

Perioperative Immunotherapy Combined with Chemotherapy Improves pCR Rate in PD-L1-Positive NSCLC with **Rare Driver Mutations**

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INTRODUCTION

- Perioperative / neoadjuvant immunotherapy (IO) is the standard of care (SOC) for early-stage resectable EGFR/ALK-negative NSCLC.
- However, considerable controversy persists over perioperative IO management of NSCLC harboring rare driver mutations.
- Neither neoadjuvant targeted therapy nor IO has been established as the SOC for stage II–III patients in this cohort.

METHODS

- This is a retrospective study.
- Patients with stage II-III NSCLC harboring rare driver mutations received perioperative targeted therapy, IO+chemo, or other regimens (e.g., ADCs, chemo plus anti-angiogenic therapy).
- Pathological assessment followed IASLC multidisciplinary recommendations for pathological response following neoadjuvant therapy.

RESULTS

► N=40

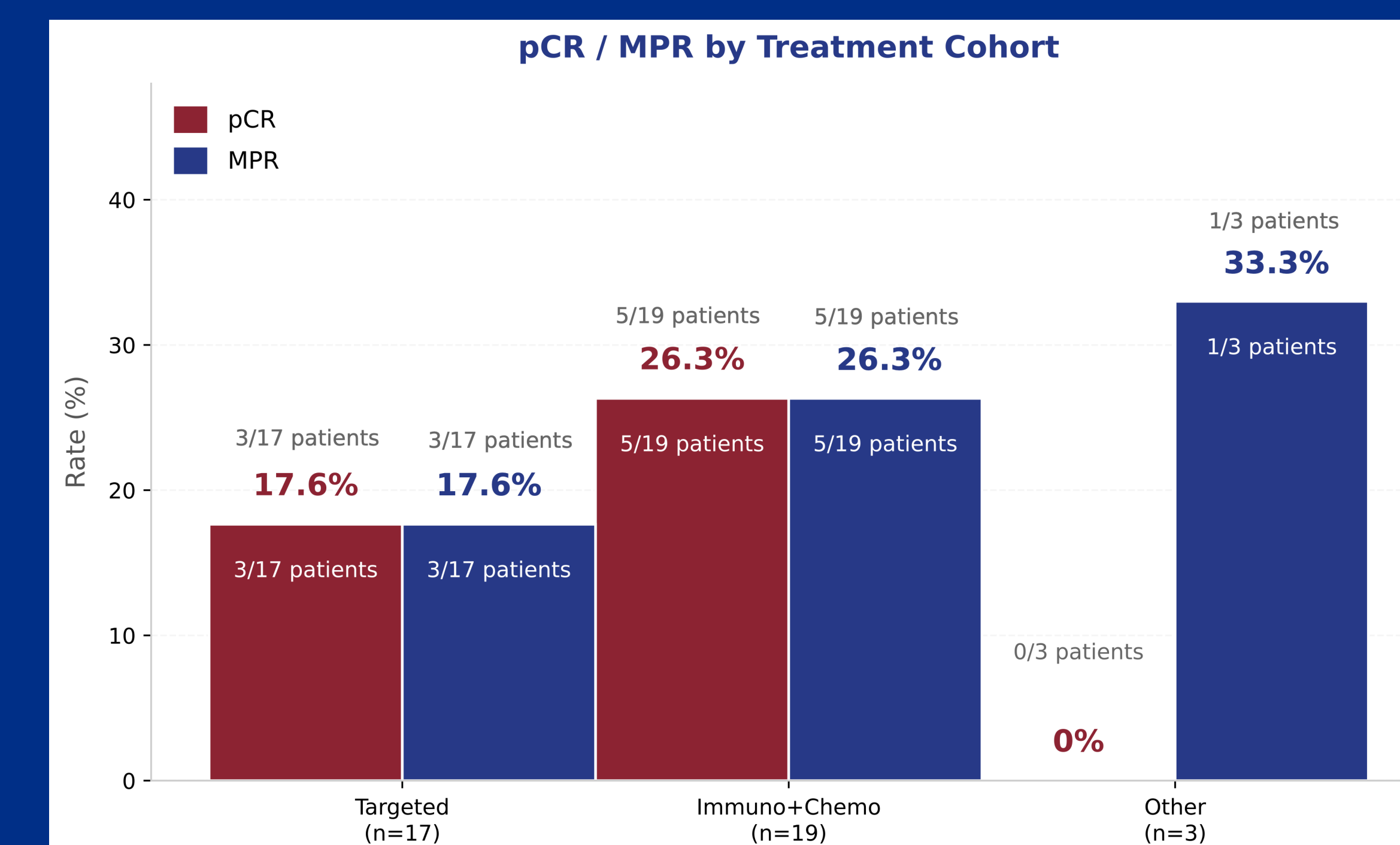
Patients with rare-mutation NSCLC were enrolled across three treatment cohorts.

