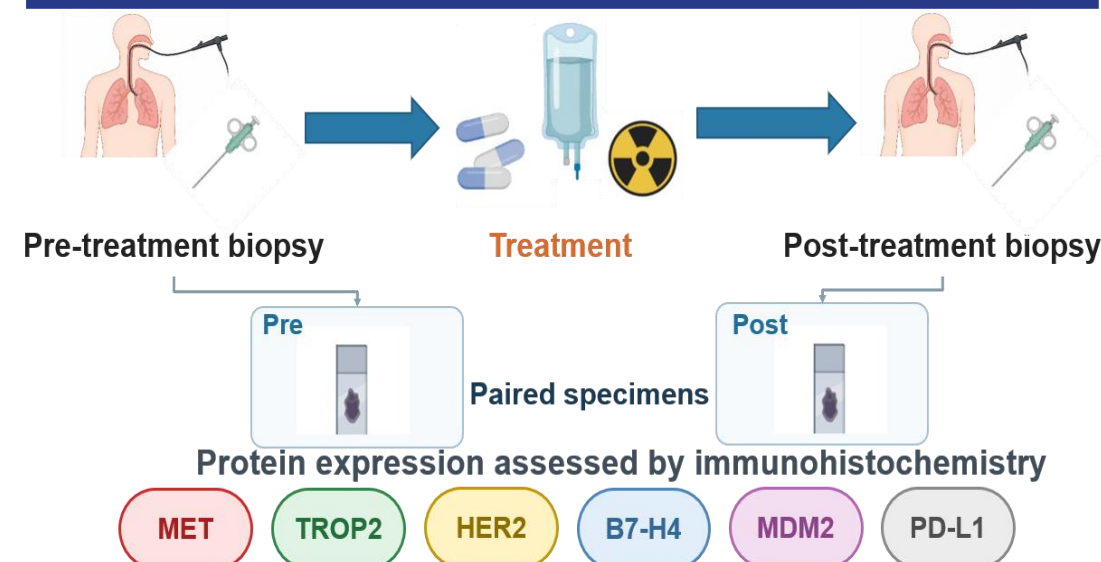


INTRODUCTION

- ✓ Antibody–drug conjugates (ADCs) targeting TROP2, MET, and HER2 have shown clinical activity, but treatment-related expression changes may limit the reliability of archival diagnostic specimens for treatment selection¹⁻³.
- ✓ We evaluated multiple target proteins in paired pre-treatment and post-treatment NSCLC biopsies and examined differences according to actionable genetic alteration (AGA) status.

METHODS



- ✓ We retrospectively identified patients with NSCLC who underwent paired biopsies at diagnosis before any treatment and at disease progression after treatment at the National Cancer Center Hospital between 2014 and 2023.
- ✓ Paired specimens were assessed by immunohistochemistry (IHC) for MET, TROP2, HER2, PD-L1, MDM2, and B7-H4 using H-score- or staining-based criteria. MET 3+ membranous staining in ≥25% of tumor cells was defined as MET overexpression (OE) and considered positive⁴; TROP2 ≥2+, HER2 ≥2+, and PD-L1 tumor proportion score ≥1% were also considered positive^{5,6}.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- ✓ **Target proteins** may individually change or become concurrently positive after treatment.
- Rebiopsy and multi-protein profiling** may better inform ADC selection than archival tissue alone.

Future Direction for Research

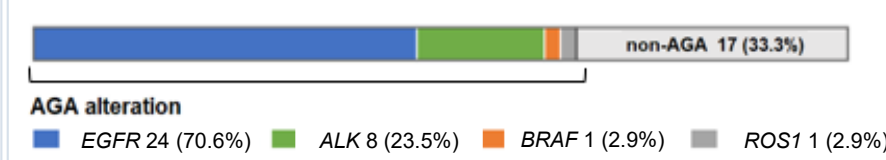
- ✓ Prospective longitudinal studies should validate treatment-associated changes and **co-positivity** across treatment settings and AGA status, defining the **optimal timing for reassessment** relative to treatment duration.
- ✓ Biomarker-integrated ADC trials should test whether updated **multi-protein profiles** can better predict response or guide **ADC selection** than archival tissue, supported by standardized, harmonized IHC assays.

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RESULTS

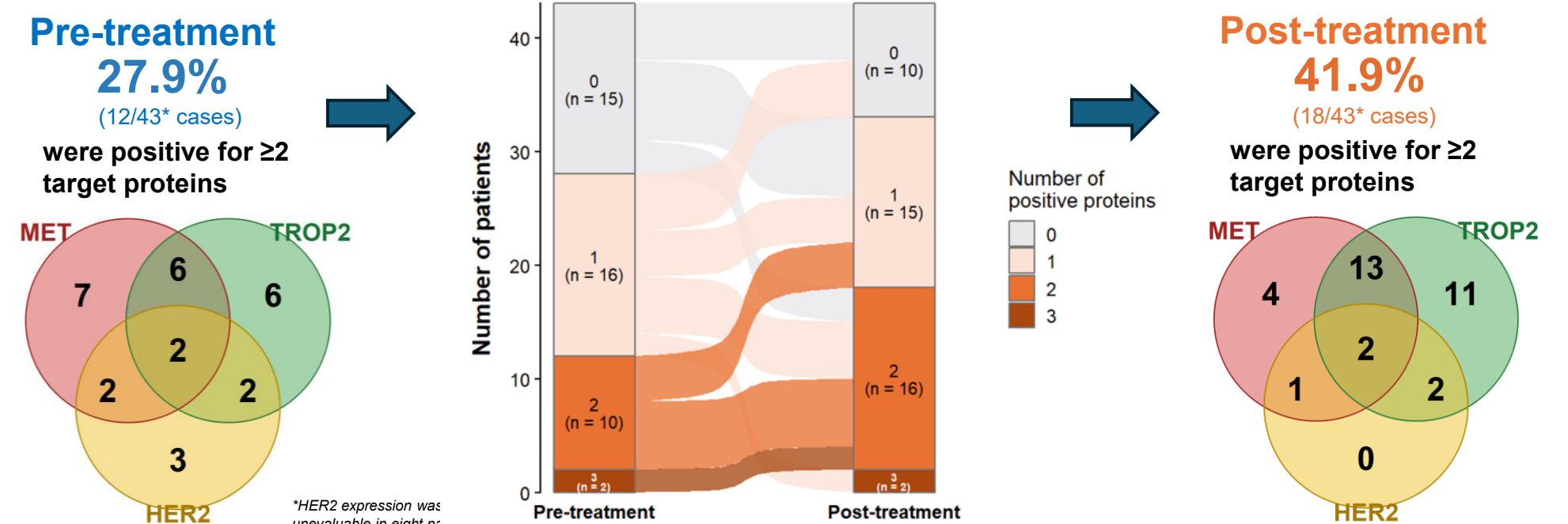
Paired biopsy in 51 NSCLC patients



Treatment-Associated Protein Expression Changes Differ by Protein and AGA Status

49.0% showed increased TROP2 expression after treatment (25/51 cases)
82.4% in non-AGA vs 32.4% in AGA

Single-Protein Expression Assessment May Overlook Coexisting Targets



Dynamic Target Protein Expression After EGFR-TKI Treatment With Emerging MET and TROP2 Positivity

