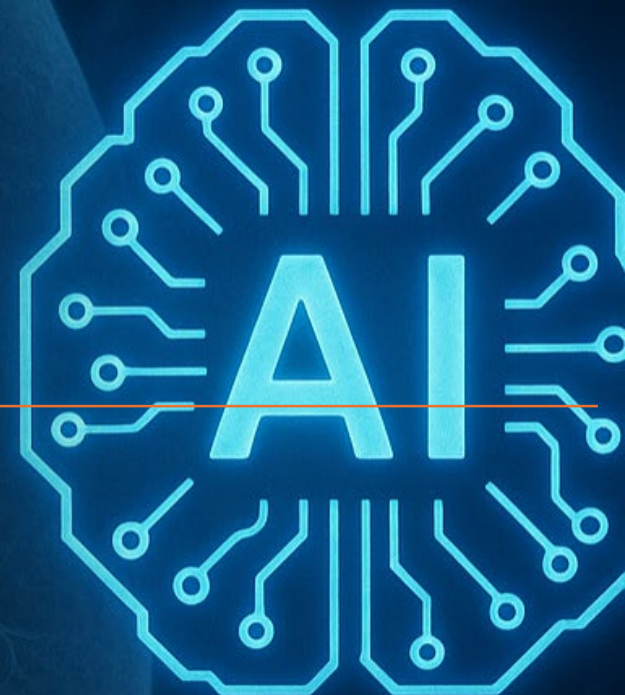


AI e nuove opportunità per la ricerca indipendente

Rebecca Romanò, MD, PhD candidate

Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

Politecnico di Milano



COORDINATION

Head of Lab




Arsela Prelaj, MD, PhD
 Vanja Mišković, PhD



FACULTY

FOUNDERS





Prof. Francesco Trovò
 Prof. Alessandra Pedrocchi
 Prof. Filippo de Braud

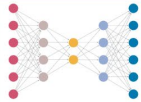
Collaborators






Prof. Emilia Ambrosini
 Prof. Marcello Restelli
 Prof. Pietro Pinoli
 Prof. Mark Carman

Trustworthy multimodal AI tools







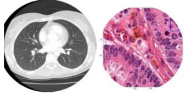
Alberto Ferrarin, Research Fellow
 Rebecca Romano, MD
 Cristina Licciardello, PhD student





Sara Ferri, Research Fellow
 Ludovica Lerma, PhD student
 Aditya Ravi, AI specialist

Medical images group





Leonardo Provenzano, MD, PhD student





Valentina Bartolomeo, PhD, MD
 Margherita Favali, PhD student
 Aleksandra Zec, PhD student





Elisa Totis, AI specialist
 Angelica Pagni, AI specialist
 Beshoy Guirges, AI specialist

LLMs and Agents






Federica Corso, PhD Post-doc researcher
 Laura Mazzeo, MD, PhD student




Vittoria Peppoloni, AI specialist
 Giuseppe Leone, MD




Francesca Chite, AI specialist
 Kristian Perriu, AI specialist

Multimomics





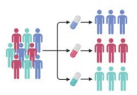
Luca Invernizzi, PhD Post-doc researcher






Ghazal Farhikhteh, PhD student
 Cecilia Silvestri, MD
 Arianna Rigamonti, PhD student
 Michela Francesconi, PhD student

Ai in clinical trials






Andrea Villa, Researcher
 Chiara Giangregorio, PhD student

Support

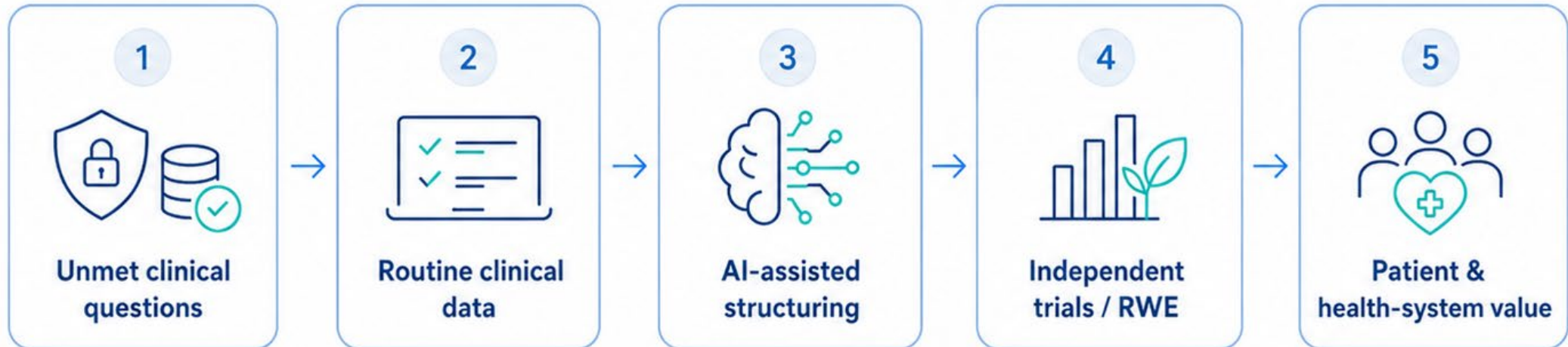



Jamalidizaji Mehrnaz, Lab/Financial Manager
 Fabrizio Baggio, Project Manager



From data to impact: AI for independent clinical research

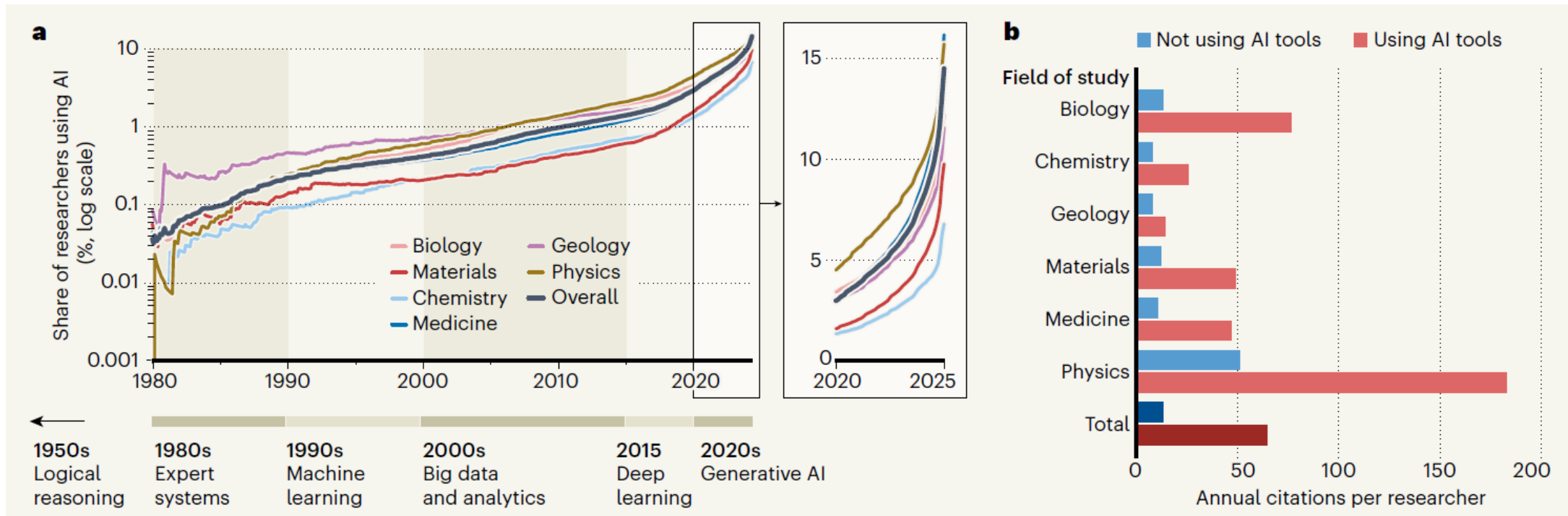
- Independent research asks **unanswered, clinically relevant questions**
- **Barriers:** data fragmentation, manual workload, slow recruitment, resources
- **AI can help transform routine clinical data into research-ready evidence**
- The goal is not automation, but **more feasible and inclusive trials**
- Condition: **validated, governed, workflow-integrated AI**



AI in Science

- AI use in science is rapidly increasing
- AI favors **data-rich**, established fields
- Risk: **more productivity, less exploration**

*Independent research should **use AI**
to ask **better questions**, not just
automate answers*

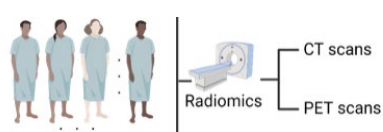
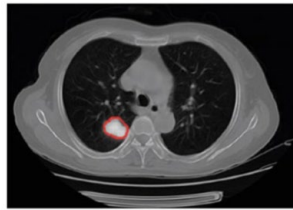


DIGITAL HOSPITAL: the foundation for AI-adoptable data

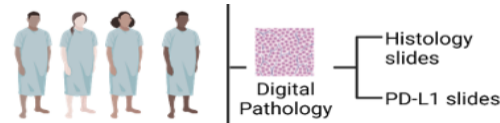
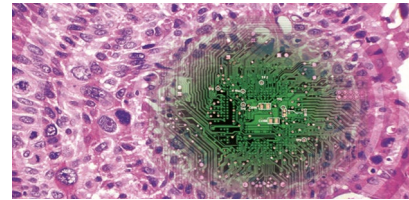
LLMs for data



