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INTRODUCTION

- Lung cancer remains the leading cause of cancer mortality worldwide.¹
- In recent decades, precision medicine has made significant breakthroughs in oncogene-driven non-small cell lung cancer (NSCLC), particularly through targeted kinase inhibitors (TKIs).²
- Acquired resistance to targeted therapies remains a major barrier to disease control.²
- This study used a precision-oncology medicine platform, MyOncoPM, to test patient-derived organoids (PDOs) for response to chemotherapies and TKIs to better predict resistance and sensitivity in real time.³

METHODS

Design:

MyOncoPM Functional Precision-Oncology platform cross referenced against real-world clinical treatment history.

Participants and Sample Collection

- 559 participants consented under IRB protocols HUM00042204 and HUM00227562; PDOs were generated from 104 participant samples (tissue, pleural fluid, ascites, and organoid).
- 55 samples (41 tissue, 12 pleural fluid, 1 ascites, 1 organoid) had documented clinical drug responses and were eligible for predictive scoring.

Predictive Scoring and Validation

- A predictive scoring protocol was set prior to evaluating PDO resistance or sensitivity to a panel of chemotherapies and TKIs.
- A python-based, AI-assisted timeline visualization tool mapped each participant's longitudinal clinical history into events over an anonymized timeframe.
- A second review using the visualization tool refined the cohort to 34 PDOs (87 drug scores) for final evaluation.
- Resistant drug scores were prevalent compared to sensitive drug scores due to participant samples collected at advanced disease stage.
- To account for the imbalanced dataset, Balanced Accuracy (Sensitivity + Specificity/2) and Mathews Correlation Coefficient (MCC) were used for final evaluation.

DISCUSSION AND CONCLUSION

Takeaway

- Genetic markers alone are generally insufficient to predict treatment response. Functional drug testing on live cells adds real time, actionable data for treatment selection, supported by 93% predictive accuracy against actual clinical outcomes.

Future Direction

- Patients with advanced NSCLC who have progressed through several lines of therapy need additional decision-support tools.
- Customize treatment selection based on drug sensitivity of live cells grown directly from the patient.
- Next steps include prospective clinical validation of MyOncoPM to estimate sensitivity, specificity, positive predictive value, and negative predictive value across therapies.

