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Clarification of oligometastasis showing survival benefit from local ablative therapies during tyrosine kinase inhibitor treatment

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Background

Oligometastasis (OM)

- A result of acquired resistance during tyrosine kinase inhibitor (TKI) treatment in patients with metastatic non-small cell lung cancer (NSCLC)

Local ablative therapy (LAT) with TKI maintenance

- A reasonable option with significantly improved clinical benefit for these patients

Lack of universal criteria for OM

- Significant challenges in determining treatment paradigms for specific patient groups

Aim

We analyzed **the feasibility of the current four OM criteria**

in assessing the clear survival benefit by LAT during TKI treatment

Methods

Retrospective study

- Patients with advanced NSCLC treated by LAT for oligometastatic lesions during TKI therapy between January 2011 and December 2020 at Asan Medical Center

The four following criteria of oligometastic disease

- TNM: M1a and M1b according to the 8th edition of TNM staging
- EORTC-LCG: Presence of ≤ 5 lesions in 1–3 organs
- NCCN: Up to three metastatic lesions
- ORGAN: A single extra-thoracic organ regardless of the number of lesions

Methods

Primary outcome

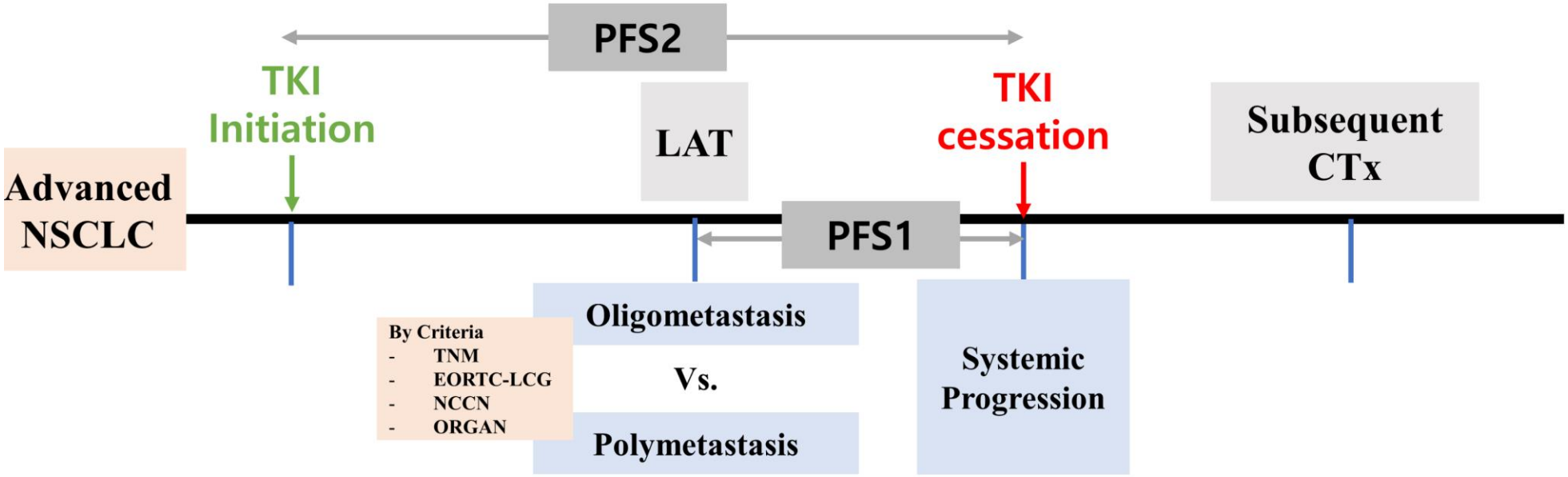
- Overall survival (OS) between the OM and non-OM under the four criteria

Secondary outcomes

- Progression-free survival (PFS)
  from OM to systemic progression (PFS1),
  from TKI to systemic progression (PFS2)
- Association between the number of involved organs and outcomes.

Methods

The schema of this study



Results

Table 1. Baseline characteristics

	Total (n = 117)
Age, mean ± standard deviation	59.3 ± 10.1
Female, n (%)	69 (59.0%)
Pathology of Adenocarcinoma	116 (99.1)
Metastasis stage of TNM 8th, n (%)	115 (98.3)
TKI treatment as 1st line, n (%)	88 (75.2)
Type of TKI, n (%)	
EGFR TKI/ALK TKI	97 (82.9)/20 (17.1)
Site of local ablative therapy (n = 120)	
Bone/Lung/Brain/Other	24 (20.0)/21 (17.5)/68 (56.7)/7 (5.8)
Type of local ablative therapy (n = 119)	
Operation/Radiotherapy/Radiosurgery	7 (6.0)/68 (58.1)/44 (37.6)

TKI = tyrosine kinase inhibitor, TNM = Tumor, Node, Metastasis, EGFR = epidermal growth factor receptor, ALK = anaplastic lymphoma receptor tyrosine kinase. *Others included pleura, lymph node, adrenal gland, and ileum.

