Onc AI

Bridging Clinical Trial and Real-World Data to Build Imaging Biomarkers for Precision Oncology

Overview

- What are imaging biomarkers and how can they be used for precision oncology?
- Real world data: challenges and opportunities
- Machine learning development at scale for software as a medical device: challenges and best practices
- Examples of Onc.AI imaging biomarkers to identify patients who respond to immunotherapy and to predict survival in advanced NSCLC throughout treatment journey

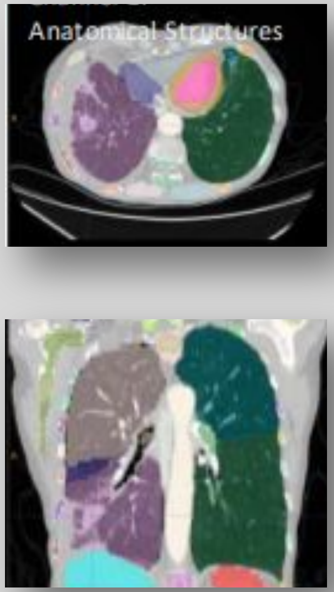
What are Imaging Biomarkers and How Can They Be Used for Precision Oncology?

Tumor Size and Quantity Routinely Assessed in Images

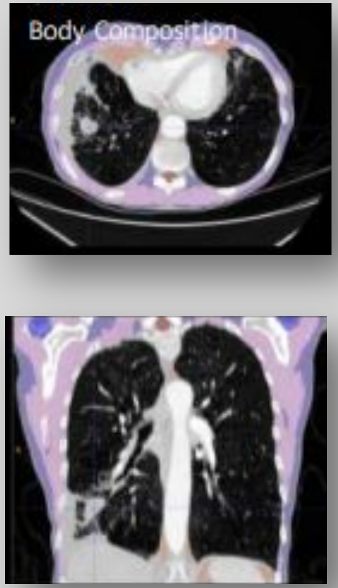
- Tumor measurements inform treatment decisions
- Clinical trial endpoints based on tumor measurements
  - Progression Free Survival (PFS)
  - Objective Response Rate (ORR)
- Tumor size does not always reflect progression
- Images contain wealth of information beyond tumor size

Diagnostic Imaging Contains Predictive and Prognostic Features That Can Be Extracted by Advanced Radiomic Analysis

