

# Rechallenge with IO in NSCLC

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# Immunotherapy Rechallenge

- Definition for this talk:
  - Resumption of immunotherapy after intervening treatment holiday or alternative anti-cancer treatment(s)
    - **Course completion, severe irAE, or progression**
  - \*Not continuation beyond progression

It depends upon what the meaning of the word 'is' is.

William J. Clinton

# Organization

- Prospective clinical trial data
  - KEYNOTE
- Meta-analysis data (retrospective cohorts)



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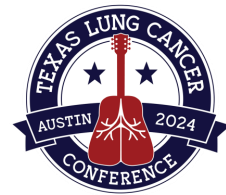


# Prospective Clinical Trial Data

- **Rechallenge upon progression after cessation for therapy completion - KEYNOTE data**
- No data from CheckMate, IMPOWER, EMPOWER, or POSEIDON
- Not to mention PACIFIC or neoadjuvant/perioperative/adjuvant IO...



Rodriguez-Abreu D, et al. Pooled analysis of outcomes with second course pembrolizumab across five phase 3 studies of NSCLC. WCLC 2022



# KEYNOTE Data

- Cohort 1: Pembrolizumab monotherapy (**n=57**), PD-L1  $\geq 1\%$ , KN-024, KN-042, KN-598
- Cohort 2: Platinum doublet plus pembrolizumab (**n=14**), any PD-L1, KN-187, KN-407
- Second course: Pembrolizumab 200mg q3 weeks for up to 1 year

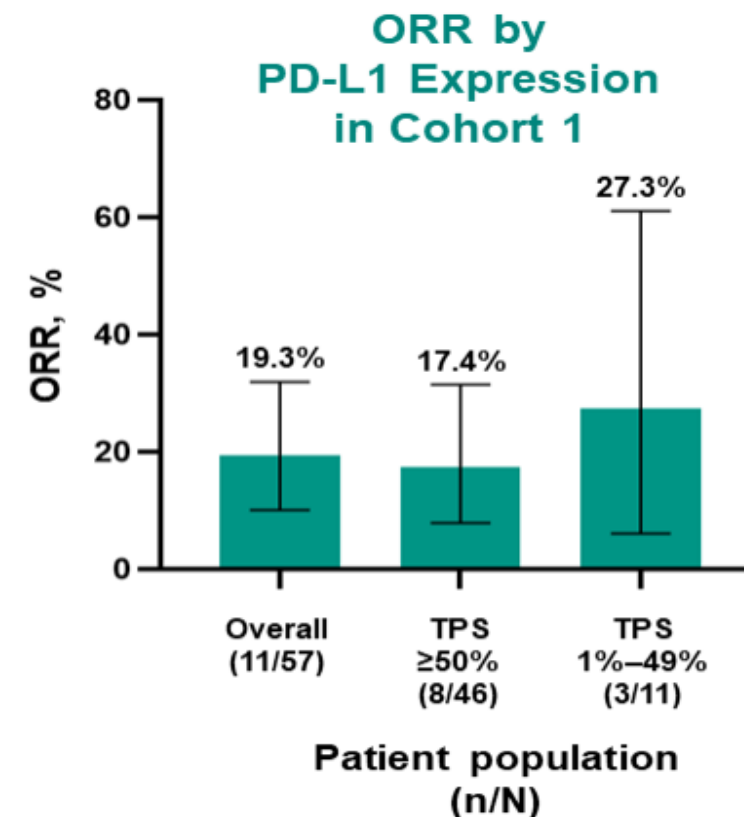
Rodriguez-Abreu D, et al. Pooled analysis of outcomes with second course pembrolizumab across five phase 3 studies of NSCLC. WCLC 2022



