Clinical Trial Notifications Triggered by Artificial Intelligence–Detected Cancer Progression

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Can we use AI to find "clinical trial-ready" patients?

Historically, less than 10% of adults with cancer enroll in clinical trials

- Yet trials often struggle to reach their accrual goals

Many trials of novel therapies have specific molecular criteria

- Tools have been developed to match patients to trials based on these criteria

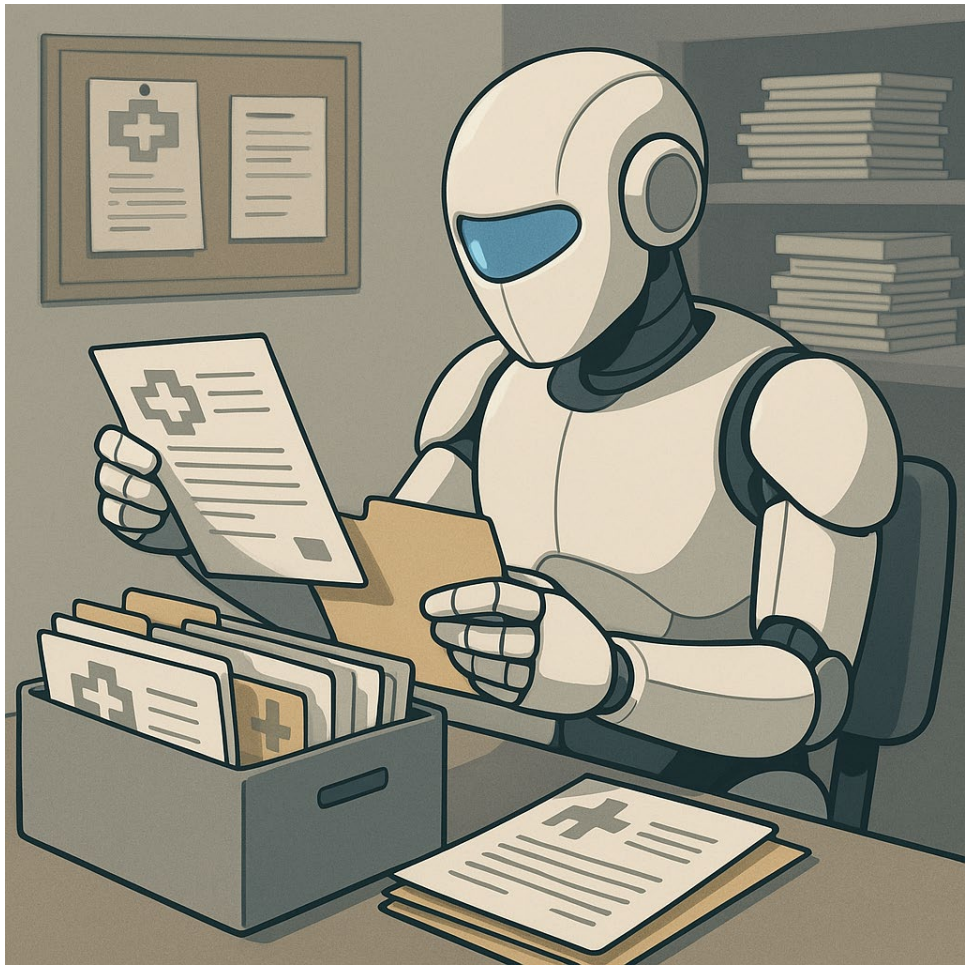
Computational clinical trial matching tools

Commercial

- IBM Watson (inactive)
- Tempus Link
- SYNERGY-AI (Massive Bio) – patient-directed/phone app
- OncoTrials (Flatiron)
- OncoLens
- Triomics / OncoLLM
- TriaLinQ (ConcertAI)
- TriNetX
- IQVIA
- Antidote (patient-directed)

Academic / open

- TrialGPT (NIH): Retrieve, criterion match, trial-level ranking
- Clinical Trial Patient Matching (CTPM): Yale
- MatchMiner: Dana-Farber

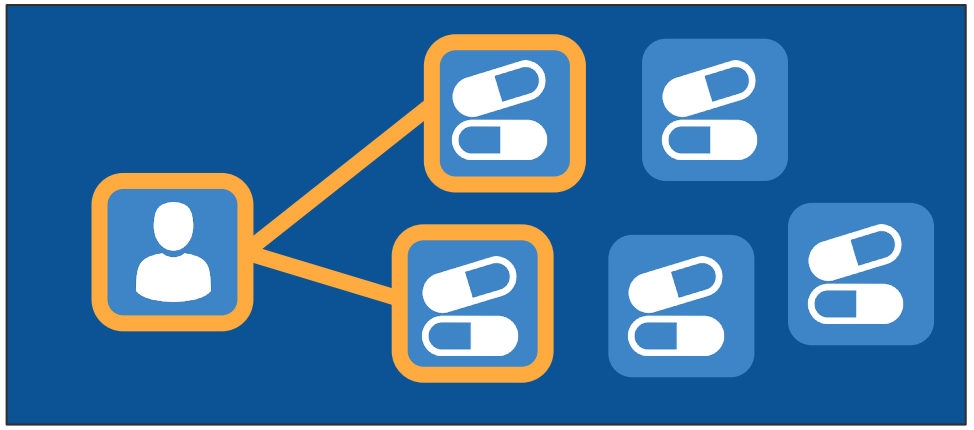


MatchMiner: Connecting Patients and Trials

Trial-centric mode

Recruit patients for a specific genomically-targeted trial

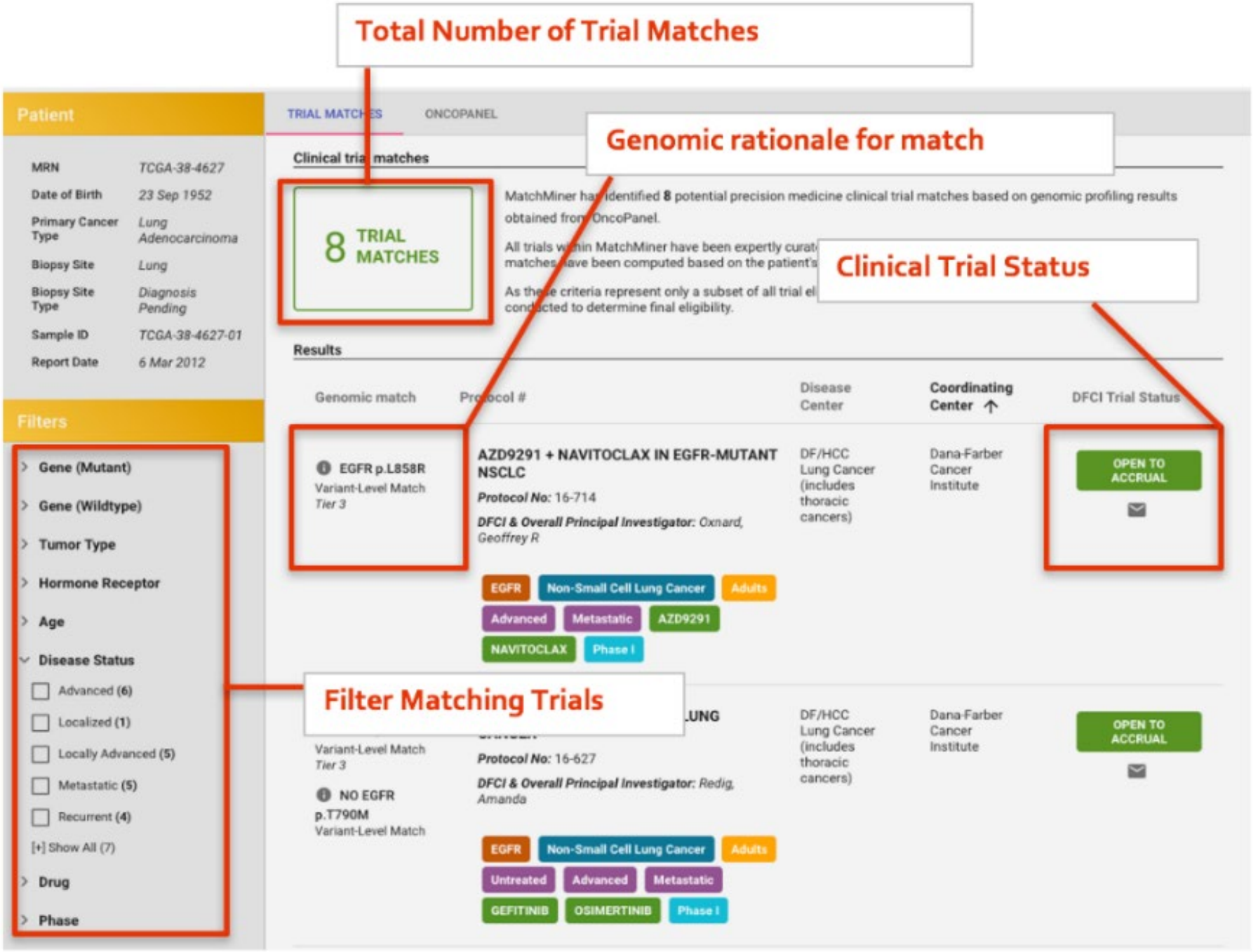
Patient-centric mode



Identify genomically-targeted trial options for an individual patient

Slide courtesy of Tali Mazor, PhD (DFCI Matchminer team)

MatchMiner interface



Screenshot of MatchMiner Patient-Centric Matching (Simulated data shown).

