iCUBE

Innovazione

Intento curativo

Immunoterapia

Comunicare il valore dell'innovazione nella cura del tumore al polmone

AstraZeneca

edra

L’immunoterapia e l’intento curativo

Massimo Di Maio

SCDU Oncologia Medica,
AO Ordine Mauriziano, Torino
Dipartimento di Oncologia
Università di Torino
massimo.dimaio@unito.it

dimaiomax

@MassimoDiMaio75

Tumore del polmone localmente avanzato: L’importanza della valutazione multidisciplinare

Oncologo medico

Radiologo

Chirurgo toracico

Patologo

Radioterapista

Infermiere

Raccomandazione clinica	Forza della raccomandazione
Nei pazienti con NSCLC in stadio IIIA/IIIB non resecabile, o IIIC, in buone condizioni generali (ECOG PS 0-1) un trattamento concomitante di chemio-radioterapia a dosi radicali dovrebbe essere preso in considerazione come opzione terapeutica di prima scelta.	**Positiva forte**

Linee guida AIOM 2019, www.aiom.it

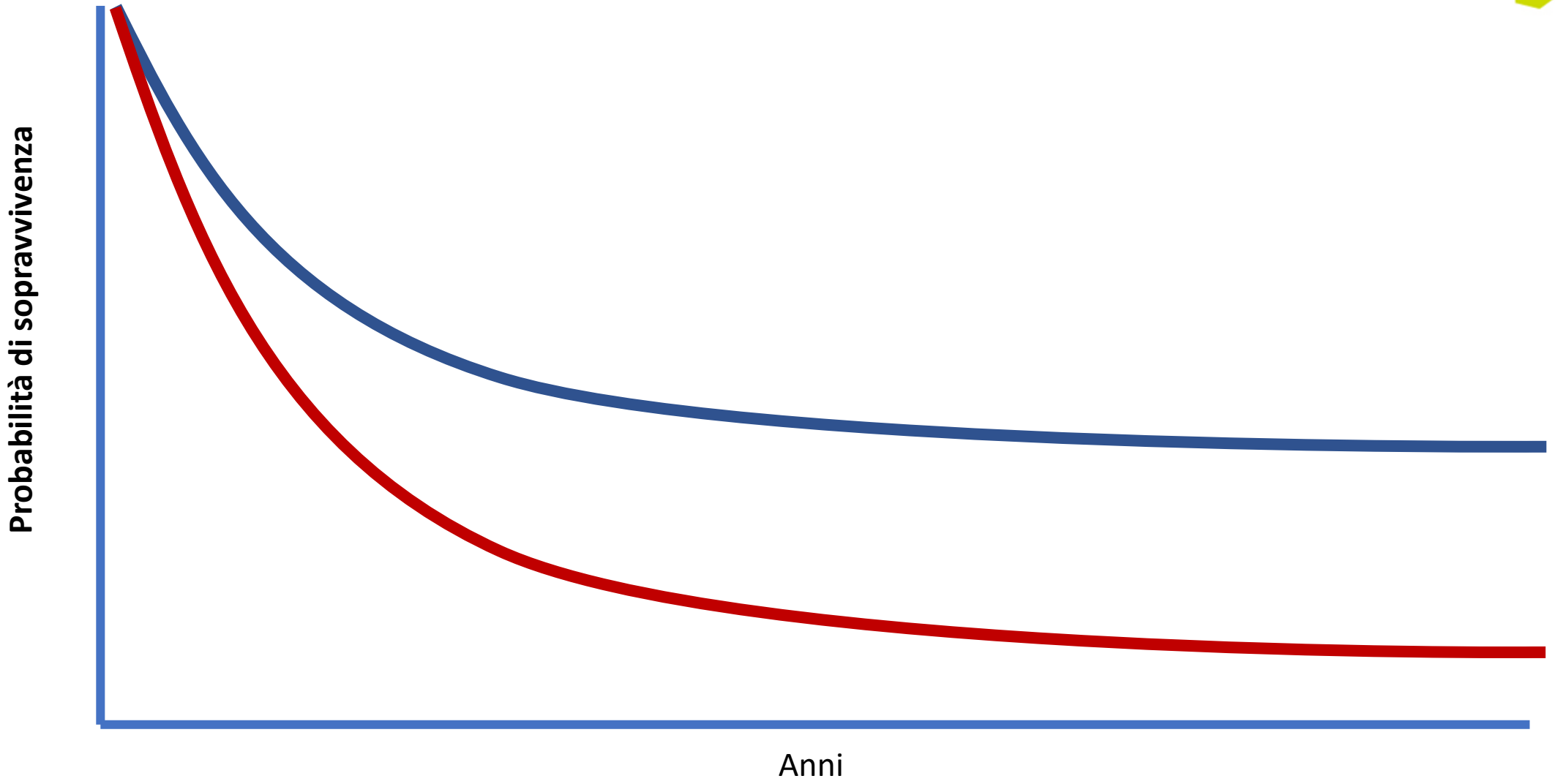
Sections

The Washington Post

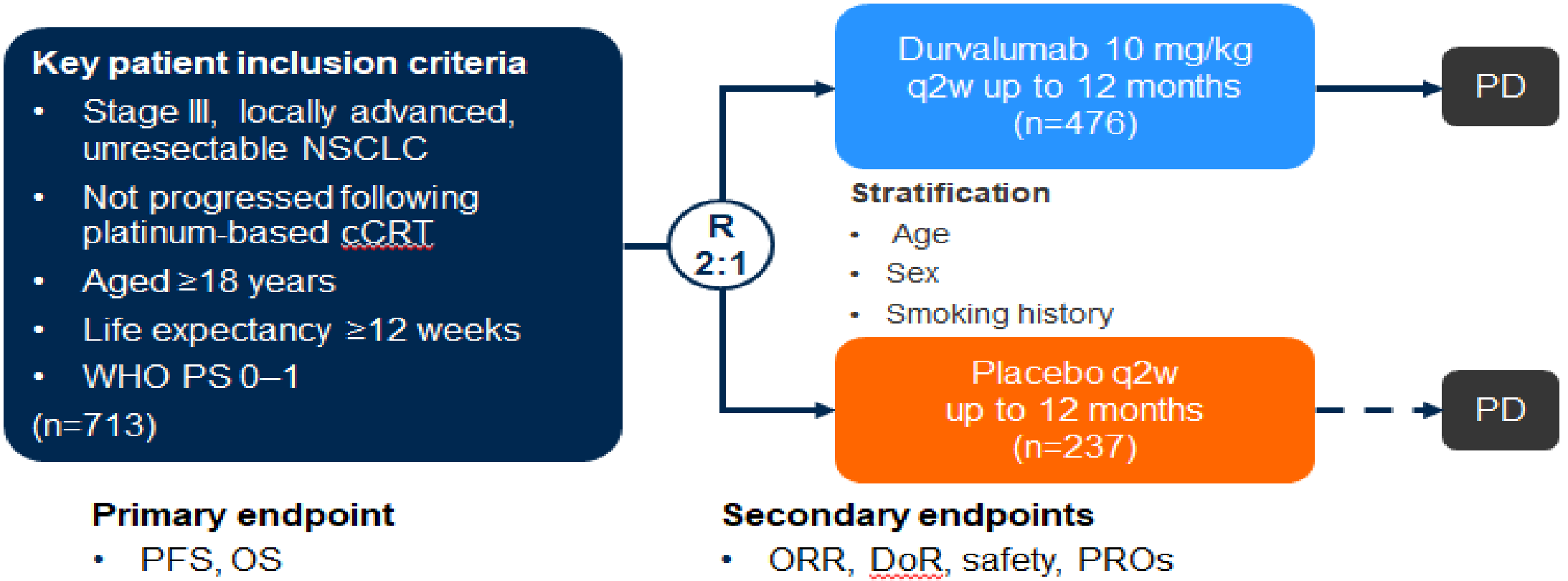
To Your Health

The list of cancers that can be treated by immunotherapy keeps growing

By Laurie McGinley April 19


Probabilità di sopravvivenza
Anni

Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial



Antonia SJ, et al.
N Engl J Med. 2017 Nov 16;377(20):1919-1929.

Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial

Patient's characteristics

- Two or more cycles of platinum-based chemotherapy
- Concurrent radiation therapy (54 to 66 Gy)
- Last dose within 1 to 42 days before randomization

Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	3 (0.4)
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Previous chemotherapy — no. (%)‖			
Induction	123 (25.8)	68 (28.7)	191 (26.8)
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	711 (99.7)
Best response to previous chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	232 (48.7)	111 (46.8)	343 (48.1)
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)

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Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial

Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Characteristic	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	23–90
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	500 (70.1)
Female	142 (29.8)	71 (30.0)	213 (29.9)
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	377 (52.9)
IIIB	212 (44.5)	107 (45.1)	319 (44.7)
Other‡	12 (2.5)	5 (2.1)	17 (2.4)
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Nonsquamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status — no. (%)			
Current smoker	79 (16.6)	38 (16.0)	117 (16.4)
Former smoker	354 (74.4)	178 (75.1)	532 (74.6)
Never smoked	43 (9.0)	21 (8.9)	64 (9.0)

