





## How to translate Al in Clinical Cancer care

#### Arsela Prelaj, MD, PhD

#### AI-ON-Lab

AI-ON-Lab leader (Artificial Intelligence for Oncology lab), and Medical Oncologist, at Istituto Nazionale Tumori di Milano PhD in Bioengineering and AI, Politecnico di Milano, Italy; ESMO Real-World Data and Digital Healt working group mem ESAC President







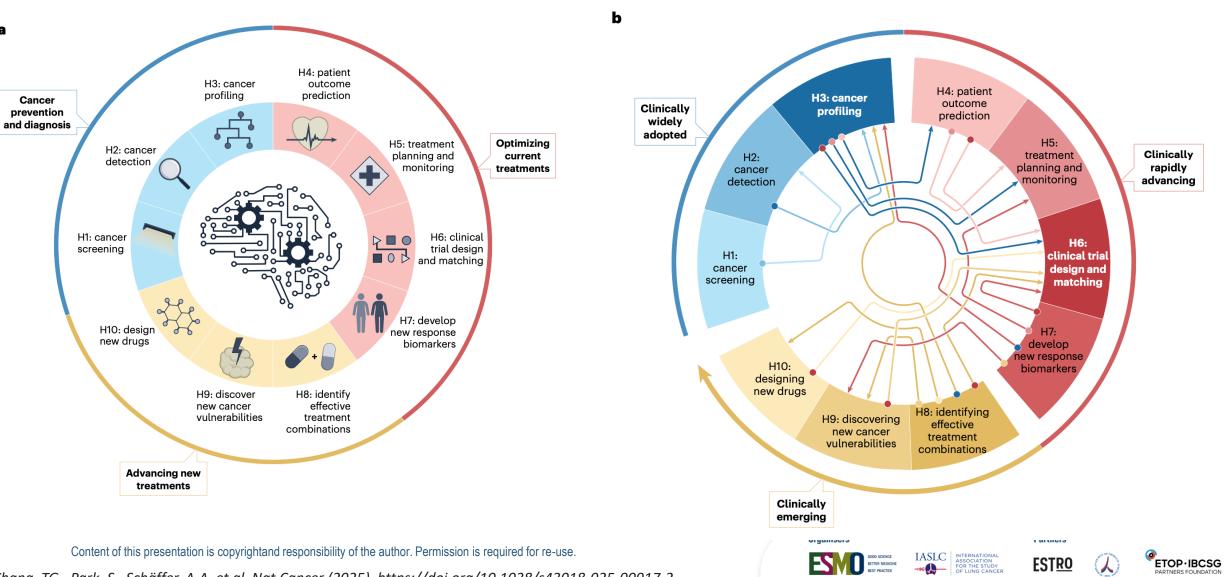
# **ORDERAL ASSEMBLY AND** Scientific Programme 11 13 June 2025

11 - 13 June 2025 Royal Olympic Hotel

# **Declaration of Interest**

Consulting/advisory role for BMS, AstraZeneca, Novartis, MSD, Lilly, Amgen, Pfizer, Jonsson & Jonsson; travel, accommodations, or other expenses paid or reimbursed by Roche and Jonsson & Jonsson; principal investigator of Spectrum Pharmaceuticals, BMS, Bayer, MSD, Lilly outside this presentation.

# HALLMARKS OF AI IN PRECISION ONCOLOGY



Chang, TG., Park, S., Schäffer, A.A. et al. Nat Cancer (2025). https://doi.org/10.1038/s43018-025-00917-2

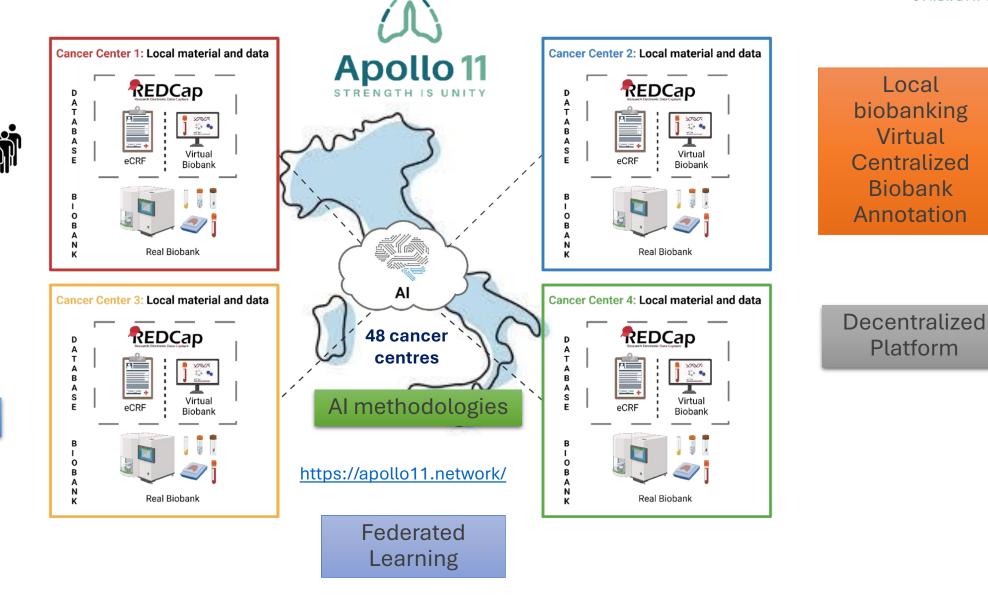
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# WE NEED BIG DATA

