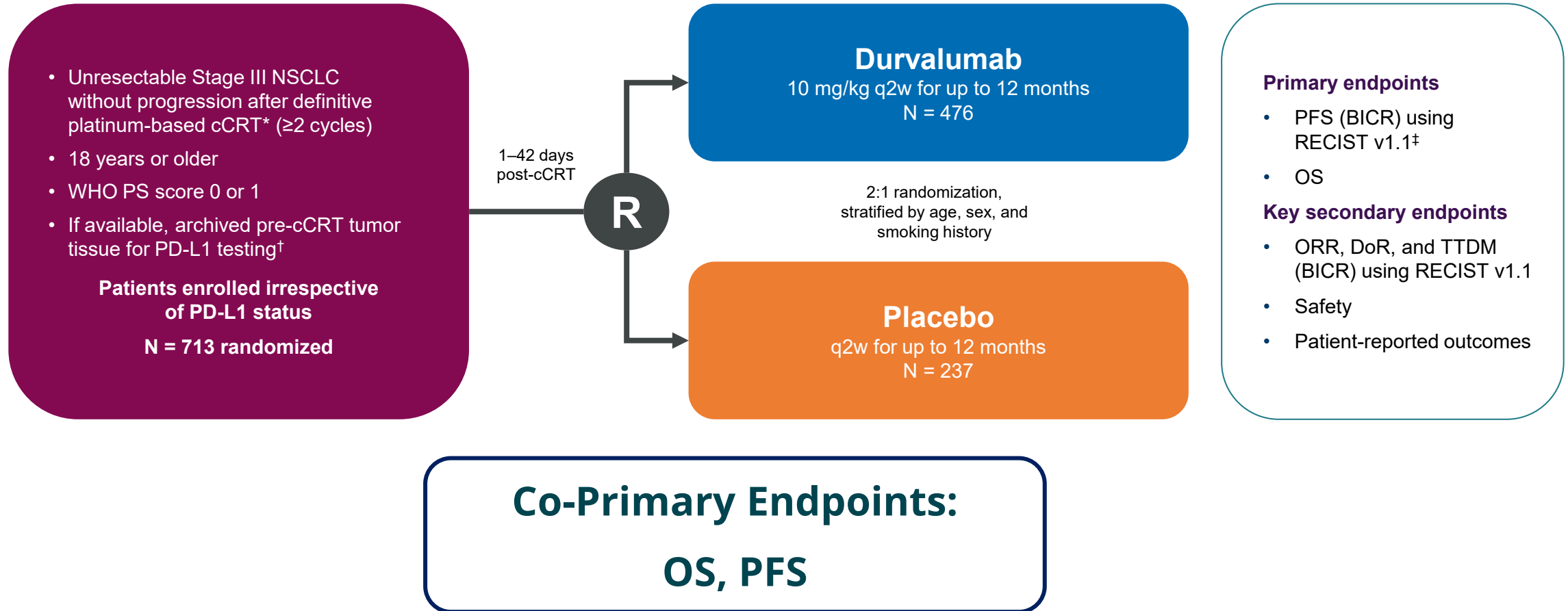


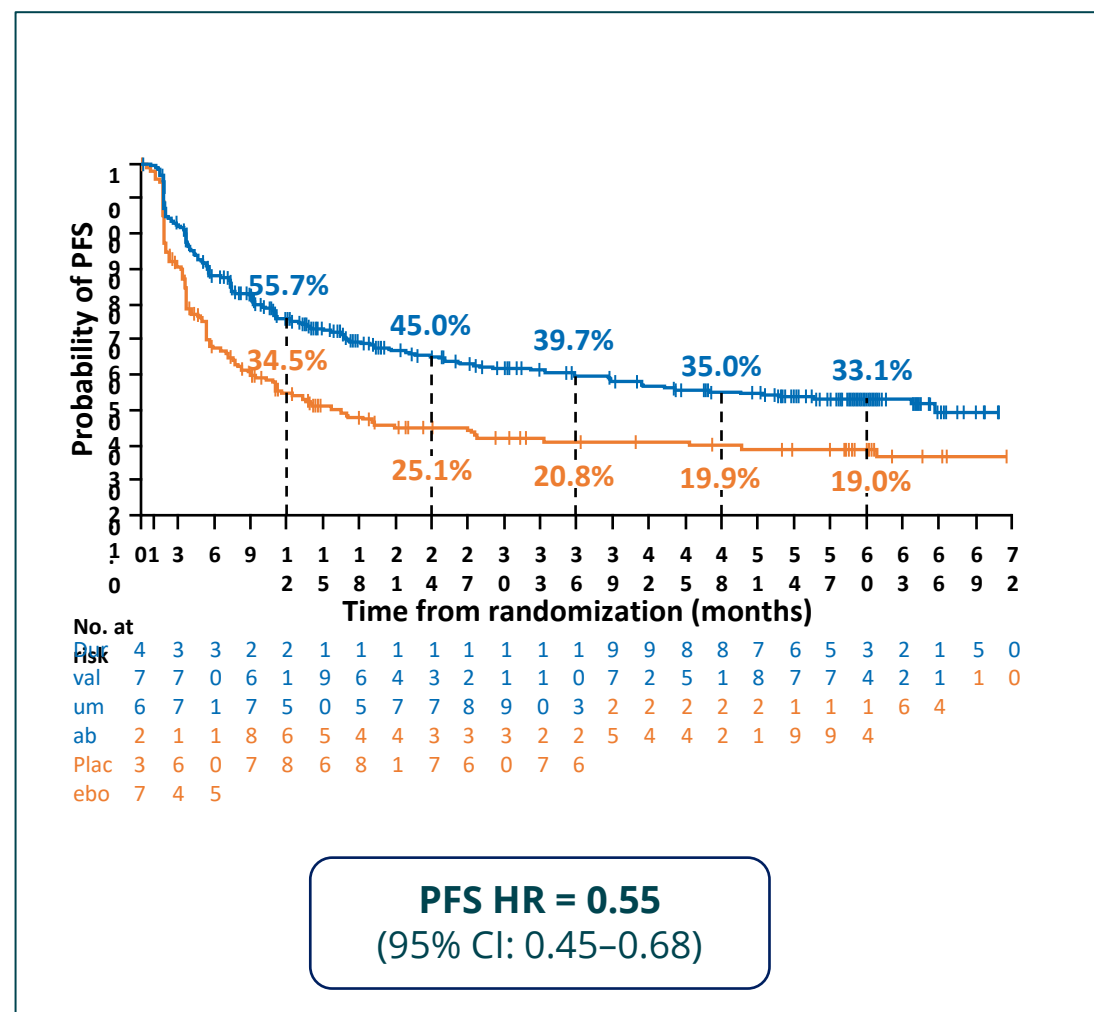
