D8.3 Impact of networking research into patients' care

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Executive summary

Multiple interdependencies exist between comprehensive cancer centers (CCC) — considering both stand-alone centres and the cancer-related area of teaching hospitals — and other providers. These interdependencies are worth to be explored in relation to the translation of research into clinical practice. For this purpose, CraNE WP8 approached the situation of precision oncology. Unlike traditional approaches, which treat cancer based on its location and histological type, precision oncology uses genomic and molecular information with the purpose of designing more individualized treatments and minimizes side effects. Both the Europe's Beating Cancer Plan (EBCP) and the Joint Actions CraNE and the upcoming EUnetCCC point out to the interface between care and research as one of the critical areas of action.

The current analysis focused on the most common instrument used in the EU health systems to realize the potential of precision oncology. The so-called Molecular Tumour Boards (MTBs), the scope of which can be hospital-based, regional or even national, stands out as the multidisciplinary committee that seeks for matching therapies for patients based on their molecular profile of the tumour as well as the natural history of the disease. Eight experiences of MTBs were evaluated and compared in order to understand their internal operation, the potential of integration in a multi-provider context (including the Comprehensive Cancer Centers, as well as their governance and accountability.

The findings show that, although MTBs are not part of standard care and operate in a research setting, they share their key functionalities such as composition, internal operation and most of timing targets. We also found different models of MTB that relate to be or less research-oriented and the discussion of patients at different moments of the processes of care, which might have an impact on the administered targeted therapies. A main conclusion of the analysis was that MTBs differences, given the regional or even national scope where they operate, relate to the efforts made in ensuring access of patients and professionals — to expert knowledge — in non-CCC settings.

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1. Introduction

Precision oncology represents a crucial advancement in the health of cancer patients, focusing on the personalization of clinical management based on the unique molecular characteristics of the tumor (Garraway & Lander, 2013). Unlike traditional approaches, which treat cancer based on its location and histological type, precision oncology utilizes genomic and molecular information to design more effective individualized treatments that minimize side effects (Chakravarty, et al., 2017).

Molecular alterations, including genetic mutations, genomic amplifications, and gene fusions, are fundamental for understanding the biology of cancer. These alterations can serve as biomarkers that help define a diagnosis, determine the prognosis of the disease, or predict the response to specific therapies, allowing oncologists to select targeted treatments that block critical molecular pathways for tumor survival and proliferation (Vogelstein et al., 2013). Molecular determination requires tumor tissue, which is usually obtained through an invasive technique that varies in method and complexity depending on its location. Additionally, recently, liquid biopsy has been developed as a minimally invasive technique that allows the determination of different biomarkers in blood (Rolfo, et al., 2018).

The identification of these alterations is currently performed through advanced techniques such as Next Generation Sequencing (NGS), either by studying a gene panel, the exome, or the whole genome, which allows the simultaneous analysis of multiple genes with high precision and speed (Tsimberidou, et al., 2014). This technology has facilitated the detection of somatic mutations in oncogenes and tumor suppressor genes, as well as alterations in copy number and genomic rearrangements, providing a comprehensive view of the cancer's molecular profile (Garraway & Lander, 2013). However, the rapid pace of advancements in precision oncology and the fact that its application involves small patient groups make it challenging to obtain robust evidence in experimental contexts (such as the validation of risk stratification and the clinical development of treatments) (Vivot, et al., 2017), as well as the evaluation of patient outcomes when these sequencing techniques are implemented in clinical practice (Regier, et al., 2022).

In this context, the European Society for Medical Oncology (ESMO) has proposed a common framework to classify genomic alterations according to their clinical relevance for precision oncology. The Scale for Clinical Actionability of Molecular Targets (ESCAT) was developed to harmonize and standardize the presentation and interpretation of clinically relevant molecular data, determine the relationship between molecular

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alterations and drugs with the best results in clinical trials, and provide a common language that could be adopted by all professionals involved (Mateo, et al., 2018).

The interpretation of results from new sequencing technologies is a complex task, requiring differentiation between findings with proven or potential clinical value, based on clinical or preclinical evidence, hypothetical relationships between molecular alterations and drugs, and findings currently irrelevant to clinical practice. Therefore, a multidisciplinary approach involving different specialists such as oncologists, hematologists, pathologists, geneticists, molecular biologists, or bioinformaticians, among others, is required (Mateo,et al., 2018; Koopman, et al., 2021). This approach must consider the indication for which the molecular study is conducted and the clinical situation of the patient, along with the interpretation of the results, to correctly adapt their clinical management.

1.1. Molecular Tumor Boards

Different European healthcare systems are proposing solutions to realize the potential of precision oncology through a common organizational approach, enabling its effective implementation in healthcare centers, supported by comprehensive public funding. Published experiences in different countries present various recently developed organizational models, although these have not yet matured enough to be consolidated as standard care processes. Among these models, a proposal centered on Molecular Tumor Boards (MTBs) stands out.

MTBs refers to a multidisciplinary group of healthcare professionals that includes oncologists, bioinformaticians, biologists, and molecular pathologists, who evaluate and interpret the specific molecular characteristics of each patient's tumor to offer individualized clinical recommendations based on available evidence and their expertise (Rolfo, et al. 2018; Koopman, et al. 2021). These MTB professionals must possess the necessary knowledge to differentiate between therapies established as standard in clinical practice, those in clinical trials, off-label treatments, and other therapeutic options based on molecular determinations (Rolfo C, et al. 2018; Koopman B, et al. 2021). The implementation of MTBs in healthcare services may present differences according to national and regional contexts. In 2021, ESMO proposed a model of MTBs with required professionals and clearly defined roles. The professionals and roles can be seen in the following image, created by the ESMO authors (Danesi et al., 2021, p. 9):

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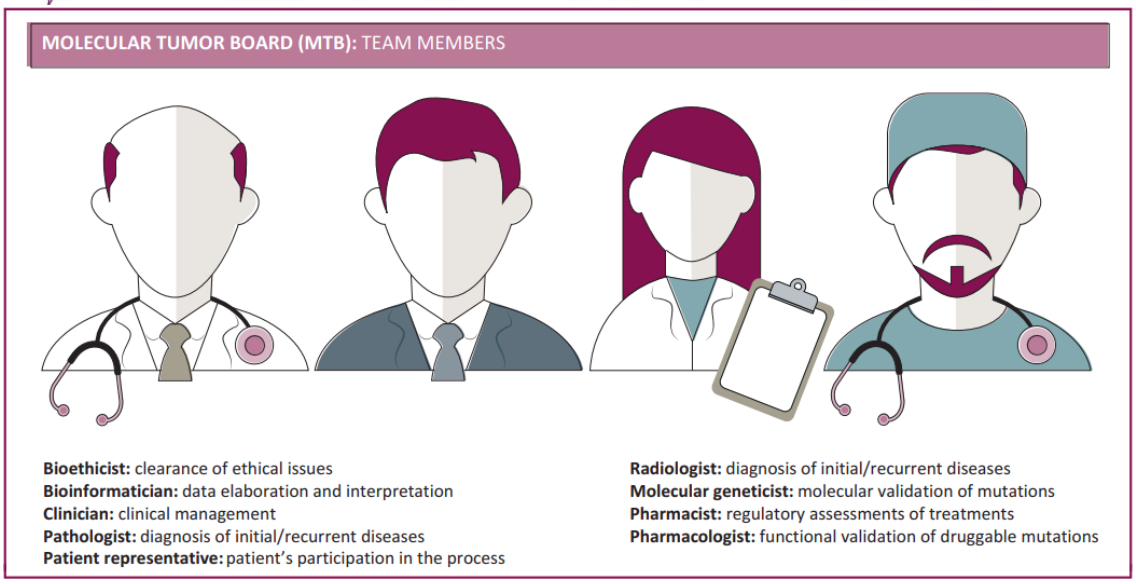