#### BIOData-driven model in lung cancer: APOLLO11 use case





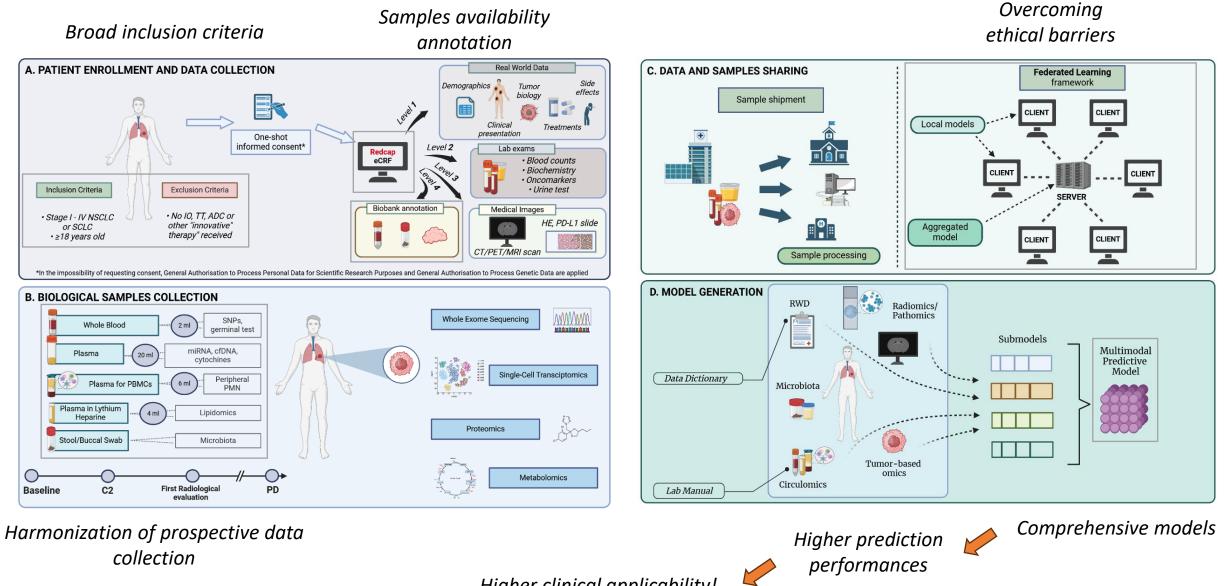


Medical Images

Prelaj A, et al. APOLLO 11. Clin Lung Cancer. 2024

## **APOLLO11 Study Design and Workflow**





*Higher clinical applicability!* 

Prelaj A et al. Submitted

# **APOLLO11: data**



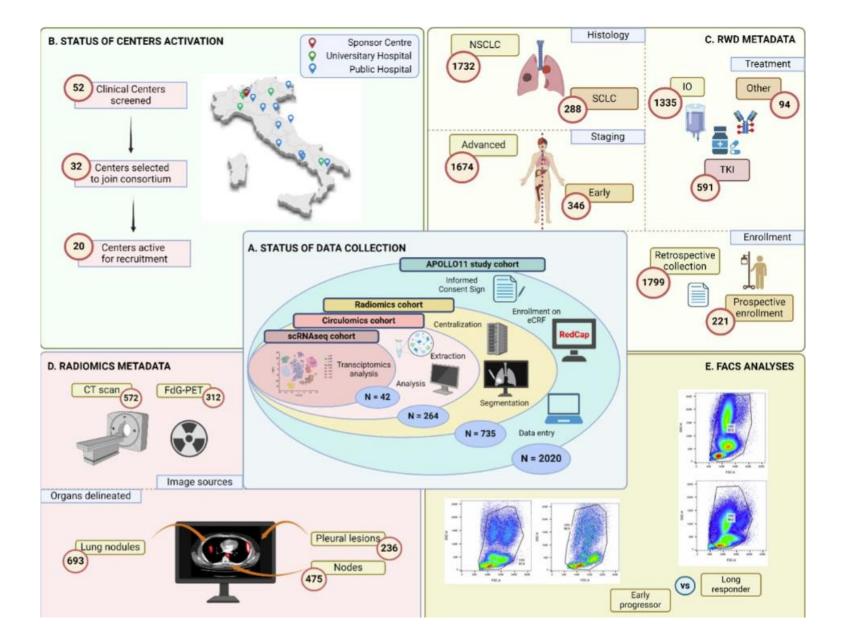
32 CENTRES WILL BE ACTIVATED IN TOT SOON

**20 CENTRES ARE RECRUITING** 

2498 PATIENTS ENROLLED

With NSCLC e SCLC

From Stage I to stage IV

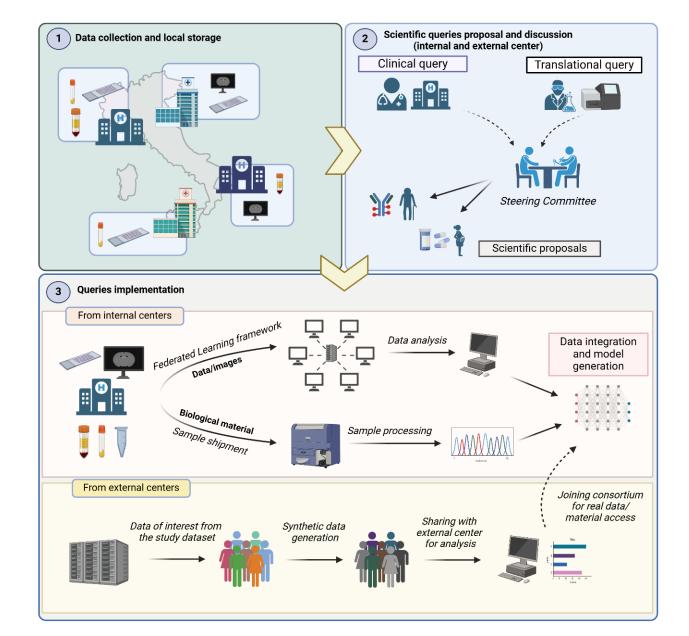


Prelaj et al. Submitted

#### **APOLLO11 Queries Implementation**



Updated collection...



#### Hypotheses Sharing

Fairness among centers

Scientific queries process as the core of data-driven research

Precision Oncology



Leveraging Synthetic Data to share data beyond the consortium f in 🛛

🗘 Apollo 11

antte la Dete Meure Desserve stamps Demande fraguenti Canta

#### Unity is Strength

Centri di ricerca italiani per strategie terapeutiche avanzate per il tumore al polmone

# APOLLO 11 2021

#### **FEDERATED NETWORK**



## 48 Centri di ricerca avanzata sul tumore al polmone

Creazione di una rete di centri italiani che si occupano di pazienti affetti da tumore del polmone NSCLC avanzati già trattati o candidati a ricevere una terapia a base di ICI



#### Real world data da tutti i centri attivi

Sviluppo di un database nazionale Real World per i pazienti affetti da tumore del polmone trattati con TERAPIE INNOVATIVE (ad es. immunoterapia, terapie target, anticorpi coniugati)



#### https://apollo11.network/



Sviluppo di una biobanca multilivello nazionale registrata con impostazione e armonizzazione delle procedure operative per la raccolta, la conservazione e la spedizione dei campioni biologici.



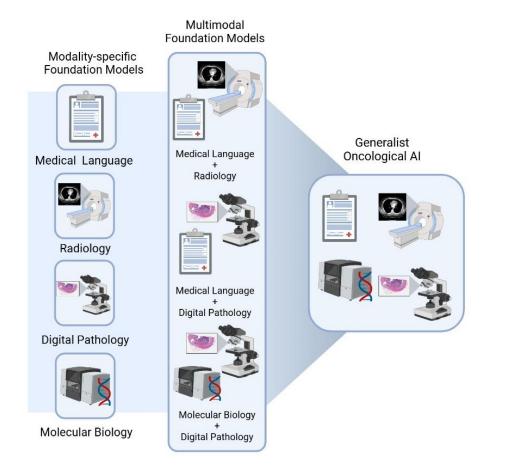
#### Intelligenza Artificiale

Creazione di un modello predittivo di intelligenza artificiale (AI) per migliorare la previsione della risposta, portando in ultima analisi a una migliore sopravvivenza e qualità di vita dei pazienti oncologici

#### **MODERN AI** 2017 + Computational resources 2010 Massive unlabeled data Computational resources 1980s Selfs-supervison at scale Massive labeled data **Big Data** TASK A TASK B Feature engineering Clustering Rule: IF-THEN Fact Tree based methods Support Vector Machine TASK C TASK D Interface engine TASK A TASK B TASK C EXPERT SYSTEMS MACHINE LEARNING DEEP LEARNING FOUNDATION MODELS Manually-crafted symbolic Less rigid (supervised/unsupervised) Automatically learns if labeled data Automatically learns from massive representations and rules Manual labor available in massive data without labels! No use of data • Extensive data preparation and feature • Limited by availability of labeled data Quick adaptation to new tasks using • Rigid limited labeled data engineering

# LLMs and Foundation Models uni and multimodal

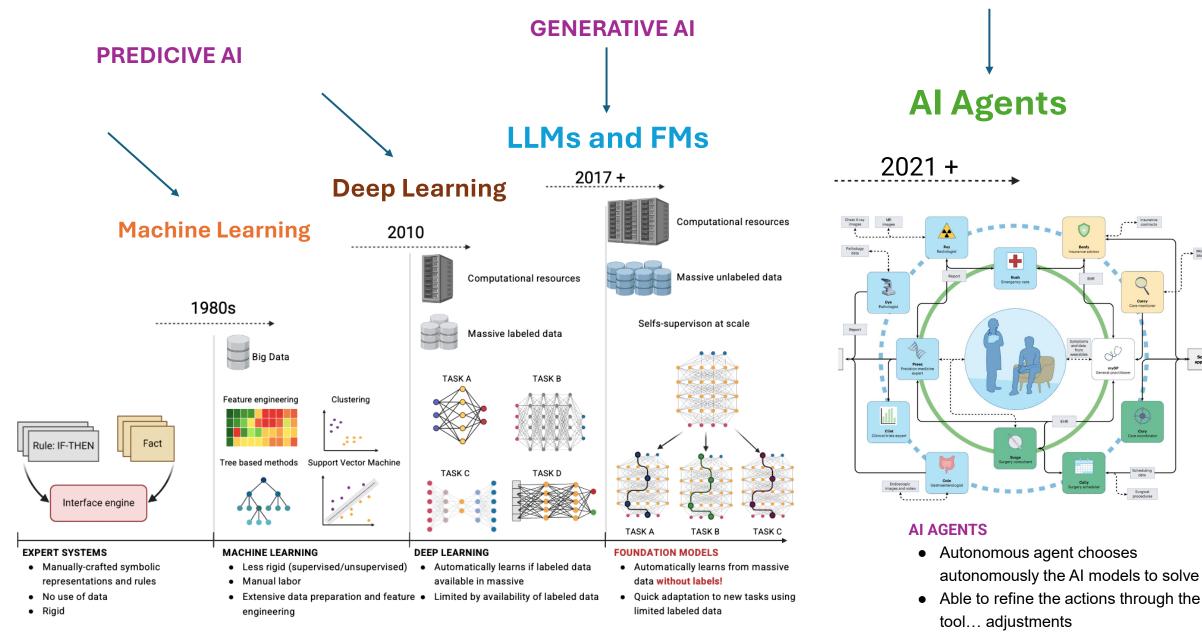
## From uni to multimodal: A PANCANCER approach