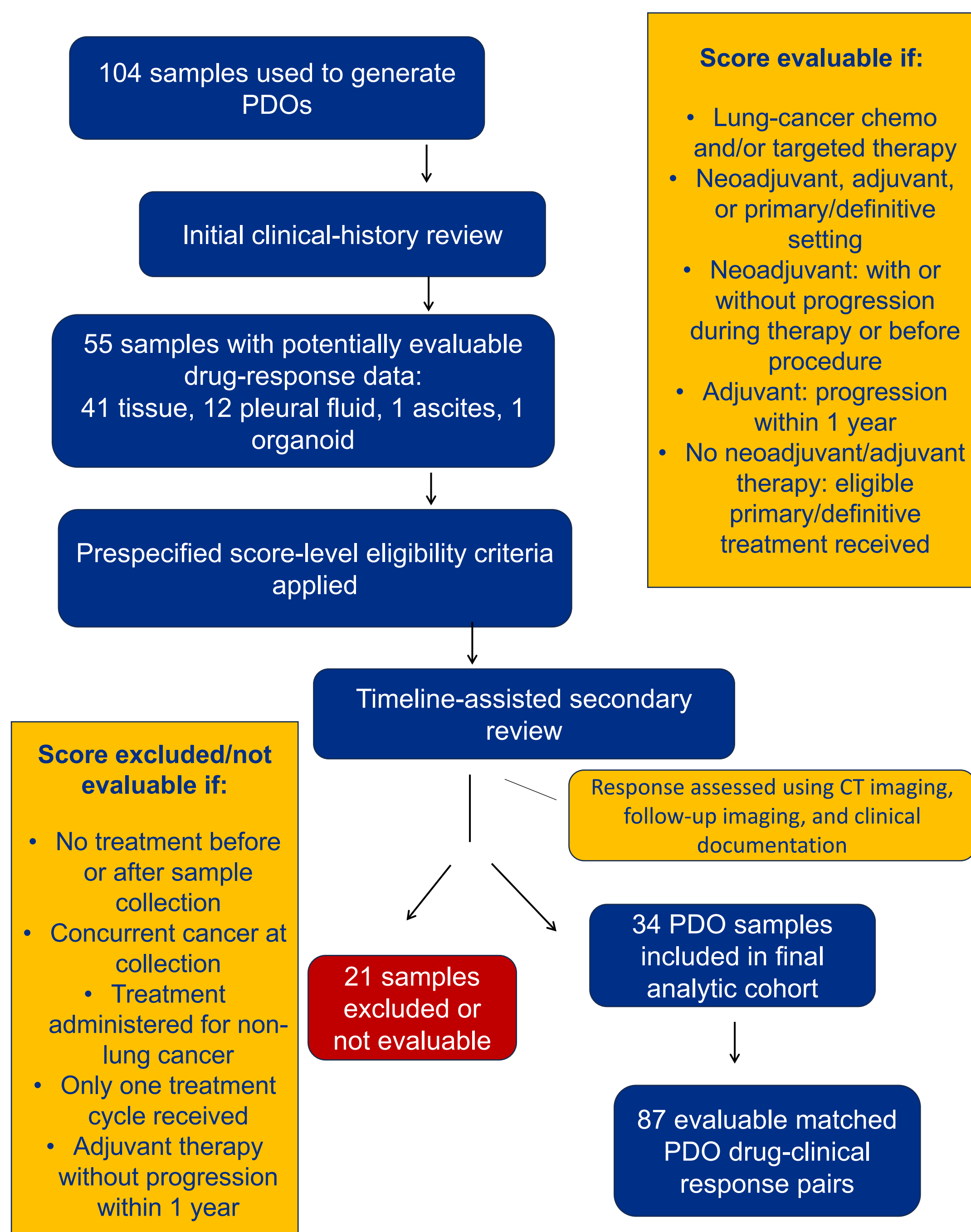


Figure 1. Clinical eligibility and predictive score evaluation workflow.