# Tumor Response and Survival During Second-Course Pembrolizumab



	Cohort 1 (pembro monotherapy) N = 57	Cohort 2 (pembro + chemo) N = 14
ORR <sup>a</sup> (95% CI), %	19.3 (10.0–31.9)	0 (0.0–23.2)
DCR <sup>a</sup> (95% CI), %	73.7 (60.3–84.5)	50.0 (23.0–77.0)
Best overall response, <sup>a</sup> n (%)		
CR	0	0
PR	11 (19.3)	0
SD	31 (54.4)	7 (50.0)
PD	8 (14.0)	2 (14.3)
NA <sup>b</sup>	7 (12.3)	5 (35.7)
DOR, <sup>a</sup> median (range), mo	NR (0.0+ to 20.0+)	–
DOR ≥6 mo, %	78.8	–
OS, <sup>c</sup> median (95% CI), mo	27.5 (21.7–NR)	NR (NR–NR)
6-mo rate (95% CI), %	85.1 (72.4–92.3)	85.1 (52.3–96.1)
PFS, <sup>a,c</sup> median (95% CI), mo	10.3 (5.6–14.0)	7.7 (1.8–NR)
6-mo rate (95% CI), %	60.8 (46.0–72.7)	54.5 (22.9–78.0)

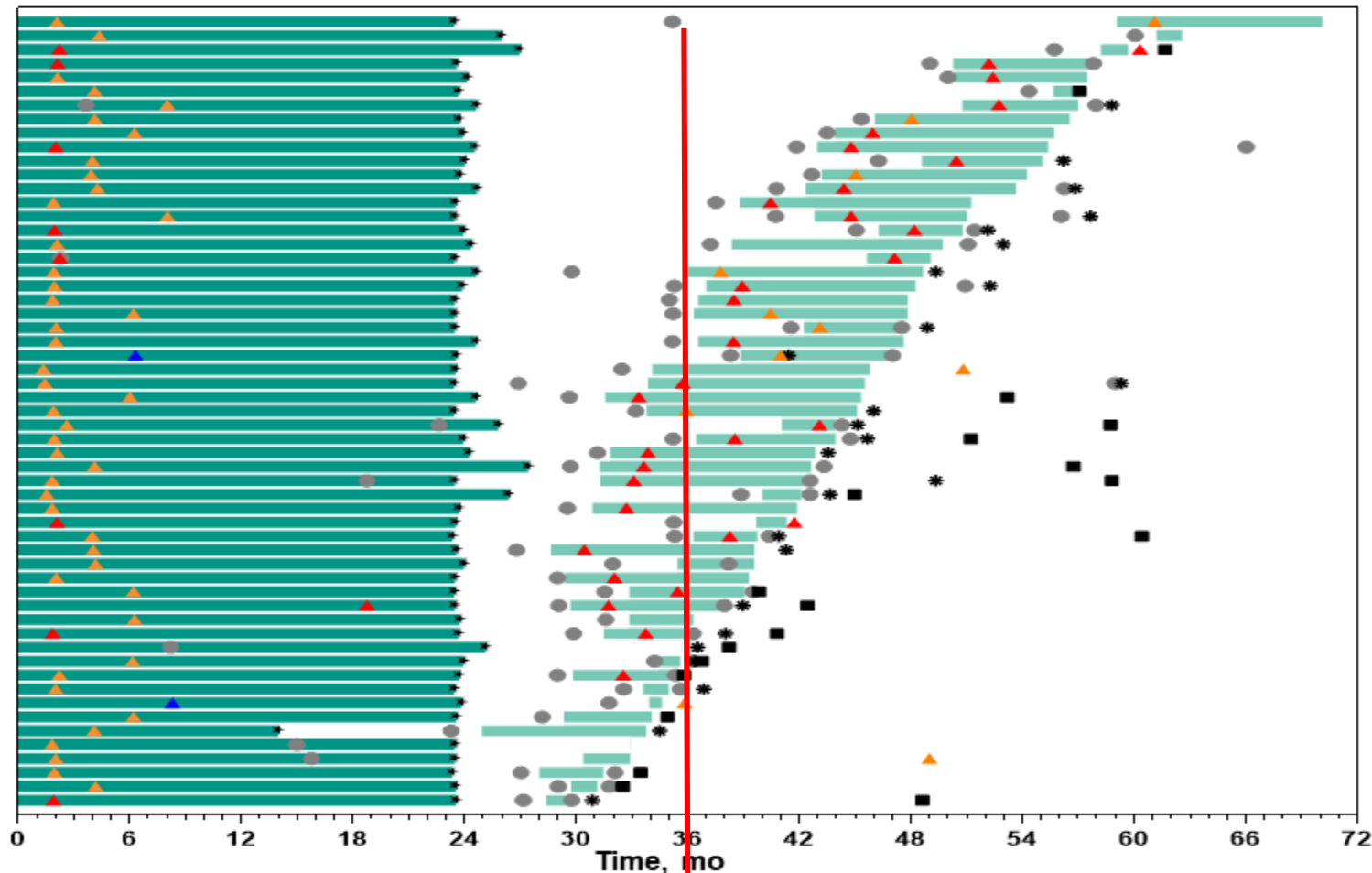


