

# Immunotherapy treatment duration

*Experience in non-small cell lung cancer*

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# Disclosures [update 02/2021, alphabetical]

- **Research funding at University Hospitals KU Leuven**
  - MSD
- **Advisory functions**
  - AstraZeneca, BMS, Boehringer, Daiichi-Sankyo, MSD, Novartis, Pfizer, Roche, Sanofi
- **Lectures**
  - AstraZeneca, BMS, Eli-Lilly, MSD, Novartis
- **Others**
  - None



# NSCLC immunotherapy duration

> will the ostrich finally reach out?

- Patient case study
- Treatment guidelines
- Clinical trial data
  - RCT: Patients treated beyond 1 year
  - Follow-up: patients treated up to 2 years & re-challenge
- Patient case study recap and discussion



# NSCLC immunotherapy

> male patient, born 1956, smoker 70 pack-years

- **04/2020**
  - Chest X-ray (work-up arterial insufficiency legs): lesion L lower lobe
  - Lung adenocarcinoma, cT2b N3 M1c (peripancreatic lesion, L adrenal gland lesion)
  - Molecular: p.Gly12Ser c.34G>A in exon 2 of KRAS. PD-L1 5%
- **05/2020**
  - Start carboplatin-pemetrexed & pembrolizumab q3w
- **08/2020**
  - OK after 4 cycles -> pemetrexed & pembrolizumab q3w maintenance
- **12/2020**
  - Still OK, but ↓ renal function (C&G clearance 48) -> stop pemetrexed, continue pembrolizumab 400 mg q6w



# NSCLC immunotherapy

> male patient, born 1956, smoker 70 pack-years

Q

If the patient continues to do well (including no irAEs), my further plan is:

1. Stop immunotherapy after 2 years in case of RECIST CR/PR
2. Stop immunotherapy after 2 years in case of RECIST CR/PR/SD
3. Continue immunotherapy until RECIST PD
4. Continue immunotherapy until loss of clinical benefit
5. I would not know since I don't treat NSCLC



# NSCLC immunotherapy duration

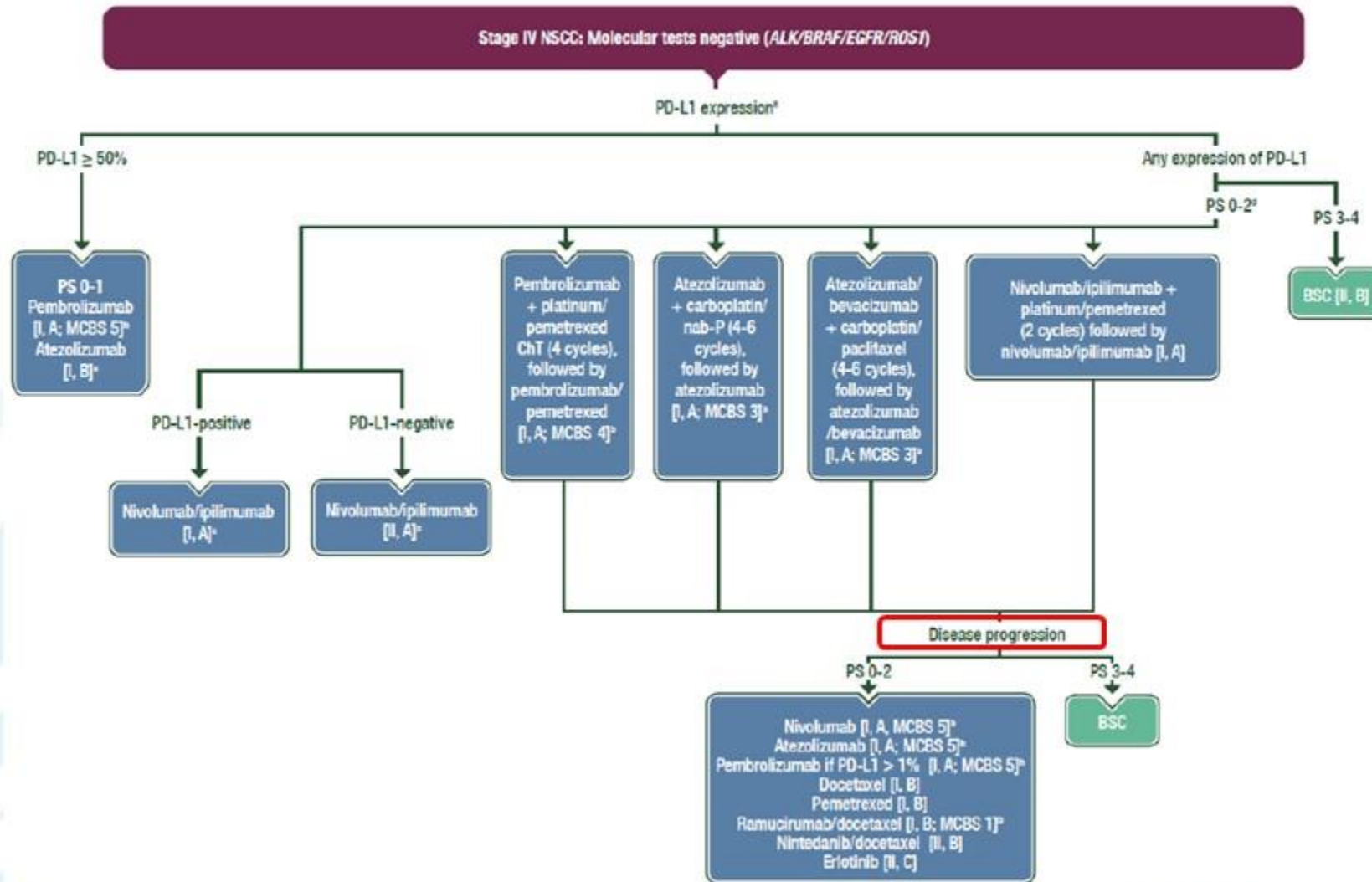
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# ESMO clinical practice guidelines