Trial Readiness: The Problem

- MatchMiner matches all living patients to genomic trials/filters
- However, patients are often not 'trial-ready'

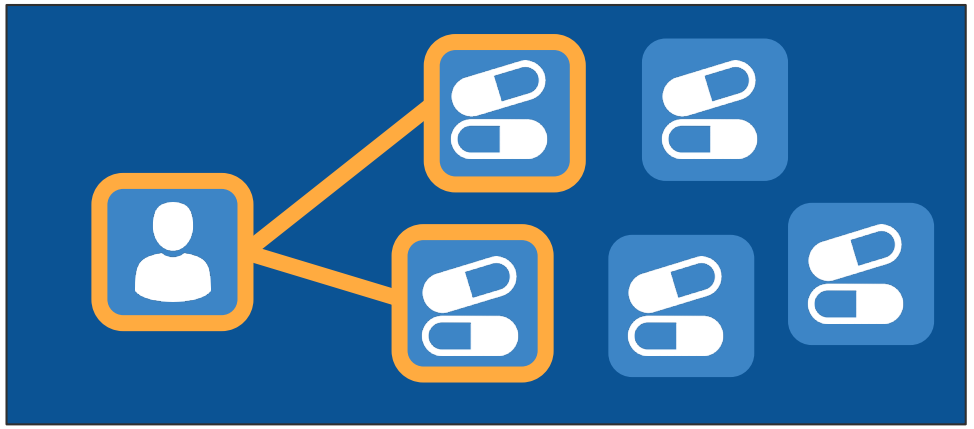
Slide courtesy of Tali Mazor, PhD (DFCI Matchminer team)

Trial readiness: The problem

Trial-centric mode

Too many patients: Filters return too many patients to review, most of whom are not trial-ready anyway.

Patient-centric mode



Notification overload: Attempts at ‘push notifications’ to providers mostly include patients that are not trial-ready, therefore providers ignore notifications (and get annoyed at us).

Slide courtesy of Tali Mazor, PhD (DFCI Matchminer team)

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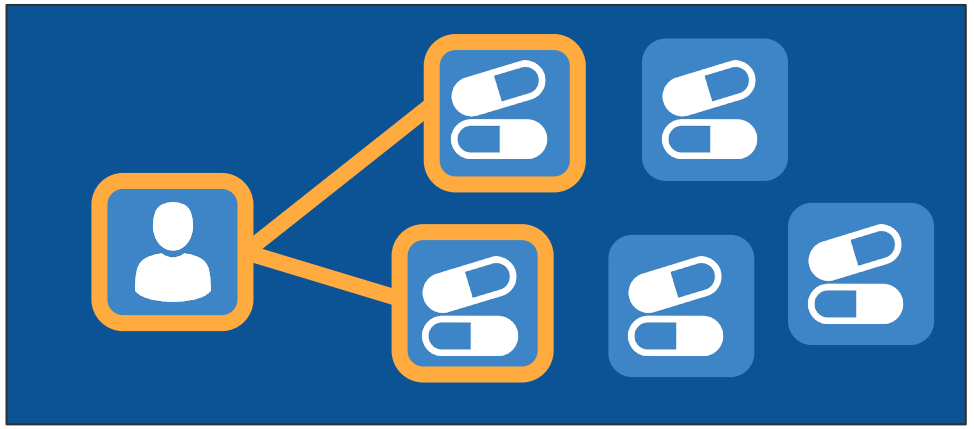

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Slide courtesy of Tali Mazor, PhD (DFCI Matchminer team)

We have AI models to extract clinical data from imaging reports

- Propensity to change treatment within 30 days
- Probability of mortality within 6 months
- Progression of disease
- Brain metastases

Clinical Inflection Point Detection on the Basis of EHR Data to Identify Clinical Trial–Ready Patients With Cancer

Kenneth L. Kehl, MD, MPH[1]; Stefan Groha, PhD[1]; Eva M. Lepisto, MA, MSc[1]; Haitham Elmarakeby, PhD[1]; James Lindsay, PhD[1]; Alexander Gusev, PhD[1]; Eliezer M. Van Allen, MD[1]; Michael J. Hassett, MD, MPH[1]; and Deborah Schrag, MD, MPH[1]

Assessment of Deep Natural Language Processing in Ascertaining Oncologic Outcomes From Radiology Reports

Kenneth L. Kehl, MD, MPH[1,2,3]; Haitham Elmarakeby, PhD[3]; Mizuki Nishino, MD, MPH[4]; et al

» Author Affiliations | Article Information

JAMA Oncol. 2019;5(10):1421-1429. doi:10.1001/jamaoncol.2019.1800

Artificial intelligence-aided clinical annotation of a large multi-cancer genomic dataset

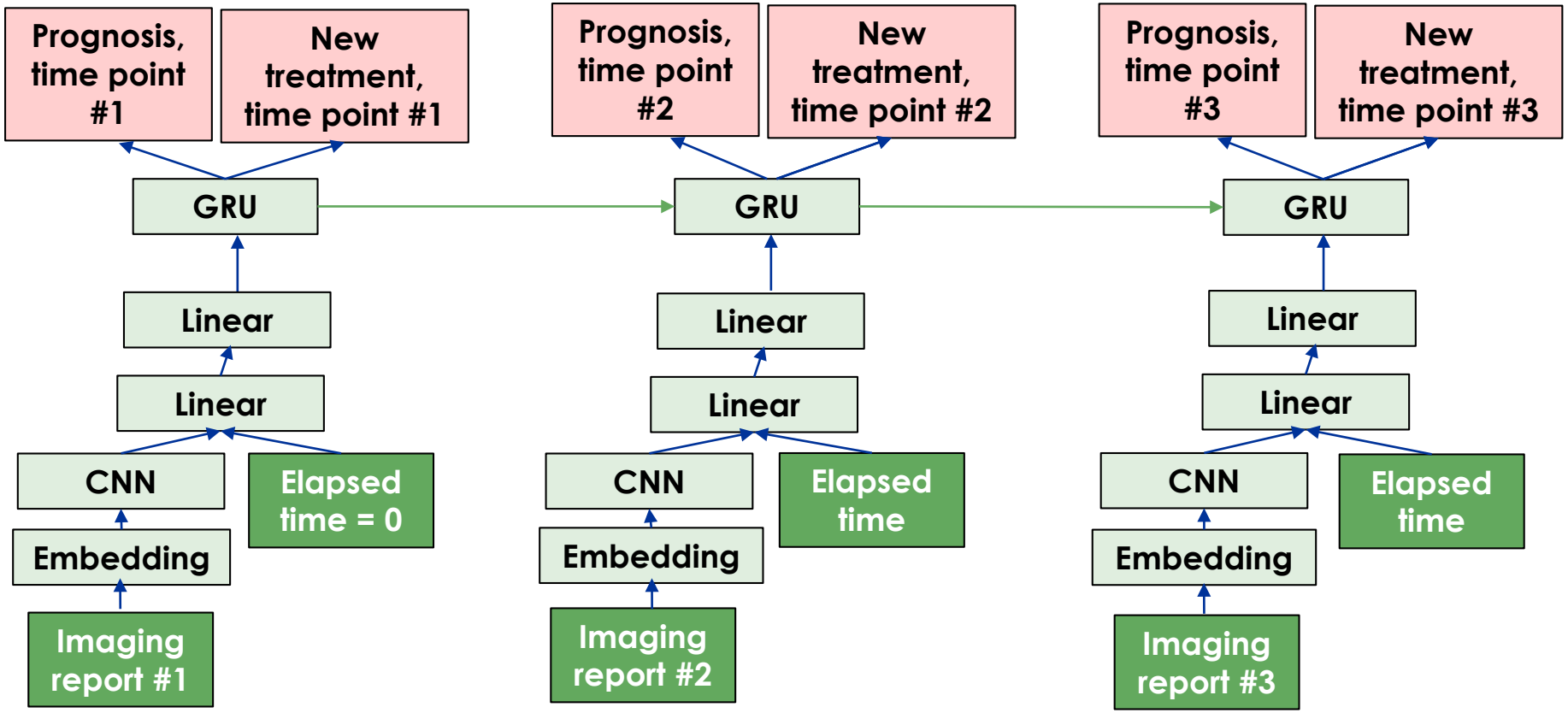
Kenneth L. Kehl ✉, Wenxin Xu, Alexander Gusev, Ziad Bakouny, Toni K. Choueiri, Irbaz Bin Riaz, Haitham Elmarakeby, Eliezer M. Van Allen & Deborah Schrag

Nature Communications **12**, Article number: 7304 (2021) | Cite this article

Trial readiness: The Problem

- MatchMiner matches patients to trials based on genomics
- However, patients are often not “trial-ready.”
- Can we train an AI model to find ”trial-ready” patients?

