“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

April 20, 2022
Brad Power

Meeting Summary

Ally Perlina, Chief Science Officer at CureMatch, presented combinations of approved drugs that are the best fit for advanced prostate cancer patient Brian McCloskey based on his cancer’s unique molecular profile. CureMatch is a San Diego-based company which takes biomarkers identified by most any diagnostic sequencing test and matches them with approved drugs in combinations. Their distinctive value is using multiple drugs in combination to achieve a better fit with the unique characteristics of a patient’s cancer, and therefore better patient outcomes.

The CureMatch system starts with input from a patient’s molecular profile, derived from DNA and/or RNA sequencing of a patient’s tumor tissue or liquid biopsy sample. The test will identify biomarkers or variants of interest (variants from normal cells, potential drivers of the cancer), usually 4 to 6. Not all biomarkers or variants go into the algorithm. Some may be rejected because they are not pathogenic (don’t drive the disease), and some because there are no therapies targeting that biomarker. The physician has latitude to include or exclude biomarkers or treatment options due to any reason, such as medical history. For example, Brian had pembrolizumab, so he might decide to remove it as a treatment option. Then CureMatch analyzes the patient’s selected biomarkers against the roughly 300 drugs that the FDA has approved in combinations of 3, 2, or 1 drugs. They do not include clinical trials in their recommendations. For example, Brian has a variant (B7-H3/CD276) which has several clinical trials targeting this pathway, but it would not be included in a CureMatch recommendation because there are no approved drugs for it yet. Off-label uses of drugs (drugs that have been approved but for a different indication) are included in the treatment combinations.

The roughly 4.5 million possible combinations of the roughly 300 approved drugs are then scored on the extent to which they address the patient’s selected biomarkers. If a drug combination addresses 4 of 6 biomarkers, the score is 67%, 3 of 6 would be 50%, and 2 of 6 would be 33%. The drug combinations are ranked on their scores, with explanations and links to support the choices. For example, Brian had 6 actionable markers, 16 on compendia drugs, 54 matching drugs, and 24,857 relevant combinations. CureMatch’s top option, with a score of 32%, was a 3-drug combination of apalutamide (FDA approved, AR target), olaparib (FDA approved, FANCA target via PARP-1, PARP-2), and trametinib (off-label, BRAF target via MAP2K1, MAP2K2, and MAP2K2 target).

As Emma Shtivelman, an experienced PhD molecular biologist and Chief Scientist at Cancer Commons summed up,

> “*... someone like me looks more for clinical trials rather than off-label treatment options. And when I look for clinical trials, I keep in mind the previous treatments... CureMatch has this assumption that a physician will be able to prescribe off-label combinations of two or three drugs. This happens rarely, even with the best specification. I know two patients who had recommendations from CureMatch and their physicians worked with*

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> *the recommendations, and it worked great. But it's an exception... It's unfortunate and very frustrating.*”

Advanced Prostate Cancer Patient Panel Report

Brian McCloskey shared highlights from a meeting of advanced prostate cancer patients who have registered with the Prostate Cancer Lab community.
Four themes emerged that they would like to see if they could change one thing about their care:

- **Better physician-patient communication**: Providing patients with simple language they can use to understand their disease and treatment options.
- **Better diagnostics for personalizing treatments**: Tailoring treatments uniquely to the profile of each individual.
- **Medical guide partner**: Finding a trusted medical advisor who will be an expert partner on the journey.
- **Access to experts**: Achieving a high quality of care in rural locations.

Requests

- Do you have any feedback on the CureMatch presentation? Would you recommend their approach to a friend or family member?
- Do you know anyone who would be a good candidate to serve on our Prostate Cancer Lab patient board? The candidate should be very active in wanting to learn more about his advanced prostate cancer and treatment options.

The information and opinions expressed on this website or platform, or during discussions and presentations (both verbal and written) are not intended as health care recommendations or medical advice by Cancer Patient Lab/Prostate Cancer Lab, its principals, presenters, participants, or representatives for any medical treatment, product, or course of action. You should always consult a doctor about your specific situation before pursuing any health care program, treatment, product or other course of action that might affect your health.

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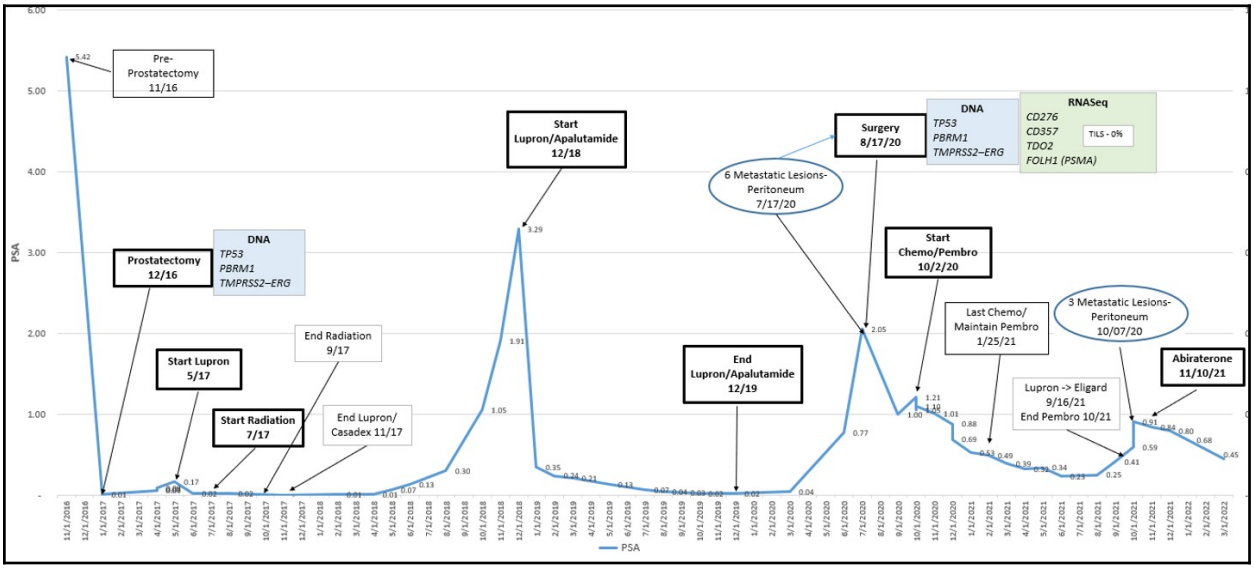
Meeting Transcript

CureMatch Recommendations for Treatment Combinations for Brian McCloskey

Brad Power: To set up Ally's CureMatch analysis, we're going to have Brian briefly set the stage with his medical history.



Brian McCloskey: I was diagnosed in 2016. I had a prostatectomy. Unfortunately, it came back, and then I went on this wild ride. I went on first line hormone therapy, then Lupron, then radiation, and then we saw an uptick in my PSA. Then I went to a second line hormone therapy with apalutamide, and saw an immediate response to that, which was great. I took a bit of a holiday in December of 2019, you can see at step 5 there. Unfortunately, I had a biochemical recurrence at that juncture, but it became visible as soon as I went off of all hormone therapy. In August of 2020, point 6 on this graph, we discovered I had six metastatic lesions in my peritoneum. We did surgery, and then I started a combination of chemo and pembro. You can see my PSA began to drop during all of that. I took six rounds of chemo and stayed on pembro for about 12 months. I began to see a bit of an uptick in September of last year. We did some more imaging and found I had 3 metastatic lesions in the peritoneum. Prior to that there were no visible mets after the surgery and after chemo. I am now on abiraterone. I have had a PSA decline from .9 to 1.45.

Saed Sayad: What was the Gleason score?

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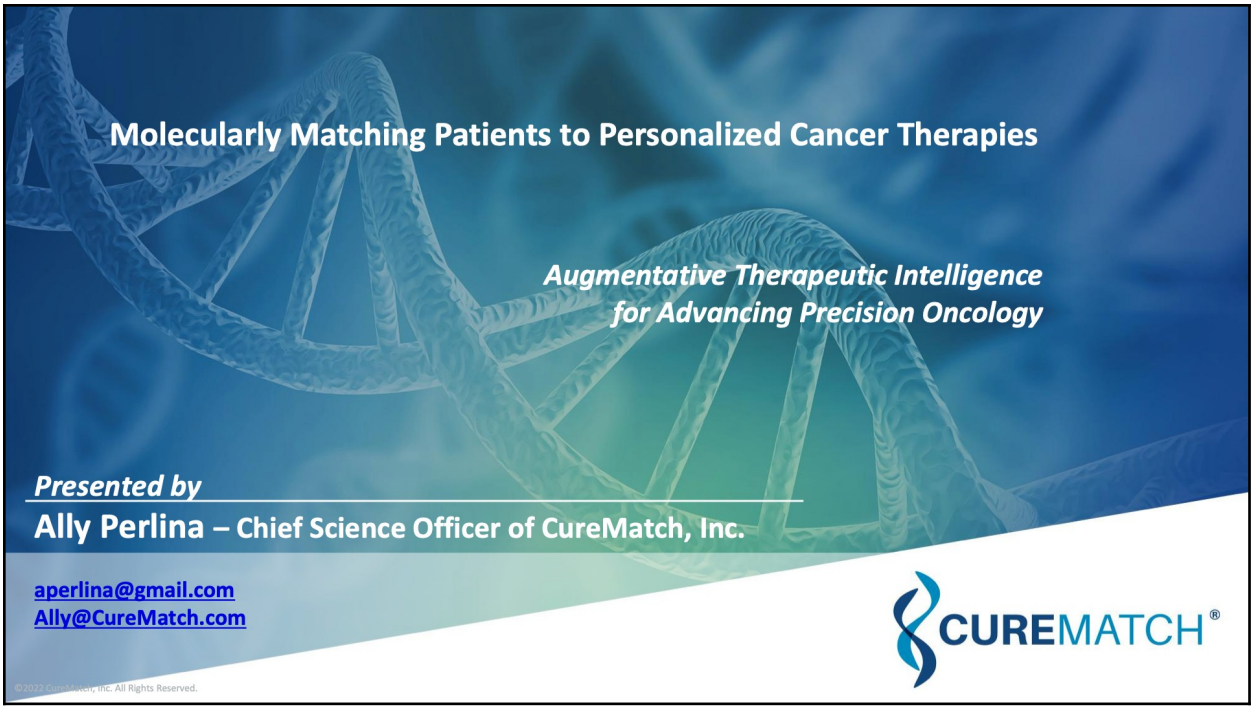
Brian McCloskey: It was a 4 + 3, with grade 5.



