EMJ

Interview

Volume 10 Supplement 9
July 2022
emjreviews.com

The Role of Molecular Pathology, Early Testing, and Informatics in the Multidisciplinary Team Approach in Cancer Care: Interviews with Two Key Opinion Leaders

Oncology

The Role of Molecular Pathology, Early Testing, and Informatics in the Multidisciplinary Team Approach in Cancer Care: Interviews with Two Key Opinion Leaders

Interviewees: Russell Petty,[1] Helmut Popper[2]

1. Ninewells Hospital and Medical School, University of Dundee and NHS Tayside, Scotland, UK
2. Institute of Pathology, Medical University of Graz, Austria

Disclosure: Petty has received individual financial support from AstraZeneca, Bristol Myers Squibb, Eli Lilly, Pfizer, Roche, Sanofi, and Servier, and institutional financial support from Amgen, Astellas, Boston Biomedical, Clovis, Eli Lilly, Five Prime Therapeutics, Janssen, Merck Serono, MSD, and Roche. Popper acted/acts as a consultant on the advisory boards of AstraZeneca, Bristol Myers Squibb, Eli Lilly, Hofmann La Roche, and Novartis, and has received unrestricted research grants from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Pfizer, and Roche.

Acknowledgements: Medical writing assistance was provided by Brigitte Scott, MarYas Editorial Services, Cowlinge, UK.

Disclaimer: The opinions expressed in this article belong solely to the named interviewees.

Support: The publication of this article was funded by a medical educational grant from AstraZeneca, with the purpose of enhancing the fundamental understanding of oncology specialists of the value of a multidisciplinary team approach in the management of patients with cancer, and the role of molecular pathology, early testing, and informatics in the multidisciplinary approach in cancer care.

Citation: EMJ Oncol. 2022;10[Suppl 9]:2-8. DOI/10.33590/emjoncol/22C0320. https://doi.org/10.33590/emjoncol/22C0320.

Interview Summary

For this article, the EMJ conducted interviews in April and May 2022 with two key opinion leaders, Russell Petty from Ninewells Hospital and Medical School, University of Dundee and NHS Tayside, Scotland, UK, and Helmut Popper from Institute of Pathology, Medical University of Graz, Austria, both of whom have a wealth of experience and expertise in the multidisciplinary care of patients with cancer. The experts gave valuable insights into topics such as the inclusion of molecular pathology, the feasibility of early testing, and the importance of informatics in the multidisciplinary team (MDT) approach.

This article discusses how molecular pathology fits alongside traditional anatomical pathology, and the role of molecular MDTs in the management of patients with cancer. The need for education of MDTs about interpretation of molecular pathology findings and the value of informatics are also explored.

MOLECULAR PATHOLOGY AND THE MULTIDISCIPLINARY TEAM APPROACH

Inclusion of Molecular Pathology in Multidisciplinary Cancer Care

Petty, a practicing oncologist specialising in gastrointestinal (GI) tract cancer, described traditional anatomical pathology as the foundation that underpins the diagnosis of cancer, and advocated that both anatomical and molecular pathology are needed in the MDT approach to cancer care. According to Petty, molecular pathology is currently of great importance, and is becoming increasingly significant as it enables more precise diagnosis and treatment selection. Petty noted that the use of molecular pathology for treatment selection has expanded rapidly in recent years, and there are now few oncology subspecialties for which molecular pathology testing is not essential. Petty considered that a "tumour agnostic approach" to treatment selection based on molecular findings is valuable, but anatomical pathology still has a role in determining clinical tumour behaviour and defining some of the key basic clinical treatment protocols, including locoregional treatments such as surgery and radiotherapy, some systemic treatment, for managing patient symptoms, and identifying the type of specialist nurse and community care the patient needs. In concurrence, Popper, a molecular pathologist specialising in lung cancer, emphasised that molecular pathology has been a part of the pathologist's workload since 2009, and is an essential element of the pathology discipline and a standard requirement in the MDT approach.

