Multidisciplinary Team Approach in Cancer Care: A Review of the Latest Advancements Featured at ESMO 2021

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Abstract

A collaborative approach from healthcare professionals is necessary for the management of patients with cancer to diagnose and treat the disease, provide support for the various needs of the patients, and optimise outcomes. A co-ordinated, multidisciplinary team (MDT) approach promotes shared decision-making and enables comprehensive care of patients with cancer through a variety of medical specialties and support initiatives. Presentations at the European Society for Medical Oncology (ESMO) Congress 2021 show MDTs are an important component of clinical studies and clinical practice, enabling guided treatment decisions and adaptive strategies at different stages of treatment, and in various patient populations, to ensure optimal individualised patient care. MDT strategies have improved understanding of diagnosis, management, clinical patterns, risk factors, and mechanisms of some specific immune-related adverse events (irAEs) and may enable patient features associated with severe irAEs to be identified. Examination of a multidisciplinary approach to early endometrial cancer highlighted that women regarded as high-risk according to traditional risk factors (stage, histological type) had varying recurrence-free survival, and overall survival according to molecular classification. Incorporating molecular classification into routine diagnosis is easy and reproducible, improves prognostic prediction, changes risk categorisation for a minority of patients, and has a major impact on personalised treatment, which may translate to better patient outcomes. The importance of sharing expertise and multidisciplinary teamwork was evident in the many multidisciplinary sessions at the congress. Strategies to improve efficiency in multidisciplinary care include clinical decision platforms, and analysis of input factors at MDT meetings. Transition of MDT meetings to a virtual format during the COVID-19 pandemic has enabled continuation of these meetings in uncertain times and may become a legacy of COVID-19. The individual studies presented at ESMO 2021 that utilise an MDT in their treatment decisions, and the numerous multidisciplinary sessions at the congress that involved contributions from a range of expertise, highlight how the oncology community is on board with the concept of a co-ordinated, cross-disciplinary approach, and is driving improvement in this area to ensure best patient care.
INTRODUCTION

The complexity of management of patients with cancer necessitates a collaborative approach from healthcare professionals to diagnose and treat the disease; provide support for the social, psychological, dietary and physical needs and survivorship of patients; and optimise outcomes. A co-ordinated, MDT approach promotes shared decision-making by a range of healthcare professionals in collaboration with specialist oncology consultants, and enables comprehensive care of patients with cancer through a variety of medical specialties and support initiatives.

ESMO VISION FOR CANCER CARE IN THE FUTURE: AN INCLUSIVE, MULTIDISCIPLINARY ONCOLOGY COMMUNITY IS KEY

In the Presidential address, Peters described the ESMO Vision 2025 as a three-tiered approach surrounding the core understanding of care to connect and engage those who care about cancer. The first ambition of ESMO is an aspiration to cultivate one oncology community in which all cancer professionals across disciplines and geographical borders are united in a diverse, inclusive culture that gives each stakeholder a true sense of belonging and enables professionals to cater for the diverse needs of patients. Commitment to providing education to cancer professionals for life to support their development, and to ensure they keep up with advancements in the field and changing standards of care along every step of the professional trajectory, forms the second ambition. The third is a drive to realise the ideal of accessible cancer care that is reliable, equally accessible, and economically sustainable.

STUDIES UTILISING A MULTIDISCIPLINARY TEAM APPROACH

Multidisciplinary Team-Guided Treatment Decisions are an Important Component of Patient Care

Numerous studies presented at ESMO 2021 describe the use of an MDT as an integral part of the conduct of the study, although these studies did not identify key performance indicators and quality metrics to track the quality of care received, or specifically measure the impact of the MDT on patient outcome.

For example, Zovato et al. reported the results of a single-centre, real-world study, the aim of which was to describe the efficacy and toxicity of lenvatinib treatment within the context of multidisciplinary-based management of patients with advanced radioactive iodine-refractory differentiated thyroid cancer. Treatment decisions were validated by a multidisciplinary board, comprising an oncologist, endocrinologist, radiotherapist, endocrine surgeon, and nuclear medicine physician, and all patients were managed by an oncologist and/or an endocrinologist. Zovato et al. noted that patients in this study experienced longer progression-free survival and improved 24 months' overall survival, compared with that reported in other clinical trials, and concluded that a multidisciplinary approach could help to establish appropriate timing for lenvatinib initiation, and may enable early detection and better management of adverse events.

