Matching cancer patients with clinical trials: overcoming current challenges through advanced technologies

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Executive summary

Clinical trials serve as the mechanism that translates research into standards of care. A higher enrollment rate in clinical trials has been shown to produce advances in treatment at a faster rate in cancer populations. Patients who participate in research are also more likely to report positive patient experiences. Yet even though the number of trials has increased exponentially in the last two decades, less than 4% of adult cancer patients worldwide enroll in clinical trials.[1]

Matching patients to trials is a lengthy and complicated process, and it varies among hospitals and clinicians. It usually begins with a conversation between the patient and the treating oncologist. Many clinicians, especially those not affiliated with an academic center, are not aware of or have no time to investigate, clinical trials. Those who do may spend several hours searching through incomplete or inaccurate clinical trials registries and sift manually through long lists of inclusion and exclusion criteria. Most patients aren't aware of clinical trials or don't understand their disease well enough to do their own research. A number of other socio-economic, geographic and financial factors present challenges for patients.

The digitization of health data, combined with recent advancements in artificial intelligence (AI) technologies, is creating an unprecedented number of opportunities for clinical decision support. Popular AI techniques, such as machine learning and natural language processing, are promising significant advancements in early detection, diagnosis, and treatment of cancer and other major disease areas.

NAVIFY® Clinical Trial Match is a clinical decision support application that currently queries 11 worldwide registries for sponsor-agnostic, patient-specific clinical trial matches based on age, gender, biomarkers, tumor info, tumor location, stage and genomic alterations. Roche has partnered with MolecularMatch Inc., who leverages technology licensed from the top-ranked MD Anderson Cancer Center. The app, part of the Roche NAVIFY Decision Support portfolio, is embedded in the tumor board workflow, saves clinicians valuable time and allows them to expand the list of trials available to patients. It can therefore help increase awareness of and participation in clinical trials, augment treatment options for cancer patients and improve the patient experience.

Introduction

The last decade has brought major advances in the understanding of cancer biology as well as breakthroughs in new diagnostic and therapeutic areas.[2] For example, sequencing technologies are entering everyday clinical practice and revealing some of the mutations responsible for abnormal cell growth. In the future, increased understanding of genetic abnormalities will allow clinicians to select personalized therapies for patients.

Clinical trials make it possible to apply the latest scientific research to standards of care. The number of trials worldwide has increased exponentially in the last two decades. As of March 2019, there were 299,634 studies registered with ClinicalTrials.gov (of which 103,507 or 35% are based in the US) compared to fewer than 1,500 registered in 2000.[3]