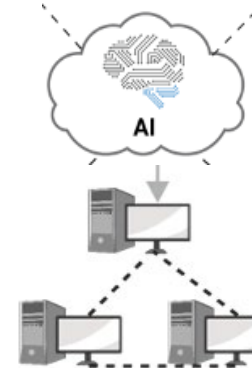
Radiomics



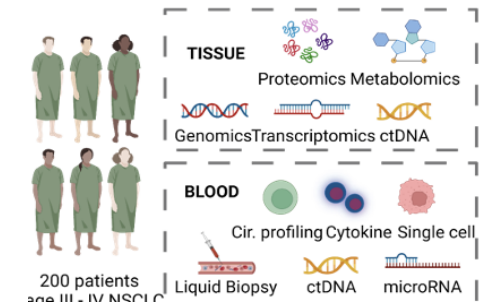
Digital Pathology



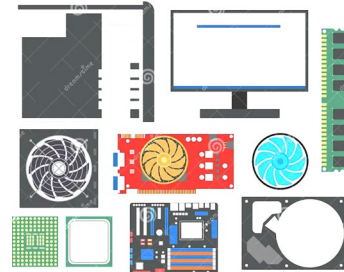
Data Sharing



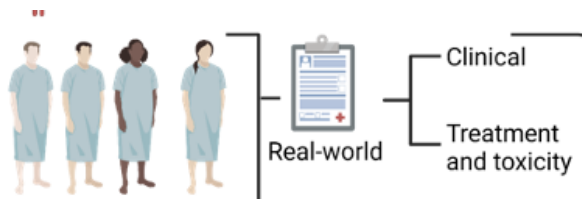
Biobank Digitalization



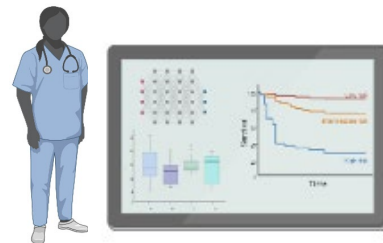
Cool Rooms



AI Agents



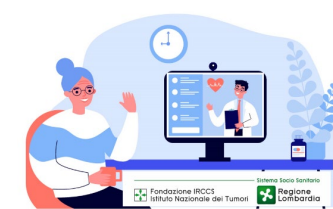
Treatment DM Tools



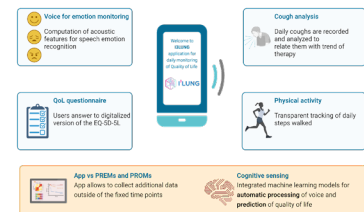
Co-DM Tools



Televisits



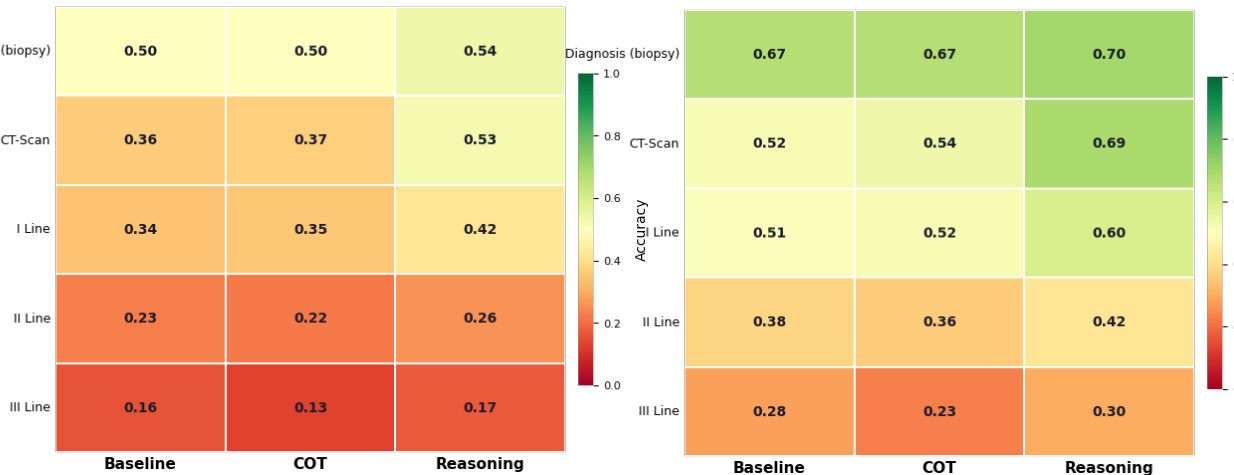
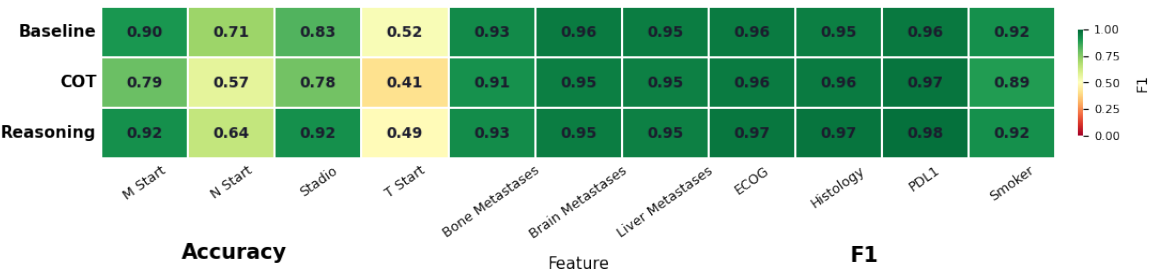
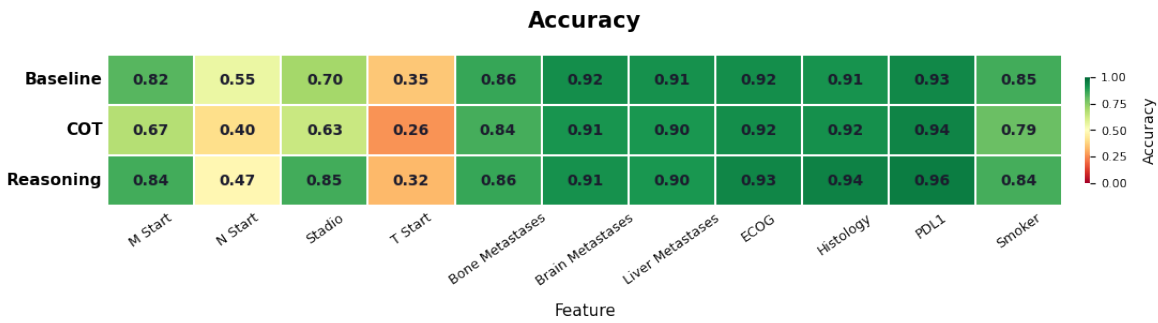
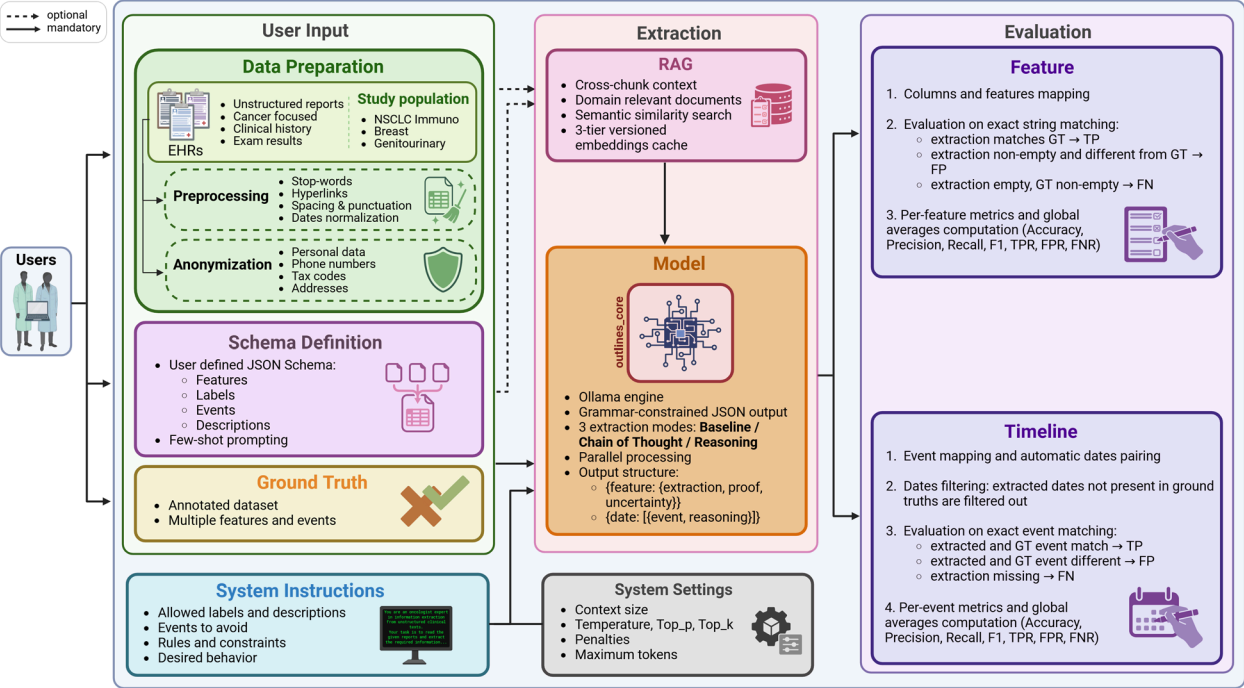
Novel QoL: App/ Wearable Device



*Accessible, standardized, interoperable,
traceable, high-quality data.*

Use case 1 — PROCESSING HEALTHCARE DATA WITH AI: LLM-ON-HUB Platform

Information Extraction & Validation in a 1.300-Patients Pan-Cancer Cohort



2025 ESMO AI & DIGITAL ONCOLOGY
Annual Congress

BERLIN GERMANY
12-14 NOVEMBER 2025



Kristian Perriu
AI specialist



Francesca Chite
AI specialist



Laura Mazzeo,
MD, PhD student

[https://www.esmorwd.org/article/S2949-8201\(25\)00278-4/fulltext](https://www.esmorwd.org/article/S2949-8201(25)00278-4/fulltext)

Use case 2 — PROCESSING HEALTHCARE DATA WITH AI:

Clinical Trial Matching

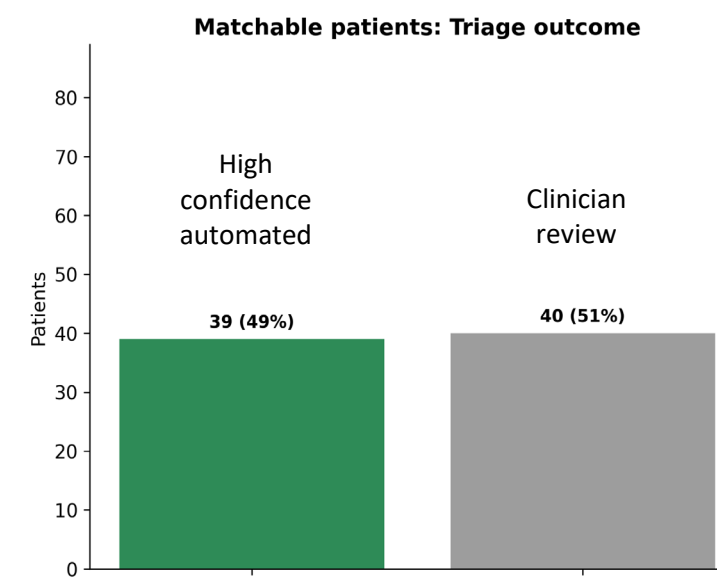
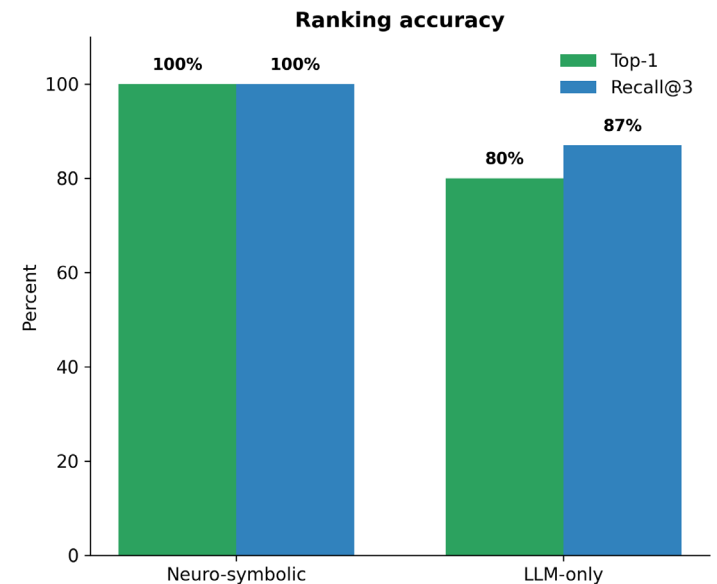
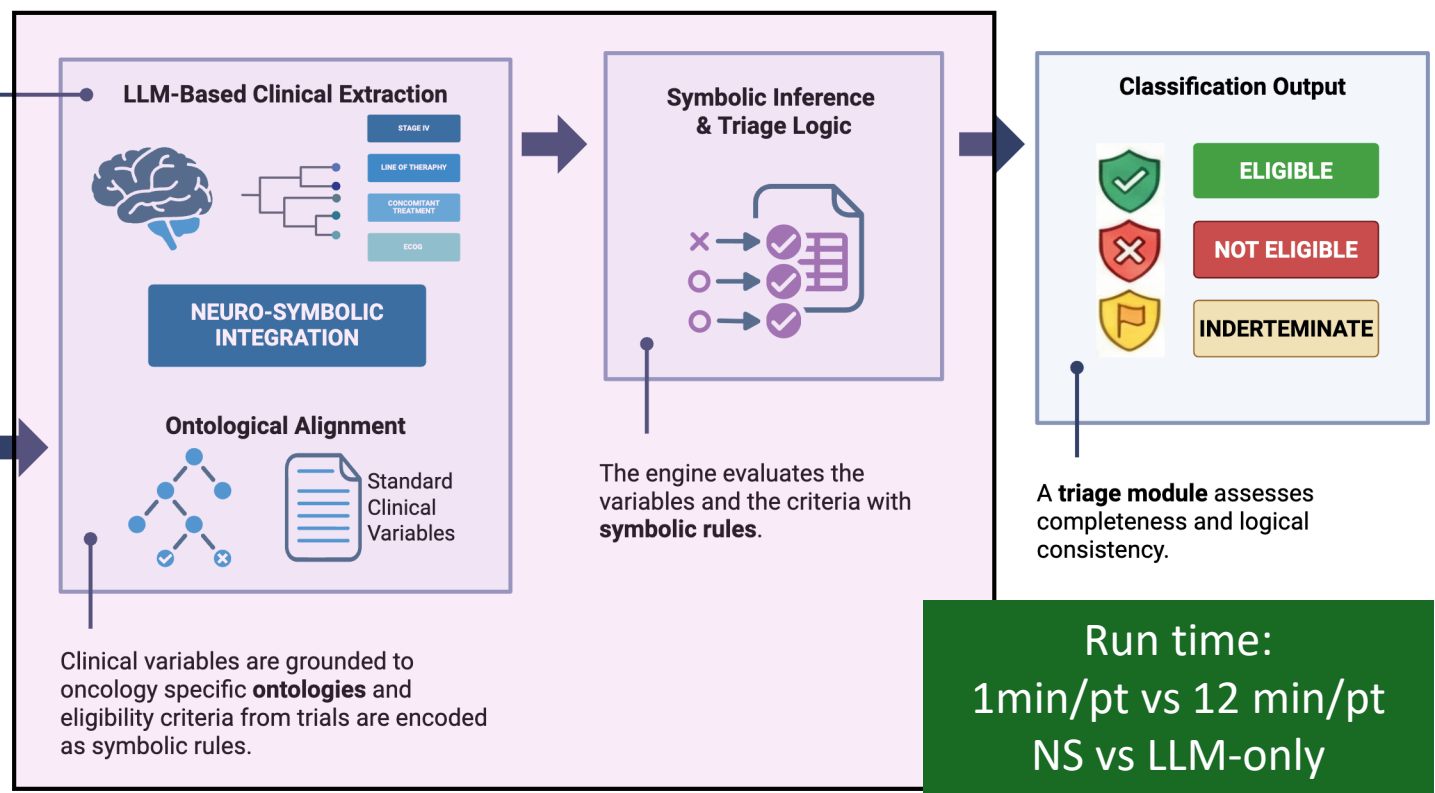
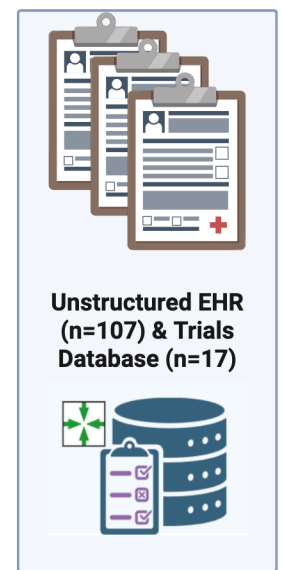


Vittoria Peppoloni,
AI specialist



Giuseppe Leone,
MD

Llama 3.1:70B extracts clinical variables from EHR.



<https://www.sciencedirect.com/science/article/pii/S2949820125002395>



Neuro-symbolic: LLM-based extraction + rule-based eligibility reasoning

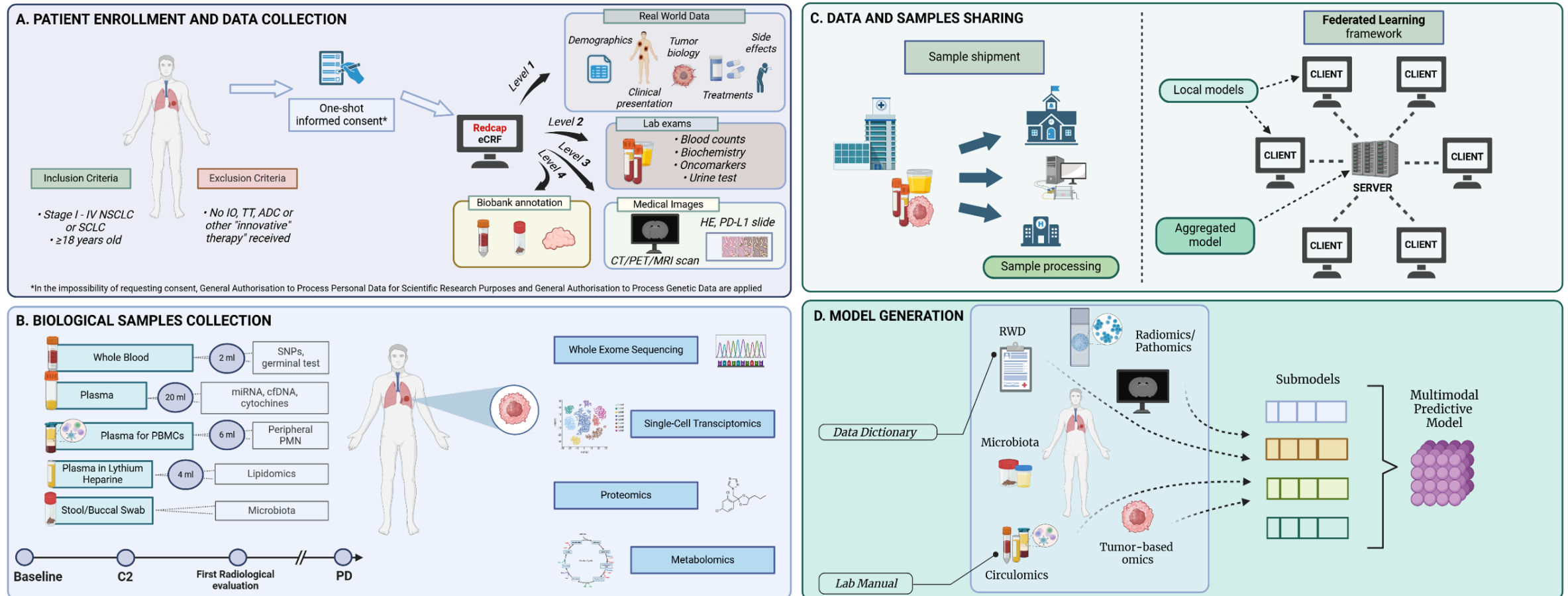
Validated on 107 lung & bladder cancer patients in 17 clinical trials

