Changes in Patient Reported Outcomes Relative to the Time of Disease Progression in Non-Small Cell Lung Cancer

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Disclosures

J. Schuchard, S.C. Bolge, M. Ennis, S. Kumar, S. Sethi, S. Shah, and M. Withelder are employees of Johnson and Johnson companies and may hold stock or other ownership interests

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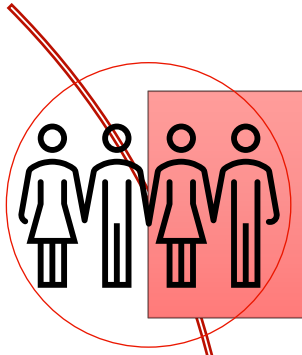
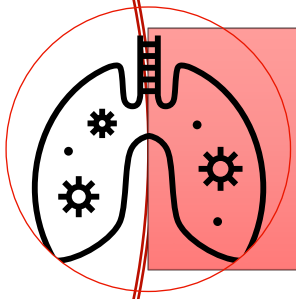
How do we measure efficacy in cancer clinical trials?



Overall survival (OS): The time from randomization until death

--Most reliable endpoint for cancer (FDA, 2018)

--Measurement often requires large sample sizes and lengthy timelines



Progression free survival (PFS): The time from randomization until disease progression or death

--Measured using radiographic tumor assessments

--Not universally accepted as being patient relevant (Giuliani et al., 2018; Hwang & Gyawal, 2019; Kovic et al., 2018)

Disease symptoms and impacts on **health-related quality of life** (HRQoL)

--Typically measured using patient-reported outcomes (PROs)

--In prior studies, measurement often ended at the time of disease progression (Marschner et al., 2020)

Study Objective and Data

- **Study objective:** Assess how symptoms and functioning change relative to the time of radiographic disease progression in non-small cell lung cancer (NSCLC)
- **Data sources:** Two randomized, phase 3 clinical trials evaluating amivantamab-based treatment regimens in adult patients with EGFR-mutant advanced NSCLC
  - MARIPOSA (NCT04487080): first-line treatment (Cho et al., 2024)
  - MARIPOSA-2 (NCT04988295): second-line treatment (Passaro et al., 2024)

Key Variables	Assessment
Core PROs (FDA, 2024): EORTC QLQ-C30 global health status, physical functioning, role functioning (Aaronson et al., 1993) NSCLC-SAQ total lung cancer symptom severity (Bushnell et al., 2021; McCarrier et al., 2016)	MARIPOSA: Every 8 weeks on treatment & every 12 weeks for one year after study treatment discontinuation MARIPOSA-2: Every 3 weeks on treatment & every 12 weeks for one year after disease progression
Disease progression date based on blinded independent central review	MARIPOSA: Every 8 weeks for the first 30 months and then every 12 weeks MARIPOSA-2: Every 6 weeks for the first 12 months and then every 12 weeks
Sociodemographic and clinical covariates: Age, sex, race/ethnicity, Eastern Cooperative Oncology Group (ECOG) score, history of smoking, history of brain metastasis, mutation type, and line of therapy (first/second)	At screening/baseline

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Statistical Analyses

- Longitudinal piecewise mixed effects models were used to evaluate change in PRO measure scores relative to time of disease progression
  - 0 = disease progression date
  - Negative time values = Months pre-progression
  - Positive time values = Months post-progression
- Fixed effect predictors
  - treatment group*
  - study randomization factors
  - patient age
- Fixed/random piecewise time estimates:
  - Pre-progression linear effect
  - Pre-progression quadratic effect
  - Post-progression linear effect
- Statistical significance $p < 0.05$ with no correction for multiple comparisons

**Treatment-by-time interactions were also tested. No notable differences in time trends across treatment groups were observed.*

Participants

- **Analysis 1:** Subset of MARIPOSA participants who experienced disease progression
- **Analysis 2:** Subset of MARIPOSA participants who experienced intracranial disease progression
- **Analysis 3:** Replication of Analysis 2 with subset of MARIPOSA-2 participants who experienced intracranial disease progression

