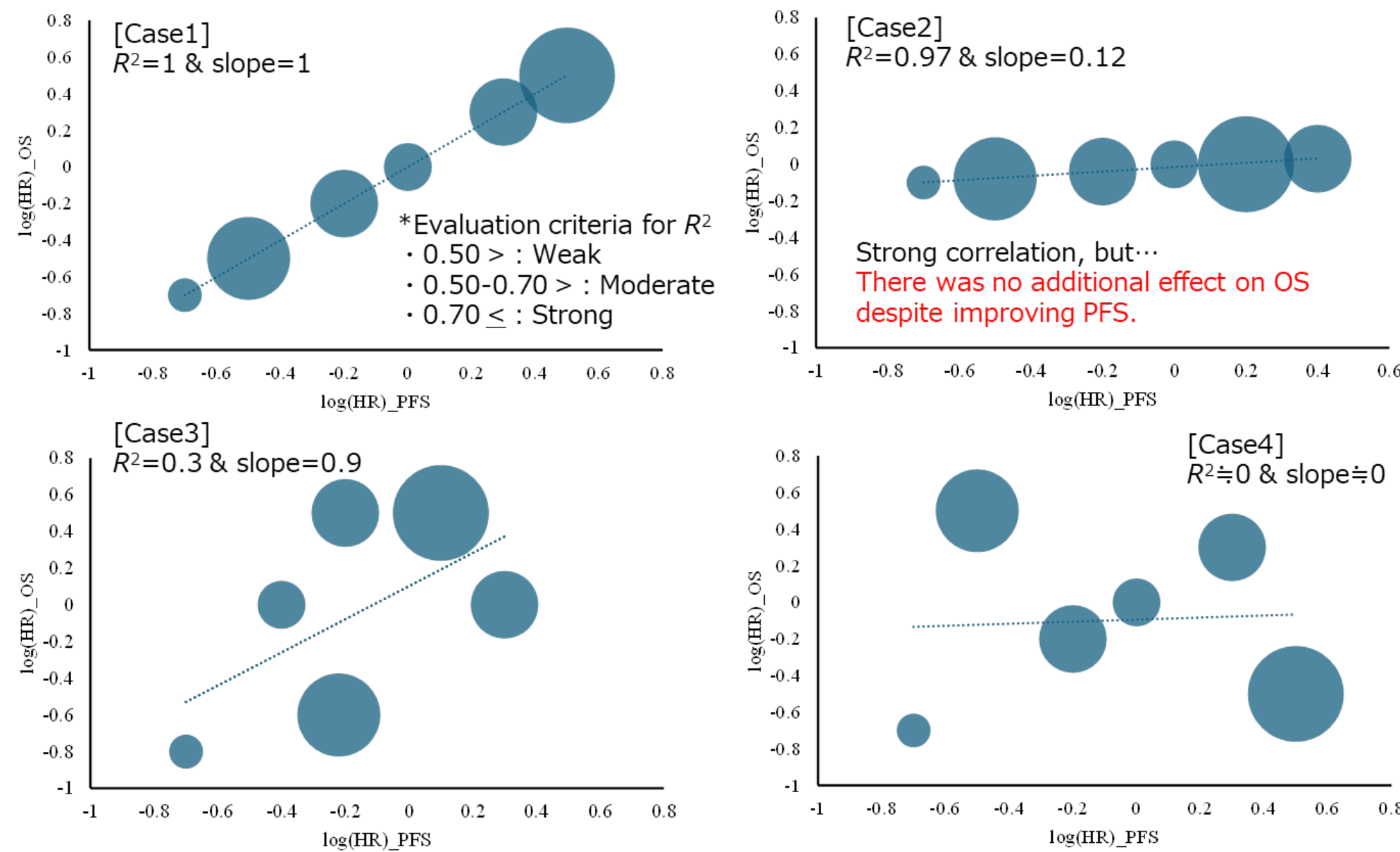


INTRODUCTION

- Surrogate endpoints for overall survival (OS) can help reduce trial-related resources, such as study duration and required sample size.
- Although a previous report assessed PFS as a surrogate for OS in advanced malignant pleural mesothelioma (Wang, 2017), it relied on 17 small trials published before 2012 and did not include trial-level analyses.
- While surrogacy of OS for immune checkpoint inhibitors (ICI) has been reported (Skelin, 2025), the evidence was limited to seven trials. To the best of our knowledge, no data are available for other mechanisms of action, including molecular-targeted therapies.
- We evaluated OS surrogacy in patients with advanced pleural mesothelioma across various trial settings.



METHODS

Literature Search

A PubMed search identified phase II and III trials involving patients with advanced mesothelioma published between January 1, 2000, and December 31, 2025.