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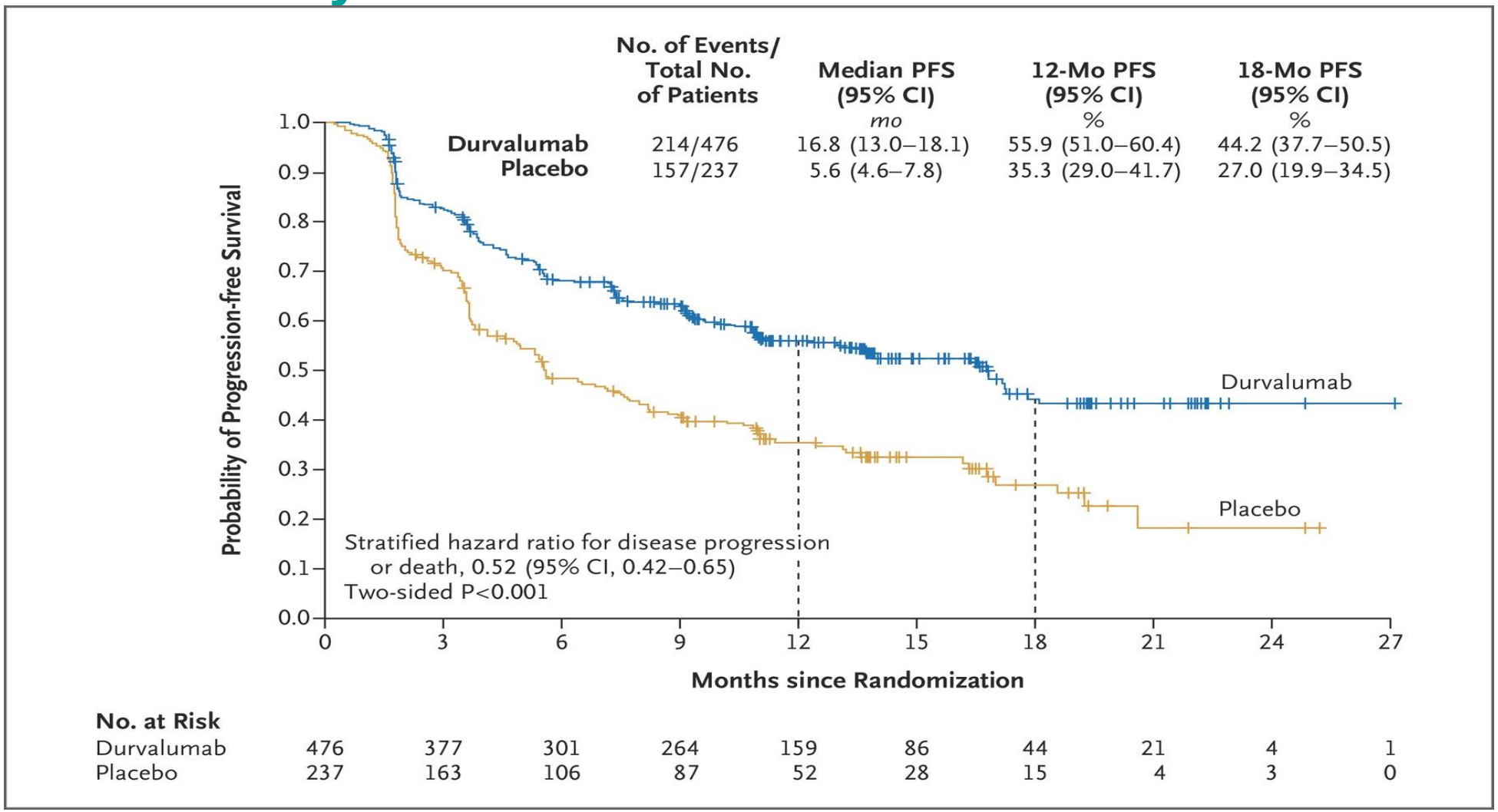
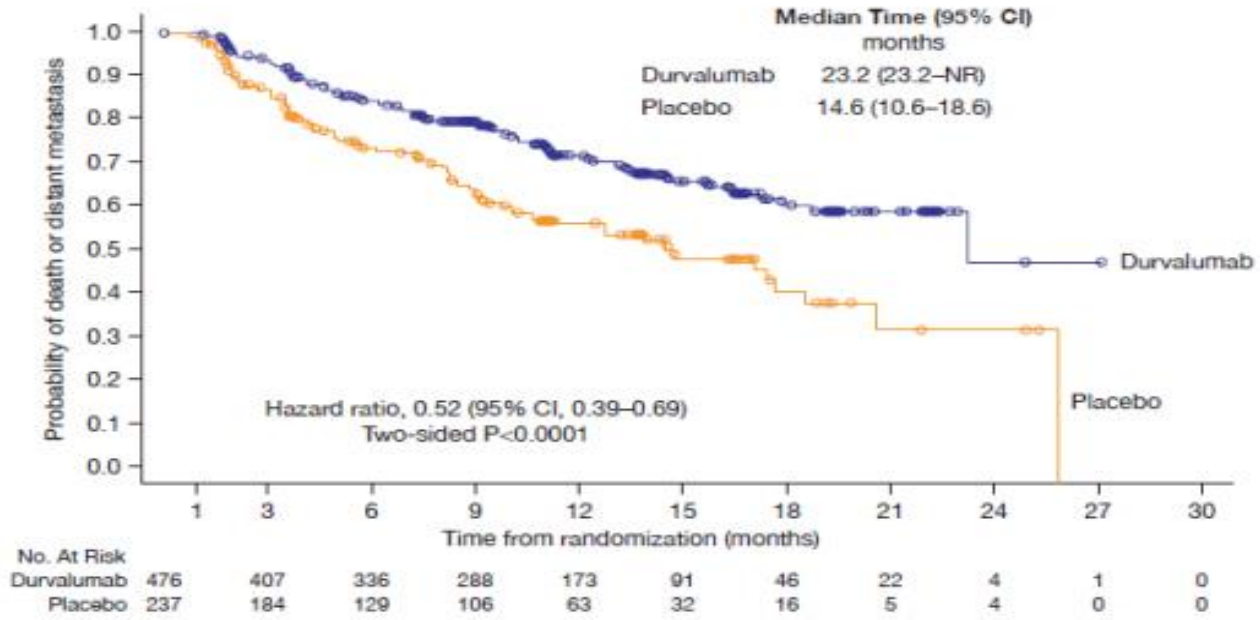
Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial



Antonia SJ, et al.
N Engl J Med. 2017 Nov 16;377(20):1919-1929.

Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial

Time to death or distant metastasis



New lesion site†	Durvalumab (N=476)	Placebo (N=237)
	number of patients (percent)	
Any new lesion	97 (20.4)	76 (32.1)
Lung	56 (11.8)	41 (17.3)
Lymph nodes	27 (5.7)	27 (11.4)
Brain	26 (5.5)	26 (11.0)
Liver	9 (1.9)	8 (3.4)
Bone	8 (1.7)	6 (2.5)
Adrenal	3 (0.6)	5 (2.1)
Other	9 (1.9)	5 (2.1)

Antonia SJ, et al.
N Engl J Med. 2017 Nov 16;377(20):1919-1929.

Immune checkpoint inhibition in locally advanced NSCLC: the PACIFIC trial

Table 3. Adverse Events of Any Cause.

Event	Durvalumab (N=475)		Placebo (N=234)	
	Any Grade*	Grade 3 or 4	Any Grade*	Grade 3 or 4
	number of patients with event (percent)			
Any event	460 (96.8)	142 (29.9)	222 (94.9)	61 (26.1)
Pneumonitis or radiation pneumonitis†	161 (33.9)	16 (3.4)	58 (24.8)	6 (2.6)
Diarrhea	87 (18.3)	3 (0.6)	44 (18.8)	3 (1.3)
Pruritus	58 (12.2)	0	11 (4.7)	0
Rash	58 (12.2)	1 (0.2)	17 (7.3)	0

Discontinuation to AEs	15.4%	9.8%
Serious AEs	28.6%	22.6%
Death due to AEs	4.4%	5.6%
High-dose glucocorticoids	8.8%	5.1%