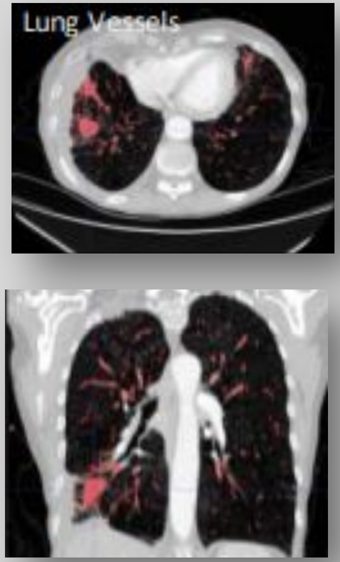
Anatomical structures



Body composition

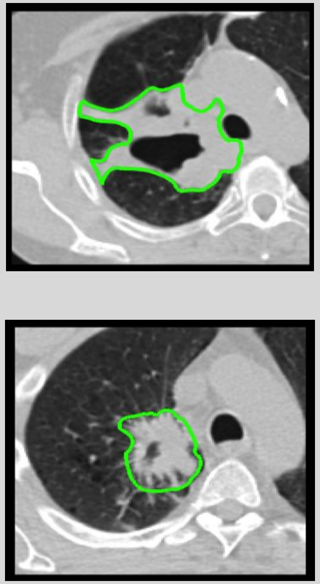


Vasculature



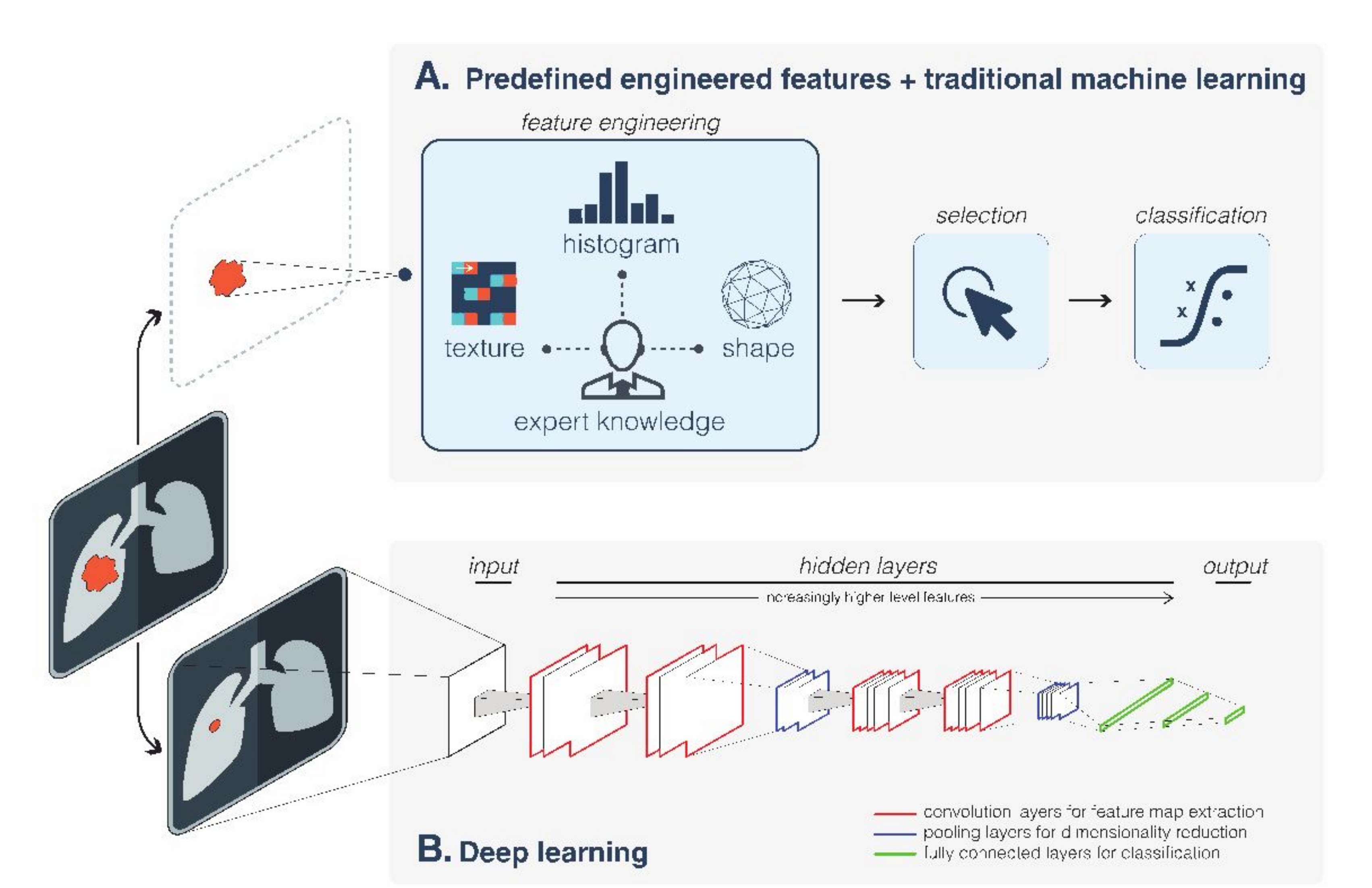
Tumor size & location

Tumor appearance



These features comprise the foundation of **imaging biomarkers**

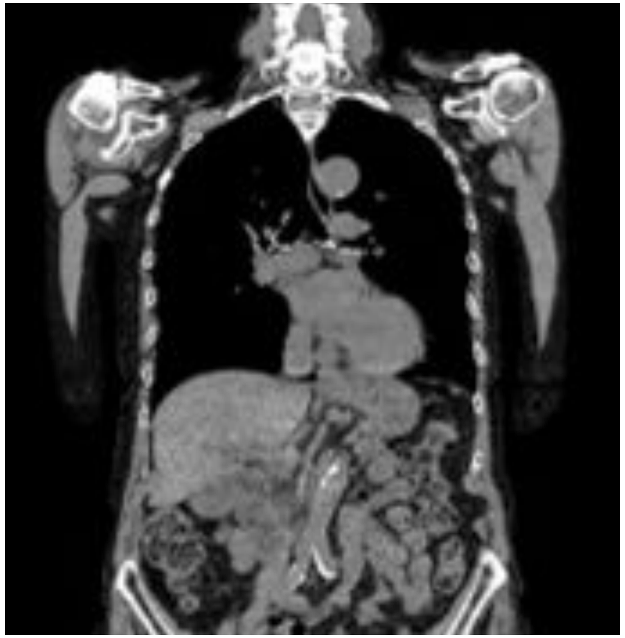
Deep Learning Increases Performance of Imaging Biomarkers



