



**2023 World Conference
on Lung Cancer**

SEPTEMBER 9-12, 2023 | SINGAPORE



Pulmonary – From Diagnostics to Therapeutics

Best of WCLC 2023

**Nicholas Stollenwerk, MD
University of California, Davis**





Overview

- 1) Pulmonary nodules evaluation
- 2) Bronchoscopic and pleural interventions



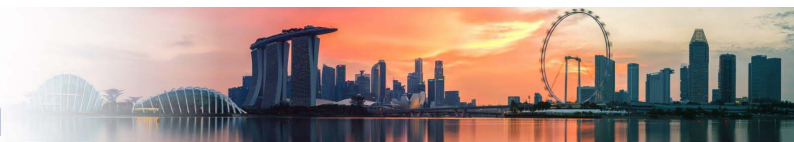


Pulmonary nodules

Incorporating Biomarkers into Lung Cancer Screening: Who Benefits?

Hilary A. Robbins, PhD
International Agency for Research on Cancer
RobbinsH@iarc.who.int

International Agency
for Research on Cancer



Development and validation of a protein-based lung cancer risk prediction model: Initial results from the Lung Cancer Cohort Consortium (LC3)

Hana Zahed, PhD student
International Agency for Research on Cancer (IARC/WHO), Lyon, France

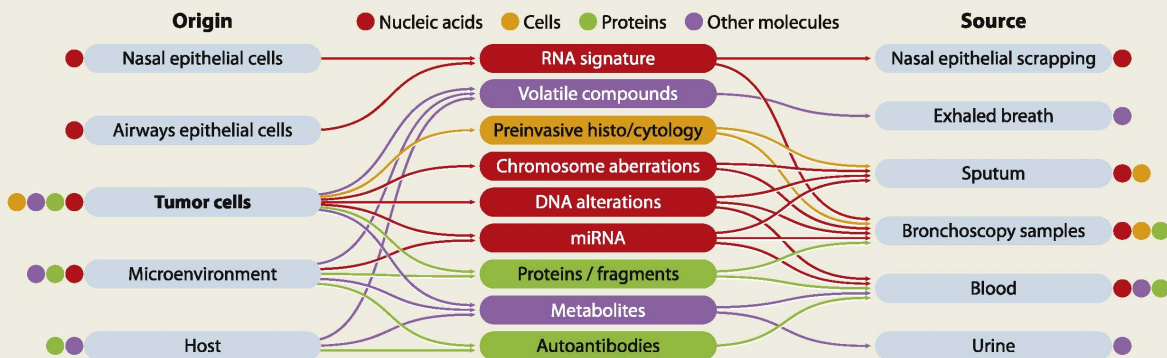
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Pulmonary nodules

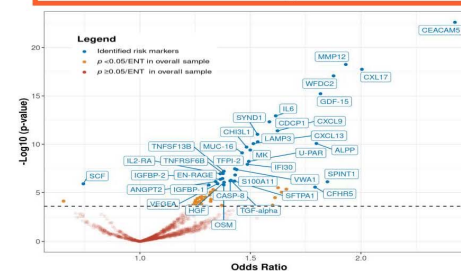
Types of biomarkers proposed for lung screening