► pCR/MPR by treatment

17 patients received perioperative TKI; both pCR and MPR rates were 17.6% (3/17).

19 patients received perioperative IO + chemo; both pCR and MPR rates were 26.3% (5/19).

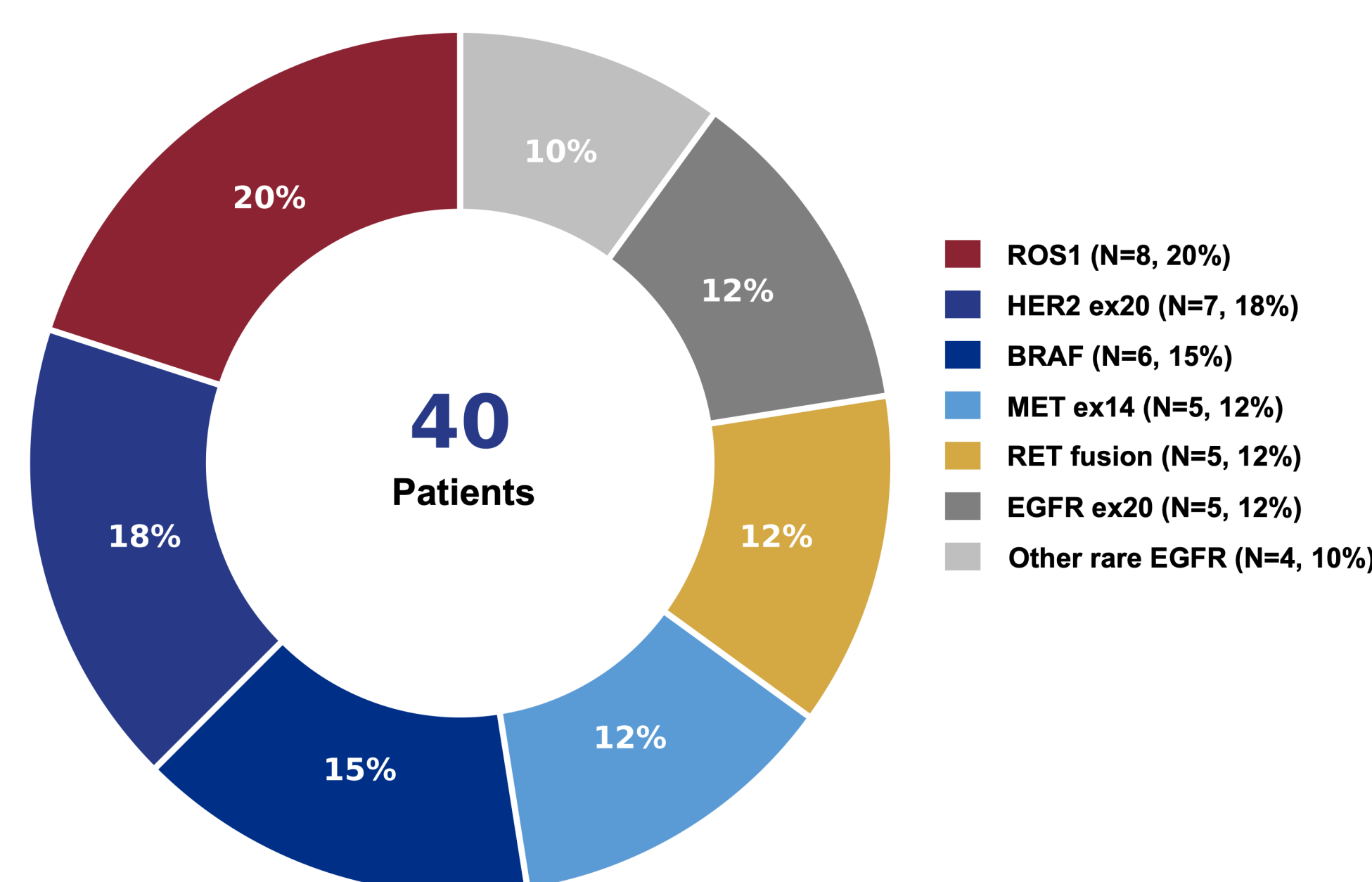
3 patients received other treatments; the MPR rate was 33.3% (1/3).