Statistical Analysis

To evaluate PFS and ORR as surrogate endpoints for OS, the coefficient of determination (R^2) and regression slopes were calculated using a sample-size-weighted least-squares model. In the trial-level analysis, log-transformed hazard ratios (HRs) and between-group differences (Δ) were used. Leave-one-out cross-validation (LOOCV) was performed to assess the variability of R^2 and the discrepancy between the predicted and observed HRs for OS. In the arm-level analysis, surrogacy was examined using the median PFS and median OS.

RESULTS

Table1. Trial characteristics (n=93)

Factors	n (%)
Region	
Europe	47 (50.5)
North America	24 (25.8)
Asia	5 (5.4)
Global	13 (14.0)
Others	4 (4.3)
Study phase	
phase II	79 (84.9)
phase III	14 (15.1)
Line of Therapy	
1st-line	40 (43.0)
2nd-line	49 (52.7)
1st & 2nd	4 (4.3)
Primary endpoint *	
OS	18 (19.4)
PFS	26 (28.0)
ORR	39 (41.9)
DCR	3 (3.2)
Others	9 (9.7)
Central Review	
No	69 (74.2)
Yes	24 (25.8)

* Duplicate counting due to co-primary endpoints.

Figure6. medianPFS $\times$ medianOS (ICI) (n=23)

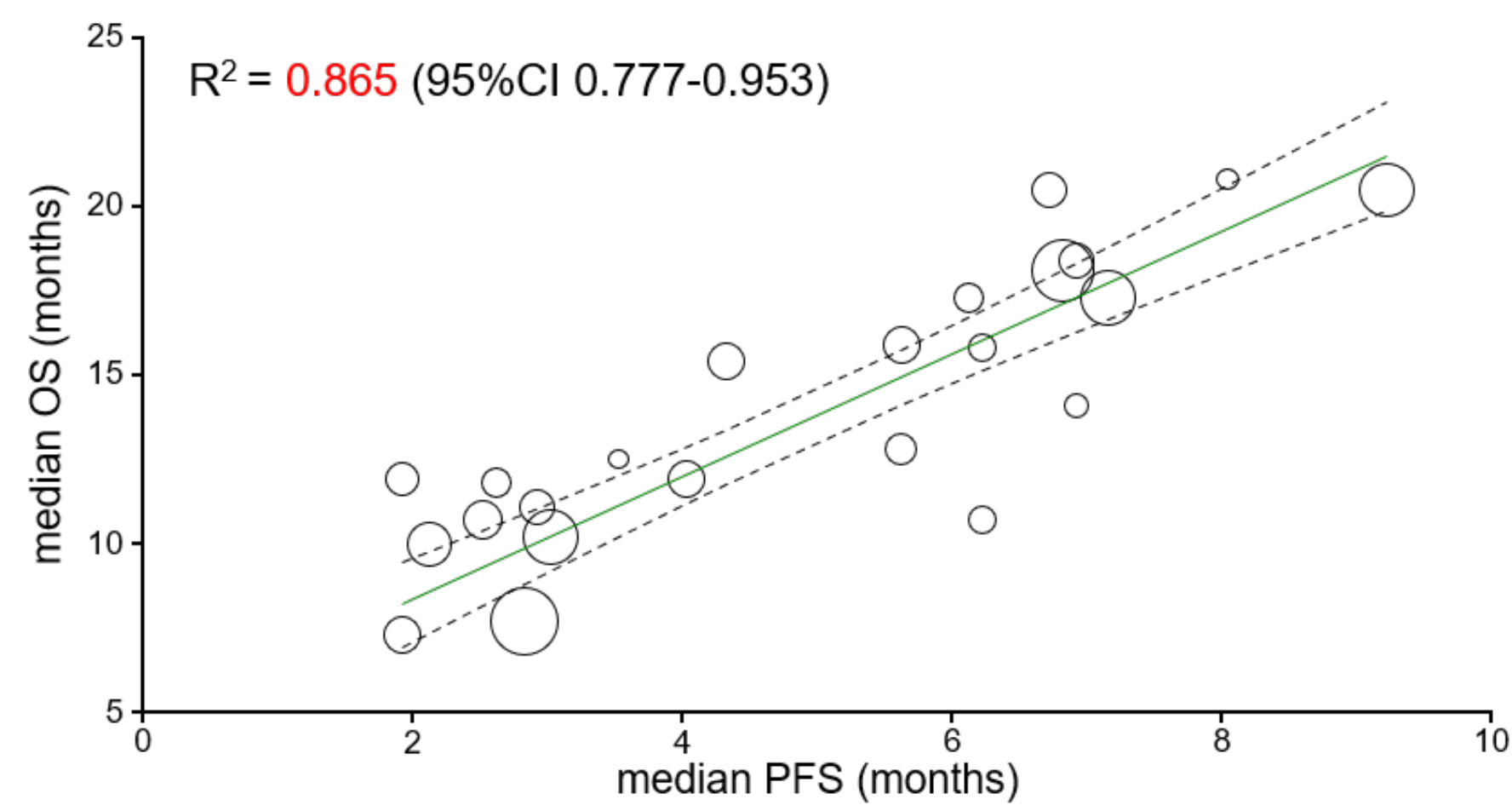


Figure1. log(HRPFS) $\times$ log(HROS) (n=28)