<sup>a</sup>+ indicates no PD at the time of last disease assessment.

<sup>b</sup>Per RECIST v1.1 by investigator review. <sup>c</sup>No postbaseline assessment available for response evaluation. <sup>d</sup>From the start of second course.

Database cutoff dates: Jun 1, 2020 (KN024); Apr 28, 2021 (KN042); Oct 1, 2021 (KN598); Aug 28, 2020 (KN189); Sep 30, 2020 (KN407).

# Individual Patient Profiles: Cohort 1 (initial pembrolizumab monotherapy)



	Median (range), mo
Time from stopping first-course pembro to starting second course	12.0 (3.8–35.6)
Time from start of second course to data cutoff	21.5 (0.6–46.5)

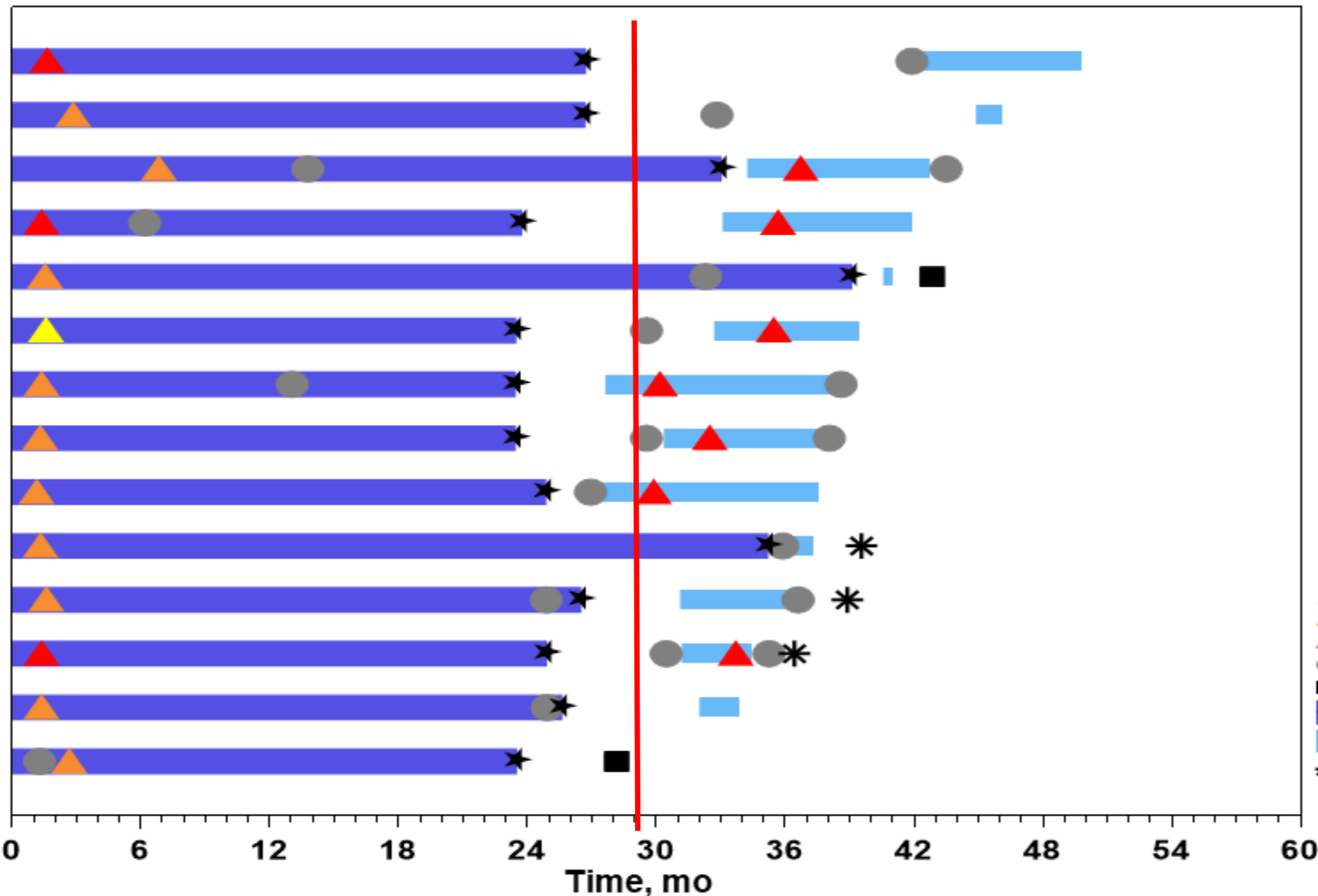
- ▲ CR
- ▲ PR
- ▲ SD
- PD
- Death
- End of first course
- Second course
- \* Began subsequent therapy