- Help us to maximize the use of small datasets as extractors
- Help us to specialize the tasks as predictors
- Al Agents: Interactive, adapted for all tasks

# **SHIFT AI**

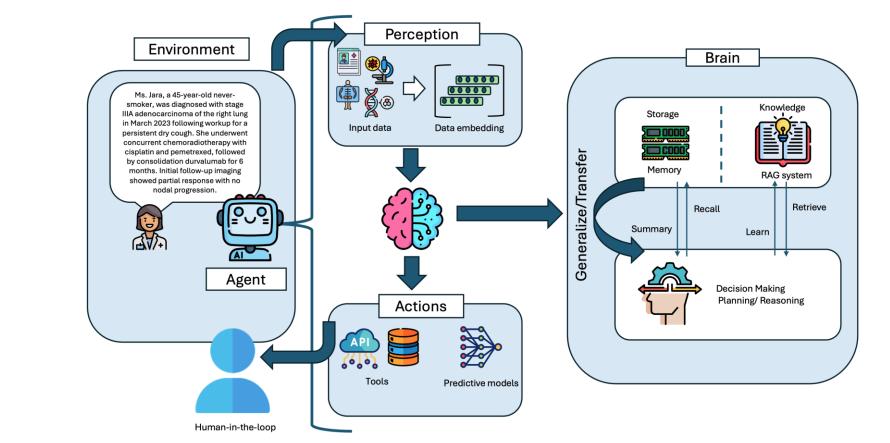
#### **PREDICIVE AI + GENERATIVE AI**



# **Al Agent**

#### **Agent-Layers**

#### **Agent-Workflow**



Al Agent

Foundation / Generative Al (LLMs, Vision-Language Models)

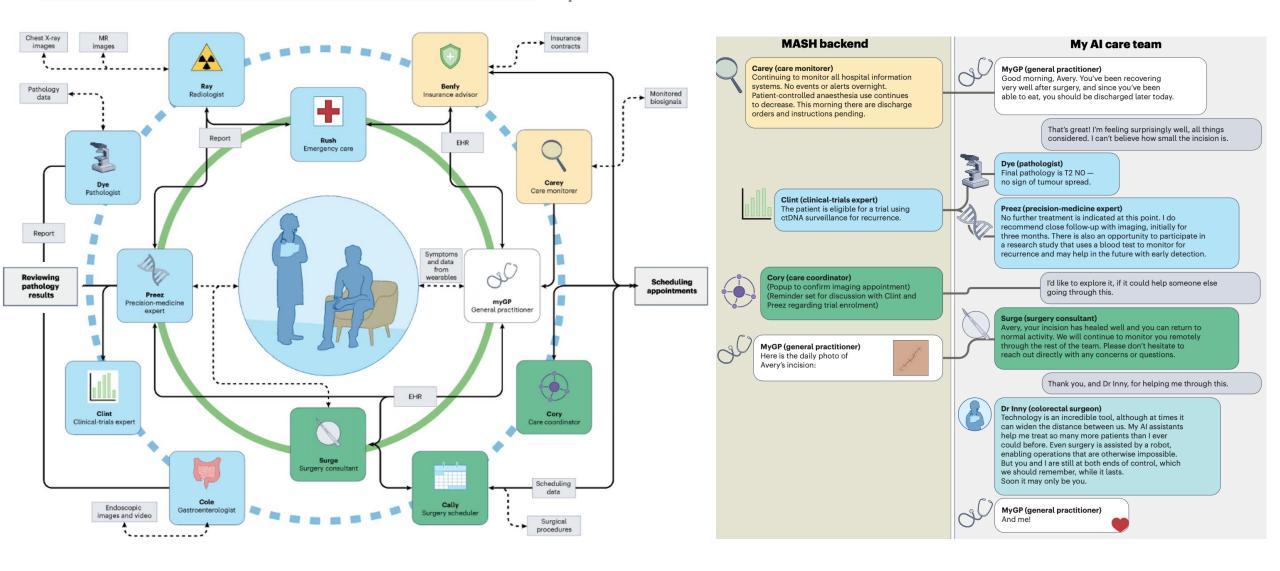
Predictive AI / Specific Tools (QA, Image Captioning, etc.)

Knowledge Integration / RAG (External Sources & Internal Data) Check for updates

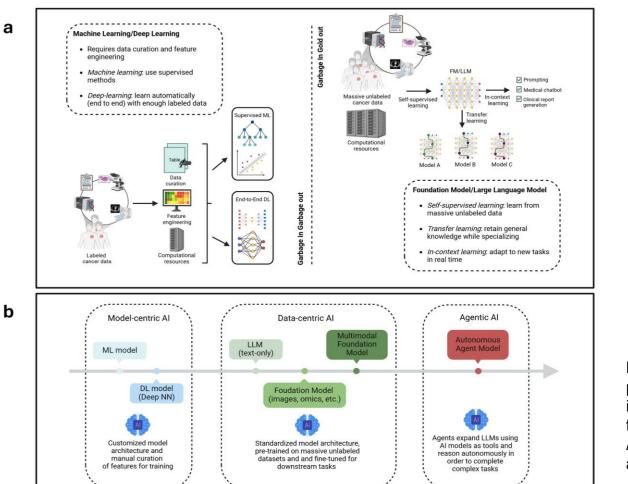
# Coordinated AI agents for advancing healthcare

Michael Moritz, Eric Topol & Pranav Rajpurkar

# Autonomous (Al independent) & Assistive (Human in the loop)

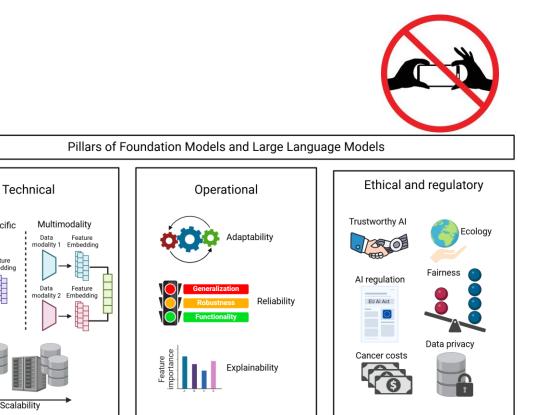


# **GIGO: GARBAGE IN - GOLD OUT**



Arsela Prelaj, MD, PhD, Fondazione IRCCS Istituto Nazionale Tumori of Milan, Italy

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Panel a: Garbage In Gold Out is the paradigm shift in oncology driven by FMs and LLMs. This paradigm enhances the potential of FMs and LLMs in transforming cancer data, i.e., Garbage In, into highly valuable insights, i.e., Gold Out . Panel b: Evolution of AI models in cancer research from traditional model-centric AI, to data-centric AI (FMs and LLMs) and very recently to Agentic AI (autonomous AI Agent). Panel c: These pillars are requested for effective and safe development and deployment in clinical oncology.

Modality-specific

Feature embedding

Data

modality

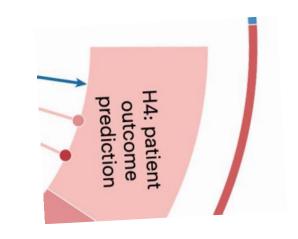
#### Corso et al. Under revision Nature Cancer