Modeling for one patient



Kehl et al, *JCO-CCI*, 2021

Finding patients for trials: Implementation pilot

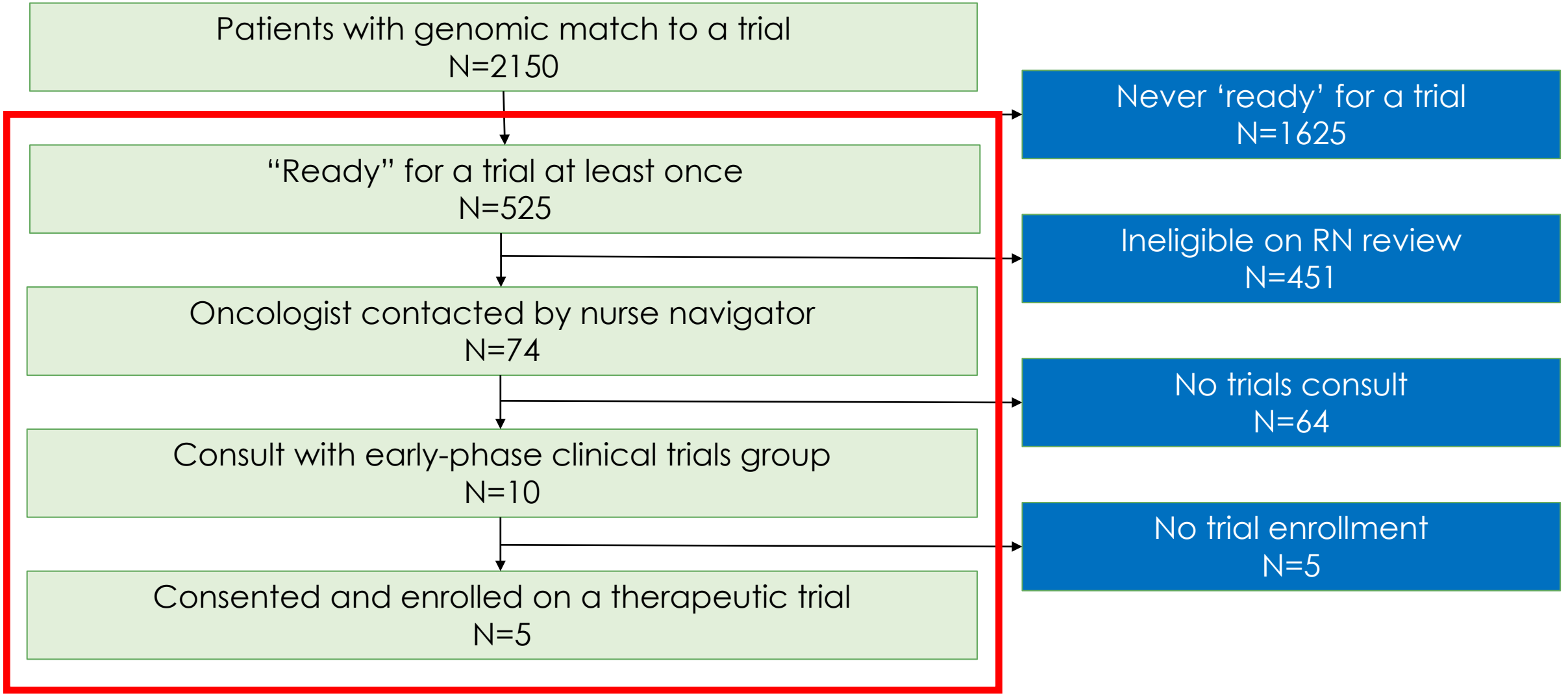
Disease center

- Center for Cancer Therapeutic Innovation
  - Early-phase studies

Intervention

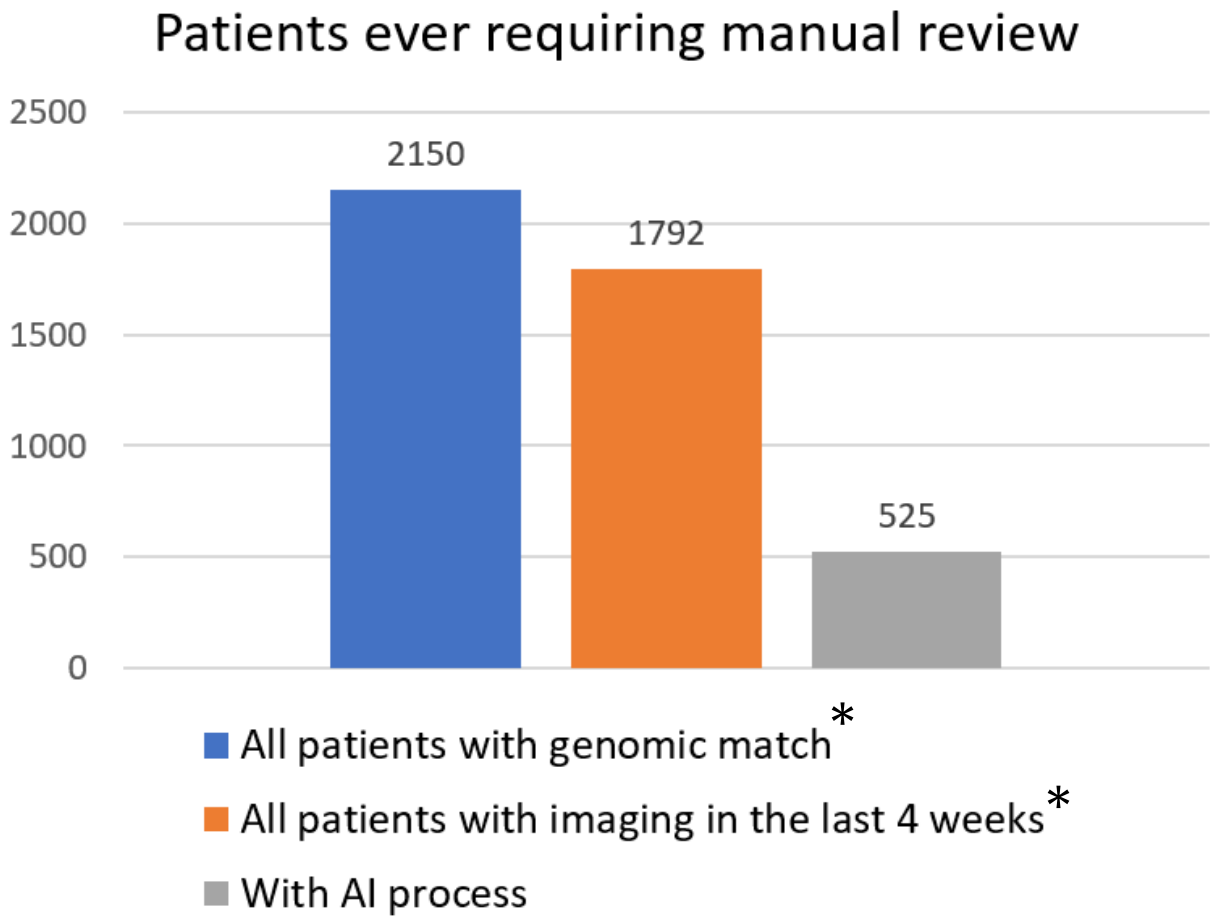
- Weekly spreadsheets providing predictions of clinical trial "readiness" based on propensity to initiate new treatment within 30 days
- Emailed to small group of clinicians and research staff in each disease center

