

P2.18: Phase III trial of systemic therapy ± primary tumor resection for NSCLC with radiologically undetermined pleural dissemination (JCOG2103)

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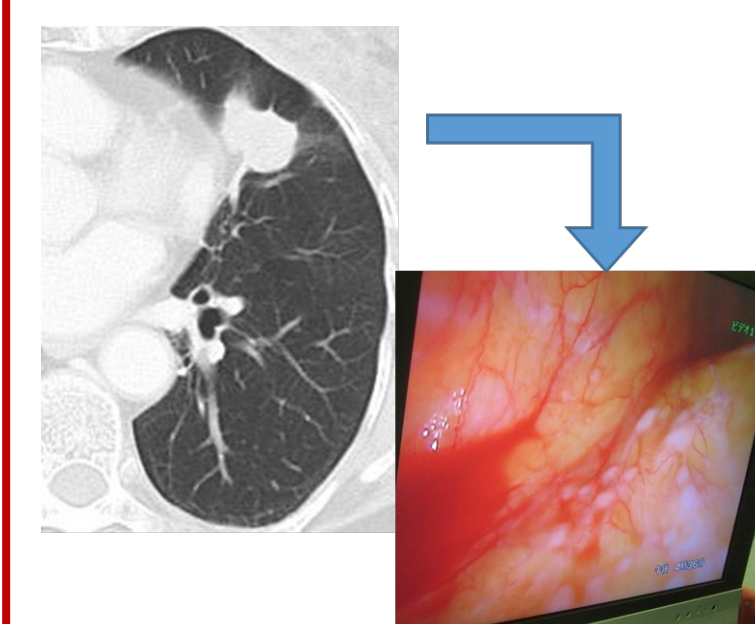
INTRODUCTION

Toward cure in low-volume pleural dissemination?

Types of NSCLC with pleural dissemination (PD)

Pattern 1

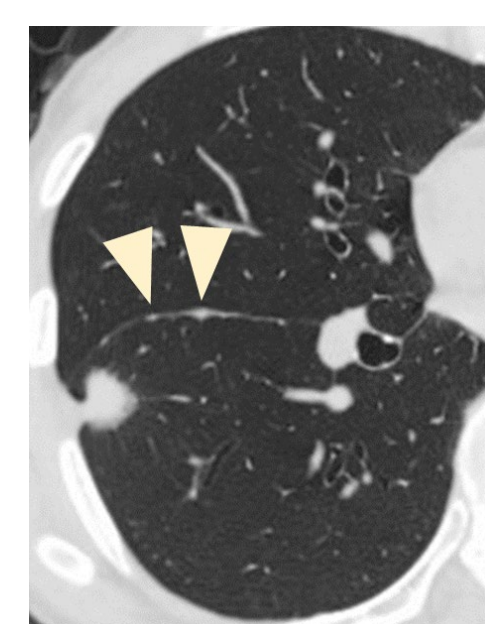
- No radiological findings suggestive of PD
- Curative-intent surgery initiated
- Unexpected PD at surgery



Radiologically undetermined PD (RUPD)

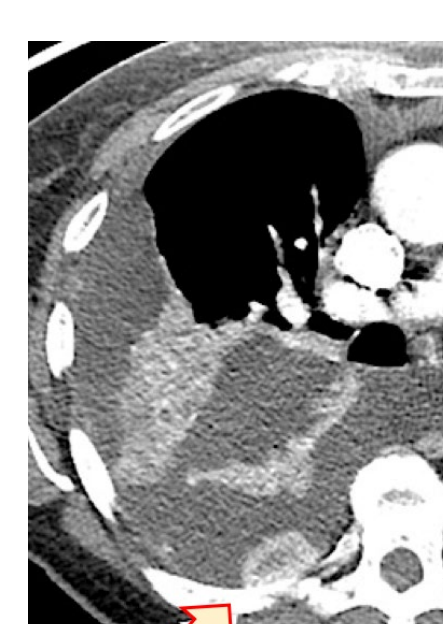
Pattern 2

- Possible PD but small pleural nodules on CT (≤ 10 mm)
- PD confirmed by thoracoscopy



Pattern 3

- Overt PD
- Large pleural nodules on CT (>10 mm)
- Grade 2 or higher pleural effusion



- **RUPD is characterized by:**
 - **Minimal PD and occult disease on preoperative imaging**
 - **A distinct low-volume subset of M1a disease.**
- Systemic therapy remains the standard treatment for RUPD.
- Retrospective studies have suggested a potential survival benefit from primary tumor resection in selected RUPD.