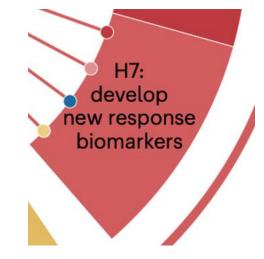


### TAILORING TREEATMENT STRATEGIES: DELAY

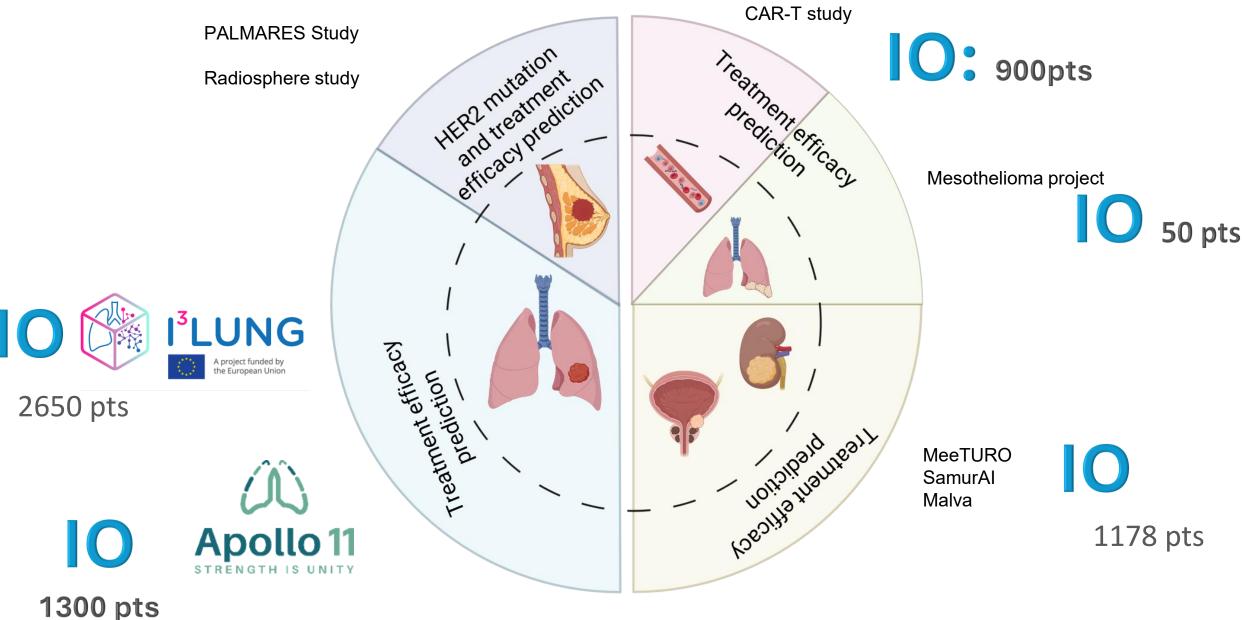
H4. Patient outcome prediction

H7. New Response Biomarker





# Ongoing projects: analyzed 6078 pts with IO-based



Physician Decision Support Systems (PDSS) for Immunotherapy

Integrating Predictive AI and Generative AI for clinical decision making

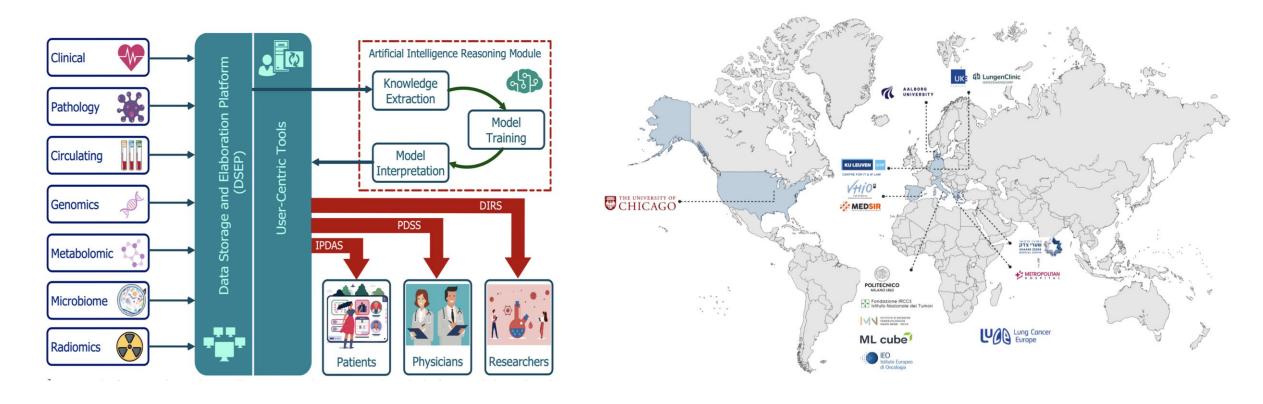




A project funded by the European Union

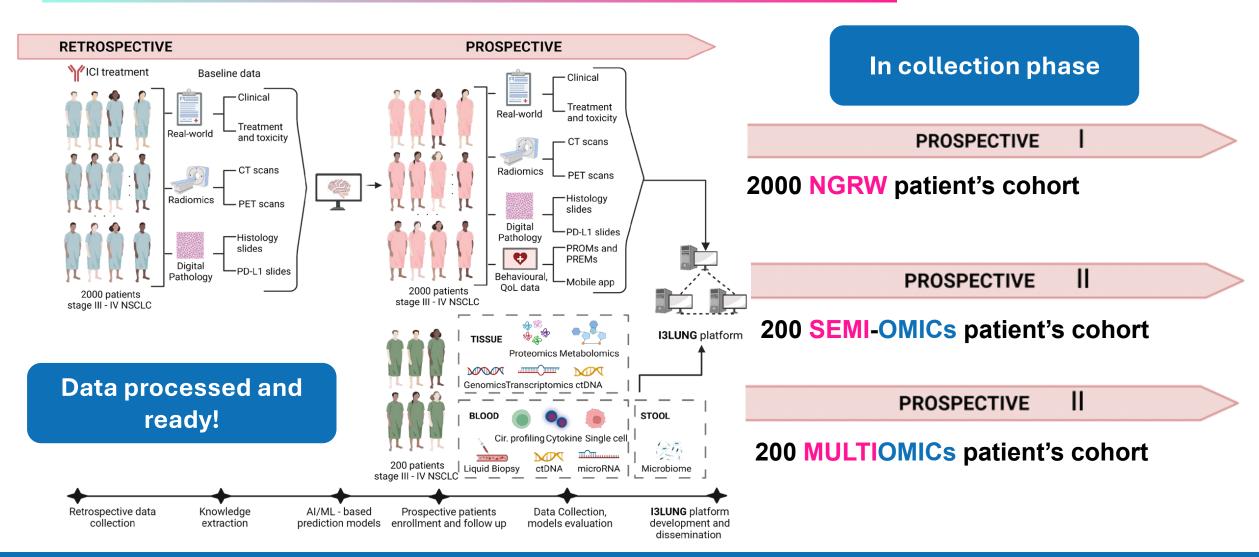
# I3LUNG: A European and beyond project on AI, IO and NSCLC





**Goal:** Develop a Data storage and Elaboration Platform (DESP) by integrating **Real world** and **multiomics** data in NSCLC patients treated with immunotherapy with the aim to produce a clinical decision-making tool using AI approaches

