Clinical trial matching summit summary (January 31-February 1, 2019)

Executive summary

While most patients enrolled in a cancer clinical trial became aware of the trial opportunity through either their provider, or a member of the study team, somewhere between 10 and 20 percent of patients find their clinical trial through the use of patient advocacy organizations or patient-facing clinical trial matching services. Approximately 50 individuals representing a broad array of stakeholders attended a two-day summit focused on identifying policy and infrastructure recommendations to improve patient-facing cancer clinical trial matching. The summit, held January 31-February 1, 2019, was sponsored by the American Cancer Society (Society) and the American Cancer Society Cancer Action Network (ACS CAN).

The summit was an outgrowth of a larger initiative focused on addressing patient barriers to cancer clinical trial enrollment begun two years earlier. That initiative produced a Landscape Report describing the barriers and a set of 23 recommendations for overcoming those barriers, both of which were released in April 2018 (fightcancer.org/clinicaltrialbarriers). Two of the recommendations deal with matching tools and formed the basis of the summit.

- **Recommendation #5**: Stakeholders should collaborate to develop free or affordable technology, tools, and processes targeted toward non-research sites/ providers that make matching patients to trial opportunities and referral of patients interested in trial participation easier.
- **Recommendation #10:** Non-site specific trial matching and navigation services should be available for patients not provided trial options by their provider or institution. These services should clearly communicate roles and objectives.

The meeting addressed three key areas of clinical trial matching challenges:

- **Clinical trial database challenges**: The completeness and accuracy of trials to which patients are matched. Two main public databases, clinicaltrials.gov and the National Cancer Institute's (NCI's) clinical trial reporting program (CTRP) exist, along with numerous institutional or proprietary databases
- **Patient/proxy interface challenges:** Patient-facing matching services require a patient, or their representative to typically manually enter clinical data about the patient into pre-specified fields.
- **Provider use of non-commercial matching services:** A significant portion of providers in the U.S. still practice in settings that do not have automated trial pre-screening as part of their workflow. If these providers are to help patients match to a clinical trial, they must use third-party matching tools, in many cases the same ones accessed by patients.

The first day involved discussions of the three issue areas and brainstorming of potential solutions. The second day of the meeting the group further discussed recommendations and identified priority recommendations within each area. The final recommendations are listed below:

Clinical trial database recommendations

1) Develop a stakeholder group (includes patients) to:
    - Select a limited number of high-impact trial criteria critical to matching to focus on—e.g. biomarkers
    - Develop consensus on standards and structure for these criteria
    - Pilot their use to demonstrate value
2) Develop standards for protocol-writing tools/templates to promote the collection of more standardized eligibility criteria amenable to searching
3) Enhance existing cancer trial database to ensure the most complete and updated data on cancer clinical trials. This would utilize multiple data sources already in existence that are currently not linked. This database would also be structured to optimize clinical trial matching.
4) Develop and use common ontology/terminology/taxonomy

Patient data input recommendations

5) Develop blue button policies and functionality tailored to clinical trial matching
6) Create data standards around critical EHR data points needed for matching and incentivize EHR developers to adopt these standards
7) Develop "middleware" to convert between participant entries and recognized standards

Provider use of non-commercial matching services action items

8) Survey community providers about their use of matching services and tools, inquiring about needed tools and incentives (such as a reimbursement code for clinical trial discussion) would prompt them to match and refer more patients to trials.
    a. Enlist the help of the Association of Community Cancer Centers (ACCC), American Society of Clinical Oncology (ASCO), and the Oncology Nursing Society (ONS) to conduct the survey.
9) Follow-up in one year with the Leukemia and Lymphoma Society (LLS) about their pilot program with American Society of Hematology (ASH) members.

Detailed meeting notes

Day one

Session One-Overview (Led by Mark Fleury)

The conference began with a review of the history of the work undertaken to date as well as the goals and logistics of the meeting. Specifically, the summit was an outgrowth of recommendations #5 and #10 from the Landscape Report (fightcancer.org/clinicaltrialbarriers), and the summit goal was to identify prioritized policy and infrastructure solutions to challenges encountered by patient facing cancer clinical trial matching services. Patient-facing services are those used outside of an institution by patients or their proxies and include sites like clinicaltrials.gov or emergingmed.com.

