

P 3.258: Guiding Dabrafenib-Trametinib Dosing in BRAF V600E-Mutated NSCLC A Prospective Biomarker Cohort

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BACKGROUND

- Dabrafenib-trametinib (D-T) is an effective first-line treatment for advanced *BRAF V600E*-mutated NSCLC^{1, 2}
- Treatment-related toxicity frequently requires dose reductions³
- The clinical impact of dose reductions remains unclear

AIM

Evaluate the impact of dose reductions on toxicity and PFS, characterize dabrafenib/trametinib pharmacokinetics, and explore the clinical utility of therapeutic drug monitoring (TDM).

METHODS

- Prospective Dutch biomarker cohort (NCT05221371)
- Advanced *BRAF V600E*-mutated NSCLC treated with first-line D-T
- Enrollment: September 2018 to Juni 2025
- Data cut-off: June 2026
- All available pharmacokinetic (PK) samples collected at baseline and every 3 months thereafter were included; pre-Tmax samples were excluded
- Documented adverse events were extracted from clinical records and graded according to CTCAE
- Dose reductions at physician discretion

RESULTS

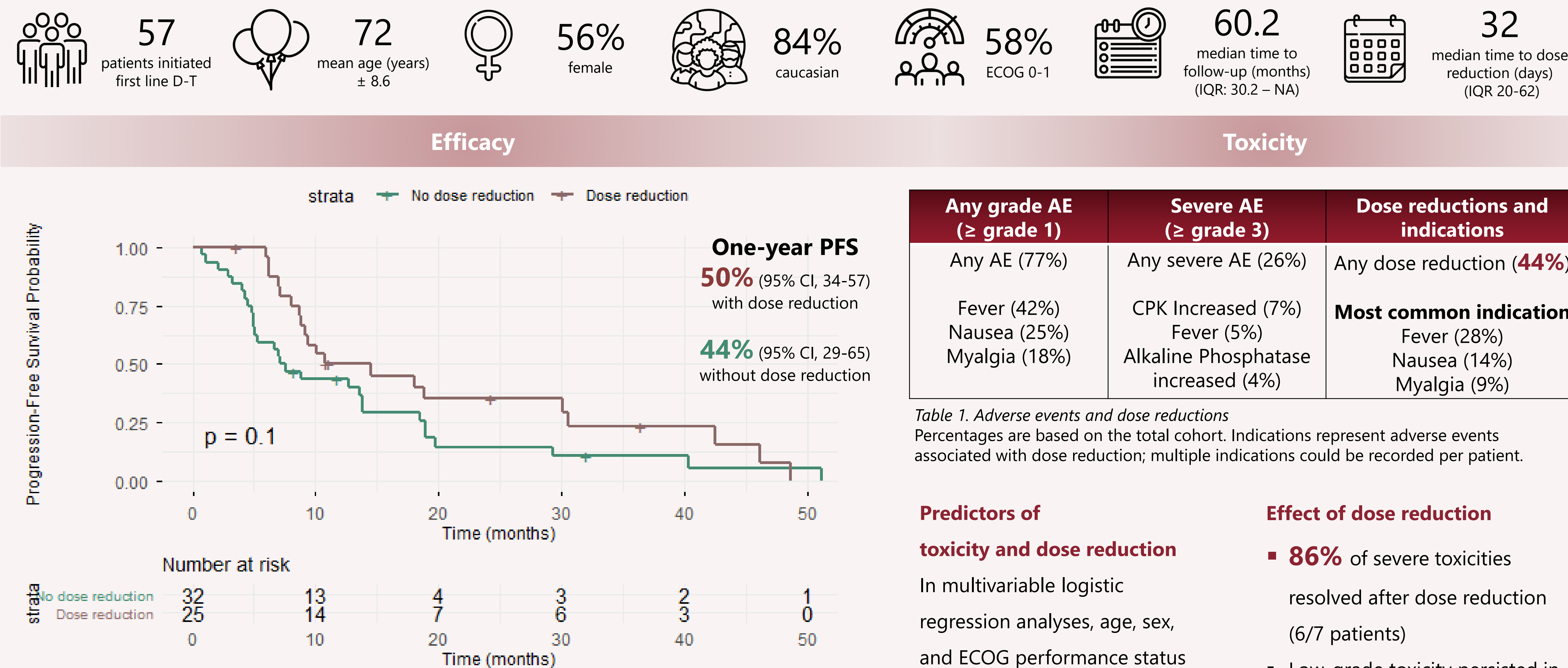


Figure 1. Impact of dose reduction on PFS
Dose reduction was not associated with an increased risk of progression. Multivariate HR 0.89 (95% CI 0.49 – 1.61)