Prelaj et al. CLC 2023



# **I3LUNG: Patients Cohort**



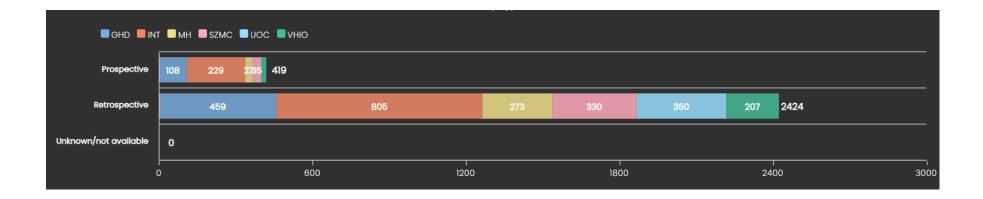
# **I3LUNG: Platform and patients**



**Cancer clinical centers:** 

Select the section you want to use today

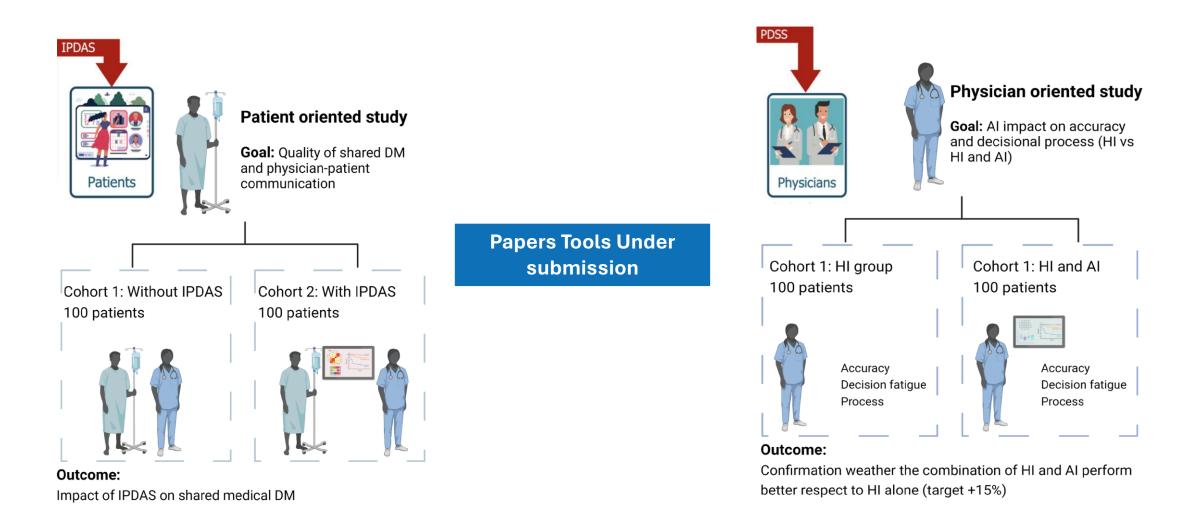




Updated to April 2025

#### 13LUNG: tools, for PATIENTS AND DOCTORS



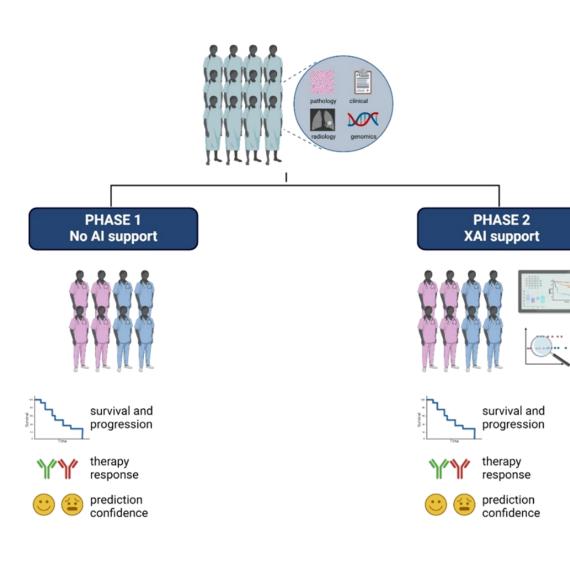


Arsela Prelaj

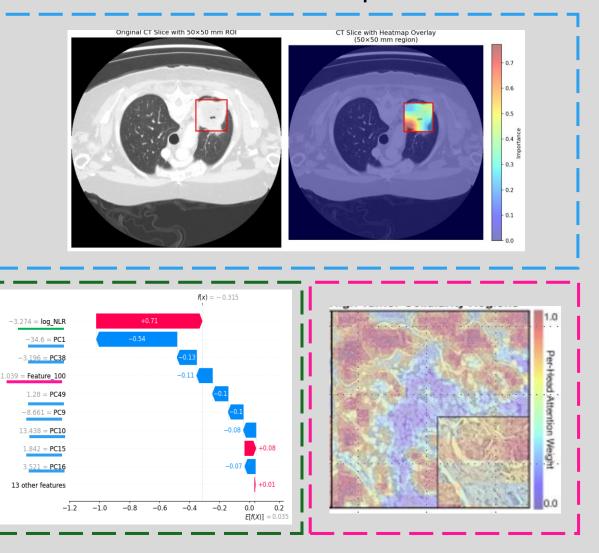
www.i3lung.eu

## **I3LUNG: Clinical Usability of the tool**



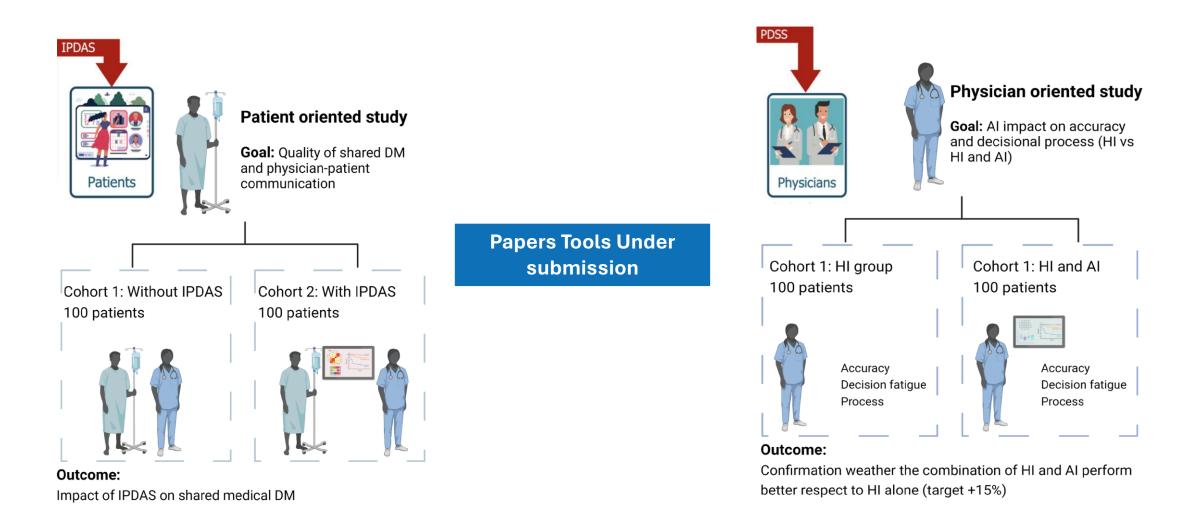


**Multimodal Model Explanation** 



#### 13LUNG: tools, for PATIENTS AND DOCTORS



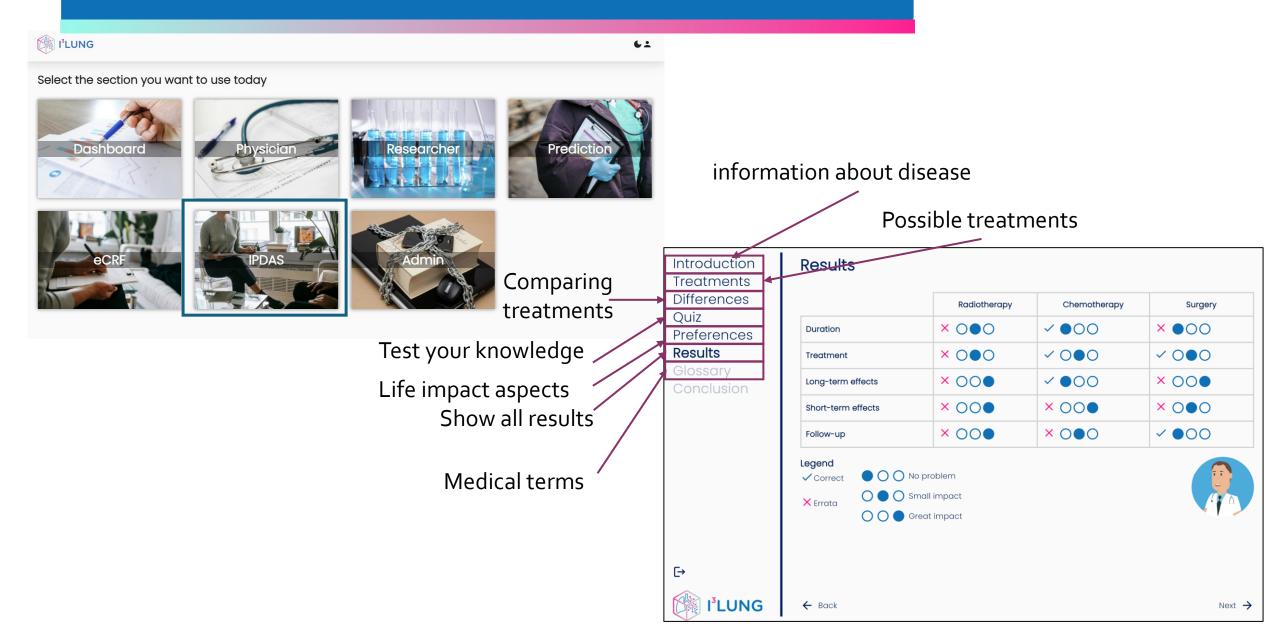


Arsela Prelaj

www.i3lung.eu

### I3LUNG: Co-Decision Making tool for patient





# **Mobile App for**

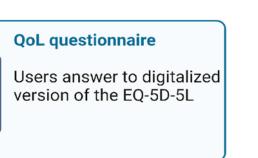
- **Detection of Toxicity**
- **Detection of progression**
- **Detection of Relapse**

## I3LUNG: mobile app – QoL monitoring

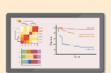












App vs PREMs and PROMs

App allows to collect additional data outside of the fixed time points



Cognitive sensing Integrated machine learning models for automatic processing of voice and prediction of quality of life