Ally Perlina: Thanks for having me. I hope what I have will be helpful.

I spoke to Brian last year. We met virtually. I know there is a history of his getting a different CureMatch report in 2017. It was different data then, and there was different knowledge out there in the world.

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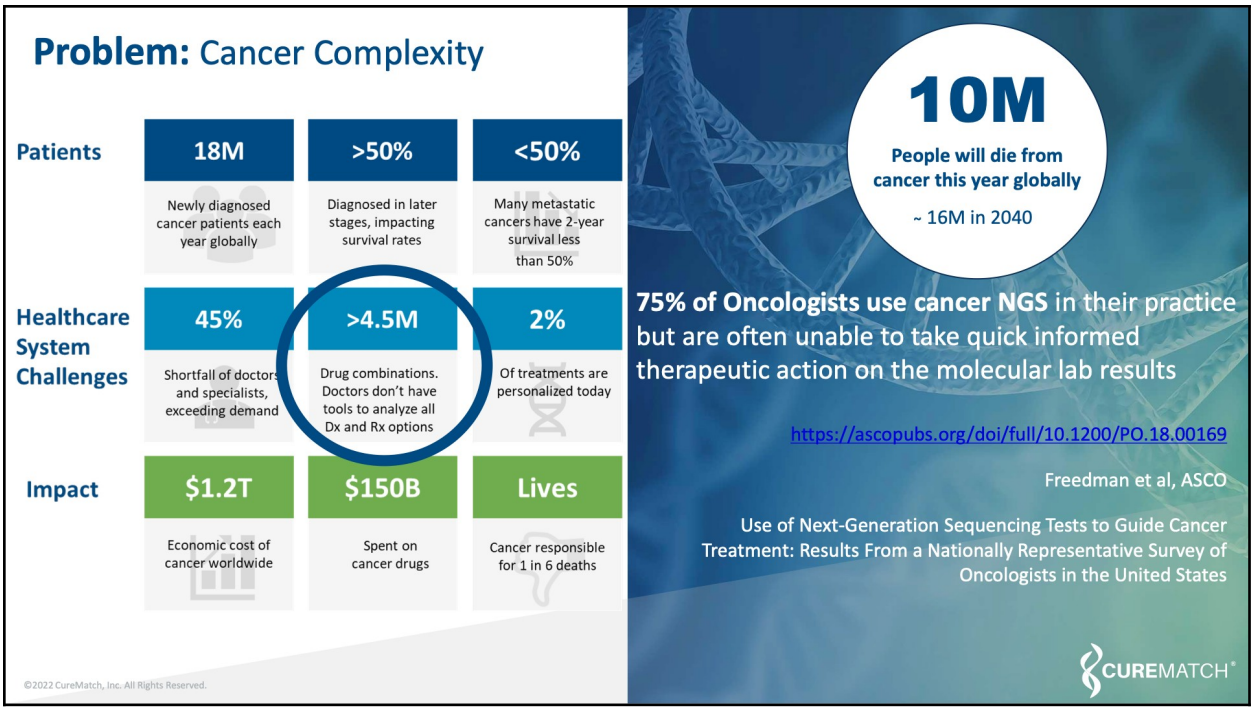