MDT-guided treatment decisions were an important component of a Phase II clinical trial by Zhu et al., which demonstrated that neoadjuvant toripalimab (a programmed cell death protein 1 inhibitor) plus chemotherapy is safe and effective for patients with locally advanced non-small cell lung cancer. In this study, patients were reassessed by the MDT after the second treatment cycle and candidates for complete resection underwent surgery, whereas all other patients received the remaining treatment cycles. Similarly, in a study by Humayun et al. to assess radiological and pathological response to neoadjuvant concomitant chemotherapy and radiotherapy (RT) versus sequential short course RT followed by chemotherapy in locally advanced
rectal cancer, cases amenable to surgical resection were identified at an MDT meeting. Although these and further studies\textsuperscript{13-17} presented at ESMO 2021 that reported involvement of an MDT did not specifically measure the impact of the decisions made by the MDT compared with non-MDT care in terms of patient outcomes, they show the broad utilisation of this approach.

**Multidisciplinary Teams in Studies of Elderly Patients with Cancer**

Cancer is diagnosed frequently in elderly patients, and treatment can be complicated by comorbidities and/or frailty. An MDT can play a role in improving outcomes for this particularly vulnerable population.

In a study by Pang et al.,\textsuperscript{18} patients aged \( \geq 65 \) years with cancer underwent evaluation with the comprehensive geriatric assessment (CGA) tool, and then MDT-recommended interventions were implemented based on the CGA findings. In total, 92\% of patients who were considered to require interventions actually received the interventions, 31\% of whom reported improved quality of life, and 29\% of caregivers described reduced burden. Pang et al.\textsuperscript{18} concluded that early identification and MDT-recommended tailored interventions based on CGA improve quality of life in elderly patients with cancer and reduce their caregivers’ stress.

An MDT played a key role in the evaluation by Bossi et al.\textsuperscript{19} of the role of CGA as a tool to personalise the therapeutic approach implemented for elderly patients with locally advanced head and neck squamous cell carcinoma. The MDT proposed a therapeutic strategy prior to CGA performed by a geriatrician, then subsequently re-evaluated the strategy in the light of the CGA results. The major therapeutic strategy changed after CGA in 12\% of cases, and there was an increased demand for supportive care, such as nutritional and psychological support, psychiatric treatments, and chronic therapy modification.\textsuperscript{19}

The positive impact of an MDT approach was also noted in a study by Alekseeva et al.\textsuperscript{20} of older patients with metastatic colorectal cancer. The correction of geriatric syndromes by the MDT improved geriatric status, tolerability of chemotherapy, clinically significant response, and event-free survival.\textsuperscript{20}

**A MULTIDISCIPLINARY APPROACH TO EARLY ENDOMETRIAL CANCER**

A multidisciplinary approach to early endometrial cancer was encapsulated by presentations at an ESMO 2021 multidisciplinary session comprising molecular classification,\textsuperscript{21} surgical approaches,\textsuperscript{22} adjuvant radiotherapy (RT),\textsuperscript{23} and adjuvant systemic therapy.\textsuperscript{24} Although these presentations did not refer specifically to MDTs, they demonstrate how approaching cancer (in this case, endometrial cancer) from different disciplinary angles promotes cross-discipline thinking, planning, and execution of care, and that this is a valuable approach to enable optimum patient management.

**Molecular Classification of Endometrial Carcinoma and its Implications for Clinical Management**

The inclusion of molecular classification in multidisciplinary cancer care is an evolving concept and needs to be considered for patients who are likely to benefit from personalised treatment.

Singh\textsuperscript{21} highlighted the global burden and rising incidence and mortality of endometrial carcinoma, noting that personalised treatment will improve clinical outcomes. Management of endometrial carcinoma involves treatment decisions such as surgical versus non-surgical treatment, location, and extent of surgery, and whether to administer adjuvant RT and which type. These decisions are currently based on traditional clinical pathological risk factors (histological type, grade, stage, lymphovascular space invasion).\textsuperscript{21,25} Singh\textsuperscript{21} explained that there are molecular insights that can add valuable prognostic information to this traditional clinical pathological risk assessment.