Use case 3 — Multimodal RWD collection

APOLLO11: BIO DATA-DRIVEN MODEL

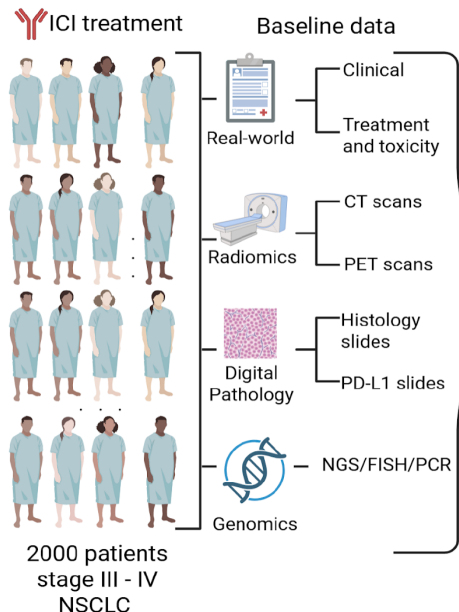
APOLLO11: a bio-data-driven model for clinical and translational research in lung cancer

[Arsela Prelaj](#) , [Leonardo Provenzano](#), [Vanja Miskovic](#), [Monica Ganzinelli](#), [Laura Mazzeo](#), [Maria Gemelli](#),

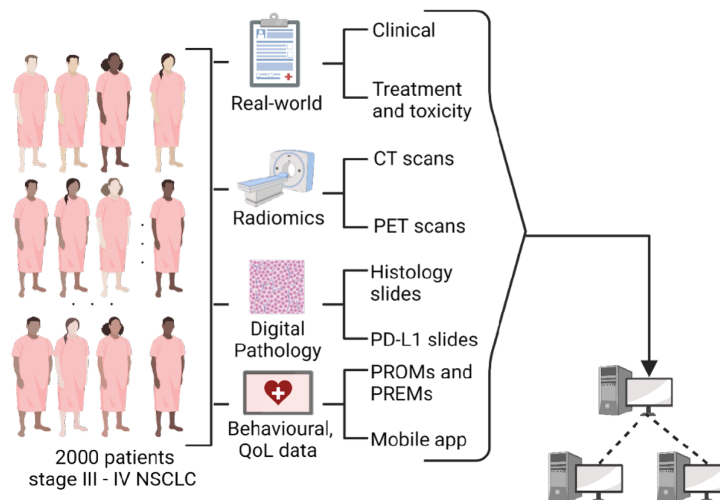


Use case 4 — Multimodal AI and clinical usability: I3LUNG study

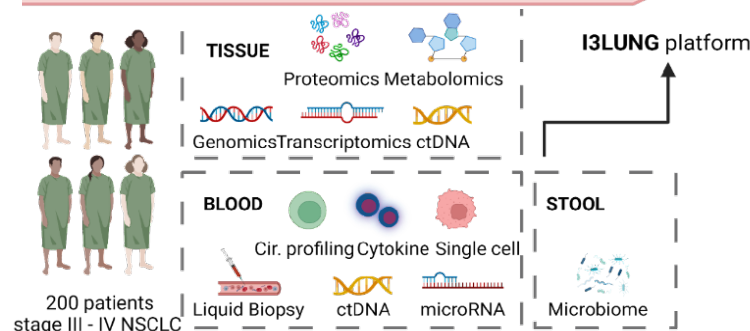
RETROSPECTIVE ARM



PROSPECTIVE ARM 1



PROSPECTIVE ARM 2 (OMIC)



CLASSIFICATION ENDPOINTS

Primary:

- Overall Survival at 24 months (OS24)
- Overall Survival at 6 months (OS6)

Secondary:

- Objective Response Rate (ORR)
- Disease Control Rate (DCR)

SURVIVAL PREDICTION ENDPOINT

Primary:

- Overall Survival (OS) from IO start

Secondary:

- Progression-Free Survival (PFS) from IO start

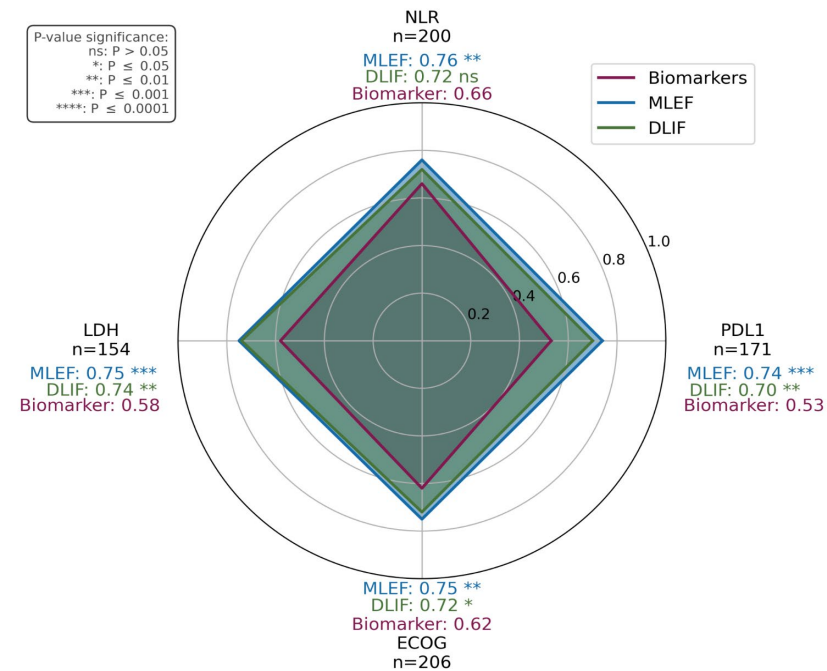


RWD Unimodal MLEF/DLIF outperform

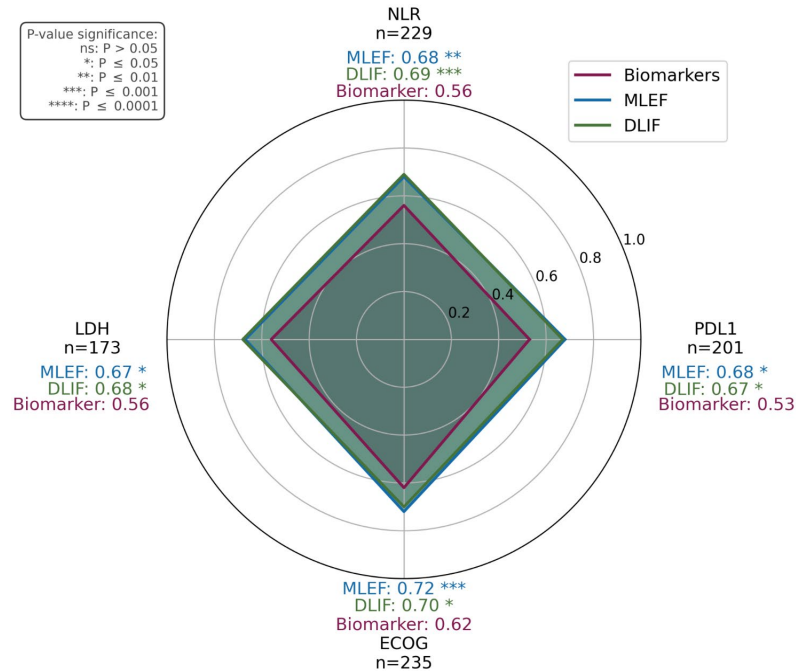
Single Biomarkers:

- PD-L1 → tumor protein expression
- NLR/LDH → systemic inflammation
- ECOG PS → patient fitness

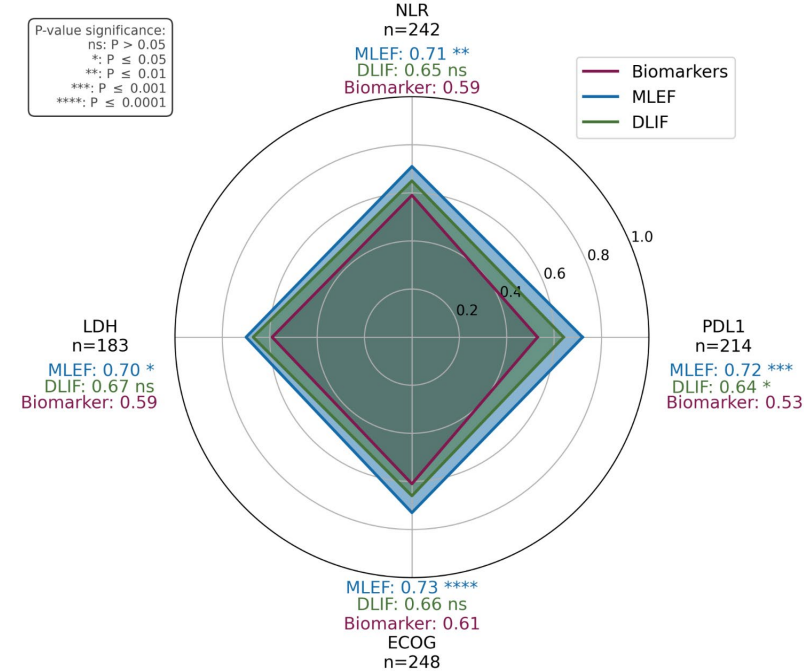
OS24: AUCs up to **0.76** vs
0.66



OS6: AUCs up to **0.72** vs
0.62

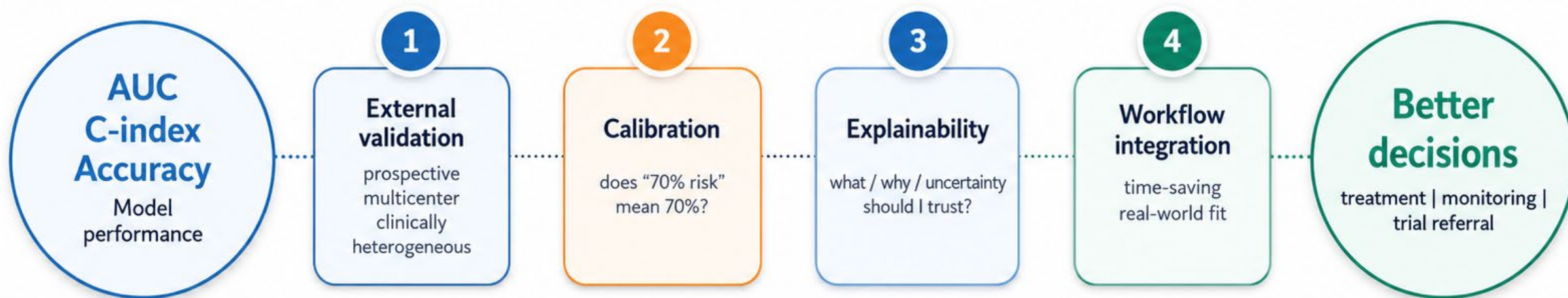


DCR: AUCs up to **0.73** vs
0.61



From AUC to clinical utility

A good model is not enough: it must improve a real oncology decision.