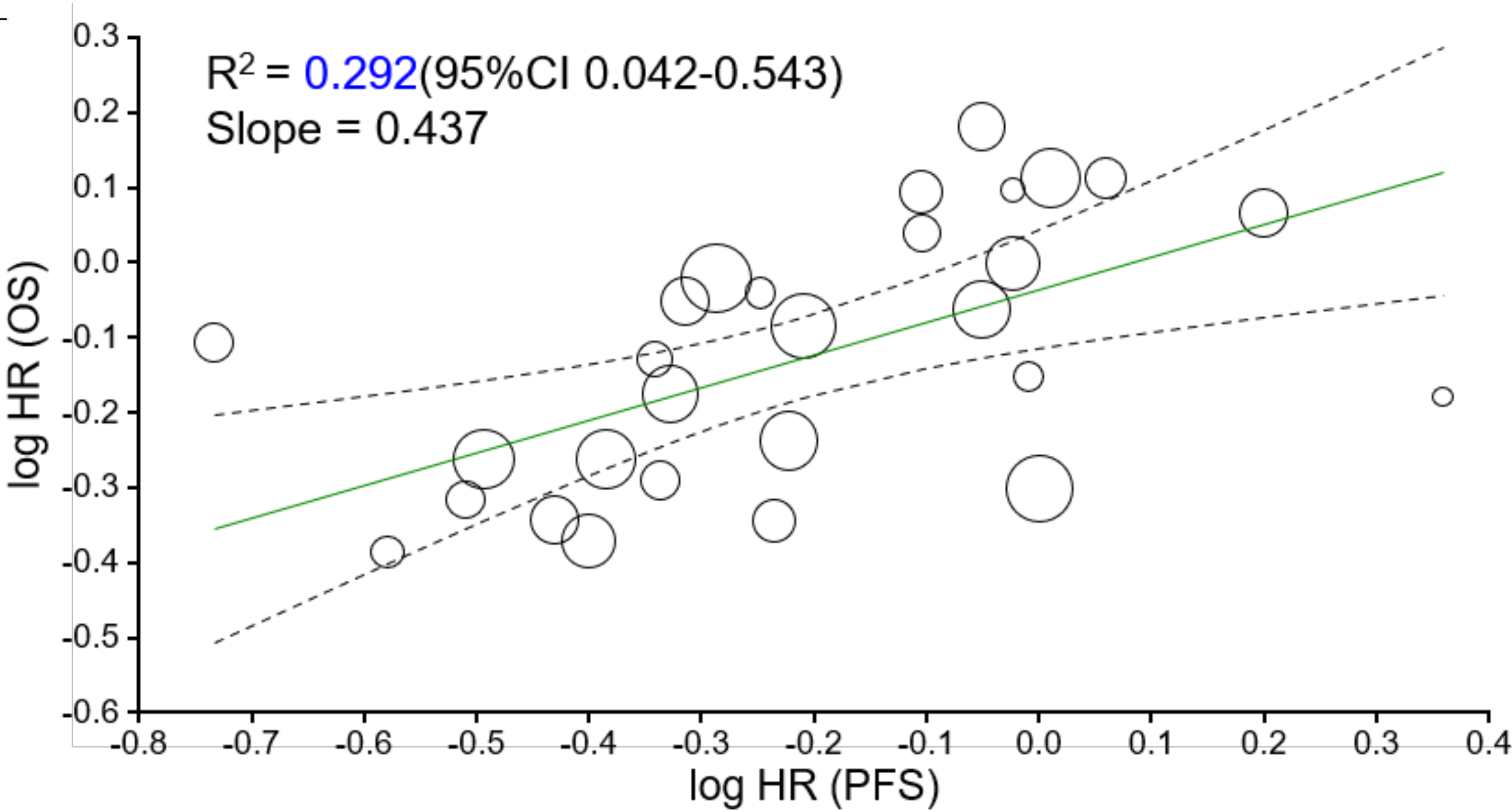


Figure4. Δ ORR $\times$ log(HROS) (n=25)