Participant Characteristics

	MARIPOSA		MARIPOSA-2
	Disease Progressed (N=590)	Intracranial Progressed (N=135)	Intracranial Progressed (N=105)
Age (years), Mean (SD)	62.1 (11.0)	61.4 (10.9)	59.3 (10.7)
Race, n (%)			
Asian	333 (56.4%)	80 (59.3%)	53 (50.5%)
White	239 (40.5%)	51 (37.8%)	48 (45.7%)
Other	18 (3.1%)	4 (3.0)	4 (3.8)
Sex, n (%)			
Male	255 (43.2%)	67 (49.6%)	36 (34.3%)
Female	335 (56.8%)	68 (50.4%)	69 (65.7%)
Baseline ECOG, n (%)			
0	181 (30.7%)	46 (34.1%)	39 (37.1%)
1	409 (69.3%)	89 (65.9%)	66 (62.9%)
Treatment Group*, n (%)			
Amivantamab and Lazertinib	203 (34.4%)	58 (43.0%)	29 (27.6%)
Group 2	260 (44.1%)	53 (39.3%)	18 (17.1%)
Group 3	127 (21.5%)	24 (17.8%)	58 (55.2%)

Notes. All results are presented as n(%) unless otherwise specified. ECOG = Eastern Cooperative Oncology Group (ECOG) Performance Status. N = total sample size. SD = standard deviation. *In MARIPOSA, Group 2 = Osimertinib, Group 3 = Lazertinib. In MARIPOSA-2, Amivantamab and Lazertinib are also combined with Carboplatin and Pemetrexed; Group 2 = Amivantamab, Carboplatin and Pemetrexed, Group 3 = Carboplatin and Pemetrexed.

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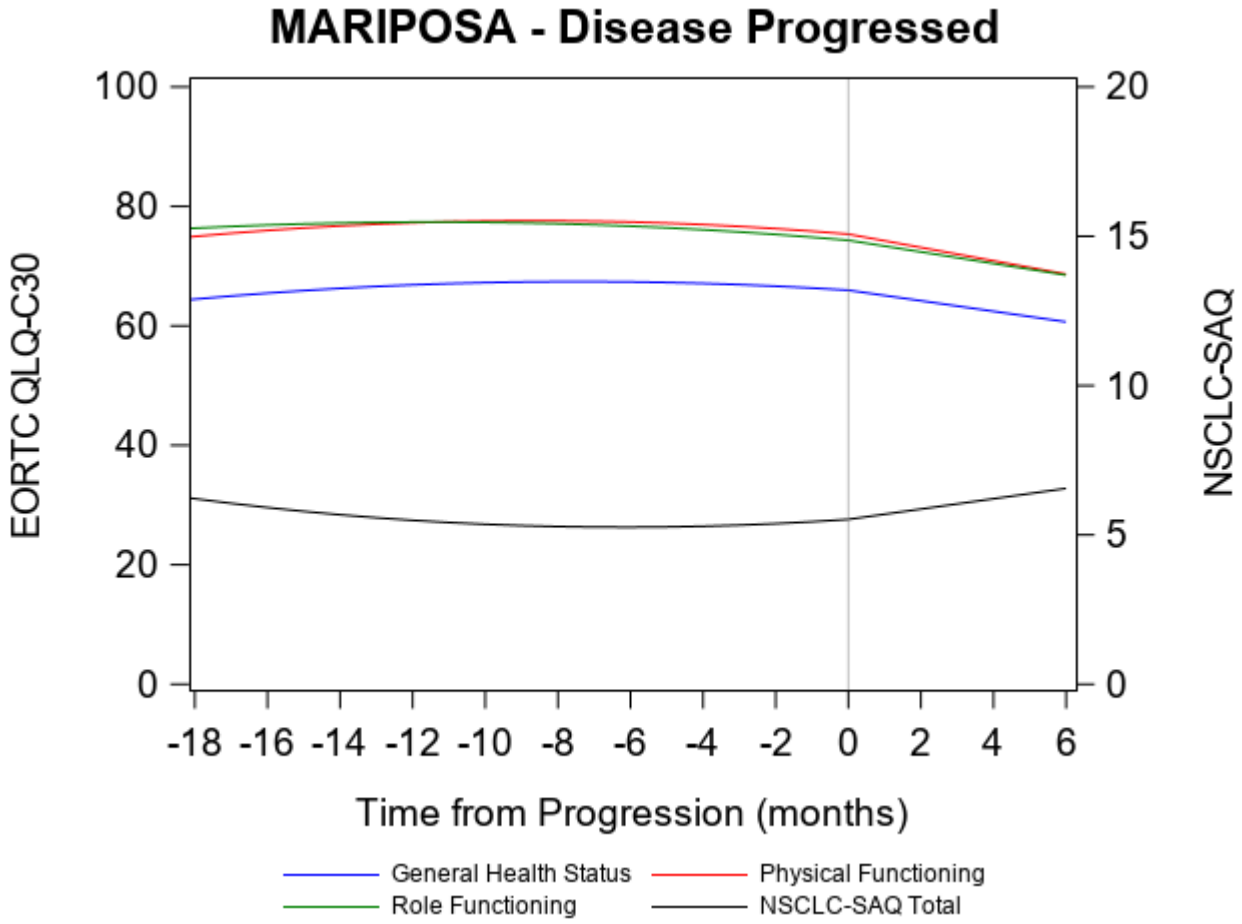
PROs worsened leading up to, at the time of, and after disease progression