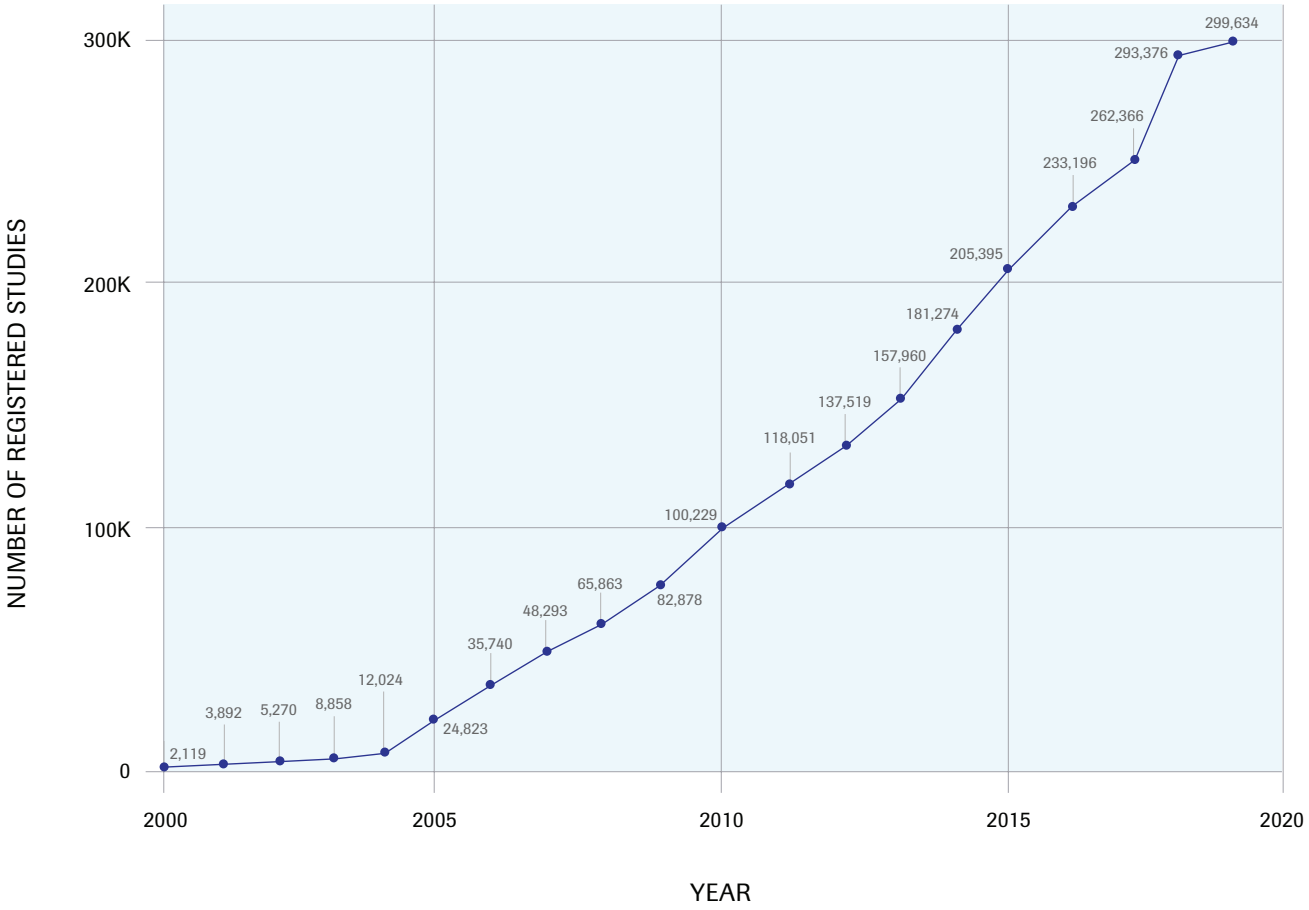

Figure 1. Number of registered studies over time as of March 11, 2019. Source: https://ClinicalTrials.gov.

In a 2017 study, Unger et al. suggest that a higher enrollment rate in clinical trials produces "treatment advances at a faster rate and corresponding improvements in cancer population outcomes."[4] A study conducted in Europe found that "patients who participated in research were more likely to rate their overall care and treatment as 'very good/excellent' and to describe positive patient experiences, such as better access to non-standard care, better interactions with staff and being treated as an individual."[5]

The success of a clinical trial depends on its ability to enroll a specified number of participants within a planned time frame. Despite the growth of the total number of registered trials, the rate of cancer trial participation hasn't changed significantly over time.[6] Numerous barriers have kept enrollment rates low: less than 4% of adult cancer patients enroll in clinical trials.[7]

This paper explores the practice of matching cancer patients with clinical trials; the challenges involved; how technology enhances clinical decision support; and how a new application that streamlines the clinical trial matching process promises to help clinicians and patients on the path to personalized healthcare.

Matching cancer patients to clinical trials: current practices

Identifying and recommending clinical trials to cancer patients is one of the functions of the treating oncologist. Conversations about clinical trials occur regularly during tumor board meetings when pathologists, oncologists and other specialists meet to discuss cancer cases and treatment. "All tumor boards involve conversations about clinical trials," says Richard Hammer, MD, a pathologist and leader of the hematopathology tumor board at University of Missouri (MU) Health Care. Not only is it important for the patient, it is a requirement for hospital accreditation and national cancer reporting.

Donald Doll, MD, a medical oncologist at MU Health Care, participates in a number of tumor boards each week: hemopathology, ear, nose, throat (ENT), multi-disciplinary, genitourinary (GU), and neuro-oncology. "For every new patient, we try to find a clinical trial if possible," he says.

MU Health Care is staffed with a Clinical Trials Office, whose role is to screen patients and discuss options with the patients' treating oncologists. A clinical trials coordinator from this office also attends tumor board meetings regularly, informs the clinicians of upcoming trials, and meets with the referred patients.

There may not be trials available for the rare forms of cancer. Assuming a trial is found and a match made the patient may not be willing or able to participate, for a number of reasons we explore in this paper. Only a small percentage of cancer patients will ultimately participate in a clinical trial.

Unger et al. mapped the pathway from cancer diagnosis to trial enrollment in the manner shown in Figure 2.

In a study performed in a large metropolitan region from 1993 to 1995, 147 physicians discussed 245 patient cases and their own knowledge, attitudes and practices toward clinical trials.[8] The study found that "physicians in university settings and who had formal support from a cooperative group were more likely to refer patients to trials. More specifically, surgeons referred more patients to trials when they felt comfortable explaining trials or believed that treatment should not stray from protocol. Oncologists were less likely to make referrals if they perceived the paperwork to be onerous or entry requirements to be too stringent."