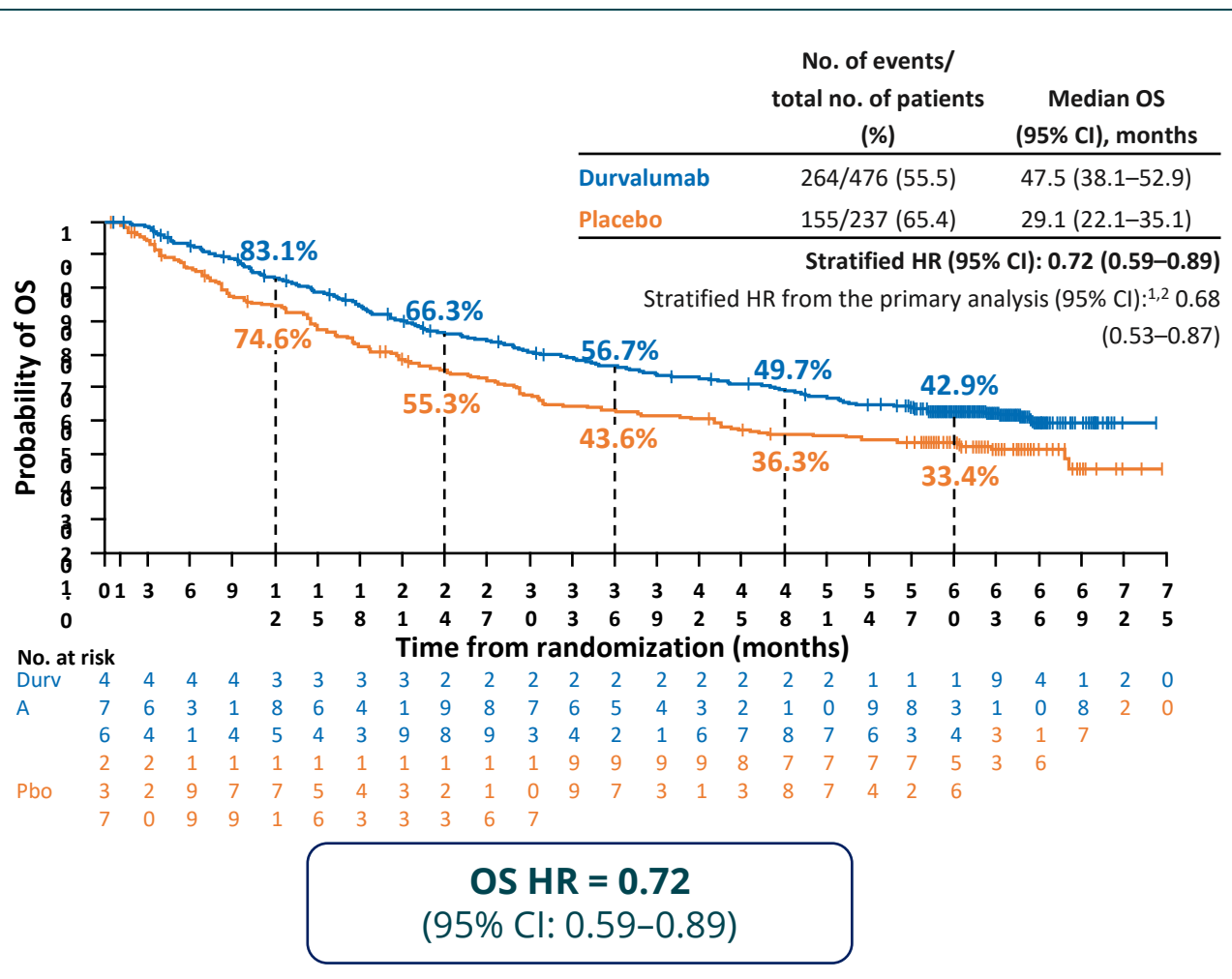
# Case 5: Stage III NSCLC after progression on maintenance durvalumab