These MTBs meet regularly to discuss individual cases, integrating diverse knowledge and experiences to reach optimal therapeutic decisions. This approach not only enhances the personalization of treatment but also promotes interdisciplinary collaboration and continuous learning among the professionals involved. The effective implementation of MTBs requires adequate infrastructure and institutional support, as well as the availability of advanced sequencing technologies and data analysis. Additionally, it is crucial to ensure the continuous training of professionals in the advances of precision oncology and next-generation sequencing techniques (Shin, Bode, & Dong, 2017; Rolfo, et al., 2018).

Therefore, MTBs represent an innovative and collaborative approach to precision oncology, offering personalized clinical recommendations based on a multidisciplinary evaluation of the molecular characteristics of each patient's tumor. This approach can significantly improve clinical outcomes and the quality of life of cancer patients (Groisberg, Roszik, Conley, Patel, & Subbiah, 2017) (Schwaederle, et al., 2015). Several approaches of the organizational concept have tried in different EU countries. One relevant case is the experience of Norway, which has a national MTB that aims to: establish equitable access to molecular tumour analysis, enabling patient stratification for clinical trials; increase the volume of trials in the field of precision oncology, such as the national adaptive precision oncology trial (IMPRESS; Helland Å et al. 2022); and work on mechanisms to implement precision oncology as a care standard (Taskén, et al., 2022). In Germany, the German Network for Personalized Medicine (DNPM) aims to integrate molecular characterisation of advanced-stage tumours and personalised therapeutic strategies in the national health system. It has regional personalised medicine networks in all Comprehensive Cancer Centres (CCCs), where the MTBs are based; and a national strategy for harmonising and guaranteeing the quality of the process, financing MTB activities and recommended treatments, and providing the necessary training to the professionals involved (Illert, et al., 2023).

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The Netherlands has a national organisational model that focuses on collaborative workflows aligned at the national level, the interinstitutional level, and between the different MTBs. This model aims to standardise the identification/prioritisation of molecular alterations to be analysed, and improve the consistency and quality of targeted treatment recommendations for tumours with rare or complex molecular profiles. The MTBs are based in tertiary referral hospitals, but experts from other local hospitals can participate. MTBs operate independently of the cancer-specific

The scope of an MTB can be limited to a specific institution (e.g. a CCC), as in the case of Germany (Illert, et al. 2023); or they can cover a network (of which we have identified no published experiences) or a whole region/country, as in Norway and Germany (Taskén K et al. 2022; Illert AL et al. 2023). In any case, with the increasing implementation of MTBs in cancer care, more and more cancer types are being analysed and evaluated, which increases the urgency of standardising and centralising the molecular analysis process.

One limitation of MTBs is that relatively few people are currently benefiting from the results of discussions, which frequently may produce non-informative results: after MTBs have discussed available therapeutic options based on the molecular profile, they usually issue no recommendations because they have found no biomarkers with available matched therapies. One systematic review published in 2021 evaluated the clinical outcomes of MTBs, including a total of 14 studies with 3328 patients. It found that 61% to 89% of patients with a molecular profile could not receive treatment due to "lack of actionable mutations [or] rapidly progressive disease", or because "when clinical trials were recommended by the MTB, patients were unwilling to travel or ineligible" (Larson, et al., 2021, p. 1127). However, although most analyses end up being non-informative, most cancer therapies approved in the last five years are targeted therapies (Luzán 5 Health Consulting, p. 8).

1.2. CraNE Joint Action

The framework of this initiative is the CraNE Joint Action, which responds to flagship 5 of Europe's Beating Cancer Plan: "The Commission will establish, by 2025, an EU Network linking recognised National Comprehensive Cancer Centres in every Member State". One specific aim of CraNE is to create an EU Network of National CCCs (EUnetCCC) in order to improve care and reduce disparities across the EU. This implies preparing the necessary preconditions for the integration of both existing CCCs and newly categorised CCCs across all EU Member States. One key precondition is the establishment of a specific certification process based on criteria and standards resulting from an assessment on sustainability and feasibility of networking of CCCs (https://crane4health.eu).

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In view of MTBs' growing scope of action, we aimed to explore how they coordinate to facilitate access of patient from different hospitals. This perspective is of utmost interest for CraNE Work Package 8 (WP8; Equitable Access to High-Quality Care and Research: Networks in the context of CCCs). MTBs constitute an excellent case study for evaluating the organisational methods and options used by networks built around CCCs to translate research progress into clinical practice. It seems logical that CCCs should occupy a leading position in the field of precision oncology, and it is worth exploring the shared strategies of provider networks organised around CCCs for facilitating equitable patient access.

Specifically, Task 3 of WP8 is to analyse the potential role of networks in supporting translation of research findings into patient care. This multiple case study will consider MTBs' implementation and the use of real-world data to assess outcomes in cancer care within networks. We have analysed eight cases from different European health systems to explore the role of CCCs in terms of the design, implementation, and integration of MTBs at the regional and/or national level.

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2. Methodology

The present report is a qualitative study based on semi-structured interviews. The phenomena being studied is the translation of research into clinical practice based on MTBs' role while taking into account the role of CCCs. The research question was:

> How do molecular tumour boards (MTBs) provide and align their services in a multi-provider context, including the Comprehensive Cancer Centers?

2.1 Objectives

The main objective of this research was the following:

- Analysing the embedment of MTBs with a regional scope, that is, involving different providers with a different degree of expertise in cancer.

Two secondary objectives were formulated:

- Understanding the internal organization, patient access, and decision delivery/reporting of MTBs by focusing on lung cancer.
- Gain insight into potential differences in access to MTBs' services between CCCs and non-CCC providers.