Modern systemic therapy + primary tumor resection
→ Improved local control → Longer survival?
Prospective evidence is lacking

PATIENTS and METHODS

Main eligibility criteria

- cT1-2bN0-1M1a (stage IVA) NSCLC with RUPD (patterns 1 and 2)
- Histological diagnosis of PD by thorascopic or open chest biopsy (positive pleural cytology alone is not acceptable)
- No prior treatment

Endpoint:

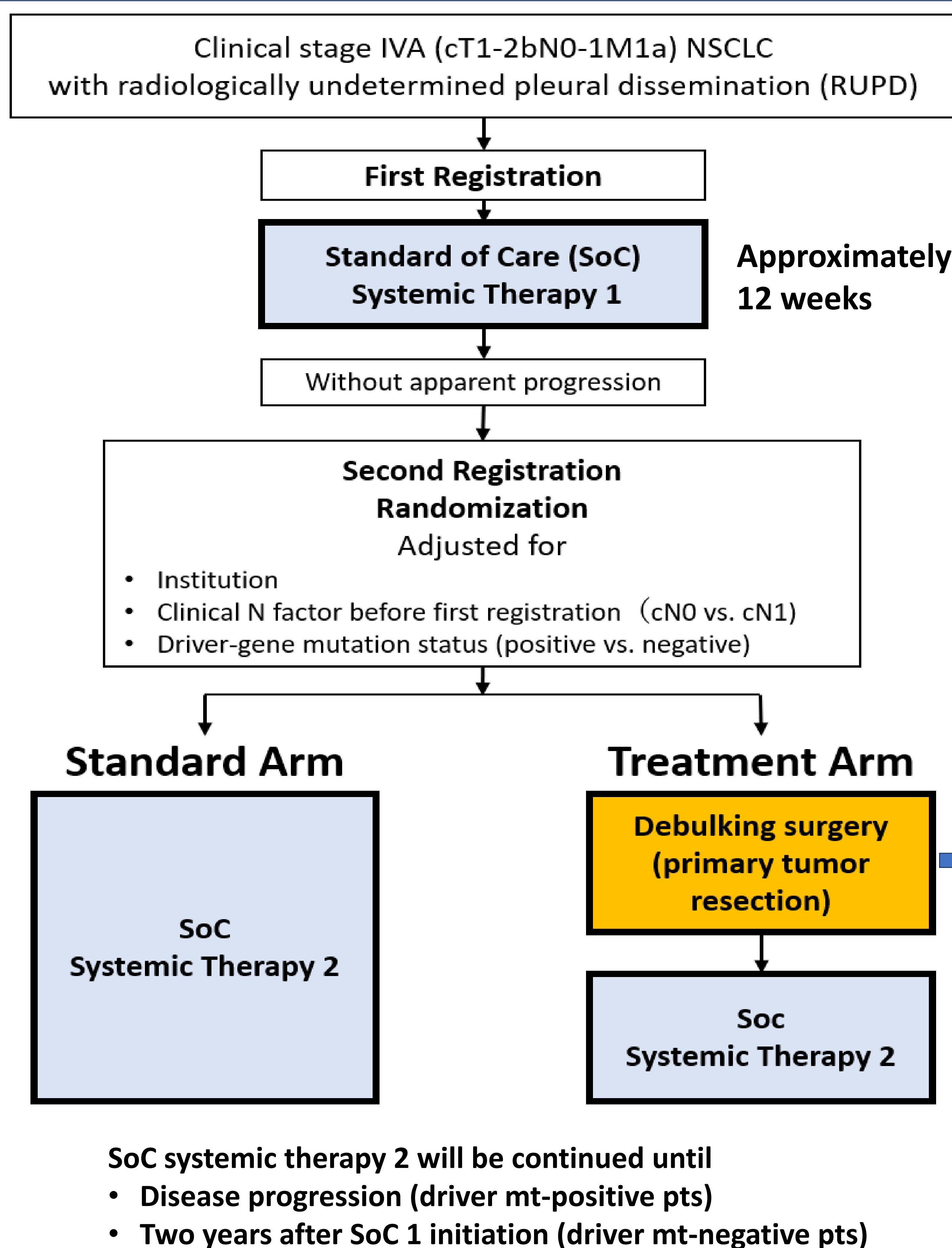
- **Primary: overall survival (OS)**
- Secondary: progression-free survival, local progression-free survival, distant progression-free survival, cumulative incidence proportion of pleural effusion (Grade 2 or above), adverse events and quality of life (EQ-5D, FACT-L).

