Clinical and Translational Radiation Oncology 48 (2024) 100838

Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

Clinical management of oligometastatic cancer: Applying multidisciplinary tumor board recommendations in practice

Sebastian M. Christ [a,1,*], Minsu Breitenstein [b,1], Philip Heesen [b], Brandon Turner [c], Urs J. Muehlematter [d], Kaspar Pohl [b], Jonas Willmann [a], Alexander Maurer [d], Sukhdeep K. Nagpal [e], Maiwand Ahmadsei [a], Eugenia Badra Vlaskou [a], Esmée L. Looman [a], Astrid E. Heusel [a], Michael Mayinger [a], Panagiotis Balermpas [a], Andreas Wicki [f], Nicolaus Andratschke [a], Tracy Balboni [c], Mai Anh Huynh [c], Martin Huellner [d], Matthias Guckenberger [a]

[a] Dept. of Radiation Oncology, University Hospital & University of Zurich, Zurich, CH, Switzerland
[b] Faculty of Medicine, University of Zurich, Zurich, CH, Switzerland
[c] Dept. of Radiation Oncology, Brigham and Women's Hospital, Dana Farber Cancer Institute, Boston, MA, USA
[d] Dept. of Nuclear Medicine, University Hospital & University of Zurich, Zurich, CH, Switzerland
[e] Radiotherapy Dept., The Royal Marsden NHS Foundation Trust, London, UK
[f] Dept. of Medical Oncology & Hematology, University Hospital & University of Zurich, Zurich, CH, Switzerland

ARTICLE INFO

Keywords:
Oligometastasis
Multidisciplinary tumor board
Therapeutic management

ABSTRACT

Aims: Multidisciplinary tumor boards (MDTs) are an integral part of ensuring high-quality, evidence-based and personalized cancer care. In this study, we aimed to evaluate the adherence to and implementation of MDT recommendations in patients with oligometastatic disease (OMD).
Methods: We screened all oncologic positron emission tomography (PET) scans conducted at a single comprehensive cancer center in 2020. Patients were included if they had evidence of imaging-based OMD from a solid organ malignancy on the index scans, had their OMD case discussed at an MDT, and were treated and followed up at the same center. A switch away from the MDT-recommended treatment modalities was classified as a *major deviation*; non-MDT-mandated adjustments to a recommended treatment modality were coded as *minor deviation*. Clinical data was obtained via chart review; statistical calculations were computed using the R software.
Results: After review of PET and/or concurrent brain scans, 787 cases of OMD were identified. Thereof, 347 (44.1 %) cases were discussed at MDT, of which 331 (42.1 %) were therapeutically managed and subsequently followed. The three most commonly recommended therapies were systemic therapy (35.6 %), multimodality treatment including definitive local therapy (17.8 %), and radiotherapy (13.9 %). A major deviation was recorded in 16.3 % of cases (most commonly: none of the MDT-recommended treatment modalities were performed: 19 (35.2 %); not all MDT-planned treatment modalities were performed: 12 (22.2 %); and additional treatment modality was performed: 11 (20.3 %). A minor deviation was found in 1.5 % of cases. On multivariable regression, number of distant metastases ($n > 1$) was associated with a major deviation (OR: 1.85; 95 % CI, 1.0–3.52). Major deviations were associated with a significantly worse OS ($p = 0.0034$).

Abbreviation: BASEC, Business Administration System for Ethics Committees; CCCZ, Comprehensive Cancer Center Zurich; CI, Confidence interval; CONSORT, Consolidated standards of reporting trials; CT_x, Chemotherapy; DGB, Data governance board; EORTC, European Organisation for Research and Treatment of Cancer; ESTRO, European Society for Therapeutic Radiology and Oncology; FDG, [Fluorine-18]-fluorodeoxyglucose; GIT, Gastrointestinal tract; IQR, Interquartile range; MDT, Multidisciplinary tumor board; MRI, Magnetic resonance imaging; MVA, Multivariable analysis; NSCLC, Non-small-cell lung cancer; OMD, Oligometastatic disease; OR, Odds ratio; OS, Overall survival; PET, Positron emission tomography; PFS, Progression-free survival; PSMA, [Gallium-68]-prostate specific membrane antigen; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; USZ, University Hospital Zurich; UVA, Univariable analysis; vs, versus; WHO, World Health Organization.

* Corresponding author at: Department of Radiation Oncology, University Hospital & University of Zurich, Rämistrasse 100, 8091 Zurich, CH, Switzerland.
E-mail address: sebastian.christ@usz.ch (S.M. Christ).

[1] Both authors contributed equally to this study.

https://doi.org/10.1016/j.ctro.2024.100838
Received 19 May 2024; Received in revised form 5 August 2024; Accepted 7 August 2024
Available online 10 August 2024

Conclusions: Adherence to and implementation of MDT recommendations in OMD patients was generally high (83.7%). Major deviations might be further reduced by more careful and elaborate discussions of OMD patient characteristics s and patient preferences.

Introduction and background

Multidisciplinary tumor boards (MDTs) are a mandatory component of comprehensive cancer centers to discuss patient management and provide interdisciplinary treatment recommendations. MDT discussions are important for every cancer patient, yet especially so for complex cases and rapidly changing treatment indications such as oligometastatic disease (OMD). Desirable goals of the use of MDTs consist in basing treatment decisions on the best available evidence, developing tailored treatment regimens for every individual patient, decreasing variation in clinical practice across cases and institutions, ensuring the reasonable use of healthcare resources, guarantee the implementation of clinical practice guidelines, decreasing time between diagnosis and multidisciplinary management and treatment, and, last but not least, ensuring patient safety [1,2,3]. Following the widespread adoption of MDTs, significant improvements in assessment and management, improvement in diagnostic accuracy, and improvement in overall survival (OS) have been demonstrated [4,5]. In addition, there is evidence for specific cancers, for example, breast cancer patients, that MDT recommendations improve patient compliance in complex cases [6].