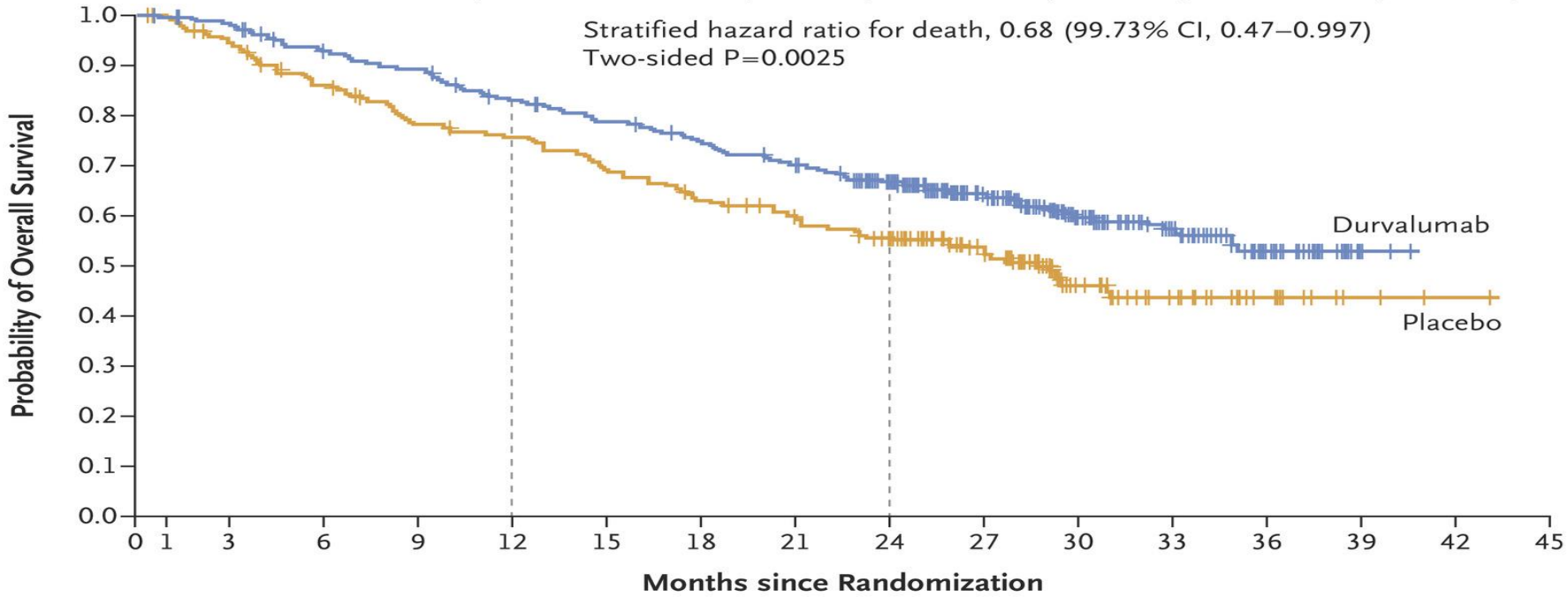
Antonia SJ, et al.
N Engl J Med. 2017 Nov 16;377(20):1919-1929.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC

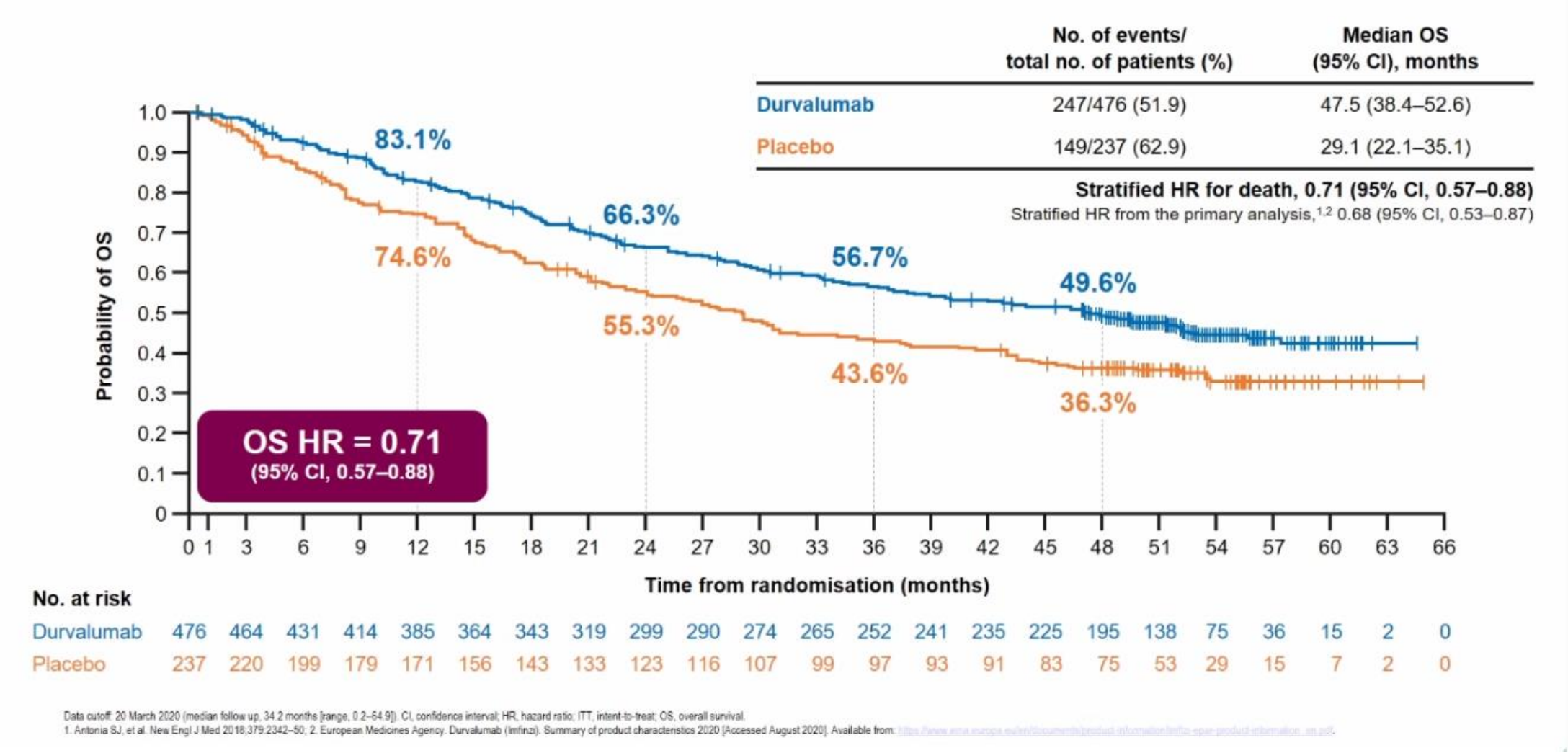
	No. of Events/ Total No. of Patients	Median Overall Survival (95% CI)	12-Mo Overall Survival Rate (95% CI)	24-Mo Overall Survival Rate (95% CI)
		mo	%	%
Durvalumab	183/476	NR (34.7–NR)	83.1 (79.4–86.2)	66.3 (61.7–70.4)
Placebo	116/237	28.7 (22.9–NR)	75.3 (69.2–80.4)	55.6 (48.9–61.8)



No. at Risk															
Durvalumab	476	464	431	415	385	364	343	319	274	210	115	57	23	2	0	0
Placebo	237	220	198	178	170	155	141	130	117	78	42	21	9	3	1	0

Antonia SJ et al,
N Engl J Med. 2018 Dec 13;379(24):2342-2350.