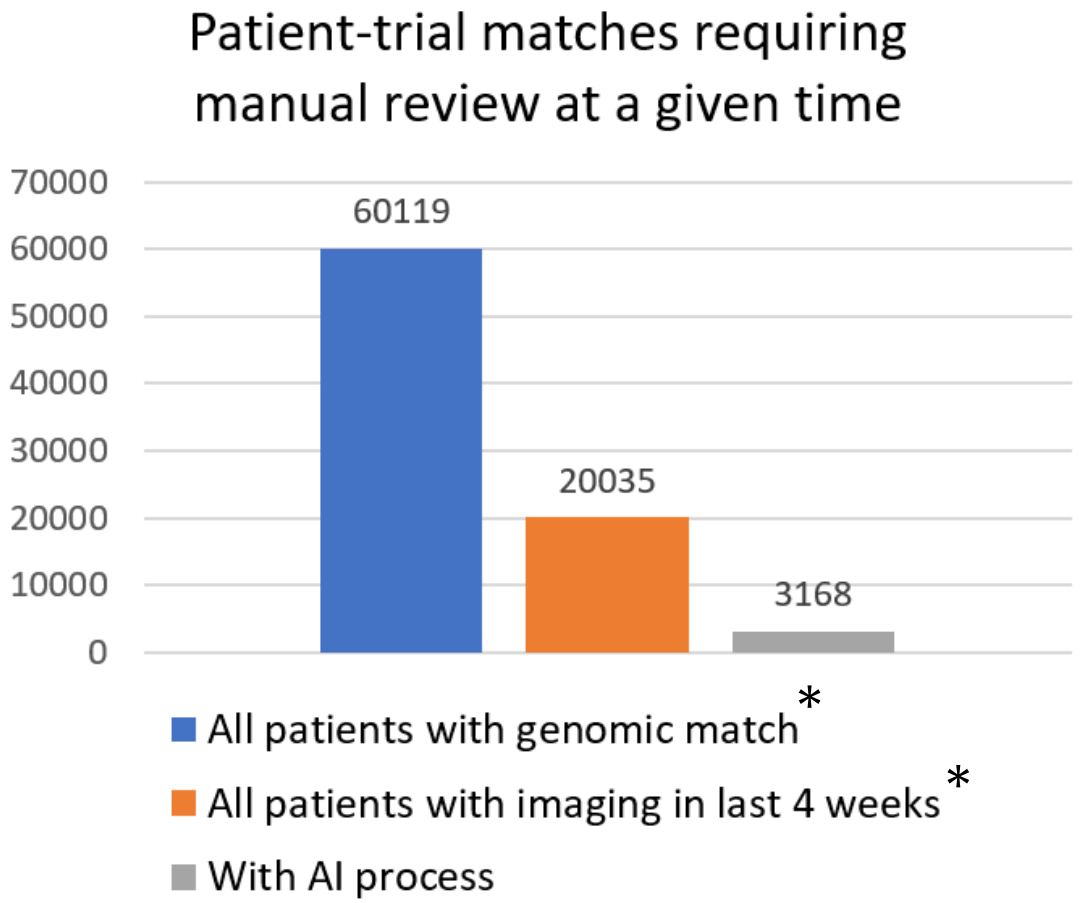
Nine-month pilot results



Kehl et al, *JCO-PO* 2024

Volume of manual review required

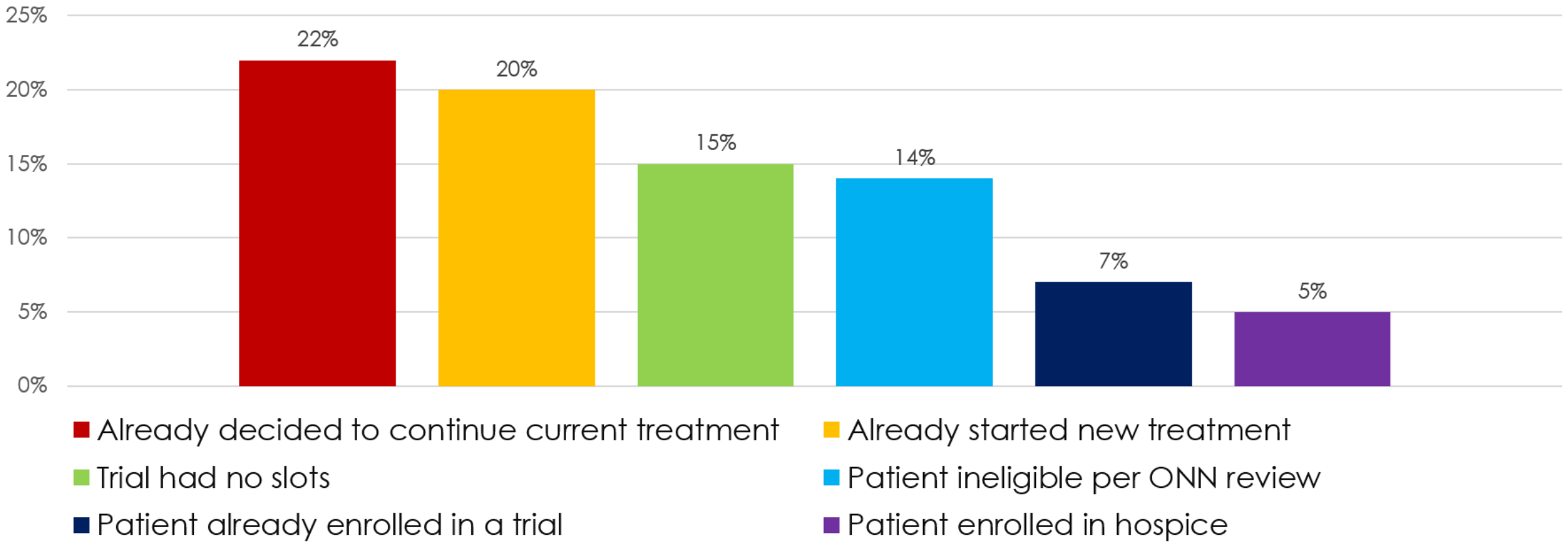




* Hypothetical

Kehl et al, *JCO-PO* 2024

Reasons for oncologist non-contact



Kehl et al. JCO Precis Oncol. 2024 Mar;8:e2300507.

Finding trials for patients: OPTIONS

(Optimizing **P**recision **T**rials with an artificial **I**ntelligence driven **O**ncologist **N**otification **S**ystem)

All adults with OncoPanel results for solid tumors as of January 2023

Group 1:
Standard MatchMiner workflows
No proactive AI-based provider notification

Control group

Group 2:
Email notifications sent to treating oncologists when patients:
1) Had genomic matches,
2) Were likely to change treatment (AI), and
3) Had progressive disease (AI)

Group 3:
Email notifications sent to treating oncologists when patients meet Group 2 criteria and additional manual review criteria

Intervention group

Interlude: What is this study?

Research?

- Is it a clinical trial? What 'accrual' do I report?
  - Zero?
  - 50,000?

Operational?

- The operations of clinical research?
- What do we do when trial PI's ask for lists of patients with progressive disease who match their trials?