#### Name of speaker/presenter

#### www.i3lung.eu



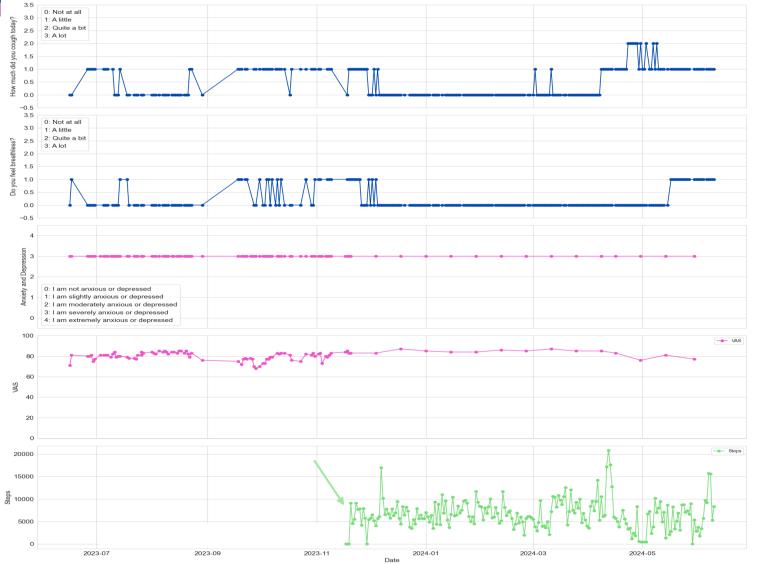
How much cough

Breathlessness

EQ-5D-5L Feelings of depression and anxiety

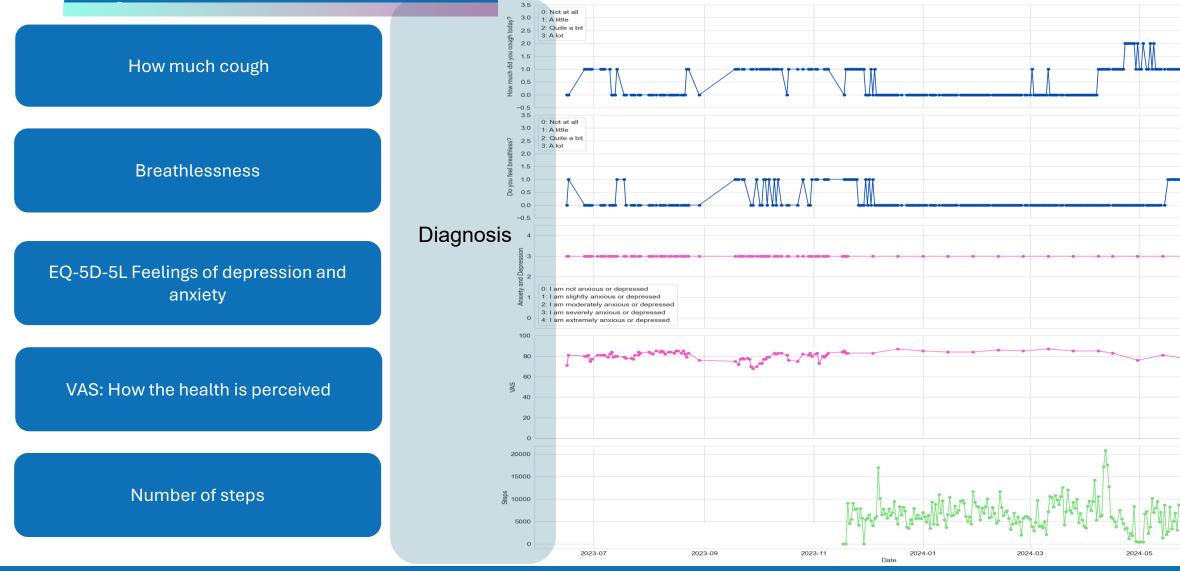
VAS: How the health is perceived

Number of steps



Chiara Giangregorio





Chiara Giangregorio

--- VAS



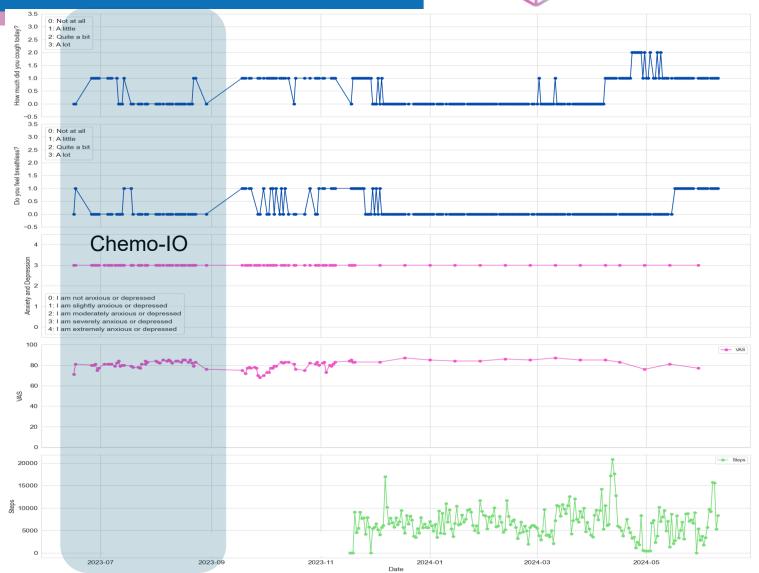
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Chiara Giangregorio



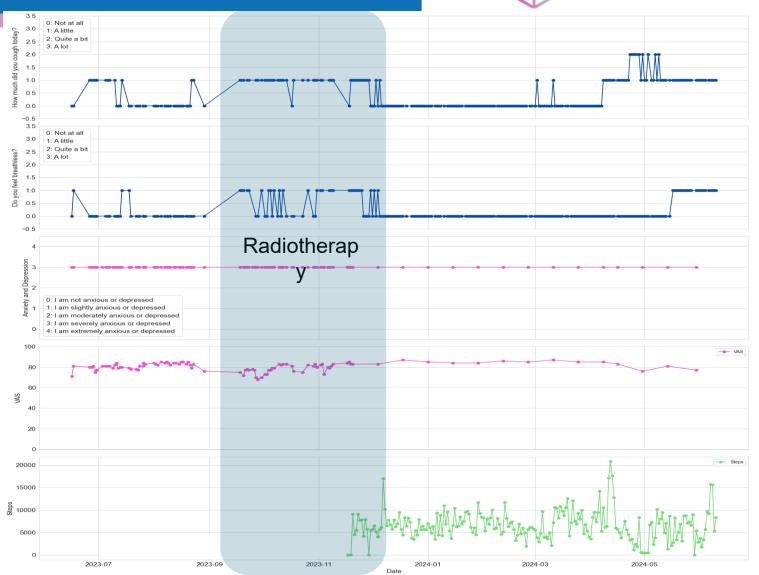
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Chiara Giangregorio



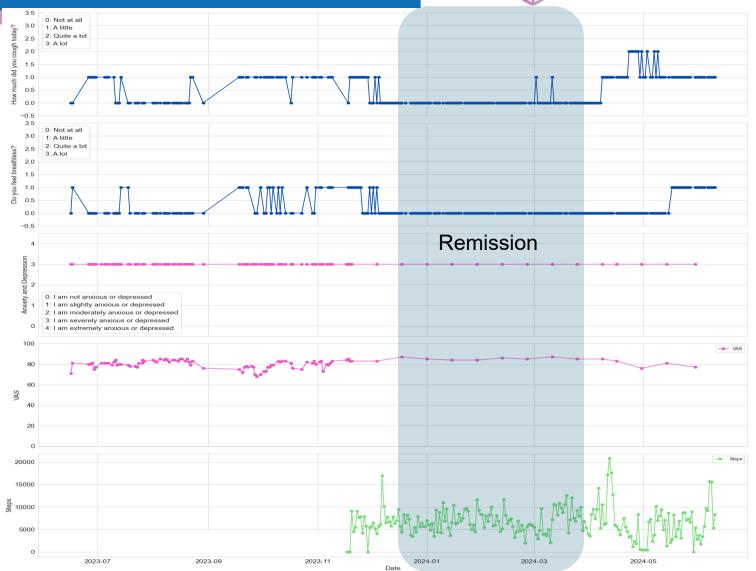
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Chiara Giangregorio



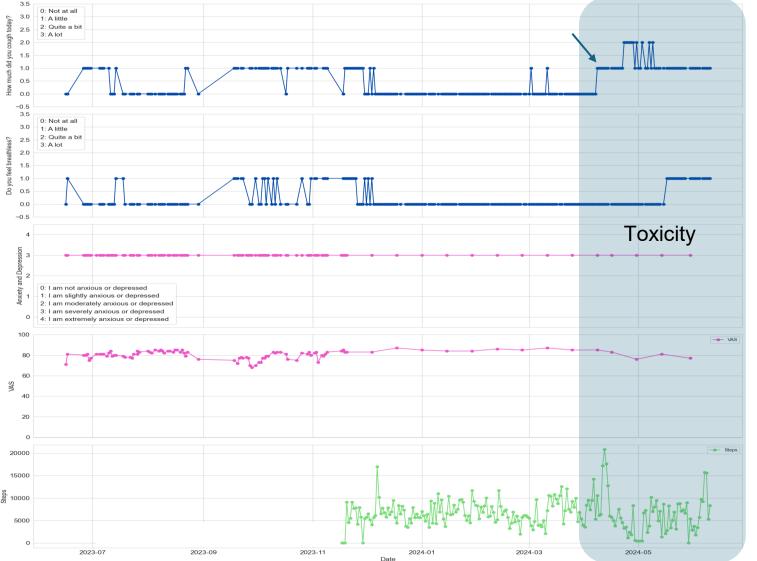


April 2024: onset of cough symptoms

Mid-May 2024: CT confirms treatmentrelated pneumonia

Fatal if not timely treated

Can we detect intrasubject variations in cough depending on the trend of treatment?