Seijo et al, J Thorac Oncol 2019

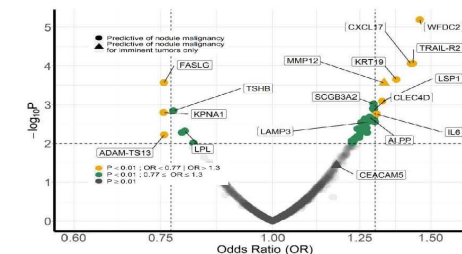
Identification of proteins

Markers for lung cancer risk



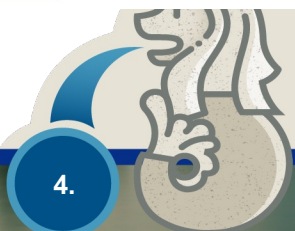
LC3, Nat Commun, 2023

Markers for nodule malignancy



Moez et al., JNCI, 2023

Custom panel
Measures absolute concentrations of 21 selected proteins

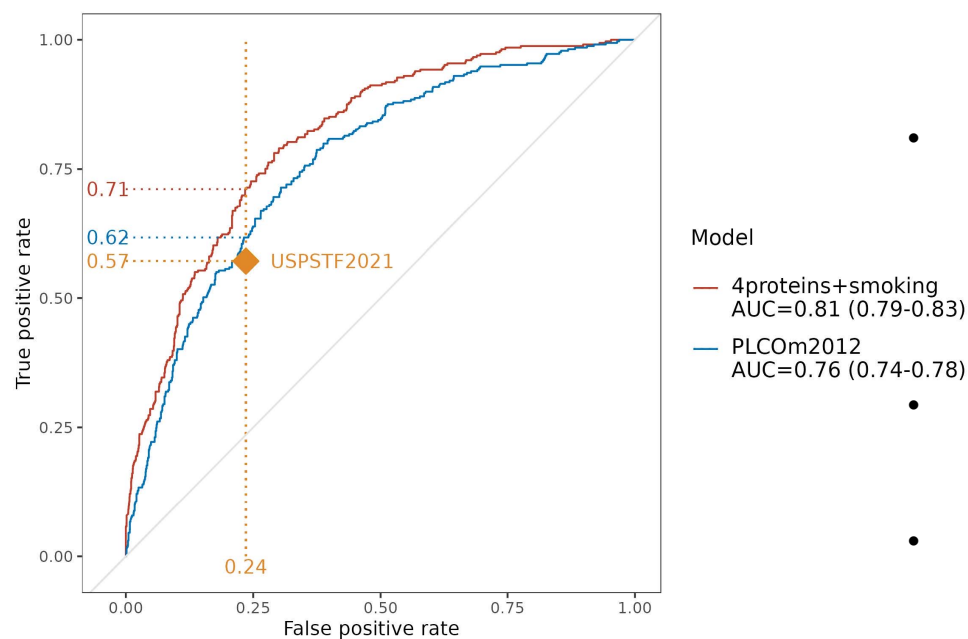




Take home messages:

Performance of **preliminary** model in independent **testing** set (3 cohorts):

- 4 selected proteins: MMP12, CEACAM5, SCF, LPL
- Age, smoking intensity, smoking duration



- Biomarkers offer a promising diagnostic test to augment CT based screening. They can help develop screening plans for high-risk patients that don't meet standard criteria and patients that meet standard criteria, but are otherwise felt to be low risk.
- It is agreed upon by most that lung cancer screening benefits patients.
 - It helps identify early disease in high-risk patients.
 - There are multiple guidelines on who should be screened: NLST, NELSON, USPSTF 2021, and the PCLoM2012 prediction model.
- The data presented by Hilary Robbins, PhD, and Hana Zahed, PhD student, are preliminary, but represent a growing area of study.
- The 4 selected proteins outperforms USPSTF2021 and PLCOm2012. The significance of this is limited at this time, but this is early data.





Pulmonary nodule risk



Development Of A Clinico-Proteo-Metagenomic Classifier For Risk Stratification Of Incidentally-Detected Pulmonary Nodules

Harvey I. Pass MD⁺, Leo Segal MD⁺, Serena Fraraccio*, Stephen Wandro*, Akanksha Singh-Taylor*, Sandrine Miller-Montgomery*, Eddie Adams*, Gregory Sepich-Poore*, Rob Knight*