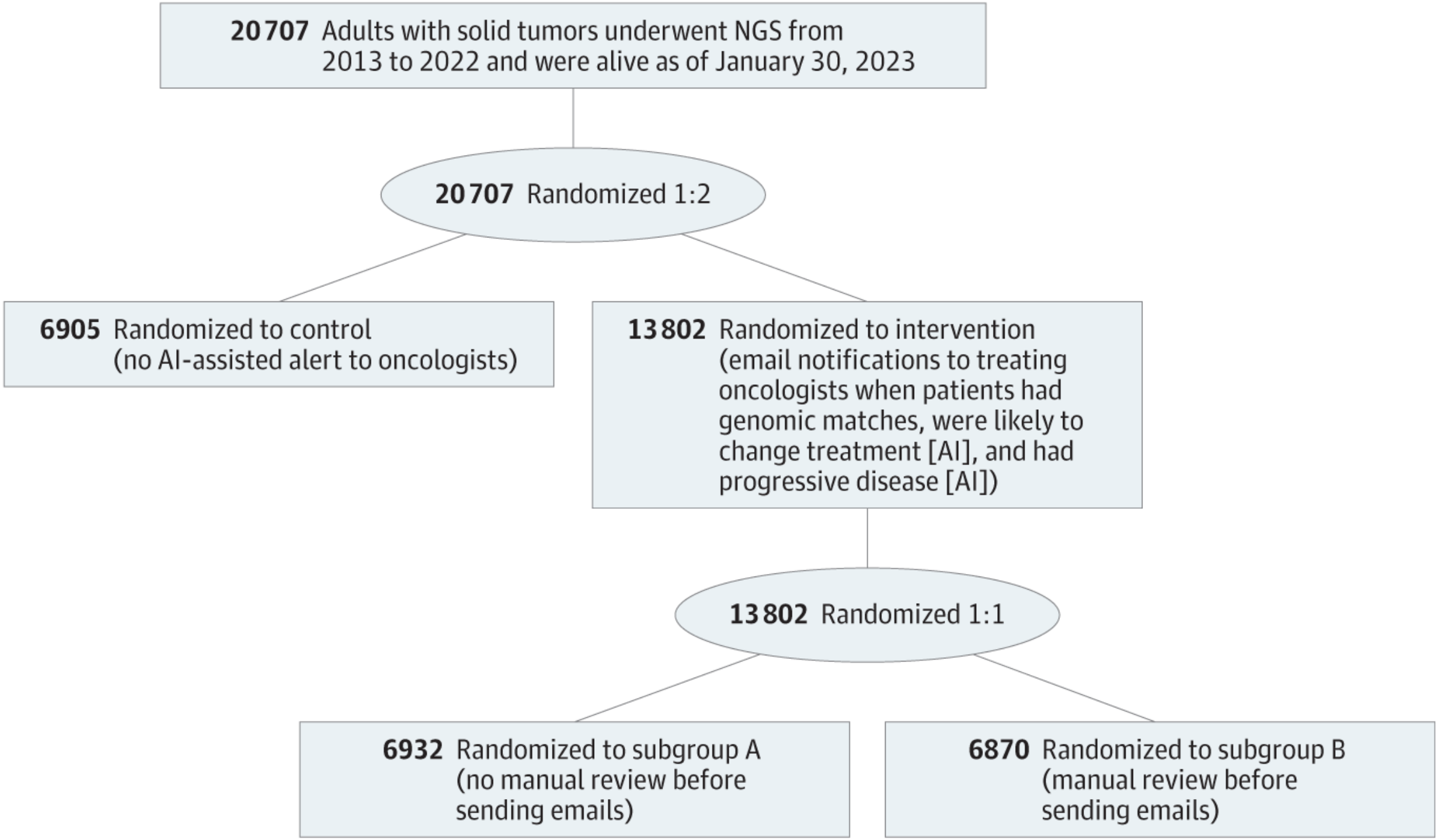
OPTIONS: Outcomes

Primary

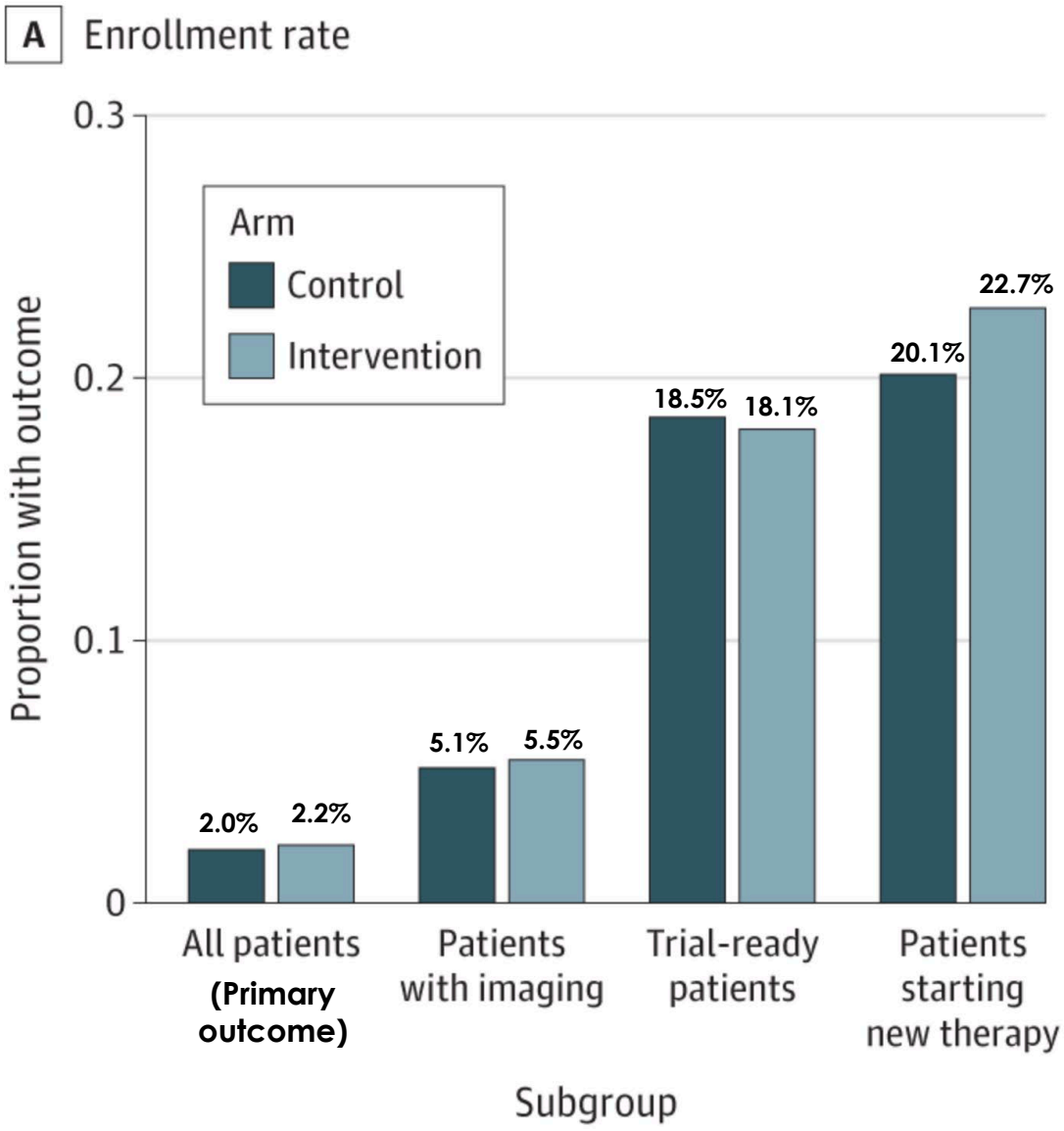
- **Enrollment in any DFCI therapeutic (anti-cancer medicine) clinical trial by end of follow-up 7/1/24**
  - **Groups 2+3 versus group 1**

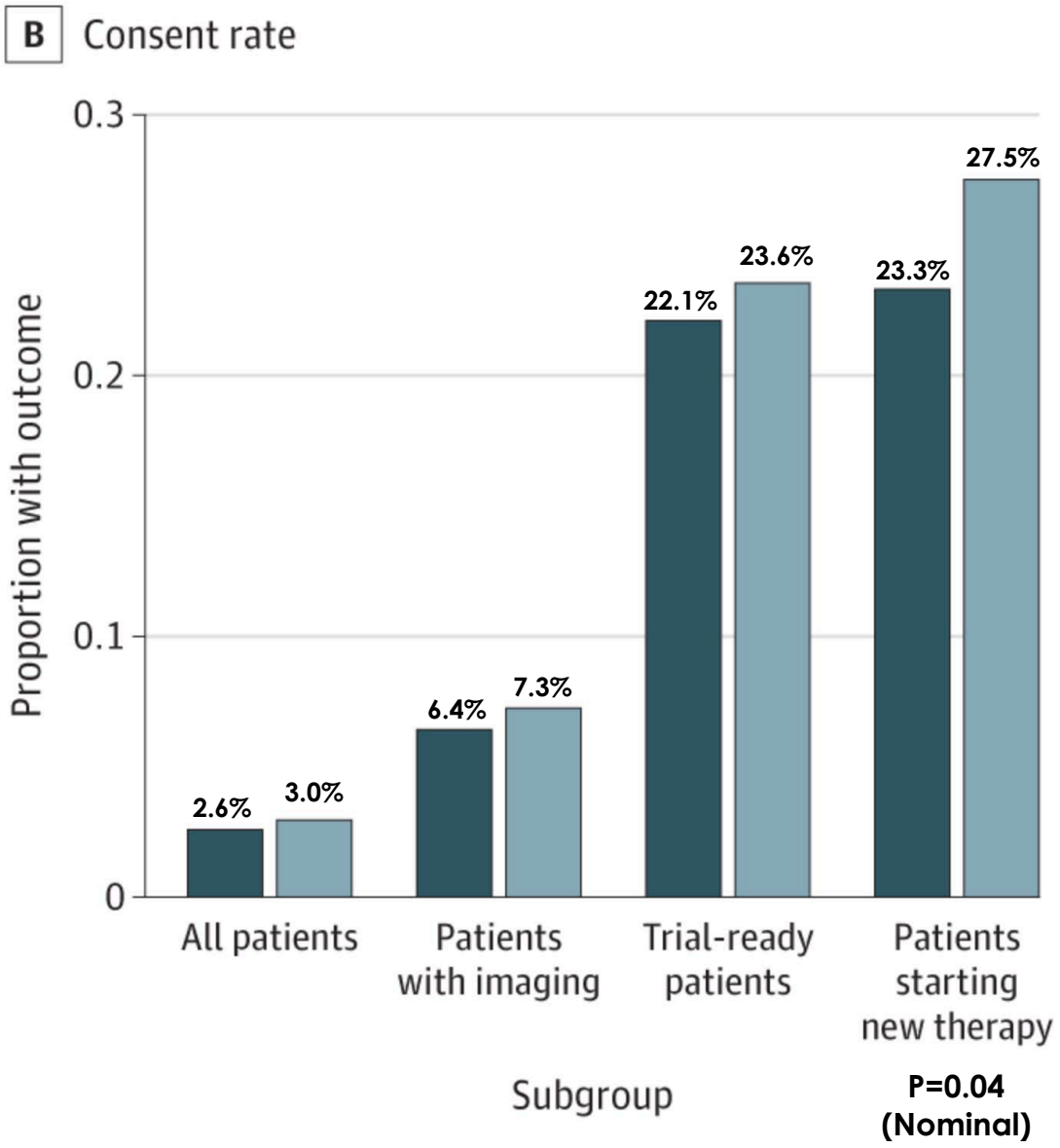
Secondary

- Enrollment in therapeutic trials across all three groups
- Consultations in Center for Cancer Therapeutic Innovation
- Consents to any therapeutic trial
- Consents and enrollments among patients deemed likely to change treatment
- Proportion of new treatments that were trials
- Clinician survey results

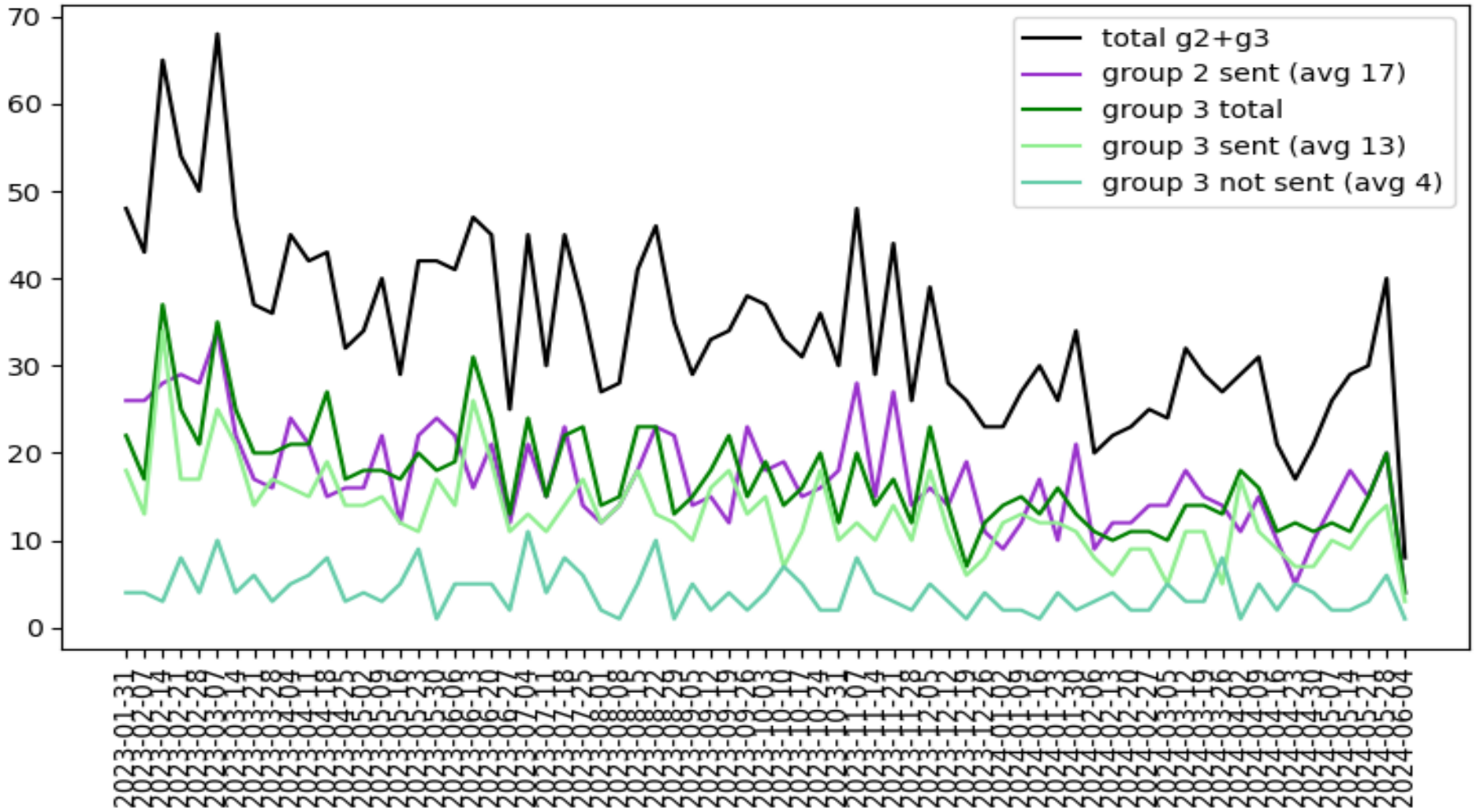

20 707 Adults with solid tumors underwent NGS from 2013 to 2022 and were alive as of January 30, 2023
20 707 Randomized 1:2
6905 Randomized to control (no AI-assisted alert to oncologists)
13 802 Randomized to intervention (email notifications to treating oncologists when patients had genomic matches, were likely to change treatment [AI], and had progressive disease [AI])
13 802 Randomized 1:1
6932 Randomized to subgroup A (no manual review before sending emails)
6870 Randomized to subgroup B (manual review before sending emails)