## > NSCLC



Planchard et al, Ann Oncol 29 Suppl 4: iv192-237, 2018 and e-update Sept 15, 2020

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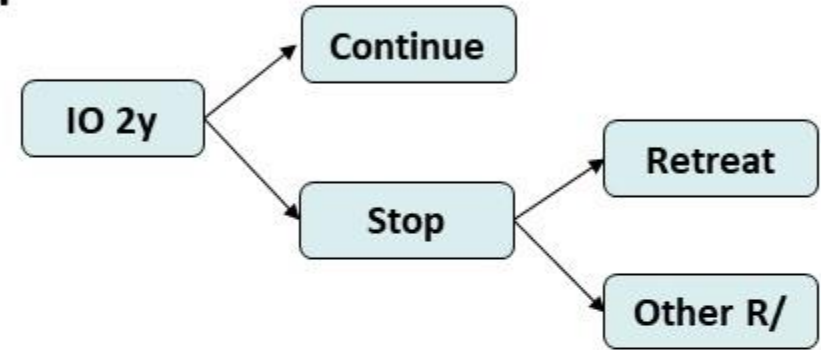
# NSCLC immunotherapy duration

> where is the horizon?



## Possible answers

- Ostrich action
- RCT



- Learn from follow-up of available trials
- Regulatory decision (e.g. 2y max. UK)
- Practice according to RCTs (up to 2 years)
- ...



# NSCLC immunotherapy duration

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# NSCLC immunotherapy

## > continuous vs. fixed 1-year 2L/3L nivolumab [Checkmate 153]

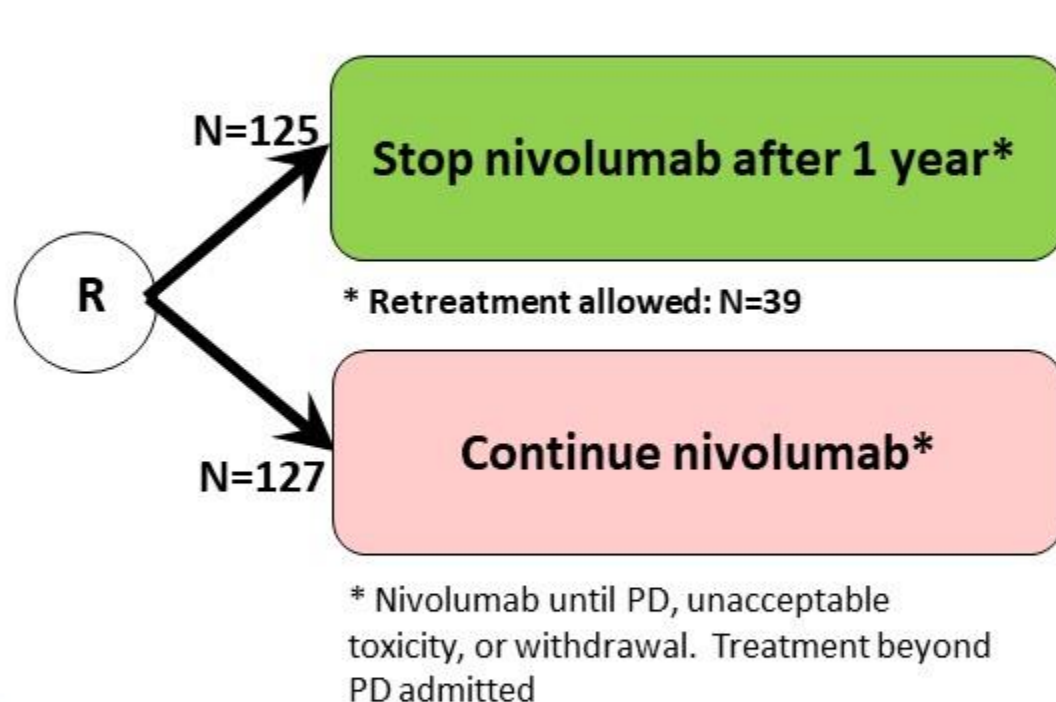
### Checkmate 153

#### Pre-treated advanced NSCLC

- ≥1 prior systemic therapy
- PS 0–2
- Treated CNS mets allowed
- Started Nivolumab (N=1245)

- Nivolumab at 1 year (N=252)\*

\* All patients on treatment at 1 year were randomised **regardless of response status**