With the rise of the concept of OMD and the absence of clinical outcomes from phase III trials, phase II trials have demonstrated improved outcomes with ablative therapy strategies in addition to standard of care [7]. Due to the increasing implementation of ablative therapy in the diverse group of OMD patients, interdisciplinary case discussions are becoming more and more important [8,9,10,11,12].

While MDT implementation has clear clinical benefits, little is known about the execution of the recommendations that result from MDTs. Higher adherence to MDT decisions leads to a greater use of therapy guidelines. The literature currently provides mixed results regarding adherence to MDT recommendations. *Krause et al.* (2023) demonstrated a relatively low adherence of 64 % in patients with gastrointestinal tumors, while *Walter et al.* (2023) demonstrated an adherence of 89.6 % in lung cancer patients and *Rangabashyam et al.* (2020) demonstrated an adherence of 77.9 % in patients with head and neck cancer [13,14,15]. Taking into account the demand of resources for the healthcare system, it is even more important to achieve the highest possible adherence to MDT recommendation [16].

Against this background, the goal of this retrospective single-center cohort study was to analyze adherence to and implementation of MDT recommendations in OMD patients. Our hypothesis was that both are generally high at a comprehensive cancer center, yet lower in oligometastatic patients as compared to other disease states due to the lack of randomized phase III data and the heterogeneity of the OMD state. We also assessed reasons for non-adherence to MDT recommendations in this patient cohort, and tried to identify factors that correlated with non-adherence.

Materials and methods

Patient cohort

All consecutively conducted oncological [fluorine-18]-fluorodeoxyglucose positron emission tomography (FDG-PET) and [gallium-68]-prostate specific membrane antigen (PSMA)-PET scans conducted at the Department of Nuclear Medicine, University Hospital Zurich (USZ), Comprehensive Cancer Center Zurich (CCCZ), between January and December 2020 were screened for this study. Patients were included if (1) they were adults, (2) there was evidence of an extracranial solid organ malignancy, (3) there was evidence of oligometastatic spread after PET- and cranial-magnetic resonance imaging (MRI) scan review, and (4) oncological MDT discussion as well as follow-up took place at the CCCZ, and patients were not lost to follow-up at the time of implementation of MDT recommendation (Fig. 1*)*. This research group previously reported on the MDT treatment recommendations for this patient cohort [17].

OMD definition

No single definition of OMD exists at this point, with phase II trials and guidelines using slightly different definitions [18,19,20]. For the purposes of this study, a definition of maximum five extra- and intracranial metastases was used, which was also employed for previous assessments of this patient cohort [17,21]. Following the ESTRO-EORTC classification of OMD, OMD status was further sub-divided into *synchronous OMD* (OMD imaging diagnosis $\leq$ 6 months of primary diagnosis) and *metachronous OMD* (OMD-imaging diagnosis $>$ 6 months of primary diagnosis) [7].

Adherence to and implementation of MDT recommendations

MDT recommendations at CCCZ are usually recorded in writing and summarize the MDT discussion and interdisciplinary recommendation for each patient case. For the purposes of this study, the written MDT recommendations were reviewed in detail for each OMD patient and classified into “systemic therapy alone”, “radiotherapy alone”, “surgery alone”, “multimodal therapy”, “further evaluation”, “watch & wait”, “other”, and “unclear”. The category “other” included, for example, measures such as biopsy of possible metastasis, therapy break or continuation of treatment without any therapeutic change. Adherence to MDT recommendations was regarded as the baseline scenario and the MDT recommendation was regarded as implemented if a patient underwent the treatment as specified in the MDT report. Deviations from MDT recommendations were coded as either “major” or “minor”, following a methodology used in similar studies [13]. A major deviation was defined as a change of treatment modality, deviating away from the one recommended by the MDT. A minor deviation was defined as adherence to the recommended treatment modality, yet there were, nonetheless, minor changes to the planned therapy regimen, for example, a change away from the recommended systemic therapy agent or radiation treatment intent. If a change to the initially recommended MDT was mandated by a second MDT before the initiation of therapy, this was counted neither as major nor as minor deviation.

Data collection and statistical analysis

Demographic, clinical, and imaging data was obtained either from the electronic medical record system or the hospital imaging depository. All MDT recommendations and their classification were undertaken by one researcher (MB) and cross-checked by a second researcher (SMC). Descriptive summary statistics were calculated for all relevant variables under study. Inferential statistical analysis included both univariable and multivariable logistic regression analysis (UVA; MVA) to assess what variables might be associated with non-adherence to MDT recommendations. Independent variables were dummy coded based on commonly employed definitions and mostly median value cut-offs, and they were dichotomized as follows: gender (male vs. female), age ($<$70 vs. $\geq$ 70 years of age), OMD state (synchronous vs. metachronous) and number of distant metastases ($\leq$1 vs. $>$ 1). The Kaplan-Meier method was used for OS estimation; patients were censored at the date they were