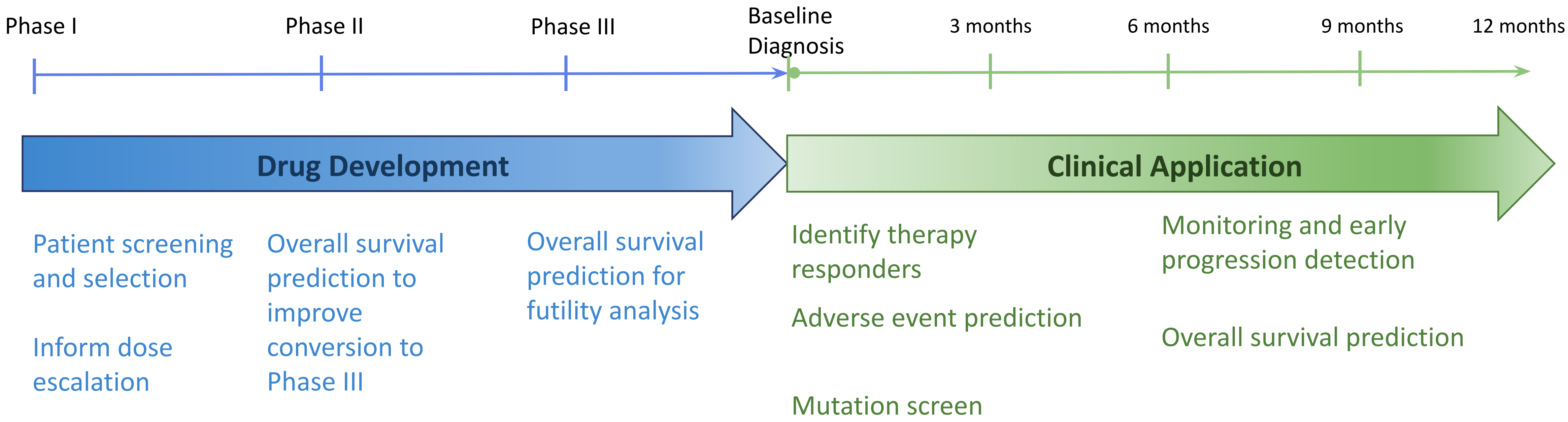
Hosny, Nature Reviews Cancer 2018

Advantages of Radiological Imaging-Based Biomarkers

- Calculated from radiological images already acquired in routine care
- No blood or tissue samples needed
- Captures multiple tumors, peritumoral regions, and other anatomical signals
- Rapid calculation
- Can be combined with clinical, genomic, and other data to create multi-omic biomarkers



Predictive and Prognostic Imaging Biomarkers Inform Precision Oncology at Every Stage



AI-imaging biomarkers (radiomics) are **showing strong potential** in academia, but commercialization limited by data needs and machine learning development challenges

Real World Data: Challenges and Opportunities

Building a Robust, Unbiased, Generalizable Dataset: Randomized Clinical Trial (RCT) Data vs. Real-World Data (RWD)

RCT Data

- **Controlled Cohorts**: Carefully selected groups minimize variability
- **Standardized Treatment Protocols**: Uniform guidelines ensure consistent patient care
- **Regular Follow-Up Intervals**: Regular imaging schedules facilitate consistent monitoring
- **Consistent Data Handling**: Uniform collection and imaging protocols ensure consistency

- **AI Implication**: Controlled environments reduce bias, leading to **models with higher internal validity**

RWD

- **Potential Cohort Biases**: Lack of randomization can introduce selection biases
- **Diverse Treatment Approaches**: Reflects variability in clinical practice
- **Variable Follow-Up Schedules**: Imaging intervals differ based on individual needs and resources
- **Inconsistent Data Handling**: Variations in collection and imaging protocols pose challenges
- **Expanded Data Volume**: Larger datasets provide broader patient outcome perspectives

- **AI Implication**: Diverse data enhance generalizability, making **models more applicable to varied real-world scenarios**

Bridging the Gap Between RCT and RWD in AI Model Development: Comprehensive Real-World NSCLC Dataset

Patient Cohort: 3,000+ patients with advanced NSCLC

Robust Imaging Data: 60,000+ CT scans totaling 18 million ima

Diverse Sources: 10+ hospital networks
- Academic, community, and rural settings
- U.S. and Europe
- 6 scanner manufacturers
- 117 scanner models

Extensive Data: Imaging at baseline and follow-ups
- Clinical Notes
- Pharmacy
- Laboratory
- Genomic Data
- Demographics

Indication Specific

Multimodal

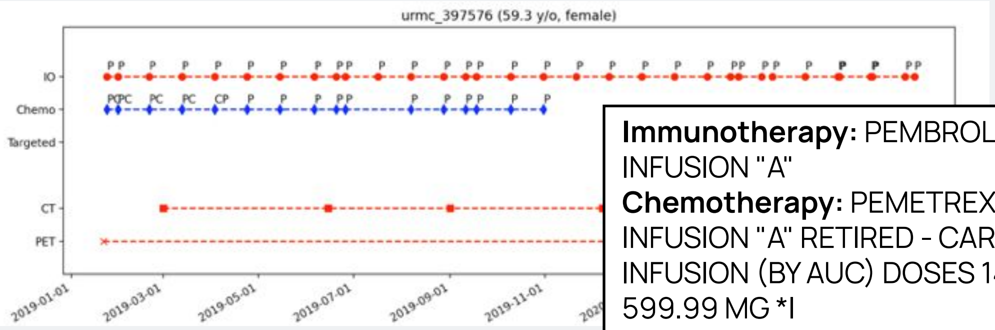
Comprehensive Outcomes

Bridging the Gap Between RCT and RWD in AI Model Development: Image Standardization and Harmonization

ML-Ready Patient Profiles: Standardized representations for seamless AI integration