- 65-year-old man
- Undergoing treatment for stage III unresectable squamous NSCLC (T4N2M0)
- The tumoral PD-L1 score is 50%
- There are no actionable genomic alterations
- He commences consolidation durvalumab
- Within 6 months of therapy, he develops progressive disease in the bones on his first restaging CT
- **What is the most appropriate next treatment?**

# PACIFIC: Durvalumab Post cCRT in Stage III Unresectable NSCLC: Study Design

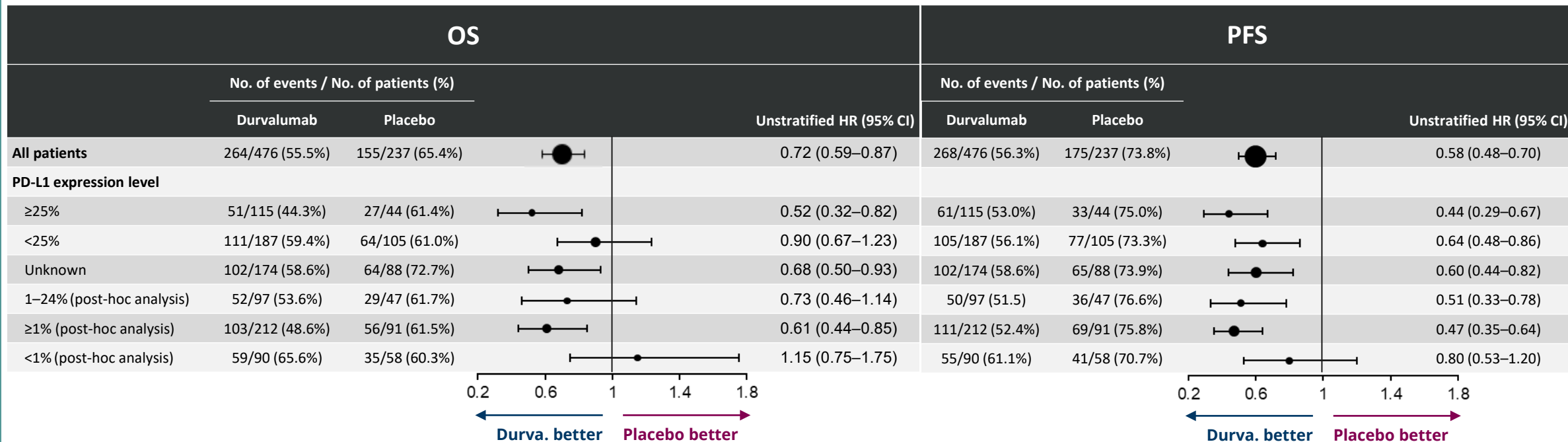


# PACIFIC: OS and PFS Benefit

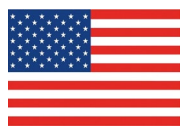


Spigel DR, et al. *J Clin Oncol.* 2022;40(12):1301-1311.