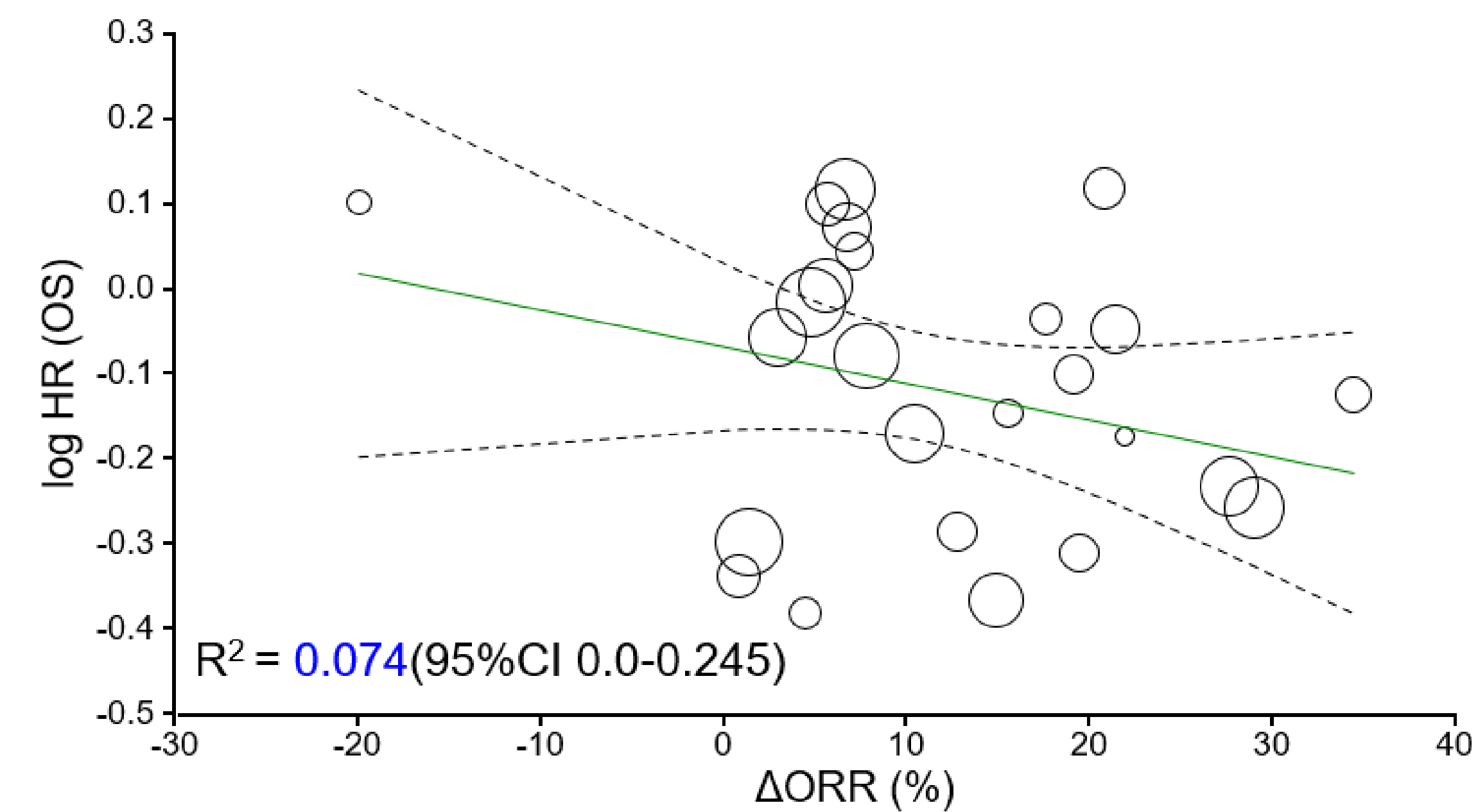


Figure7. medianPFS $\times$ medianOS (Molecular-targeted) (n=36)