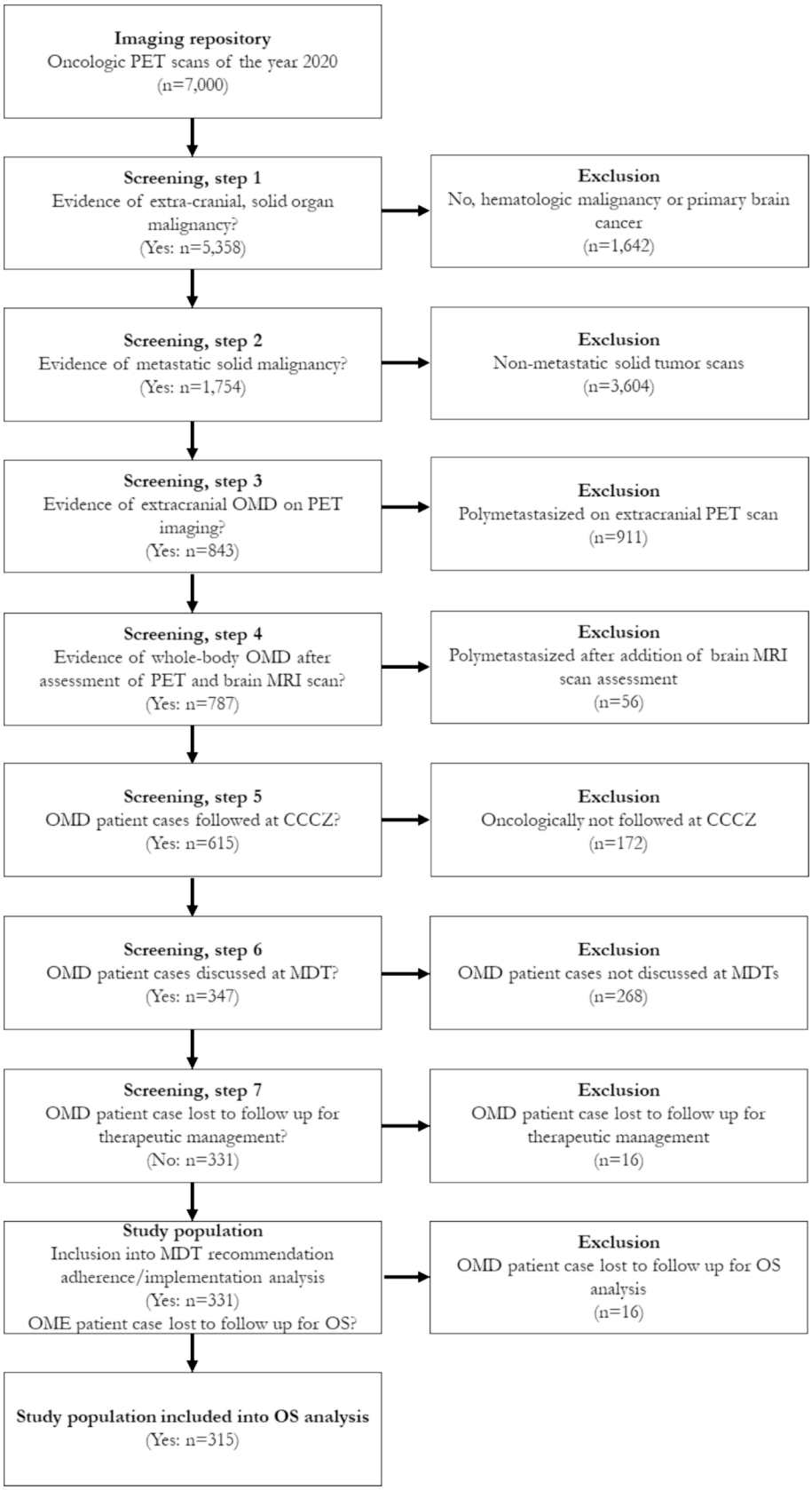

Fig. 1. Patient screening, inclusion and exclusion criteria. Abbreviations: CCCZ=Comprehensive Cancer Center Zurich; MDT=Multidisciplinary tumor board; MRI=Magnetic resonance imaging; OMD=Oligometastatic disease; OS=Overall survival; PET=Positron emission tomography.

last known alive (≤6 months at the time of data collection). A significance level of < 0.05 was employed for this study. For UVA and MVA, the statistical software program R was used. CONSORT diagram and other graphics were created using the Microsoft PowerPoint software.

Ethical approval and data reporting

This study was approved by the Cantonal Ethics Committee of Zurich (BASEC ID No. 2018–01794) and the hospital-level data governance board (DGB) before the initiation of the project. In addition, this study complied with the Ethical Code of the World Medical Association International Code of Medical Ethics, as well as the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist (*Supplementary Table 1*).

Results

Out of the 787 identified OMD cases identified on PET imaging, 347 OMD cases (44.1 %) met the inclusion criteria for this study, which formed the basis for the MDT analysis. N=172 and n = 268 patients were excluded, as they were not followed at CCCZ or discussed at an MDT, respectively. Out of the eligible 347 OMD cases, 16 (2.0 %) where furthermore excluded because of a loss to follow up during the therapeutic management. Thus 331 patients were included in our MDT recommendation adherence and implementation study. For the overall survival (OS) assessment, 16 (2.0 %) additional patients were excluded, because they were lost to follow up, resulting in a total number of 315 (40.0 %) patients for OS analysis (CONSORT diagram; Fig. 1).

Median age at diagnosis of the 347 OMD patients was 65 (IQR, 56–73). Of those, 65 % (n = 215) were male and 35 % (n = 116) were female. The most common primary was skin cancer with 34.1 % (n = 113), followed by lung and pleural carcinoma with 20.5 % (n = 68). Most patients presented with a metachronous OMD stage (74.3 %, n = 246). In 58.6 % (n = 194) of cases, the primary tumor was controlled at the time of OMD diagnosis. The median number of distant metastases at the time of OMD diagnosis was 2 (IQR, 1–3). At the time of data analysis, 53.9 % (n = 170) of patients were alive. The median OS since OMD diagnosis was 2.2 years (IQR, 1.0–2.6). For a summary of demographic and clinical information, consult Table 1.

The two most commonly assessed MDT recommendations originated from the dermato-oncologic MDT (33.5 %; n = 111) and the thoracic MDT (23.9 %; n = 79). In terms of MDT recommendations across all MDTs assessed, “systemic therapy alone” was recommended most frequently (35.6 %, n = 118), followed by “multimodality therapy” (palliative systemic therapy plus ablative local therapy) (17.8 %, n = 59), and “radiotherapy alone” (13.9 %, n = 46). Treatment intent was documented as largely palliative (n = 242; 73.1 %). If local therapy was recommended, the primary tumor was most frequently treated directly (72.2 %; n = 91), metastatic disease was treated in 15.1 % (n = 19) of cases, and in 12.7 % (n = 16) cases, both the primary tumor and metastasis were recommended to be targeted. Ablative local therapy was recommended to be applied to all active lesions in 58.2 % (n = 53/n = 91) of cases. Before starting treatment, 58 (17.5 %) cases were discussed at a secondary MDT within 30 days of the initial MDT. The three most common secondary MDT discussions were molecular oncologic (n = 16; 27.6 %), thoracic-oncologic (n = 15, 25.9 %), and head and neck oncology (n = 7, 12.1 %). For an overview of MDT details, see Table 2.