+NYU Langone Health, New York, *Micronoma, San Diego
USA

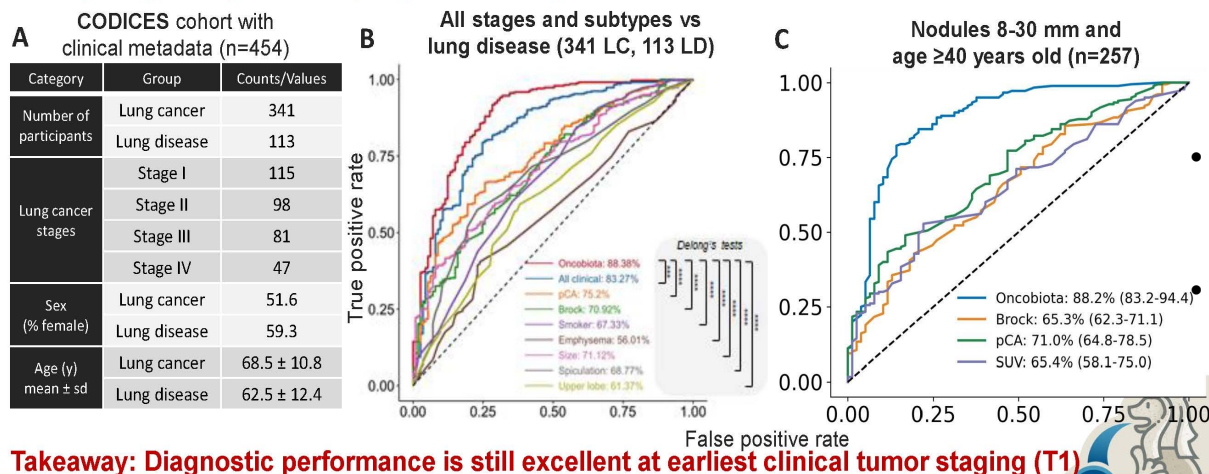
Pass, HI: NYU Langone Health, USA





Take home messages:

Developing a microbe + human, multi-omic diagnostic ("Oncobiota") for early-stage lung cancer (i.e., clinical T1)



There are multiple lung nodule scoring calculators: Brock University, Mayo, VA, Pan Canadian, Peking University Peoples Hospital, and Herder (incorporates PET).

- Accuracy (ROC AUC) ranges are good, but have room for improvement (~0.65-0.79)
- Biomarkers offer a promising diagnostic test to augment CT based screening.

Biomarkers will help with low-risk nodules, and moderate-risk nodules in patients at risk for complication with biopsy.

Currently there is a commercially available blood test that uses proteomics. It utilizes 2 different testing strategies:

- 7 auto antibodies to known cancer proteins. This is helpful in the high-risk patient.
- Ratio of 2 markers is used to further risk stratify, which is helpful for the low-risk patient.

The data presented by Pass, et al., is an example the many possible biomarkers that are to come.

- It outperforms Brock U, PanCA, and PET.



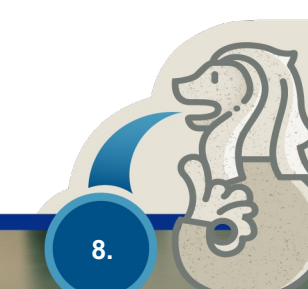


Pulmonary nodule risk



Saliva metabolic profiling for benign and malignant pulmonary nodules distinguish and early lung cancer detection