Utilising Molecular Pathology Alongside Traditional Anatomical Pathology: Impact on Patient Diagnosis, Management, and Outcomes

Petty explained that current clinical practice comprises anatomical and histopathological definitions of cancer, and these are subdivided by molecular pathology into biomarker-defined subcategories that direct how an oncologist can best treat their patient. Petty acknowledged that molecular subgroups have not yet been fully defined for many of the common cancers; however, molecular subclassification of cancer is an expanding area, and Petty expected molecular subclassification to be available to increasing numbers of patients in the future. According to Petty, the incorporation of molecular pathology in the MDT approach for patients with cancer is most advanced in the field of non-small cell lung cancer (NSCLC), with clinical practice in this area leading the way in terms of developing and implementing diagnosis and treatment paradigms. He added that the lessons learned in NSCLC in this regard are valuable to clinicians and MDTs managing patients with other types of cancer.

Popper described molecular pathology as a critical part of the diagnostic process. He explained that in his native Austria, a pathologist, rather than a specialist molecular pathologist, presents the traditional anatomical pathology data and the molecular pathology findings to the MDT. The MDT then makes an informed decision about the most suitable therapy for the patient based on the molecular data and factors such as patient status and tumour characteristics, with the oncologist making the final decision about treatment. Popper explained that molecular pathology adds to traditional anatomical pathology by identifying gene mutations that provide a rationale for a particular treatment option (e.g., mutations in the epidermal growth factor receptor gene in patients with lung cancer prompt clinicians to consider treatment with tyrosine kinase inhibitors). This enables clinicians to optimise treatment for the patient, which may translate to improved patient outcomes.

Petty considered that molecular pathology in the past has "smouldered, rather than caught fire," as there was little available evidence that it would direct targeted treatments or immunotherapies and improve patient outcomes. He now believes that there is ample clinical trial evidence to support the concept that molecular pathology alongside traditional anatomical pathology improves patient outcomes, and the availability of this evidence explains why molecular pathology has recently gained so much traction, and is evolving so quickly.

Who Drives the Incorporation of Molecular Pathology into Multidisciplinary Cancer Care?

In Petty's opinion, the incorporation of molecular pathology into multidisciplinary cancer care is usually driven by oncologists, who review the clinical trial data and follow up with molecular pathologists to see which biomarker evaluations are possible. Popper considered that the driver of the collaboration between clinicians and molecular pathologists depends on the tumour type, the geographical location of the institution, and the historical set-up of the collaboration. For example, in Austria, a diagnosis of NSCLC, particularly adenocarcinoma or squamous cell lung carcinoma, automatically prompts an in-house molecular diagnostics work-up without having to wait for oncologists to request molecular data; so-called "reflex testing". Popper clarified that although reflex testing is standard practice for NSCLC in Austria, this is not the case for all other types of cancer, and reflex testing is not established in every country. In agreement with Petty, Popper noted that in GI tract cancer, molecular pathology data are usually produced following a request by the oncologist. Petty described that reflex molecular testing across all types of cancer is increasing in the UK as part of the expansion of molecular pathology. The driver for this is to ensure timely availability of results for clinical decision-making at the optimal time in patient diagnostic pathways.

Which Patients Might Benefit From a Combined Molecular Pathology–Traditional Anatomical Pathology Approach?

Petty described the combined molecular pathology–traditional anatomical pathology approach as a day-to-day reality within oncology practice and, therefore, potentially applicable to all patients with cancer. He clarified that it would be difficult to find a tumour subspeciality where molecular pathology does not have a role. Popper pointed out that molecular testing benefits patients for whom a driver mutation is identified because this result guides clinicians towards prescribing specific driver-blocking therapy, rather than standard of care chemotherapy or chemoradiotherapy.

Do Multidisciplinary Teams Fully Utilise Biomarker Testing?

Petty noted that clinical MDTs are mostly tumour-site-specific; therefore, molecular testing is conducted on this basis. Although these MDTs are likely to fully utilise biomarker testing, Petty expressed concern about whether they can keep up with the rate of progress in this area, including developing and maintaining the level of expertise required to offer full molecular profiling in the future. Popper stated that in Austria, molecular pathology testing is expected, and the cost is reimbursed. He acknowledged that this is not the case globally, and that testing is more likely to be conducted in institutions and countries where the cost will be reimbursed. In cases where reimbursement is not guaranteed, Popper questioned who would pay for molecular testing, as the cost is unlikely to be covered by the molecular pathology budget.