#### Primary endpoint

- Incidence of high-grade TRAEs

#### Exploratory endpoints

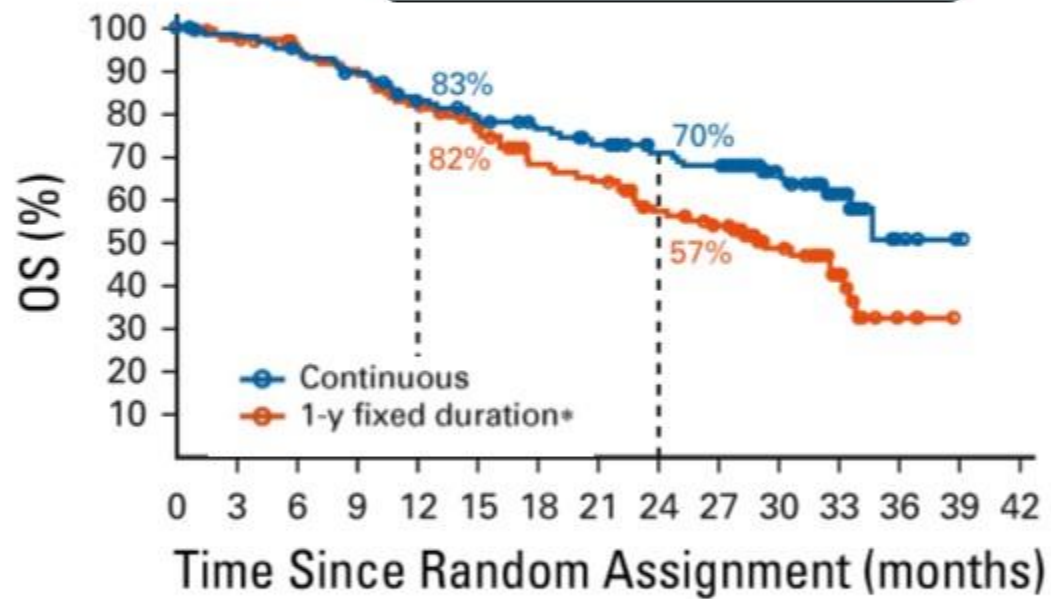
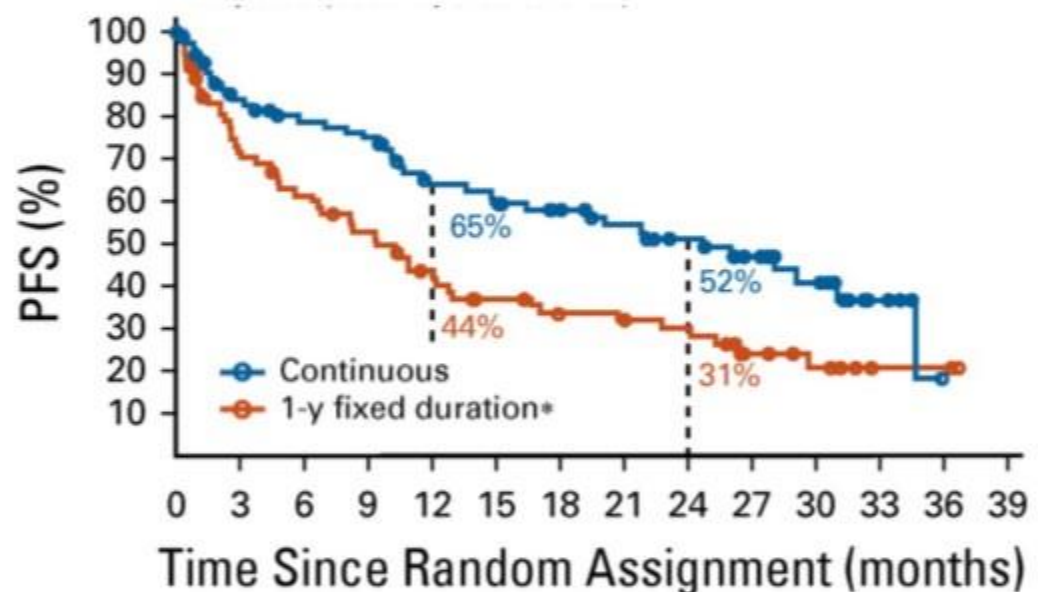
- Efficacy
- Biomarkers

# NSCLC immunotherapy

> continuous vs. fixed 1-year 2L/3L nivolumab [Checkmate 153]

PFS HR 0.56 [0.37-0.84]

OS HR 0.62 [0.42-0.92]



No. at risk:

|                    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |
|--------------------|----|----|----|----|----|----|----|----|----|----|----|---|---|---|
| Continuous         | 89 | 68 | 61 | 58 | 45 | 42 | 37 | 32 | 27 | 20 | 13 | 5 | 0 | 0 |
| 1-y fixed duration | 85 | 53 | 44 | 37 | 29 | 23 | 19 | 18 | 16 | 9  | 6  | 2 | 2 | 0 |

No. at risk:

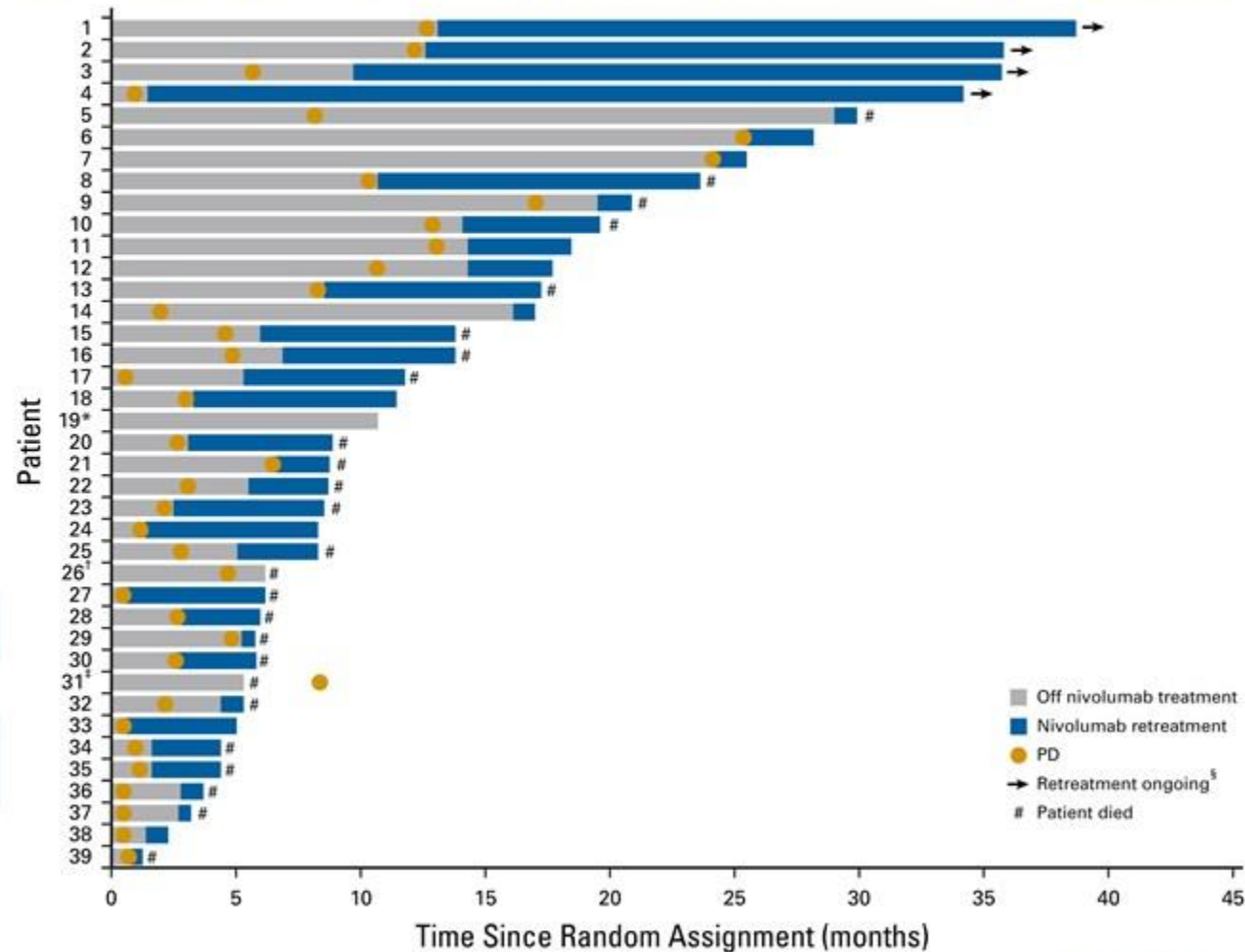
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|--------------------|-----|-----|-----|-----|----|----|----|----|----|----|----|----|---|---|---|
| Continuous         | 127 | 121 | 116 | 109 | 98 | 92 | 86 | 79 | 70 | 67 | 44 | 22 | 4 | 1 | 0 |
| 1-y fixed duration | 125 | 116 | 109 | 102 | 93 | 85 | 70 | 66 | 53 | 47 | 32 | 15 | 4 | 0 | 0 |