For decades, endometrial cancer risk stratification was based largely on histological type, grade, and stage. In 2013, however, The Cancer Genome Atlas (TCGA)\textsuperscript{26} discovered four molecular subtypes, with each group having distinct clinical outcomes: POLE ultramutated (POLEmut), mismatch repair deficiency (MMRd), p53 abnormal (p53abn), and no specific molecular profile.\textsuperscript{27} Singh\textsuperscript{21} discussed this new classification and emphasised that the traditional binary approach to endometrial
cancer diagnosis of endometrioid (no specific molecular profile/copy-number low: 50% of patients with endometrial cancer) versus serous-like/non-endometrioid (p53abn/copy-number high: 12% of patients with endometrial cancer) was too simplistic.26,27 Two other endometrial cancer subtypes are now considered: the POLEmut subtype comprises polymerase epsilon mutations (ultramutated cancers: 9% of patients with endometrial cancer) and the MMRd subtype is composed of mismatch repair system defects (hypermutated: 28% of patients with endometrial cancer). Singh21 noted that the inclusion of POLEmut and MMRd subtypes in an expanded classification provides more accurate prognostic prediction than traditional clinical pathological risk assessment. Singh21 concluded that incorporating molecular classification into routine diagnosis is easy and reproducible, improves prognostic prediction, changes risk categorisation for a minority of patients, and has a major impact on personalised treatment, which may translate to better patient outcomes.

Surgical Approach to Early Endometrial Cancer

Surgery has an important place in the multidisciplinary care of patients with cancer. Abu-Rustum22 explained that treatment of apparent uterine-confined endometrial cancer (most new cases) is total hysterectomy and bilateral salpingo-oophorectomy to remove the primary tumour, followed by procedures to identify any extraterine disease, and that surgical staging remains the gold standard. He advocated that women with endometrial cancer should be treated by gynaecologic oncologists, and that pathologic assessment of pelvic nodes remains the most accurate method to determine metastatic disease. There has been an important change in surgical culture from quantity to quality, with increasing precision in surgery with sentinel lymph node mapping28,29 now becoming the standard of care, and lymphadenectomy for staging purposes less commonly performed.22

Role of Adjuvant Radiotherapy and the Benefits of Adding Chemotherapy in Early Endometrial Cancer

Radiotherapy and chemotherapy are crucial treatment approaches in multidisciplinary cancer care, and it is vital for the MDT to understand how to utilise these treatments optimally to provide the best care for the patient.

The role of adjuvant radiotherapy with or without chemotherapy in early endometrial cancer has been studied in depth in the PORTEC and other studies. An overview of the findings, plus the additional benefits of molecular classification were presented at ESMO by de Boer.23

De Boer23 emphasised that external beam radiotherapy (EBRT) alone is still standard treatment for early-stage endometrial cancer with high-risk factors; however, molecular classification has changed the landscape for endometrial cancer treatment and should be incorporated into management strategies for all endometrial cancers, particularly in high-grade tumours.23

The 10-year results from PORTEC-2,30 in which women with high-intermediate risk (Stage I–IIA) endometrial carcinoma were randomised to EBRT or vaginal brachytherapy (VBT), support treatment based on molecular-integrated risk profiles.31 Higher risk of pelvic recurrence in women treated with VBT was restricted to a subgroup of patients with unfavourable features (e.g., substantial lymphovascular space invasion, p53abn). In contrast, there was no increase in pelvic recurrence in women treated with EBRT who had unfavourable features.31

PORTEC-4a32,33 (currently recruiting) is the first study to investigate individualised treatment based on the molecular risk profile versus standard adjuvant treatment in endometrial cancer, with the aim to reduce both over- and undertreatment. In this study, women with Stage I endometrial cancer will be randomised 1:2 to standard adjuvant VBT versus adjuvant treatment based on molecular-integrated profile. Patients with a favourable molecular-integrated profile will undergo observation, patients with an intermediate risk profile will receive VBT, and patients with an unfavourable risk profile will receive EBRT.