2.2 Selection Criteria

A diverse sample of MTBs from different European regions and health systems were selected. Four criteria were used in this process:

- **Appropriateness**: MTBs selected by cancer plans or gatekeepers with a regional scope including CCCs and other providers.
- **Variability**: MTBs from different EU regions to ensure diversity of experiences, with CCCs either holding the MTBs at a functional level or being mere referring centers to "external" MTBs.
- **Feasibility**: Based on contacts provided by gatekeepers and professional networks of the researchers, including members of the CraNE Joint Action.
- **Maturity**: More than 5 years in operation.

2.3 Case Selection and data collection

The preliminary review of potential cases was conducted based on task 8.2 of the CraNE Joint Action, which focused on care pathways for lung cancer and implied onsite visits.

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This initial phase ensured a first understanding of the functionalities and context surrounding related to the MTBs.

Regional MTBs – our study cases - had to be proposed and endorsed by representatives from national cancer control plans (NCCPs) and/or health authorities. Such endorsement process was crucial to validate the relevance and appropriateness of each selected MTB.

Information retrieval was initiated by contacting NCCP managers in several EU countries. A brief study protocol, describing the purpose, motivation, and methodology of the study, was distributed among gatekeepers and interviewees (Annex 2). An interview guide was developed for the purposes of this study.

Relevantly, the lead members of the respective cases of analysis selected the interviewees. We should consider the interviewees both key informants and representatives of the MTB. The protocol and the interview questions were shared in advance to select the most suitable key informant. In general, the key informants were either the lead members or professionals with a strong presence both in clinical deliberation and in the process of connecting results of the deliberation to the hospitals.

2.4 Ethical Considerations

- Ethical approval and consent were obtained from all participants.
- Confidentiality and anonymity of the interviewees were maintained throughout the study.

2.5 Selected MTBs

A total of 8 cases were successfully selected for the study, though many other potential cases declined the invitation to participate due to time constraints. This section provides detailed insights into the structure, functioning, and regional engagement of each MTB, contributing to the overall understanding of their roles and impact within their respective health systems.

1. IMPRESS - Norway

MTB scope: National.

Description: Norway's MTB is materialized under the clinical study IMPRESS.

Laboratories: A total of 6 laboratories located in different university hospitals.

Interview Format: On-site, 22/06/2023.

2. Midtjylland (Aarhus) - Denmark

MTB scope: Regional.

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Description: Regional lung cancer MTB focused explicitly on adenocarcinoma.

Laboratories: Only one laboratory located in Aarhus CCC.

Interview Format: On-site, 25/09/2023.

3. Málaga - Province of Andalucia, Spain

MTB scope: Regional.

Description: Regional MTB situated in the Medical Health Research Center (CEMES), which houses the only laboratory.

Laboratories: One laboratory located in CEMES.

Interview Format: On-site, 13/12/2023.

4. Tuscany - Italy

MTB scope: Regional.

Description: Regional MTB celebrated online

Laboratories: One laboratory for the region, located in Careggi University Hospital.

Interview Format: Online, 25/04/2023.

5. ICO – Bellvitge, Catalonia, Spain

MTB scope: Regional.

Description: ICO/ Bellvitge is one of the six reference laboratories designated as expert centres in Catalonia by the Catalan Health Service. Catalonia has a program for the MTB covering the whole region.

Laboratories: Catalan Institute of Oncology (ICO) - Bellvitge.

Interview Format: On-site, 16/04/2023 and 23/04/2023.

6. Curie Institute - France

MTB scope: Regional and National.

Description: Institut Curie serves as a reference center for Paris with two programs: one regional and one national. The regional program is locally financed, while the national program covers about 50% of the country and is nationally financed.

Laboratories: The reference laboratory for the region.

Interview Format: Online, 26/04/2024.

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7. Instituto Português de Oncologia do Porto (IPO-Porto) - Portugal

MTB scope: National and Regional.

Description: IPO-Porto is the only formalized MTB in the country, though many hospitals conduct genetic profiling independently. IPO-Porto functions as a consultancy board for the region.

Laboratories: Located in the CCC IPO-Porto.

Interview Format: Online, 08/05/2024.

8. Heidelberg - Germany

MTB scope: National.

Description: The MTB of Heidelberg is part of the National Center for Tumor Diseases (NCT) Heidelberg CCC. It has a national scope with 152 associated partners.

Laboratories: One of the main laboratories in the country.

Interview Format: Online, 13/05/2024.

2.6 Analysis

All interviews were recorded and transcribed verbatim. Each interview was check by two independent research to ensure the validity of the translation. Data analysis was conducted using thematic analysis, which allowed for the emergence of new categories without adhering to a predefined study framework (Clarke & Braun, 2017; Alhojailan, 2012). This approach facilitated a comprehensive exploration of the data, enabling the identification of novel themes and patterns. Labels were assigned freely, allowing new categories to emerge organically from the data. The analysis revealed three main categories that served to organise the study contents: (1) *Internal Organization*: This category includes the structure and management of MTBs, roles and responsibilities, and decision-making processes; (2) *Integration into healthcare systems*: This category examines how MTBs are embedded within broader healthcare systems, their collaborations, and their impact on patient care; and (3) *Governance Mechanisms*: This encompasses policies, regulations, and frameworks that guide the operation of MTBs, as well as the relations that MTBs have as organizations to the healthcare authorities.

We used ATLAS.ti 9 for the data analysis process, providing robust tools for coding, categorizing, and interpreting the data.

2.7 Study limitations

This study has some limitations that may affect the generalizability and comprehensiveness of the findings. First, the degree of representativeness of the

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professionals in relation to their MTB should be discussed. MTBs are multidisciplinary committees with defined roles, and we only included accessed one or two professionals per MTB. Second, the positions of the interviewees differed depending on the selected case, making some interviews without counterpart positions. Some interviewees were heads of the organization with close ties to its development, while others were members with significant coordinating and clinical roles, focusing more on internal organization and patient access. Lastly, the study only includes interviews with MTB professionals. Treating physicians, managerial positions from local hospitals and healthcare authorities might bring other insights into MTBs' operations and roles. A broader and more varied sample of interviewees, including hospital professionals and healthcare authorities, would enhance the comprehensiveness and validity of the results. In order to anonymize our informants, all of them have been described as researchers, so the link with the position and name cannot be followed back. We had the objective to collect some data on the access of patients by centre of origin. Most of MTBs couldn't share with us this data for confidential reasons, while other did not have these data segregated.

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3. Results

The results are structured in three complementary sections: internal operation of MTBs, regional healthcare services' integration, and governance and accountability. In the first two sections, we have differentiated between how professionals in the MTB experience the internal process of their tasks, and how their functions relate to the formal or informal networks they are working for. In the third section, we have tried to combine these two visions to explain why MTBs adopt these kinds of procedures.

