



P3.209: Population Pharmacokinetics and Exposure-Response Analysis of Rezipertinib in Patients with EGFR-Mutated Advanced or Recurrent NSCLC

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INTRODUCTION

Rezipertinib is a novel third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI). It has demonstrated promising efficacy in patients with advanced or relapsed non-small cell lung cancer (NSCLC) harboring EGFR mutations. This study aimed to develop a population pharmacokinetics (PopPK) model for rezipertinib and evaluate exposure-response relationships for efficacy.

METHODS

A PopPK model was developed for rezipertinib in 104 patients with EGFR-mutated advanced or recurrent NSCLC. AUC_{ss} served as the exposure metric in logistic regression for ORR, adjusting for covariates (sex, age, BMI, EGFR mutation histology).

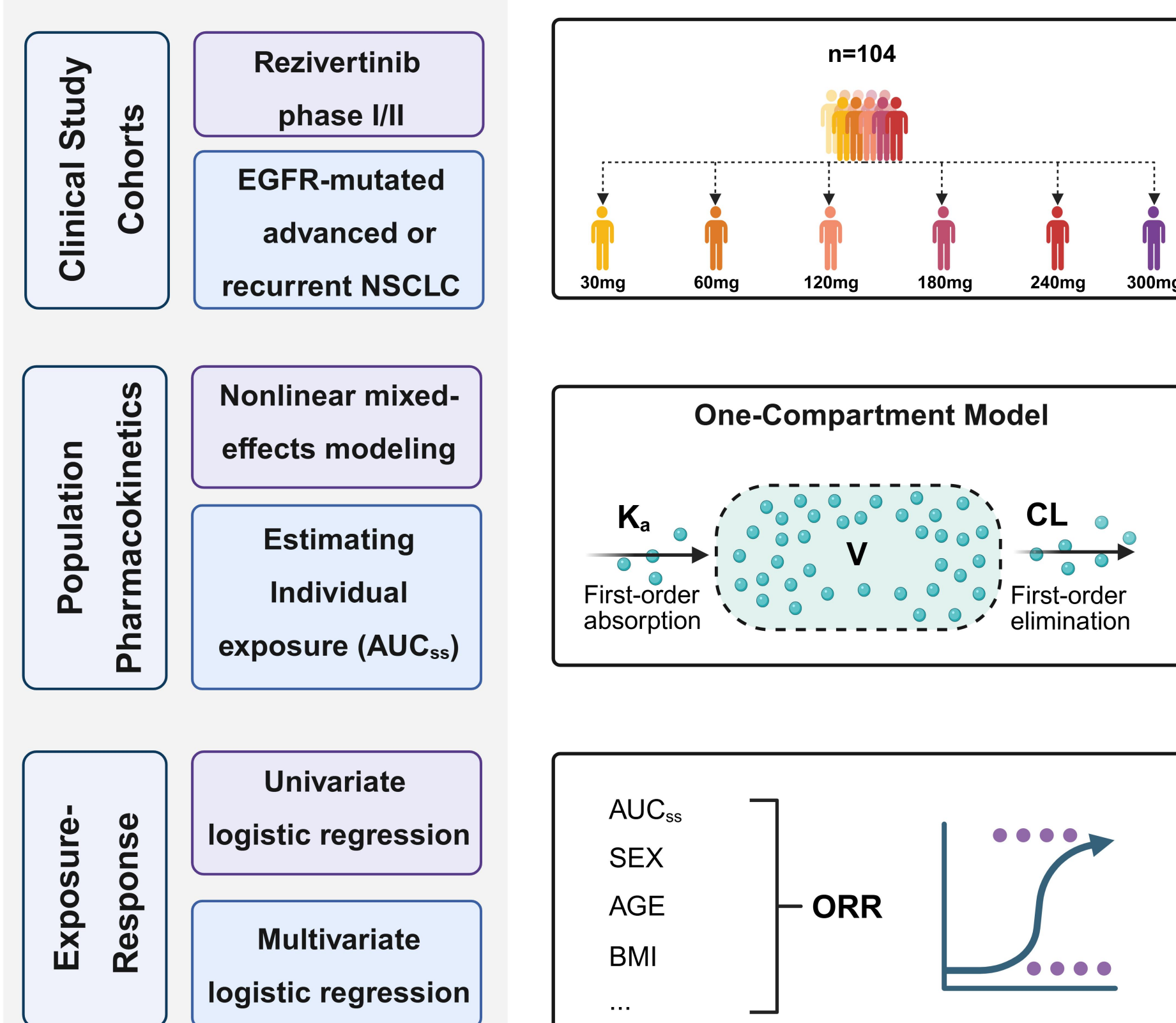


Figure 1 Study design flowchart.