De Boer explained that in PORTEC-334 the 5-year overall survival benefit seems not to outweigh the toxicity of adding chemotherapy to RT in Stage I–II endometrial cancer with high-risk factors (84% versus 82% with and without chemotherapy, respectively), and there was excellent pelvic control with RT alone. Similar
conclusions were drawn from the GOG-249 trial. Patients with Stage III disease in PORTEC3 showed 5-year overall survival benefit with the addition of chemotherapy (79% versus 69%), as did women with serous cancer (71% versus 53%). These results indicate the benefits of adding chemotherapy to RT are dependent on tumour stage.

Reporting on an analysis using samples from the PORTEC-3 study, de Boer stated that women regarded as high-risk according to traditional risk factors (stage, histological type) had varying recurrence-free survival according to molecular classification (e.g., 5-year recurrence-free survival ranged from 48% for patients with p53abn cancers to 98% for patients with POLEmut cancers). The benefit of adding chemotherapy to RT also differed between molecular subgroups, with only patients with p53abn tumours experiencing significant benefit versus RT alone.

De Boer concluded that molecular classification should be incorporated into clinical diagnostics, treatment decisions, and new trials for endometrial cancer, and that several trials are ongoing or in set-up. For example, activation of the RAINBO studies is expected by early to mid-2022.

Unmet Needs in Adjuvant Systemic Therapy for Endometrial Cancer

Unmet needs in adjuvant systemic therapy for endometrial cancer highlighted by Mirza include the risk for under- and over-treatment. Clinical trials evaluating adjuvant therapy for patients with early-stage disease have been criticised because treating all patients with high-intermediate risk features with RT has potential for significant over-treatment rates. In addition, the heterogeneous clinical course of endometrial cancer was identified as being an obstacle to individualised patient care, and patients with high-risk histologies or poor prognostic molecular markers are considered to be unlikely to do well with standard therapies, even if treated when the disease is early stage. Mirza concluded that the landscape of endometrial cancer management is changing dramatically, molecular classification has helped define this disease more precisely, and therapies are being developed to target specific subpopulations.

MULTIDISCIPLINARY SESSIONS AT ESMO 2021

A multidisciplinary approach to cancer management was highlighted by the numerous multidisciplinary sessions at ESMO 2021, in which speakers from different disciplines contributed to the discussion. A few representative examples follow.

Biology-Guided Combination Cancer Therapy: A Multidisciplinary Perspective

During a multidisciplinary session on biology-guided combination cancer therapy, Cuppen considered the value of genomics information for trial design and patient stratification using whole-genome sequencing. He described whole-genome sequencing as a clinically validated tool that provides a comprehensive view of the genomic landscape of a tumour, efficiently detects all types of simple and complex biomarkers, and facilitates identification of patients for clinical trials.

Also in this session, Chalmers noted that although RT is often curative and organ preserving, tumour size, location, and inherent resistance contribute to treatment failure with RT. He proposed that tumour control and cure rates could be increased by combining RT with molecular targeted drugs that inhibit the DNA damage response. Obenauf added to the session by explaining that cross-resistance can develop between targeted therapy and immunotherapy during management of a patient with cancer, and that this can be best prevented by using immunotherapy as a first-line treatment, using targeted therapy for only a short time, and switching to immunotherapy before progression.

Multidisciplinary Teamwork is Essential to Achieve Better Outcome in Patients Receiving Neoadjuvant Chemotherapy for Breast Cancer

Several presentations at ESMO 2021 highlighted the need for an MDT approach to optimise the treatment of breast cancer. Neoadjuvant chemotherapy (NACT) is currently indicated for locally advanced invasive breast cancers and, according to Hung, is compatible
with mastectomy with or without breast reconstruction, and does not increase risk of major surgical complications. In a session on tailoring surgical treatment after NACT, Hung highlighted a significant need for greater uniformity and guidelines regarding treatment following NACT, and suggested that multidisciplinary teamwork is essential to achieve better outcomes in patients receiving NACT.

In this session, Chua reported that indications for RT after primary surgery for breast cancer are informed by high-level evidence from randomised trials based on pathologic staging information, and that neoadjuvant systemic therapy enables tailoring of RT based on the extent of treatment response. According to Chua, there are limited data to define indications for RT after neoadjuvant systemic therapy, and the future of personalised local-regional RT will be driven by integrating residual disease burden with tumour biology and efficacy of systemic therapy in a multidisciplinary context.