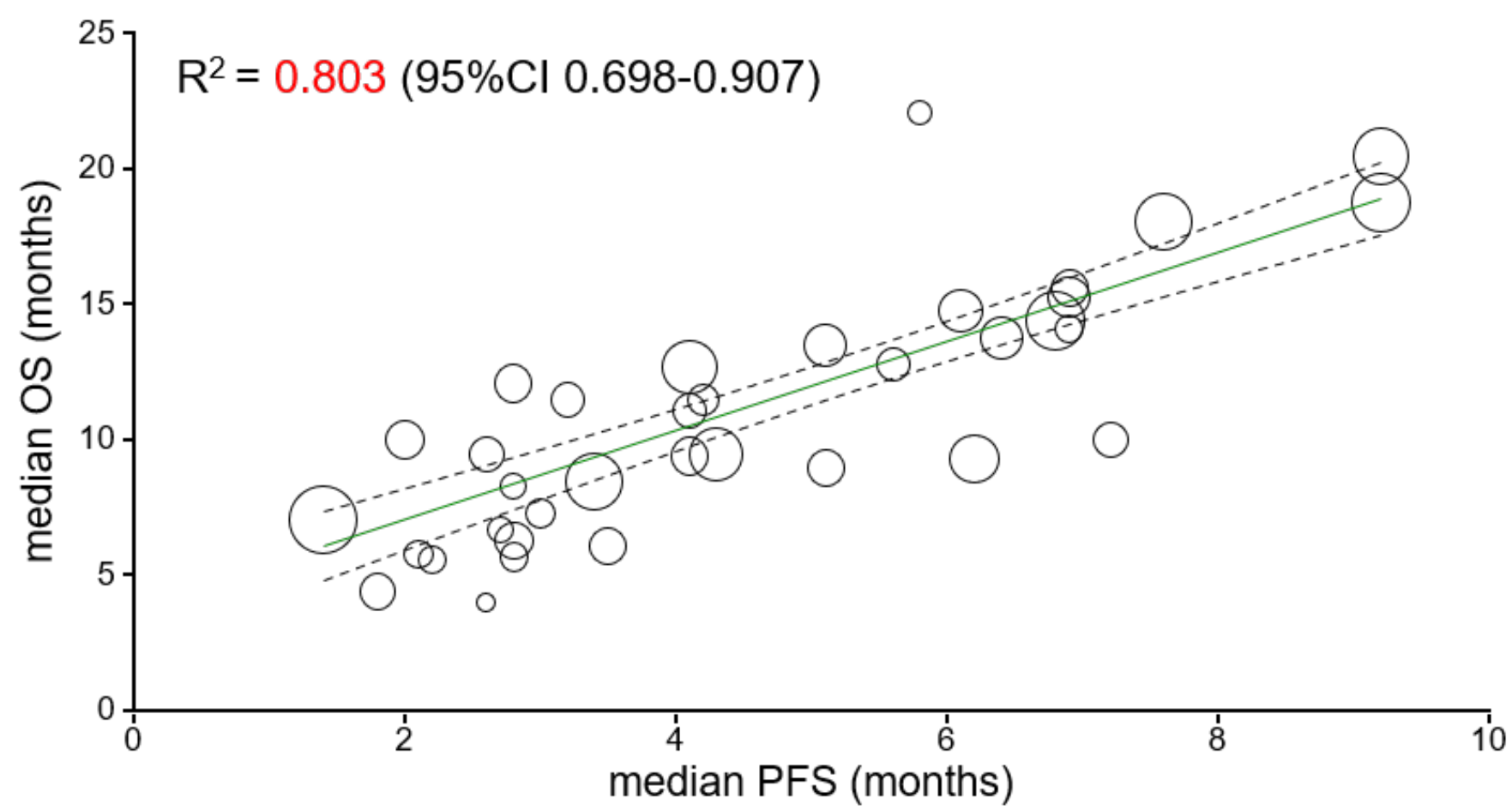


Figure2. LOOCV