The meeting was organized around three key topic areas of clinical trial matching:

- **Clinical trial database challenges**
- **Patient/proxy interface challenges**
- **Provider use of non-commercial matching services**

Session Two-Secret Shopper (Led by Mark Fleury)

Prior to discussing the three topic areas, findings were presented from a "secret shopper" study conducted by ACS CAN. The project involved creating a mock lung cancer patient with relevant clinical variables and using eight different patient-facing matching services to look for clinical trials. The searches were conducted on each site using the same four variables, which were diagnosis/type of cancer (non-small cell lung cancer), location (Jacksonville, FL), acceptable travel distance (up to 50 miles), and study type (treatment/interventional).

The number of matches returned per matching service varied from three to 25, with a total of 37 unique trials identified across all services. No single trial was found by all 8 matching services, two trials were found by seven of the eight services, only five were found by more than half the services and 13 trials were found by a single matching service.

To determine the cause of the different findings, each of the matching services was evaluated for whether the 37 trials were in the services database, and by and large, with the exception of one sponsor-specific matching service, almost all trials were in database. On closer examination, many of the trials were found to have significant differences in the number of sites reported open. In one case three different matching services had the same trial, but the reported number of sites ranged from seven to 93.

Differences in terminology typed in to the patient interface sometimes made a difference in search results even within the same service (e.g., 'NSCLC' vs 'non-small cell lung cancer' vs 'non-small cell lung carcinoma'). In some services this was prevented by the use of drop-down boxes that required selection

of a specific cancer type. One additional finding was that not all matching services recognized a cancer's ontology. For example, one trial was located by a single matching service despite that trial's presence in all but one matching service's databases. The trial was for any solid tumor, and the one service identifying that trial recognized that lung cancer is a type of solid tumor despite no specific mention of "lung cancer" in the trial protocol.

Several areas of interest were not explored in this study, but may be the focus of future analysis. These include the quality and readability of the trial information provided, how matching services using call centers might differ, and how matching performance would change if more clinical variables were used.

Session Three-Clinical Trial Database Challenges (Led by Mark Fleury)

Clinical trial databases contain information about the trials including patient eligibility criteria, trial locations, contact information, and information regarding the purpose of the trial. Currently the main sources of clinical trial data include:

- National Library of Medicine (NLM) clinicaltrials.gov (CT.gov)
- National Cancer Institute (NCI) clinical trials reporting program (CTRP)
- Trial sponsor-provided information
- Institution-specific protocols

A pre-meeting survey was sent out to attendees, and nine organizations responded indicating they had some sort of CT matching service. Of these, the data sources were as follows:

- 6 pulled from NLM CT.gov
- 3 pulled from institutions
- 3 pulled from NCI's CTRP
- 2 pulled from trial sponsors

These services varied in whether they combined data from multiple sources. Four services used only one data source, four services used two data sources, and one used all four sources. Most (7) modified the data in some way.

Brief perspectives on challenges with clinical trial databases were presented by Wenora Johnson, a patient advocate with Fight Colorectal Cancer, and Gisele Sarosy, with NCI.

Wenora Johnson – Fight Colorectal Cancer

Fight Colorectal Cancer has a clinical trial search tool that helps late-stage colorectal cancer (CRC) patients search for microsatellite stable (MSS-CRC) clinical trials. The list is reviewed (curated) with a patient's point of view in mind. The original data is populated daily from ClinicalTrials.gov then reviewed by trained curators. The database is not comprehensive, each week the list of trials goes through a review process done by a combination of patient volunteers and healthcare experts. Wenora is one of the patient curators. As a curator, she is

trained to remove non-relevant trials, to help clarify language and add more non-clinical information to the record, including logistical aspects of the trials that patients are likely to care about.

Gisele Sarosy – NCI

The NCI clinical trials reporting program (CTRP), is a comprehensive database of NCI supported trials. It includes trials directly supported by NCI, including industry trials if they are conducted at NCI-Designated cancer centers. It is estimated that CTRP contains about 90% of US interventional cancer clinical trials in ClinicalTrials.gov. A group of abstractors produce a clinical trial record and apply cancer specific coding terms to facilitate search and retrieval. Information on clinical trials taking place in NCI's Networks, i.e., the NCTN and NCORP trials, including the sites in which patients can enroll is updated via an automatic data feed nightly. For pharma trials at NCI cancer centers, NCI asks submitters to provide contact info for those sites. Recently NCI has initiated efforts to improve searching for cancer clinical trials.