PACIFIC: analisi aggiornata di sopravvivenza



Data cutoff: 20 March 2020 (median follow up, 34.2 months [range, 0.2–64.9]). CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival.
1. Antonia SJ, et al. New Engl J Med 2018;379:2342–50; 2. European Medicines Agency. Durvalumab (Imfinzi). Summary of product characteristics 2020 [Accessed August 2020]. Available from:

Faivre Finn, ESMO 2020

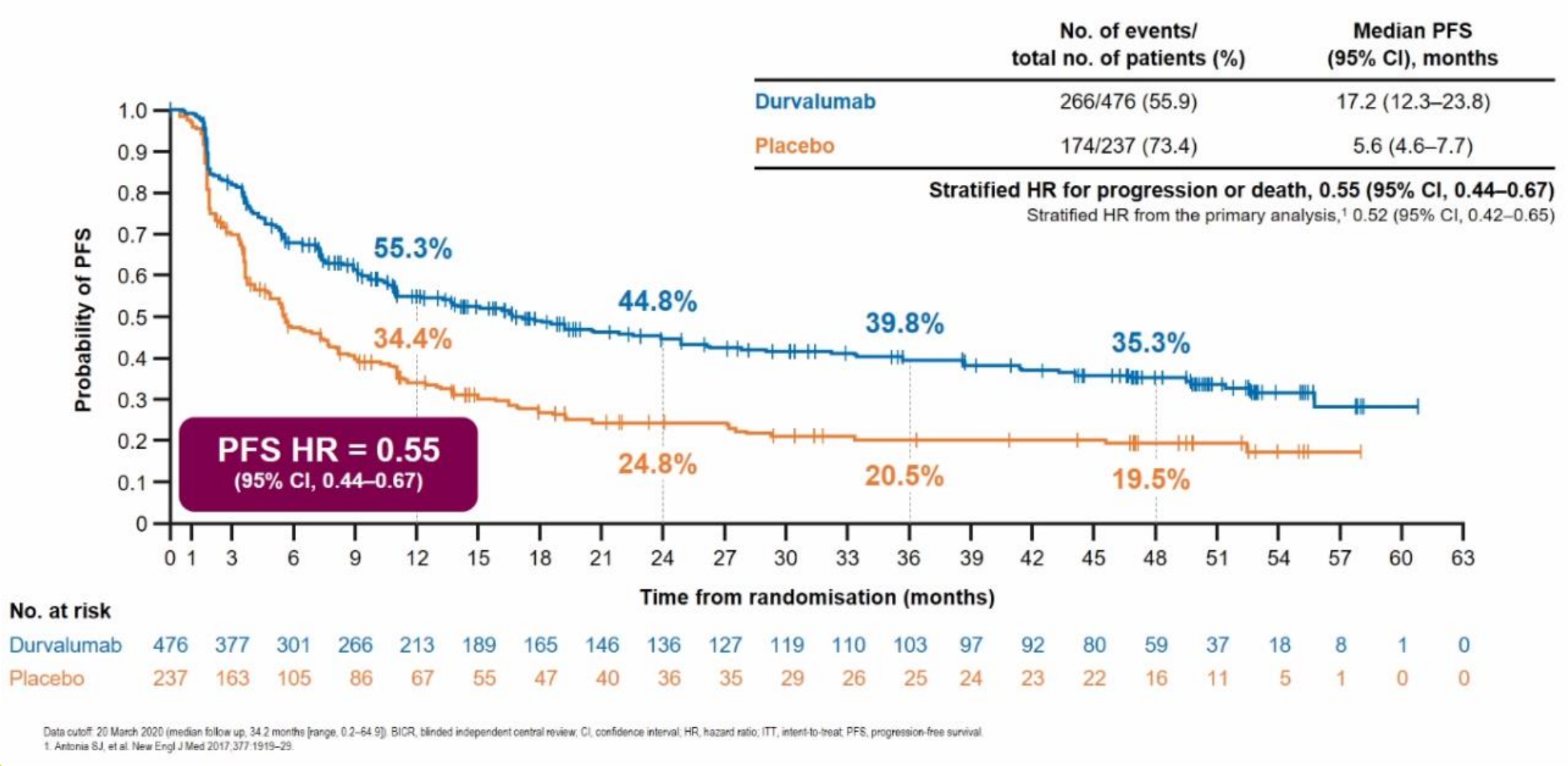
PACIFIC: analisi aggiornata di sopravvivenza

- Delta pazienti vivi a 4 anni: **+13.3%**

- Number needed to treat: **7.52**

Bisogna trattare 7.5 pazienti con durvalumab perché 1 in più sia vivo a 4 anni.