Statistics

- 3-year OS: 50%→65%, one-sided α : 5%, power: 70%
- Planned accrual period: 5 years, follow-up: 3 years
- Sample size: 170 (1st registration) and 140 (randomized)

STUDY DESIGN

- The Japan Registry of Clinical Trials (JRCT) number JRCTs031220666.
- Supported by AMED under Grant Number (25ck0106942h0002 and 24ck0106942h0001)

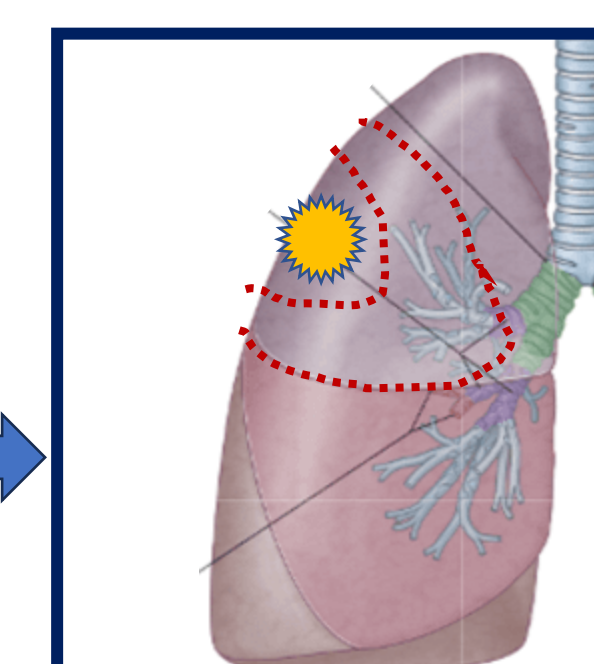


Regimens of standard of care (SoC) systemic therapy

	SoC systemic therapy1	SoC systemic therapy 2
Driver mutation-positive	Targeted therapy (TKI)	
EGFR (ex19 del, L858R($\pm$ T790M)) ^{1,2}	Osimertinib	
EGFR (ex18-21 (except for 19 del, L 858R, ex20)) ¹	Afatinib	
ALK	Alectinib	
ROS1	Crizotinib	
BRAF (V600E)	Dabrafenib + Trametinib	
MET (ex14 skip)	Tepotinib	
RET	Selpercatinib	
Driver mutation-negative	Chemotherapy+ ICI	ICI maintenance
Non-Squamous cell carcinoma	CBDCA + Pemetrexed + Pembrolizumab	Pemetrexed + Pembrolizumab
	CBDCA + Nab-paclitaxel + Atezolizumab	Atezolizumab
Squamous cell carcinoma	CBDCA + Nab-paclitaxel + Pembrolizumab or CBDCA + Paclitaxel + Pembrolizumab	Pembrolizumab

¹Any unlisted EGFR gene mutations are classified as EGFR-mutation negative.

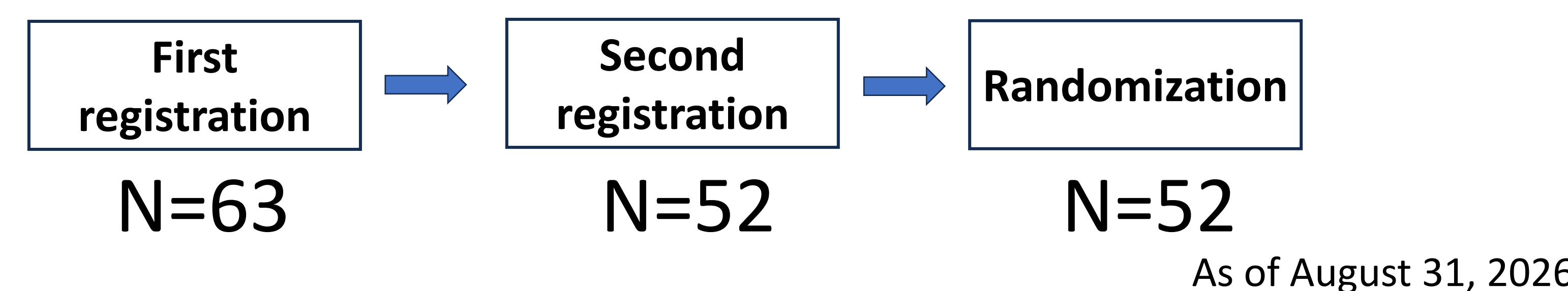
²Osimertinib + cis-based chemotherapy (FLAURA2 regimen) will be adapted in next protocol amendment.



- **Limited lung resection (LR, wedge or segmentectomy)**
 - If LR is not feasible, lobectomy is allowed.
- **Lymph node dissection is not required.**
 - In cN1 cases, clinically involved N1 nodes should be resected.

Enrollment status

- Joint study by 71 institutions in JCOG-LCSSG and JCOG-LCSG
- Enrollment initiation: March 2023



TAKE AWAY MESSAGE

- JCOG2103 is the first randomized phase III trial evaluating the role of primary tumor resection in c-stage IVA NSCLC with RUPD.
- This trial may establish a new treatment paradigm integrating systemic therapy with primary tumor resection for selected stage IV disease.

REFERENCES

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Conflict of Interest (COI) Statement

The authors declare no COI associated with this presentation.

Artificial Intelligence (AI) Use Disclosure

Generative AI (ChatGPT-Plus) was used only for English editing. The authors review and accept full responsibility for the final content.

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Protocol summary