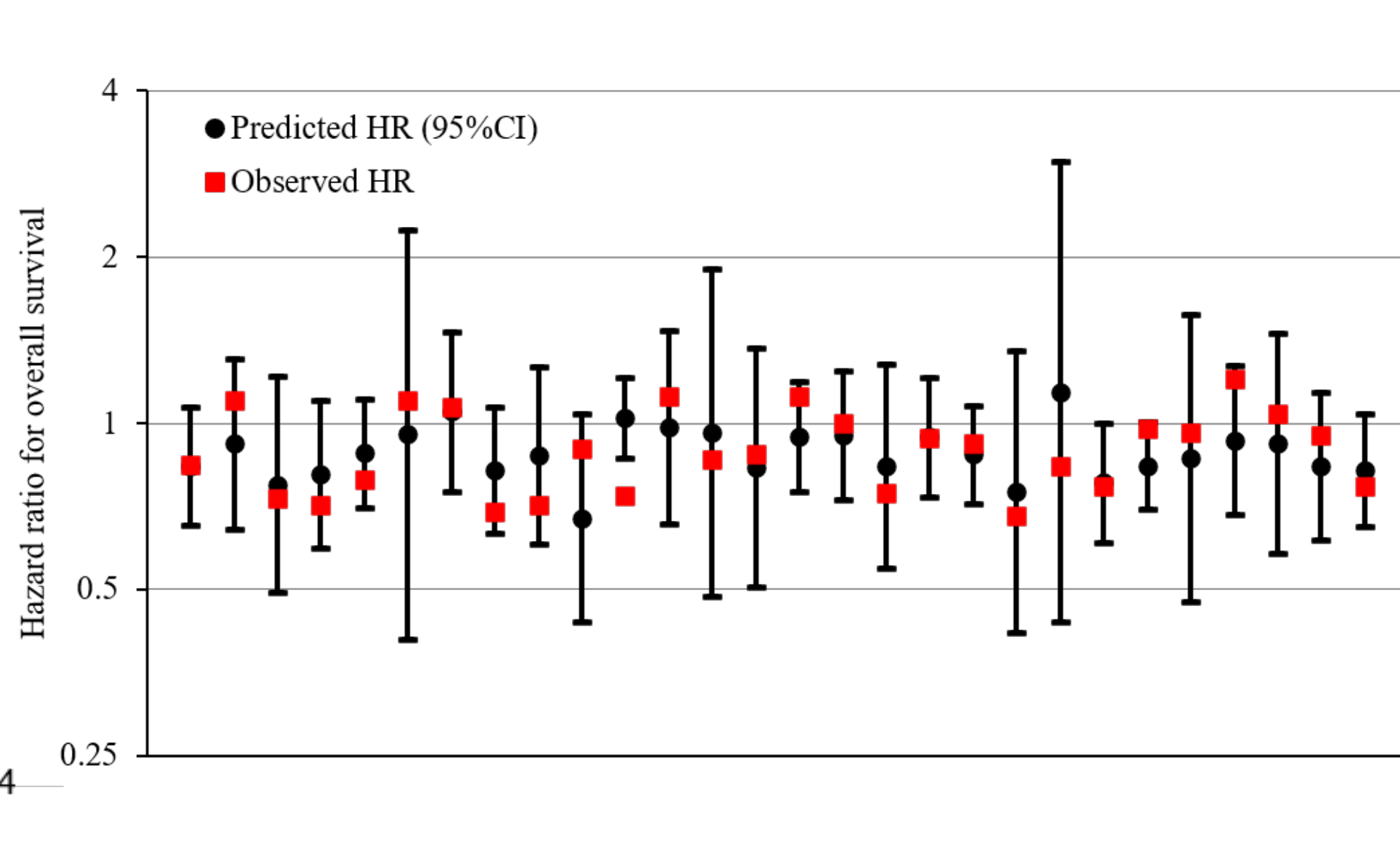


Figure5. Δ ORR $\times$ log(HRPFS) (n=25)