Beyond AUC, the oncology question is:

- ✓ Will this output change my treatment choice?
- ✓ Will it identify uncertainty earlier than routine care?
- ✓ Will it help select monitoring intensity or a clinical trial?



Clinical utility:
**better calibrated decisions
without over-reliance**

AI should reduce uncertainty — not replace clinical judgement.

Clinical Usability: Methods



PATIENTS COHORT



100 NSCLC pts
treated with ICI,
6 I3LUNG centers



PHYSICIANS



10 experts in
lung cancer



10 non-
experts in lung
cancer

PHASE 1 - NO XAI support

Patients'
data

Clinical
demographic
lab
Genomics
molecular



CT scan



H&E slide

Questions

Will this patient achieve DCR with IO-based treatment?

YES

NO

What is the most likely survival range
for this patient?

<6m, 6-12m, 12-18m, ≥24m

PHASE 2 - WITH XAI support

Patients'
data

Clinical
demographic
lab
Genomics
molecular



CT scan



H&E slide

Questions

After seeing the XAI DCR prediction
will this patient achieve DCR with IO-
based treatment?

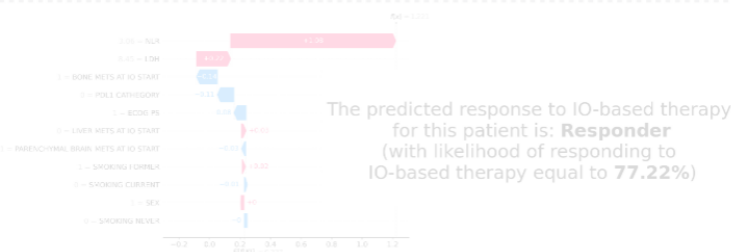
YES

NO

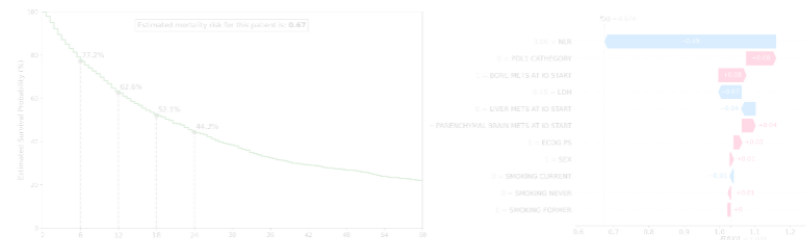
After seeing the XAI OS prediction
what is the most likely survival range
for this patient?

<6m, 6-12m, 12-18m, ≥24m

XAI DCR
prediction



XAI OS
prediction

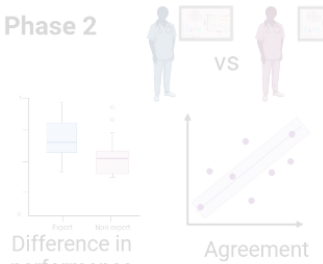


ANALYSIS

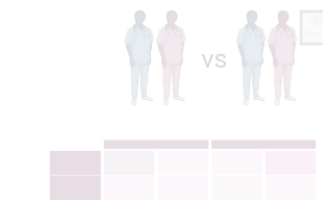
Phase 1



Phase 2



Phase 1 vs 2



Confusion matrix of correctness of
physician-XAI collaboration

Clinical Usability: Methods



PATIENTS COHORT



100 NSCLC pts
treated with ICI,
6 I3LUNG centers



PHYSICIANS



10 experts in
lung cancer

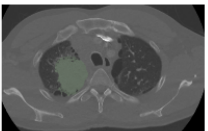


10 non-
experts in lung
cancer

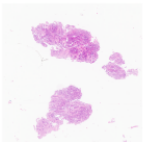
PHASE 1 - NO XAI support

Patients'
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Clinical
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CT scan



H&E slide

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PHASE 2 - WITH XAI support

Patients'
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CT scan



H&E slide

Questions

After seeing the XAI DCR prediction
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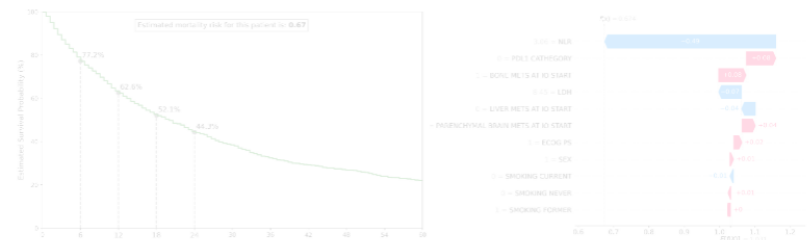
After seeing the XAI OS prediction
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XAI DCR
prediction



XAI OS
prediction

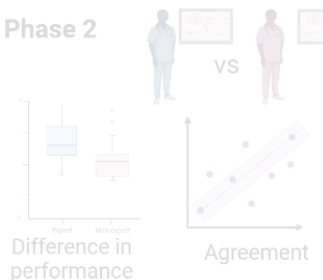


ANALYSIS

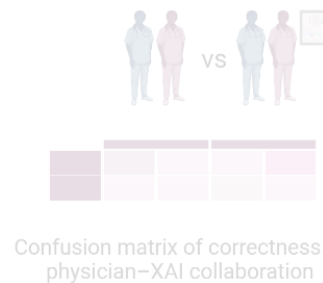
Phase 1



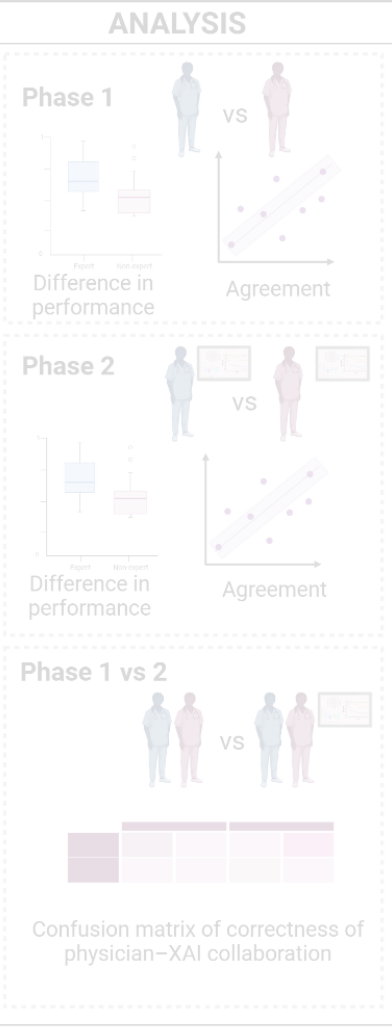
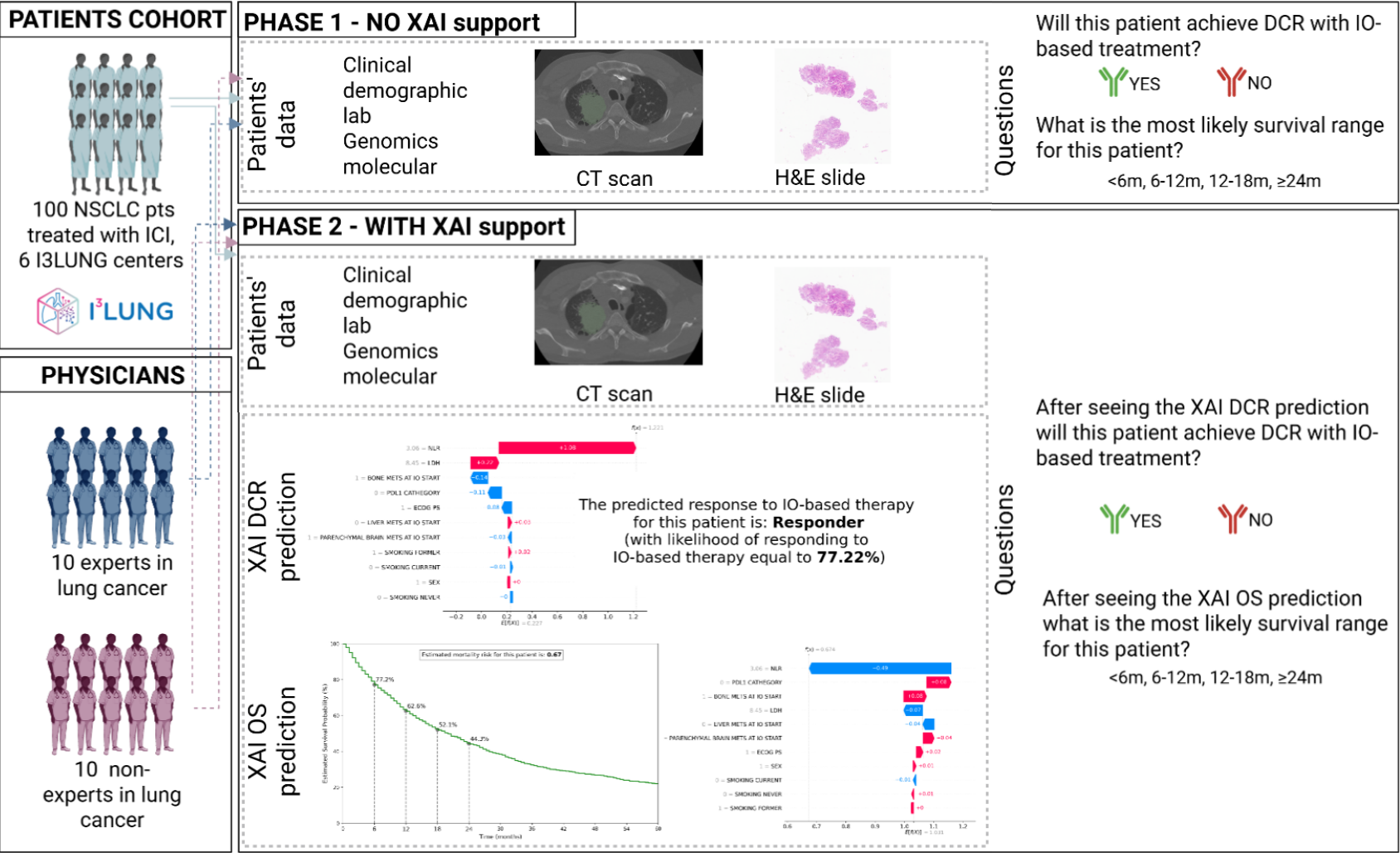
Phase 2



