotherapy	Surgery: immunotherapy in case of residual tumor

Table 1 (*Continued*)

Case	Cancer type	Genomics data available	Previous treatment	Suggested management
14	Triple-negative breast cancer	*BRCA1*	Neoadjuvant pembrolizumab	Pembrolizumab for 1 year; do not start PARPi due to pCR
15	Pulmonary Fibrosis + High Risk Pulmonary nodule	*TP53* A276D	N/A	Bone-marrow aspirate; if negative, it confirms somatic *TP53* mutation
16	Metastatic colorectal cancer	Foundation: *EGFR* exon 19 deletion (L747_S752del); *CDK4* amplification; *MDM2* amplification; *MYC* amplification; *MAP3K1* rearrangement exon 3; *RAD21* amplification; guardant: (cfDNA): ATM: R3008H (0,3%); EZH2: V626M (0,2%)	Osimertinib	Chemotherapy (low response to immunotherapy due to *MDM2* amplification)
17	Luminal B breast cancer; clear cell renal carcinoma	Missense variant *MLH1* c.794G > A: p.(Arg265His) rs63751448: VUS	N/A	Probable pathogenic *MLH1* mutation; perform broader NGS panel
18	Stage-IV NSCLC (squamous)	PD-L1 negative	N/A	Low TMB: carboplatin/nab-paclitaxel + pembrolizumab; high TMB: ipilimumab/nivolumab
19	Serous ovarian carcinoma + peritoneal carcinomatosis	*RAD51C* variant: c.656T > C; p.(Leu219Ser): VUS	N/A	Needs broader NGS panel
20	Extra-hepatic colangiocarcinoma; pancreatic adenocarcinoma	N/A	N/A	Neoadjuvant durvalumab -> surgery; or FOFLIRINOX; immunotherapy only if MSI-high
21	Stage-IV sigmoid adenocarcinoma	*TMB* 13,23; guardant: PIK3CA H1047R	Oxaliplatin + irinotecan + panitumumab	Trifluridine- tipiracil and bevacizumab
22	Metastatic papillary thyroid carcinoma	IHC: *BRAF* V600E +; TTF-1 +; CK19 +; HBME-1 +; Galectin-3 + foundation one (lung): PDL-1 10%; *BRAF* V600E mutation; loss of CDKN2A/B on exon 1 and CDKN2B Oncofoco: *BRAF* p. Val600Glu; amplifications: *MET*, *BRAF*, *CDK6*, *HGF*, *NKX2-1*, *PIK3CG*, *SMO*; genomic instability analysis: MSS; TMB: low/intermediate (5,8 mutations/Mb)	Trametinib and dabrafenib	Thyroidectomy + iodine-131; or cabozantinib or lenvatinib

Abbreviations: ADC – Antibody–Drug Conjugate; AKT1 – AKT Serine/Threonine Kinase 1; ATM – Ataxia Telangiectasia Mutated; BRAF – B–Raf Proto–Oncogene, Serine/Threonine Kinase; BRCA1 / BRCA2 – Breast Cancer Gene 1 / 2; CBFB – Core–Binding Factor Subunit Beta; CDK4 / CDK6 – Cyclin–Dependent Kinase 4 / 6; CDKN2A / CDKN2B – Cyclin-Dependent Kinase Inhibitor 2A / 2B; cfDNA – Circulating Cell–Free DNA; CK19 – Cytokeratin 19; ctDNA – Circulating Tumor DNA; DAKO – Dako (commercial antibody diagnostic platform); EGFR – Epidermal Growth Factor Receptor; ER – Estrogen Receptor; ERBB2 – Erb–B2 Receptor Tyrosine Kinase 2 (also known as HER2); ETV6 – ETS Variant Transcription Factor 6; FOLFIRINOX – 5-Fluorouracil + Leucovorin + Irinotecan + Oxaliplatin; fs – Frameshift; HBME-1 – Hector Battifora Mesothelial Cell 1; HER2 – Human Epidermal Growth Factor Receptor 2; HR+ – Hormone Receptor Positive; IHC / IHQ – Immunohistochemistry; KRAS – Kirsten Rat Sarcoma Viral Oncogene Homolog; LP (variant) – Likely Pathogenic (variant classification); MAP3K1 – Mitogen-Activated Protein Kinase Kinase Kinase 1; MDM2 – Mouse Double Minute 2 Homolog; MET – Mesenchymal–Epithelial Transition Factor; MLH1 – MutL Homolog 1; MMR – Mismatch Repair; MSH2 / MSH6 – MutS Homolog 2 / 6; MSI–H – Microsatellite Instability–High; MSS – Microsatellite Stable; MYC – MYC Proto–Oncogene; N/A – Not Available; NGS – Next-Generation Sequencing; NKX2-1 – NK2 Homeobox 1; NTRK – Neurotrophic Tyrosine Receptor Kinase; NSCLC – Non–Small Cell Lung Cancer; PARPi – Poly (ADP–Ribose) Polymerase Inhibitor; PD–1 – Programmed Cell Death Protein 1; PD–L1 – Programmed Death–Ligand 1; PIK3CA / PIK3CG – Phosphatidylinositol–4,5–Bisphosphate 3–Kinase Catalytic Subunit Alpha / Gamma; PMS2 – Postmeiotic Segregation Increased 2; PR – Progesterone Receptor; RCC – Renal Cell Carcinoma; RAD21 / RAD51C – RAD21 Cohesin Complex Component / RAD51 Paralog C; RB1 – Retinoblastoma 1; STK11 – Serine/Threonine Kinase 11; T–DM1 – Trastuzumab Emtansine; TMB – Tumor Mutational Burden; TP53 – Tumor Protein p53; TTF–1 – Thyroid Transcription Factor 1; VAF – Variant Allele Frequency; VUS – Variant of Uncertain Significance; wt – Wild Type