DISCUSSION AND CONCLUSION

BMI affects rezipertinib distribution

- A PopPK model was established for rezipertinib, identifying BMI as a significant covariate on the apparent volume of distribution, suggesting that BMI should be considered for individualized dosing.

Sex & T790M predict ORR

- Female patients had a significantly higher ORR, whereas patients with positive tissue T790M status had a significantly reduced ORR.

Supports dose optimization

- These results provide a basis for clinical individualized dose optimization of rezipertinib, emphasizing that treatment strategies should integrate both baseline patient characteristics and exposure metrics.

REFERENCES & ACKNOWLEDGEMENTS

REFERENCES

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RESULTS

For the PopPK model, the typical population estimates were $K_a = 0.149 \text{ h}^{-1}$, $V = 1618 \text{ L}$, and $CL = 29.3 \text{ L/h}$, while the standard deviation of the additive residual error was 36.7 ng/mL. Covariate analysis identified BMI as a significant covariate on the apparent volume of distribution, and the effect was estimated as 1.87. Goodness-of-fit plots and visual predictive checks confirmed adequate model performance (Figure 2).

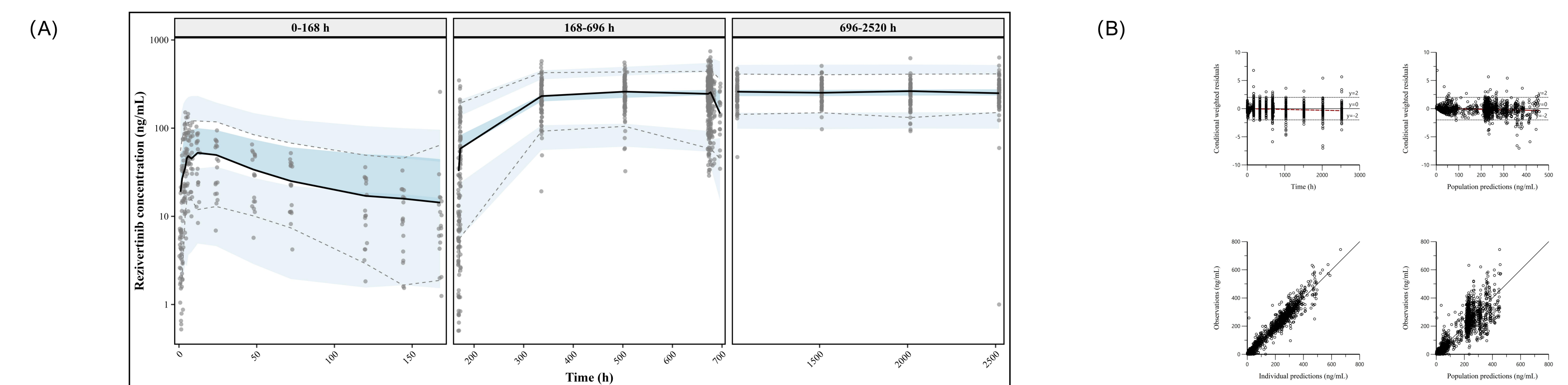


Figure 2 Prediction-corrected visual predictive check results and goodness-of-fit plots.

In the exposure-response analysis, ORR numerically increased across ascending AUC_{ss} quartiles. Consistently, logistic regression yielded an $OR > 1$, suggesting a positive exposure-response trend for rezipertinib (Figure 3).