In 83.7 % (n = 277) OMD cases, the MDT recommendation was implemented, and treating physicians and patients adhered to the recommended treatment schedule. In 16.3 % (n = 54) of the assessed cases, a major deviation was identified. The most common major deviations were (1) “none of the MDT-planned treatment modalities were performed” (35.2 %; n = 19), (2) “not all MDT-planned treatment modalities were performed” (22.2 %; n = 12), and (3) “additional treatment modality was performed” (20.3 %; n = 11), see *Supplementary Table 2*. The three most common reasons for major deviations were: (1) physician decision (n = 20; 36.4 %), (2) patient comorbidity (n = 12; 21.8 %), and (3) patient decision (n = 9, 16.4 %). In ten cases (18.2 %) no clear explanation for the major deviation could be identified. Minor deviations were identified in five cases only (1.5 %). They included (1) “additional RT-site added” (40 %; n = 2), (2) “additional chemotherapy given” (20 %; n = 1), and (3) “not all planned chemotherapy agents were given” (20 %; n = 1), and (4) a different chemotherapy was administered” (20 %; n = 1), see *Supplementary Table 2*. The most frequent reason was physician decision (80 %). The deviations were discussed in only seven (11.7 %) cases in the following MDT before the treatment regimen was changed. For a comprehensive summary regarding the adherence to and implementation of MDT recommendations for the evaluated OMD cases, see Table 3.

On UVA and MVA, number of distant metastases (1 (reference) vs. 2 to 5) was found to be significantly associated with adherence to MDT recommendations (UVA: p = 0.046; MVA: p = 0.05). The UVA showed an odds ratio (OR) of 1.84 (95 % confidence interval (CI), 1.02;3.40), and the MVA showed an OR of 1.85 (95 % CI, 1.0;3.52). No statistically significant association was found for other variables such as age at diagnosis (>65 vs. ≤ 65), gender (female vs. male), OMD state (metachronous vs. synchronous), treatment intent (curative vs. palliative), primary tumor state (controlled vs. not controlled), MDT recommendation (combination vs. evaluation, other, radiotherapy, surgery, systemic therapy and watch & wait) and Type of MDT (breast vs. dermato-oncology, upper and lower GIT oncology, head and neck oncology, hepatobiliary oncology, thoracic oncology, neuro(−endocrine), neuro-oncology, sarcomas, thyroid tumors and uro-oncology). For the results of the UVA and MVA analysis, consult Table 4.

Fig. 2 shows a timeline from the date of OMD diagnosis to first MDT, start of therapy, second MDT, duration of therapy, and first re-staging exams. Median duration between date of OMD diagnosis and first MDT was 7 days (IQR, 5–15), with a sample size of n = 331. Median duration between OMD diagnosis and start of therapy was 26 days (IQR, 14–44, n = 287). It lasted a median of 30 days (IQR 24.25–43.5) to the second MDT discussion (n = 58).

Fig. 3 shows a Kaplan-Meier plot, where patients with and without

Table 1
Demographic data for the sample patient population.

Variable	Data (n = 331 MDT cases)
Median age at OMD diagnosis, years (range)	65 (56–73)
Gender, n (%)	
• Female	116 (35.0)
• Male	215 (65.0)
Primary cancer, n (%)	
• Skin[1]	113 (34.1)
• Lung[2] and pleura	68 (20.5)
• Head and neck	38 (11.5)
• Prostate	35 (10.6)
• Other[3]	77 (23.3)
Oligometastatic state, n (%)	
• Synchronous	85 (25.7)
• Metachronous	246 (74.3)
Primary tumor controlled at time of OMD diagnosis, n (%)	
• Yes	194 (58.6)
• No	137 (41.4)
Number of distant metastases at OMD diagnosis, n (IQR)	2 (1–3)
Number of patients alive at time of analysis, n (%)[4]	170 (53.9)
Median OS from imaging OMD diagnosis, years (IQR)	2.2 (1.0–2.6)

Abbreviations.
IQR=Interquartile range; MDT=Multidisciplinary tumor board; OMD=Oligometastatic disease; OS=Overall survival.
[1] Skin includes malignant melanoma and squamous cell carcinoma. [2]Lung includes non-small cell and small cell carcinoma. [3]Other includes colorectal, breast, gallbladder, liver, pancreas, and upper GIT cancers as well as cancers of unknown primary. [4]This data refers to n = 315 patients.

Table 2
Multidisciplinary tumor board discussions and treatment regimens.

Variable	Data (n = 331 MDT cases)
Type of first MDT, n (%)	
• Dermato-oncology	111 (33.5)
• Thoracic oncology	79 (23.9)
• Uro-oncology (incl. prostate cancer)	41 (12.4)
• Head & neck oncology	31 (9.4)
• Upper & lower GIT oncology	25 (7.6)
• Other[1]	44 (13.3)
MDT recommendation, n (%)	
• Systemic therapy alone	118 (35.6)
• Multimodality treatment[2]	59 (17.8)
• Further evaluation/discussion, e.g., with the patient	53 (16.0)
• Radiotherapy alone	46 (13.9)
• Surgery alone	23 (6.9)
• Watch & wait	21 (6.3)
• Other[3]	5 (1.5)
• Unclear/no decision	6 (1.8)
Treatment intent, n (%)	
• Curative	89 (26.9)
• Palliative	242 (73.1)
Site of definitive local therapy, n/n (%)	
• Primary tumor	91/126 (72.2)
• Metastasis	19/126 (15.1)
• Both	16/126 (12.7)
Discussion of case in second MDT within 30 days, n (%)	
• Yes	58 (17.5)
• No	273 (82.5)
Type of second MDT, n (%)	
• Molecular oncology	16 (27.6)
• Thoracic oncology	15 (25.9)
• Head & neck oncology	7 (12.1)
• Dermato-oncology	6 (10.3)
• Upper & lower GIT oncology	5 (8.6)
• Other[4]	9 (15.5)

Abbreviations: GIT=Gastrointestinal tract; IQR=Interquartile range; MDT=Multidisciplinary tumor board.