Also in this session, the use of systemic therapy, which is an important component of multidisciplinary cancer care following NACT, was discussed by Marmé. He outlined that factors to consider in post-NACT systemic treatment of patients with triple-negative breast cancer who did not achieve pathologic complete response include BRCA status, platinum and immune checkpoint inhibitor (ICI) use during NACT, and dihydropyrimidine dehydrogenase status. In post-NACT systemic treatment in patients with non-pathologically complete response human epidermal growth factor receptor 2 early breast cancer, potential factors to consider include dual blockade during NACT, hormone receptor status, and post-NACT human epidermal growth factor receptor 2 status.

Multidisciplinary Discussion is Recommended in Retroperitoneal Sarcoma

Multidisciplinary discussion of retroperitoneal sarcoma (RPS) revealed that resectability is not only a technical issue, and that patient- and tumour-related factors need to be considered in the decision-making process. In this situation, a strategic delay can be useful to enable selection of the proper treatment strategy in the recurrent setting in selected patients. Haas outlined the lessons learned from the STRASS trial, in which 75% of patients had liposarcomas, and there was no benefit of preoperative RT for unselected RPS. According to Haas, preoperative RT should not be considered as standard of care for RPS, and the appropriate perspective for this subgroup of liposarcomas should be multidisciplinary discussions, with patients counselled about the results in a shared decision-making process. Consideration of systemic therapy in RPS by Penel showed palliative systemic treatment can be used, but preoperative and adjuvant chemotherapy should not be given outside clinical trials.

The Value of a Multidisciplinary Team for Immune-Related Toxicity

According to Naidoo, early recognition of irAEs experienced by patients with cancer receiving ICI therapy affects outcomes, and irAE MDTs may help to innovate in this area. The irAE MDT includes professionals from different disciplines such as rheumatology, pulmonary, endocrinology, neurology, cardiology, gastroenterology, nephrology, pathology, and radiology, and takes different forms, including virtual referral, irAE tumour boards, inpatient services, and fellowships. Goals of the irAE MDT, as defined in a pilot project conducted by Naidoo et al., are to centralise the discussion of complex irAEs, identify new irAEs, characterise risk factors and mechanisms of irAEs, and propose prospective irAE clinical trials, including biomarker studies, to address unanswered questions. Data generated by MDTs in irAE biorepositories and disease- or organ-specific clinical databases have improved understanding of clinical patterns, risk factors, and mechanisms of irAEs. Naidoo considered that irAE MDTs will not only assist with diagnosis and management of complex irAEs, but may enable patient risk factors associated with the development of severe irAEs to be identified.

A Multidisciplinary Approach Is Needed to Manage Neurotoxicity

In a discussion of the neurological complications of cancer treatment, Hottinger pointed out that although chimeric antigen receptor T cell therapies offer great promise to improve clinical outcomes, neurotoxicity occurs typically about 1 week after chimeric antigen receptor T cell infusion, and an early multidisciplinary approach is needed to manage toxicity.
Integration of Patient-Reported Symptoms into Cancer Care

In a multidisciplinary session on integration of patient-reported symptoms into cancer care, Eicher\textsuperscript{52} indicated that clinicians may be unaware of many of their patients’ symptoms, and that systematic symptom monitoring with patient-reported outcomes can help to close this gap.\textsuperscript{53,54} The success of this approach relies on patients being willing and able to self-report their symptoms, and clinicians to trust the patient-reported information. Eicher\textsuperscript{52} considered that patient-reported outcome measures can be used to tailor supportive care as part of a multidisciplinary approach, including screening that guides the assessment of patient-reported symptoms based on validated measures. Ideally, this should be integrated in a model of care that enables patients with cancer to be supported in their symptom self-management.