## CAREFUL INTERPRETATION

- Phase IV community study – no preplanned study hypothesis
- Primary endpoint = safety – outcome added as exploratory
- Moderate numbers

# NSCLC immunotherapy

## > CM-153: nivolumab retreatment in patients who progressed after randomization



Waterhouse et al, J Clin Oncol 38:3863-3873, 2020

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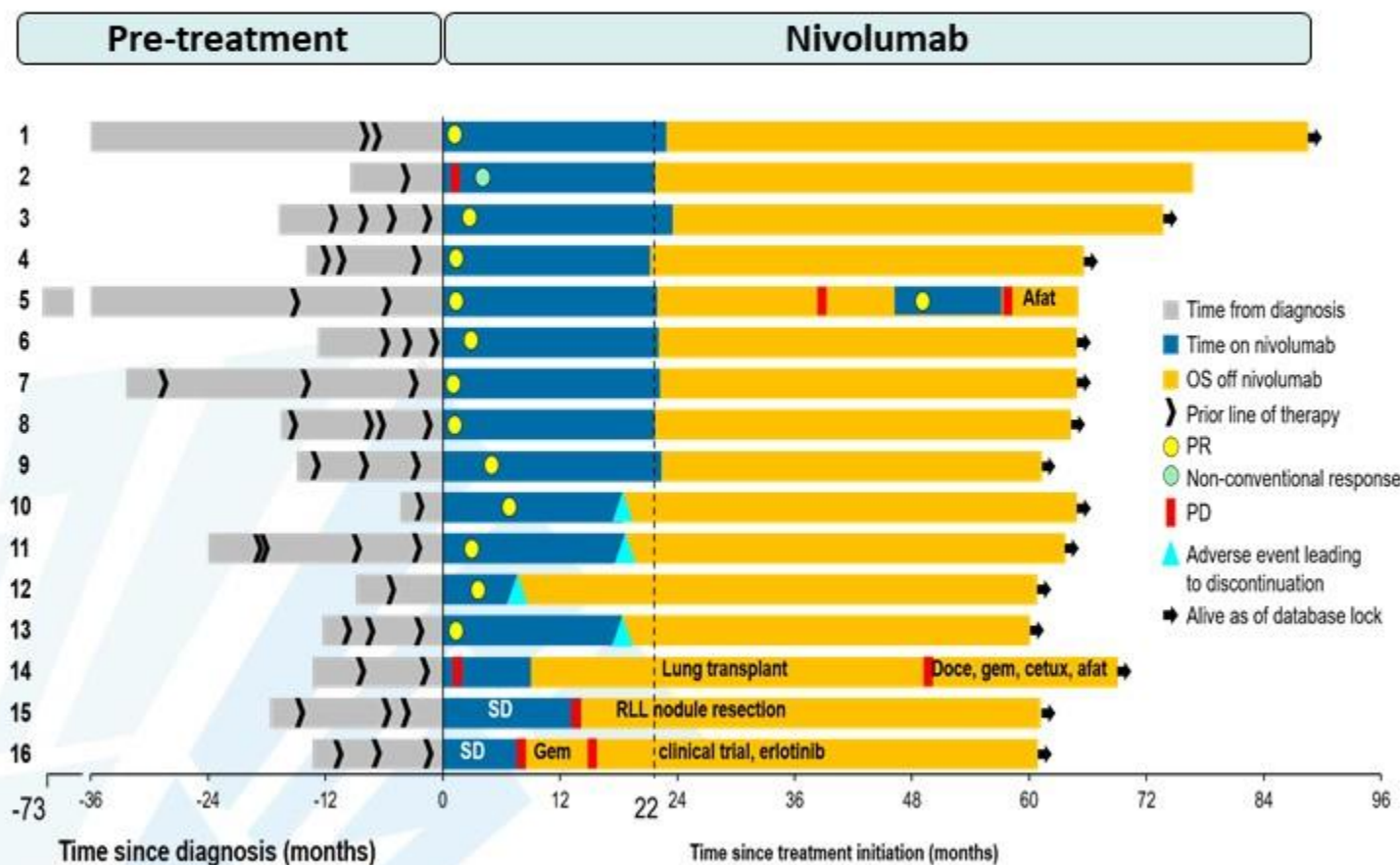


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# NSCLC immunotherapy

> Nivolumab ph1 CM-003 study – relapsed NSCLC subset: outcome of 5Y survivors (n=16)



## Nivolumab ph1 NSCLC subset

16/129 (12.4%) are 5Y survivors

- 13 of these were responders
- 4 of these responders: stop for toxicity

At data cut-off

- 12 patients alive without PD
- 4 had subsequent other Tx

Brahmer et al, AACR 2017

Copyright permission requested.