Prior to breaking up into smaller groups, previously identified challenges with databases were reviewed, and include:

1) **Inaccurate/outdated data:** Trial status, recruiting locations, etc., are often out of date in public databases
2) **Lack of standards** for clinical trials data, which makes searching more difficult
3) **Lack of structured data:** Even when data standards are used, the data may not be stored in a structured manner within trial databases, making searching difficult.
4) **Detailed eligibility and protocol information often not available in public trial databases**.
5) **Non-clinical trial information that patients care about missing:** Patient participation decisions might depend on additional information about trials like number of visits, type of intervention, etc.

Attendees were broken into five smaller groups of approximately ten people each for focused discussions. These groups were charged with first reviewing, and modifying if necessary, the challenges, and then brainstorming potential policy and infrastructure solutions to overcome these challenges.

Breakout Reports

Following breakouts, the groups shared feedback with all the attendees. It was suggested that challenge #4 be modified slightly to indicate that it is a challenge primarily with industry trials. **Detailed eligibility and protocol information for industry trials often not available in public trial databases**.

It was also suggested that challenge #5 include the need for patient-friendly language. **Non-clinical trial information that patients care about missing and language is not patient-friendly**:

Additionally, other observations about databases were made:

- Some databases were initially designed for different purposes than they're currently used
  - For use by oncologists and not machine reading
  - Not intended to be recruitment tool
- No singular solution to all challenges
- Lack of incentives for stakeholders to change

Session Four-Patient/Proxy Interface Challenges (Led by Nina Bianchi)

Brief perspectives on challenges with clinical trial databases were presented by Elly Cohen, the director of Breastcancertrials.org, and Alissa Gentile, Director, Clinical Trial Support Center, Leukemia and Lymphoma Society (LLS)

Elly Cohen – Breastcancertrials.org

Breastcancertrials.org is a domain-specific application focused on breast cancer using a curated database derived mostly from clinicaltrials.gov. The site does a deep dive on patient characteristics, asking patients for detailed clinical and treatment information. The site regularly communicates with clinical trial investigators to improve records. The curation of the original CT.gov record tries to approximate protocol author's intent in easier to understand language.

The site has developed an offshoot tool, called Metastatic Trial Search (MTS). They found metastatic patients want their own portal/space. It was developed in 2015 in collaboration with five breast cancer organizations, and uses common screening criteria. MTS is currently embedded on 17 advocacy group websites.

Through research, they found that patients and providers want different information. For example, patients don't want to see the list of eligibility criteria up front, but providers do. Patients are intimidated by scientific trial titles, so the site creates their own titles. Breastcancertrials.org has an API to its curated trial registry that enables other applications to integrate trial matching in their suite of services. Using this API, the Metastatic Breast Cancer Alliance will provide trial matching for users of its MBC Connect App in Spring 2019.

Alissa Gentile– Leukemia and Lymphoma Society (LLS)

LLS has an Information Resource Center (IRC) that is a free phone service that allows patients to call social workers, nurses and health educators and discuss range of issues. If the caller is interested in clinical trials, they are referred to the Clinical Trial Support Center which is staffed by Nurse Navigators who work with patients and caregivers throughout their cancer journey.

The majority (about 55%) of their customers are patients. LLS's matching service, involves significant patient support. Nurses educate patients about clinical trials and gather details about a patient's diagnosis, genetic profile, past treatments, physical condition and medical history; they also review a patient's financial situation, insurance coverage, support network and ability to travel. Nurses will reach out to trial sites and work with the IRC to help to overcome barriers to enrollment.

Prior to breaking up into smaller groups, previously identified challenges with databases were reviewed, and include:

1) Methods, tools, and considerations needed to obtain accurate and sufficiently detailed patient data to facilitate good matches--e.g. relying on patient memory to provide clinical data)
2) User-friendly inputs that facilitate easier search for good matches (e.g. manually typing in data rather than import)
3) Goals and design of matching services potentially yielding different results for the same patient. Patients may not be aware of these differences.

Attendees were again broken into five smaller groups for discussion.