3.1. Internal operation

The MTB professionals we interviewed described relatively similar internal processes, regardless of their geographical location, with the exception of the Portuguese Institute of Oncology (IPO) in Porto, which provides a forum for discussion but not analysis (see section 3.2.4).

3.1.1. Inclusion of patients

All MTBs offer their services to the hospitals in a region, territory, or, in the case of Norway, the whole country. Even so, several MTBs are physically located in one or more hospitals, usually CCCs, and share the hospitals' information technology (IT) infrastructure (Institut Curie, France; Tuscany, Italy; Catalan Institute of Oncology [ICO], Spain; IPO-Porto, Portugal; Heidelberg, Germany). Consequently, patients treated in the CCC have more direct access to the MTB, and oncologists from other hospitals have to make a different type of online request (usually by email). Patients treated in CCCs may also have more direct access to clinical information. Requests to the MTB for patient assessments are made online in all cases.

Three cases in this study offer two different options for inclusion requests: Midtjylland (Denmark) has a single healthcare IT infrastructure for the whole region, while Norway and Málaga separate the infrastructures of the CCC and the MTB. The MTB in Norway is part of a national clinical trial, and patient access is only possible through a clinical trials unit in any hospital. This requirement separates MTBs from CCCs, although the analysis laboratories are located in six university hospitals.

These solutions do not always generate "equitable" results. For example, although Málaga (Spain) has separate infrastructure for MTBs, only tertiary care hospitals can make requests on behalf of patients.

3.1.2. Targeted patients

The main difference between the MTBs studied is the time of patient inclusion. The MTB of Midtjylland provides upfront genetic profiling when the patient is diagnosed. The only

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inclusion criterion is suspicion of adenocarcinoma during the initial diagnostic phase. This means NGS is performed on some patients who do not need it:

> "Because sometimes we do order them so early on in the diagnostics that we later on discover that it is a squamous cell carcinoma or perhaps a neuroendocrine carcinoma. And then we didn't have to order it, but we already have because we want it to be as quickly as possible" (researcher, Midtjylland).

In Málaga and the ICO, upfront genetic profiling is reserved for very specific cases, usually starting from the second line of treatment. In the Institut Curie and in Tuscany, requests for sequencing are usually made after second-line treatment. In Norway, Heidelberg, and IPO, molecular diagnostics begins when patients no longer have viable therapeutic options. However, the definitions of targeted patients appear to be gradually broadening, according to different interviewees:

> "I'd say this is still the majority of cases, but we're trying to use molecular diagnostics earlier. It's very difficult to give a general answer. But for example, we have the experience that in many patients with rare cancers, often there is no good standard treatment and you only have one or two lines. So, we typically try to use molecular profiling early on. But it's a moving target, I'd say (Researcher, Heidelberg)."

3.1.3. Molecular Tumour Board meetings

In all the cases studied, the MTB meetings have a chairperson or coordinator, usually a pathologist or oncologist. The meetings are always virtual/mixed and are held twice weekly, weekly, or twice monthly, though the frequency of meetings can be reduced if there are no cases to discuss. Requests for patient inclusion in MTBs are made online, and there are no systems in place for prioritising patients. Oncologists can request that the process be accelerated in very specific cases, but the team in charge of molecular profiling normally does not offer this possibility. In general, the requests are resolved on a "first in, first out" basis.

3.1.4. Molecular Tumour Board programmes

In some cases, there are several MTB programmes, understood to mean catchment areas covered by the MTB. Heidelberg has two different programmes, each of which has twice-weekly meetings. One programme focuses on whole genome sequencing (WGS), while the other is more experimental and considers other sequencing techniques (transcriptome sequencing and methylation profiling). Finally, Institut Curie has a national programme and a hospital-based programme. The national programme covers half of the territory, and the hospital-based programme works in a network with nearby hospitals, without a strict scope.

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During meetings, board members discuss the clinical information of each patient, referring to medical records and molecular profiling results, to find the best therapeutic option. According to our interviewees, 65% to 85% of analyses either show no biomarkers or show genetic alterations that do not match any available treatment.

3.1.5. Molecular Tumour Board composition

The composition of MTBs varies across the cases, as shown in Table 1. The only speciality present in all MTBs is pathology, although all boards have members with a strong background in molecular biology. Furthermore, none of these MTBs have a patient representative, as recommended by ESMO.

Table 1. Experts required in MTBs by case.

	Norway	Midtjylland	Tuscany	Málaga	IPO	ICO	Institut Curie	Heidelberg
Experts by need	X		X	X	X	X	X	X
Clinical oncology	X		X	X	X	X	X	X
Haematologist	X							X
Gyn. oncology	X							
Pathologist	X	X	X	X	X	X	X	X
Medical genetics	X	X	X		X	X		X
Molecular biologist	X	X		X	X	X	X	
Bioinformatic	X	X	X			X		
Pharmacologist	X				X	X		
Radiotherapist				X		X	X	
Project manager								X

3.1.6. Molecular profiling for solid tumours

The methodology used to evaluate the molecular characteristics of tumors is typically NGS, with the number of genes evaluated varying depending on the panel or whether it involves whole exomes or genomes (Table2). There is considerable heterogeneity between the processes, due to both the specific objectives of each MTB and the resources assigned to them. For example, the MTB in Norway is part of a national clinical trial with research objectives as well as clinical objectives, following the format of the Drug Rediscovery protocol (DRUP; van der Velden et al. 2019). This kind of study, which we can define as an adaptive precision oncology trial, monitors the results of therapies according to genetic profiles to discover which off-label therapies are effective and which are not. The particularity of the Norwegian MTB is that it seeks an appropriate therapy based on the country's ongoing clinical trials and only proposes off-label treatment when there are no other options.

In Catalonia, the Precision Oncology Program (POPCat) was established through Instruction 03/2021. This program spans the entire region with the objective of

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integrating precision medicine into the public healthcare system in an organized manner, using healthcare planning criteria and leveraging the experience of the centers to ensure quality and equitable access for all patients with a clinical indication. The program harmonizes processes by establishing quality criteria and providing specific funding for the analysis of gene panels in reference centers, linked to the fulfilment of these criteria. The Catalan Institute of Oncology (ICO) is one of the reference centers for these programs.

Table 2. Molecular profiling characteristics in each case.

	Norway	Midtjylland	Tuscany	Málaga	IPO	ICO	Institut Curie	Heidelberg
Tumour biopsy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Liquid biopsy	Yes	No	Yes	For some cancers	For some cancers	For some cancers	Yes	No
Type of testing	Gene panel	Gene panel	Gene panel	Gene panel	Gene panel	Gene panel	Gene panel, WGS	Gene panel, WGS, transcriptome sequencing, methylation profiling
Nº of genes	523	72	572	120	500	80-500	500	80-500
Unique panel	Yes	Yes	Yes	Yes	No	No	Yes	Yes

3.1.7. Deliberation and recommendation report

Once the board has the results of the test, they discuss the findings and the actionable biomarkers during the meeting. After the deliberation process, the MTBs write up a report with the most important alterations and a recommendation (except in Midtjylland). The report is posted in the patient's electronic medical record. MTBs do not always have access to the medical records of all patients (because they are stored in separate IT systems); in these cases, they send the results and the recommendation to the professional who made the request:

> "So if it's a patient at our hospital, it's entered into the electronic health record. With other centers where we simply provide the report, we actually don't know to what extent somebody in [City], enters the information" (anonymous).