Brahmer J et al. Five-year follow-up from the CA209-003 study of Nivolumab in previously treated advanced non-small cell lung cancer: Clinical characteristics of long-term survivors. Presented at: AACR 2017 Annual Meeting; April 1-5, 2017, Washington DC



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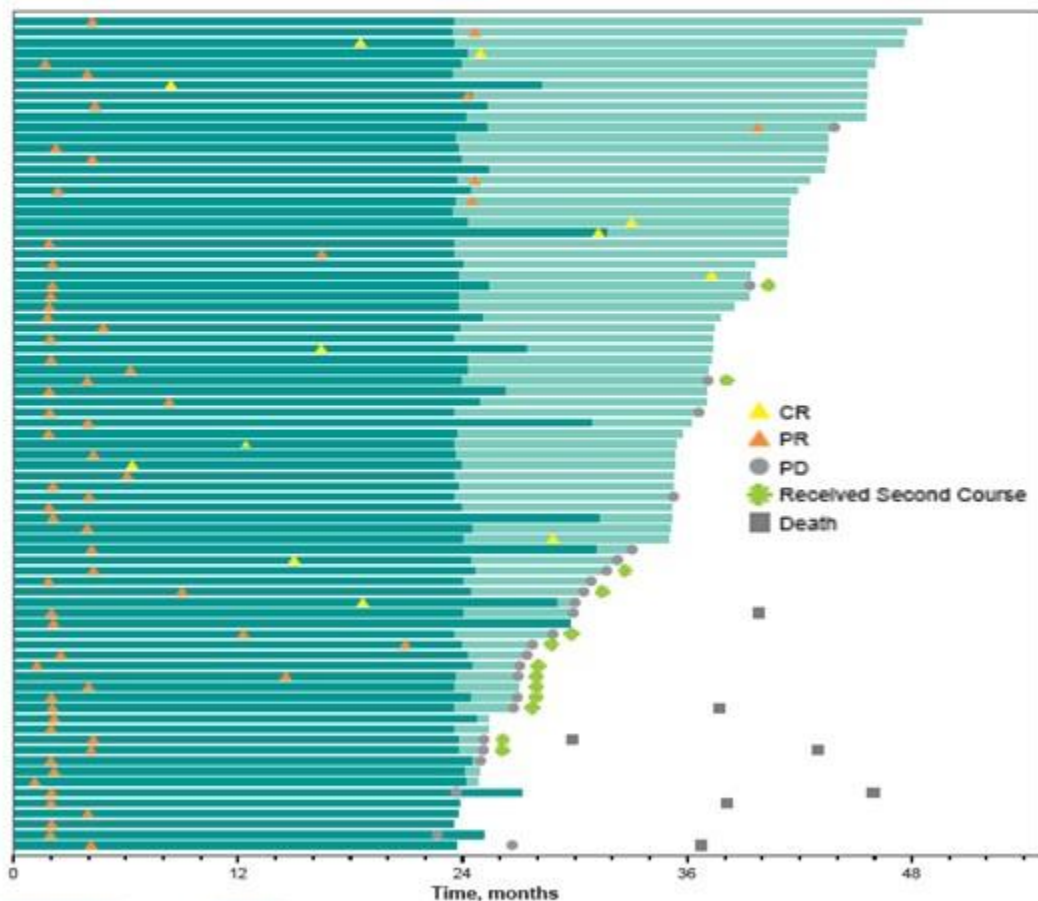


# NSCLC immunotherapy

## > ph3 Pembro 2L/3L study [Keynote-010]: 5-year update

Patients who completed 2 years (N=79) \*

\*this figure is from the 3Y update



KN-010: 2L/3L in PD-L1  $\geq 1\%$

79/690 (11.4%) patients had 2Y of pembro

- 74 of these were responders
- 3Y survival rate from pembro discontinuation was 83%

At data cut-off: 61 patients alive

- 38 patients alive without PD
- 21 had 2<sup>nd</sup> course as subsequent Tx
- ? had other subsequent Tx
- 4 died without further Tx

Herbst et al, J Clin Oncol 38:1580-1590, 2020 and Herbst et al, WCLC 2020

Copyright permission requested.

Herbst R et al. 5-year survival update from KEYNOTE-010: Pembrolizumab versus docetaxel in previously treated PD-L1-positive advanced NSCLC. Presented virtually at the 2020 WCLC, January 28-31, 2021



