

Biomarker-Driven Neoadjuvant Therapy in Resectable NSCLC: Interim Results From the PURPOSE Phase II Umbrella Study

Interim results from a phase II umbrella study | Poster Tour Presenter: GUO SONGYUAN

Clinical challenge

Resectable NSCLC is biologically heterogeneous, and optimal neoadjuvant strategies remain undefined across molecular subgroups.

Study concept

PURPOSE evaluated a biomarker-guided and adaptive treatment strategy integrating driver alterations, PD-L1 expression, and treatment response.

Biomarker-guided treatment allocation framework

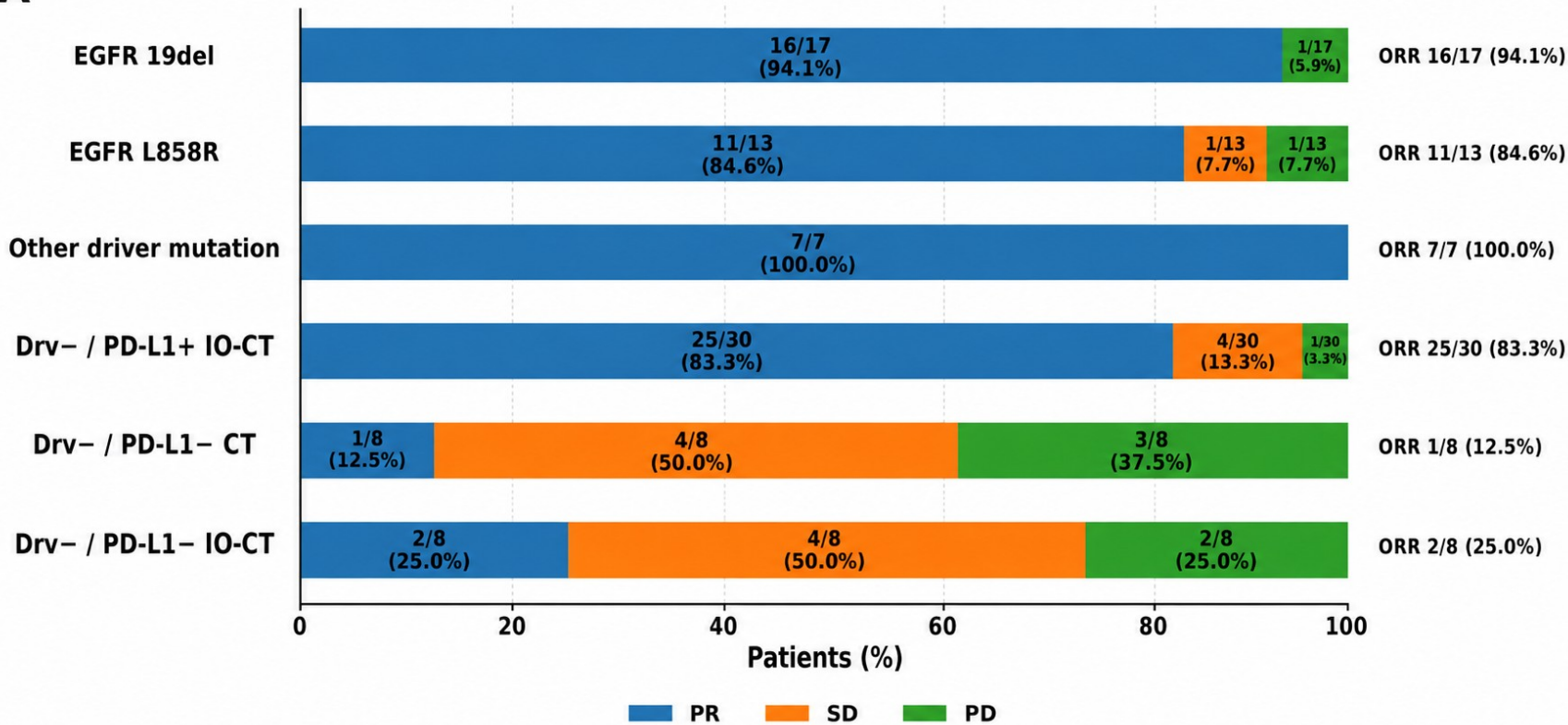
Baseline molecular profiling

- Driver alteration → matched targeted therapy
- No driver alteration → PD-L1-guided strategy
 - PD-L1 positive → IO + CT
 - PD-L1 low/negative → CT

Adaptive exploration: inadequate response to CT followed by IO-CT conversion (F→G)

Primary endpoint: objective response rate (ORR)