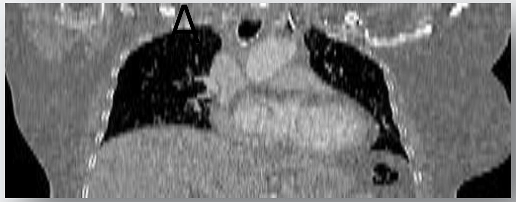
Uniform Annotation Protocol: Centralized radiographic annotation ensures consistency across institutions

Image Harmonization: Techniques reduce biases from varying scanners and protocols

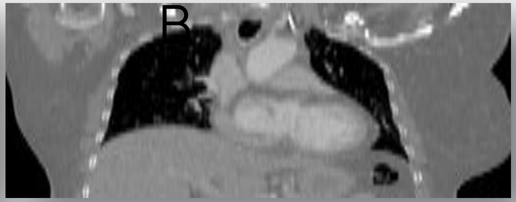


Immunotherapy: PEMBROLIZUMAB INFUSION "A"
Chemotherapy: PEMETREXED INFUSION "A" RETIRED - CARBOPLATIN INFUSION (BY AUC) DOSES 145 MG - 599.99 MG *I
Histology: PD-1 Score: 0.55 Mutation Status: EGFR: unknown, KRAS: unknown, TP53: unknown, ALK: unknown

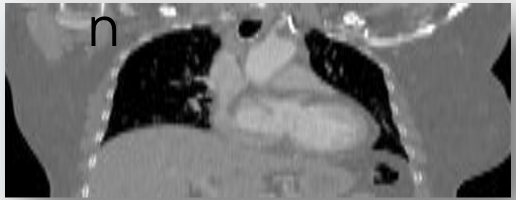
Protocol A



Protocol B



Harmonization



ML Development at Scale: Challenges and Best Practices

Building a Production Model: Machine Learning Operations (MLOps)

Challenges

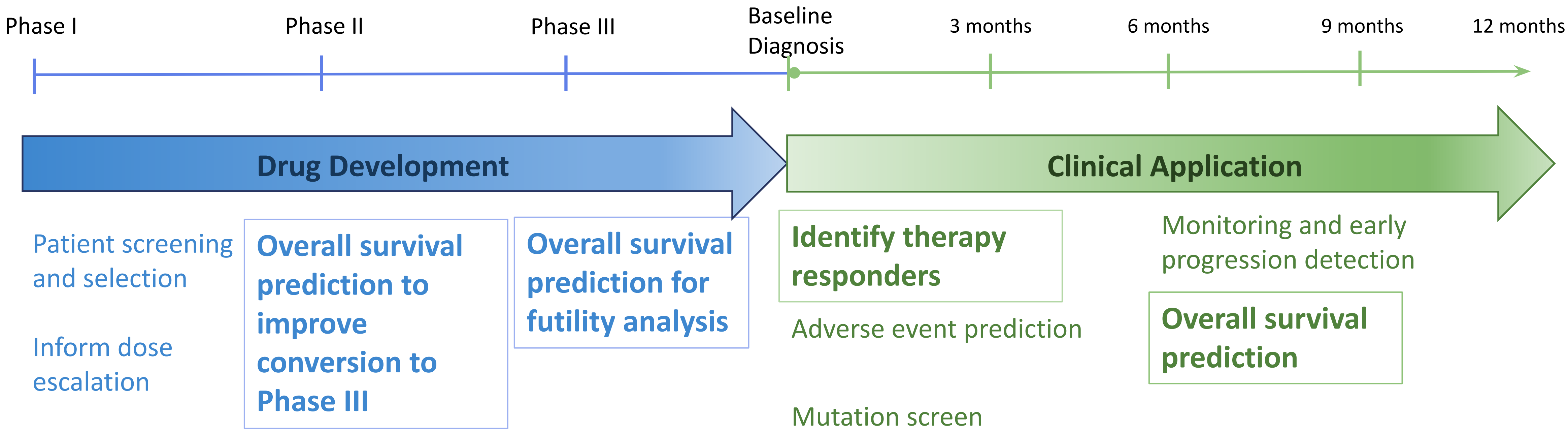
- Integrating ML data, training, evaluation tasks
- Committing to a cloud vendor and managing cloud resources
- Facilitating experimentation
- Repeatability
- Creating auditable lineage of dataset generation and model training

Best Practices

- Automated modular pipeline on one platform
- MLOps tool that is an abstraction layer used on any cloud provider
- Automated parameter searches
- All runs reproducible by design
- Automatically track and store every asset (code, data, logs, hyperparameters, weights) during run

Examples of Onc.AI Imaging Biomarkers Developed Using These Best Practices

Onc.AI Predictive and Prognostic Imaging Biomarkers Inform Precision Oncology at Every Stage