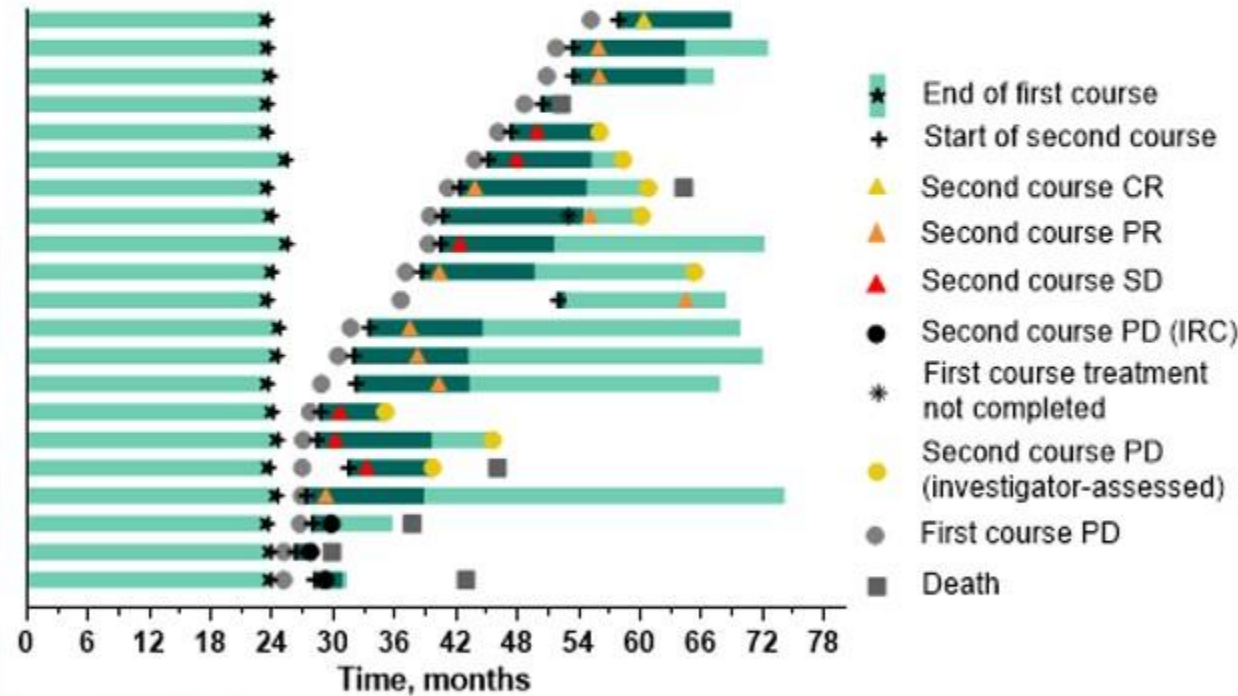
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# NSCLC immunotherapy

## > ph3 Pembro 2L/3L study [Keynote-010]: 5-year update

2<sup>nd</sup> course (N=21)



KN-010: 2L/3L in PD-L1 ≥1%

### Response

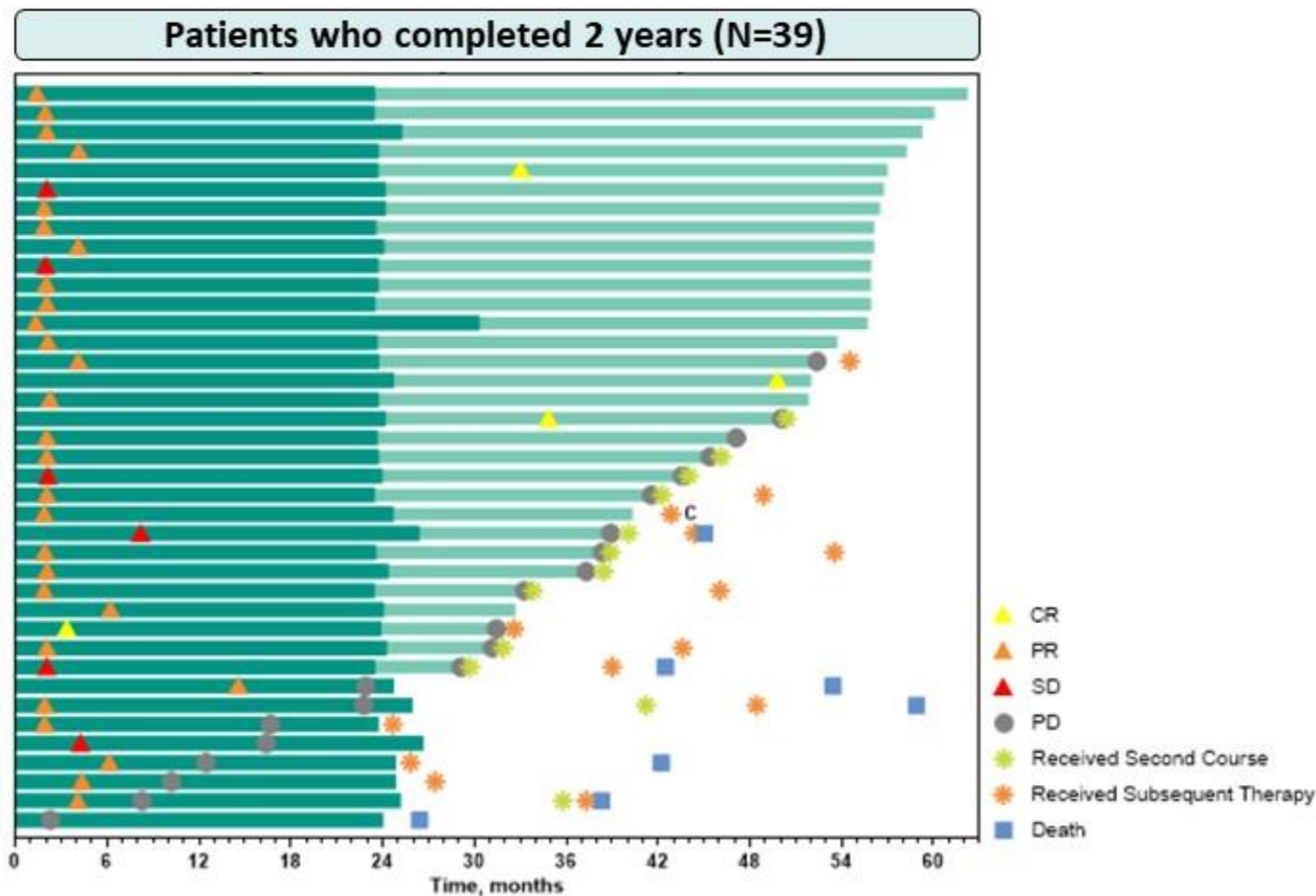
- CR 1
- PR 10
- SD 6
- PD 3
- NE 1

### Outcome

- 15/21 alive at data cut-off

# NSCLC immunotherapy

## > ph3 Pembro 1L study [Keynote-024]: 5-year update



### KN-024: 1L in PD-L1 $\geq 50\%$

39/154 (25.3%) patients had 2Y of pembro

- 32 of these were responders
- 3Y survival rate from pembro discontinuation was 81%

#### At data cut-off

- 15 patients alive without Tx
- 12 had 2<sup>nd</sup> course as 1<sup>st</sup> relapse Tx
- 10 had other 1<sup>st</sup> relapse Tx
- 2 died without further Tx

Brahmer et al, ESMO 2020

Copyright permission requested.