[1] Other includes breast, sarcoma, hepato-pancreato-biliary, medical oncology, neurosurgical, neuroendocrine, neurological and thyroid MDTs. [2]Comprises palliative systemic therapy plus definitive local therapy. [3]Other includes cannulation of possible metastasis, therapy break and continuation of treatment without any therapeutic change. [4]Other includes breast, neurosurgical, sarcoma, neurological, dermatology and hepato-pancreato-biliary MDTs.

major deviation were compared. At each time point after OMD diagnosis, the group without major deviation showed a better OS. There was a statistically significant difference with a p-value of 0.0034.

Discussion

The literature on adherence to and implementation of MDT recommendation shows relatively large discrepancies. General adherence to MDT-recommended therapy ranges from 58.2 %-89.6 % (esophageal and gastric cancer: 58.2 %; gastrointestinal cancer: 64 %; head and neck squamous cell carcinoma: 77.9 %; sarcomas and musculoskeletal tumors: 73.5 %; neuro-oncologic tumors 79.9 %; hepatocellular carcinoma: 85.3 %; lung cancer: 81.0 %) [13,15,22,23,24]. The generally high adherence to the MDT recommendation observed in this study is in line with expectations given a university center setting like at CCCZ. This is also reflected by the fact that there was no deviation in any of the 331 MDT cases due to logistical reasons or lack of timely access to diagnostic or therapeutic resources. The reasons for deviation from the recommendations were largely medical in nature, most likely due to discrepancies between the interpretation of the individual patient condition as presented at the MDT versus actual patient condition as assessed in the outpatient clinic setting. The main reasons for non-adherence to the MDT recommendation also correspond to what is described in the literature [13,14,15,22,23]. Since the most frequent

Table 3
Overview of deviations from multidisciplinary tumor board recommendations.

Variable	Data (n = 331 MDT cases)
Major deviation, n (%)	
• Yes	54 (16.3)
• No	277 (83.7)
Reason for major deviation, n (%)	
• Physician decision	20 (36.4)
• Patient comorbidities	12 (21.8)
• No reason detectable	10 (18.2)
• Patient decision	9 (16.4)
• Death	4 (7.3)
• Study inclusion	0 (0)
• Logistical reasons	0 (0)
Minor deviation, n (%)	
• Yes	5 (1.5)
• No	326 (98.5)
Reason for minor deviation, n (%)	
• Physician decision	4 (80.0)
• Patient comorbidities	1 (20.0)
• No reason detectable	0 (0)
• Patient decision	0 (0)
• Death	0 (0)
• Study inclusion	0 (0)
• Logistical reasons	0 (0)
Deviations discussed in next MDT before changing therapy, n (%)	
• No	53 (88.3)
• Yes	7 (11.7)

Abbreviations.
MDT=Multidisciplinary tumor board.

deviation was due to a physician decision, this also raises the question, why concerns about the therapeutic strategy were not raised during the initial MDT discussion. Relatively rarely, in 11.9 % of cases, the deviation of the MDT recommendation was discussed in the next MDT, which was attributed to a lack of time in an MDT and motivation to make medical judgments.

Given the diagnostic uncertainties and clinical heterogeneity associated with OMD, the high level of adherence to and implementation of MDT recommendations could be considered noteworthy. Navigating the complexities of OMD demands a nuanced approach, given the significant variability in disease severity among patients. It is crucial to determine whether a patient falls within the oligometastatic spectrum, characterized by a limited number of treatable metastases, or if a polymetastatic scenario is present. Tailoring effective treatment strategies hinges on this distinction. The diagnostic evaluation must go beyond mere numerical counts, delving into the patient's complete disease history, the dynamics of metastatic progression, and the biological behavior of the metastases. Recognizing both the diagnostic uncertainties and the inherent diversity in OMD presentations, treating physicians must contend with these challenges, underscoring the significance of adherence to MDT treatment recommendations. It can be argued that this adherence not only signifies the evolving comprehension of OMD among healthcare providers but also highlights the necessity for an individualized approach in managing patients with differing levels of metastatic involvement.

With the use of locally ablative therapies, several phase II trials have demonstrated improved progression-free survival (PFS), 5-year survival, and OS in patients with non-small cell lung carcinoma (NSCLC) [7,25,26,27]. We were positively surprised by a high rate of local therapy at 31.7 %, especially considering the composition of cases with respect to timing of imaging and their histology as well as the fact that treatment intent for most patients was palliative in this cohort. This can be attributed to high MDT recommendation adherence, which is reflected in the implementation of the recommendations provided by the MDT [8,9,10,11,12].

The significant difference in the correlation of major deviation and

Table 4
Uni- and multivariable regression testing for factors associated with major deviations.