<sup>†</sup>Patient stopped treatment at cycle 21 due to CR assessed per investigator and not BICR (PR). At the time of progression, patient was eligible for second-course pembrolizumab, per protocol.  
Database cutoff dates: Jun 1, 2020 (KN024); Apr 28, 2021 (KN042); Oct 1, 2021 (KN598); Aug 28, 2020 (KN189); Sep 30, 2020 (KN407).



# Individual Patient Profiles: Cohort 2

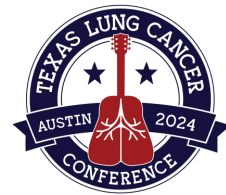
(initial platinum + pembrolizumab)



	Median (range), mo
Time from stopping first-course pembro to starting second course	5.4 (0.9–18.2)
Time from start of second course to data cutoff	10.3 (1.9–18.0)

- ▲ CR
- ▲ PR
- ▲ SD
- PD
- Death
- ★ End of first course
- Second course
- \* Began subsequent therapy

Database cutoff dates: Jun 1, 2020 (KN024); Apr 28, 2021 (KN042); Oct 1, 2021 (KN598); Aug 28, 2020 (KN189); Sep 30, 2020 (KN407).



# KEYNOTE Data

- Toxicity during second course pembrolizumab

AE, n (%)	Cohort 1 (pembro monotherapy) N = 57	Cohort 2 (pembro + chemo) N = 14
Treatment-related AEs	14 (25)	4 (29)
Grade 3/4 AEs	3 (5)	1 (7)
Led to discontinuation	1 (2)	0
Led to death	0	0