# PACIFIC: 5-year OS and PFS by PD-L1 Subgroups



## FDA approval:



- Feb 16 2018
- 42 days after cCRT
- PDL1 all-comers

## EMA approval:



- September 21 2018
- 42 days after cCRT
- PDL1 ≥1% only

# Treatment Beyond Progression: Definitions



## Defining tumor resistance to PD-1 pathway blockade: recommendations from the first meeting of the SITC Immunotherapy Resistance Taskforce



ORIGINAL ARTICLE

Clinical definition of acquired resistance to immunotherapy in patients with metastatic non-small-cell lung cancer

**Table 1** Definitions of primary and secondary resistance in advanced disease setting

Resistance phenotype	Drug exposure requirement	Best response	Confirmatory scan for PD requirement	Confirmatory scan timeframe
Primary resistance	≥6 weeks	PD; SD for <6 months*	Yes†	At least 4 weeks after initial disease progression‡
Secondary resistance	≥6 months	CR, PR, SD for >6 months*	Yes†	At least 4 weeks after disease progression‡

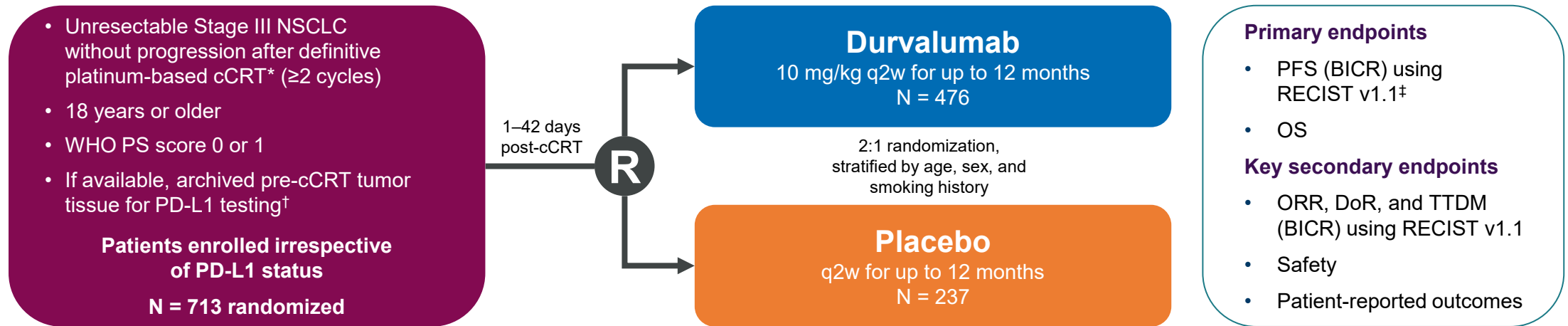
### Modification of Acquired Resistance Definition for NSCLC:

- PD-(L)1 mono or IO/IO combinations can be grouped
- Objective response (CR/PR), SD is excluded
- No need for confirmation scans
- AR if there is progression within 6 months of last IO (Receptor occupancy of PD-1)

**Table 4** Definitions of resistance after discontinuing treatment for metastatic disease

Stopped therapy (CR/PR/end of study/other social rationale)	Duration of time after last dose of PD-(L)1 inhibitor	Confirmatory scan requirement
Primary resistance	No CR/PR prior to discontinuation	No
Secondary resistance	Prior CR/PR and ≤12 weeks from last dose	Yes
Late progression	Prior CR/PR and >12 weeks from last dose	Yes