A

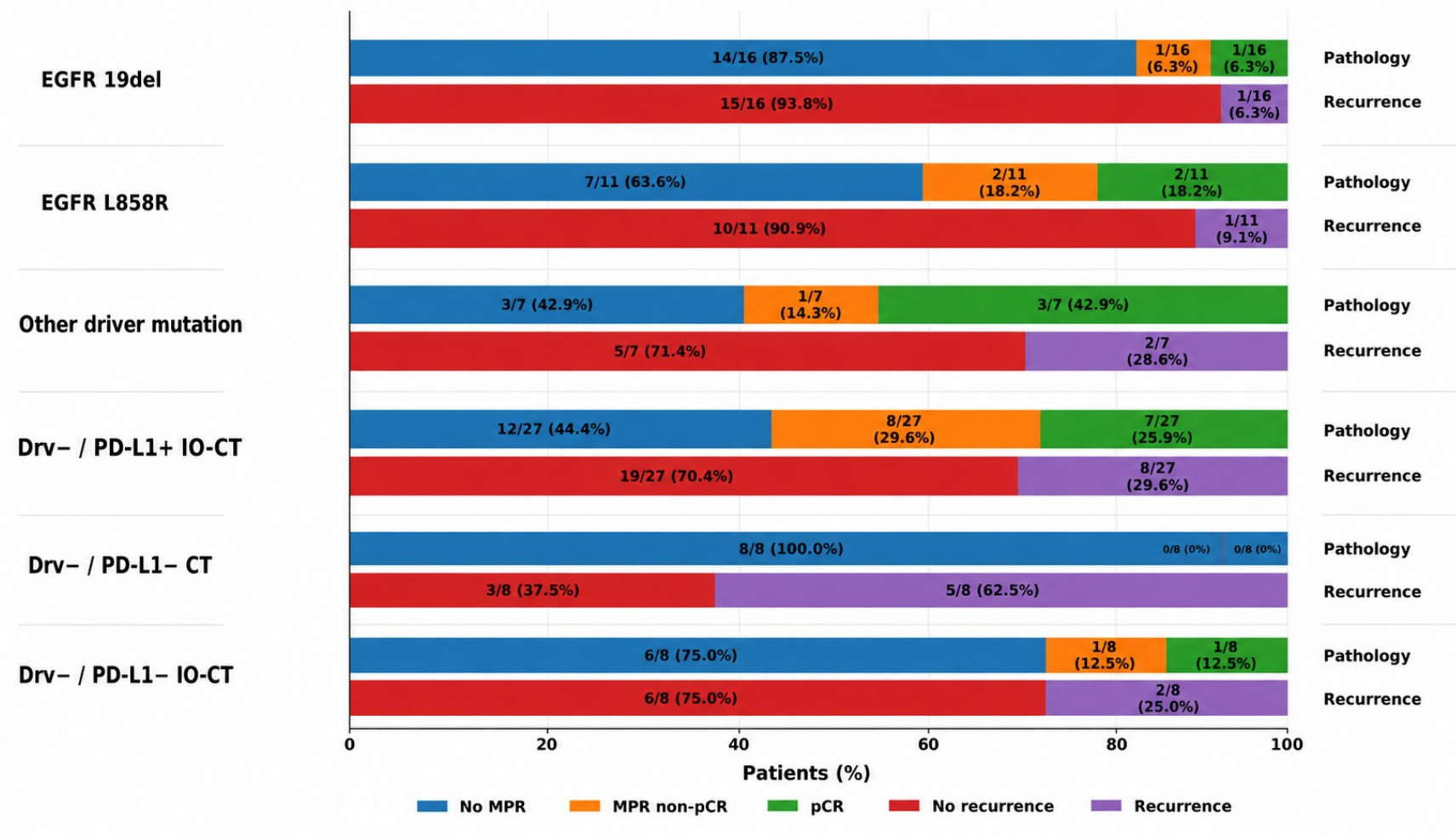


Key findings

- Treatment sensitivity differed substantially across biomarker-defined cohorts.
- **Driver-positive tumors** showed high activity with matched targeted approaches.
- **Driver-negative/PD-L1-low tumors** showed limited activity with chemotherapy alone, while IO-containing strategies demonstrated potential activity.