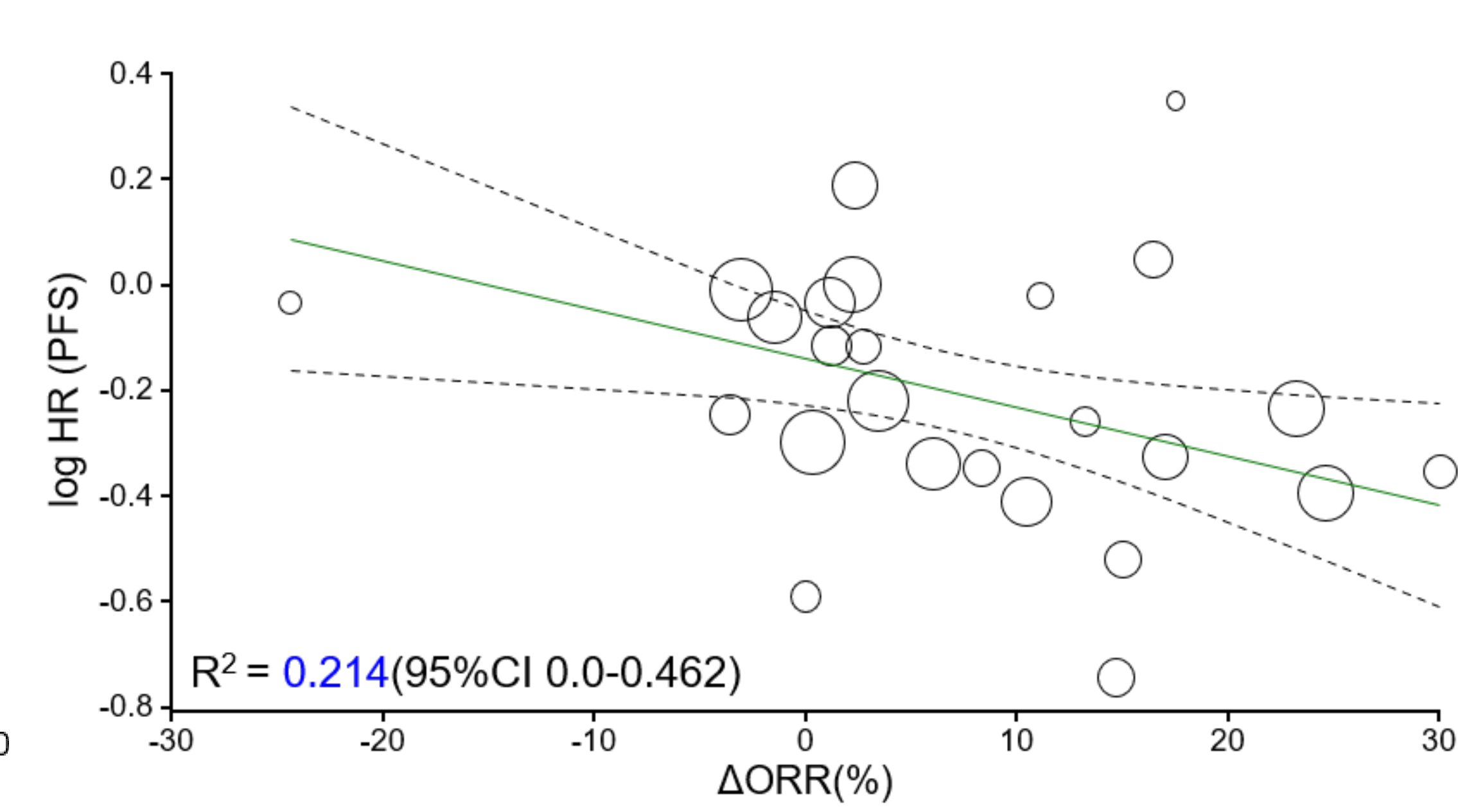


Figure8. medianPFS $\times$ medianOS (Cytotoxic) (n=66)

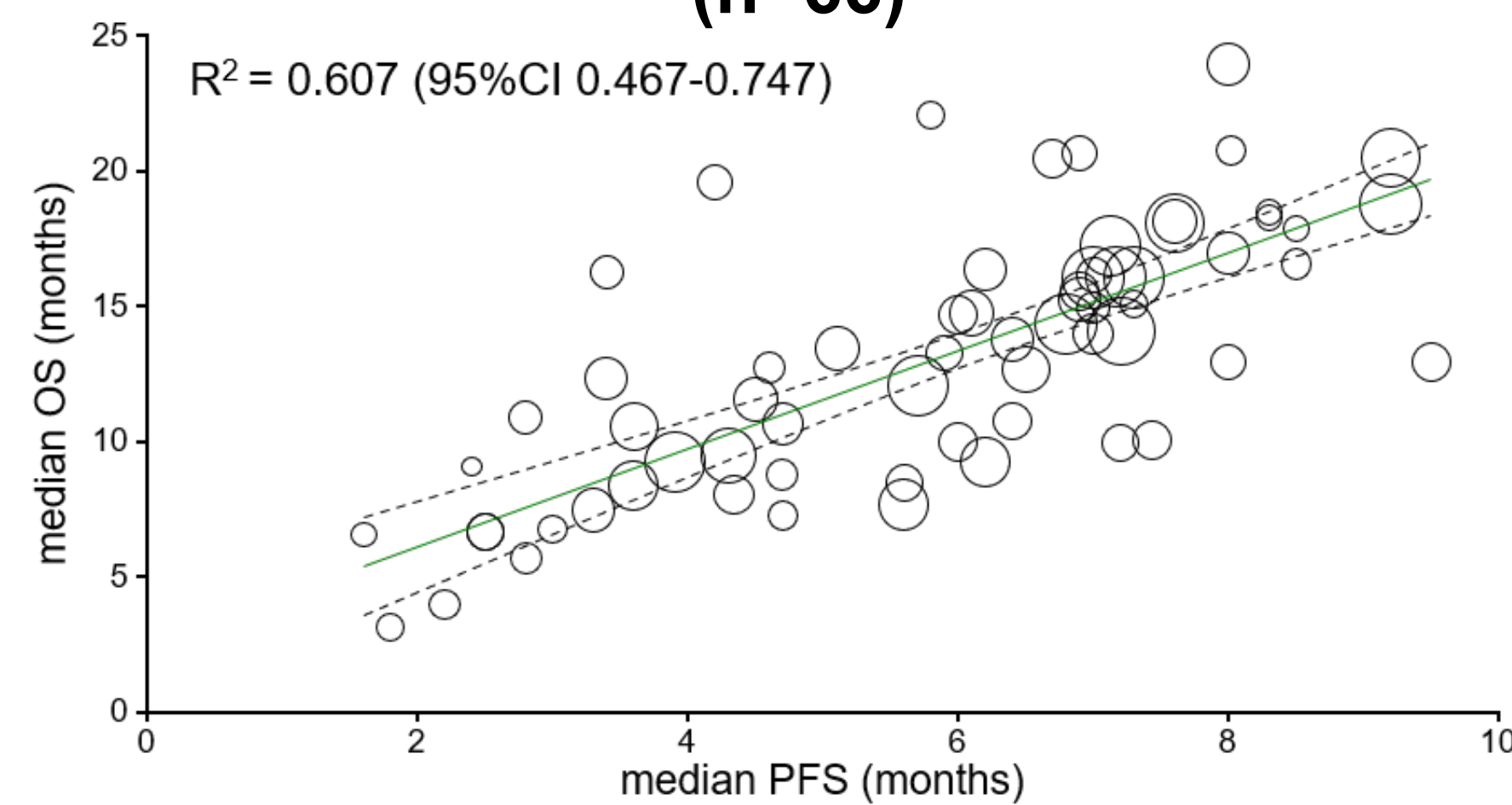
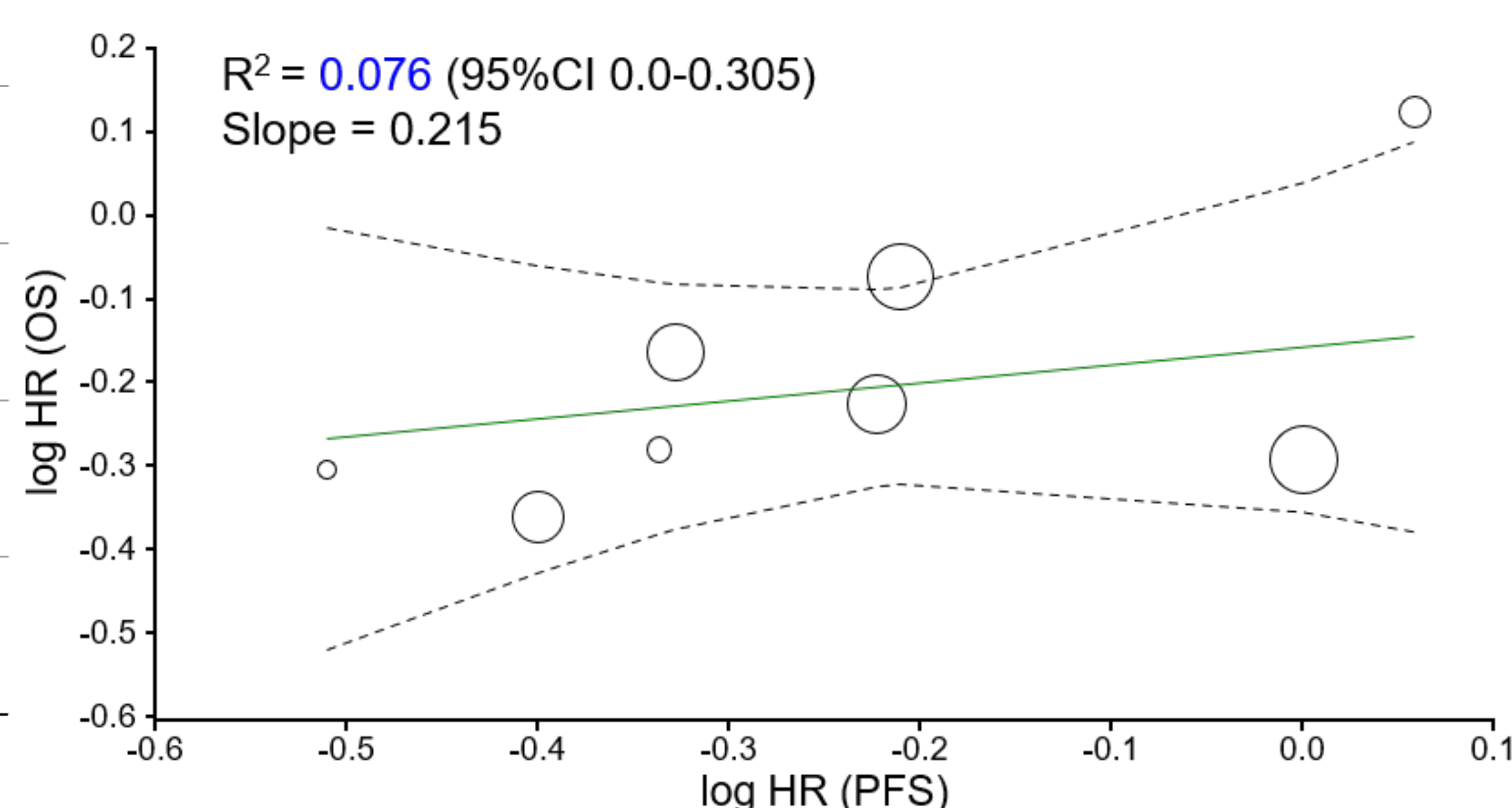


Figure3. log(HRPFS) $\times$ log(HROS) (ICI) (n=8)



DISCUSSION & CONCLUSION

- At the trial level, neither PFS nor ORR showed a strong correlation with OS, indicating that they are not valid surrogate endpoints in advanced pleural mesothelioma.
- In the ICI subgroup, the correlation between PFS and OS was even weaker than previously reported.
- In contrast, arm-level analyses demonstrated strong correlations between median PFS and median OS, particularly in ICI and molecular-targeted therapy cohorts.
- Median PFS may therefore serve as a useful endpoint for early efficacy assessment in exploratory phase II trials, although it should not replace OS in confirmatory trials.

COI & AI DISCLOSURES

Conflict of Interest (COI) Disclosure:

The authors have no conflicts of interest to declare relevant to this presentation.

AI Use Disclosure:

No artificial intelligence (AI) tools were utilized in the development of the content or materials for this presentation.