MARIPOSA – Disease Progression

- All three piecewise slopes were statistically significant and in the projected direction for all scores
  - *Pre-Progression*: Scores worsened more and more leading up to progression (quadratic effect; all p<0.01) and at the time of progression (linear effect; all p<0.001)
  - *Post-Progression*: Scores continued to worsen post-progression (linear effect; all p<0.001)

	Disease Progression			
	Global Health Est(SE), P	Physical Function Est(SE), P	Role Function Est(SE), P	Lung Symptoms Est(SE), P
Pre-Linear	-0.39(0.12), 0.0007	-0.52(0.12), <0.0001	-0.54(0.16), 0.0008	0.08(0.02), <0.0001
Pre-Quadratic	-0.03(0.01), <0.0001	-0.03(0.01), <0.0001	-0.02(0.01), 0.0065	0.01(0.00), <0.0001
Post-Linear	-0.88(0.13), <0.0001	-1.12(0.17), <0.0001	-0.97(0.20), <0.0001	0.17(0.03), <0.0001

Notes. Est = Estimate. SE = Standard error. P = p-value.



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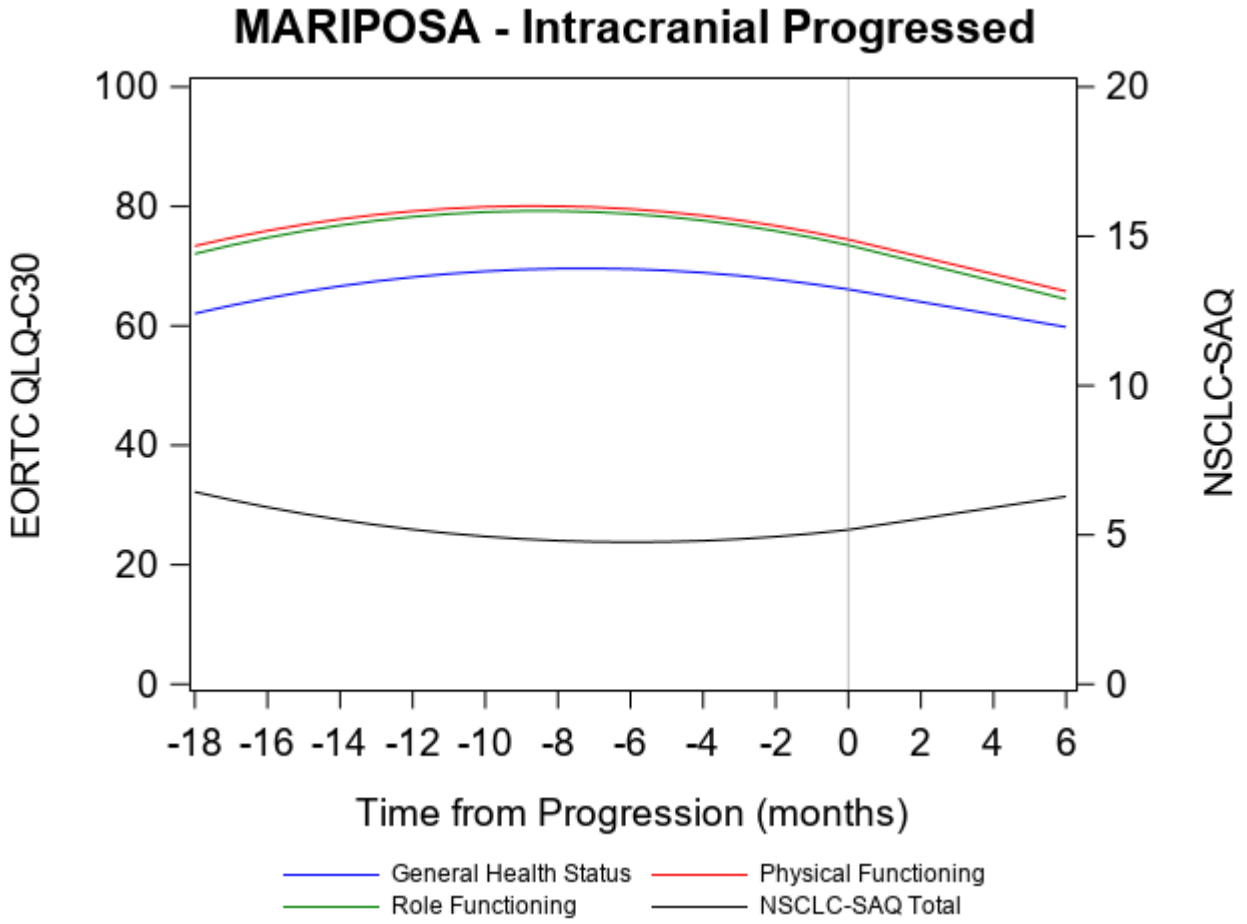
PROs worsened leading up to, at the time of, and after intracranial disease progression

MARIPOSA – Intracranial Progression

- All three piecewise slopes were statistically significant and in the projected direction for all scores
  - *Pre-Progression*: Scores worsened more and more leading up to progression (quadratic effect; all p<0.001) and at the time of progression (linear effect; all p<0.01)
  - *Post-Progression*: Scores continued to worsen post-progression (linear effect; all p<0.001)

	Intracranial Progression			
	Global Health Est(SE), P	Physical Function Est(SE), P	Role Function Est(SE), P	Lung Symptoms Est(SE), P
Pre-Linear	-0.96(0.25), 0.0002	-1.31(0.27), <0.0001	-1.35(0.36), 0.0002	0.14(0.04), 0.0021
Pre-Quadratic	-0.07(0.02), <0.0001	-0.08(0.02), <0.0001	-0.08(0.02), 0.0003	0.01(0.00), <0.0001
Post-Linear	-1.05(0.26), 0.0002	-1.44(0.31), <0.0001	-1.51(0.36), 0.0001	0.19(0.05), 0.0008

Notes. Est = Estimate. SE = Standard error. P = p-value.