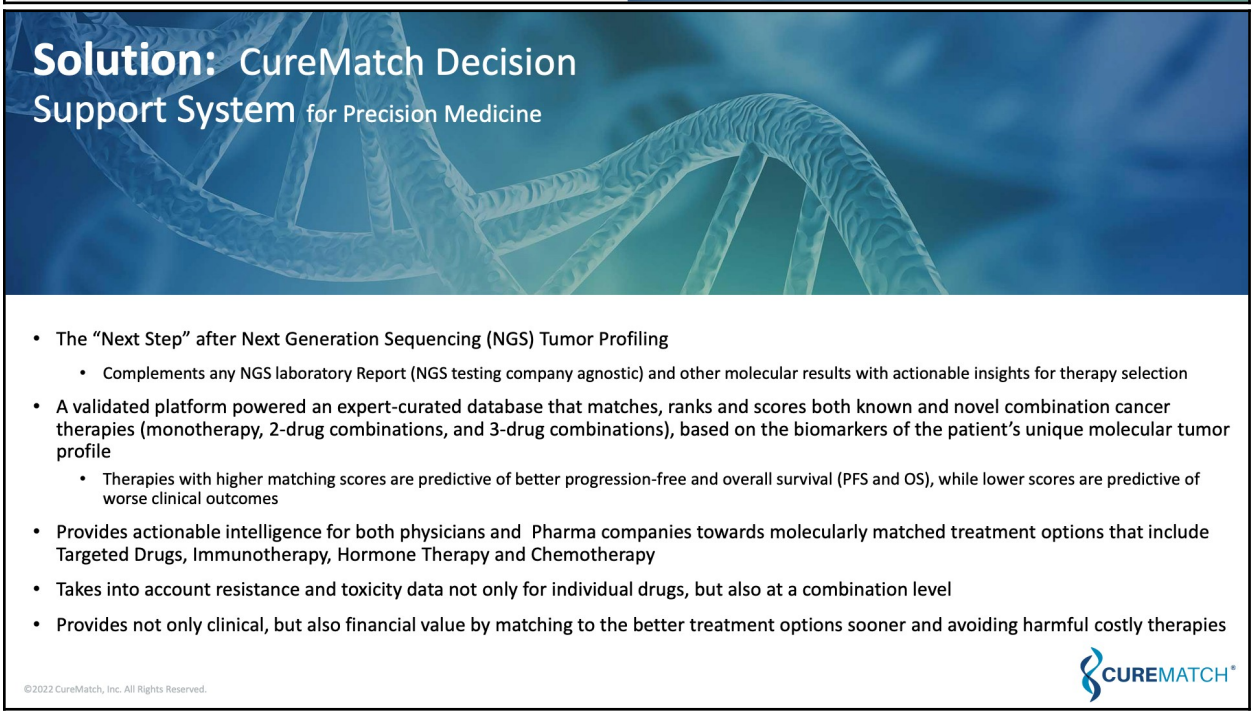

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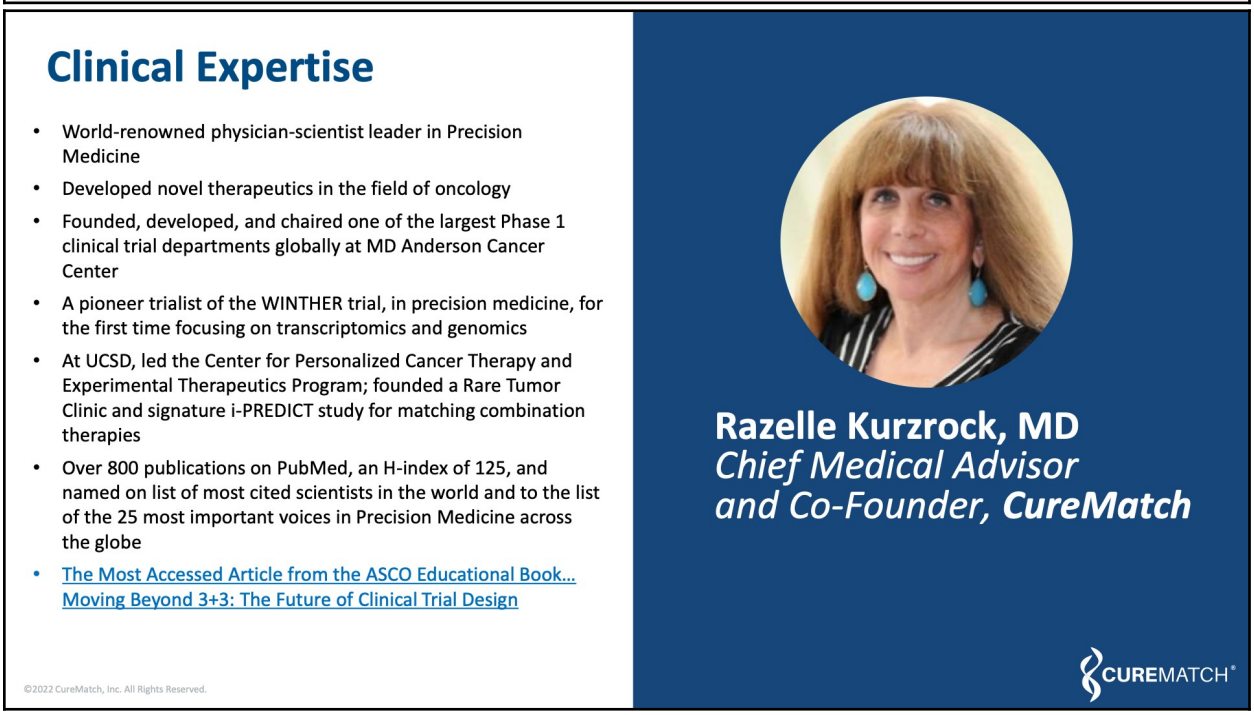
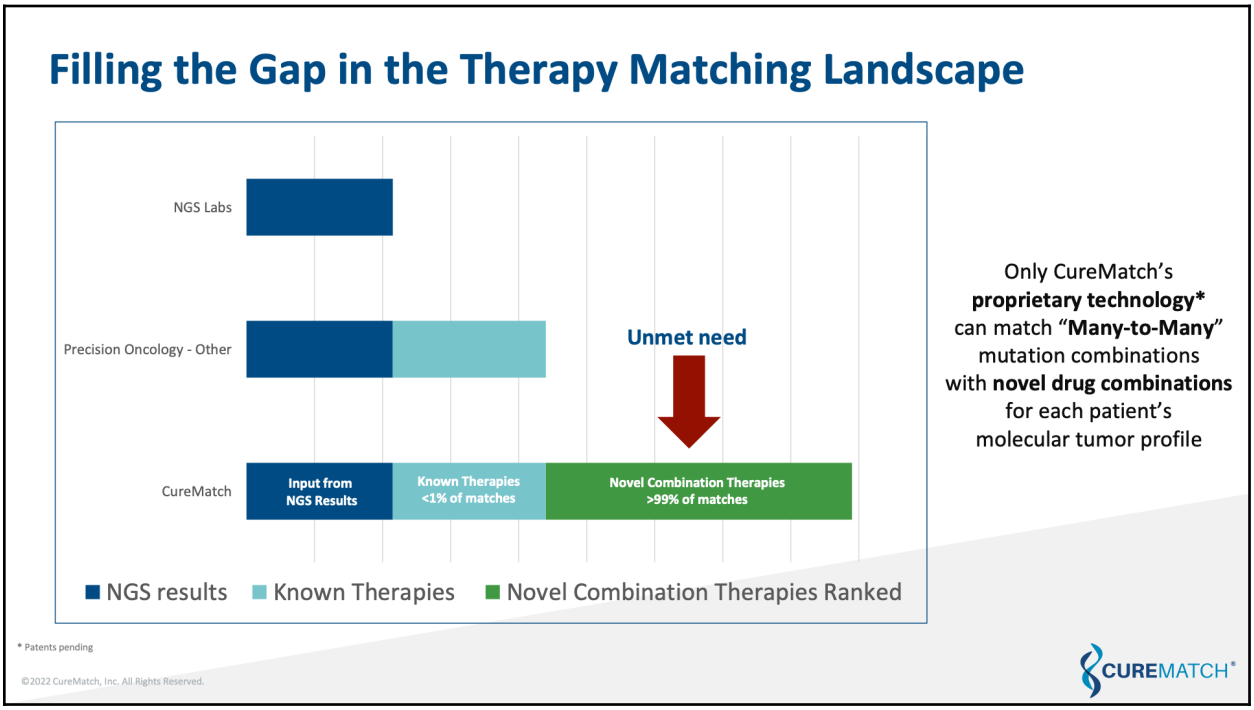
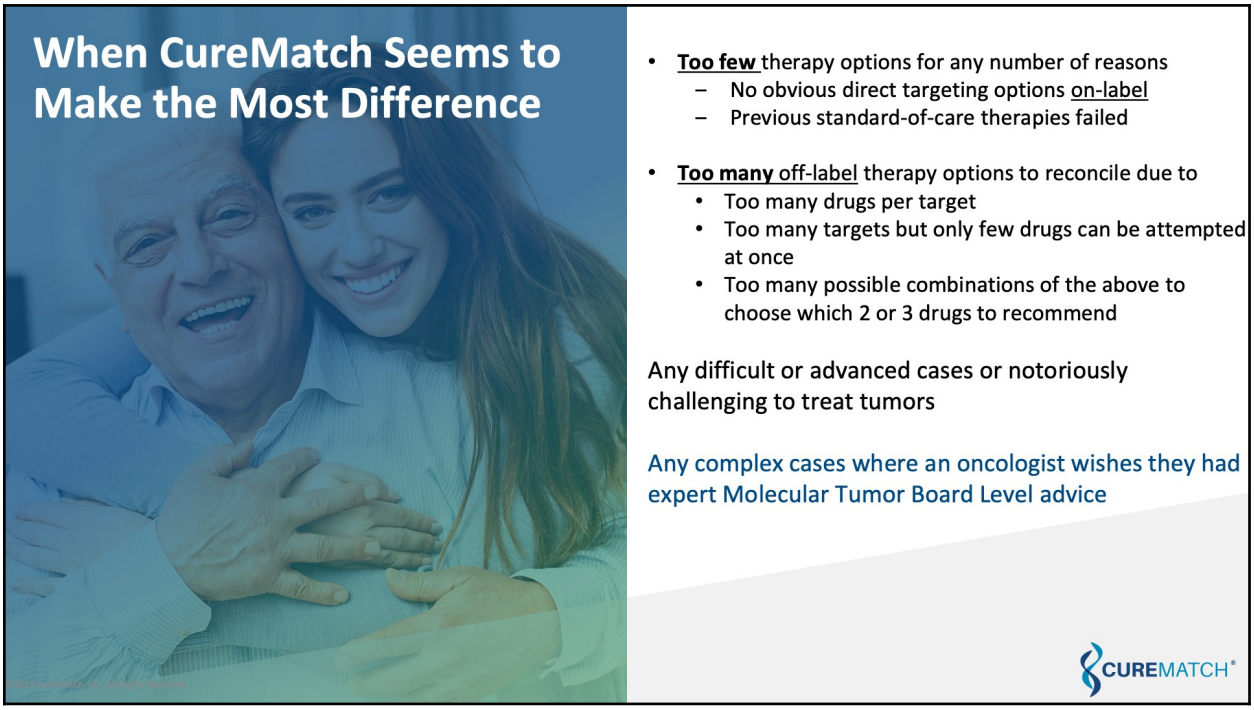


You can think of CureMatch as knowledge representation and reasoning, as opposed to a machine learning kind of AI. We are not trying to make a prediction. It's more like scoring molecular fitness of treatments (therapies, drugs) to the markers of molecular type in each individual patient profile. As our founder and chief medical advisor Dr. Razelle Kurzrock said, it's like a snowflake, everybody's cancer is unique. The idea of her CureMatch brainchild that was born in 2015 was to be able to emulate molecular tumor board reasoning, with all the knowledge at hand, so that for any unique new case, even if some mutations have never been seen before

in the arrangement that they align in a give patient, no matter how unique a case is, if there is a way to therapeutically address or drug the target, then the match will be considered by our system.



I'm going to tell you how it fits in the therapy-matching space, and then go to the reports.



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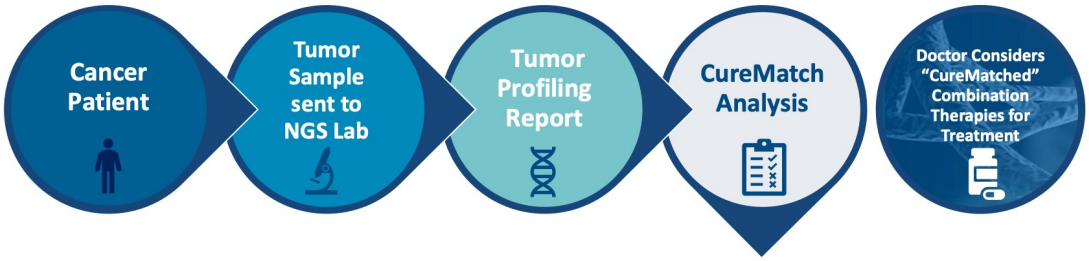
The “Next Step” in Elevating Cancer Care



Agnostic to lab, sample type, cancer type, or types of omic data
(genomic, transcriptomic, proteomic)

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Types of Inputs Needed from NGS Labs to Produce a CureMatch Report

Required Inputs

NGS Report (PDF is standard, other types of formats possible):

- Age and Sex
- Diagnosis
- Country of Residence
- Laboratory Name
- List of biomarkers
  - with clear determination of clinical relevance
  - Somatic **DNA** Alterations

Additional Optional Inputs

- Non-pathogenic or VUS markers
- TMB, MSI, HRD, and MMR markers – if determined by the lab
- Pathology Reports
- RNA or Protein or Immune Markers can be included in addition to the Somatic DNA Alterations
- Pharmacogenomics (PGx), if any
- Physician’s choice of drugs or combination therapies to be scored or excluded