Variable	UVA		MVA	
	OR (95 % CI)	p-value	OR (95 % CI)	p-value
Age at diagnosis				
• >65 *(reference)*	0.98	>0.9	0.95	0.9
• ≤65	(0.54; 1.76)		(0.51; 1.80)	
Gender				
• Female *(reference)*	0.99	>0.9	0.97	0.9
• Male	(0.54; 1.86)		(0.52; 1.89)	
OMD state				
• Metachronous *(reference)*	1.74	0.083	1.44	0.3
• Synchronous	(0.92; 3.21)		(0.69; 2.93)	
Number of distant metastases				
• 1 *(reference)*	1.84	**0.046**	1.85	**0.05**
• 2–5	(1.02; 3.40)		(1.0; 3.52)	
Treatment intent				
• Curative *(reference)*	1.53	0.2	1.47	0.3
• Palliative	(0.78; 3.26)		(0.70; 3.31)	
Primary tumor state				
• Controlled *(reference)*	0.66	0.2	0.91	0.8
• Not controlled	(0.37; 1.19)		(0.46; 1.83)	
MDT recommendation				
• Combination *(reference)*				
• Evaluation	0.33 (0.09; 0.99)	0.064	0.33 (0.09; 0.99)	0.064
• Other	0.16 (0.01; 0.90)	0.09	0.16 (0.01; 0.90)	0.09
• Radiotherapy	0.53 (0.18; 1.39)	0.2	0.53 (0.18; 1.39)	0.2
• Surgery	0.44 (0.09; 1.52)	0.2	0.44 (0.09; 1.52)	0.2
• Systemic therapy	0.75 (0.36; 1.59)	0.4	0.75 (0.36; 1.59)	0.4
• Watch & wait	0.00 (0.00; 16.40)	>0.9	0.00 (0.00; 16.40)	>0.9
Type of MDT				
• Breast *(reference)*				
• Dermato-oncology	1.88 (0.33; 35.40)	0.6	2.00 (0.32; 39.20)	0.5
• Thoracic oncology	3.84 (0.69; 72.00)	0.2	4.34 (0.70; 84.80)	0.2
• Other	2.58 (0.47; 48.0)	0.4	3.05 (0.49, 59.60)	0.3

Abbreviations.
CI=Confidence interval; GIT=Gastrointestinal tract; MDT=Multidisciplinary tumor board; MVA=Multivariable analysis; OR=Odds ratio; OS=Overall survival; UVA=Univariable analysis.

number of metastatic sites (1 vs. 2–5) was consistent with our clinical experience. We explain this association based on a correlation between increased number of metastatic sites and worse overall survival, in metastatic cancer patients in general as well as in oligometastatic patients [28,29,30,31,32,33]. From clinical experience we dare to suggest that an increased number of metastatic sites is associated with a worse performance status, although there are no studies on this relationship yet. Since lower WHO performance status and increased comorbidity are associated with increased non-adherence, this would explain the significant difference between major deviation and number of metastatic sites [34,35].

This study found a statistically significantly worse OS with the presence of major deviations. While this is a very intriguing finding, it needs to be appreciated with caution, as this association might be influenced by confounders. While indeed deviation from the recommended treatment strategy might be a reason for shorter OS, notable confounding factors might include the presence of comorbidities, worse actual medical conditions than was assumed during MDT discussion, rapidly deteriorating conditions, or even patient wish to forego a potentially life-prolonging, yet intensive treatment regimen.

As reported above, recommendation for local therapy was limited to few cases in our study (multimodality therapy, incl. ablative local therapy: 17.8 %, n = 59, and radiotherapy alone: 13.9 %, n = 46). Several reasons for this finding might be postulated: Firstly, the absence of robust phase II/III evidence supporting the efficacy and safety of local treatment options might present a significant challenge in MDT discussion. Secondly, limited availability of data on local interventions, particularly in the context of rare tumors, poses a remaining substantial knowledge gap, making it challenging to confidently advocate for such approaches during MDT discussion. Additionally, the lack of standardized recognition for OMD further complicated decision-making, as clear criteria for identifying patients suitable for local therapy might not be universally acknowledged amongst all disciplines. Lastly, uncertainty surrounding the comprehensive understanding of prior treatments, particularly in cases where imaging history was incomplete or treatment details were unknown, might have contributed to the cautious approach in recommending local therapy during MDT discussion. These nuanced considerations further underscore the need for more comprehensive research, standardized guidelines, and improved diagnostic tools to better underpin potential benefits of local treatment strategies in a

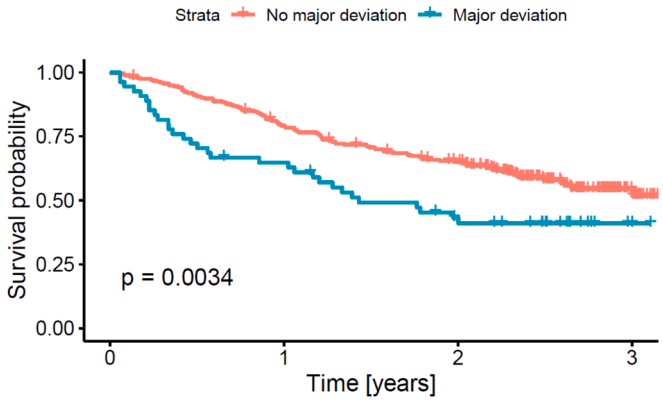

Fig. 3. Kaplan-Meier overall survival plot with log-rank p-value, stratified by major deviation.

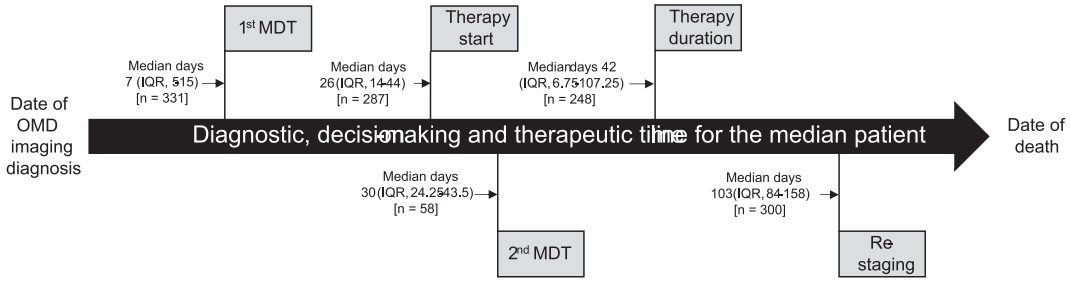

Fig. 2. Timeline from OMD diagnosis to MDT discussion, treatment and follow-up for the median OMD patient. Abbreviations: IQR=Interquartile range; MDT=Multidisciplinary tumor board; OMD=Oligometastatic disease; OS=Overall survival.

broader spectrum of OMD cases.