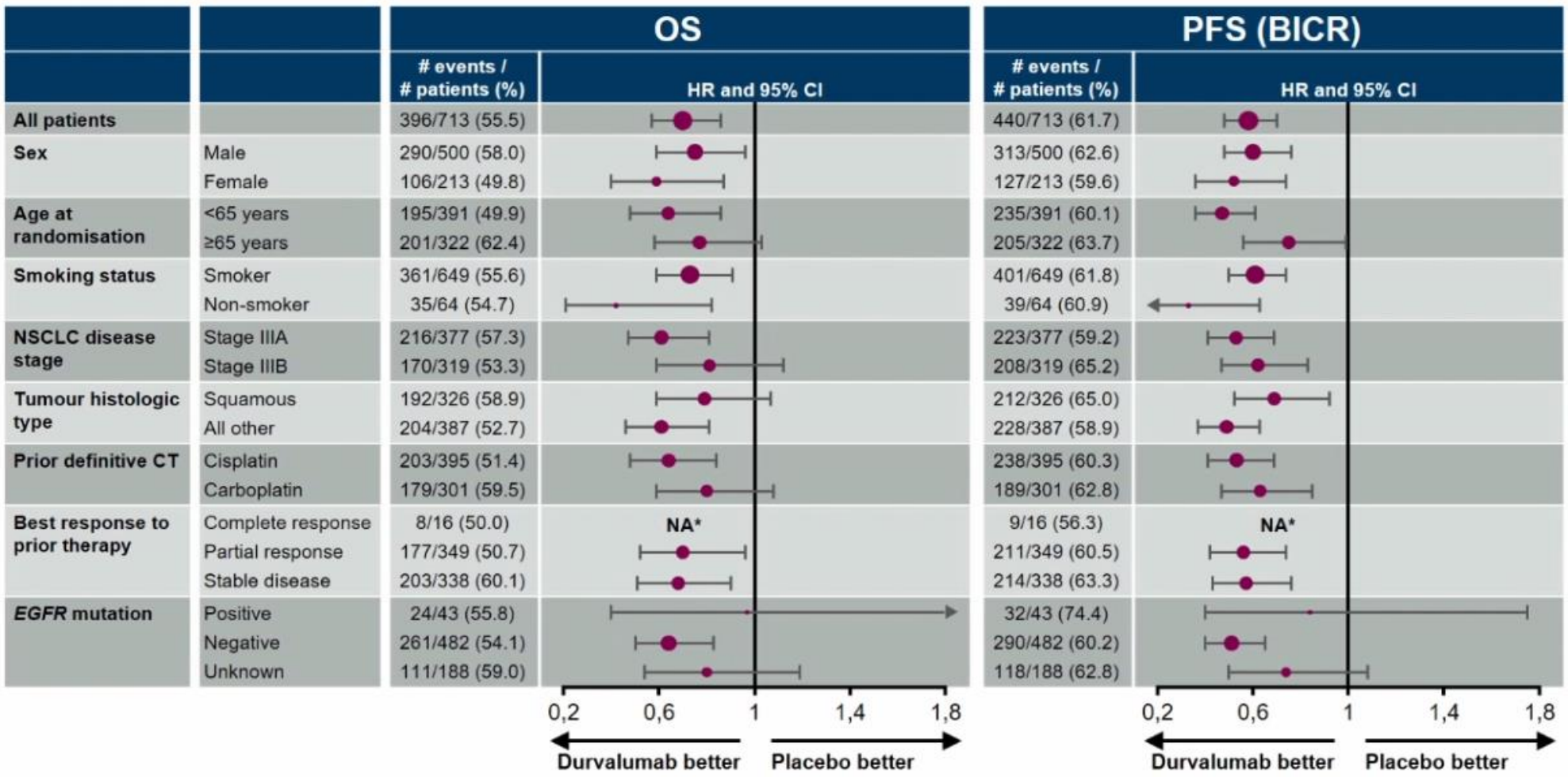
PACIFIC: analisi aggiornata di PFS



Data cutoff: 20 March 2020 (median follow up, 34.2 months [range, 0.2–64.9]). BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival.
1. Antonia SJ, et al. New Engl J Med 2017;377:1919–29.