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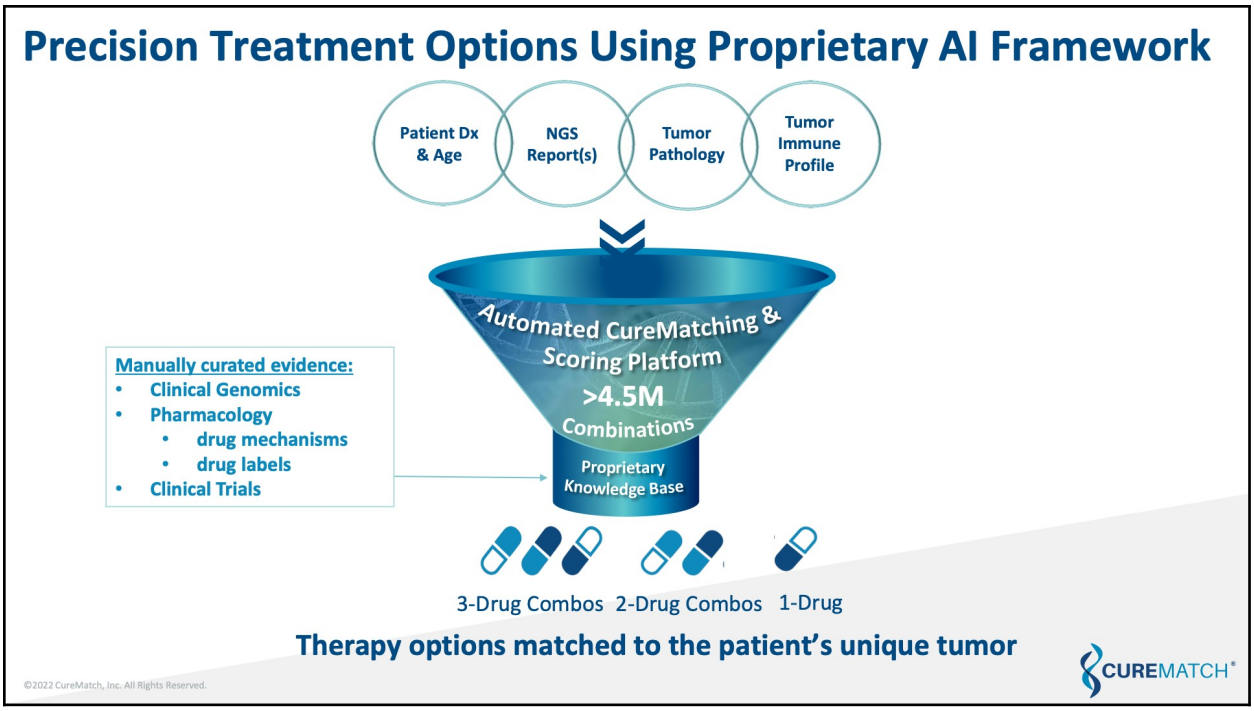

We don't attempt to call variants or markers as pathogenic or not. We are not trying to assign the initial clinical interpretation and variant curation of significance the way that labs do. We go next in line after an NGS report, and also consider molecular data on a proteomic or gene expression level from other types of reports. Unlike some companies that do a beautiful job of showing what are the known therapies associated with actionable markers, we also cover novel combinations. We work with the over 300 or so available cancer drugs to consider the millions of ways to mix and match them into customized two-drug or three-drug combinations, which is what molecular tumor boards often recommend. They take drugs that are available and combine them in ways that have possibly not been tested in clinical trials or approved. But the drugs themselves are available. The novel combinations cover about 99% of the top molecular matches for each patient.

Brad Power: Can you please define some terms? NGS is for Next Generation Sequencing. They are typically looking at an oncopanel of about how many genes?

Ally Perlina: We are not limited by the panel or number of genes that the lab looks at. Larger panels from CLIA-certified labs may be better, but we will take any sample type, liquid biopsy or solid tissue, any company or lab that does NGS analysis, whether they interpret the results or therapies or not. We will take the molecular profile markers that are discovered, from DNA level or RNA level tests, and and will CureMatch that.

Brad Power: To get a sense of scale, one of these companies, like Foundation Medicine, looks at 200 or 300 genes, and then identifies variants in a half dozen or dozen markers that might be useful?

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Ally Perlina: Usually what we see are 5 or 6 markers on average. When patients turn to CureMatch is when the decision is not trivial to choose from among millions of possible combinations to come up with the best combination of two to three drugs. Often this is too late. We hope that NGS will be ordered sooner and more frequently, and CureMatch will become the standard of care. We get quite complex cases. We see anywhere between 2 to 15 or even 20 markers coming out of the tests, particularly if you have RNA expression data, which adds markers.

Rick Stanton: On the slide where you have "known therapies less than 1% of matches", let me say what I think that might mean. If I have a mutation that has a known therapy that is directly targetable, that is kind of rare. And for the other 99%, you need the CureMatch system to target it.

Ally Perlina: It's not just mutation to drug matches that are one-to-one. What this is saying is that out of all the reports we have done, we have seen one therapy address the overall molecular profile on the top (with the best score) 1% of the time, and we have seen a combination address all of the pathogenic markers 99% of the time. You need to take the drugs out of the 300 and mix and match them in customized, individualized ways that are molecularly precise and justifiable.

Jeff Waldron: Does CureMatch incorporate drugs that are investigational, under clinical trials or available to patients through compassionate use or expanded access?

Ally Perlina: This came up in my correspondence with Brian. We just work with available drugs. Investigational drugs are not included in our system. If it is approved for some indication, even a non-cancer indication, then it is included.
Our clients, doctors of patients, have not been turning to us for clinical trial matching for investigational drugs. When they turn to us, they know that they are going to be trying something different and the case is very complex and often advanced, and they don't know if the patient will qualify for a clinical trial. We take care of what we do uniquely, which is taking care of the complexity of choosing from millions of possible combinations, then filtering and scoring for targeting the overall profile. We will expand from there. We are focused, and we are a small startup.

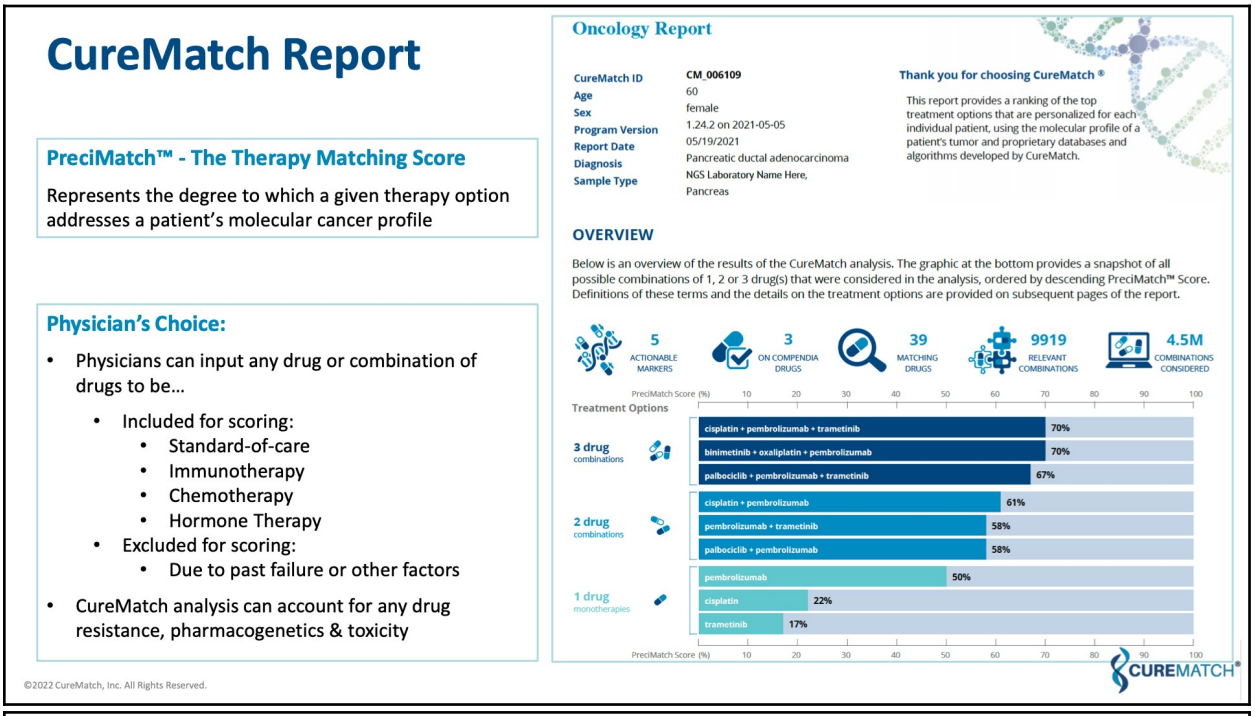
Glenn Sabin: You are also looking at non-cancer agents that are also FDA-approved?