# Treatment Beyond Progression Early-Stage NSCLC: Post PACIFIC

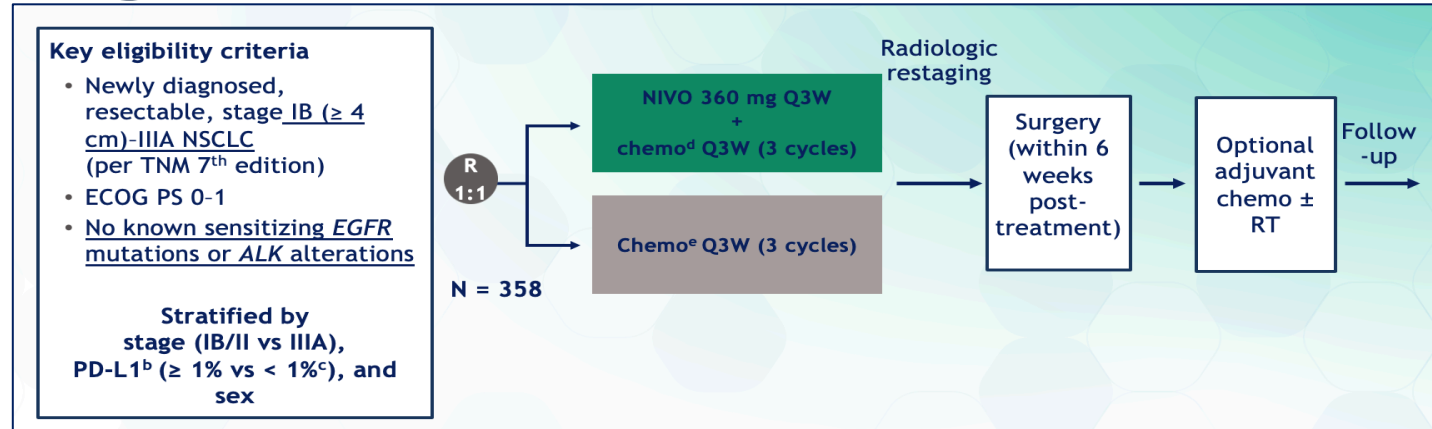


Type of Therapy	Durvalumab (n = 476)	Placebo (n = 237)
Any therapy, No. (%)	231 (48.5)	139 (58.6)
Radiotherapy	97 (20.4)	61 (25.7)
Immunotherapy <sup>a</sup>	60 (12.6)	69 (29.1)
Cytotoxic chemotherapy	157 (33.0)	85 (35.9)
Other systemic therapies <sup>b</sup>	53 (11.1)	35 (14.8)
Other	2 (0.4) <sup>c</sup>	0

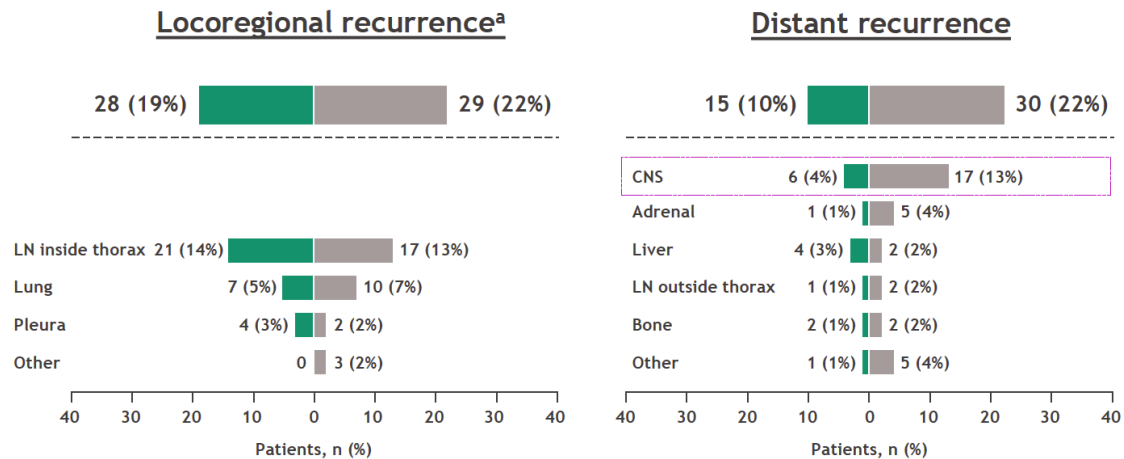
- 34 pts completed 12-months of initial consolidation durvalumab (7%)
- Of these patients, 4 (12%) completed 12 months of re treatment

# Treatment Beyond Progression

## Early-Stage NSCLC: Lessons From CM816



### Patterns of Recurrence



### 5-yr Follow-up