OPTIONS results





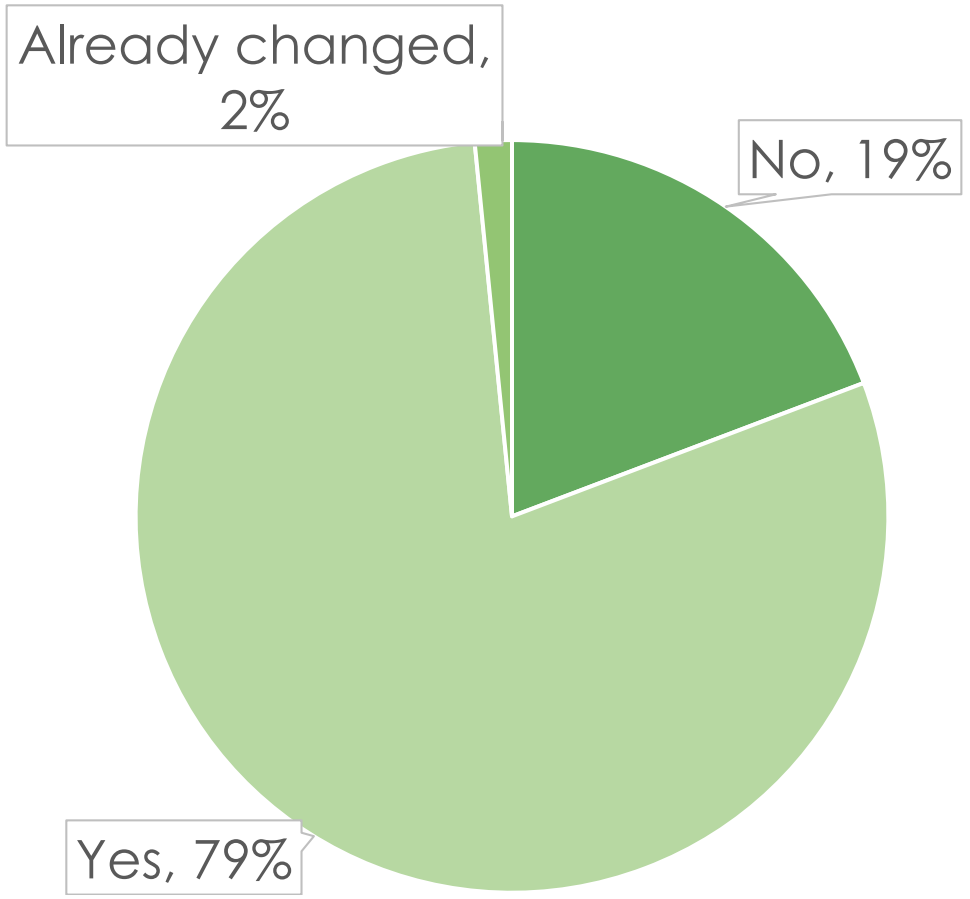
OPTIONS: Email counts



Data courtesy of Tali Mazor, PhD (DFCI Matchminer team)

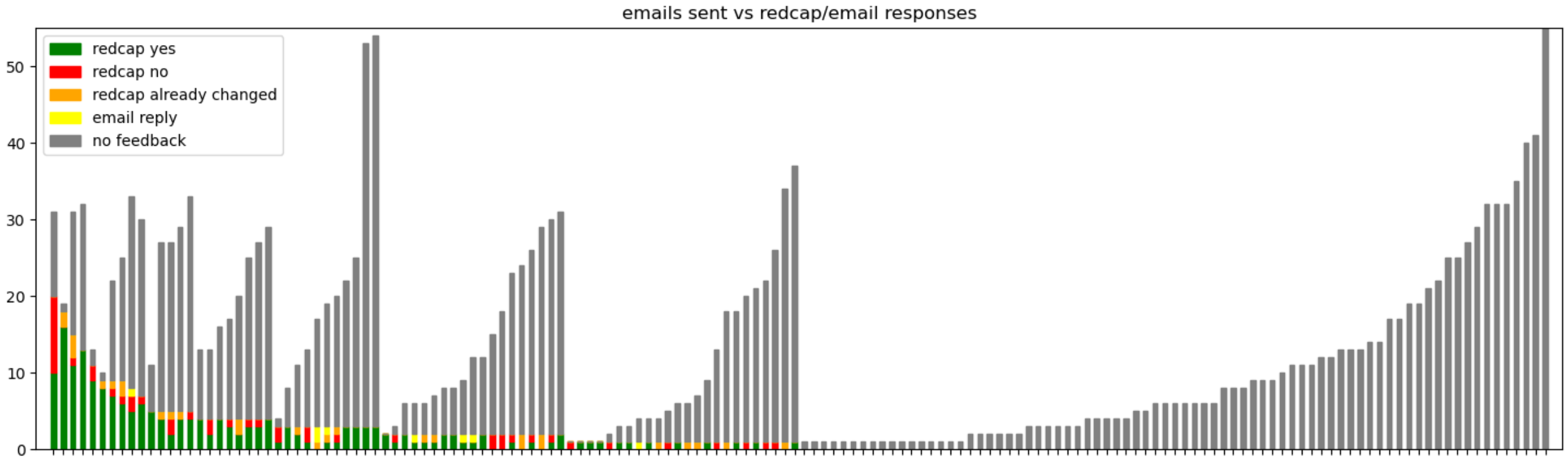
OPTIONS: Oncologist survey results

Do you agree that this patient is likely to change treatment in the next 30 days?



OPTIONS: Survey results by provider

Survey response rate on per-email basis: 12%
About half of email recipients responded at least once.