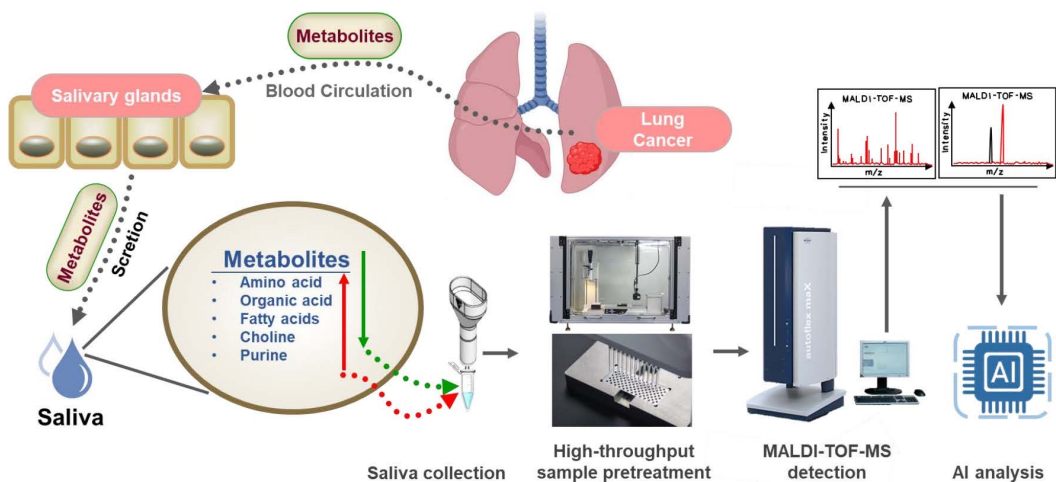
Jianmin Wu
Zhejiang University, Hangzhou
The People's Republic of China





How it works

1. Principle & Methods



High-throughput MS platform for salivary metabolic profiling and lung cancer detection

Home-made collection device:
Metabolites kept stable in 7 days



High-throughput pretreatment:
96 samples treated within 1 h



MALDI-TOF-MS :
Each sample detected within 5 s



AI data analysis : Biomarker
screening & model construction

AI Model: **GA+SVM Algorithm**

- Biomarkers being used include proteomics, metabolomics, cells, autoantibodies, DNA/RNA, and VOCs.
- Wu, et al., has shown that saliva can be used to detect early-stage lung cancer.
- This offers a very non-invasive method.
- They used MALDI-TOF Mass Spec analysis.
- AI was used to assist in the analysis of the MS.





Take home messages:

4. AI model performance

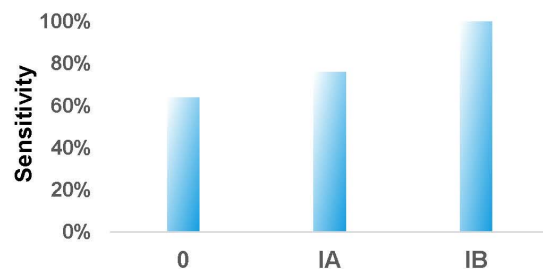


Fig1. Sensitivity of early stage lung cancer

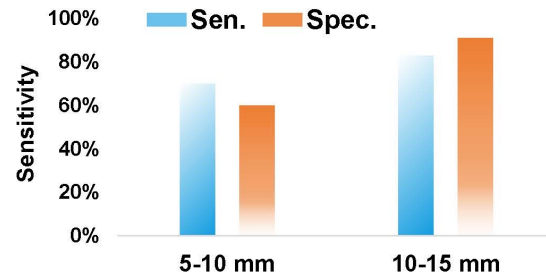


Fig2. Sensitivity and Specificity of pulmonary nodules with size 5-15 mm

Summary:

Saliva metabolic AI model shows high potential in diagnosis of early stage lung cancer and small size of pulmonary nodules

- This non-invasive biomarker test using saliva offers potential screening for early-stage lung cancer and a possible adjunctive test in the evaluation of small pulmonary nodules.
- The sensitivity is not adequate to be used alone, but this method offers future potential.



What about other thoracic malignancies



Using a breath test to potentially screen an asbestos-exposed population for Pleural Mesothelioma.