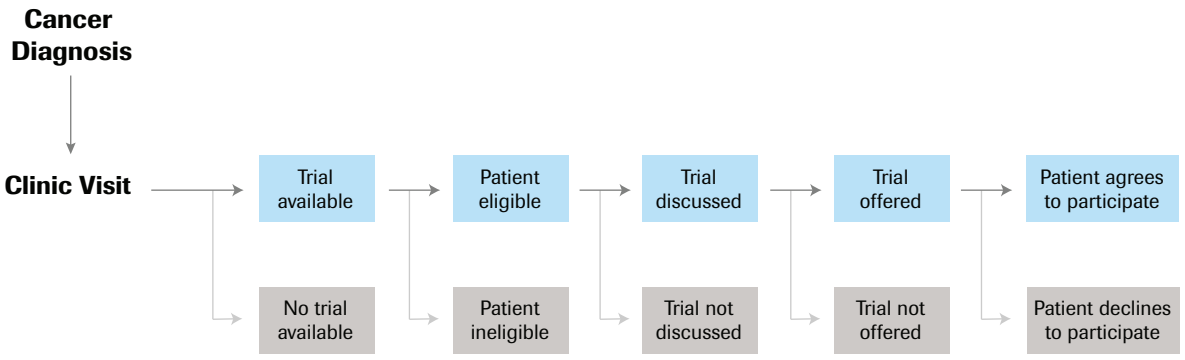

Figure 2. Pathway of trial enrollment process. Adapted from source: Unger et al., "Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies." 2016 ASCO Annual Meeting

Matching patients to trials: challenges for physicians

Awareness

Clinical trials are usually sponsored by academic medical centers, pharmaceutical companies or federal agencies, such as the National Institutes of Health (NIH). According to a survey by Embi et al.,"patients are much more likely to participate in a study if their physician has suggested it to them."[9] Yet, according to the same survey, few clinicians, mostly those in university settings, do the majority of the recruiting. One of the reasons is clinicians may not be aware of all the clinical trials.

Doctors in university hospitals are informed of clinical trials through the efforts of the academics and researchers leading the trials. They, in turn, depend on clinical trial coordinators and graduate students to increase awareness among clinicians and to enroll patients. Clinical trial coordinators are often present in tumor board meetings. However, their focus is on trials run by the institutions they are affiliated with and often doesn't extend to a broader geographic area.

MU Health Care, an academic health system, runs a number of clinical trials. "The Clinical Trials Office is down the hall," says Dr. Doll, who pages the office regularly. Dr. Doll and the Clinical Trials Office try to find the best match for their patients at MU Health Care. Clinical trials at other locations are considered if a trial isn't available at MU or if the patient requests it.

Doctors outside the hospital environment are not informed of clinical trials in the same way. It is up to them to actively search for trials and stay informed, according to an article by Dr. Anita Wolfer, Senior Oncologist and Head of Unit in Oncological Research, Lausanne University Hospital.[10]

Time and cost

Assuming clinicians are aware of the enrolling trials, they still have to examine the inclusion and exclusion criteria, assess whether the patients are eligible, and discuss all this with each patient. The time involvement on behalf of the clinician limits the number of patients who can be evaluated, points out Matthew Prime MD, PhD, Medical Director, Diagnostic Information Solutions at Roche. Dr. Doll depends on his Clinical Trials Office at MU to find the best match for the patient. He often searches clinical trials himself, something he'd rather not do; he'd rather be treating his patients.

Eligibility screening for trials, which includes a review of all clinical data, is, for the most part, still done manually.[11] A single evaluation can take hours, according to a study by Penberthy et al. "[The] screening process is made more difficult by the need to repeatedly evaluate patients over their disease course and by the number of CTs and detailed eligibility requirements that research staff and physicians must consider at each patient visit."[12]

In their 2012 study, Penberthy et al. calculated that the cost of eligibility screening, based on time spent by research nurses and clinical research associates, ranges from $129.15 to $336.48 per patient. The estimated annual cost of screening to the institution was more than $90,000.[13]

> *"A higher enrollment rate in clinical trials produces treatment advances at a faster rate and corresponding improvements in cancer population outcomes."*[4]

Inclusion and exclusion criteria

Eligibility criteria define the patient sample under study and are designed to determine effectiveness of treatment in a well-defined population. Clinical trials need to reach threshold enrollment to present statistically significant results, and enrolling patients can take years.