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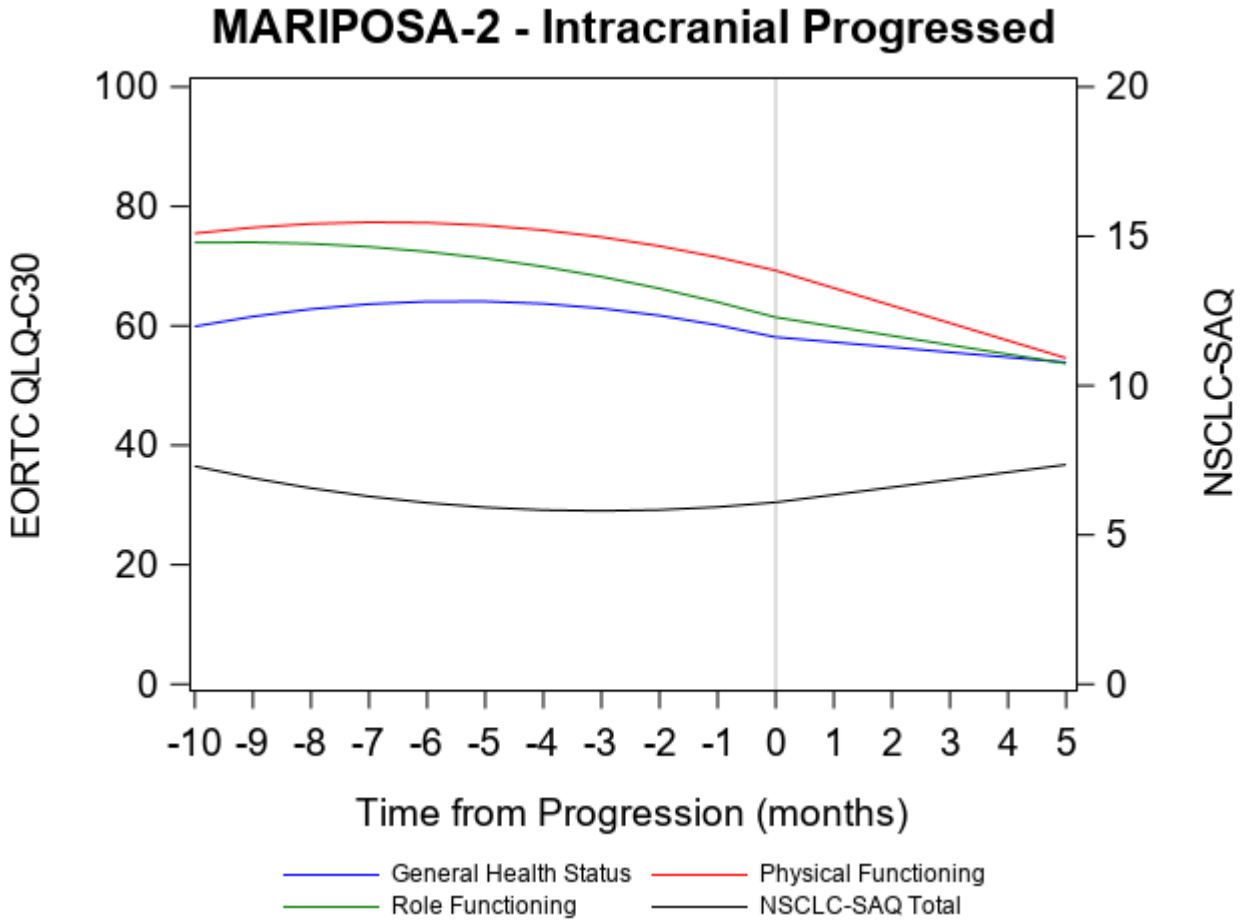
MARIPOSA 2 intracranial disease progression results were consistent with findings from MARIPOSA

MARIPOSA-2 – Intracranial Progression

- Statistical significance for piecewise slopes varied across scores; all slopes were in the projected direction
  - *Pre-Progression:* Scores worsened more and more leading up to progression for all outcomes except Role Functioning (quadratic effect; p<.01) and at the time of progression for all outcomes except NSCLC-SAQ Total scores (pre-progression linear effect; p <.01)
  - *Post-Progression*: Scores continued to worsen post-progression only for Physical Functioning (linear effect; p<.01)

	Intracranial Progression			
	Global Health Est(SE), P	Physical Function Est(SE), P	Role Function Est(SE), P	Lung Symptoms Est(SE), P
Pre-Linear	-2.21(0.63), 0.0005	-2.40(0.62), 0.0002	-2.70(0.81), 0.0010	0.19(0.11), 0.0752
Pre-Quadratic	-0.20(0.07), 0.0021	-0.18(0.06), 0.0030	-0.15(0.08), 0.0843	0.03(0.01), 0.0046
Post-Linear	-0.84(0.63), 0.1909	-2.93(0.84), 0.0010	-1.54(0.85), 0.0786	0.25(0.13), 0.0603

Notes. Est = Estimate. SE = Standard error. P = p-value.