## Mobile app as a digital biomarker



#### **Idea and Goal**



NSCLC Early Detection Gap: Screening mainly target smokers, leaving non-smokers undiagnosed. Late Diagnosis Issue: Most cases are detected at advanced stages, limiting treatment options.



Cough as an Underutilized Biomarker Potential for NSCLC Detection: Currently unexplored, but promising for screening



Investigate Al-based cough analysis for distinguishing NSCLC patients on immunotherapy (IO) treatment from healthy individuals.



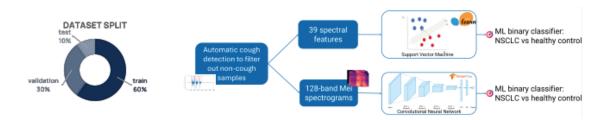
Cough samples

collected

through a

#### Research (s. Disard Analysis (s. Disard Analysis (s. Control (s. C

#### Workflow



Support vector Machine (SVM): Hyperparameter tuning on validation set Convolutional Neural Network (CNN): Adam optimizer with binary cross entropy loss function + early stopping with 15-epoch patience





Giangregorio, Licciardiello et al. ELCC 2025

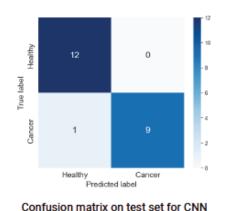
#### Dataset:

- 91 patients with stage III-IVB NSCLC treated with IO
- 109 healthy controls

Model	Accuracy	Sensitivity	Specificity
SVM	82%	70%	92%
CNN	95%	90%	100%

Results

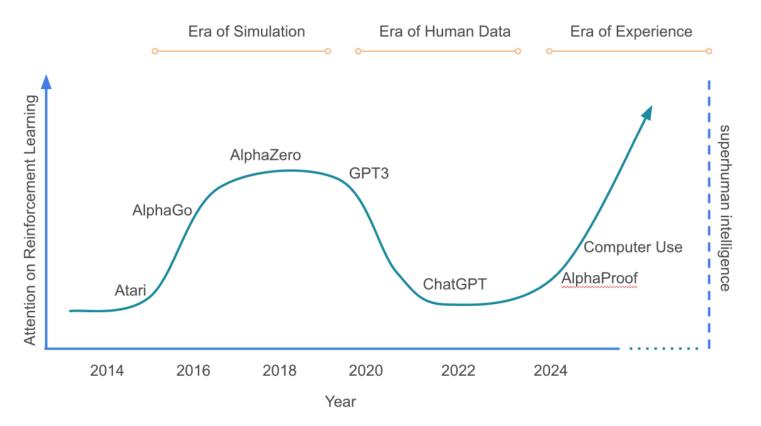
Model performances evaluated on test set for classical machine learning model SVM and CNN.



#### Potential of using cough as a digital biomarker!

Name of speaker/presenter

# The Era of Experience



- AI must move beyond static human data.

- Continuous, real-world experience is key.

- Grounded rewards from the environment, not just human feedback.

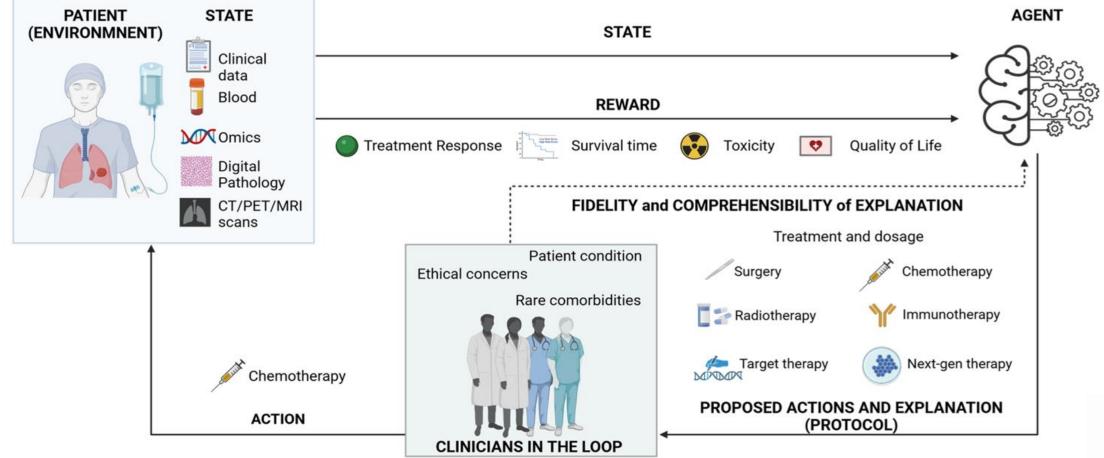
- Autonomous agents adapt to the real world over time.

- Reinforcement learning drives superhuman capabilities.

David Silver, Richard S. Sutton\* Deep Mind June 2025

# **Modeling The Patient Journey With RL**



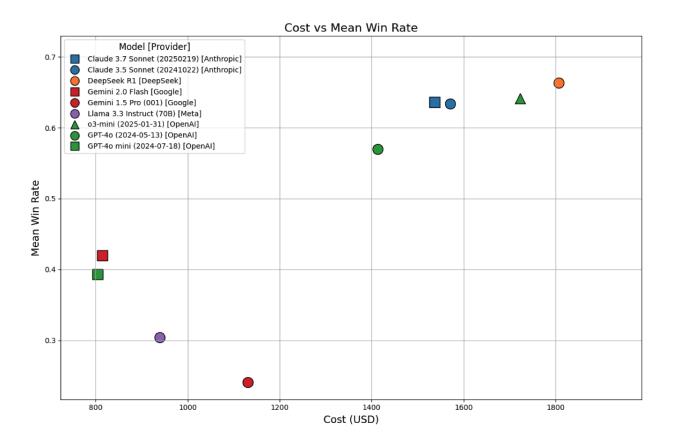




Zec, Aleksandra, et al. "Open Problem: Leveraging Reinforcement Learning to Enhance Decision-Making in Oncology Treatments.", ARLET workshop @ICML 2024

AI-ON-Lab

# **Cost-analysis in the LLMs era: MedHELM**



Overall, non-reasoning models (GPT-40 mini: \$805, Gemini 2.0 Flash: \$815) had the lowest costs and decent win-rates (0.39-0.42).Llama 3.3 Instruct (\$940) reached a 0.30 win-rate, while Gemini 1.5 Pro (\$1,130) achieved 0.24. In contrast, reasoning models cost more DeepSeek R1 (\$1,806) and o3-mini (\$1,722) but performed better (0.66 and 0.64). Claude 3.5/3.7 Sonnet (\$1,571/\$1,537) offered a solid costperformance balance ( $\sim 0.63$  win-rate).



**European Interdisciplinary Society of Artificial** Intelligence in Cancer research. Founded in 19<sup>th</sup> Dec 2024

Helena Linardou

Treasurer

**Loic Verlingue** 



Arsela Prelaj President



President-elect

**Daniel Truhn** 



**Claes Lundström** 

**Jakob Nikolas Kather** 



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Vanja Mišković

**Mireia Crispin** 

**General Secretary** 

**Raquel Pérez-López** 

**Mihaela Aldea** 



Truly effective AI integration hinges on the combined expertise of a variety of research figures: medical oncologists, imaging specialists (nuclear) radiologists, pathologists, physicists, bioinformaticians and AI engineers.