3.1.8. Cancers treated

All the MTBs studied are tumour-agnostic, which means the discussions are based on genetic and molecular features rather than the type of cancer. They select sequencing techniques according to tumour location, according to the expected clinical benefits and

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the analysis time. The only exception is Midtjylland, where the MTB is for lung cancer only.

3.1.9. Molecular Tumour Board models

MTBs are classified according to several variables of interest. The time point of their application during the diagnosis or treatment process is one of the most important defining features. In this study, we found that molecular profiling of cancer patients can be performed upfront, deferred, or both:

- In upfront MTB evaluations, molecular profiling is part of initial patient testing. Upfront evaluation has become routine clinical practice for some tumours, such as non-small cell lung cancer, because ESMO recommends performing a genetic analysis before beginning treatment (Planchard et al. 2020). This is the case of Midtjylland.

- Backend MTB evaluations take place when the patient has no alternative therapeutic options (i.e. when the oncology team has exhausted all conventional options). This is how the IPO and the Norwegian MTBs operate.

- MTBs that adopt a mixed approach act after the first line of treatment but before exhausting all therapeutic options. They offer a wide range of intermediate options. Heidelberg and Tuscany started with the deferred approach but are now moving towards the mixed model. The other mixed MTBs are the in the ICO, Málaga, and Institut Curie.

These categories are not mutually exclusive. As almost all MTBs are tumour agnostic, they can apply an upfront, deferred, or mixed model according to the tumour location.

3.2. Integration of Molecular Tumour Boards in oncology networks

Successful integration of MTBs in oncology networks depends on whether existing mechanisms facilitate equal access of patients from other hospitals to the MTB. Since the MTBs included in this study are regional or national entities, they place special emphasis on the mechanisms of referral between different hospitals to facilitate patient access.

To explore the degree of MTB integration, we have described the procedures considered most significant by our interviewees, as well as the problems they face and the different solutions put into practice.

Table 3 shows the MTB workflows and activities, which are similar across all the MTBs, but with relevant differences in their implementation.

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Table 3. MTB workflows by case.

	Patient inclusion	Patient information	Molecular profiling and interpretation	Discussion of results and report	Follow-up
Norway	Yes	Yes	Yes	Yes	Yes
Midtjylland	Yes	Yes	Yes	Yes	No
Málaga	Yes	Yes	Yes	Yes	No
Tuscany	Yes	Yes	Yes	Yes	No
ICO	Yes	Yes	Partially	Yes	No
Institut Curie	Yes	Yes	Yes	Yes	Yes
IPO	Yes	Yes	Only local	Yes	Yes
Heidelberg	Yes	Yes	Yes	Yes	If possible

3.2.1. Patient inclusion

The first point to consider is the capacity of professionals to refer eligible patients to the MTB (i.e. the type of gateway). All the MTBs in this study are part of national health systems, meaning they are accessible to all patients who meet certain criteria. The MTB with the fewest inclusion criteria is Midtjylland, which requires only the suspicion of lung adenocarcinoma during the initial diagnostic phase; nearly 80% of patients meet this criterion, according to the expert we interviewed. The most restrictive MTBs, such as that of the IPO, require patients to have exhausted the standard lines of treatment, have no available alternatives, and have a performance status of 0 to 1.

In Institut Curie, Málaga, Tuscany, the IPO, and Heidelberg, because there is no automated and standardised computer system with the inclusion and exclusion criteria, the treating physicians are responsible for deciding when to include patients in MTBs. With gateways like this, two treating physicians could make different decisions for the same patient related to the decision for referral, which could generate access disparities if decisions on inclusion are mediated by knowledge of precision oncology. When we asked our interviewees how much they thought the average treating physician knows about their field, they indicated that the knowledge is outdated due to the inherent difficulty of keeping up with this continually evolving field:

> “I mean, I think the knowledge is quite low indeed. And I mean, if we think about it, only a minority of patients are discussed in MTBs, even in our institution. So because, you know, we discuss patients every week. So, it's a very low proportion in comparison to all patients we treat every year in the recurrent setting. And then at the national level, it's even lower. So, at the end, you know, it's only a small minority of patients who are discussed, meaning that the knowledge in molecular biology is indeed very limited and concentrated” (Medical Oncologist, Institut Curie).

> “I think for some oncologists it's difficult to explain their results to the patient, because they have not as strong and knowledge or understanding about the

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results. And that's why we try and we try to discuss it quite thoroughly at the MTB meetings so that they actually understand as much as possible" (Oncologist, Norway).

> "I think that yes there is a difference, probably at the information level, because the oncologists who are in the regional hospitals or more second-level hospitals, yes it could be that they have had less exposure to clinical trials, sometimes they have fewer opportunities to attend conferences as well, because that is also important from a training perspective, and sometimes they have pretty good overall knowledge, but yes it may be that the field is evolving at such a rapid pace and sometimes as well the findings can be so diverse that probably the knowledge they have is sufficient, but it could be better"(Oncologist, ICO).

On the other hand, inclusion cannot simply be automated, as many factors associated with the patient's place of residence can facilitate or hinder their inclusion in the MTB. These factors include the need to travel to another region for the clinical trial, the patient's support network, or their preferences regarding continuation of therapy.

We identified two methods for safeguarding against these disparities in the cases studied. One is removing the treating physicians' exclusive capacity to decide on patient referral, for example by greater protocolisation of inclusion. This is one goal of the precision programme in Catalonia, where a regional government directive stipulates that patients who meet certain criteria must be included in the MTB. This protocolisation has not been top-down; rather, different experts representing the stakeholders agreed on the requirements:

> "If it's in the instruction, it should always be done as indicated. This is wonderful. This means you don't have to fight and ask for favours to get things done" (Anonymous).

Norway provides another example of this approach. As previously described, access to the Norwegian MTB is through clinical trial units in hospitals. When patients run out of therapeutic options, they are sent to the clinical trials unit for an evaluation of possible curative options. In this way, the role of intermediary passes to the clinical trials units of the hospitals. However, our interviewees indicated that this approach has drawbacks, since not all clinical trials units are equally established in tertiary hospitals. The know-how of each clinical trials unit determines their use of the MTB. One interviewee explained that 30% of all MTB cases come from Oslo University Hospital, the largest hospital in the country.