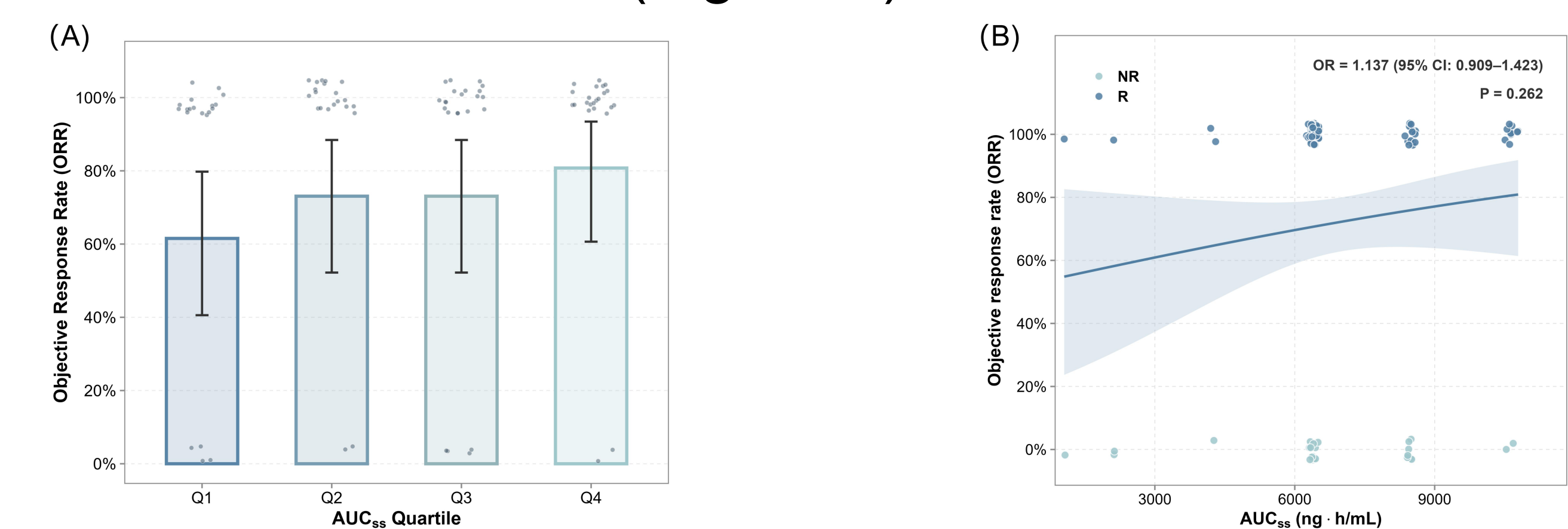


Figure 3 Exposure-response analysis of rezipertinib.

In univariate analysis, female patients had a significantly higher ORR ($OR = 3.16$, 95% CI: 1.30-7.70, $P = 0.011$). Multivariable analysis confirmed female sex as an independent predictor of better response ($OR = 5.34$, 95% CI: 1.70-16.76, $P = 0.004$), whereas positive tissue T790M status was significantly associated with lower response ($OR = 0.25$, 95% CI: 0.08-0.82, $P = 0.022$) (Figure 4).

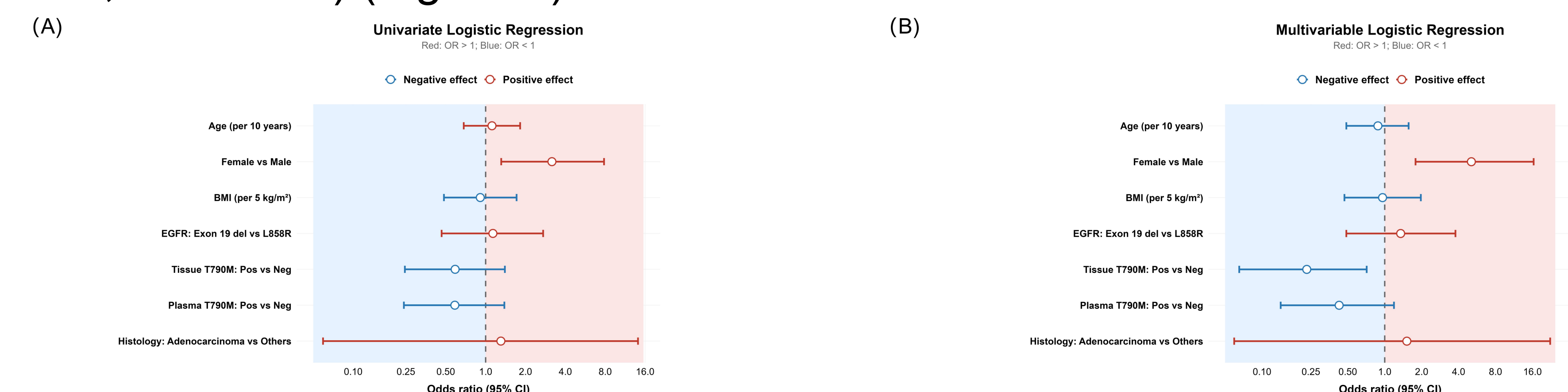


Figure 4 Univariate and multivariate analyses of ORR.