registration numbers were allowed. Consent for molecular testing and subsequent discussion was obtained by the treating physicians as per institutional standards.

Discussions followed a semistructured format. Treating physicians presented molecular and clinical data in writing, and other members contributed asynchronously with their opinions, literature references, or management suggestions. While the exchanges were not moderated in real time, the treating physician summarized the discussion to ensure clarity and to highlight potential management strategies.

For each case, management options were suggested based on the genomic findings and clinical context provided by the treating physician. However, apart from some cases in which the treating physician shared treatment decisions and outcomes voluntarily, we did not prospectively follow whether these recommendations were implemented in the clinical practice, nor did we collect systematic information on patient outcomes.

Results

From September 2022 to May 2024, we discussed 22 cases, with an average of 3.3 patients discussed per month (►**Table 1**). The group suggested management options for all cases to the treating physicians.

As an illustration, we discussed the case of a 65-year-old female patient previously diagnosed with metastatic lung cancer carrying a *BRCA2* mutation that had spread to the central nervous system and was treated with olaparib after failing cisplatin-based chemotherapy and brain radiation therapy. Olaparib had a stabilizing effect on her tumor for approximately 30 months. During a routine follow-up, a new triple-negative breast tumor was identified. Genetic testing revealed the presence of two separate *BRCA2* gene mutations in the breast tumor. The initial mutation (p.Val220Ilefs4) caused a frameshift, producing a truncated and non-functional BRCA2 protein. However, the second mutation, K437fs22, corrected the reading frame of exon 11, enabling Rad51 to bind to BRCA2 properly. This new mutation restored the functionality of BRCA2, explaining the clinical resistance observed in the breast tumor. The patient underwent breast tumorectomy and radiation therapy, and she continues olaparib, with a stable disease.[3]

Discussion

The present study showed that creating a multidisciplinary virtual group to discuss oncological cases with complex genomic information is a feasible and affordable alternative even for developing countries where financial resources are scarce to fund single institutional MTBs. The group's role was limited to generating and sharing potential management strategies; clinical implementation remained at the discretion of the treating physician. This distinction is important because, while the discussions demonstrated that a WhatsApp-based MTB is feasible, the absence of follow-up prevents us from drawing conclusions about its real-world impact on treatment decisions or patient survival.

An important strength of our model is that patient confidentiality was preserved by using only de-identified case summaries, while allowing broad access to expert input. The discussions were semistructured and conducted asynchronously, which lowered barriers to participation compared to traditional MTB meetings.

The advantages of the WhatsApp group are the low costs involved, the non-synchronic means of communication, in which the professionals may answer at any time they prefer and not need to meet at a particular time, unlike the usual MTBs, which meet either in person or virtually.

The current study has several limitations, such as its non-prospective design, the small number of cases discussed, and the lack of systematic follow-up on all patients. While some outcomes were shared by the treating physicians, a structured collection of follow-up data would strengthen future studies. Another limitation is that case presentations were not structured based solely on the abbreviated information posted by the treating physicians, and we could not ascertain if all relevant specialists saw each case, as only a few physicians in the group posted their comments on each case. Furthermore, other non-medical professionals such as pharmacists could complement the physicians' inputs and further contribute to the case discussions.

Conclusion

In conclusion, implementing virtual MTBs through crowdsourcing of molecular knowledge through a virtual group of physicians has proven to be a feasible and effective solution for developing countries facing financial constraints to fund single institutional MTBs. This approach has enabled comprehensive discussions of complex genomic information and has provided valuable management options for treating physicians. The case herein reported illustrates the potential of this approach, as it resulted in a successful treatment outcome for a patient with metastatic lung cancer and a secondary breast tumor carrying multiple *BRCA2* gene mutations. Further research and implementation of this approach in other countries with limited access to traditional MTBs could greatly benefit cancer patients and improve their outcomes.

Author Contributions

BM: data curation, investigation, methodology, writing - original draft, writing - review and editing, project administration; DGA: conceptualization, supervision, validation, writing - review and editing; AMM: writing - review and editing, conceptualization, investigation.

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Conflict of Interests

The authors have no conflict of interests to declare.

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