MOLECULAR MULTIDISCIPLINARY TEAMS

Tumour-Site-Specific Multidisciplinary Teams and Molecular Multidisciplinary Teams as Separate Entities

Molecular MDTs created to provide personalised treatment recommendations tailored to the genetic footprint of individual patients were founded with the onset of precision oncology (PO), as many clinicians were inexperienced in the interpretation of results and their relevance to clinical practice.[1,2]

Petty indicated that molecular MDTs were perhaps considered a research exercise in the past, but are now reaching into clinical practice. He explained that there is no definitive model for the integration of information from molecular MDTs into clinical tumour-site-specific MDTs, but that work was continuing in this area. Petty proposed that molecular MDTs and tumour-site-specific MDTs should be maintained as separate entities to maximise time efficiency, and to ensure that the MDT does not become large and unwieldy. He also emphasised that molecular MDTs must ensure that the molecular pathology information is presented to the tumour-site-specific MDT in an understandable form for oncologists, and this requires the molecular MDT to educate practicing oncologists on this subject.

Popper stated that clinical tumour-site-specific MDT and molecular MDT practices differ between countries. He suggested that there is no need for molecular MDTs in Austria, as pathologists present and explain the molecular data to the tumour-site-specific MDTs; however, in other countries where there is no such close collaboration between molecular pathology and traditional anatomical pathology, there may be a need for molecular MDTs.

How Do Multidisciplinary Teams Assign Clinical Relevance to Molecular Pathology Findings?

Petty, who is based in the UK, reasoned that while molecular testing is centred on only a few available actionable biomarkers, there is currently sufficient expertise within tumour site-specific MDTs to assign clinical relevance to molecular pathology findings presented by a tumour-site-specific pathologist. Petty acknowledged that the role of molecular pathology in multidisciplinary care is evolving, however, and the potential requirement for broader panels and whole-genome sequencing in the future necessitates a separate molecular MDT with molecular genetics expertise to interpret data, assign clinical relevance, and report this information to the tumour-site-specific MDT. Petty questioned whether there is a need for a member of the tumour-site-specific MDT (e.g., a clinical oncologist) to attend the molecular MDT meetings and vice versa, to promote collaboration and ensure that the information exchanged between the two types of MDT is relevant, focused, and understood.

Popper recounted that in Austria, the pathologist presenting the anatomical and molecular pathology data to the MDT may express an opinion about the most appropriate treatment for the patient, but the MDT makes and records the final decision. Popper considered that there is no need for specialist molecular pathologists to be included in MDTs in Austria because pathologists take responsibility for informing and educating the MDT about the molecular pathology data.

Educating Multidisciplinary Teams About Interpreting Molecular Pathology Results

Considerable effort needs to be put into education, for both clinical oncologists and molecular pathologists, Petty advocated, with the structure of the learning based around tumour sites because that is how clinical oncology and molecular pathology are currently organised. This is a huge task that needs to be undertaken in a variety of medical education settings. Petty claimed there is an immediate need to educate oncologists and pathologists, including educating oncologists about realistic expectations for which and how many tests are possible with a small amount of tumour tissue, and how long the tests might take. Petty suggested that in the future, education could take the form of postgraduate specialist medical training in oncology and pathology, perhaps even "planting the seeds" on these topics in undergraduate medical training.

Popper explained that any questions surrounding the molecular data are discussed by the laboratory personnel, molecular pathologist, and pathologist before the MDT meeting to ensure that comprehensive and correct data are presented to the MDT. For example, an unusual gene mutation for which there is currently no therapy but there are relevant clinical trials, would be discussed beforehand, and the clinical trial information presented to the MDT, thereby providing another option for the patient.

Barriers to the Evolution of Molecular Multidisciplinary Teams

PO has evolved rapidly, and is now integrated into standard of care practices for most cancer patients; however, molecular MDTs have not evolved accordingly.[1,2] Petty reflected that the need for education and understanding of molecular data, along with regulatory considerations, may contribute to the slower evolution of molecular MDTs compared with PO. Furthermore, the MDT relies on evidence-based data on biomarkers that influence treatment decisions and improve patient outcomes, and these data take time to accrue.

The slower evolution of molecular MDTs compared with PO may be related to the historical use of commercial companies to conduct molecular analysis, Popper suggested,

as pathologists were not necessarily familiar with the data, and quality control was lacking for this process. For this reason, Popper specified, the European Society of Pathology (ESP) recommends that all molecular testing is conducted in-house, rather than by commercial companies, to ensure reliability of data and quality control.[3] Popper explained that the ESP has established a quality system to regulate molecular testing across Europe. Individual institutions conduct annual molecular testing on samples sent by the ESP, and the results are assessed to define the testing performance of the institution, thus creating a European standard.