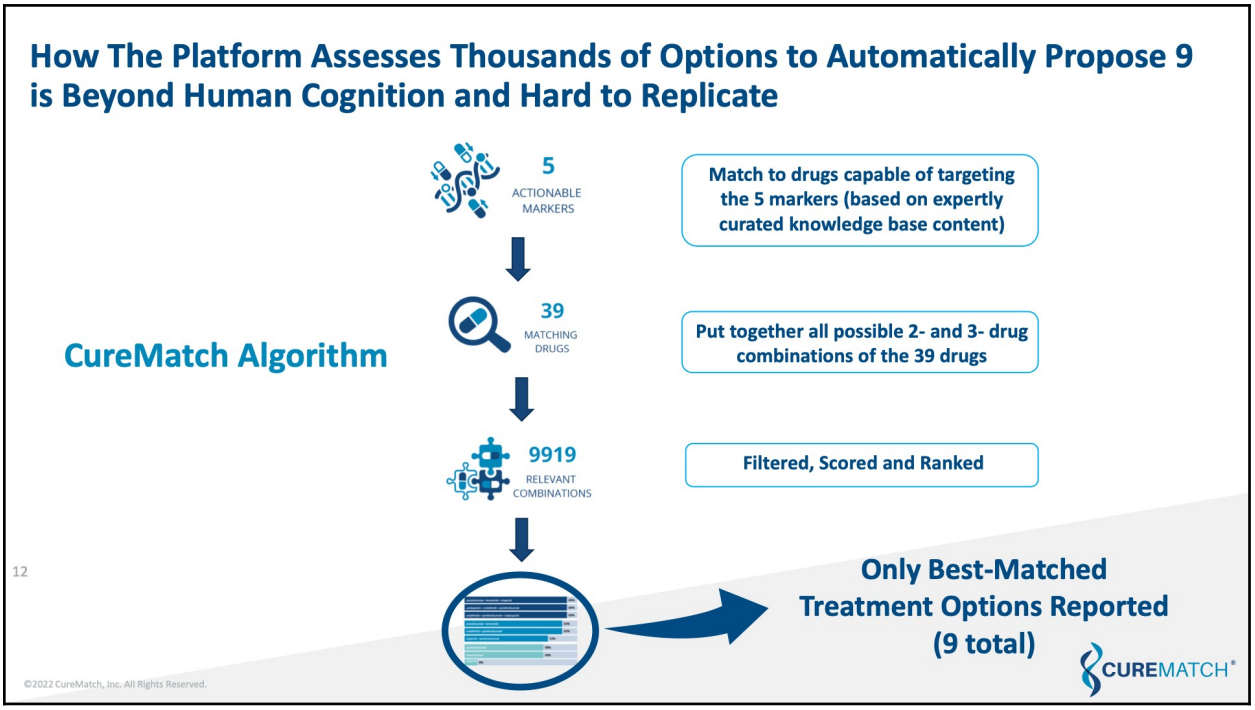
Ally Perlina: There are relatively fewer of those, but they are included.

John Laird: When you say that you identified 5 or 6 pathogenic markers, what does that mean? Not every mutation is pathogenic. To be chasing mutations that are irrelevant to the progression of the disease would be a concern.

Ally Perlina: Sometimes we don't have enough markers to produce a report. I participated in several of these hackathons, and at one stage, there weren't enough markers to run a report,

and then later more markers were identified, and then there was. And there are pathogenic markers that are not actionable. In Brian's case there is a fusion that is not considered actionable. But there are other markers that are actionable.





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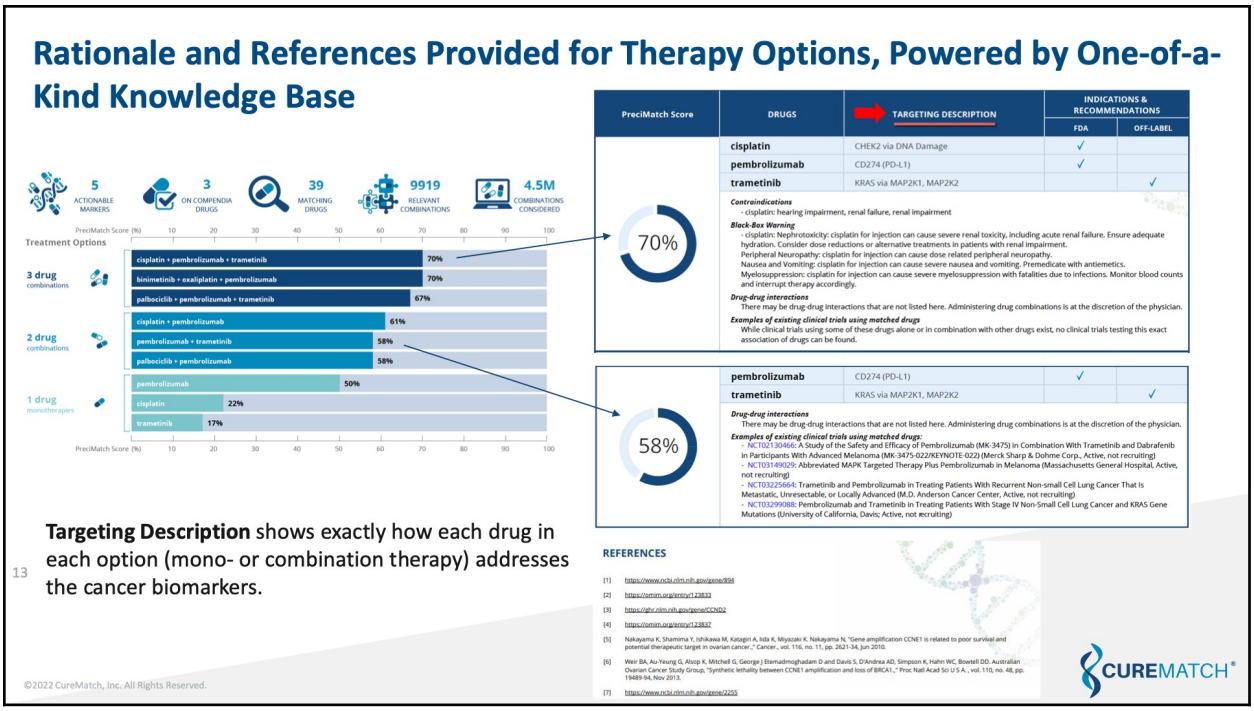

This example is not Brian's report, but in this case, there were 5 actionable markers, but there were 6 or 7 pathogenic or clinically significant markers reported from the NGS results. Unless the clinical team overrides this and says that this or that is pathogenic, we will take whatever the lab report says, and we will CureMatch that. We don't reinterpret CLIA-certified results.

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Oncology Report

Patient's Name	**Brian M.**
Medical Record #	**BM012876**
CureMatch ID	**CM_006190**
Age	56
Sex	male
Program Version	1.47 on 2022-04-14
Report Date	04/15/2022
Diagnosis	Prostate adenocarcinoma
Sample Type	Tempus xO 1714 Genes, Prostate; Tempus xT 648 Genes, Abdominal Wall; Tempus RNA, Abdominal Wall

Thank you for choosing CureMatch ®

This report provides a ranking of the top treatment options that are personalized for each individual patient, using the molecular profile of a patient's tumor and proprietary databases and algorithms developed by CureMatch.

OVERVIEW

Below is an overview of the results of the CureMatch analysis. The graphic at the bottom provides a snapshot of all possible combinations of 1, 2 or 3 drug(s) that were considered in the analysis, ordered by descending PreciMatch™ Score. Definitions of these terms and the details on the treatment options are provided on subsequent pages of the report.

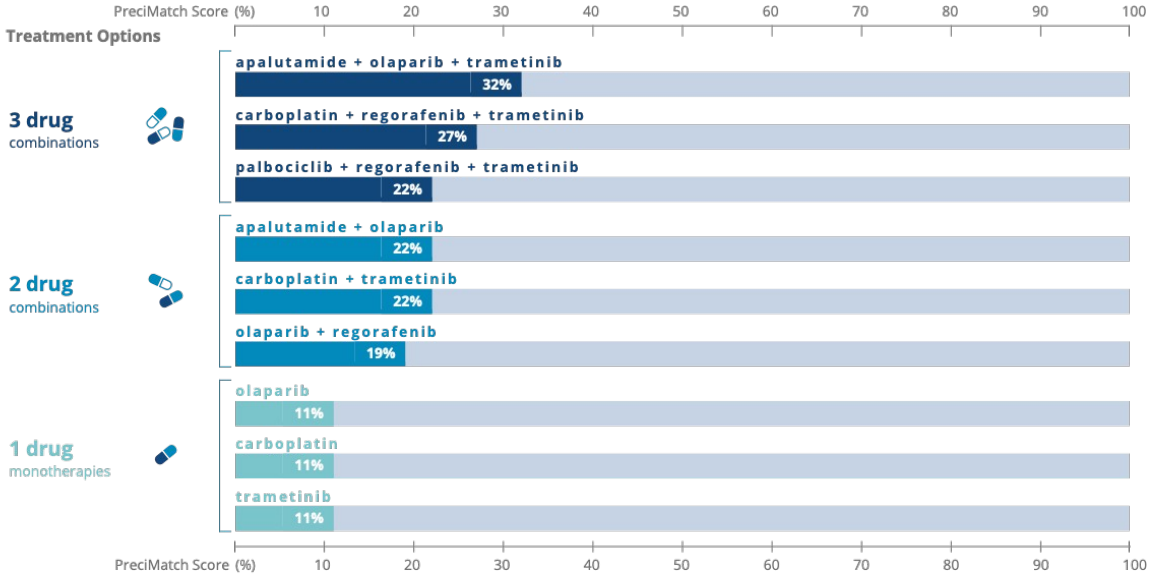
6 ACTIONABLE MARKERS

16 ON COMPENDIA DRUGS

54 MATCHING DRUGS

24857 RELEVANT COMBINATIONS

4.5M COMBINATIONS CONSIDERED



Note: The therapeutic options above may have alternative drug choices listed on pages 3-7 (see Targeting Description table column). Drugs are considered alternatives when they share analogous mechanisms of action and impact on the score.

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DESCRIPTION OF MARKERS

Detailed description of actionable markers is given in subsequent pages of the report.