Inclusion criteria specify the characteristics required for entry in the trial, such as age, stage of disease, and specific pathological characteristics. Exclusion criteria disqualify patients from participating. Such criteria include comorbidities, concomitant treatment or other – that can mask the effect of the drug or treatment being tested. Clinical trials often have very long lists of exclusion criteria, says Dr. Hammer.

On the topic of excluding patients from clinical trials, the US Food and Drug administration (FDA) reports "a tension between balancing the desire to minimize heterogeneity ('noise'), which can mask a finding of the effect [during a clinical trial], and the desire to generate data that are generalizable to the broader patient population that is likely to be treated."[14] According to the FDA, "narrow eligibility criteria can diminish the understanding of the risk-benefit of the study treatment relevant to the patient population likely to take the drug if the drug is approved."[15]

"Care teams and patients have to overcome a number of hurdles before an appropriate clinical trial is identified."

Clinical trials databases

In 2007, the FDA mandated that all clinical trials in the US register and report summary results for reasons of transparency, scientific accountability and public benefit. Similar regulations are in place by the European Medicines Agency (EMA). The FDA and EMA require that registration takes place prior to the first patient being enrolled. The International Committee of Medical Journal Editors requires registration of a clinical trial in a registry as a prerequisite for publication of its results.

Clinical trials are registered in databases, such as ClinicalTrials.gov in the US, the European Clinical Trials Registry in Europe and the University Hospital Medical Information Network in Japan. However, no unified registry of all clinical trials worldwide exists today. Probably the largest meta-register of clinical trials is WHO's International Clinical Trials Registry Platform. All registries in the ICTRP have to fulfill the WHO ICTRP criteria regarding content, quality and validity, accessibility, unambiguous identification, technical capacity, administration and governance.[16]

Searching the clinical trial registries isn't as easy as one might think. A study of ClinicalTrials.gov and 13 primary registries in the WHO network, published in 2014, evaluated each registry for website content; navigation; search and whether the website could be used in multiple languages; website function, design and accessibility. The study found that the content and characteristics of the online registries were different for each organization. It also reported that few websites provided useful clinical trial information to patients and the general public.[17]

ClinicalTrials.gov is not always updated or entirely accurate, says Dr. Hammer. This makes it difficult to match a patient with studies outside MU Health Care. Often, the best clinical trial for a patient may be in a different state or even a different country. But finding one can be onerous.

Matching patients to trials: challenges for patients

Awareness

A study by Leiter et al. that used data from the Health Information National Trends Survey (HINTS) found that clinical trial awareness increased between 2008 and 2012, "though a large subset of the population still lacks general awareness of clinical trials."[18]

Many clinicians have a concept of the "engaged patient," one who understands the disease and its impact and researches treatment options. But in reality, most patients don't even know about trials, says Dr. Doll. They rely on their doctor to recommend them.

Understanding the disease and treatment process

How can the "engaged patient," one who is aware of clinical trials, get more information? Dr. Prime says they typically start by talking to their clinician. Much depends on the patient-clinician relationship. With guidance from their clinician, patients may use Google, research medical databases such as PubMed, visit the website of the American Cancer Society, or search ClinicalTrials.gov in the US.

However, in order for patients to understand their clinical trial options, they first have to understand the disease and the very specific inclusion and exclusion criteria. A patient may only know the anatomical position of their cancer, e.g. colon or breast cancer. Most patients don't know or understand the disease specifics, such as the sub-variant. Cancer is very complicated, says Dr. Prime. Today we not only classify cancer anatomically, but specific to the cell type and down to the precise genetic mutation. Sequencing allows us to examine the genetic code for clues of the exact cancer variant, and we can match the disease to a very specific treatment. All this increases the amount and complexity of information patients and their families have to sort through if they wish to educate themselves and weigh their options.

Socio-economic factors

While tracking clinical trial awareness between 2008 and 2012, Leiter et al. found that "in the 2012 dataset, higher education level, higher yearly income, and Internet-use were significantly associated with clinical trial awareness." The study also points out ethnic and racial disparities in trial awareness.[19]

A recent study in early-stage trials at a comprehensive cancer center found that cancer-related internet use was associated with an income of over $60,000.[20] The patients in the study used the internet to learn about their cancer (85%), treatment adverse effects (65%), clinical trials (52%), new alternative treatments (42%), and symptom management (41%).

But being a "very engaged patient" doesn't necessarily lead to better odds of signing up for a clinical trial; this isn't due strictly to the exclusion criteria or other factors mentioned at the beginning of this paper. The "very engaged patient," one who consistently reads medical reports and is up to speed on the latest research, approaches their treating physician with the expectation that the physician is also on top of the latest research. But this is rarely the case, says Dr. Prime. "Clinicians just don't have the time for that. Their primary goal is to treat patients."