The study's inherent limitations originate primarily from its singular institutional focus. This constraint may have introduced potential biases, thus restricting the generalizability of the study's findings to other centers and a broader population. A further shortcoming consists in the fact that MDT recommendations in written might not always capture the potentially rich discussions and arguments presented when assessing different treatment algorithms during the MDT sessions. Lastly, patients that were OMD-diagnosed at CCCZ, yet received oncological therapy and follow-up at other centers, could not be evaluated in the context of this study.

In conclusion, this study found a generally high adherence to and implementation of MDT-recommended algorithms for OMD patients. Given the diagnostic uncertainties surrounding OMD, the heterogeneity of the OMD state, and the lack of phase III evidence, this study underscores the importance and validity of careful and elaborate patient discussions at MDTs to achieve more personalized care for OMD patients.

Prior publication

The abstract of this project was presented at the Annual Meeting of the SASRO in Bern, Switzerland in 2023.

Ethical approval

This study was approved by the Cantonal Ethics Committee in Zurich before the initiation of the project (BASEC ID # 2018–01794). All methods were carried out in accordance with relevant guidelines and regulations of the Declaration of Helsinki.

Availability of data and material

Collected patient data are confidential and not available for publication.

Code availability

Not applicable for this publication.

Funding

SMC and MA received support through the "Young Talents in Clinical Research" Beginner's Grant from the Swiss Academy of Medical Sciences (SAMW) and the Bangerter-Rhyner Foundation. This project was also supported by the SNF project "CRSII5_183478" as well as the "CCCZ Oligometastatic Disease Program – OMD-ZH".

Authors' contributions

All authors made substantial contributions to this project and manuscript. SMC and MG had the initial project idea. SMC, MG, BT, AW, TB, and MAH subsequently conceptualized the project. UJM, AM and MH provided the basis for the imaging database. SMC, MB, PH and KP did the majority of the data collection and data analysis. ELL presented the project at SASRO 2023. SMC, MB and MG prepared the first version of the manuscript, which was critically reviewed and improved by all co-authors. The final version of the analysis and manuscript was agreed on by all co-authors before submission.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: AW received research grants through a research collaboration ("POP") of the University of Zurich with Hoffmann-La Roche Ltd. MAH received research grants from Immune-Sensor, Inc. and ViewRay, Inc., as well as speaking honoraria for presenting at the Harvard Medical School Breast Cancer Symposium. M.H. received grants and speaker honoraria from GE Healthcare, a fund by the Alfred and Annemarie von Sick legacy and a grant from the clinical research priority program (CRPP) Artificial Intelligence in Oncological Imaging Network of the University of Zurich. NA has received grants from ViewRay Inc. and BrainLab and personal fees from AstraZeneca, Debiopharm, ViewRay and BrainLab, and non-financial support from ViewRay, all outside of the submitted work. MG has received grants from AstraZeneca and Varian and personal fees from AstraZeneca, all outside of the submitted work. Moreover, the USZ Department of Radiation Oncology has research and teaching agreements with Siemens/Varian, ViewRay and VisionRT. PB cited research grants to the institution from ViewRay Inc. (Mountain View, CA, USA).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2024.100838.

References

[1] Mano MS, Çitaku FT, Barach P. Implementing multidisciplinary tumor boards in oncology: a narrative review. Future Oncol 2022;18(3):375–84. https://doi.org/10.2217/fon-2021-0471. Future Medicine Ltd.
[2] Brauer DG, et al. Utility of a multidisciplinary tumor board in the management of pancreatic and upper gastrointestinal diseases: an observational study. HPB 2017;19(2):133–9. https://doi.org/10.1016/j.hpb.2016.11.002.
[3] Tamburini N, et al. Multidisciplinary management improves survival at 1 year after surgical treatment for non-small-cell lung cancer: a propensity score-matched study. Eur J Cardiothorac Surg 2018;53(6):1199–204. https://doi.org/10.1093/ejcts/ezx464.
[4] Pillay B, et al. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: a systematic review of the literature. Cancer Treatment Rev 2016;42:56–72. https://doi.org/10.1016/j.ctrv.2015.11.007. W.B. Saunders Ltd.
[5] Di Pilla A, et al. The impact of tumor boards on breast cancer care: evidence from a systematic literature review and meta-analysis. Int J Environ Res Public Health 2022;19(22). https://doi.org/10.3390/ijerph192214990. MDPI.
[6] Leff DR, et al. A multidisciplinary team approach minimises prophylactic mastectomy rates. Eur J Surg Oncol 2015;41(8):1005–12. https://doi.org/10.1016/j.ejso.2015.02.017.
[7] Guckenberger M, et al., "Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation," 2020. [Online]. Available: www.thelancet.com/oncology.
[8] NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Kidney Cancer Version 2.2023 [Internet]. 2022. Available from: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
[9] NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Prostate Cancer Version 4.2022 [Internet]. 2022. Available from: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.
[10] NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Non-Small Cell Lung Cancer Version 3.2022 [Internet]. 2022. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
[11] ESMO Clinical Practice Guidelines Metastatic NSCLC [Internet]. 2020. Available from: https://www.esmo.org/content/download/347819/6934778/1/ESMO-CPG-mNSCLC-15SEPT2020.pdf.
[12] ESMO Consensus Guidelines for the Management of Patients with Metastatic Colorectal Cancer [Internet]. 2016. Available from: https://www.annalsofoncology.org/article/S0923-7534(19)34754-4/pdf.
[13] Krause A, et al. Guideline adherence and implementation of tumor board therapy recommendations for patients with gastrointestinal cancer. J Cancer Res Clin Oncol 2023;149(3):1231–40. https://doi.org/10.1007/s00432-022-03991-6.
[14] Walter J, et al. Guideline adherence of tumor board recommendations in lung cancer and transfer into clinical practice. J Cancer Res Clin Oncol 2023;149(13):11679–88. https://doi.org/10.1007/s00432-023-05025-1.
[15] Rangabashyam MS, et al. Adherence of head and neck squamous cell carcinoma patients to tumor board recommendations. Cancer Med 2020;9(14):5124–33. https://doi.org/10.1002/cam4.3097.
[16] Algwaiz G, Salam Y, Bustami R, Ferwana M, Jazieh AR. Do multidisciplinary tumor board discussions correlate with increase in 5-year survival? a meta-analysis study. Global Journal on Quality and Safety in Healthcare 2021;4(1):3–10. https://doi.org/10.36401/jqsh-20-23.
[17] Christ SM, et al. Imaging-based prevalence of oligometastatic disease: a single-center cross-sectional study. Int J Radiat Oncol Biol Phys 2022;114(4):596–602. https://doi.org/10.1016/j.ijrobp.2022.06.100.
[18] Palma DA, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET Phase