MARKERS OF KNOWN SIGNIFICANCE

GENOME VARIANTS

MARKER	DESCRIPTION	ACTIONABLE
FANCA	copy number loss/ deletion	**Yes**
TP53	G244fs	**Yes**
FLCN	copy number loss/ deletion	No
PBRM1	R710*	No
TMPRSS2-ERG	rearrangement/ fusion	No

TRANSCRIPTOME VARIANTS

MARKER	DESCRIPTION	ACTIONABLE
AR	high expression (mRNA)	**Yes**
BRAF	high expression (mRNA)	**Yes**
CDK4	high expression (mRNA)	**Yes**
MAP2K2	high expression (mRNA)	**Yes**

PROTEIN VARIANTS

MARKER	DESCRIPTION	ACTIONABLE
CD274 (PD-L1)	no expression (protein)	No

REPORTED POLYMORPHISMS

MARKER	DESCRIPTION	ACTIONABLE
None		

ADDITIONAL MARKERS

MARKER	DESCRIPTION	ACTIONABLE
Homologous Recombination	unknown	No
Microsatellite Status	stable	No
Mismatch Repair Status	unknown	No
Octreotide Scan	No	No
Tumor Mutation Burden	low 2.3 Muts/Mb	No

MARKERS OF UNKNOWN SIGNIFICANCE

MARKER	DESCRIPTION	ACTIONABLE
PPFIA1	V551fs	No
PTEN	K102_P103dup	No
RYR2	A1008V	No
SOX8	R256H	No

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TOP RANKED 3-DRUG COMBINATION THERAPIES

PreciMatch Score	DRUGS	TARGETING DESCRIPTION	INDICATIONS & RECOMMENDATIONS	
			FDA	OFF-LABEL
32%	**apalutamide**	AR	✓	
	olaparib	FANCA via PARP1, PARP2	✓	
	trametinib	BRAF via MAP2K1, MAP2K2 MAP2K2		✓

Alternative drug(s) for apalutamide
nilutamide[1]

Alternative drug(s) for olaparib
rucaparib[1], niraparib, talazoparib

Alternative drug(s) for trametinib
binimetinib

Contraindications
- apalutamide: pregnancy

Drug-drug interactions
There may be drug-drug interactions that are not listed here. Administering drug combinations is at the discretion of the physician.

Examples of existing clinical trials using matched drugs
While clinical trials using some of these drugs alone or in combination with other drugs exist, no clinical trials testing this exact association of drugs can be found.

27%	**carboplatin**	FANCA via DNA damage	✓	
	regorafenib	BRAF TP53 via FLT1, KDR		✓
	trametinib	BRAF via MAP2K1, MAP2K2 MAP2K2		✓

Alternative drug(s) for carboplatin
cisplatin[1], oxaliplatin

Alternative drug(s) for trametinib
binimetinib

Black-Box Warning
- regorafenib: Severe and sometimes fatal hepatotoxicity has occurred in clinical trials. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue STIVARGA for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence.
- carboplatin: Carboplatin injection should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate treatment facilities are readily available.
Bone marrow suppression is dose related and may be severe, resulting in infection and/or bleeding. Anemia may be cumulative and may require transfusion support. Vomiting is another frequent drug related side effect.
Anaphylactic-like reactions to carboplatin have been reported and may occur within minutes of carboplatin injection administration, Epinephrine, corticosteroids, and antihistimines have been employed to alleviate symptoms.

Contraindications
- carboplatin: bleeding

Drug-drug interactions
There may be drug-drug interactions that are not listed here. Administering drug combinations is at the discretion of the physician.

Examples of existing clinical trials using matched drugs
While clinical trials using some of these drugs alone or in combination with other drugs exist, no clinical trials testing this exact association of drugs can be found.

Here are the report results for Brian. The report gives you a score, the "PreciMatch Score". This score represents how well any given option is covering all of the pathogenic markers with the

drugs that are included. We show top 3-drug and 2-drug combinations and monotherapies. Physicians like to see that, and sometimes they score quite well. When we have something that covers therapeutic markers of the profile of the patient 100%, then the score is 100. If there is no molecular matching for the treatment, then the score will be zero. There has to be molecular justification or indication for a drug.
With this molecular score, the higher the score, the better we have seen progression-free survival and overall survival outcomes, and the worse the score, the worse the outcomes. This CureMatching and scoring has merit. We have been able to collect evidence that shows that our algorithm and knowledge base is predictive of outcomes. That is where we come in with intelligent therapeutic decision support.

The 4.5 million doesn't change, but the number of potentially relevant two- or three-drug combinations that the engine considers does change. Here there were 6 actionable markers. But on the second page, there are more than 6 markers. For example, if somebody had 20 markers, but you could only hit 8 with a combination of 3 drugs, then you're not going to get a score of 100%, because you're at best hitting under 50% of the markers. How many birds can you shoot with three stones? These drug combinations shown do not address the marker that is the fusion because we're not counting it as an actionable marker. We do not consider it targetable. All other markers from transcriptomic and genomic data were taken into account. When you go through the targeting description in the report, you can see what is being targeted by the top 3-drug combination, and how it is directly or indirectly acting on the markers. Sometimes it may not be drugged directly, it is a marker of sensitivity. Whenever possible, we have alternative drugs presented. To qualify as an alternative, the drugs have to not only be of the same therapy type and targeting mechanism, they also have to have the same score. This is where you will see alternative PARP inhibitors, or a MEK inhibitor, because BRAF showed up. This is how to navigate through the report and the rationale for the recommendations.
Then we move onto monotherapies.
We show an option for indirect targeting of P53. This is unusual because P53 is not usually targeted because downstream of P53 there are angiogenesis pathways that are related to growth and proliferation that have been clinically shown that target VEGF growth factor have shown some promise.

Brian McCloskey: In 2017 we did a CureMatch report for me, and my highest PreciGene score was 70%. Now it's 32%. The decline is not good. Why is there that change?

Ally Perlina: We had this flagged as actionable, and now it's not.

This is a rudimentary, simplistic way to think about our scoring algorithm. If you had two markers, and you addressed one of them, your score would be 50%. If you have 20 markers, and you address five of them, your score would be 25%.
One point is it's not actionable.
The other point is that there are more markers, so if you had the same drugs, the score would be lower.

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More markers means there are more options, but there are only so many you can target with any 3-drug combination. If you can address 4 with a 3-drug combination, but not all 7 at once, that will affect your score.
Some doctors use 4-drug combinations at low doses and titrate up, but we limit ourselves to 3 drugs in a combination.

Brian McCloskey: I saw that you didn't include my CD276 because that's being addressed by a clinical trial, and you don't include clinical trials. This marker came out of my work with CD274.

Emma Shtivelman: B7-H3/CD276 is a popular target for CAR-T trials and ADCs (antibody drug conjugates).

Ally Perlina: In our system, if it's already approved, and can be mixed and matched in a combination, we would have included it. For example, if PD1 or PDL1 were included as a marker, then pembrolizumab would be included in most combinations.

Emma Shtivelman: I worked with CureMatch before and I am very fond of the company, but in this case I'm not sure it has been taken into account because Brian has already had pembrolizumab.

Ally Perlina: We didn't take it into account because there was no explicit reason to tell me to exclude this or count this. We have this as the physician's choice to include or exclude drugs, possibly based on previous history.

Emma Shtivelman: The difference is that someone like me looks more for clinical trials rather than off-label treatment options. And when I look for clinical trials, I keep in mind the previous treatments, the number and the nature of them. CureMatch has this assumption that a physician will be able to prescribe off-label combinations of two or three drugs. This happens rarely, even with the best specification. I know two patients who had recommendations from CureMatch and their physicians worked with the recommendations and it worked great. But it's an exception in general. It's unfortunate and very frustrating.

Ally Perlina: You're absolutely right. That's a reality. We exist to provide this information to help inform decisions when off-label combinations are to be considered. There are other companies that do clinical trial matching very well, but they won't do this molecular tumor board style of review. As soon as you have even five drugs that are available, to pick which two to give, or which three to give out of five, is not so trivial because we also take into account toxicity, resistance, and which drugs should not be given with another drug if it has a certain profile. It's very hard for any physician to keep on top of all of that. But I know we're not the majority case scenario right now. I hope we will be. We are in the process of getting our CPT code later this year from the AMA, which we hope to get later this year, so we can be more easily reimbursable.

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Clinical Evidence

Genome Medicine

[Molecular profiling of advanced malignancies guides first-line N-of-1 treatments in the I-PREDICT treatment-naïve study](#)

Sicklick....Kurzrock, Genome Medicine 2021

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

[Significance of scores generated by a cancer therapy matching engine for patient outcomes.](#)

Perlina, ASCO, 2021

nature medicine

[Molecular profiling of cancer patients enables personalized combination therapy: the I-PREDICT study](#)

Sicklick, Nature Medicine 2019

nature COMMUNICATIONS

[Real-world data from a molecular tumor board demonstrates improved outcomes with a precision N-of-One strategy patients](#)

Kato, Nature, 2020

cancers

[The Crossroads of Precision Medicine and Therapeutic Decision Making](#)

Boichard.....Kurzrock, Cancers, 2020

ESMO Open Cancer Horizons

[Comparison of Three Commercial Decision Support Platforms for Matching of Next-Generation Sequencing Results with Therapies in Patients with Cancer](#)

Perakis, ESMO Open, 2020

Molecular Cancer Therapeutics

[Precision Oncology: The UC San Diego Moores Cancer Center PREDICT Experience](#)

Schwaerderle...Kurzrock, Molecular Cancer Therapeutics, 2016

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Real-world validation study from a molecular tumor board demonstrates improved outcomes with precision therapy matching approach

Problem/ Objective

Does a treatment of multiple drugs that targets the patient's genetic mutations in lethal cancers improve the patient's outcome *and* is it safe and feasible?