Identifying Patients Likely to Benefit from Treatment

Identifying ICI Responders at Baseline

- Approximately 30% of patients benefit from immune checkpoint inhibitor (ICI) therapy
- Limited predictive values for existing approved biomarkers in advanced NSCLC
- **Clinical Need**: Identify patients who will benefit from ICI monotherapy versus combination therapy with chemotherapy
- **Our Contribution:** Developed deep learning imaging biomarker to predict response to ICI in NSCLC using routine baseline CT scans

Predicting OS From Longitudinal Imaging

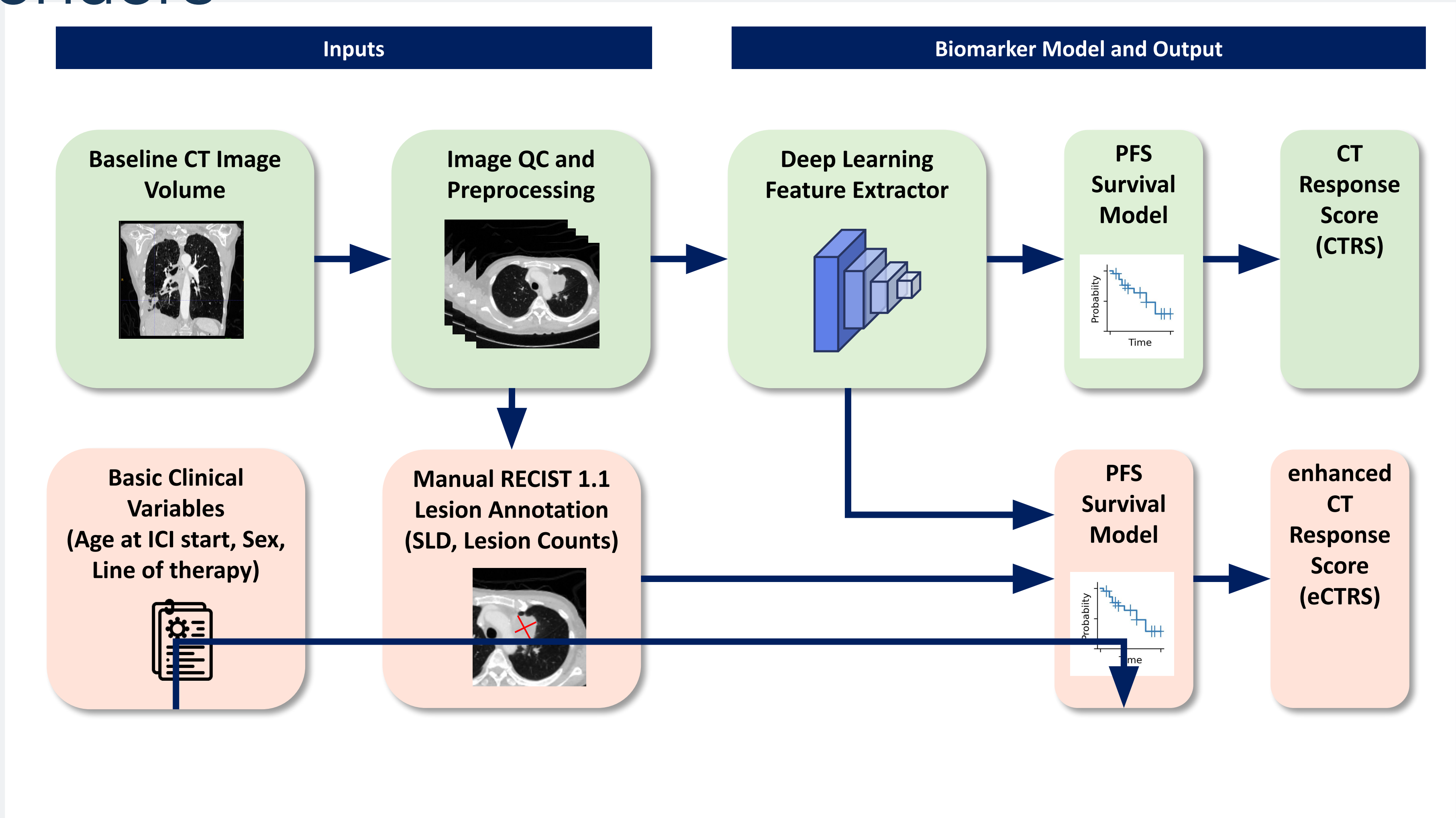
- Variability of outcomes in patients with early stable disease complicates treatment decisions and early-phase clinical trials
- **Clinical Need**: Identify patients who will benefit from continued treatment
- **Drug Development Need:** Predict OS with higher accuracy than current tumor size-based metrics
- **Our Contribution:** Developed deep learning serial imaging biomarker to predict OS in advanced NSCLC using routine CT scans