Pathological response and recurrence patterns

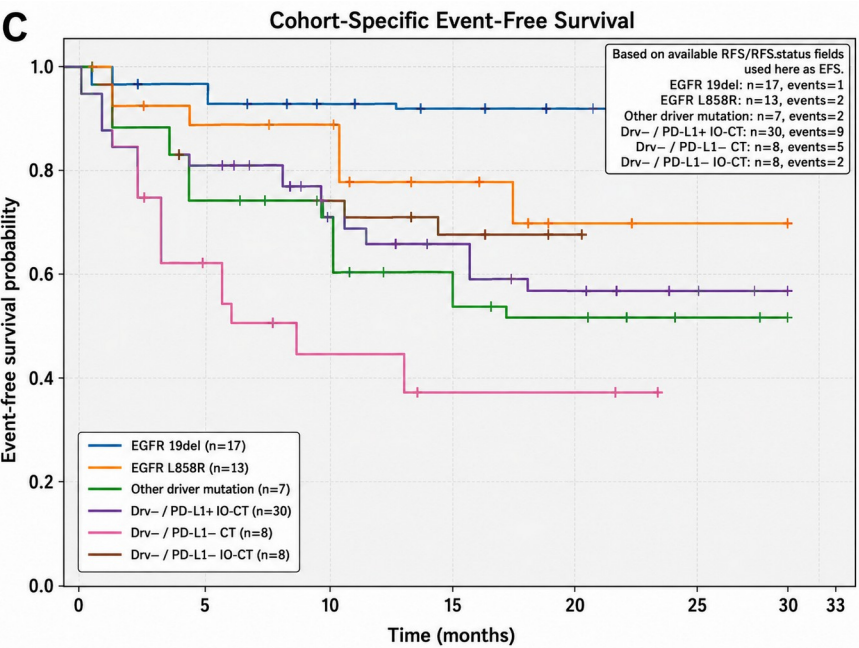
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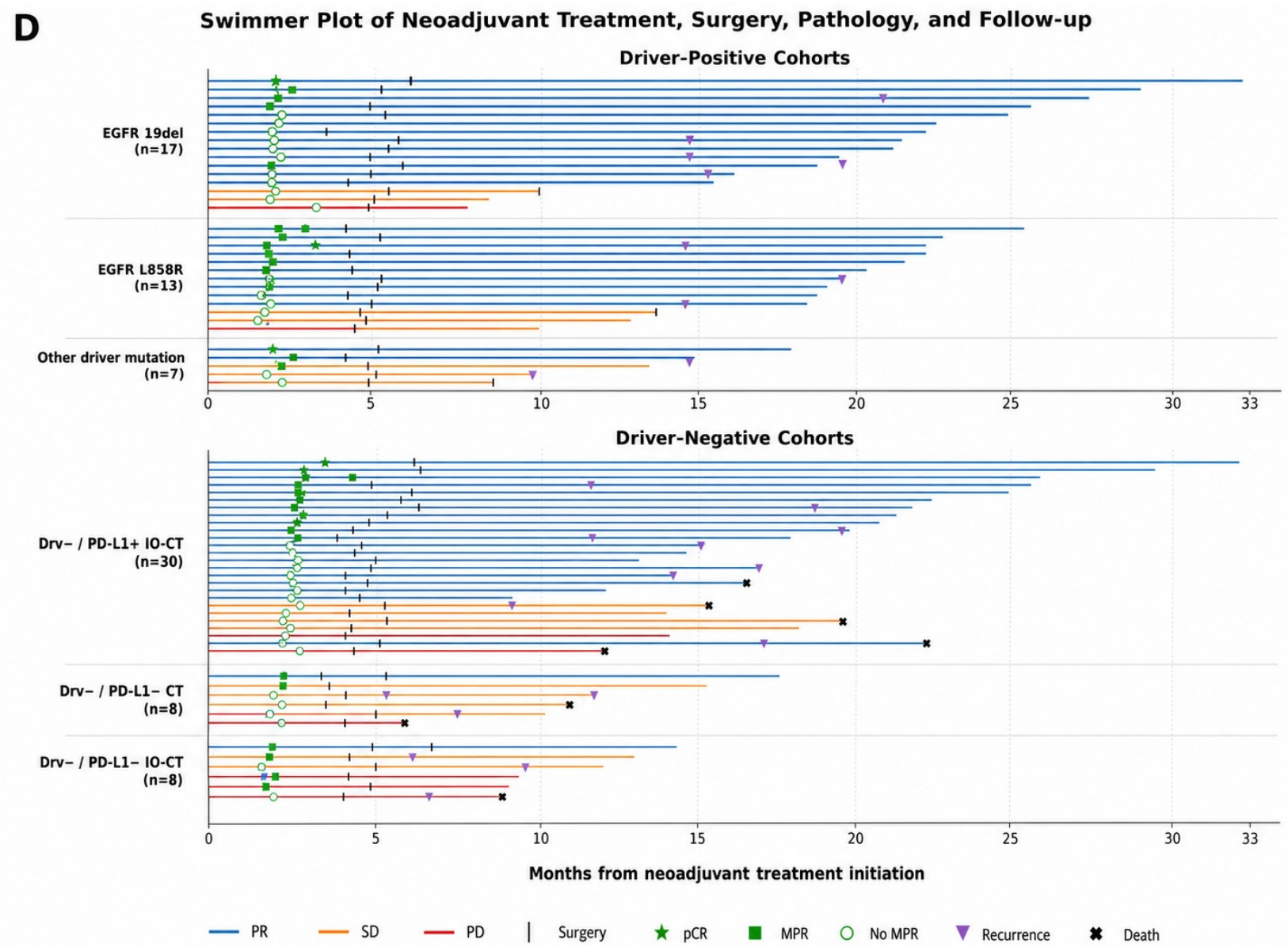
Key findings