Approach

Prospective Trial Conducted

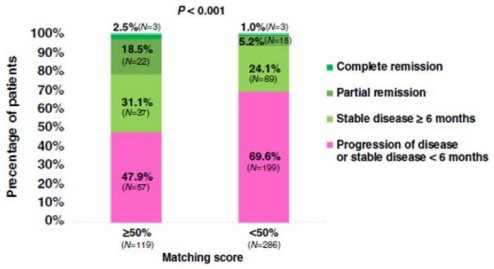
Participants: 715 patients with metastatic cancer

Method: Match patient with a personalized combination of drugs that targets more of the cancer's mutations. Score each patient's molecular-to-drug "matching," **the higher the matching score (≥ 50%), the better the match**

Results

With Precision Medicine Matching

- Rate of matching multiple drugs to numerous genomic alterations —typical in metastatic tumors—was high
- **High score = independent predictor of longer progression free survivability (PFS) and overall survival (OS)**



nature COMMUNICATIONS

Real-world data from a molecular tumor board demonstrates improved outcomes with a precision N-of-One strategy - High matching score leads to better clinical outcomes." *- Shumei Kato, MD, et al*

Source: Nature Communications https://www.nature.com/articles/s41467-020-18613-3

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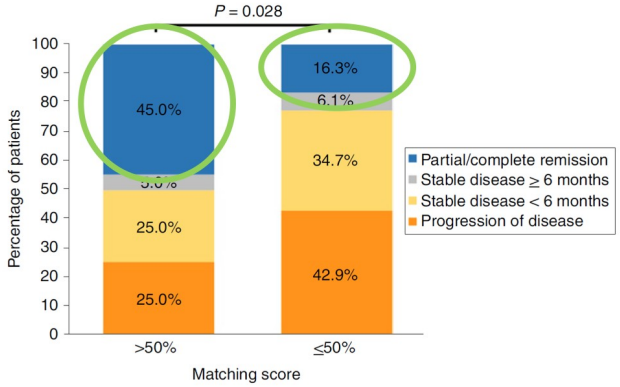
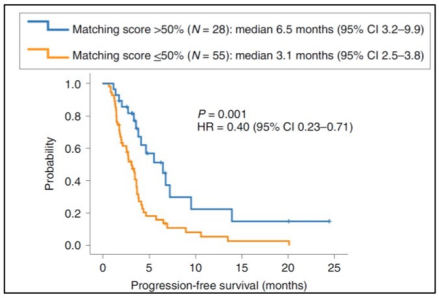
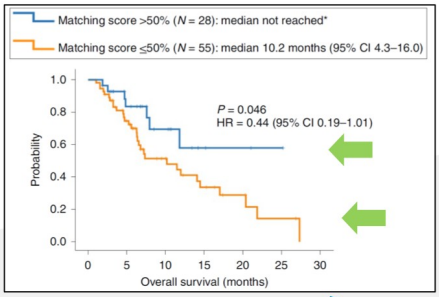
“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

Published Results from I-PREDICT Study: Metastatic, treatment refractory



Higher matching score (>50%) translated into significantly better response, progression-free survival and overall survival





Source: Sicklick et al, Nature Medicine 2019

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Precision Matched Therapies Across All Tumor Types

I-PREDICT CASE STUDY

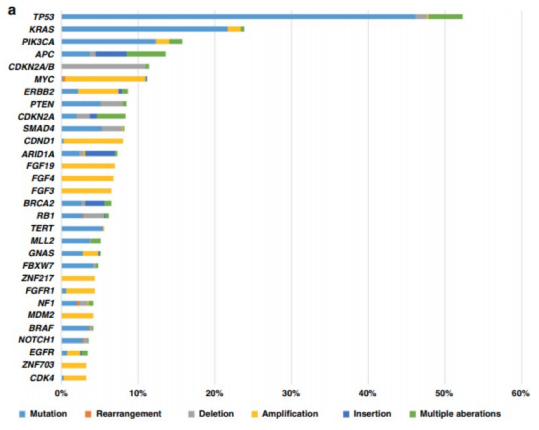
Table 1 Baseline demographics of patients presented at the Molecular Tumor Board (*N* = 715 unique patients)[a].

Period	December 2012–September 2018
Number of meetings	200
Age	Median, 61 years; Range, 3–92 years
Gender, *N* (%)	Men, 295 (41.3%); Women, 420 (58.7%)
Number of physicians who presented ≥1 case	58
Diagnosis, *N* (%)	
Breast cancer	129 (18.0)
Colorectal cancer	87 (12.2)
Hematologic malignancies	51 (7.1)
Gastroesophageal cancer	51 (7.1)
Pancreatic cancer	48 (6.7)
Biliary cancer	37 (5.2)
Lung cancer	36 (5.0)
Gynecologic cancer	36 (5.0)
Other GI malignancies[b]	33 (4.6)
Sarcoma	32 (4.5)
Bladder/Ureter cancer	20 (2.8)
Head and neck cancer	19 (2.7)
Hepatocellular carcinoma	18 (2.5)
Neuroendocrine malignancies	17 (2.4)
Prostate cancer	13 (1.8)
CNS malignancies	12 (1.7)
Thyroid cancer	5 (0.7)
Other malignancies	71 (9.9)

[a]Among the 858 presented patients, 99 patients were presented more than once. Only the first records were included in the analysis. Forty-four patients without complete discussion record were excluded (Supplementary Fig. 1). Only patients in face-to-face Molecular Tumor Board meetings were included.
[b]Other GI malignancies include appendiceal adenocarcinoma (*N* = 27), duodenal cancer (*N* = 4) and small bowel adenocarcinoma (*N* = 2).
CNS central nervous system, GI gastrointestinal.

Source: https://www.nature.com/articles/s41467-020-18613-3

NATURE COMMUNICATIONS | https://doi.org/10.1038/s41467-020-18613-3 ARTICLE



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“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

Clinical Significance of scores generated by the CureMatch cancer therapy matching engine for patient outcomes

Problem

Can precision medicine tools (from CureMatch) help oncologists navigate the myriad of therapy options to best address each patient’s unique tumor profile?

Approach

Based on I-PREDICT study (published in Nature)

Participants: Patients with available Progression Free Survivability (PFS) and sequencing data who received <3 matched non-experimental cancer drugs in combination (n=77).

Data set: Binarized at 36 possible thresholds (higher vs. lower score bins). Limit of >25 patients per bin.

Kaplan-Meier plots (p-value, hazard ration, confidence intervals)

Results

Therapies with high scores were predictive of better progression free survivability (PFS).

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

“The utility of this system provides digital guidance to oncologists in selecting the most suitable treatment.”

- Perlina, ASCO

Source: J Clin Oncol 39, 2021 (suppl 15; abstr e15099)

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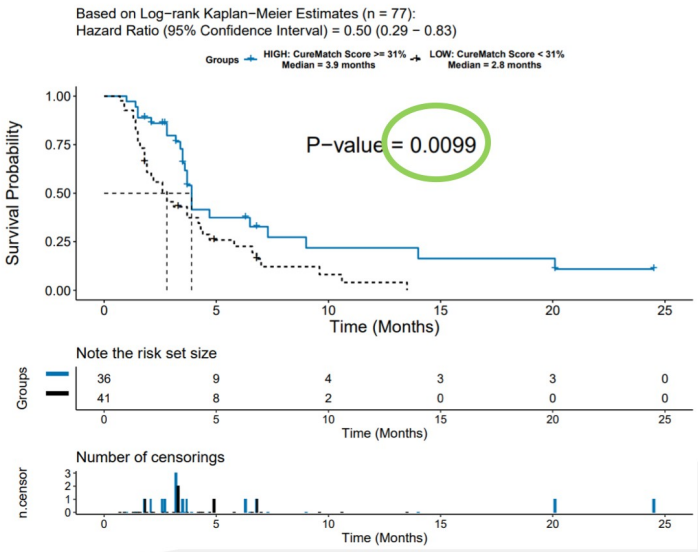
CureMatch’ed scores correlate with clinical outcome



Progression-Free Survival (PFS): Pan-Cancer

Romm…..Perlina, ASCO

J Clin Oncol 39, 2021 (suppl 15; abstr e15099)

The higher the score, the better the outcome.

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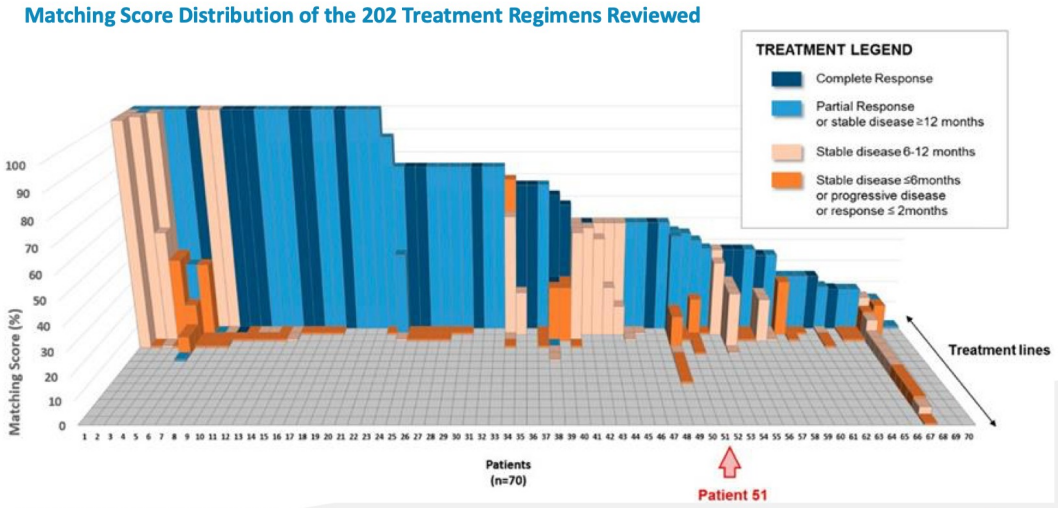
“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