EARLY STAGING AND MOLECULAR TESTING AND THE MULTIDISCIPLINARY TEAM

Histopathological Diagnosis and Disease Staging

Accurate staging of cancer is vital in determining stage-appropriate treatment and prognosis.[4] One role of the clinical tumour-site-specific MDT is to ensure focused and timely investigations for histopathological diagnosis and disease staging. Petty described a scenario in the management of patients with oesophageal cancer in the UK, in which the endoscopist observes a tumour on endoscopy and conducts a biopsy, at which point the MDT may trigger basic staging investigations (e.g., CT scan) before histopathology results are available. Popper declared that early staging of lung cancer is difficult because staging is not possible until surgery, and he estimated that only one in four or five patients with lung cancer are eligible for surgery.

Is Early Molecular Testing Likely to Improve Patient Outcomes?

Petty described two routes for triggering molecular testing in GI tract oncology. In one, the patient undergoes basic staging investigations and the MDT then triggers molecular pathology testing, and in the other, the patient receives a histopathology diagnosis and the pathologist triggers molecular pathology testing ahead of the MDT discussion about the patient. The latter reflex testing approach can be advantageous, as it saves time; however, it can be wasteful, as molecular pathology is not relevant for all patients. For example, very ill, elderly, or frail patients who would not be able to tolerate treatment do not need to undergo biomarker testing to define optimum treatment. Petty remarked that early reflex molecular testing is likely to lead to early implementation of a personalised treatment plan for patients at a cohort level, but not on an individual patient basis.

Popper outlined that there have been research attempts for early molecular testing in lung cancer with cell-free tumour DNA (ctDNA) or liquid biopsy; however, these methods do not yet enable clinicians to predict the development of lung cancer. Studies in early stage lung cancer mostly do not detect ctDNA because at this stage of disease, the tumour is very small and does not shed much tumour DNA. Therefore, ctDNA may be present in the local environment of the tumour, but would not be detectable in the bloodstream. Popper indicated that a new test or a new signature for early lung cancer is still awaited.

THE ROLE OF INFORMATICS IN MULTIDISCIPLINARY CANCER CARE

Cancer informatics is the intersection of information science, computer science, medical oncology, communication, and healthcare.[5] Informatics comprises the resources, devices, and methods required to optimise the acquisition, storage, retrieval, and use of information.[5] Comprehensive and reliable informatics is essential to deliver the information to the MDT and patients.[6]

Informatics Systems and Support

According to Popper, the ThermoFisher Scientific (Waltham, Massachusetts, USA) and Illumina, Inc. (San Diego, California, USA) systems are the two most commonly used systems for molecular testing and associated informatics, and these systems are well-regulated and very reliable. He explained that information technology (IT) support is essential for institutions that conduct molecular testing, and that the size of the IT team may vary considerably. Popper considered there is a need to standardise informatics across MDTs; however, different institutions are bound

to the systems that they are using for molecular testing.

Petty explained that molecular pathology analysis and informatics occur at the molecular testing, pre-MDT meeting stage. Therefore, for most oncologists, informatics is considered a "black box": they know that it happens, that it is quality controlled, and what the output looks like, but they do not know much about the details of the analysis. Petty acknowledged that oncologists may benefit from understanding more about the "black box" in terms of what the analysis involves, the expertise required, and timescales. He stated that arguably, one of the major advantages of the whole MDT process is the increased understanding of colleagues' roles, which creates a more cohesive multidisciplinary approach, and that a greater awareness of the tasks and issues of molecular pathologists is an important part of that understanding.

How Might Informatics Contribute to the Effectiveness of the Multidisciplinary Team and Improve Patient Outcomes?

Popper underscored the importance of informatics for the interpretation and organisation of molecular data according to clinical relevance, including establishing the presence of a real mutation versus a patient-based variation. Filtering out the molecular abnormalities that are treatable to present to the MDT enables clinicians to make quicker and more efficient treatment decisions. Popper highlighted that it is also important to maintain a record of all mutations for each patient in case of disease recurrence and new treatment options becoming available, or relevant future clinical trials.