II randomized trial. J Clin Oncol 2020;38(25):2830–8. https://doi.org/10.1200/JCO.20.00818.
[19] Lievens Y, et al. Defining oligometastatic disease from a radiation oncology perspective: an ESTRO-ASTRO consensus document. Radiother Oncol 2020;148:157–66. https://doi.org/10.1016/j.radonc.2020.04.003.
[20] Iyengar P, et al. Treatment of oligometastatic non-small cell lung cancer: an ASTRO/ESTRO clinical practice guideline. Pract Radiat Oncol 2023;13(5):393–412. https://doi.org/10.1016/j.prro.2023.04.004.
[21] Kroese TE, et al. Incidence and survival of patients with oligometastatic esophagogastric cancer: a multicenter cohort study. Radiother Oncol 2022;173:269–76. https://doi.org/10.1016/j.radonc.2022.06.012.
[22] Soon JJY, Zhao Y, Shannon NB, Tan JTH. Adherence to multidisciplinary tumor board recommendations in patients with curable esophageal and gastric cancers. J Gastrointest Cancer 2023;54(2):614–22. https://doi.org/10.1007/s12029-022-00847-7.
[23] Hollunder S, et al. Cross-sectional increase of adherence to multidisciplinary tumor board decisions. BMC Cancer 2018;18(1). https://doi.org/10.1186/s12885-018-4841-4.
[24] Cao Y, Mezzacappa C, Jaffe A, Strazzabosco M, Taddei TH. Adherence to tumor board recommendations in the treatment of patients with hepatocellular carcinoma. J Multidiscip Healthc 2023;16:1531–40. https://doi.org/10.2147/JMDH.S407908.
[25] Jasper K, Stiles B, Mcdonald F, Palma DA. Special Series: thoracic oncology: current and future therapy review articles practical management of oligometastatic non-small-cell lung cancer. J Clin Oncol 2022;40:635–41. https://doi.org/10.1200/JCO.21.
[26] Katipally RR, Pitroda SP, Juloori A, Chmura SJ, Weichselbaum RR. The oligometastatic spectrum in the era of improved detection and modern systemic therapy. Nat Rev Clin Oncol 2022;19(9):585–99. https://doi.org/10.1038/s41571-022-00655-9. Springer Nature.
[27] Iyengar P, et al. Consolidative radiotherapy for limited metastatic non-small-cell lung cancer: a phase 2 randomized clinical trial. JAMA Oncology 2018. https://doi.org/10.1001/jamaoncol.2017.3501. American Medical Association.
[28] Dziggel L, Gebauer N, Bartscht T, Schild SE, Rades D. Performance status and number of metastatic extra-cerebral sites predict survival after radiotherapy of brain metastases from thyroid cancer. Anticancer Res 2018;38(4):2391–4. https://doi.org/10.21873/anticanres.12488.
[29] Oh Y, et al. Number of metastatic sites is a strong predictor of survival in patients with nonsmall cell lung cancer with or without brain metastases. Cancer 2009;115(13):2930–8. https://doi.org/10.1002/cncr.24333.
[30] Owonikoko TK, et al. Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. J Clin Oncol 2007;25(35):5570–7. https://doi.org/10.1200/JCO.2007.12.5435.
[31] Pallis AG, et al. Efficacy and treatment tolerance in older patients with NSCLC: a meta-analysis of five phase III randomized trials conducted by the hellenic oncology research group. Ann Oncol 2011;22(11):2448–55. https://doi.org/10.1093/annonc/mdq772.
[32] Seve P, Sawyer M, Hanson J, Broussolle C, Dumontet C, Mackey JR. The influence of comorbidities, age, and performance status on the prognosis and treatment of patients with metastatic carcinomas of unknown primary site: a population-based study. Cancer 2006;106(9):2058–66. https://doi.org/10.1002/cncr.21833.
[33] Kim TH, Nam TK, Yoon SM, Kim TH, Choi YM, Seong J. Stereotactic ablative radiotherapy for oligometastatic hepatocellular carcinoma: a multi-institutional retrospective study (KROG 20–04). Cancers (Basel) 2022;14(23). https://doi.org/10.3390/cancers14235848.
[34] Lindqvist J, Jekunen A, Sihvo E, Johansson M, Andersén H. Effect of adherence to treatment guidelines on overall survival in elderly non-small-cell lung cancer patients. Lung Cancer 2022;171:9–17. https://doi.org/10.1016/j.lungcan.2022.07.006.
[35] Wulaningsih W, et al. Determinants of non-adherence to adjuvant endocrine treatment in women with breast cancer: the role of comorbidity. Breast Cancer Res Treat 2018;172(1):167–77. https://doi.org/10.1007/s10549-018-4890-z.