Kevin Lamote, PhD

Laboratory Experimental Medicine & Pediatrics
University of Antwerp, Belgium





Take home messages:

Results

Model Characteristics Value (95% Confidence interval)

Sensitivity	1.000 (0.652 – 1.000)
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Potential use to rule out disease in an at-risk population

Negative Predictive Value	1.000 (0.950 – 1.000)
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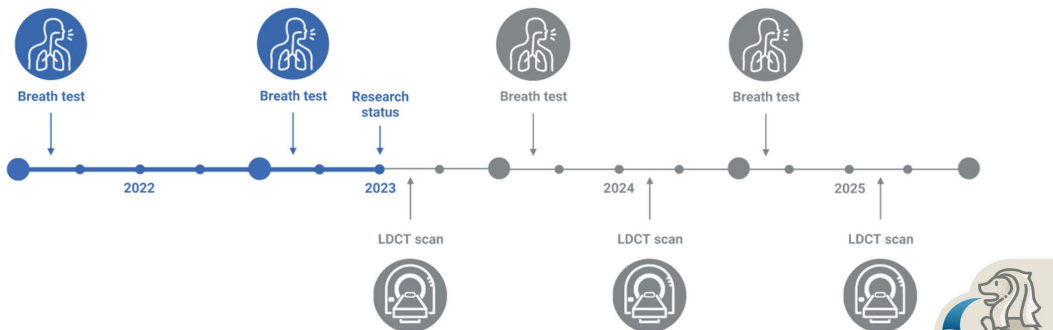
Accuracy	0.291 (0.235 – 0.354)
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AUC _{ROC}	0.791 (0.735 – 0.847)
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- Mesothelioma is difficult to diagnose.
 - No blood testing available
 - Imaging is often inconclusive
 - Biopsy can require thoracotomy
- Screening high-risk asbestos-exposed populations requires a highly sensitive test with a high NPV.
 - It should also be minimally invasive and readily available.
 - Lamonte, et al., has shown exhaled breath analysis of Volatile Organic Compounds (VOCs) offers a test with high NPV.
- Potentially an algorithm using repeat testing and low-dose CT scan be used.
 - This will help triage more invasive procedures like pleural biopsy and thoracotomy.

Future perspectives

Correlation of breath test results to CT imaging of double positive participants





Bronchoscopic Therapeutics

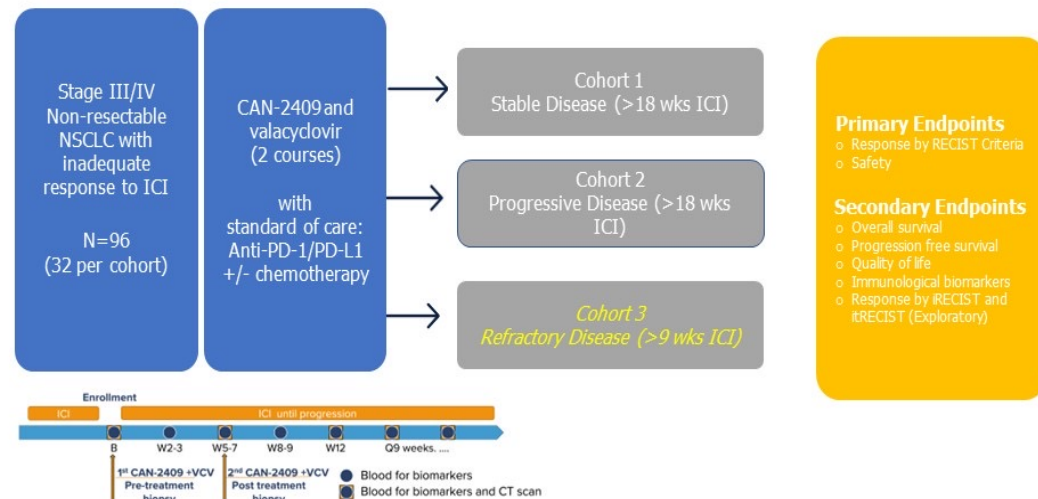


Therapeutic Bronchoscopic Interventions for Modification of Tumor and Nodal Microenvironments in Non-Small Cell Lung Cancer