Breakout Reports

Participants provided the following clarifications and additions to the previously identified challenges

- No clear definition on what is meant by a "good" match
- Lack of consensus on acceptable level of precision – i.e., how many data points are needed for a good match?
- Patient understanding of their diagnosis and treatment options may be limited
  Information provided to patients by providers may be limited
- Matching services do not consider patient's full medical record/ medical history
- Patient interface challenges and solutions need to be discussed in tandem with database challenges and solutions – many issues are intertwined

Provider use of non-commercial matching (Led by Mamta Kalidas)

This session was focused on provider access to non-commercial matching services that were not institution based. This type of access is relevant to report recommendation #5: *"Stakeholders should collaborate to develop free or affordable technology, tools, and processes targeted toward non-research*

sites/ providers that make matching patients to trial opportunities and referral of patients interested in trial participation easier." The goal of the session was to better understand issues associated with how providers at non-research sites could help their patients locate clinical trials available at other sites.

Brief perspectives on provider access to non-commercial matching services were presented by Blair Burnett, Senior Policy Analyst at the Association of Community Cancer Centers (ACCC) and Alissa Gentile, Director, Clinical Trial Support Center, LLS

Blair Burnett – Association of Community Cancer Centers (ACCC)

There is little to no internal clinical trial matching services or matching infrastructure at community cancer centers but there is the desire for it among providers. Community cancer centers want their patients to get the best care possible, including a clinical trial if appropriate, but also face financial pressures that make referring patients to other centers challenging. In many cases clinical trials can function in a collaborative fashion with smaller centers providing testing and support with trial treatments occurring at affiliated larger medical centers where the trial is run from. Some sites are also investigating the use of telemedicine to bring trials to the community, but little consensus exists in the community on how to enable clinical trials at smaller sites.

Alissa Gentile – LLS

LLS underwent a 7-month pilot study with the American Society of Hematology (ASH) to provide 53 ASH members in seven geographically diverse centers in U.S. and Canada to work with LLS's existing Clinical Trial Support Center. Through this pilot, the physicians had direct access to the Nurse Navigators. In the pilot, doctors provide information about patients to LLS Nurse Navigators directly rather than the patients being responsible for reporting these data. The nurses reported that this resulted in more accurate information. The goal is of program is to increase access to clinical trials by open communication between patients, providers, and clinical trial investigators, so LLS still works with the patients and caregivers to help with medical and non-medical needs to overcome barriers to enrollment. Data gathered from the pilot showed that the CTSC service reduced the burden on the physicians and their staff in identifying clinical trials for their patients. Physicians found the service to be timely, comprehensive and highly individualized to the patients' medical and non-medical needs. Utilizing the CTSC enabled physicians to have an informed discussion with their patients about clinical trials as a possible course of treatment. Experience from the pilot indicate that once providers refer one patient, they often came back to LLS with additional patients. Community hospitals tended to send easier cases, and academic medical centers sent more difficult cases when patients had exhausted other local options.

The pilot is expected to transition into a more broadly offered service within the next year, with any ASH member being able to use their service.

Unlike the previous sessions, participants did not break up into small groups, but rather discussed the issue together. The primary questions for discussion were:

- Are there open access provider facing matching services that integrate into the workflow for providers at non-research institutions?
- Is/should access to public marching services by providers be different than for patients/proxies? How?

Significant discussion revolved around the role of electronic medical records and how they might be leveraged by providers. Several participants pointed to matching services that already have two interfaces, one for patients and the other for providers. In such cases the provider interface can use fewer questions to arrive at a complex medical concept by using medical terminology, while patient facing questions may need to ask multiple simple questions to arrive at the same medical concept. When multiple interfaces exist to the same service, participants shared experiences where this dual interface left patients with questions about what their providers are seeing through their interface that the patients weren't in theirs. Lastly, Foundation Medicine discussed how their tumor profiling reports contain potential clinical trial matches based on identified genetic mutations. These kinds of third-party test reports can be used by any provider and can be especially useful for providers who otherwise do not have access to clinical trial matching infrastructure. Their weakness is that the laboratories typically do not have any additional clinical information about the patient beyond their tumor sample, so patient matching is based on very limited information.