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# Meta-Analysis Data

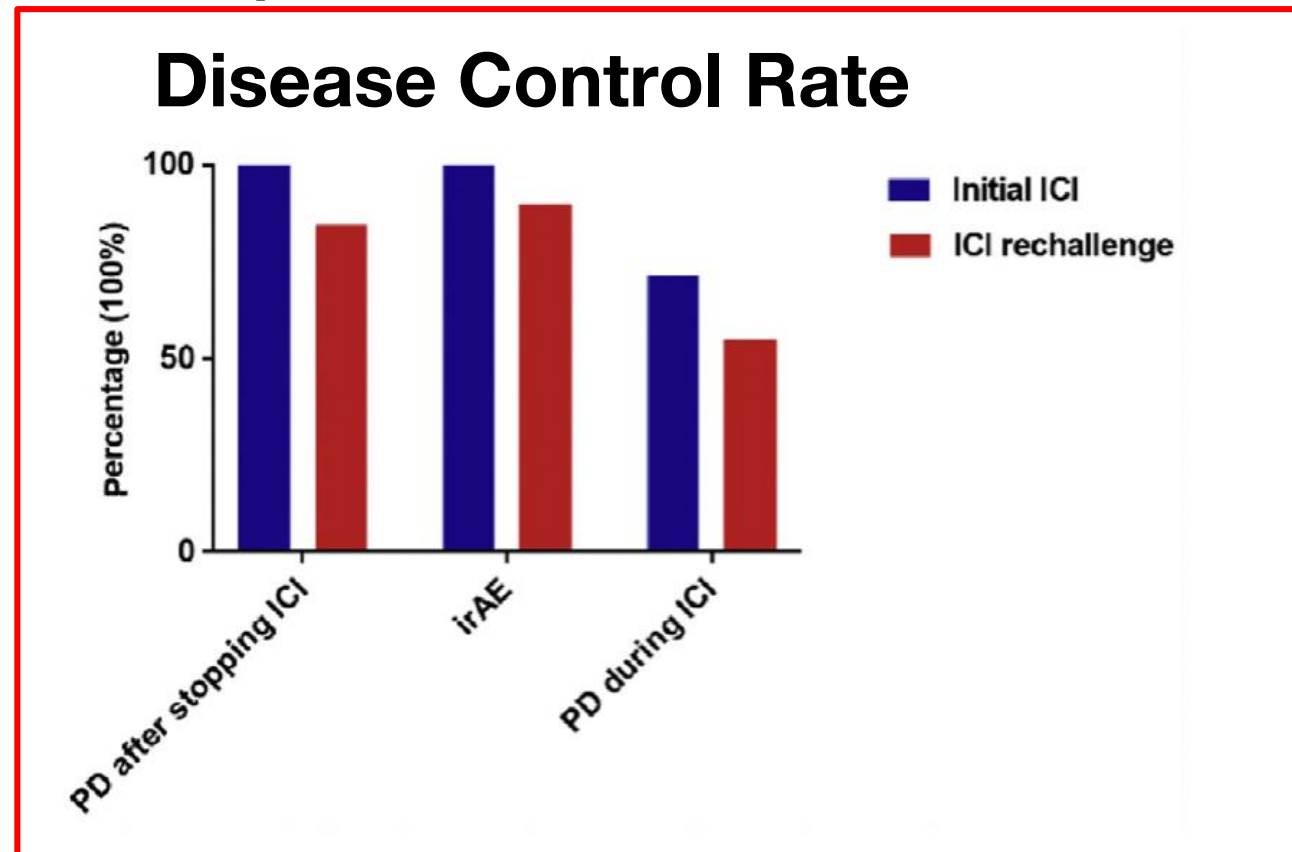
- Rechallenge upon progression:
  - Cessation for therapy completion
  - Cessation for irAE
  - Cessation for previous progression on immunotherapy

Xu S, et al. Heterogenous outcomes of ICI rechallenge in NSCLC: A meta-analysis. *JTO CRR* 2022

# Meta-Analysis Data

- 15 retrospective studies, 442 patients

- Grade  $3/4$  irAE:
  - 9% rechallenge
  - 17% initial use

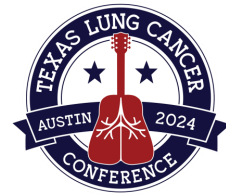


Xu S, et al. Heterogenous outcomes of ICI rechallenge in NSCLC: A meta-analysis. *JTO CRR* 2022

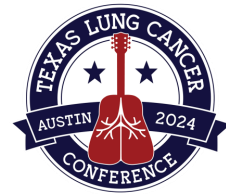


# Conclusions

- Rechallenge upon progression after cessation for therapy completion - GOOD IDEA 😄 😄 😄
- Rechallenge upon progression after cessation for toxicity - REASONABLE IDEA 😐 😐 😐
- Rechallenge upon progression after cessation for previous progression - PROBABLY NOT 😞 😞 😞



# Thank you for your attention



# Immunotherapy Rechallenge

- Case:
  - MD: “I recommend stopping immunotherapy and monitoring with CT scans because you’ve completed 2 years or you’ve had a severe side effect.”
  - Patient: “What if the cancer grows again?”