Phase 1 vs 2



Clinical Usability: Methods



Clinical Usability: Methods



PATIENTS COHORT



100 NSCLC pts
treated with ICI,
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10 experts in
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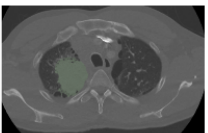


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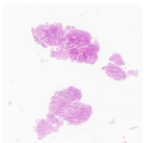
PHASE 1 - NO XAI support

Patients'
data

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demographic
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molecular



CT scan



H&E slide

Questions

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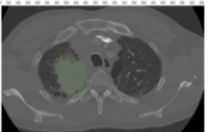
What is the most likely survival range
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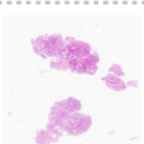
PHASE 2 - WITH XAI support

Patients'
data

Clinical
demographic
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Genomics
molecular



CT scan



H&E slide

Questions

After seeing the XAI DCR prediction
will this patient achieve DCR with IO-
based treatment?

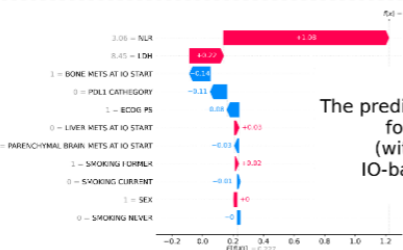
YES

NO

After seeing the XAI OS prediction
what is the most likely survival range
for this patient?

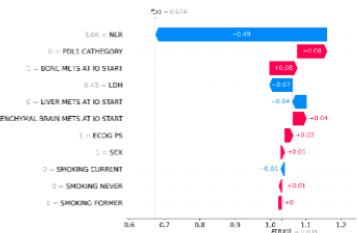
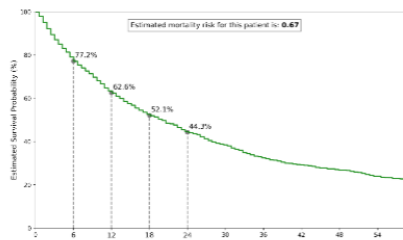
<6m, 6-12m, 12-18m, ≥24m

XAI DCR
prediction



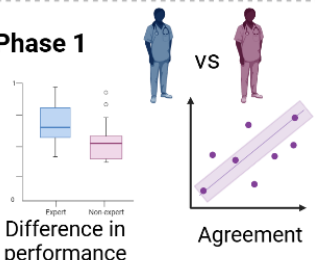
The predicted response to IO-based therapy
for this patient is: **Responder**
(with likelihood of responding to
IO-based therapy equal to **77.22%**)

XAI OS
prediction

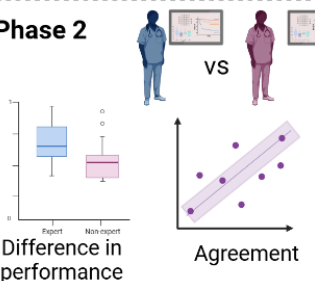


ANALYSIS

Phase 1



Phase 2

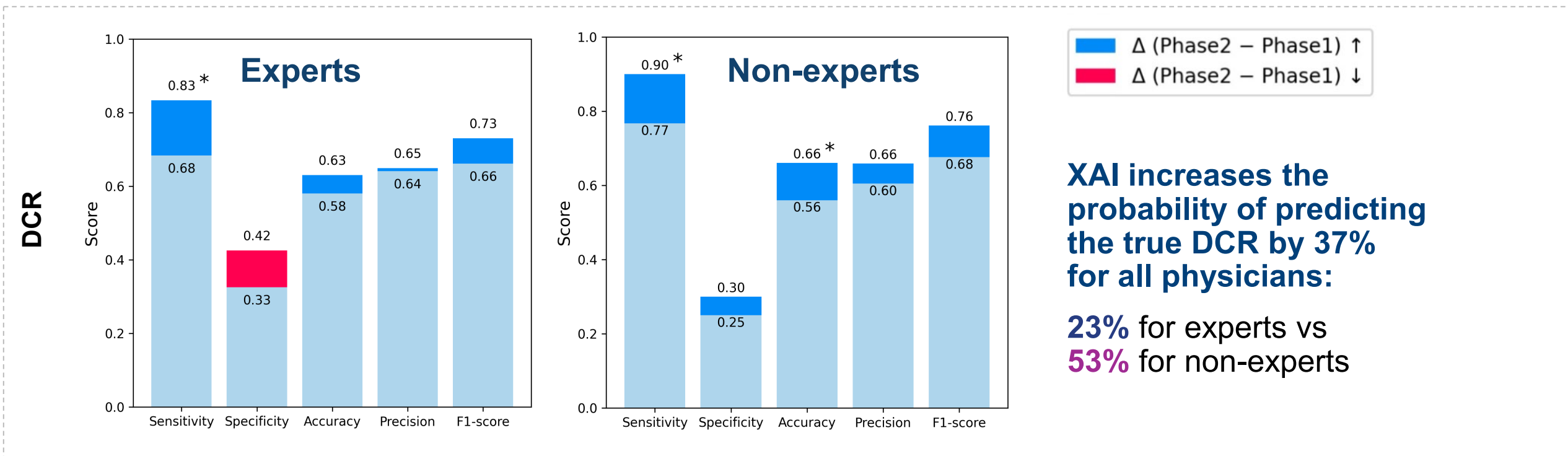


Phase 1 vs 2



Confusion matrix of correctness of
physician-XAI collaboration

Clinical Usability: Results



OS **XAI increases the probability of predicting the true OS by 36% for all physicians:**
 14% for experts vs **61%** for non-experts

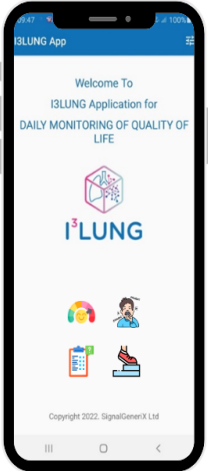
Automatic Cough Analysis: Pre-screening tool & Patient monitoring



Voice for emotion monitoring
Real-time computation of acoustic features for speech emotion recognition