> "In Oslo university hospital, there's quite a large department for clinical research and that lacks in the smaller hospitals, there's no such department of clinical research. So and they have to learn and they have to sort of establish their routines. They have to get the persons involved. But I think it's really good that

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> they do that and they are very eager. And I think some years from now they will be more competent and they will have things in place" (Oncologist, Norway).

The other method for facilitating patient entry is educating treating physicians on the latest molecular oncology research, or including the same treating physician in the MTB and the Multidisciplinary Team Meeting (MTM), as occurs in Málaga (and in Midtjylland with the specific pathology dealt by the MTB). Currently, in the province of Málaga, there are three tertiary hospitals and four local hospitals, all working in the same network. This networking consists of sharing physical resources, such as positron emission tomography–computed tomography (PET-CT) scanners, and having oncologists travel to regional and county hospitals. During these trips, the oncologist from the tertiary care hospital or from the local team in the MTM can request the inclusion of a patient in the MTB. To do this, the oncologist from the tertiary care hospital makes an online request from their hospital, as only tertiary hospitals can make this request. According to our interviewees, this extra step is an additional effort but does not constitute a barrier to the inclusion of eligible patients.

This process also attenuates any differences in knowledge that may exist between CCCs and non-CCCs. The same professionals request inclusions, and when the local MTM discusses the inclusion of the patient, it is the CCC oncologist who argues for the admission or exclusion of the patient following the same criteria as in the CCC. In this way, information about the advantages, disadvantages, capabilities, and uses of the MTB is transmitted from CCCs to non-CCCs through dialogue in the MTMs.

3.2.2. Patient information

The second role of MTBs is to provide information to all patients and obtain their informed consent to perform molecular profiling. MTBs should also provide detailed and accessible information about their functions. According to one interviewee, managing patients' expectations is an important task in their clinical practice, since some patients are overly optimistic about the current possibilities of precision oncology.

> "Some patients put a lot of hope in the MTB and they think that, you know, if they come to see us, it's because we will find something. So I find it very important to tell them we'll try to find something, but it's very likely we don't. So that, you know, they are not disappointed if we don't find nothing" (Medical Oncologist, Institut Curie).

One example of good practice for informing patients comes from Heidelberg, where they have produced informative videos (link). These videos explain the inclusion criteria, the objective of the analysis, data privacy, and the information needed from patients, among other aspects.

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3.2.3. Molecular profiling and interpretation

The third function of MTBs is sample preparation, molecular analysis, and reporting. Before molecular profiling of tumour samples, the biopsies must be treated to extract DNA and RNA. All MTBs except those of the ICO and the IPO perform this process. In Catalonia, the pathologists in smaller hospitals have to take on an additional workload, which can generate delays in the dispatching of samples. In Heidelberg, some of the hospitals that send the sample also extract the DNA and RNA, although the MTB also performs this process.

The sample must be of sufficient quality to be sequenced and produce informative results. The main determinants of biopsy quality, according to one interviewee, is the time needed to extract the sample, the time needed for formalin fixation and paraffin embedding, the time from sample extraction to sequencing, and the quantity of tissue extracted. In one case, a non-CCC hospital provides a larger proportion of non-informative biopsy results:

> "Because they are not fixed with the same cure. This is something that worries us and that we have never said and maybe it's something we have done wrong, because listen, something is going on with the biopsies from [Hospital], which are non-informative more often than ours" (Anonymous).

MTBs also prepare the libraries for sample sequencing. This procedure enables subsequent reporting of mutations, fusions, insertions, duplications, etc. found in the tumour sample.

The main difference in access to MTBs for molecular profiling is related to the location of the analysis laboratories, which are centralised in CCCs or leading research hospitals. There are three reasons for this centralisation, according to our interviewees: the number of analyses to be performed, the cost of the sequencing panels, and the knowledge required to perform the analyses.

First, the more samples sent for analysis, the more staff members needed. MTBs with broader entry criteria require more laboratories to respond to the volume of requests. Secondly, the panels are more cost-effective when all the available slots are used, since different patient samples can be sequenced at the same time on a single panel. In some MTBs, the panels must be full before sequencing begins. Finally, molecular analysis is a complex task carried out by bioinformaticians. When we asked our interviewees about the capacity of other hospitals to carry out this task, they advocated caution:

> "They can't do it. They're not prepared yet" (Anonymous).

> "Is it also a matter of expertise, of passing quality tests, because it is important to have a closed machine in the hospital, but in the end, it is also the knowledge that accompanies this device. And this is happening now in Spain, there are many

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> new laboratories that want to start and have obtained the machine, but they are having a lot of problems, because it's not just a case of putting the material in" (Anonymous).

The samples must be sent to the centralised laboratories, normally in the pathology department of the CCC or a research centre located near the CCC. This can generate a delay, because the panel plates must be filled with biological samples from several patients to reduce the average cost of sequencing. Therefore, when a hospital receives the sample, it can take up to four more days to be sequenced.

Our interviewees indicated that for external hospitals, the analysis of samples takes between one and two additional weeks on average, except in Málaga. In addition, as mentioned above, it is sometimes necessary to repeat the biopsies. Norway, Midtjylland, and Catalonia track the average times according to centre of origin.

The province of Málaga has a single circuit that promotes equity in MTB access, regardless of where the patient receives treatment. This is due to the centralisation of the samples and the analysis laboratory. All hospitals in the province send their biopsies to the same biobank. Consequently, when NGS is requested for a tumour, all samples are sent from the same place, eliminating any time differences related to patient location. In addition, all analyses are performed in a single research institute, meaning the delivery time is the same for all samples. In this way, the whole region has a homogenised circuit for sending and receiving samples. The average response time is between eight and 10 days, with no differences between hospitals.

Finally, in one case that wishes to remain anonymous, the MTB suspects that the hospitals in a certain healthcare area are sending samples to a laboratory outside the national/regional MTB:

> "In [City] we believe that they are performing the molecular diagnostics by themselves, outside the regional MTB" (Anonymous).

3.2.4. Reports and discussion of results

Regarding the fourth function of MTBs, we found no differences in access to NGS reports according to the origin of the sample, since reporting is mostly computerised. The discussion process is also similar in CCCs and non-CCCs. The board members discuss the results and decide on the best plan of action, which will depend on the molecular profile, the available medications, and the profile of the MTB professionals.

In one case, different reference laboratories use different panels. This means the molecular profile differs depending on the residence of the patient, since samples are sent to a specific laboratory based on the healthcare area of the hospitals.