Results

Table 2. Clinical outcomes for the entire cohort	
	Total (n = 117)
Overall survival	70.8 months (95% CI 56.6-85.1 months)
Progression-free survival 1	10.3 months (95% 5.5-15.1 months)
Progression-free survival 2	30.9 months (95% CI 20.6-41.1 months)

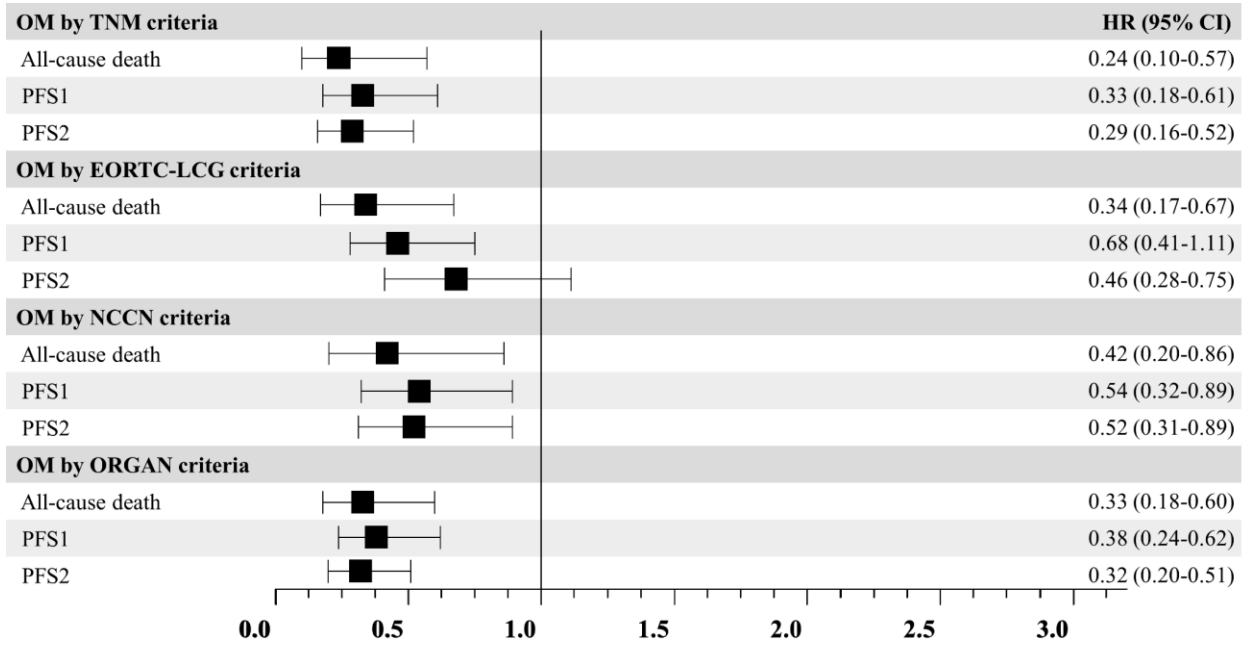
CI = confidence interval

Table 3. Profiles of patients according to the four criteria		
	OM group	**Non-OM group**
TNM criteria	30 (25.6%)	87 (74.4%)
EORTC-LCG criteria	42 (35.9%)	75 (64.1%)
NCCN criteria	34 (29.1%)	83 (70.9%)
ORGAN criteria	71 (60.7%)	46 (39.3%)

OM = Oligometastasis, Non-OM = Non-oligometastasis

Results

Figure 1. Risk-adjusted hazard ratios associated with clinical outcomes according to the criterion of oligometastasis. A hazard ratio of less than 1.00 indicates a lower risk of clinical outcomes with oligometastasis group than non-oligometastaic group



OM = Oligometastasis, PFS = progression-free survival, OS = overall survival, HR = hazard ratio, CI = confidence interval

Table 4. Cox Proportional-Hazards Analysis of the number of involved organs and outcomes

	PFS2	OS
	Adjusted HR (95% CI)	**Adjusted HR (95% CI)**
Number of extra-thoracic metastatic organs		
1 (n = 57)	1.38 (0.61-3.13)	1.97 (0.59-6.62)
2 (n = 33)	4.32 (1.80-10.35)	5.28 (1.49-18.62)
3 (n = 9)	2.98 (1.08-8.26)	3.01 (0.67-13.59)
4 (n = 4)	15.20 (4.11-56.24)	21.27 (4.50-100.60)

PFS = progression-free survival, OS = overall survival, HR = hazard ratio, CI = confidence interval

Conclusion

Our results found that **patients with OM defined by all four criteria** showed prognostic benefits from LAT during TKI therapy

In addition, **the increased number of extra-thoracic metastatic organs to two or more** was an independent predictive factor for worse outcomes