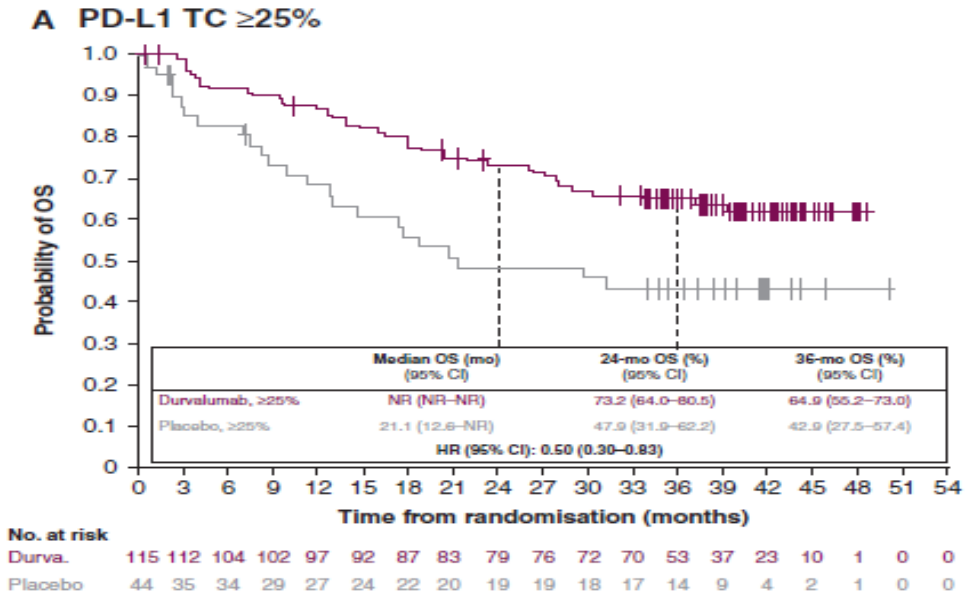
Faivre Finn, ESMO 2020

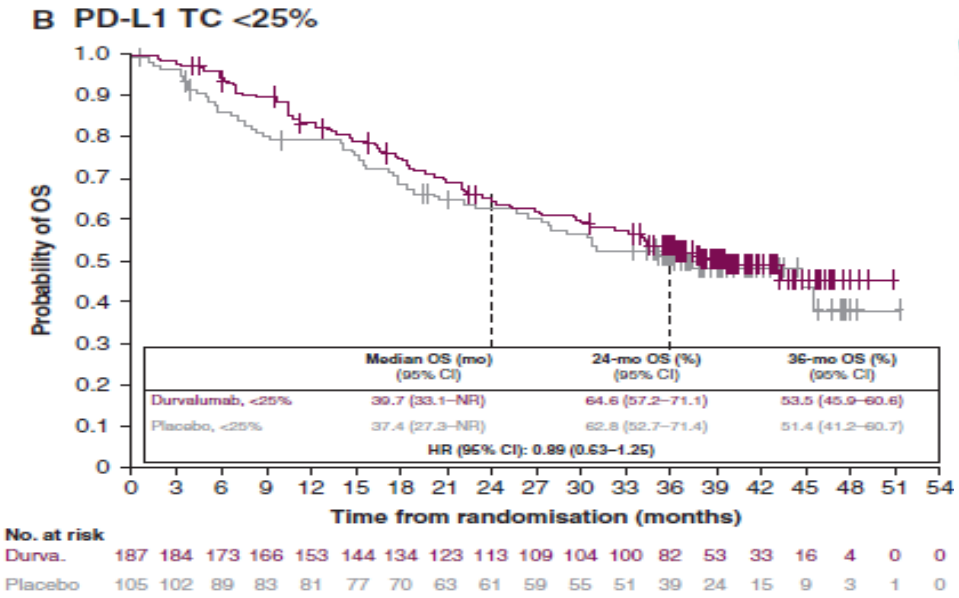
PACIFIC: analisi di sottogruppo



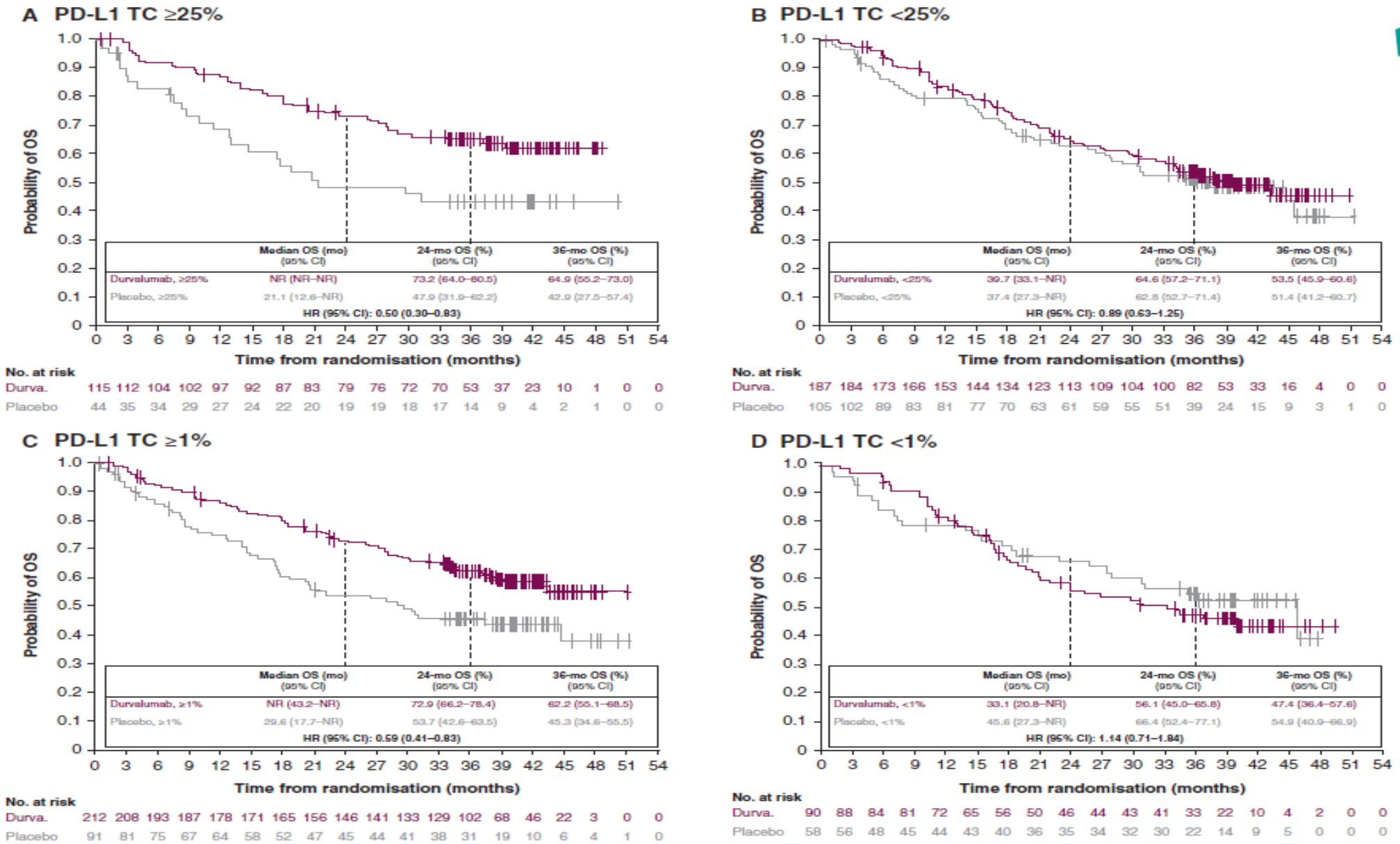
*Hazard ratio and 95% CI not calculated if the subgroup has less than 20 events.
Data cutoff: 20 March 2020. BICR, blinded independent central review; CI, confidence interval; CT, chemotherapy; EGFR, epidermal