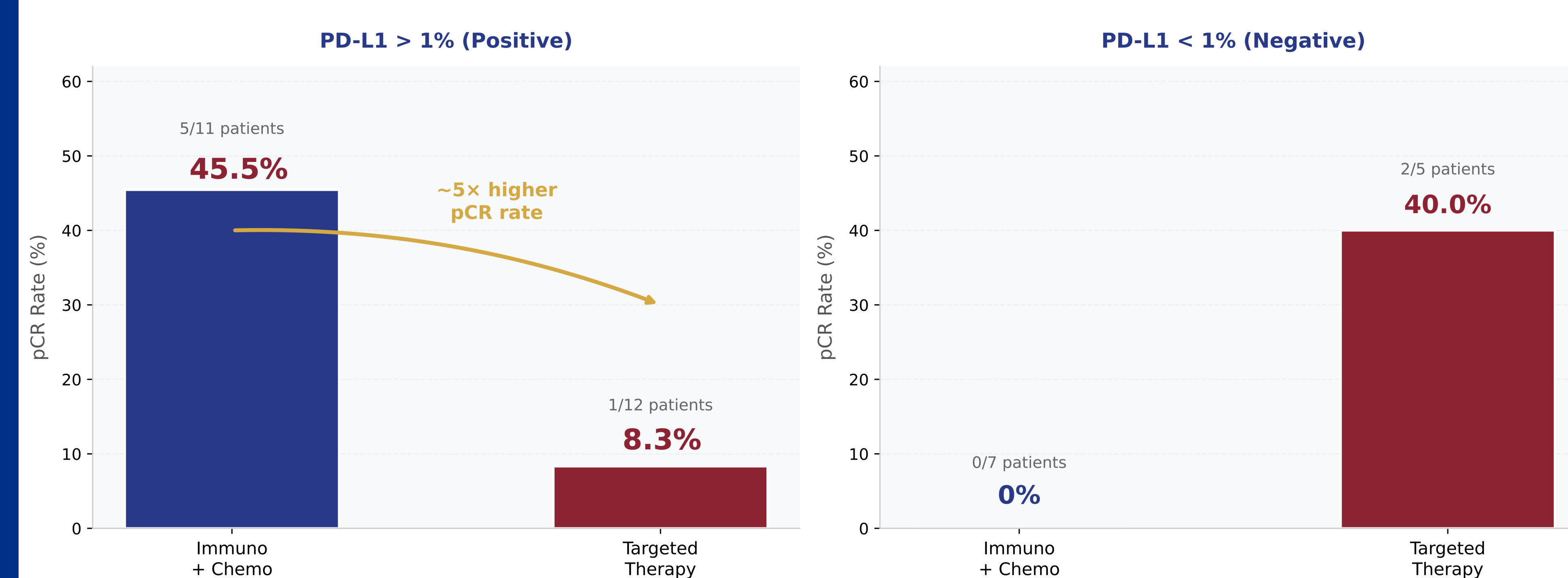
► Stratified by PD-L1 expression:

- PD-L1 > 1%: The pCR rate reached 45.5% (5/11) with immunotherapy + chemo versus only 8.3% (1/12) with targeted therapy — a striking ~5-fold benefit.
- PD-L1 < 1%: The pCR rate was 0% (0/7) with immunotherapy + chemo versus 40.0% (2/5) with targeted therapy — chemoimmunotherapy provides limited benefit for PD-L1-negative patients.

Mutation Type Distribution (n=40)



pCR Rate Stratified by PD-L1 Expression



CONCLUSIONS

► Key Takeaway

Perioperative IO+chemo may serve as a potential treatment option for early-stage patients with NSCLC harboring rare driver mutations, particularly those with PD-L1 positivity. Further validation in prospective large-sample studies is warranted.