Daniel H. Sterman, MD
 Thomas and Suzanne Murphy Professor of Pulmonary & Critical Care Medicine
 Departments of Medicine and Cardiothoracic Surgery
 Director, Division of Pulmonary, Critical Care, and Sleep Medicine
 Principal Investigator, NYU Pulmonary Oncology Research Team (PORT)
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 New York, NY USA
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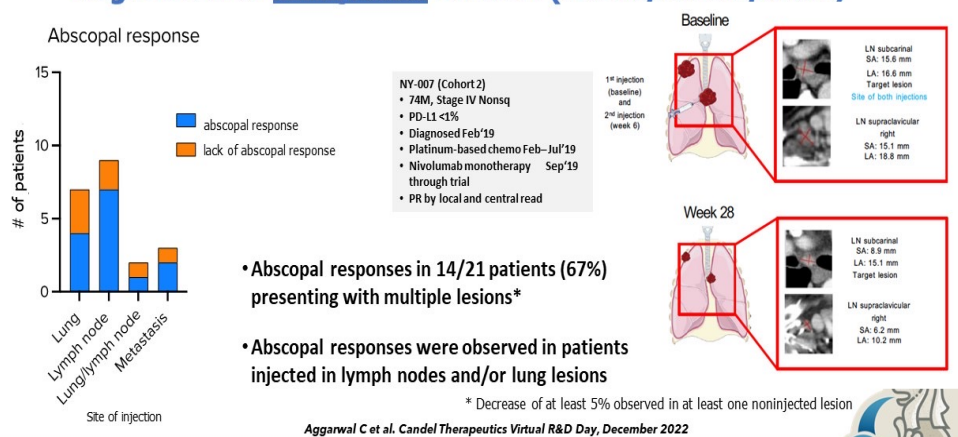
Ongoing Multicenter Phase 2 Clinical Trial of IT CAN-2409 in Combination with ICI in Stage III/IV NSCLC





Take home messages:

Regression of Uninjected Lesions (*Abscopal Response*)



• Abscopal responses in 14/21 patients (67%) presenting with multiple lesions*

• Abscopal responses were observed in patients injected in lymph nodes and/or lung lesions

Preliminary Conclusions LuTK02 Trial:

- Intralesional CAN-2409 plus valacyclovir in patients with advanced NSCLC and an inadequate response to first-line checkpoint inhibitor appears to be well-tolerated
- Promising clinical activity in the first 20 evaluable patients:
 - Evidence for disease regression in both injected and uninjected lesions (abscopal effect)
 - In Cohort 2 (patients who entered the study with progressive disease), a DCR of 87.5% with durable disease stabilization ongoing in 10 out of 16 patients
 - PR in 3 patients
 - Boosted CD8+T cell infiltration in the TME and increased levels of activated T cells in the peripheral blood
- Phase III Randomized Controlled Trial in Planning Stages
- Potential Applications in Multimodality Therapy of Early-Stage Lung Cancer

Aggarwal C et al. Candel Therapeutics Virtual R&D Day, December 2022

- Bronchoscopic interventions for lung cancer are currently in early-stage clinical trials.
- Current endobronchial treatments include brachytherapy and photodynamic therapy.
- Treatments including radiofrequency ablation, microwave ablation, cryotherapy, electroporation, and endoluminal injections are being studied.
- They are not standard of care and there is no current data to suggest they will replace surgery or stereotactic radiosurgery.
- Dr. Sterman has presented data from the Phase 2 Clinical Trial of IT CAN-2409 that shows intralesional CAN-2409 is a promising adjunct to treatment.
- Bronchoscopic intervention represents possible treatments for patients that can not tolerate surgery or SRS, in early disease, and as possible adjunctive therapies in the multimodal treatment of lung cancer.