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In the different MTBs, the aim of the discussions is to issue a recommendation that will provide the greatest benefit for the patient. According to our interviewees, financial constraints influence the recommendations in all cases except Málaga. In Portugal and Catalonia, the MTB only recommends treatments that are publicly funded or available through clinical trials. In Norway, Institut Curie, Heidelberg, and Tuscany, the MTBs can recommend off-label and compassionate-use treatments, although they always try to find clinical trials or approved treatments first. The MTB in Málaga recommends the best treatment according to ESMO criteria, regardless of whether it is publicly funded. Finally, the MTB in Midtjylland makes no specific recommendations and only reports the genetic alterations identified, although the pathologist (who has created the genetic analysis report) participates in the discussion during the MTMs. In Midtjylland and Málaga, one professional from the MTB is also in the MTM.

More differences may arise after the MTB has issued a therapeutic recommendation, because it is up to the oncologist to decide whether to follow it. MTB recommendations can be difficult to apply, because the patients have usually gone through several therapeutic cycles with all the difficulties this entails, including reduced physical health. In addition, according to our interviewees, the information patients receive is insufficient for them to understand the MTB results. If the MTB proposal is an off-label treatment that the hospital must pay for, recommending the treatment may generate conflicts of interest for oncologists, who will have to justify this extra cost to their superiors. Oncologists in regional or county hospitals may be less likely to follow the recommendation, as they may have less knowledge of and be located further from the MTB:

> “Now, if we say, that patient has that molecular iteration, but we don't have any clinical trial, so then they might follow or not to give off label or to try to get compassionate use of that drug. It’s easier to decide for the treating physician when it’s a clinical trial” (Anonymous).

To overcome this barrier, Norway has transferred the responsibility of deciding on patients’ treatment from the oncologist to the MTB, since it operates as a clinical trial. The IPO MTB is unique in that it is open to all hospitals that request its deliberation services. It covers the whole country and is the only MTB in Portugal. Other hospitals perform the molecular profiling, but only the IPO has a funded committee that discusses the results of these analyses.

Its function as a national MTB is to discuss the results and offer recommendations to all hospitals that make a patient inclusion request. But other hospitals perform the molecular profiling, except in the case of local patients treated in the IPO. Therefore, the IPO MTB discusses the results presented and offers recommendations, especially if it has a relevant clinical trial; indeed, given its size, the IPO is more likely than other hospitals to have an available clinical trial according to the results of the analysis:

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> "So they already come with a test already done outside. So in their hospital, they just want an opinion on the actionability of those alterations or an opinion on possible clinical trials that we could have" (Researcher, Portugal).

3.2.5. Follow-up

The fifth function of MTBs is monitoring the results of the recommendations, both to check whether the suggested therapies have been applied, and to evaluate their effects. Norway follows the criteria of the DRUP studies, considered the gold standard by ESMO for follow-up and reporting of results (Schmid et al. 2022). In Midtjylland, Málaga, Tuscany, and Catalonia, the MTBs do not follow up on their recommendations. The Heidelberg MTB monitors the results every three months, but not all spokes respond to follow-up requests. Moreover, because each hospital has a separate IT system, the MTB cannot access patient data to monitor the application of treatments.

3.3. Governance and accountability

The MTBs studied are regional or national entities that are mostly integrated into research institutes or CCCs. The professionals interviewed in Málaga, Portugal, Catalonia, Tuscany, Norway, and Midtjylland are hospital staff as well as members of the MTB. Since MTBs are centrally located but offer their services to a broader geographical area, this integration could generate conflicts of interest depending on the loyalty of professionals towards the MTB and the hospital they work in, unless appropriate safeguards are implemented. Similarly, the funder of the panels is not always the regional or national health authority:

> "If we have a frozen tissue, what we do is that we send our analysis to the French National Initiative, which is France Genomic Medicine, where it is a whole exome and RNA-Seq. Why do we do that? Because it's free, right?"

For this reason, we asked our interviewees who is in charge of the MTBs from an institutional point of view. The general response revealed a certain lack of knowledge or a situation of unorganised accountability regarding MTB activity. Sometimes, the healthcare authorities play a supervisory role, even regulating MTB activity; but on other occasions, the MTB members operate in a framework without a clear institutional link. One point the professionals did emphasise was the economic problems faced by MTBs. They are financed only under certain conditions, which can limit their operation when they have to obtain funds.

Another important element is the increasing implementation of precision oncology and the routinisation of MTBs. Results that used to be novel and that required discussion or expert knowledge have been assimilated by treating physicians and the MTB. As a result, professionals who previously participated in the MTB discussions no longer do so:

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> "And sometimes, something like a specific molecular alteration that used to be a topic in a molecular tumor board then becomes standard of care, and this is then discussed in the regular, say, lung cancer board and no longer a topic of the molecular tumor board. So this is, I think, a continuous process" (oncologist, Heidelberg).

> "And in the past, we had the bioinformaticians, but we no longer have them because everything is pretty much standardized now" (Oncologist, Institut Curie).

At the same time, in the case of Catalonia, the directive indicates treating physicians to include specific patients has greatly increased the number of cases analysed and discussed. This has repercussions on MTBs´ response capacity, since the number of cases analysed is directly proportional to the hours needed to complete the whole MTB workflow:

> "This has been increasing. It seems to me we do 3000... Of solid cancer. We do 3000 cases a trimester in Catalonia. Last year we did 1000" (Pathologist, ICO-Bellvitge).

The last source of disparity mentioned by our interviewees is reimbursement. As described in section 3.2.3, one healthcare region is implementing its own laboratory for molecular profiling, without regional MTB funding. This means the healthcare authority is designing and financing a regional MTB, and one of the hospitals that also receives funding for its local services is independently implementing part of the MTB.

Another aspect of reimbursement is related to who pays what. In one of the cases studied, the hospital and not a territorial health agency pays for genetic profiling. For this reason, the hospital requests that patients be referred to them, in order to enrol them in their clinical trials. If the patient has the same clinical trial at a closer location, they can be enrolled there.

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4. Conclusions

The following conclusions can be drawn from the analysis:

1. The technological capacities give to Comprehensive Cancer Centers (CCC) a prominent role in precision oncology within healthcare systems. Although MTBs may respond to regions or even entire countries—and not solely to the CCC they functionally depend on—efforts must be made to ensure that patient access is equivalent in different scenarios, whether with an MTB functionally dependent on the CCC or not.

2. In some cases MTBs are not part of standard care and operate in a research setting, but in others are integrated into the healthcare system for therapeutic decision-making. However, they share similarities in having a multidisciplinary team specialized in precision oncology, with comparable roles performing the standard functions of an MTB.

3. The MTB model and how it work is related to whether they are implemented "upfront", backend, or mixed, which can have consequences on the targeted therapies administered (i.e., whether they are approved therapies off-label or proposed access to clinical trials).

4. The concentration of technology and the link between MTBs and CCCs must be compatible with a broad circulation of knowledge to have a local impact. The participation of local healthcare professionals in MTBs (e.g., facilitating medical oncologists to present their cases) is relevant for their training and, by extension, the equitable access of their patients. The development of tele-medicine and/or IT system to enable participating in meeting may support professional's access.