Published Results: CureMatch scores predict exceptional responses



Source: Cancers 2020, 12, 166; doi: 10.3390/cancers12010166

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- Provides therapeutic intelligence to empower oncologists to address the molecular complexity of cancer
- The next step in cancer care after NGS tumor profiling
- A validated expertly curated database that matches, ranks and scores known and novel combination cancer therapies (monotherapy, 2-drug combinations, and 3-drug combinations), based on the biomarkers of the patient's unique molecular tumor profile
- Matches any of the top recommended therapy selections to ongoing clinical trials in addition to reporting out potential interactions/toxicities
- Therapies with higher matching scores are predictive of better PFS, while lower scores are predictive of worse PFS.-ASCO 2021
- Complements your current NGS Laboratory report (NGS testing company agnostic) with actionable insights
- Provides actionable intelligence towards advanced therapy treatment options in both, clinical practice, as well as clinical trials.
- Reduced Medical System financial burden by saving on harmful treatments and getting the better matched treatments sooner. https://www.einpresswire.com/article/566566644/new-study-validates-payer-physician-use-of-ai-to-cut-wasteful-spending-on-high-cost-low-value-cancer-drugs

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“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

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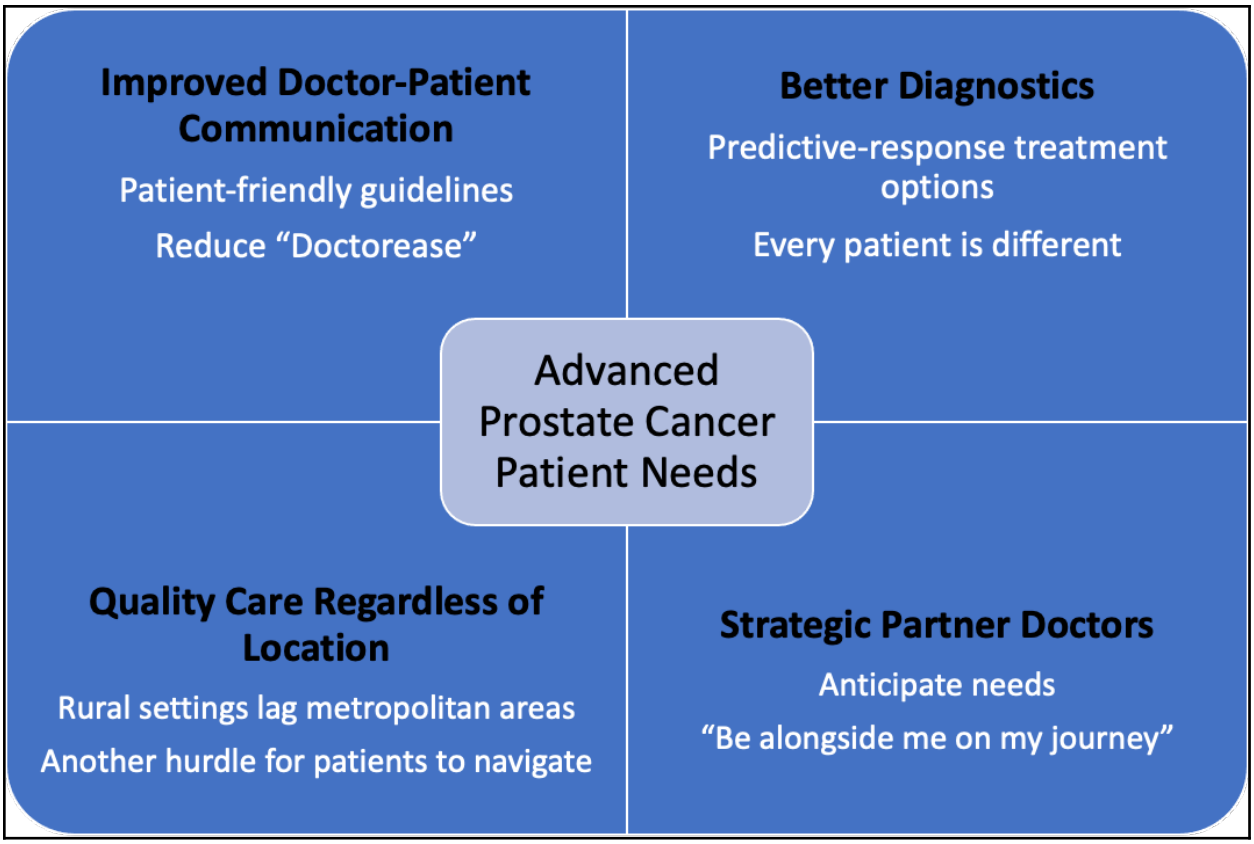
We're working towards publishing even more evidence this year. The field is pivoting even more. When I worked at Human Longevity with Rick and we were just starting the whole oncology program there, there were some progressive thinkers, but the majority weren't ready. Now the field is in a completely different shape than when we launched our comprehensive cancer program in 2015 or 2016 at HLI. Hopefully it is happening faster, rather than slower.

Brian McCloskey: Ally, thank you again very much. Please extend my appreciation to the team. I am really grateful. I will have a conversation with Rana McKay and share her thoughts.

Prostate Cancer Patients Meeting Report - Key Themes

“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]



Brian McCloskey: On Friday, April 15, Brad and I convened a meeting with four of the ten prostate cancer patients who have registered to join the Prostate Cancer Lab community over the last several weeks. We wanted to do a little market research to understand what their needs are and what they want on their healthcare journey. Mike Yancey, who is on this call, was one of the four patients.
After a round of introductions, I asked, "If you could change one thing with your healthcare, what would that be?"
Four themes emerged:

- **Improved doctor-patient communication**: Steve Abbott, the executive director of Cincinnati Cancer Advisors, raised the need for improved doctor-patient communication, especially simplified language. He is starting an initiative to try to improve "doctor-ese", the terminology that doctor's throw at patients. It is particularly difficult for cancer patients who are newly diagnosed to come up the learning curve on all the things they need to know, and the language doctors use doesn't help.
- **Better diagnostics for personalized treatments**: Ken Anderson, a member of AnCan, shared his interest in better diagnostics, as is being discussed at the Prostate Cancer Lab. Every patient is different. We both have prostate cancer, but genomically we are completely different. We want to have more data-driven decision-making and predictive-response treatment options. Jonathan Starr is interested in clinical trials for Provenge, and Ken pointed him to Larry Fong at UCSF.

“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

- **Strategic partner doctors**: Mike Yancey needs somebody who is going to be alongside him on his journey. He has bounced around between a number of doctors. Luckily he has gotten care at MD Anderson in Houston.
- **Quality care regardless of location**: Also from Mike Yancey, who is based in rural Oklahoma: it's clear that rural areas lag metropolitan areas in their access to expert advisors. Mike has fewer options in Oklahoma than Rick or I do in southern California. The Prostate Cancer Foundation has the issue of raising medical knowledge among all providers on its agenda, and now we have Mike's story to bring to them.

We talked about how often we want to meet. We will put together a patient board and meet monthly, and take information from those discussions and feed them into this format.

John Laird: On the theme of strategic partnerships with doctors, I heard two possibilities: (1) a treating physician, an integrative oncologist, or an integrative naturopath who specializes in oncology. Or (2) a medical advocate, a role that I and other doctors play, where we are more like an independent consultant. I am looking over everything in the case. Is the diagnosis accurate? Do we need to send it to a specialist who can overturn the diagnosis or make it more accurate? Where are the oncologists who might expand the range of options? Who might be in your area, and you might not know about them? What are new testing options, like I suggested to Rick? There is a whole world of advocacy. There are medical doctors. I was trained by Mark Renneker, a founder in the field.

Brian McCloskey: I know him. He's a big surfer. He's at UCSF.

John Laird: Laura Pool is another model of an advocate. She's a nurse. She is research-driven. She works for the Commonweal group in Marin. She gives strategic ideas.

Brian McCloskey: There is also the element that patients only get 20-30 minutes with their doctor, which is often not enough. Maybe there is an opportunity to scale these advocate roles or change the model a little bit.

John Laird: On your topic of physician-patient communications, sometimes in my advocacy work I'm prepping the patient for a conversation with their oncologist. My model is to empower the patient. We might spend a half hour to prepare the questions, to know what's going on and make effective requests.

Saed Sayad: I've been working with personalized data for many years, and the number one issue I see is the design of experiments, especially the predictive part. Some just try to explore, not predict. They don't start with a question and try to answer it. Exploration generates thousands of questions. For this patient, what is the most important question? Can we answer it with existing information? How much time do I have? Question-based predictive approaches are much better.

“Drug Combinations Promise Precision” (Ally Perlina, CureMatch) [#5]

Brian McCloskey: Rick Stanton is working on (NCCN-type) guidelines, and we had a good conversation about how to integrate diagnostics to eliminate certain treatments that wouldn't benefit a patient. For example, understanding your hormone sensitivity. There is an AR-V7 test for that. There are potentially organoid models that would help us understand if a patient is going to respond to chemotherapy.

Brad Power: Dr. Laird is pointing out that there are different kinds of people that can help guide patients, educating them, so they can ask the right questions.
Saed is saying patients need help in asking the right questions.