Training and Independent Validation Datasets

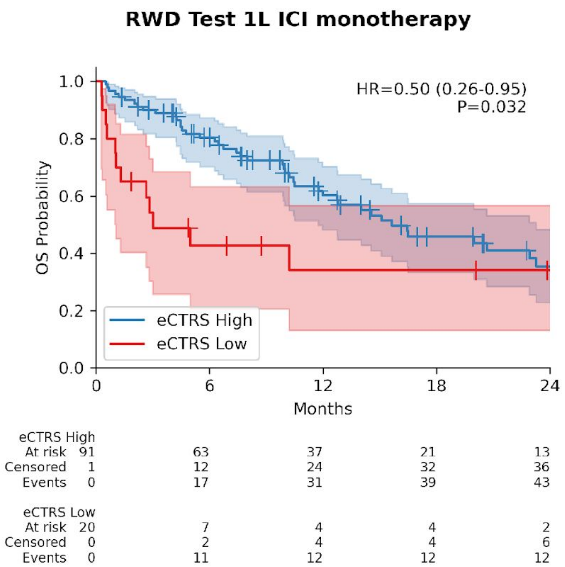
Training	Independent Validation	
Dataset A	**Dataset B**	**Dataset C**
RWD Discovery 1,173 patients 19,148 CT series 9 institutions, >50 clinical sites from US/Europe ICI start year: 2013-2021 Model development and internal cross-validation	RWD Holdout Excludes confirmed EGFR/ALK mut+ 458 patients 10 institutions ICI start year: 2013-2022	NCT02573259 (Pfizer, Inc.) 54 patients ICI start year: 2018 Phase I dose escalation study of Sasanlimab (anti-PD-1 checkpoint inhibitor) in ICI-naïve patients with advanced NSCLC

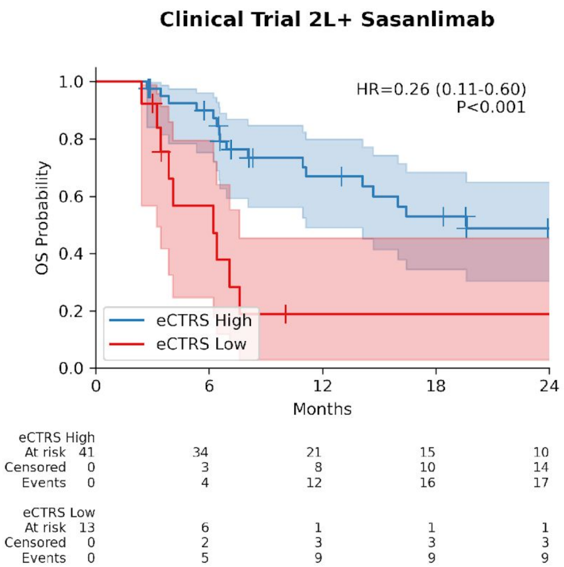
Data was collected under approval of the institutional review board or independent ethics committee of the participating institutions.

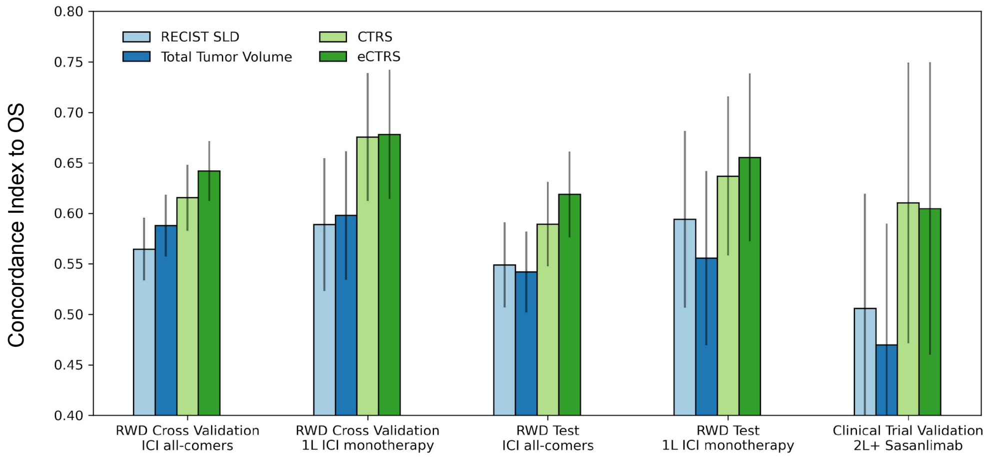
Deep Learning CT Response Score for Identifying ICI Responders