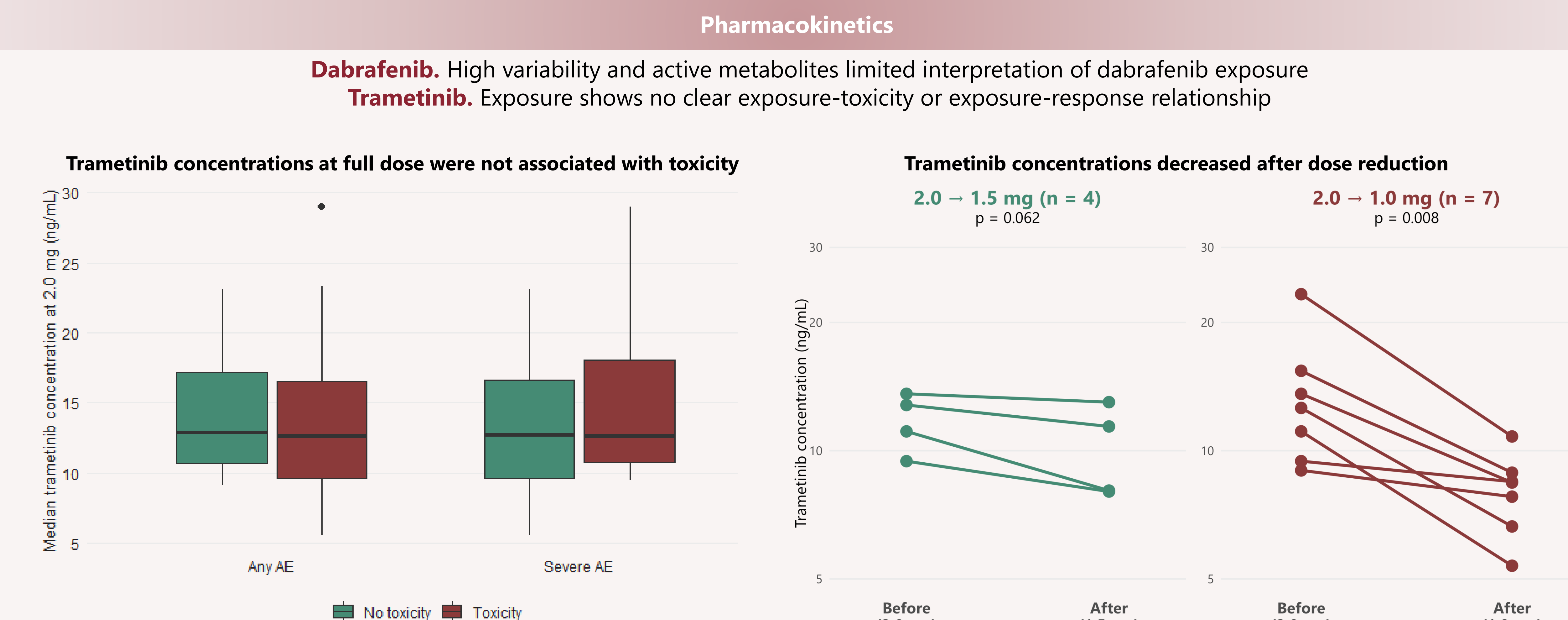
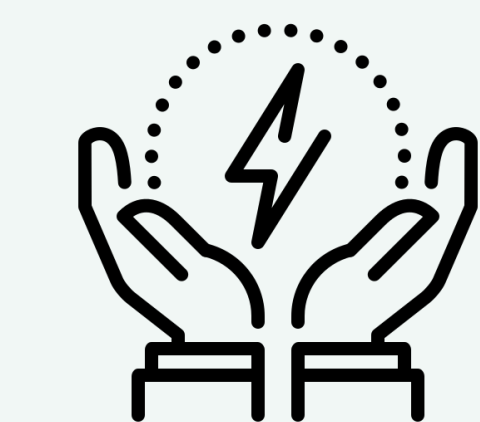


Figure 2. Trametinib concentrations by toxicity outcome
Median trametinib concentrations at 2.0 mg in patients with and without any grade or severe toxicity. Both comparisons were non-significant (p > 0.5).

Figure 3. Within-patient trametinib concentrations before and after dose reduction
Median trametinib concentrations decreased from 11.95 to 9.73 ng/mL after reduction from 2.0 to 1.5 mg (n = 4; p = 0.062) and from 12.60 to 8.42 ng/mL after reduction from 2.0 to 1.0 mg (n = 7; p = 0.008)

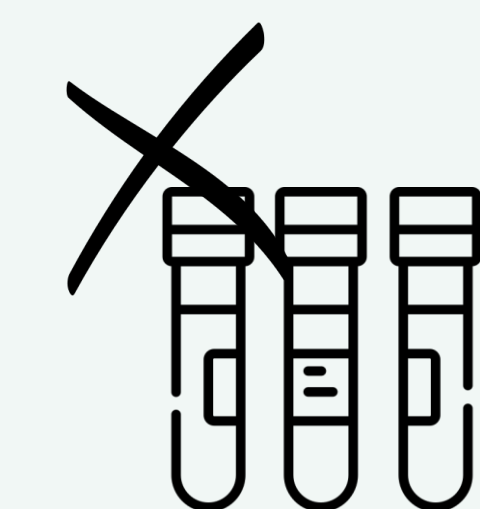
KEY MESSAGES



DOSE REDUCTION DID NOT COMPROMISE EFFICACY.



DOSE REDUCTIONS EFFECTIVELY MANAGED SEVERE TOXICITY



LIMITED ROLE FOR THERAPEUTIC DRUG MONITORING

CLINICALLY INDICATED DOSE REDUCTION APPEARS TO BE A SAFE AND EFFECTIVE STRATEGY FOR MANAGING SEVERE TOXICITY WITHOUT COMPROMISING TREATMENT EFFICACY.

CORRESPONDENCE



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1. Planchard D et al. Dabrafenib plus trametinib in patients with previously untreated *BRAF*^{V600E}-mutant metastatic non-small-cell lung cancer: an open-label, phase 2 trial. *Lancet Oncol.* 2017

2. Hendriks LE et al. Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol.* 2023

3. Auliac JB et al. Efficacy of Dabrafenib Plus Trametinib Combination in Patients with *BRAF V600E*-Mutant NSCLC in Real-World Setting: GFPC 01-2019. *Cancers (Basel).* 2020