Milton Packer, MD, in an article in MedPageToday.com writes: "In the past, physicians pretended to keep up with the medical literature. If they missed a recent relevant paper, they felt a bit guilty. Now, physicians do not even pretend. There is no guilt associated with 'not keeping up.' Everyone has conceded that they can't – and won't – be current in their medical reading."[21]

Location, finances and other factors

Many other factors present challenges for patients and impact their willingness to participate in trials.

- Location. Clinical trial sites are often located near academic medical centers, and traveling to these sites presents difficulty for many patients, especially those in rural areas.
- Finances. Patients may have to take time off work or incur transportation expenses.
- Limited access to high speed internet and social networking. High speed internet connections, access to social networking websites, and smartphone mobile applications empower patients to seek information about medical conditions that impact them or their families.[22]
- Mistrust. The FDA has reported a "historical mistrust" and suspicion in clinical trials among the American public following abuses of the public's trust, including questionable human radiation experiments conducted by the US Government.[23] The FDA has called for "careful attention to the communication processes for clinical trial recruitment and participation" and community outreach to overcome the mistrust.

> *"A large subset of the population still lacks general awareness of clinical trials."*[18]

The role of technology

Clinical decision support, through the use of artificial intelligence (AI), is in many ways revolutionizing the healthcare ecosystem and promising significant advancements in early detection, diagnosis and treatment of major disease areas, such as cancer, neurology and cardiology.

The digitization of health data, combined with increased computing power, has created a number of opportunities for the use of AI in healthcare. JASON, an independent group of scientists and academics, reports: "The availability of and access to high quality data are critical in the development and ultimate implementation of AI applications in health care."[24]

AI techniques, such as machine learning (ML) and natural language processing (NLP), can uncover critical information hidden in the large amounts of patient data and assist clinical decision making. Machine learning methods analyze structured data, such as imaging and genetic data, and allow researchers to cluster patients' traits or infer the probability of the disease outcomes.[25] Natural language processing, which combines AI with linguistics, turns unstructured data (clinical notes, lab reports, operative notes, etc.) to machine-readable structured data in order to extract the attributes necessary to diagnose and treat the patient.

"Narrow clinical trial eligibility criteria can diminish the understanding of the risk-benefit of the treatment relevant to the patient population likely to take the drug."[14]

A number of issues specific to medical data make the application of AI in healthcare particularly challenging.

1. The data resides in multiple places, such as different electronic medical record systems that lack interoperability or different departments, like radiology and pharmacy.
2. Both structured and unstructured data have to be processed in order to extract the necessary attributes that can lead to diagnosis and treatment.
3. Data is complex. Because of the complexity of the human body, the number of variables in healthcare data require more sophisticated AI techniques.
4. Patient data is sensitive. Privacy and security concerns demand constant vigilance to protect the patients' privacy.

Despite the challenges, applications of AI technologies in healthcare have already demonstrated results, particularly in clinical decision support. A recent study that used AI techniques to analyze pathology images distinguished with 97% accuracy between adenocarcinoma and squamous cell carcinoma — two lung cancer types that are difficult to parse without confirmatory tests.[26] The Google-developed tool Lymph Node Assistant detected images with metatastic cancer 99% of the time after examining scans of breast patients' lymph nodes.[27]

It is worth noting that personalized healthcare, the tailoring of treatment to each patient, is also triggering fundamental changes in clinical trial design: besides the traditional organ- and tissue-based cancer trials, there is an increasing number of umbrella trials, which are designed around molecular characteristics of the tumor regardless of location. These trials require sophisticated query mechanisms. A question for clinicians in the future will be not only "Is there a trial for my patient?" but also "Do I enroll my patient in an organ-based or an umbrella trial?" The latter question can only be answered by analyzing more patient data with the help of clinical decision support tools.

"Every clinical trial out there has the chance to recruit enough cancer patients to meet its stated goals. We need better ways of offering trial options to patients."

Matthew Prime, MD, PhD, Medical Director
Diagnostics Information Solutions, Roche

NAVIFY® Clinical Trial Match

NAVIFY Clinical Trial Match (CTM), a clinical decision support application, is part of the Roche NAVIFY Decision Support portfolio, which combines patient-specific structured, unstructured, medical literature and clinical trial data to support treatment decisions. The application is embedded in the NAVIFY Tumor Board, a workflow product which, according to one study, can reduce tumor board preparation time by 53% for oncologists and 12% for radiologists.[28] The NAVIFY Tumor Board has been designed to aggregate and display patient data, including data from EHR, streamline the workflow of multi-disciplinary meetings and document treatment decisions.