growth factor receptor; HR, hazard ratio; ITT, intent-to-treat; NA, not applicable; OS, overall survival; PFS, progression-free survival.

Faivre Finn, ESMO 2020





Paz-Ares L et al,
Ann Oncol. 2020 Mar 21:S0923-7534(20)36374-2.



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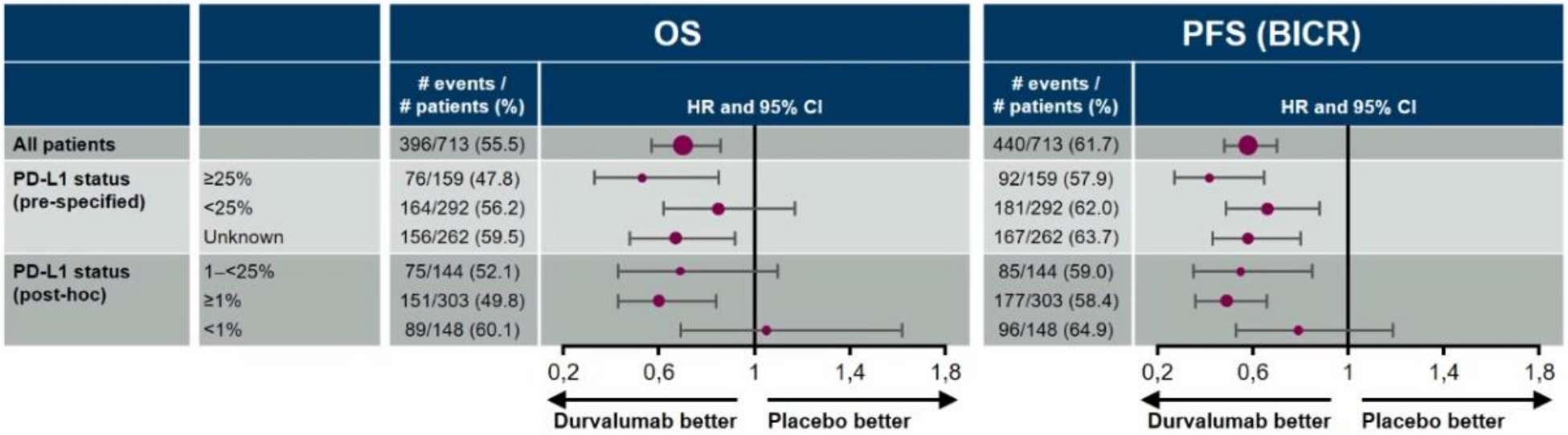
Ann Oncol. 2020 Mar 21:S0923-7534(20)36374-2.