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Conclusions

- **PROs worsen more rapidly as progression approaches and tend to continue to worsen** from that time forward in NSCLC.
- Findings support the importance of **prolonging time to disease progression and new / worsening brain metastases** as **patient relevant endpoints** in NSCLC.
- This study contributes to a growing body of evidence showing that **disease progression is associated with worsening HRQoL** in cancer. (e.g., Cella et al., 2018; Marschner et al., 2020)

- Future Work
  - Replicate these exploratory, post-hoc analyses in other types of cancer and with other PRO measures.
  - Examine changes in PRO scores relative to the time of clinically relevant events to gain novel, patient-relevant insights.

Disease progression, including intracranial progression, is associated with worsening of patients' NSCLC symptoms and health-related quality of life.

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References

Aaronson, N. K., et al. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. JNCI: Journal of the National Cancer Institute, 85(5), 365-376.

Bushnell, D.M., et al. (2021). Non-small Cell Lung Cancer Symptom Assessment Questionnaire: Psychometric performance and regulatory qualification of a novel patient-reported symptom measure. Current Therapeutic Research, 95, https://doi.org/10.1016/j.curtheres.2021.100642

Cella, D., Traina, S., Li, T., Johnson, K., Ho, K. F., Molina, A., & Shore, N. D. (2018). Relationship between patient-reported outcomes and clinical outcomes in metastatic castration-resistant prostate cancer: post hoc analysis of COU-AA-301 and COU-AA-302. Annals of Oncology, 29(2), 392-397.

Cho, B. C., et al. (2024). Amivantamab plus Lazertinib in Previously Untreated EGFR-Mutated Advanced NSCLC. The New England Journal of Medicine. https://doi.org/10.1056/NEJMoa2403614

Food and Drug Administration (2024). Core Patient-Reported Outcomes in Cancer Clinical Trials. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/core-patient-reported-outcomes-cancer-clinical-trials

Food and Drug Administration (2018). Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trial-endpoints-approval-cancer-drugs-and-biologics

Giuliani, G., Chassagnol, F., Traub, D., Gyldmark, M., Hebborn, A., Ducournau, P., & Ruof, J. (2018). Leveraging EUnetHTA's conceptual framework to compare HTA decision drivers in France, Italy, and Germany from a manufacturer's point of view. Health Economics Review, 8, 1-11.

Hwang, T. J., & Gyawali, B. (2019). Association between progression-free survival and patients' quality of life in cancer clinical trials. International Journal of Cancer, 144(7), 1746-1751.

Kovic, B., Jin, X., Kennedy, S. A., Hylands, M., Pędziwiatr, M., Kuriyama, A., ... & Xie, F. (2018). Evaluating progression-free survival as a surrogate outcome for health-related quality of life in oncology: a systematic review and quantitative analysis. JAMA Internal Medicine, 178(12), 1586-1596.

Liao, K., et al. (2022). Prognostic value of patient-reported outcome measures (PROMs) in adults with non-small cell Lung Cancer: A scoping review. BMC Cancer, 22(1), 1076.

Marschner, N., Zacharias, S., Lordick, F., Hegewisch-Becker, S., Martens, U., Welt, A., ... & Jänicke, M. (2020). Association of disease progression with health-related quality of life among adults with breast, lung, pancreatic, and colorectal cancer. JAMA network open, 3(3), e200643-e200643.

McCarrier, K.P., et al. (2016). Qualitative development and content validity of the Non-small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ), a patient-reported outcome instrument. Clinical Therapeutics, 38(4), 794 – 810

Movsas, B., et al. (2009). Quality of life supersedes the classic prognosticators for long-term survival in locally advanced non–small-cell lung cancer: An analysis of RTOG 9801. Journal of Clinical Oncology, 27(34), 5816–5822.

Passaro, A., Wang, J., Wang, Y., Lee, S. H., Melosky, B., Shih, J. Y., ... & MARIPOSA-2 Investigators. (2024). Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study. Annals of Oncology, 35(1), 77-90.

Pilz, L. R., Manegold, C., & Schmid-Bindert, G. (2012). Statistical considerations and endpoints for clinical lung cancer studies: Can progression free survival (PFS) substitute overall survival (OS) as a valid endpoint in clinical trials for advanced non-small-cell lung cancer?. Translational lung cancer research, 1(1), 26.