5. MTBs are playing an increasingly significant role in routine clinical practice. How this growing need of precision medicine will be organised should be carefully evaluated. The model based on a CCC and network of associated providers, through using an approach based on a whole range of tumours and biomarkers, seems to be a pragmatic option. Laboratories can also be organized based on a tumor-specific approach (e.g., Midtjylland) compatible with a situation of laboratories highly concentrated in a single geographical location. These decisions are framed by the capacity to respond and access to the technology in which most centers with a relevant role in oncology are interested.

6. The knowledge development among professionals involved in precision oncology and treating physicians can lead to a growing gap if specific actions are not taken to prevent it. Contact with the MTB facilitates knowledge transfer, but specific

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efforts are required in referring centers if precision oncology is to become routine clinical practice.

7. According to the analysed experiences, MTBs can focus their recommendations on treatments funded and approved by the healthcare provider or within a framework of clinical trials, where a research logic prevails. The follow-up of the effects of therapies is only found in the latter case.

8. Some MTBs receive funding for the analysis of NGS panel they discuss through various programs. This situation could affect access and the decision-making processes, as reimbursement varies by patient and program.

9. It would be needed a specific discussion at each healthcare system on how to reimburse the work of MTB as well as NGS analysis because it could be associated with this kind of resources.

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5. Lessons learned

In this section, we present the main lessons learned:

1. The supervision of MTBs by healthcare authorities is still in its early stages in most cases, where well-established indicators such as the percentage of therapies applied after discussions, as well as the clinical response of patients, do not yet exist. These indicators could be a way to monitor and even compare the effectiveness of various MTBs or evaluate how hospitals follow the recommendations. In terms of external accountability, it could also be analyzed whether there is a difference in the number of cases received depending on the referring center. These indicators could also serve as an internal tool for MTBs to set their own goals.

2. Informants pointed out possible differences in knowledge in the field of precision oncology among professionals depending on the referral center. It seems more likely that treating physicians are more knowledgeable in the field when working in CCCs. It would be required to develop training programmes to improve the knowledge of precision oncology and the implications of the NGS analysis and interpretation of results.

3. A solution for the knowledge gap involves a direct connection between MTBs and CCC, usually sharing professionals that take part in both organisational settings. Given that the reference catchment area could be different according to the MTB, it is necessary to study and propose alternative ways to link the knowledge of MTBs with that of professionals in daily clinical practice. In this regard, a universal proposal to bridge the knowledge gap would be to include the participation of medical residents in MTBs as part of their training, regardless of whether these have a national scope or are functionally part of a CCC.

4. Several professionals from MTBs have expressed difficulties in managing patient expectations towards MTBs and the intensive educational tasks they must undertake. A good example of how to provide information to the patients and support professionals is by creating informational videos aimed at patients to explain what NGS is and what they can expect from their inclusion in the programs, as it was done in Heidelberg.

5. Health systems should discuss how to organise the precision oncology area considering the high degree of dynamism and expansion. Issues such as how to reimburse the procedures, the distribution of catchment areas and programs or training of professionals, and last but not least, the background and expertise of multidisciplinary professionals required.

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Annex 1. Interview guide

Interview sheet for MTBs professionals

Internal organisation

1. Please describe your MTB: Professionals regularly involved, used criteria, tasks developed, responsible institution, scale, and who is the chair.
2. What methodology (e.g., NGS, wide genome sequencing) do you use to study the molecular biomarkers? Is there a unique gene panel across different hospitals that do this analysis?
3. Are there official guidelines/recommendations of when to start the panel/biomarker?
4. Do the MTB discussions result in decisions for approved targeted therapies or also non-approved therapies are included (encompassing off-label- and compassionate use- situations)?
5. Does the clinician responsible of the patient participate in the MTB?
6. Selection criteria to select a patient for accessing the MTB: depending on the stage, advanced situations, after failing the first line treatment...?
7. Do you have a common agenda for scheduling patients — regardless of their origin?

Access of patients to the MTB

8. Do the professionals from associated hospitals have the same possibility to ask for the inclusion of patients into MTBs? How do you provide access of patients from outside of your centre?
9. Which is the data required when referring a patient? Tumour type, stage... [request petition available?]
10. How are the tumour-based Multidisciplinary team meeting (MTM) —the clinical one— and the MTB cooperating? How is the treatment decided? Are your decisions binding?
11. Do you have data on the mean time between the petition and your result per patient? Do you have this data segregated by centre of origin?

Delivery of decisions and reporting

12. How results are disclosed (report, data...)?
13. Is there a follow up of the effective application of MTB recommendations?
14. Is the report included in patients' Electronic Health Record [EHR]?
15. Do you feel that the way drugs are reimbursed in your hospital/country has an influence on the decisions made by MTB?

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16. Please add any information that you consider relevant for the patients' QoL that we have not asked

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Annex 2. Study protocol

Research protocol CRANE's task 8.3

Molecular tumour boards (MTB) implemented in a context of CCCs and associated providers: a multiple case-study

Introduction

Molecular tumour boards (MTBs) represent the latest innovation in cancer care, as they ensure the optimal care treatment based on actionable biomarkers by interpreting the next generation sequencing results. There is currently limited evidence on the MTBs' organizational structures. To fully understand the impact of MTBs, it is important to gain a more comprehensive understanding of their potential benefits and limitations in real-life settings where top institutions in Europe collaborate with other providers in delivering cancer care.

Main question of the research

- How molecular tumour boards are engaged in a context of regionally associated hospitals?

General and specific objectives of the research project

- The general aim of this research is to analyse and compare different European cases of MTBs serving regionally and assess the enablers and pitfalls in translating research into clinical practice as well as the role that CCCs play in this process.

Case Study Methodology

The Case Study methodology is well-suited for exploring complex phenomena, especially when there is limited knowledge about its nature and boundaries, as well as the contextual conditions that are essential for understanding it. This methodology enables the collection and integration of various data sources to gain a more comprehensive understanding of the phenomenon being studied (Yin, 2003; Flyvbjerb, 2011; Baxter and Jack, 2008).

Study design

Qualitative case study based on semi-structured interviews with healthcare professionals based on experiences representative of different European regions.

Definition of cases

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Some criteria need to be specified in order to define what is our unit of analysis (or case study). These criteria are intended to produce a homogeneous context of analysis in order to compare equivalent experiences while accepting contextual variability:

- The case must have an MTB collaborating with a network of hospitals.
- The network should include at least a CCC (i.e., a teaching hospital with prominent capacities in care, and clinical and translational research).
- The cases should be representative of the different European regions.

Practical aspects of the study

- Informed consent will be ensured.

- Interviews are carried out with specific questions, recorded (voice) and last for no more than 45'.

- Once the completion of the research, a report is to be presented and discussed at CRANE Joint Action level.

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