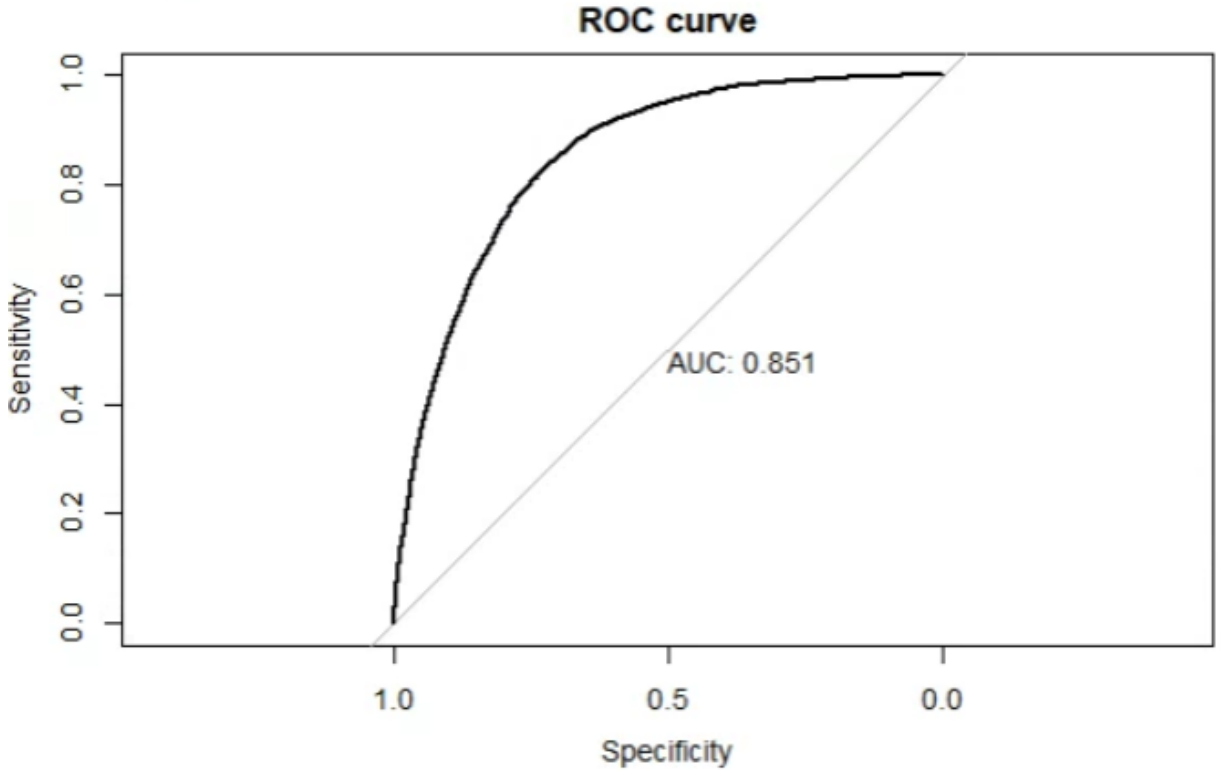


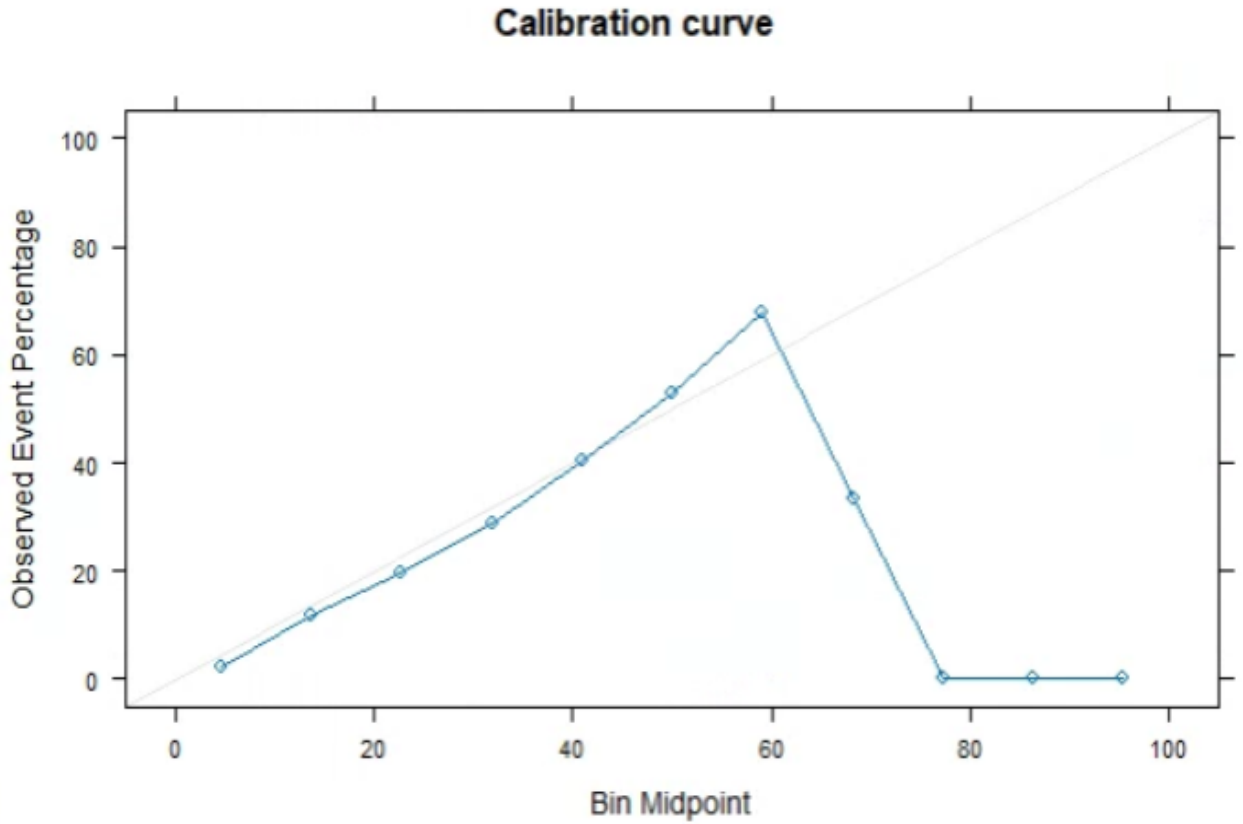
OPTIONS: Manual email rejection reasons

Of 1158 candidate clinician notifications manually reviewed for patients in group 3, 269 (23%) were rejected by our team and not sent.

Reason	N
Uncontrolled brain mets	96
No measurable disease	77
Model is wrong	46
Already changed treatment	30
ECOG	15
Hospice	11
Other	3
Multiple primary cancers	3

OPTIONS: AI model predicted treatment changes, as designed





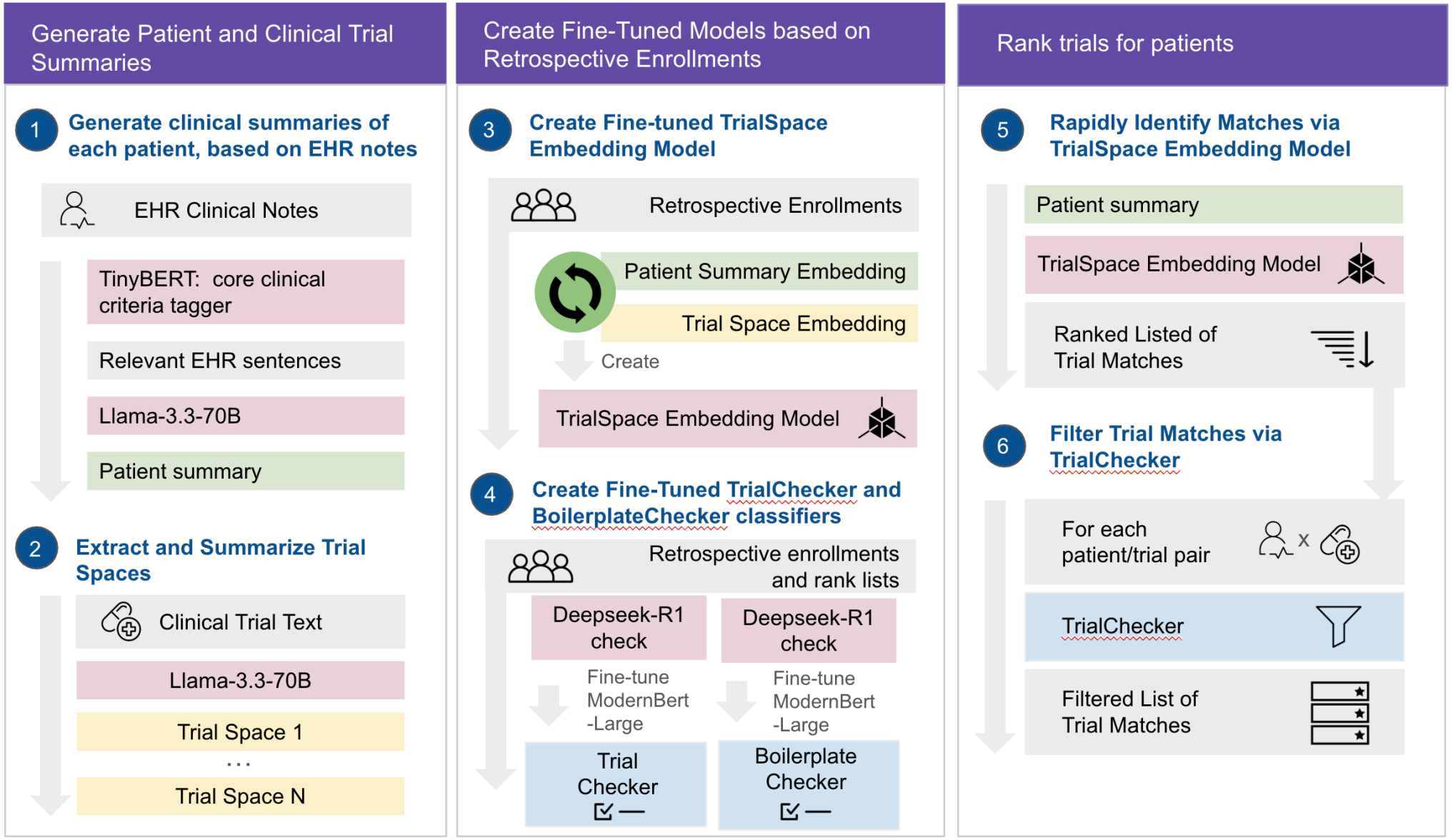
Notifying treating oncologists of trials: Conclusions to date

- Emailing academic oncologists with genomically matched trial information when their patients have progressive disease did not increase trial enrollment
- The AI models do reasonably well at finding patients with active/progressive cancer who may need treatment changes
- Our intervention addresses only one barrier to trial participation. Others may include:
  - Eligibility criteria beyond genomics and recent progression
  - Patient or oncologist preference/convenience
    - Is a trial an end in itself?
    - Complexity of trials
    - Biopsies for biomarker testing
    - Time toxicity

MatchMiner-AI: Trial matching for all

- MatchMiner selects specific trials based on genomic eligibility criteria.
- Our deployed AI pipeline can identify patients with progressive disease for whom genomic trial matches may be relevant.
- What if patients don't have genomic data or we don't have it in structured form?
- What about trials that do not select based on genomics?