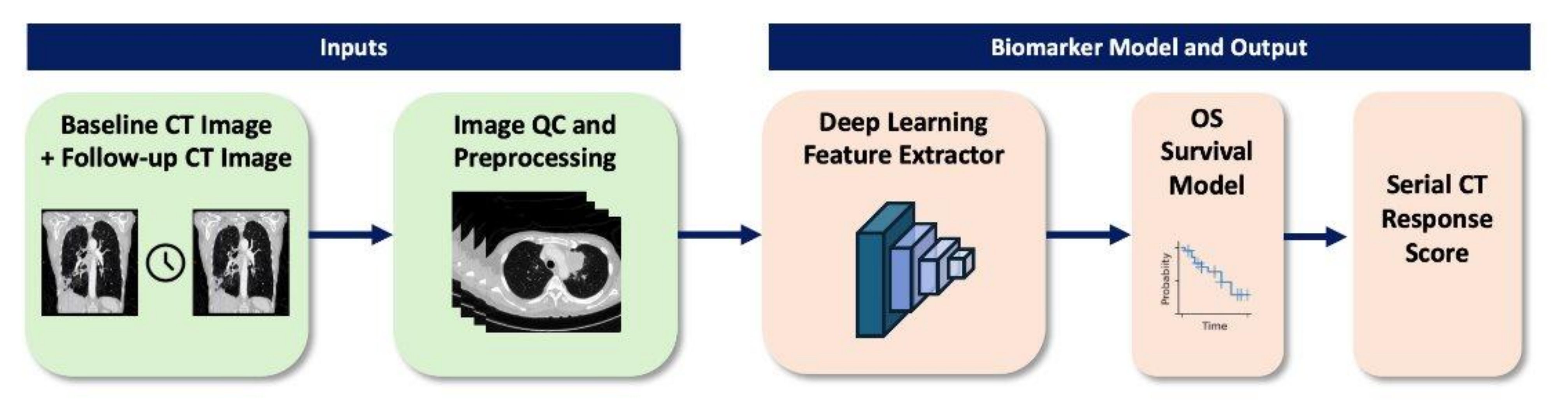
Validation Results: eCTRS Identified ICI Responders