Searching for clinical trials takes a lot of time and energy. “A tool to help with this would be great,” says Dr. Hammer. “Technology that improves the way we find clinical trials and helps us match patients will be beneficial to physicians and patients.”

How Clinical Trial Match works

Clinical Trial Match uses AI techniques to arrive at specific matches between patients and clinical trials. For this, Roche has partnered with MolecularMatch Inc., who leverages technology licensed from the top-ranked MD Anderson Cancer Center.

The app is accessed through the NAVIFY Tumor Board user interface. This can be done before, during or after the tumor board meeting. The app searches the world’s largest clinical trial registries for patient-specific matches based on the following parameters: patient age, gender, biomarkers, tumor info, tumor location, stage and genomic alterations.

A worldwide list of the following registries can be queried.

1. ClinicalTrials.gov (trials from up to 200 countries)
2. European Clinical Trials Registry (EUCTR)
3. German Clinical Trials Registry (DRKS)
4. Netherlands Trial Registry
5. Australia/New Zealand Clinical Trials Registry (ANZCTR)
6. Chinese Clinical Trials Registry
7. Clinical Research Information Service (Korea)
8. University Hospital Medical Information Network (Japan)
9. Japan Pharmaceutical Information Center – Clinical Trials Information
10. Japan Medical Association – Center for Clinical Trials
11. Iranian Registry of Clinical Trials

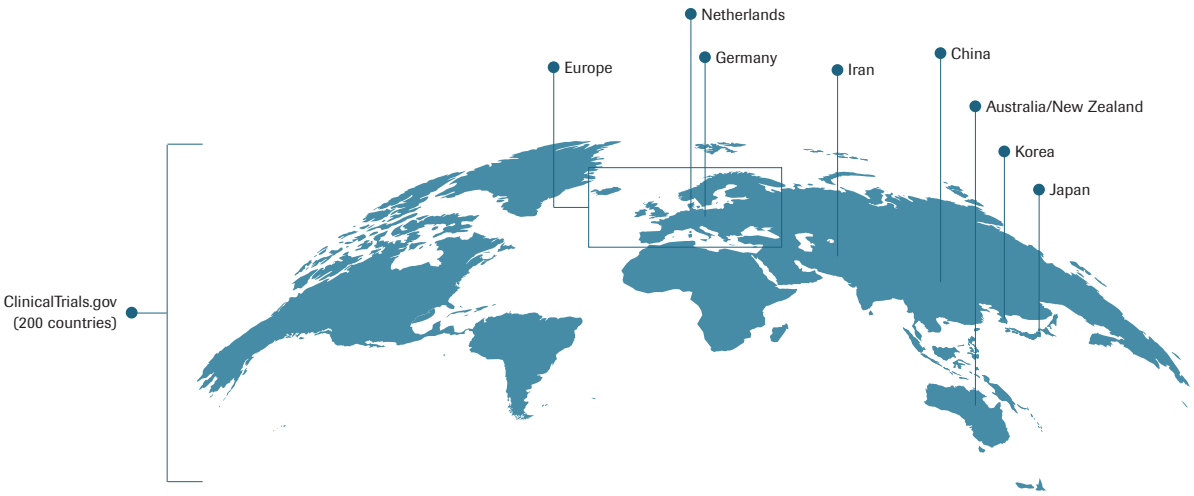

Figure 3. Worldwide registry sources for NAVIFY Clinical Trial Match

Two important aspects of the Clinical Trial Match app are the curation and validation of the clinical trial registry data by MolecularMatch. The source data is indexed, characterized and augmented with inferences, pathways and drug targets; and trials are validated with academic and other institutions.

The clinical trial results are ordered using a scoring system that displays highly applicable trials at the top. Higher phase trials will also be listed higher in the results.

The CTM app offers a number of advantages to clinicians and patients.

1. The results are unbiased. Clinical trials are displayed based on best fit to the patient regardless of trial sponsorship.
2. The application saves clinicians valuable time. Search results are usually displayed within seconds depending on connection speeds.
3. Clinicians can search for trials based on genomic alterations.
4. Non-relevant trials are automatically eliminated from the search results.
5. Clinical trials in the chosen geography are displayed first, offering the most convenient options to the patient.
6. CTM displays an explanation for each clinical trial match in the query results, which helps build clinicians' trust in the search algorithm.
7. Clinical trials at the clinician's hospital/institution are highlighted. Clinicians can also choose to search only their institution's trials. This may help increase in-house trial participation.
8. The app is embedded in the tumor board process, and the clinicians' decision to recommend a clinical trial is recorded as a next step.
9. Because of the number of registries queried, CTM expands the list of trials available to patients.
10. By making a worldwide list of trials easily accessible, CTM can increase awareness of and participation in clinical trials and improve the patient experience.