In accord with Popper, Petty advocated that informatics facilitates the presentation of molecular data in a clinically meaningful way for the MDT, thereby enabling clinicians to diagnose and treat patients more effectively, and in a timely manner. Increasing information from molecular pathology will increase the precision of MDT decisions, although the technologies remain expensive, and may not be accessible in all countries for some time.[6]

Data Acquisition, Storage and Sharing in the Multidisciplinary Team

Popper reasoned that the acquisition, storage, and sharing of data in the MDT are currently straightforward and easily maintained because few data are produced routinely, and these data can be stored separately with specific protection and restricted access. He warned that this could change if whole-genome sequencing or exome sequencing were to become routine, as this would generate huge amounts of data that would be associated with ethical and security considerations and could potentially be abused. Therefore, this type of molecular analysis is currently intended only for scientific purposes, and not for patient diagnosis or treatment, so the data are anonymised, and cannot be traced back to the patient.

Petty stated that information governance is an essential aspect of MDTs to ensure patient privacy and data protection. He added that there is no standard software for this; rather, there tends to be a piecemeal system built up over the years, with the level of software ranging from Microsoft Word (Microsoft Corp., Redmond, Washington, USA) to data platforms. Expertise in informatics, time, and money are all important factors, and unfortunately, Petty noted, lots of data are not being captured. Petty implied that there is often no overarching approach to data acquisition, storage, and sharing across tumour-site-specific MDTs for different tumour sites within the same institution.

Informatics Techniques in the Analysis of Tumours

The development of immunomodulatory cancer therapies has been paralleled by an increase in the use of informatics techniques for the analysis of tumours, the tumour microenvironment, and measures of systemic immunity.[7] Petty referred to these techniques as research tools that are not yet at the clinical practice/MDT level. Popper agreed that these techniques are currently at the research stage, but added that this might soon change in lung cancer. He explained that determining which patients with lung cancer may benefit from immunotherapy is currently based on evaluation of tumour cells (e.g., tumour cells expressing programmed death-ligand 1). However, the tumour environment rather than the tumour itself has been shown to express

immunoregulatory molecules in patients with small-cell lung cancer, and for these patients immunotherapy may be an option. Popper speculated that informatics techniques for the analysis of the tumour microenvironment may be incorporated into clinical practice quite quickly as patients with small-cell lung cancer have a very short life expectancy, irrespective of treatment, and this analysis offers new hope for these patients.

FUTURE PROSPECTS AND CONCLUSIONS

Petty concluded that the role of molecular pathology in the multidisciplinary care of patients with cancer is rapidly evolving, and it is important to bring everyone in the MDT along with this evolution. This requires education of MDTs about molecular pathology and an appropriately skilled workforce to address the challenges associated with integrating clinical and molecular MDTs, particularly as the complexity of molecular testing increases. New or expanding roles in MDTs in the future may include informatics experts, molecular geneticists, and communications experts to drive education and training, and to ensure that patients are kept informed about their care.

Popper concluded that molecular pathology is an essential part of the MDT approach, and provides valuable information to enable clinicians to make timely and effective decisions about the management of their patients, which may translate to improved patient outcomes. The integration of molecular pathology into multidisciplinary care differs between countries, but the value of molecular findings in cancer care is universally recognised. Informatics has a critical role in multidisciplinary cancer care, and currently meets the requirements for data acquisition, storage and sharing in the MDT; however, the introduction of routine whole-genome sequencing or exome sequencing is likely to challenge the status quo.

References

1. Sadaps M et al. The impact of clinical decision making in a molecular tumor board at a tertiary care center. J Clin Oncol. 2021;39(Suppl 15):3128.
2. Scott B. Multidisciplinary team approach in cancer care: a review of the latest advancements. EMJ Oncol. 2021;9[9]:2-13.
3. Cree IA et al. Guidance for laboratories performing molecular pathology for can-cer patients. J Clin Pathol. 2014;67(11):923-31.
4. Liam CK et al. Accuracy of lung cancer staging in the multidisciplinary team set-ting. Transl Lung Cancer Res. 2020;9(4):1654-66.
5. National Cancer Registrars Association. Cancer Informatics. 2022. Available at: https://www.ncra-usa.org/Education/Informatics. Last accessed: 11 June 2022.
6. Selby P et al. The value and future developments of multidisciplinary team can-cer care. Am Soc Clin Oncol Educ Book. 2019;39:332-40.
7. Hammerbacher J, Snyder A. Informatics for cancer immunotherapy. Ann Oncol. 2017;28(suppl_12):xii56-73.