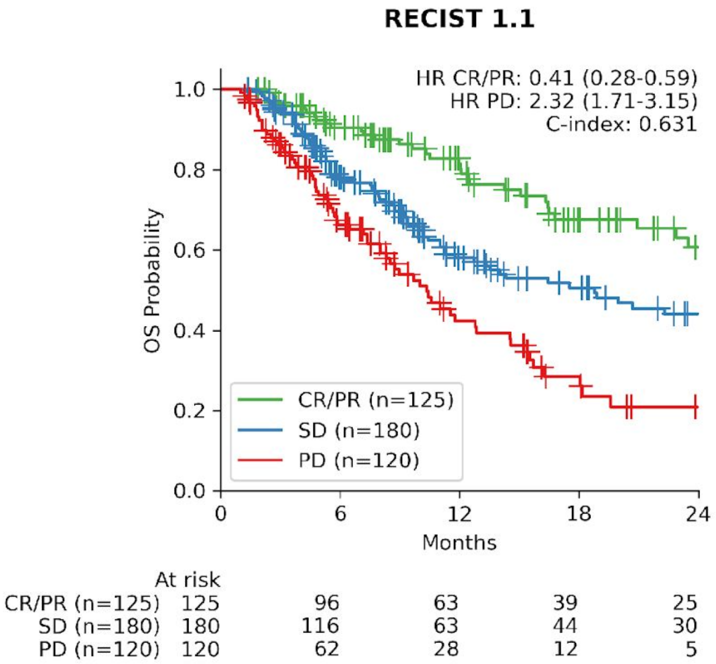


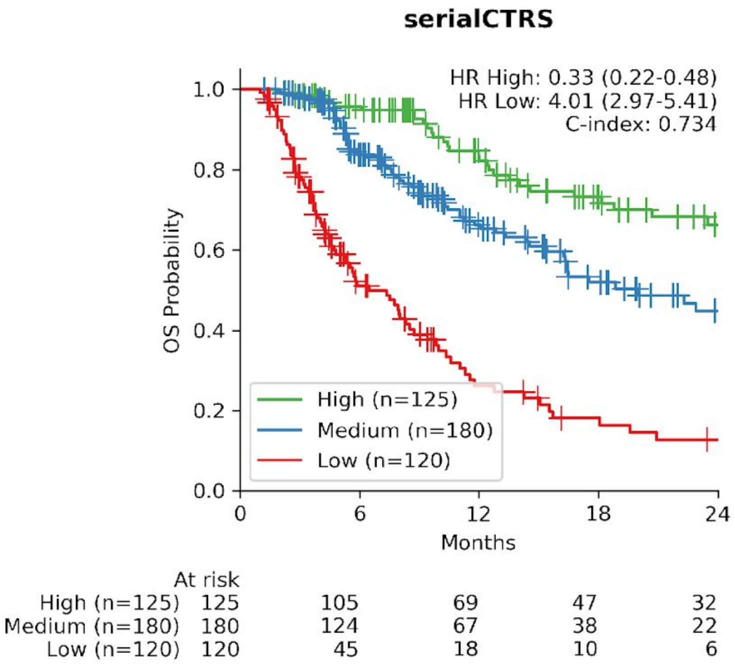


Deep Learning Serial CT Response Score for Predicting OS

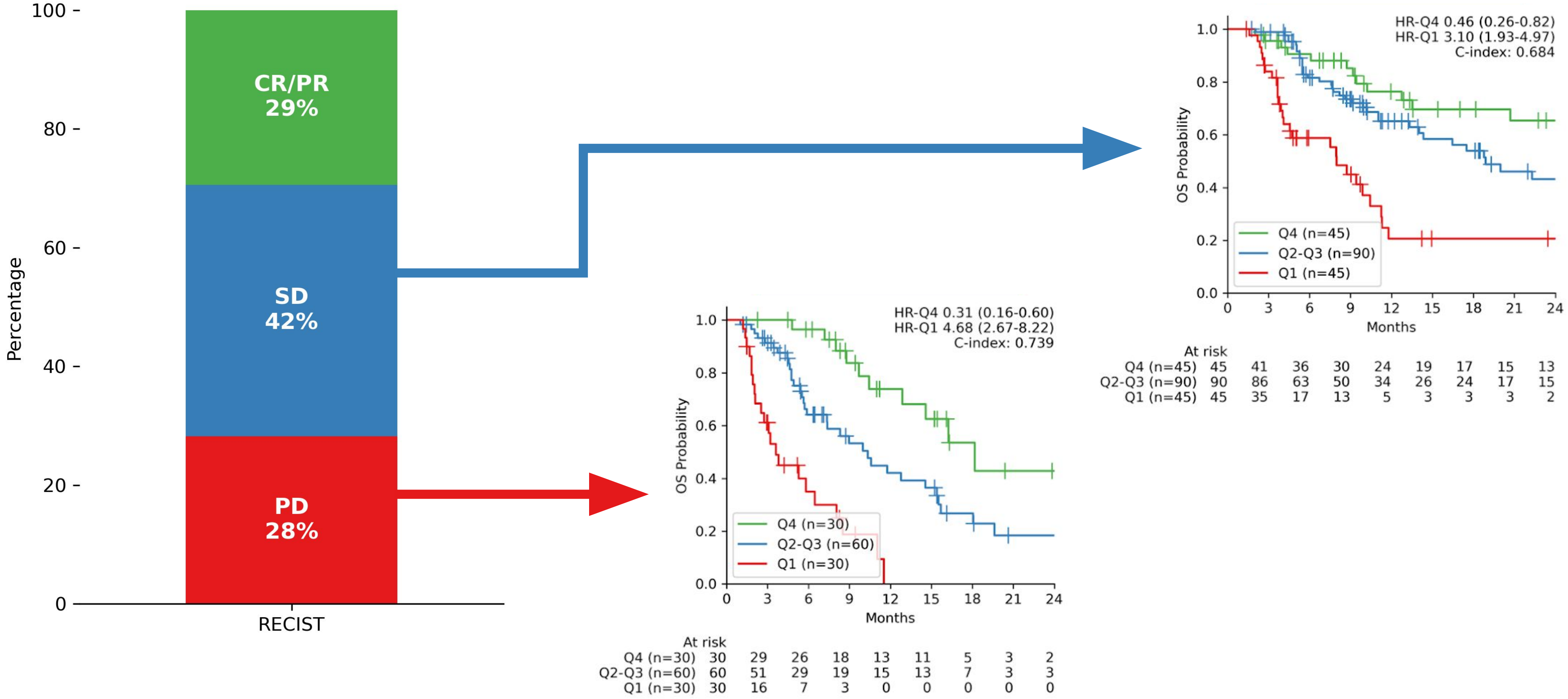


Validation Results: SerialCTRS Identified Patients With OS Benefit





SerialCTRS Further Stratified Patients in RECIST Categories



Conclusions

- Imaging biomarkers have shown potential to inform
  - Drug development
  - Treatment decisions
- Commercialization is challenged by training data and ML development needs
- Real world data is needed to train generalizable biomarkers, but data variability and potential biases must be managed
- MLOps tools accelerate AI development and productization

Acknowledgements

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- Clinical development and data partners
- Pharmaceutical industry collaborators
- Valohai MLOps provider
- Contact for questions and collaboration inquiries: tgschmidt@onc.ai

Conclusions

- **Advancements in Imaging Biomarkers**: Deep learning imaging biomarkers, such as eCTRS and serialCTRS, have demonstrated significant potential in enhancing oncology treatment decisions and clinical trial analyses.
- **eCTRS Biomarker Efficacy**: The eCTRS biomarker has proven to be a robust predictor of response to immune checkpoint inhibitors (ICI), aiding in the identification of patients most likely to benefit from such therapies.
- **serialCTRS Biomarker Superiority**: The serialCTRS biomarker offers more accurate predictions of overall survival (OS) compared to traditional imaging methods, providing valuable insights for patient prognosis.
- **Challenges in Commercialization**: Developing and commercializing these biomarkers is hindered by the need for extensive training data and sophisticated machine learning (ML) development processes.
- **Leveraging Real-World Data (RWD)**: Utilizing RWD is essential for training generalizable biomarkers. However, addressing data variability and potential biases is crucial to ensure reliability and applicability across diverse patient populations.
- **Utilizing MLOps Tools**: Implementing MLOps tools can streamline development, efficiently manage cloud resources, and provide the traceability required for regulatory approval, facilitating the transition from research to clinical application.