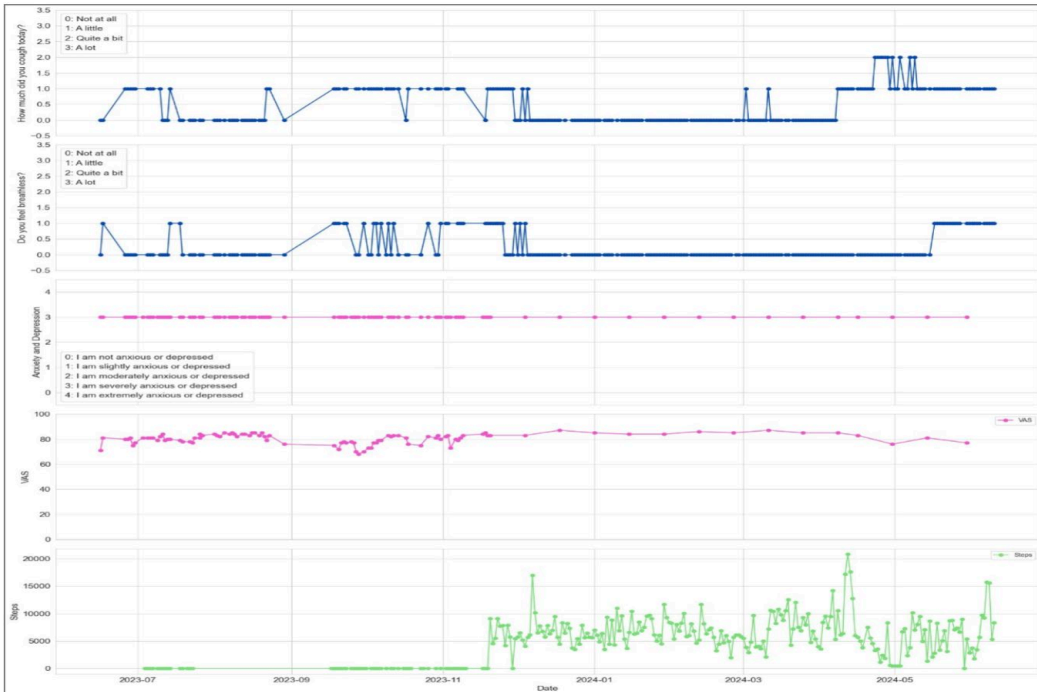
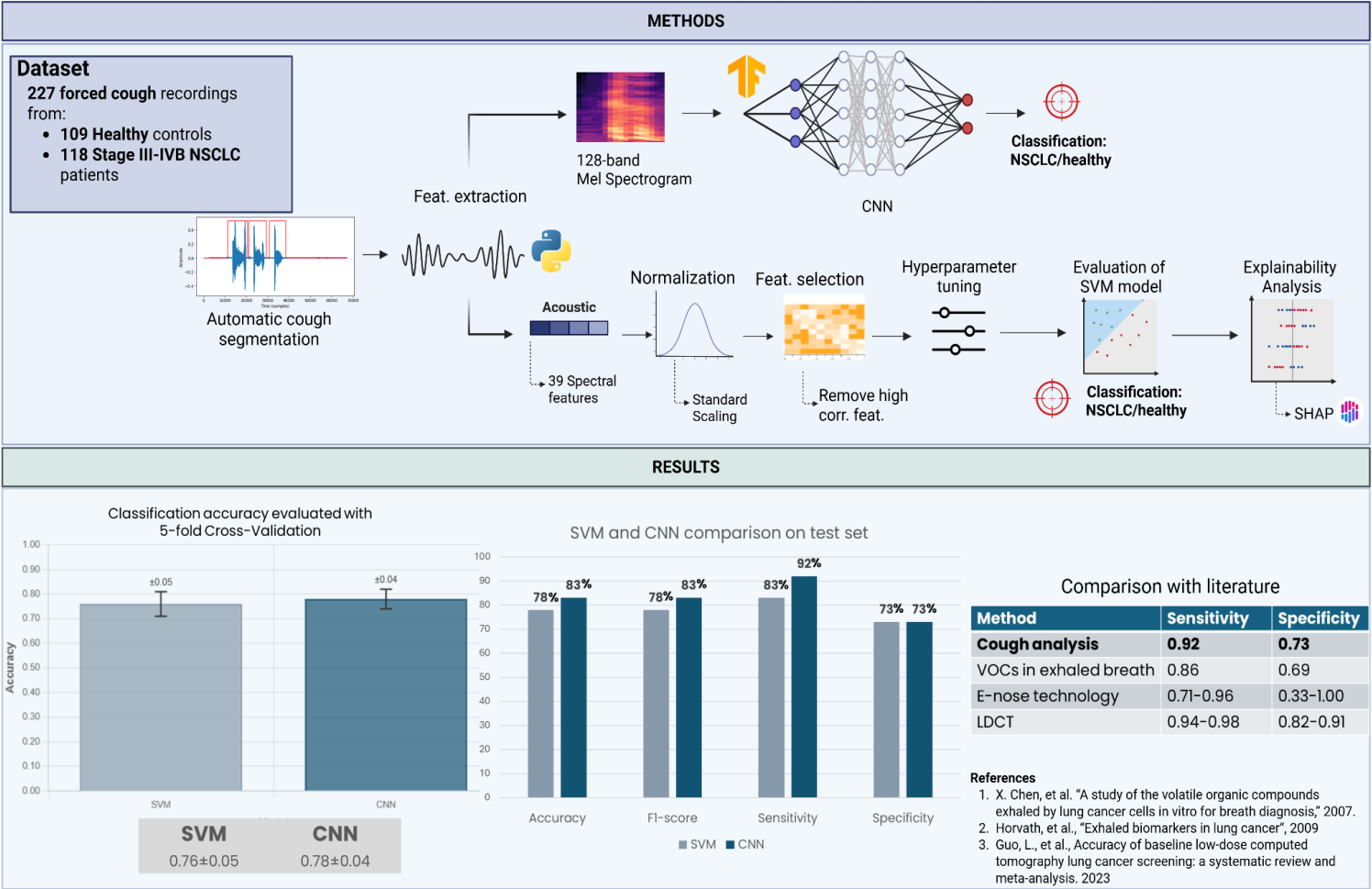
Quality of Life questionnaire
Users answer to digitalized version of the EQ-5D-5L



Cough Analysis
Daily coughs are recorded and a-posteriori analyzed to relate them with trend of therapy



Physical activity
Transparent tracking of daily number of steps walked



SPECIAL ARTICLE

ESMO guidance on the use of Large Language Models in Clinical Practice (ELCAP)

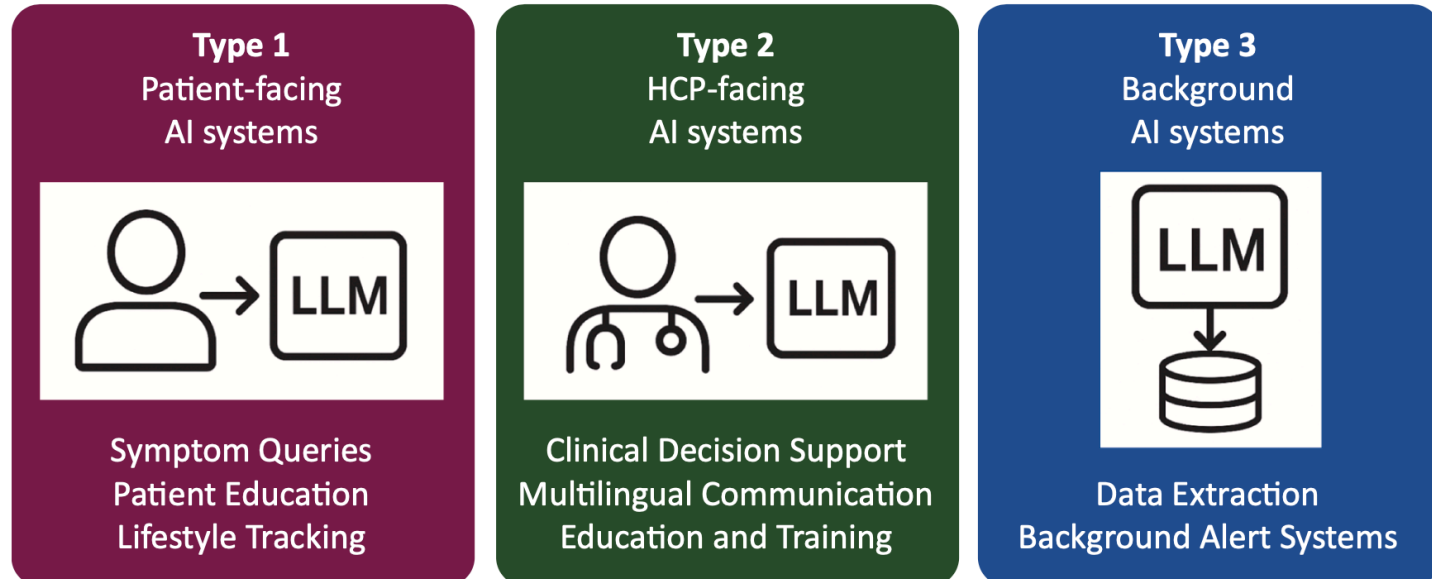
E. Y. T. Wong^{1†}, L. Verlingue^{2†}, M. Aldea^{3,4,5†}, M. A. Franzoi^{6,7}, R. Umeton^{8,9,10,11,12}, S. Halabi¹³, N. Harbeck¹⁴, A. Indini¹⁵, A. Prelaj¹⁶, E. Romano¹⁷, E. Smyth¹⁸, I. B. Tan¹, A. Valachis¹⁹, J. Vibert^{4,20}, I. C. Wiest^{21,22}, Y. H. Yang²³, S. Gilbert²¹, G. Kapetanakis²⁴, G. Pentheroudakis²⁵, M. Koopman^{26†} & J. N. Kather^{21,27,28*†}

ELCAP

ESMO guidance on the use of Large Language Models in Clinical Practice

*Patient-facing tools **should complement, not replace, professional advice** and should be embedded in **supervised care pathways**.*

*HCP-facing and background systems may **improve efficiency and decision support** but require **systematic validation, transparency, and continuous monitoring**.*



Arsela Prelaj, MD, PhD Fondazione IRCCS Istituto Nazionale Tumori di Milano

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Future direction: LLMs for clinical decision-making

Future direction: Co-trained multi-Agent for NSCLC-IO

2025 **ESMO AI & DIGITAL ONCOLOGY**
Annual Congress

71MO: Collaborative Human-Agent for Therapeutic Decision-Making In Cancer Immunotherapy Prediction

Federica Corso, PhD¹, Gabriele Carminati², Vittoria Peppoloni¹, Laura Mazzeo^{1,2}, Giulia Montelatici¹, Leone Giuseppe¹, Alberto Ferrarin¹, Daniele Lorenzini³, Rebecca Romano¹, Teresa Beninato¹, Giulia Corrao¹, Claudia Proto¹, Giuseppe Lo Russo¹, Filippo Maria de Braud¹, Alessandra Laura Giulia Pedrocchi², Marina Garassino⁴, Paolo Baili⁵, Vanja Mišković^{1,2}, Mark James Carman², Arsela Prelaj¹

Agent output

(treatment report)

#Key Findings:

1. ****Diagnosis and Staging****: [...]
2. ****Molecular Profile****: [...]
3. ****PD-L1 Expression****: [...]
4. ****Clinical Context****: [...]

#Analysis & Rationale:

While PD-L1 expression might suggest potential benefit from immunotherapy, the STK11 mutation makes it unlikely to be effective as monotherapy.