PACIFIC: analisi di sottogruppo

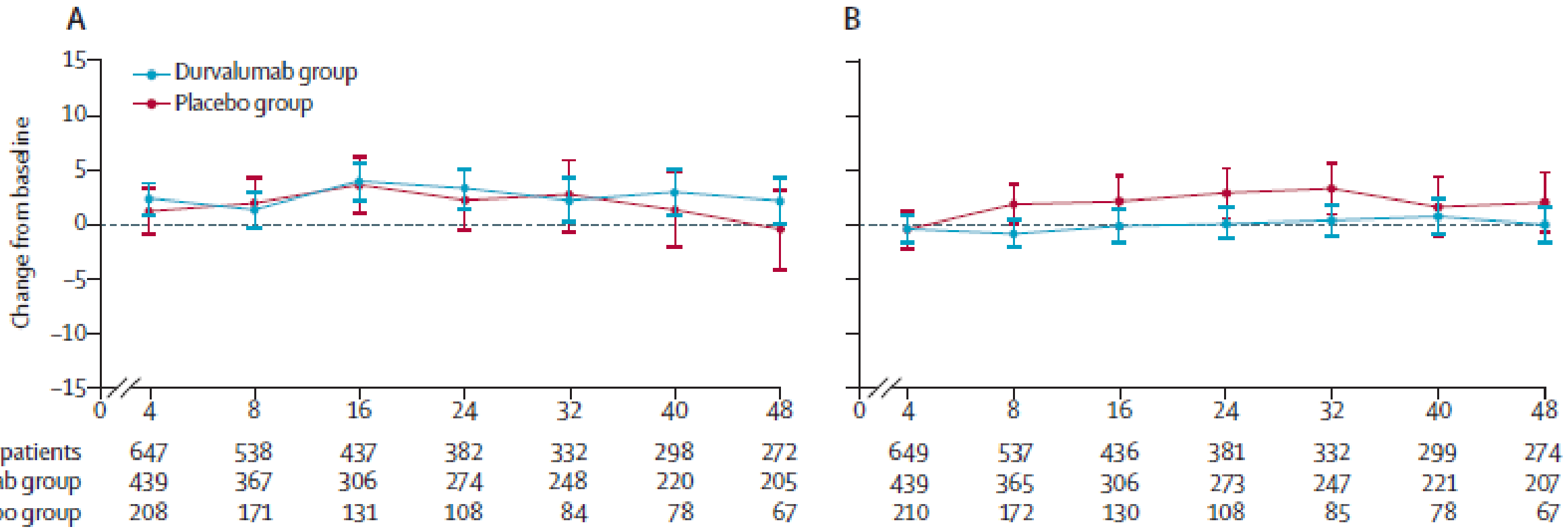


- Important facts regarding PD-L1 status:
  - PD-L1 testing was not required and 37% of all randomised patients had unknown PD-L1 status
  - PD-L1 status was determined from tumour tissue obtained pre-CRT (getting a sample post-CRT medically not feasible)
  - PD-L1 expression-level cutoff of 1% was part of an unplanned post-hoc analysis requested by the EMA

Data cutoff: 20 March 2020. BICR, blinded independent central review; CRT, chemoradiotherapy; CI, confidence interval; CR, complete response; EMA, European Medicines Agency; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

La qualità di vita è un delicato equilibrio tra il controllo dei sintomi di malattia e gli effetti collaterali del trattamento

Rispetto all'osservazione, durvalumab non compromette la qualità di vita



Number of patients	647	538	437	382	332	298	272
Durvalumab group	439	367	306	274	248	220	205
Placebo group	208	171	131	108	84	78	67

	649	537	436	381	332	299	274
	439	365	306	273	247	221	207
	210	172	130	108	85	78	67

Hui R et al,
Lancet Oncol 2019 Dec; 20(12):1670-1680.

Raccomandazione clinica	Forza della raccomandazione
Nei pazienti con NSCLC in stadio III non resecabile, in risposta o stabilità di malattia dopo trattamento chemio-radioterapico a dosi radicali, e con espressione di PD-L1 sulle cellule tumorali superiore o uguale a 1%, una terapia di consolidamento con durvalumab della durata di 12 mesi dovrebbe essere presa in considerazione come opzione terapeutica di prima scelta.	**Positiva forte**

Linee guida AIOM 2019, www.aiom.it

Conclusioni

- Il trattamento ottimale del tumore del polmone localmente avanzato richiede una discussione dei casi e una successiva gestione **multidisciplinare.**

- L'immunoterapia con durvalumab, al completamento del trattamento chemio-radioterapico, ha dimostrato un beneficio rilevante in termini di **controllo di malattia** e **prolungamento della sopravvivenza**.

- Tale beneficio avviene a prezzo di un profilo di tollerabilità ormai ben noto per i farmaci immunoterapici, e senza compromissione della **qualità di vita**.

L’immunoterapia e l’intento curativo

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SCDU Oncologia Medica,
AO Ordine Mauriziano, Torino
Dipartimento di Oncologia
Università di Torino
massimo.dimaio@unito.it

dimaiomax

@MassimoDiMaio75