- **Pathologic response** did not fully align with **early recurrence**.
- **EGFR-targeted therapy** cohorts demonstrated favorable disease control despite relatively modest MPR/pCR rates.
- **IO-containing therapy** achieved higher pCR rates, but patients without major pathological response showed increased recurrence risk.

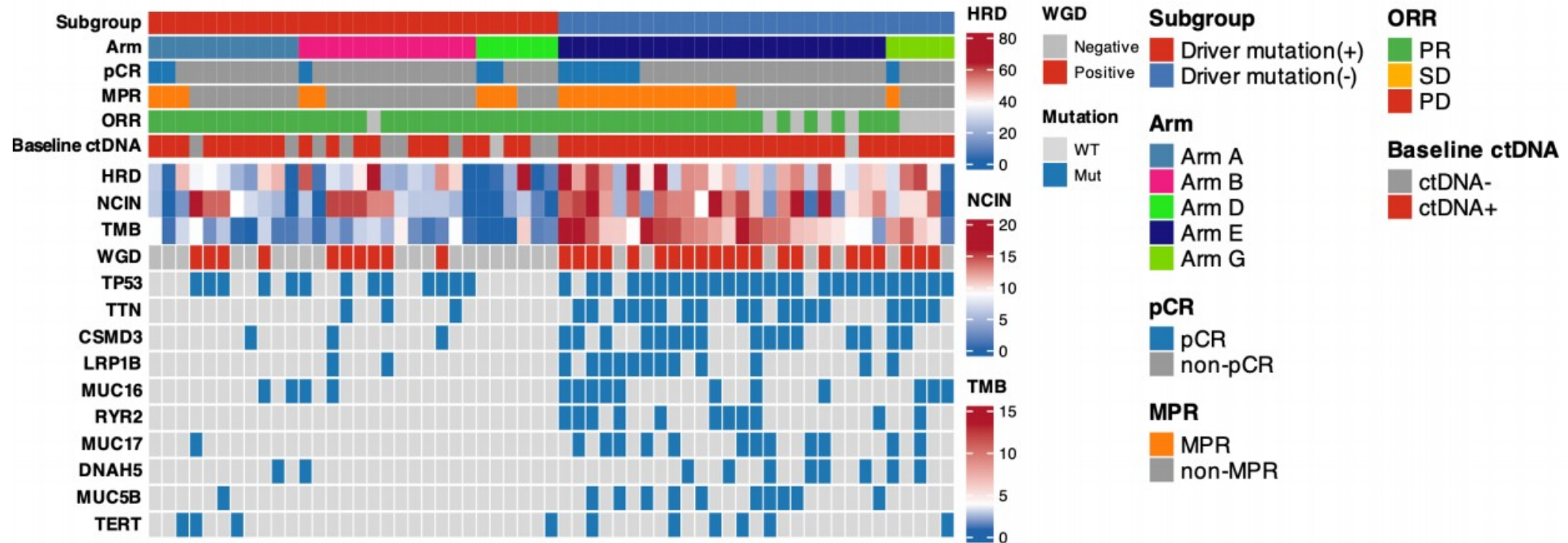
Distinct clinical trajectories after biomarker-guided neoadjuvant therapy



These findings support biomarker-guided treatment selection rather than a uniform neoadjuvant approach for all resectable NSCLC patients.



Clinical implications and future directions



Conclusions

- Biomarker-guided treatment allocation is feasible in resectable NSCLC.
- Molecular and immune-defined cohorts demonstrated distinct clinical trajectories.
- Exploratory biomarkers (NCI-N, TMB, LRP1B alterations, and longitudinal ctDNA dynamics) may further refine individualized treatment selection.

PURPOSE highlights the need for individualized perioperative strategies beyond a one-size-fits-all approach.

Further validation and longer follow-up are ongoing.

Thank You

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