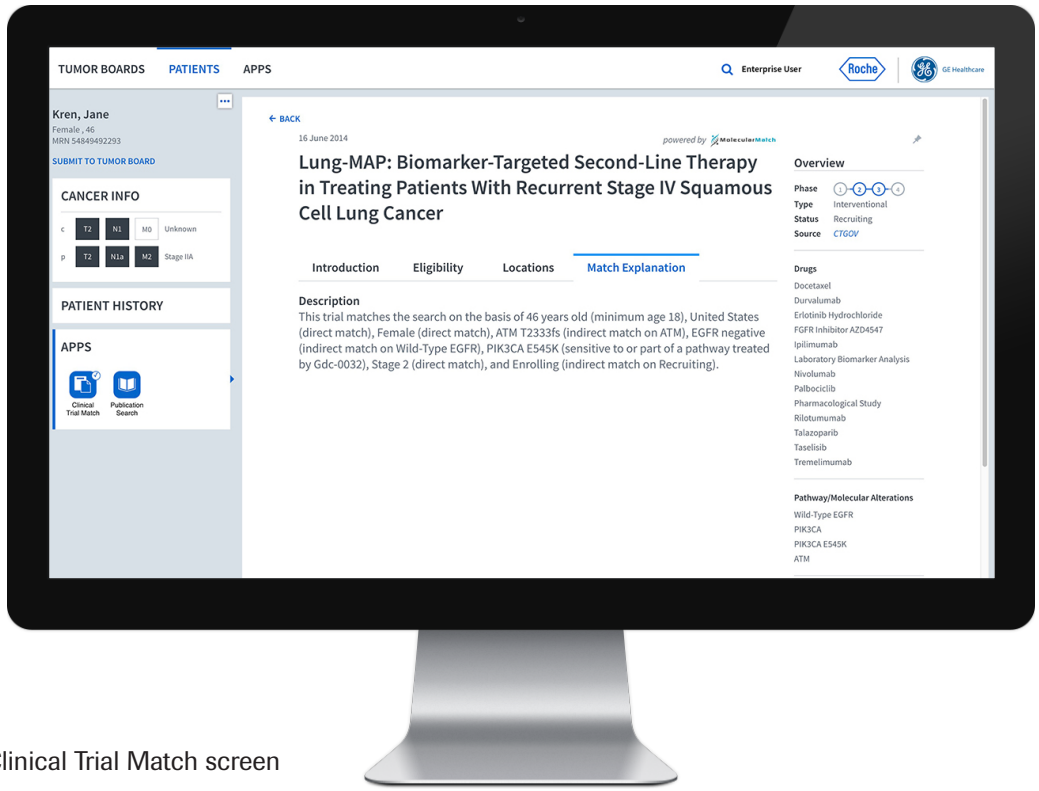

Figure 4. Clinical Trial Match screen

Conclusion

Although there are enough patients for every clinical trial in the world today, several crucial, time-consuming steps often inhibit a timely match between patients and trials: the oncologist or clinical trials coordinator has to research the open trials, pre-qualify each trial for fit to each patient, read through long lists of inclusion and exclusion criteria, discuss with the patient, and run a number of tests before patient and oncologist sign their consent. Enrolling trials may be inaccessible to patients for geographical, financial and other reasons. In the end, very few patients enroll in clinical trials.

The challenges inherent in the matching process for physicians and patients can be mitigated through the use of artificial intelligence technology. New applications, such as the NAVIFY Clinical Trial Match, can be employed to reduce the barriers that have limited participation in clinical trials, speed the matching process, save valuable time for oncologists and other clinicians, widen the pool of options for the patients, increase trial enrollment, and improve patient satisfaction. The promise of these technologies is faster access to personalized care and better outcomes for the patients.