Day Two

The second day of the summit involved further discussion of brainstormed recommendations from day one and prioritization of these recommendations through a dot-voting mechanism. The recommendations with the highest consensus include:

Clinical trial database recommendations

1) Develop stakeholder group (includes patients) to: (31 votes)
    a. Select a limited number of high-impact trial criteria critical to matching to focus on—e.g. biomarkers
    b. Develop consensus on standards and structure for these criteria
    c. Pilot their use to demonstrate value
2) Develop protocol-writing tools/templates to promote more standardized protocol design amenable to searching (27 votes)

3) Enhance existing cancer trial database to ensure the most complete and updated data on cancer clinical trials. This would utilize multiple data sources already in existence that are currently not linked. This database would also be structured to optimize clinical trial matching. (22 votes)
4) Develop and use common ontology/terminology/taxonomy (11 votes)

Patient/proxy interface recommendations

5) Develop blue button policies and functionality tailored to trial matching (21 votes)
6) Create data standards around critical EHR data points needed for matching and incentivize EHR developers to adopt these standards (19 votes)
7) Develop "middleware" to convert between participant entries and recognized standards (8 votes)

Provider use of non-commercial matching service action items

After discussion, the participants felt that not enough was known about how providers at non-research institutions use matching services to make recommendations. As next steps, the group suggested gathering further information.

8) Survey community oncologists about a provider matching service inquiring if they would use such a service and what incentives (such as a reimbursement code for clinical trial discussion) would prompt them to use it.
    a. Enlist the help of ACCC, ASCO, and ONS to conduct the survey.
9) Follow-up in one year with LLS about their pilot program with ASH members.

Stakeholder Engagement and Next Steps

Working groups will be convened to focus on individual recommendations after the conclusion of the summit. It was noted that the pharmaceutical industry was not represented at the summit and attendees urged that any future activities include all stakeholders.

Summit Attendees

Presidential Innovation Fellow	Gil	Alterovitz
National Brain Tumor Society	Amanda	Bates
Presidential Innovation Fellow	Nina	Bianch
American Society of Clinical Oncology	Suanna	Bruinooge
Philips	Anca	Bucur
Association Of Community Cancer Centers	Blair	Burnett
ResearchMatch	Loretta	Byrne
Biden Cancer Initiative	Danielle	Carnival
National Cancer Institute	Nelvis	Castro
Lung Cancer Alliance	Andrew	Ciupek
BreastCancerTrials.org	Elly	Cohen
National Cancer Institute	Andrea	Denicoff
Veterans Affairs	Nhan	Do
Lazarex Cancer Foundation	Laura	Evans Manatos
Lungevity	Andrea	Ferris
National Cancer Institute	Samantha	Finstad
ACS CAN	Mark	Fleury
Rush University Medical Center	Casey	Frankenberger
Mendel.ai	Karim	Galil
National Cancer Institute	Peter	Garrett
Leukemia & Lymphoma Society	Alissa	Gentile
Foundation Medicine	Jeff	Gruneich
Veterans Affairs	Bob	Hall
SignalPath	Brad	Hirsch
Association of American Cancer Institutes	Janie	Hofacker
Veterans Affairs	Grant	Huang
EmergingMed	Courtney	Hudson
National Library of Medicine	Nick	Ide
Fight Colorectal Cancer	Wenora	Johnson
American Cancer Society	Mamta	Kalidas
Parexel	Mwango	Kashoki
Veterans Affairs	Michael	Kelley
Jason Carter Clinical Trials Program	Scott	Kerwin
MediData	David	Kronfeld
Via Oncology	Kathleen	Lokay
Oncology Nursing Society	Barbara	Lubejko
National Cancer Institute	Patrick	Mahoney
ACS CAN Contractor	Melissa	Maitin-Shepard

Foundation Medicine	David	Marshak
Pancreatic Cancer Action Network	Cassadie	Moravek
Foundation Medicine	Lincoln	Pasquina
National Cancer Institute	Shelia	Prindiville
National Cancer Institute	Gisele	Sarosy
IBM Watson Health	Andrew	Scott
American Society of Clinical Oncology	Shimere	Sherwood
Antidote	Ariela	Silberstein
Biden Cancer Initiative	Lisa	Simms Booth
Oncology Nursing Society	Alec	Stone
National Cancer Institute	Carolyn	Ugolino
American Cancer Society Cancer Action Network	Molly	Waite
American Cancer Society	Dawn	Wiatrek
IBM Watson Health	Eric	Will
Dana-Farber Cancer Institute	Elizabeth	Williams
National Library of Medicine	Rebecca	Williams
Epic	Tom	Yosick