Neoadjuvant nivolumab in early-stage non–small cell lung cancer (NSCLC): Five-year outcomes.

Presenter : Dr. Rushabh Kothari
Director, Oncowin Cancer Center,Ahmedabad

Slide Courtesy: Dr. Siddharth Turkar
Director, Radiant Cancer Hospital, Raipur

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Background

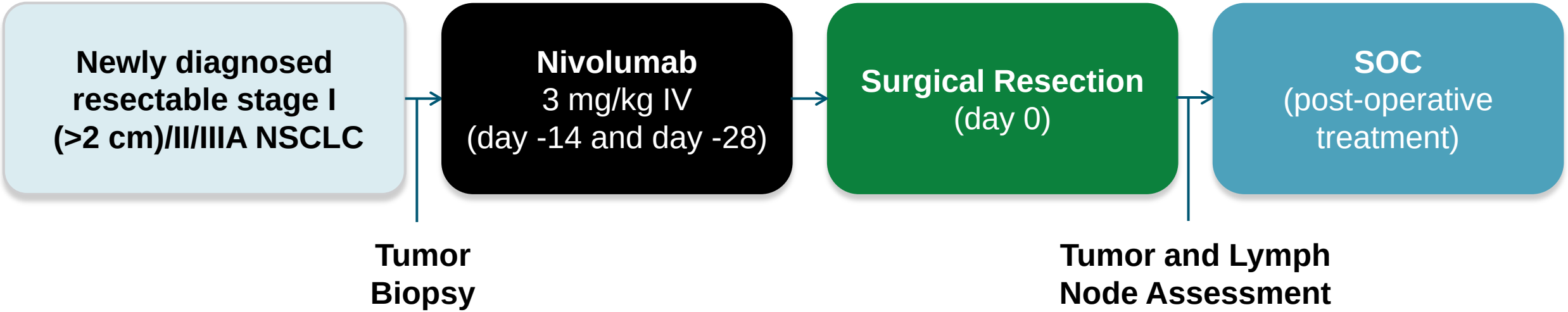
- First phase I/II trial of neoadj nivolumab (nivo) in resectable NSCLC, finding therapy to be safe and feasible.

- Final clinical results from this cohort, representing the longest follow up data for neoadj anti-PD-1 to date

Methods

- Two doses of neoadj nivo (3 mg/kg) were given prior to resection in 21 patients (pts) with resectable NSCLC.
- 5-year (yr) follow-up data, including recurrence- free survival (RFS), overall survival (OS) and association with pathologic response were tabulated.
- Event time distributions were estimated with the Kaplan-Meier method.
- All p-values are two sided with 0.05 significance level.

Neoadjuvant Nivolumab Schema[1]

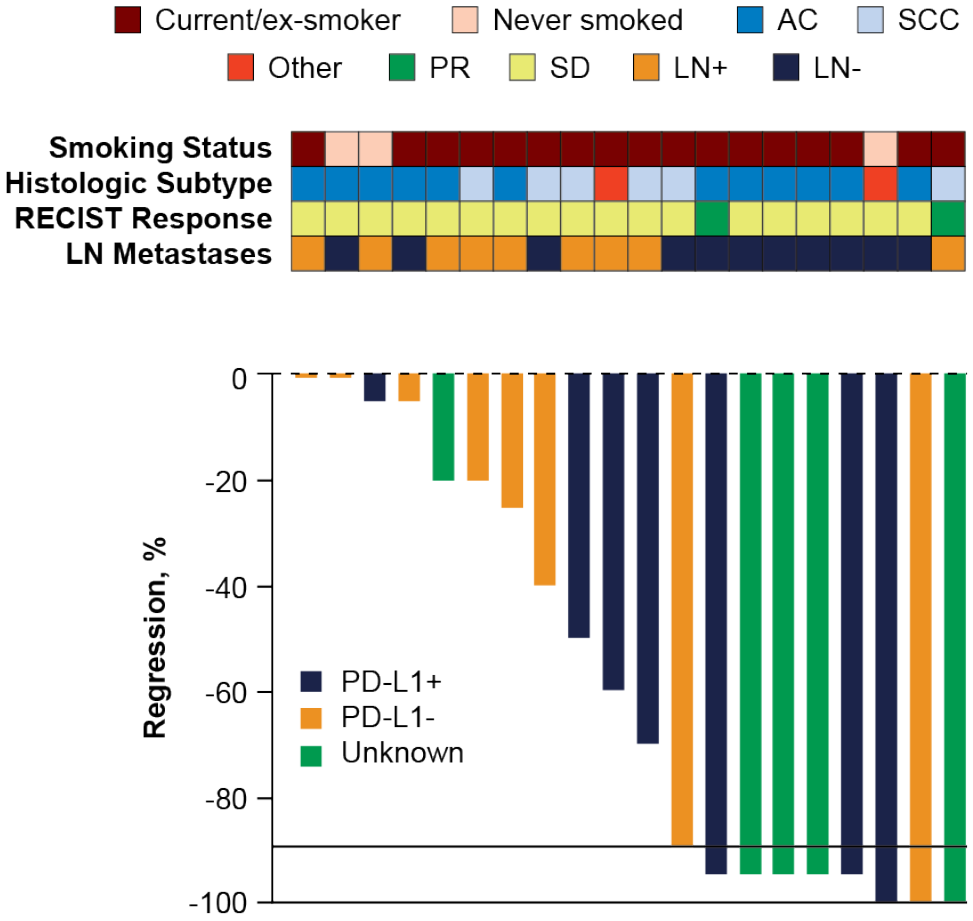


- **Primary endpoints:** Safety and feasibility
- **Also evaluated:** Tumor pathological response; expression of PD-L1; mutational burden; and mutation-associated, neoantigen-specific T-cell responses

1. Forde PM et al. *N Engl J Med*. 2018;378:1976-1986.

Pathological Assessment of Response to Neoadjuvant Nivolumab[1]

- **% of Pathological Regression According to Subgroup**



- Major pathological response occurred in 9/20 resected tumors (45%; 95% CI, 23-68)
- Responses occurred in both PD-L1–positive/–negative tumors
- 2 pCR

1. Forde PM et al. *N Engl J Med*. 2018;378:1976-1986.

Results – Five year updates

- Median follow up of 63 months
- OS: 3yr: 85%, 4yr: 80%, 5 yr: 80%
- RFS: 3yr: 65%, 4yr: 60%, 5 yr: 60%
- HR for pathologic down-staging was in the direction of improved RFS, without meeting statistical significance (HR 0.36, 95% CI 0.07-1.75, p = 0.2).
- RFS HR estimates for MPR and an alternative pathologic cut-off of less than 50% residual tumor (RT), were 0.61, (95% CI 0.15-2.44, p = 0.48) and 0.36, (95% CI 0.09-1.51, p = 0.16) respectively.

Results - Five year updates

- The direction of the effect of pre-treatment PD-L1 positivity (≥1%) was to improve RFS (HR 0.36, 95% CI 0.07-1.85, p = 0.22).
- At 5-yr follow up, 8 of 9 (89%) pts with MPR were alive and no cancer deaths have occurred. Amongst pts with MPR, 1/9 pts had a cancer recurrence in the mediastinum treated successfully with definitive chemoradiotherapy.
- Both pts with pCR are alive and without recurrence.
- No long-term immune-related adverse events have occurred other than one G3 dermatologic event.

Conclusions

- Favorable to historical trends.

- MPR trended toward improved RFS, while definitive conclusions are limited by cohort size and overall low recurrence rate.

Thank you