The Importance of Sharing Expertise

In a multidisciplinary discussion on emerging therapies, Galle\textsuperscript{55} summarised that the systemic therapy landscape for hepatocellular carcinoma has rapidly evolved since 2017, and that combination of the ICI atezolizumab with another immunotherapy and bevacizumab is the new standard of care.\textsuperscript{56} He emphasised that data on second-line therapy are not evidence-based; therefore, clinicians, particularly in MDTs, must rely on their experience to make clinically-relevant decisions to optimise patient care. Furthermore, in the closing address, Galle\textsuperscript{57} remarked that it is helpful to have a broader view, and to share not only different treatment options and experiences across tumour entities, but also to share cross-disciplinary insights to support patients in practice.

Analysis of Input Factors of Multidisciplinary Teams Provides Insight into Which Factors Influence the Quality of Recommendations

According to Galonska et al.,\textsuperscript{59} MDT meetings are a central institution in oncological decision-making, yet, apart from expert opinion, there is little evidence of factors that contribute to good recommendations. Decisions of a visceral oncology MDT meeting were analysed and, for every case discussed, predefined factors deemed necessary for effective MDTs in oncology were checked. Also, correlations between input and output factors, and which of the input factors contributed significantly to a ‘good recommendation’, were evaluated. A total of 65% of recommendations made by the MDT met all the predefined criteria of a ‘good recommendation’, and there was a strong, consistent correlation between logistical and informational input factors and the quality of the MDT output, including presence of all core team members (p<0.00001) and a clear indication of patient wishes (p<0.01). The authors concluded that analysis of input factors of MDTs provides insight into which factors influence the quality of recommendations.\textsuperscript{59}

Cardiotoxicity with Poly(ADP-Ribose) Polymerase Inhibitors: Highlighting the Role of the Cardiologist in Multidisciplinary Care

Clemente et al.\textsuperscript{60} reported that almost half of the patients receiving poly(ADP-ribose) polymerase inhibitors in their retrospective, observational study (93% of whom had ovarian cancer) experienced a cardiovascular event (the most common were hypertension [20.5%] and palpitations [18.6%]). These authors considered it important to highlight the role of the cardiologist.
in multidisciplinary management of patients taking these drugs, to optimise treatment and improve symptoms.⁶⁰

Need for a Global Standard for Neuroendocrine Tumour Care

A survey conducted by Kolarova et al.⁶¹ that measured healthcare delivery to patients with neuroendocrine tumours (NETs) showed that a multidisciplinary approach was rarely used even in Europe (35%; 143/409) and North Africa (32%; 131/410), which are the leading geographic areas for NET medical care. The authors highlighted a need for a global standard for NET monitoring, and greater expertise in NETs among healthcare professionals.⁶¹

TRANSLATION TO A VIRTUAL CANCER MULTIDISCIPLINARY TEAM MEETING DURING THE COVID-19 PANDEMIC

The results of a questionnaire by Goggin et al.⁶² to investigate the transition from in-person to virtual MDT meetings necessitated by the COVID-19 pandemic indicated that virtual MDT meetings can be implemented into routine MDT practice. Goggin et al.⁶² concluded that although challenges are encountered, transition to a virtual format enables continuation of MDT meetings in uncertain times and may become a legacy of COVID-19.

CONCLUSION

A co-ordinated MDT approach is considered the gold standard for diagnosis and treatment of cancer. Studies presented at ESMO 2021 show the positive aspects of a multidisciplinary approach in cancer care, including improved patient outcomes, the potential to establish appropriate timing of treatment initiation, co-ordinated decisions about the most appropriate treatment for the patient, and the possibility of early and better management of adverse events. The individual studies presented at ESMO 2021 that utilise an MDT in their treatment decisions, and the sheer number of multidisciplinary sessions at the congress that have pulled together a variety of expertise in a dynamic, collaborative environment, show how the oncology community is fully embracing the concept of a co-ordinated, cross-discipline approach, and is driving improvement in this area to ensure best patient care. Ongoing considerations for the realistic utilisation of a multidisciplinary approach include patient education, and how best to keep patients informed and in communication with MDTs, which are vital components for the success of this approach, and how healthcare systems cover the costs associated with running an MDT.

References

12. Humayun W et al. Randomized control trial to assess radiological and pathological response after neo-adjuvant concomitant chemo radiotherapy vs. sequential short
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46. Eicher M. Tailored supportive care based on PROMs. ESMO Congress 2021, 16 September, 2021.