Brahmer J et al. KEYNOTE-024 5-year OS update: first-line pembrolizumab vs platinum-based chemotherapy in patients with metastatic NSCLC and PD-L1 tumor proportion score  $\geq 50\%$ . Oral presentation at Virtual ESMO 2020; 19th–21st September



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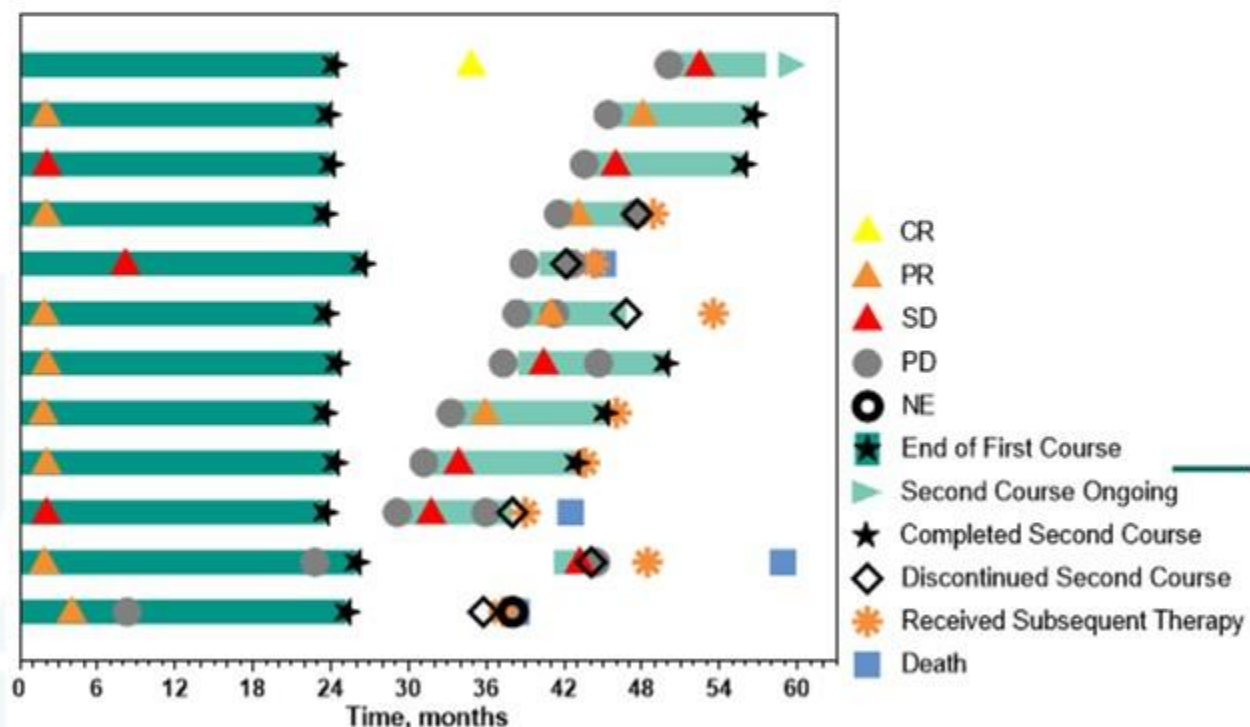




# NSCLC immunotherapy

## > ph3 Pembro 1L study [Keynote-024]: 5-year update

2<sup>nd</sup> course (N=12)



KN-024: 1L in PD-L1  $\geq 50\%$

### Response

- CR 0
- PR 4
- SD 6
- PD 1
- NE 1

### Outcome

- 8/12 alive at data cut-off
- 5/12 alive without PD

Brahmer et al, ESMO 2020

Copyright permission requested.

Brahmer J et al. KEYNOTE-024 5-year OS update: first-line pembrolizumab vs platinum-based chemotherapy in patients with metastatic NSCLC and PD-L1 tumor proportion score  $\geq 50\%$ . Oral presentation at Virtual ESMO 2020; 19th–21st September