JTI027-T-01 Timeline

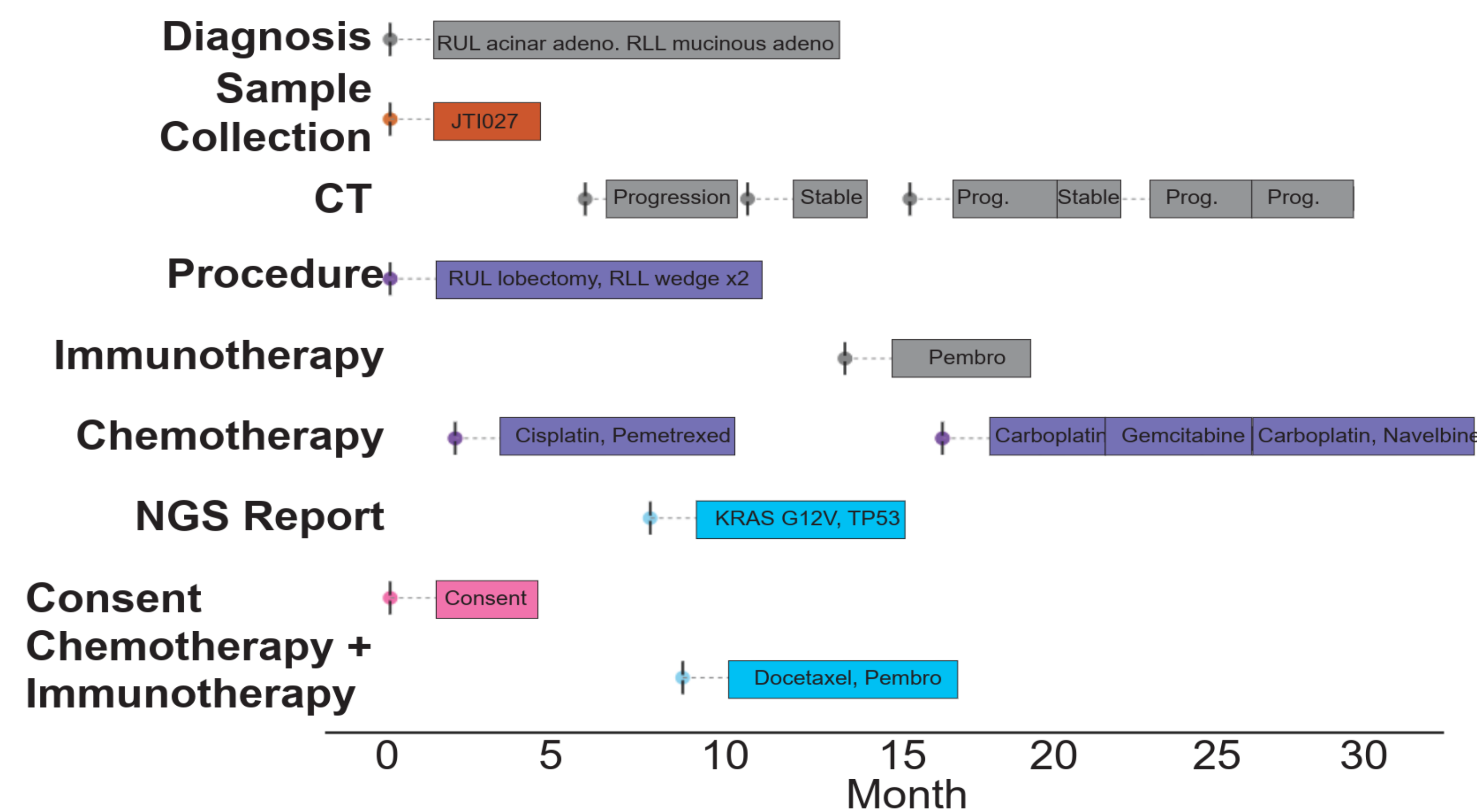


Figure 2. Longitudinal clinical timeline generated by the AI-assisted visualization tool; mapping diagnosis, therapy lines, imaging response/progression, and sample collection over time.

A.

Drug	Evaluated, n	Correct, n (%)
Alectinib	8	8 (100%)
Brigatinib	1	1 (100%)
Carboplatin	18	18 (100%)
Cisplatin	8	5 (62.5)
Crizotinib	1	1 (100%)
Docetaxel	5	5 (100%)
Gemcitabine	6	6 (100%)
Gilteritinib	1	1 (100%)
Lorlatinib	7	7 (100%)
Osimertinib	3	2 (66.7)
Paclitaxel	4	4 (100%)
Pemetrexed	21	20 (95.2%)
TPX-031	2	2 (100%)
Vinorelbine	2	1 (50%)

B.

Clinical Response	Predicted Sensitive	Predicted Resistant	Total
Sensitive	6 (TN)	3 (FN)	9
Resistant	3 (FP)	75 (TN)	78
Total	9	78	87

Sensitivity/PPV: 66.7% | Specificity/NPV: 96.2% | Overall Accuracy: 93.1%

Table 1A-B. Agreement between PDO predictions and clinical response.

RESULTS

- The precision platform accurately predicted drug scores in 93% (81/87) of drug scores, supported by the participants documented clinical history.
- A balanced accuracy of 81%; MCC 0.63 indicating moderate to strong positive correlation.
- Of the 87 drug scores across 34 PDOs, 78 scores were classified as resistant and 9 sensitive to the respective drug(s) received during clinical care.
- Chemotherapies and/or TKIs received during clinical care were significantly associated with MyOncoPM's resistance/sensitivity scores.

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Artificial Intelligence (AI) Use Disclaimer: U-M GPT was used to assist with language editing, poster organization, reference formatting. Replit Agent was used to assist with application-code development. AI was not used for data analysis, interpretation, or generation of study results.