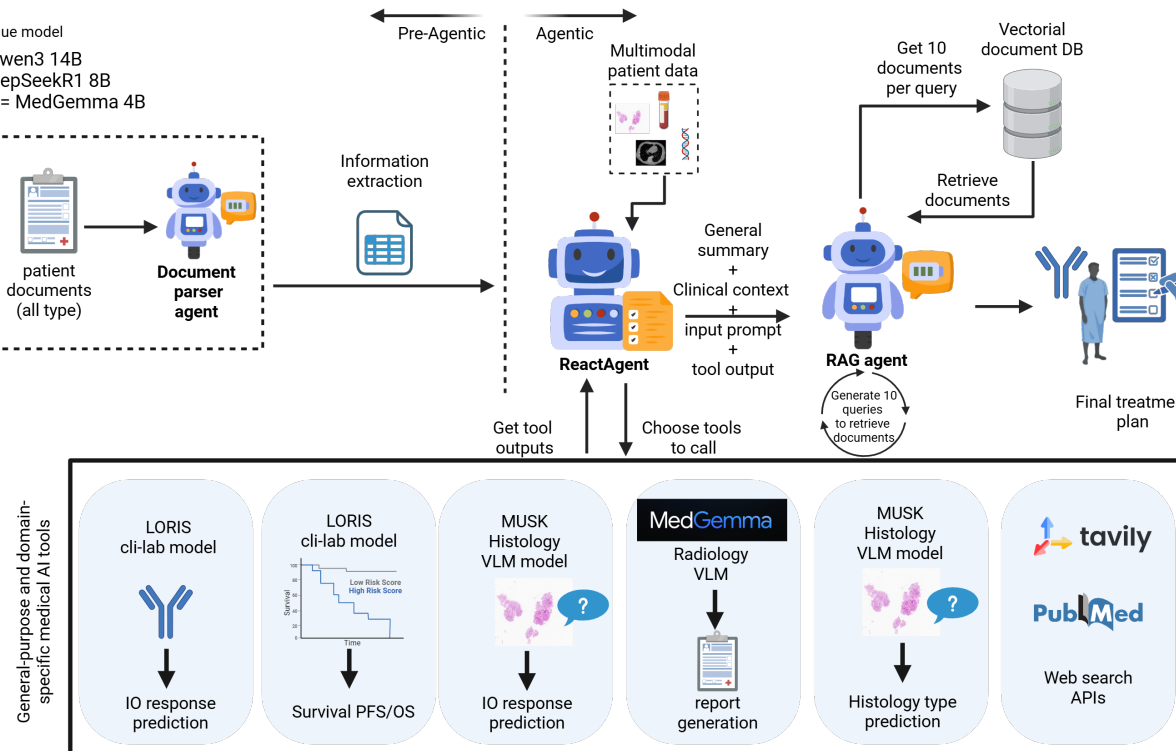
Treatment Plan:

The recommended therapy is chemotherapy + immunotherapy.

Ambiguities and Contradictions

****Missing Data****

****Regulatory Limitations****



Patient's clinical context:

{

What is the best treatment plan?

Provide the best option among the following ones:

1. chemotherapy in combination with immunotherapy
2. immunotherapy alone, either monotherapy or combination of two different immune checkpoint inhibitors

Provide a detailed summary of the new information we received from the tools.



Federica Corso, PhD

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Xiang, J., et al. *Nature* 638, 769–778 (2025)
Chang, TG, et al. *Nat Cancer* 5, 1158–1175 (2024)
Sellersgren, A., et al. arXiv:2507.05201 v3

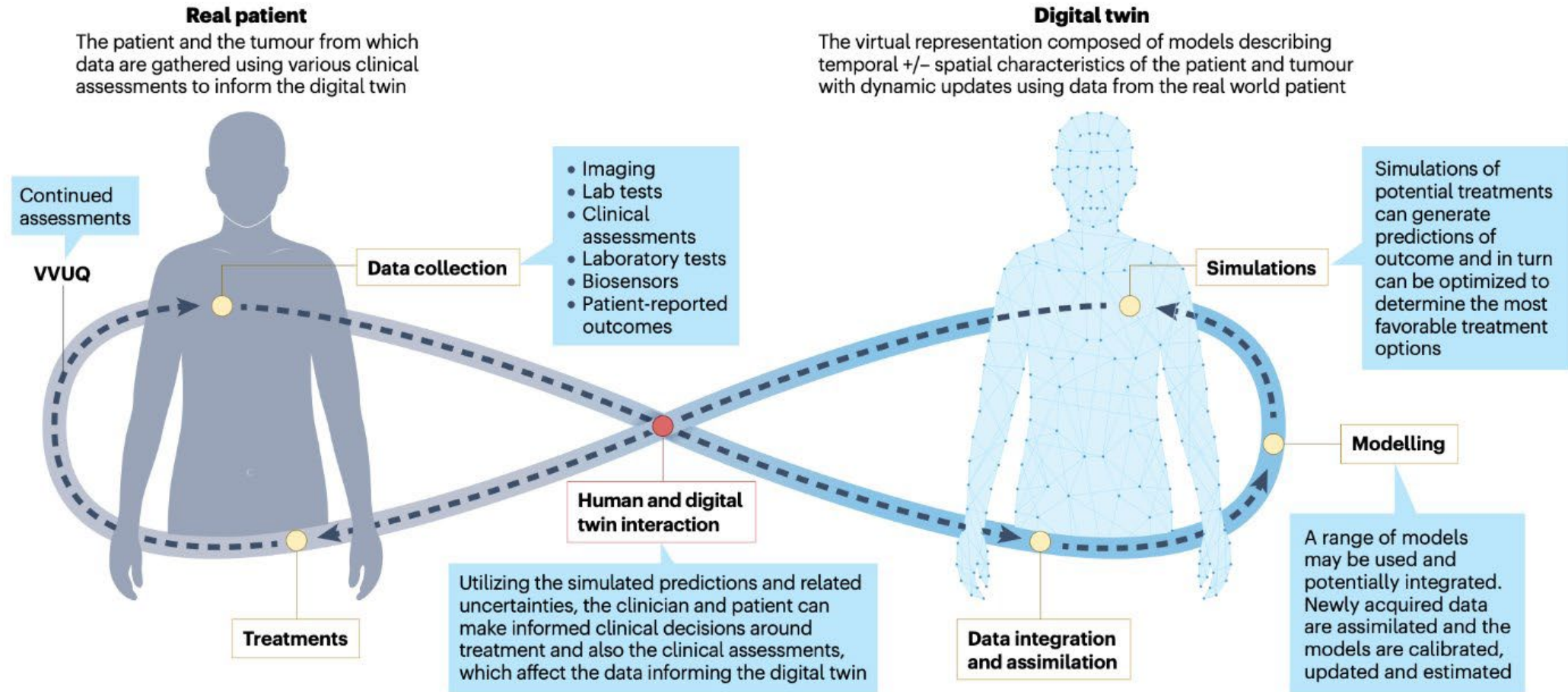


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Regione Lombardia



Future direction: Digital Twins and patient's trajectory



Uzma Saddia Asghar & Caroline Chung, *Nature Reviews Cancer*, 9 July 2025

Dr. Arsela Prelaj

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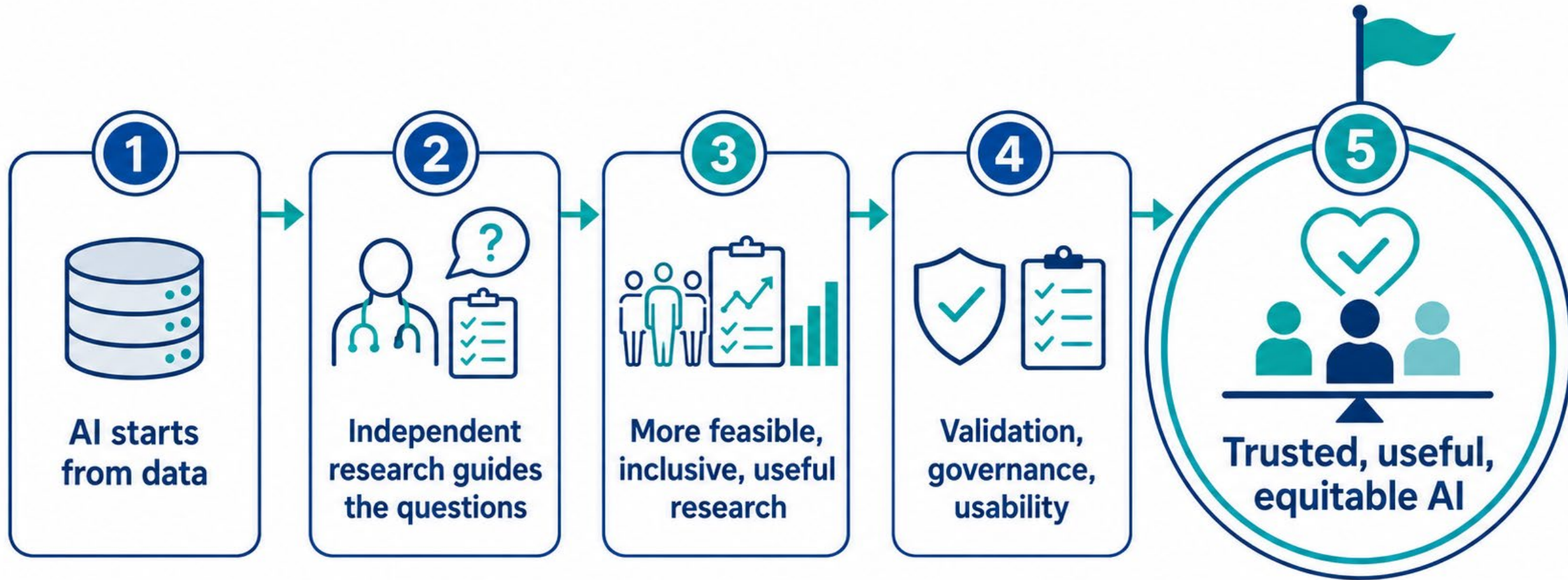
Future direction: Digital Twin platform simulator



AI-ON-Lab



Take-home message: AI is a tool, its value depends on how we use it.



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 Apollo 11



A project funded by
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<https://Ai-onlab.com>

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The Thoracic
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