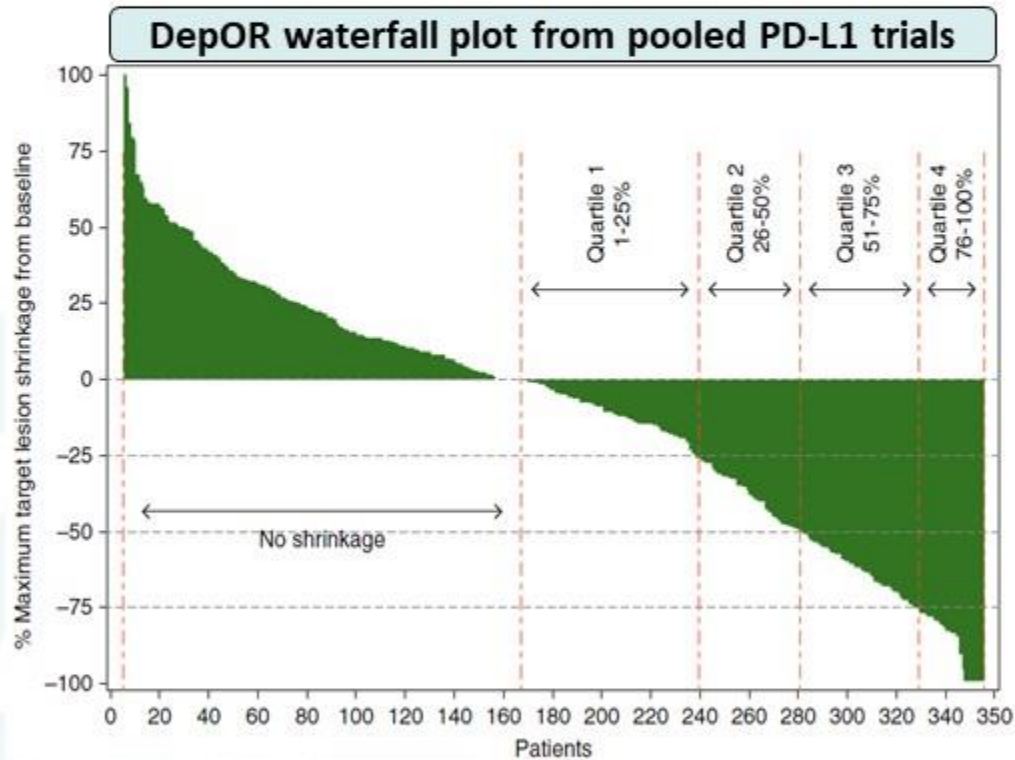
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# NSCLC immunotherapy

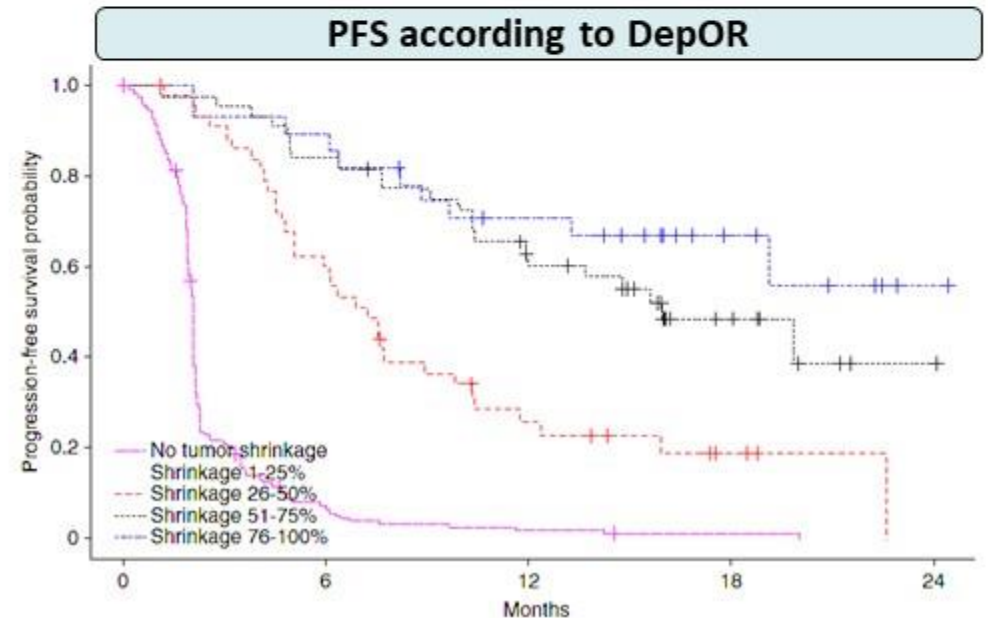
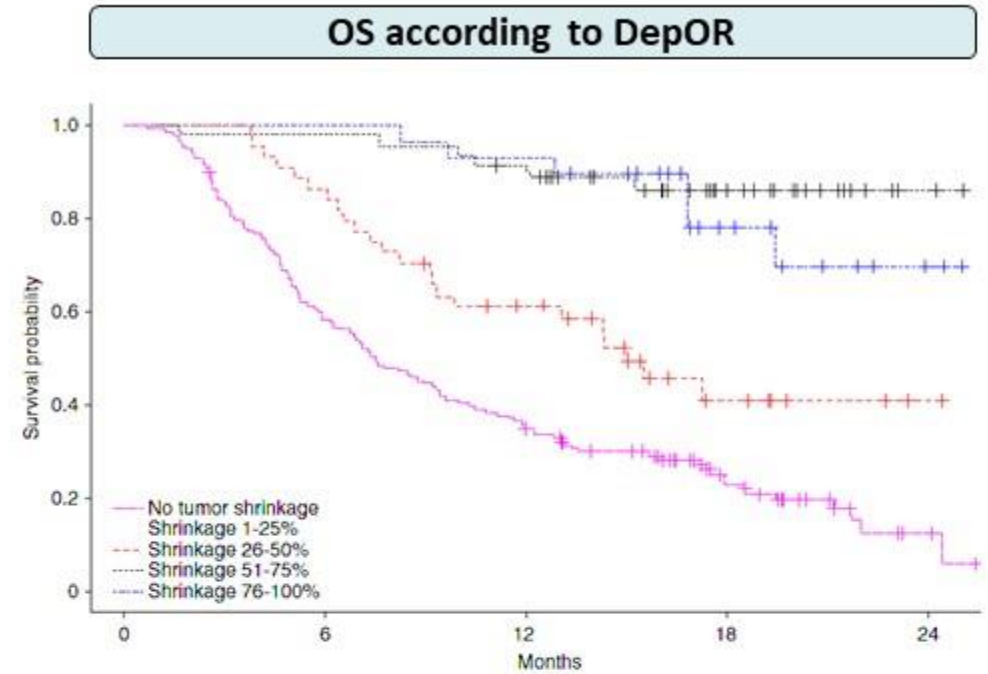
## > depth of response (DepOR)

Exploratory analysis from a pool of experimental arms from different RCTs



McCoach et al, Ann Oncol 28:2707-2714, 2017

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