SPEAK THE SAME LANGUAGE

#### **Build a multidisciplinary network**

ESAC aims to bridge strategic alliances with key European initiatives and scientific organizations to amplify AI's impact in research, diagnostic and oncology.

**DELIVER ALCARE across Cancer Societies** 

#### **Comprehensive educational programs**

Recognizing the need for specific expertise, ESAC provides training opportunities, from webinars and interdisciplinary conferences. SUMMER SCHOOL IN CANCER RESEARCH MASTER: AI IN CANCER RESEARCH

WEBSITE: https://esac-network.eu. CONTACT US by e-mail: contact@esac-network.eu





### **JOIN TODAY !**

## EARLY BIRD REGISTRATION WITHIN AUGUST 2025

#### Why join?

- > We bring together EU opinion leaders in cancer AI, from multiple fields of expertise
- > You gain access to cross-disciplinary expertise and collaborative opportunities
- > You become part of a network with strong ties to all major international cancer care and research societies
- > You can contribute to the ethical and impactful integration of AI into cancer research.

#### **Concrete benefits**

- > Participation in working groups committees and projects
- > Access to members directory and network (WIP)
- > Voting rights in the General Assembly
- > Priority access to events, workshops, and fellowships
- > Access to members-only webinars and training courses
- > Eligibility to apply for leadership roles in the WGs and Committees

#### **Membership tiers**

- > 30€/year for ordinary membership (early bird fee), 2-years discount
- > Preferential rates for students
  - \* 10€ per year for undergrad/postgrad students
  - \* 20€ per year for PhD students/medical residents

#### Join the Society

#### Become a Member

For researchers, clinicians, engineers and other stakeholders Benefits:

- Full access to ESAC's resource repository
- Participation in working groups and possibility to join WG committees
- Voting rights in the General Assembly
- Priority access to events, workshops, and fellowships
- Eligibility to apply for leadership roles within the Society
- Visibility in the ESAC member directory (under construction)
- Digital certificate and member badge





SCAN ME

Become a Sponsor

# **First ESMO AI Conference**

#### ESMO > Meeting Calendar **ESMO AI & Digital Oncology Congress 2025**

ESTO SCENE BET MACTOR



ESMO - European Society for Medical ... **ESMO** 94.157 follower 3 ore • 🕥

im #ESMOAI25: Join us in building an Al-ready community, to make sure AI enhances-not replaces-oncology expertise. Submit your... altro

Mostra traduzione







R. Fehrmann



**BERLIN** GERMANY 12-14 NOVEMBER 2025



#### **Scientific Co-Chairs**

- Mireia Crispin Ortuzar, Cambridge, UK
- Rudolf Fehrmann, Groningen, Netherlands
- Jakob Kather, Dresden, Germany

## **AI CONGRESS**

Hibrid Event organized by:

#### **Co-Local Organizers**





#### Invited speakers from:



**ECHNISCHE** 

**UNIVERSITÄT** 

DRESDEN

Memorial Sloan Kettering **Cancer** Center

VALL D'HEBRON

of Oncology



UC

School of

Medicine





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**Endorsed by:** 





ESAC

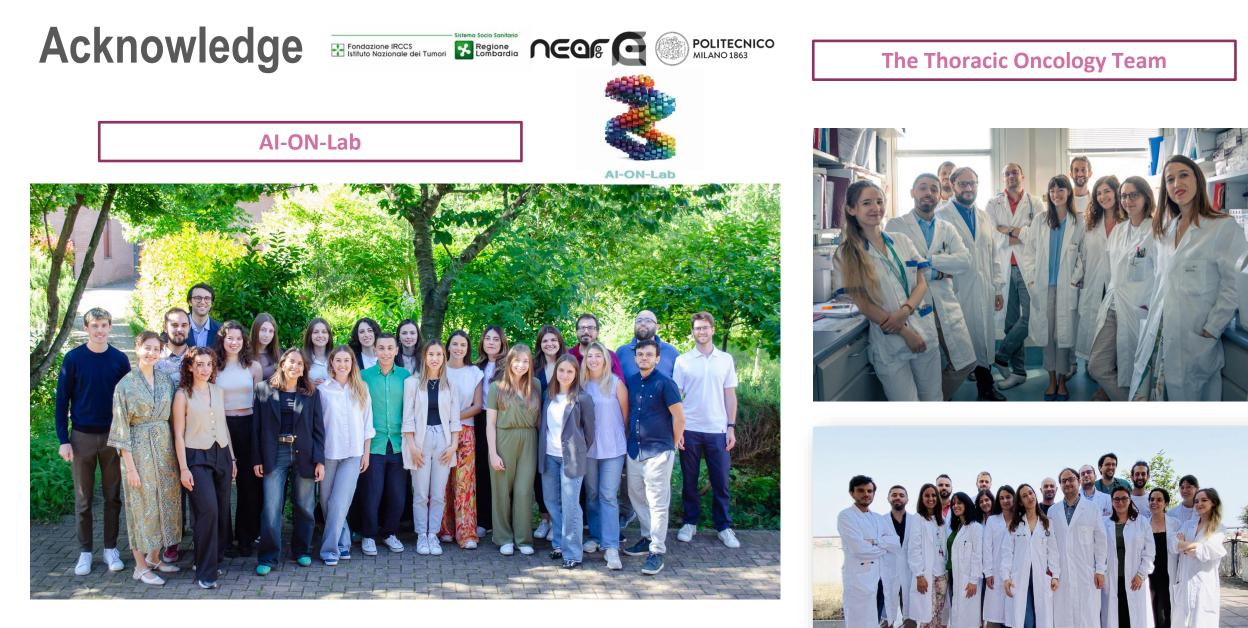
1<sup>st</sup> Annual **MEETING ESAC** (European Interdisciplinary Society

for AI in Cancer Research)

4<sup>th</sup> Edition **AI FOR ONCOLOGY** and Cancer Research

> 25 MILAN, ITALY 7th - 8th MAY 2026





http//:Ai-onlab.com

Contact Us for more info: Arsela.prelaj@istitutotumori.mi.it Adam.smith@istitutotumori.mi.it



@arselaprelaj.bsky.social

# **AI DEPLOYMENT**

- 1. High-Level Prediction Capabilities: Al now delivers accurate predictions at baseline across screening, diagnosis, prognosis and prediction tasks.
- 2. Advanced RWD, Imaging & Genomics Analysis: AI enhances real-world data (RWD), image and genomics integration improving biological insights (e.g.: from digital pathology to gene).
- **3.** Automatic Data Extraction: Significant improvements in automated and structured data retrieval streamline workflows by using NLP and LLMs.
- 4. Federated & Swarm Learning Techniques: Decentralized AI models ensure secure, privacy-preserving multiinstitutional collaborations.
- 5. New Quality of Life Monitoring through Cognitive Sensing: Al-driven mobile and wearable technologies provide realtime, adaptive health monitoring, perform much better compared to PROMs and PREMs.
- 6. Foundation Models & Generative AI: Cutting-edge advancements in LLMs and foundation models enable high-quality analysis of complex, high-dimensional data.
- 7. Al-Powered Clinical Trial Optimization: Predictive analytics improve patient recruitment, endpoint selection, and adaptive trial designs CLINICAL TRIAL MATCHING
- 8. In-Silico Drug Screening & Molecular Docking and Drug discovery: Al-powered simulations predict drug-target interactions, reducing experimental costs and time.

# Al more DELAY THAN DREAM

- 1. Privacy, Data Governance & Democracy: Ensuring compliance with data protection regulations while enabling secure data sharing.
- 2. Trustworthiness, Fairness & Diversity: Addressing bias, transparency, and ethical considerations in AI models
- 3. Advancing Treatment Selection Tools: Improving AI-driven decision support systems for personalized medicine.
- 4. Model Explainability in the Era of Generative AI: Enhancing interpretability of complex AI-driven decisions.
- 5. Scalability of Multiomics Data Integration: Overcoming small dataset limitations for robust multi-omics (Dream?)
- Longitudinal AI & Reinforcement Learning: Developing scalable models for sequencing prediction and continuous learning (Dream?).
- 7. Synthetic Data for Genomics & Imaging: Validating the use of synthetic data in clinical trial design and drug discovery.
- 8. Al Agents & Workflow Integration: Optimizing the role of AI-powered autonomous systems in clinical care applications.
- Computational Power & Cloud Resources: Addressing GPU limitations and cloud infrastructure challenges and the investments that labs/institutions need to do (Dream?).

10. Clear educational path: we need to build next generation scientist, hybrid, brining together the TECNO and HUMANITY