MatchMiner-AI: Trial matching for all

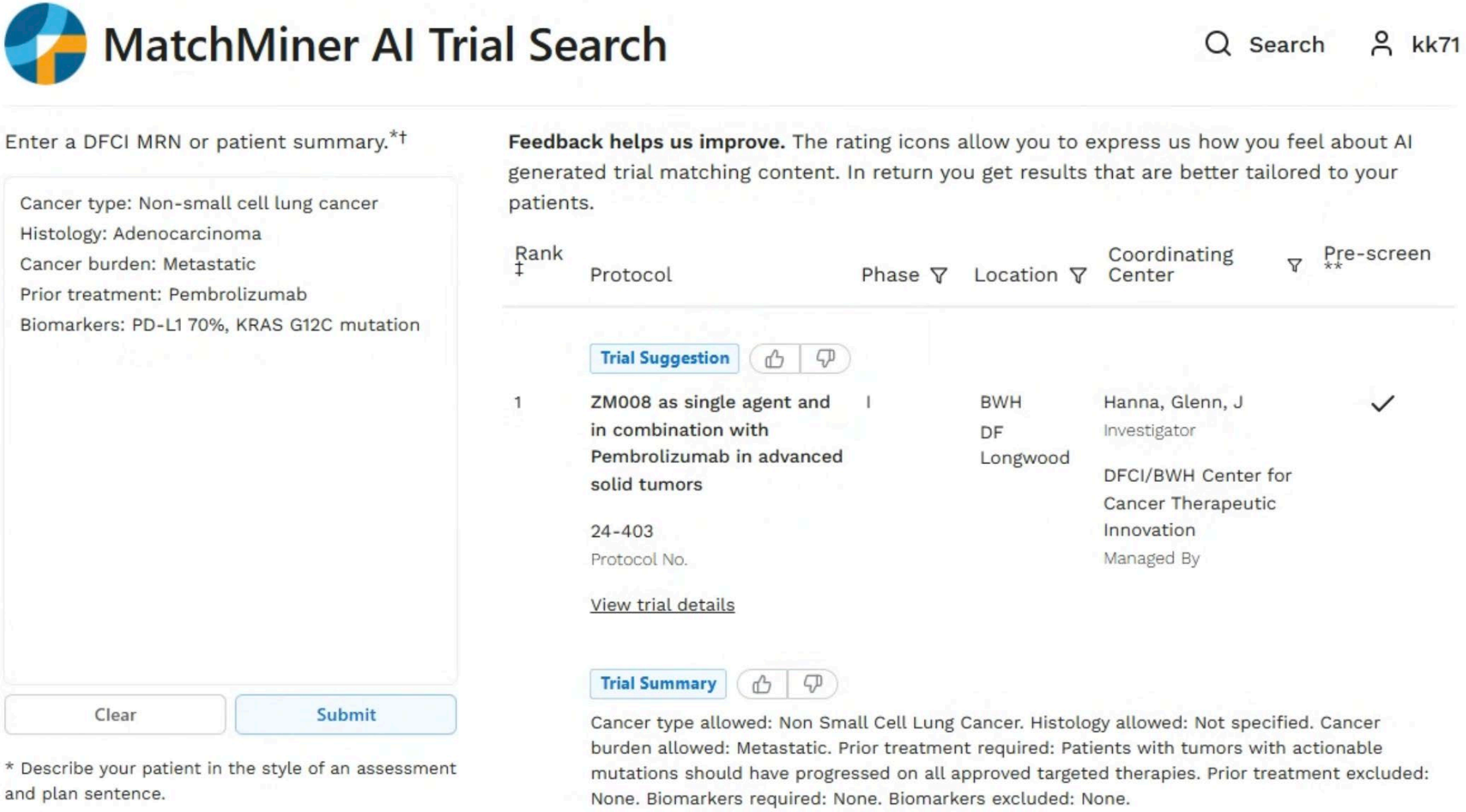


https://arxiv.org/abs/2412.17228

MatchMiner-AI: Trial matching for all

Metric	Retrospective DFCI trial enrollment dataset (Patient test split; n=1582 patient summaries queried)			DFCI standard-of-care treatment start and external trials dataset (Patient test split; n=9477 patient summaries queried)		
	Stella baseline	TrialSpace alone	TrialSpace + TrialChecker	Stella baseline	TrialSpace alone	TrialSpace + TrialChecker
Precision @ 10	0.43	0.67	0.89	0.39	0.64	0.83
MAP @ 10	0.60	0.87	0.94	0.55	0.78	0.90
Median results returned per query (N)	10	10	7.0	10	10	7.0
Mean results returned per query (N)	10	10	7.0	10	10	7.0

MatchMiner-AI: Trial matching for all



https://arxiv.org/abs/2412.17228

Caution!

Brief Communication | Open Access | Published: 19 January 2023

Racial and ethnic disparities in a real-world precision oncology data registry

Alexander T. M. Cheung, Elina L. Palapattu, Isabella R. Pompa, Christopher M. Aldrighetti, Andrzej Niemierko, Henning Willers, Franklin Huang, Neha Vapiwala, Eliezer Van Allen & Sophia C. Kamran

npj Precision Oncology **7**, Article number: 7 (2023) | Cite this article

> Cancer Epidemiol Biomarkers Prev. 2023 Mar 6;32(3):344-352.
doi: 10.1158/1055-9965.EPI-22-0875.

Elucidating Analytic Bias Due to Informative Cohort Entry in Cancer Clinico-genomic Datasets

Kenneth L Kehl [1], Hajime Uno [1], Alexander Gusev [1], Stefan Groha [1], Samantha Brown [2], Jessica A Lavery [2], Deborah Schrag [3], Katherine S Panageas [2]

Affiliations + expand

PMID: 36626408 PMCID: PMC9992002 (available on 2023-09-06)

DOI: 10.1158/1055-9965.EPI-22-0875 Paperpile

Caution!

Original Investigation

FREE

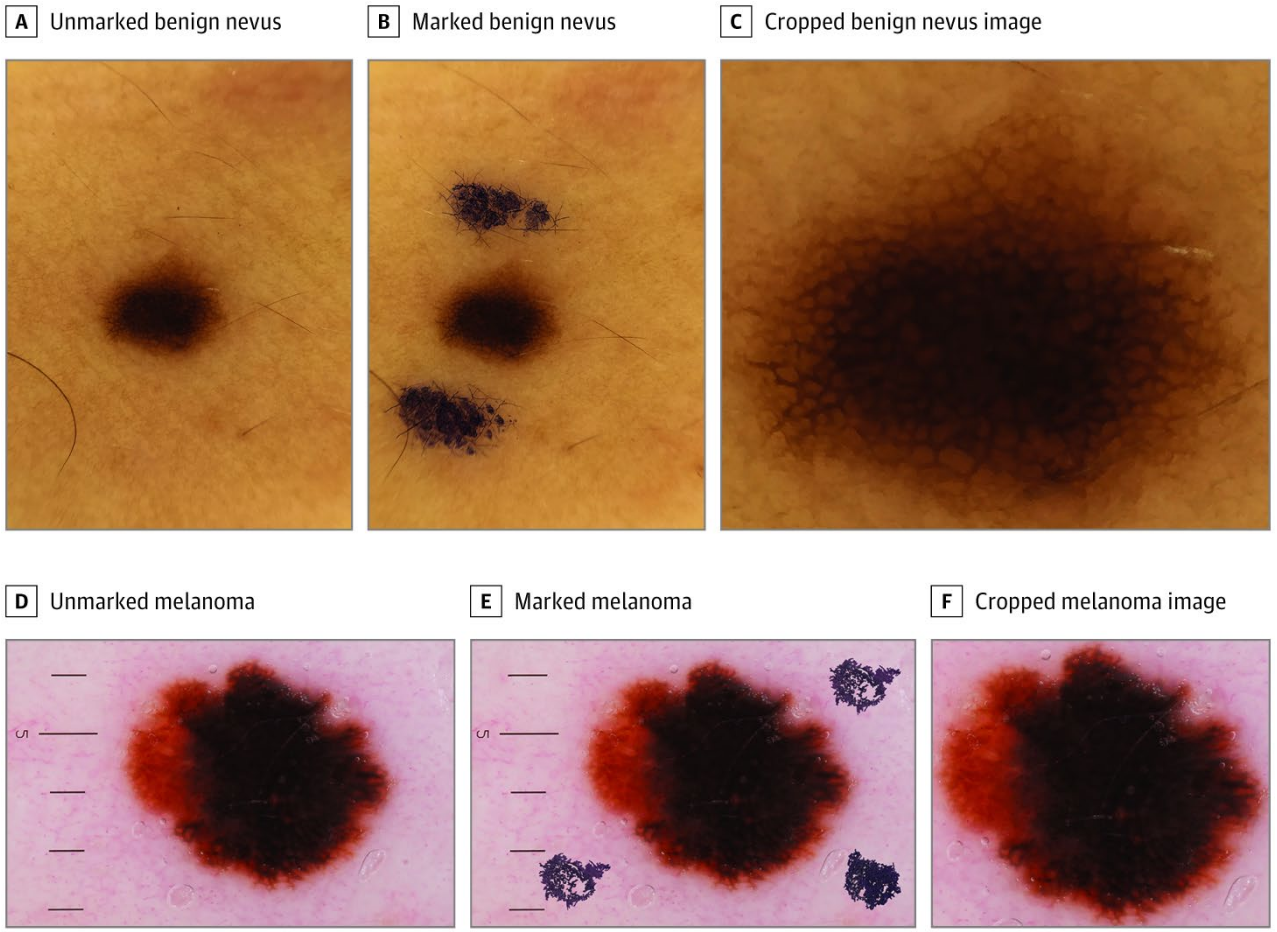
August 14, 2019

Association Between Surgical Skin Markings in Dermoscopic Images and Diagnostic Performance of a Deep Learning Convolutional Neural Network for Melanoma Recognition

Julia K. Winkler, MD[1]; Christine Fink, MD[1]; Ferdinand Toberer, MD[1]; et al

» Author Affiliations | Article Information

JAMA Dermatol. 2019;155(10):1135-1141. doi:10.1001/jamadermatol.2019.1735



Conclusions

Artificial intelligence can accelerate clinical cancer research by rapidly identifying clinical trial options for patients.

But impact requires integration.

Apply thoughtfully

Evaluate like any other technology

Beware of pitfalls and shortcuts