Pleural Therapeutics



Retrospective Analysis of Intrapleural Administration of Hypotonic Cisplatin for Malignant Pleural Effusions with Nonexpandable Lung

○Wataru Mori, Tomoyasu Mimori, Jun Ito, Yoshihiro Masui, Taichi Miyawaki, Takehito Shukuya & Kazuhisa Takahashi

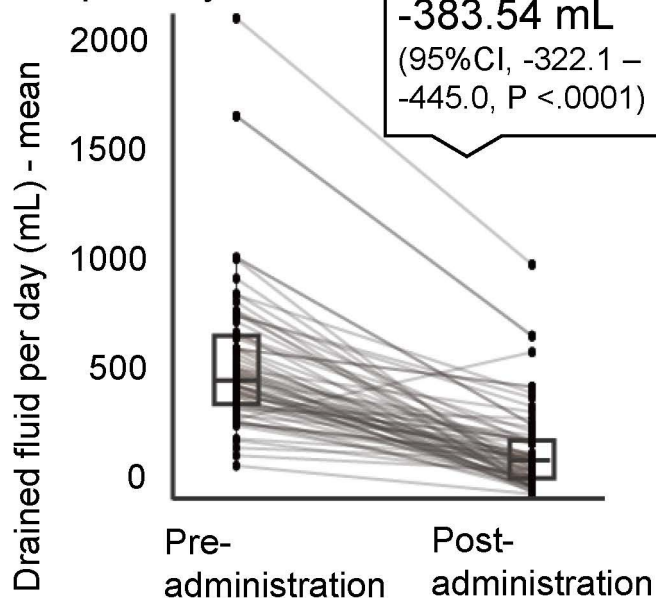
Department of Respiratory Medicine, Juntendo University, Japan
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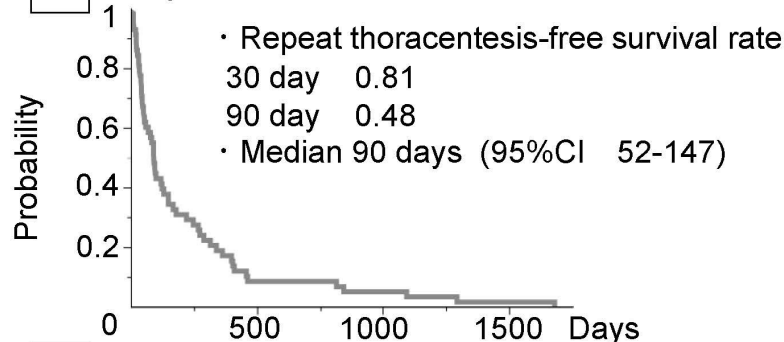


Take home messages:

3 The mean amount of drained fluid per day



4 Repeat thoracentesis-free survival



5 Adverse events

Empyema	4 (6.5)
Interstitial pneumonia	3 (4.8)
Skin metastasis	2 (3.2)



- Malignant pleural effusion represents advanced stage cancer with a poor prognosis. Patients are symptomatic and often require repeated drainage, indwelling pleural catheters, and possible chemical pleurodesis. Chemical pleurodesis is much less effective in trapped lung.

- Mori, et al., retrospectively analyzed a cohort of patients with trapped lung treated with hypotonic cisplatin. They showed a decrease in fluid output and decreased need for repeat thoracentesis. Adverse events were seen in 6.5% of patients, mainly empyema, which is a barrier to implementation.





Take Home Messages

- ✓ Biomarkers offer a promising adjunct for both lung cancer screening and pulmonary nodule risk stratification.
- ✓ Using the term biomarker is an oversimplification.
 - ✓ Methods include serum testing, nasal and airway epithelial cells, saliva, and exhaled breath analysis.
 - ✓ Testing is employing evaluation of metabolomics, proteomics, autoantibodies, DNA alterations, RNA signatures, microRNA, VOCs, and the implementation of AI.
 - ✓ This is a very active area of investigation that offers a lot of promise.
- ✓ Bronchoscopic interventions for the treatment of lung cancer appear to offer possible adjunctive therapies in the multimodal treatment of lung cancer.