References

1. Lynne T. Penberthy, Bassam A. Dahman, Valentina I. Petkov, and Jonathan P. DeShazo. "Effort Required in Eligibility Screening for Clinical Trials." *Journal of Oncology Practice.* 2012 Nov; 8(6):365–370
2. Talia Golan, Michele Milella, Aliza Ackerstein, and Ranaan Berger. "The changing face of clinical trials in the personalized medicine and immuno-oncology era: report from the international congress on clinical trials in Oncology & Hemato-Oncology" (ICTO 2017). *Journal of Experimental and Clinical Cancer Research.* 2017; 36:192
3. https://clinicaltrials.gov/ct2/resources/trends Accessed March 2019
4. Joseph M. Unger, Elise Cook, Eric Tai, and Archie Bleyer, "Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies." 2016 ASCO Annual Meeting
5. L. McGrath-Lone, H. Ward, C. Schoenborn, and S. Day. "The effects of cancer research participation on patient experience: a mixed-methods analysis." *European Journal of Cancer Care.* 2016 Nov; 25(6):1056–1064
6. Unger et al., "Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies." 2016 ASCO Annual Meeting
7. Penberthy et al. "Effort Required in Eligibility Screening for Clinical Trials." *Journal of Oncology Practice.* 2012 Nov; 8(6):365–370
8. Peter M. Ellis, Sharon M. Dowsett, Phyllis N. Butow and Martin H.N.Tattersall. "Factors that predict the referral of breast cancer patients onto clinical trials by their surgeons and medical oncologists." *Journal of Clinical Oncology.* 2000 Mar;18(6):1203-11
9. Peter J Embi, Anil Jain, and C Martin Harris. "Physicians' perceptions of an electronic health record-based clinical trial alert approach to subject recruitment: A survey." *BMC Medical Informatics and Decision Making.* 2008; 8:13
10. An Oncologist's Perspective on Clinical Trials. Patient Empowerment Network, Sept 24 2015 https://powerfulpatients.org/2015/09/24/an-oncologists-perspective-on-clinical-trials/ Accessed Sept 2018
11. Yizhao Ni, Jordan Wright, John Perentesis, Todd Lingren, Louise Deleger, Megan Kaiser, Isaac Kohane, and Imre Solti. "Increasing the efficiency of trial-patient matching: automated clinical trial eligibility Pre-screening for pediatric oncology patients." *BMC Medical Informatics and Decision Making.* 2015; 15:28
12. Penberthy et al. "Effort Required in Eligibility Screening for Clinical Trials." *Journal of Oncology Practice.* 2012 Nov; 8(6):365–370
13. Ibid.
14. US Food and Drug Administration. "Evaluating Inclusion and Exclusion Criteria in Clinical Trials" Workshop Report, Washington DC. April 16, 2018, p.2
15. Ibid.

References continued:

16. http://www.who.int/ictrp/network/criteria_summary/en/ Accessed Sept 2018
17. Daisuke Ogino, Kunihiko Takahashi and Hajime Sato. "Characteristics of clinical trial websites: information distribution between ClinicalTrials.gov and 13 primary registries in the WHO registry network." *Trials.* 2014, 15:428
18. Amanda Leiter, Michael A Diefenbach, PhD, John Doucette, PhD, William K Oh, MD, and Matthew D Galsky, MD. "Clinical trial awareness: Changes over time and sociodemographic disparities." *Clinical Trials.* 2015 Jun; 12(3):215–223
19. Ibid.
20. Goldy C. George, Adrianna Buford, Kenneth Hess, Sarina A. Piha-Paul, Ralph Zinner, Vivek Subbiah. "Cancer-Related Internet Use and Online Social Networking Among Patients in an Early-Phase Clinical Trials Clinic at a Comprehensive Cancer Center." *JCO Clinical Cancer Informatics.* 2018
21. Milton Packer, MD. "Does Anyone Read Medical Journals Anymore?" Medpagetoday.com, Mar 28 2018 https://www.medpagetoday.com/blogs/revolutionandrevelation/72029 Accessed Sept 20, 2018
22. Fox S, Duggan M. "Health Online 2013" PewResearchCenter.org, accessed Sept 2018.
23. US Food and Drug Administration. "Evaluating Inclusion and Exclusion Criteria in Clinical Trials." Workshop Report, Washington DC. April 16, 2018 p.7
24. JASON, The Mitre Corporation. "Artificial Intelligence for Health and Health Care." Dec 2017; JSR-17-Task-002
25. Darcy AM, Louie AK, Roberts LW. "Machine Learning and the Profession of Medicine." *JAMA.* 2016 Feb 9;315(6):551-2
26. https://ecancer.org/news/14754-artificial-intelligence-can-determine-lung-cancer-type.php Accessed Sept 2018
27. Yun Liu, Timo Kohlberger, Mohammad Norouzi et al. "Artificial Intelligence–Based Breast Cancer Nodal Metastasis Detection." *Archives of Pathology & Laboratory Medicine.* Oct 2018 https://doi.org/10.5858/arpa.2018-0147-OA
28. Elizabeth A Krupinski, Merce Comas, Leia Garrote Gallego, on behalf of the GISMAR Group. "A new software platform to improve multidisciplinary tumor board workflows and user satisfaction: A pilot study." *Journal of Pathology Informatics.* 2018, 9:26

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