XXIV Simposio de Revisiones en Cáncer

"Tratamiento médico del cáncer en el año 2022"

Dando un paso más en PACIFIC: ¿qué respuestas nos están dando los datos en vida real?

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Disclosures

- **Advisory/Consultancy:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda

- **Speaker Bureau/Expert testimony:** AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda, Amgen

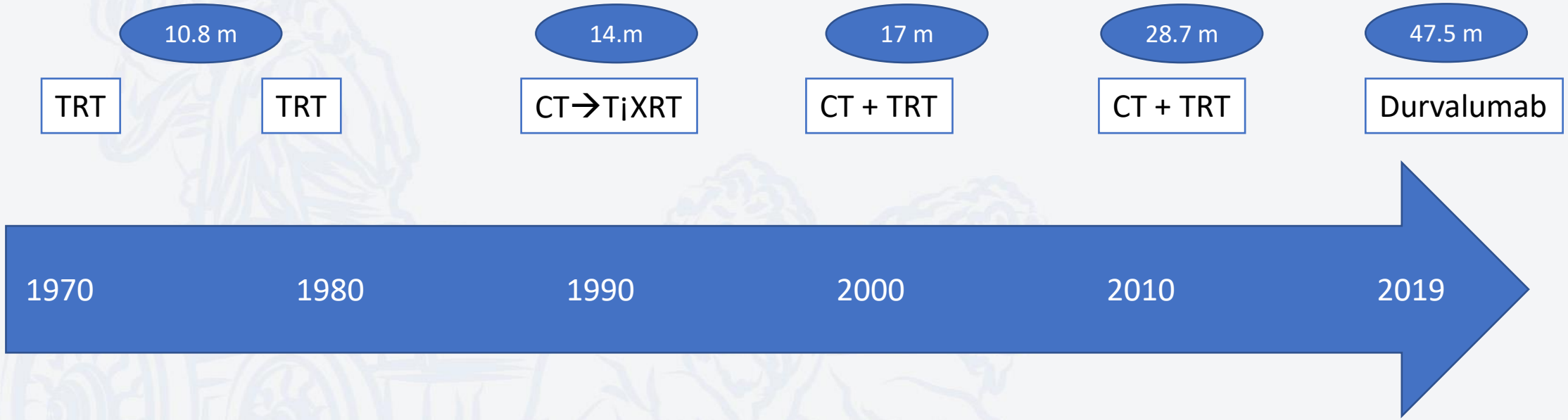
- **Travel/Accommodation/Expenses**:Bristol-Myers Squibb, Pfizer, Roche, Takeda

El secreto del cambio es enfocar toda tu energía no en luchar contra lo viejo, sino en construir lo nuevo.

Sócrates

Background

Over the last 50 years, combined modality regimens for inoperable stage III NSCLC have almost tripled the mOS of this disease

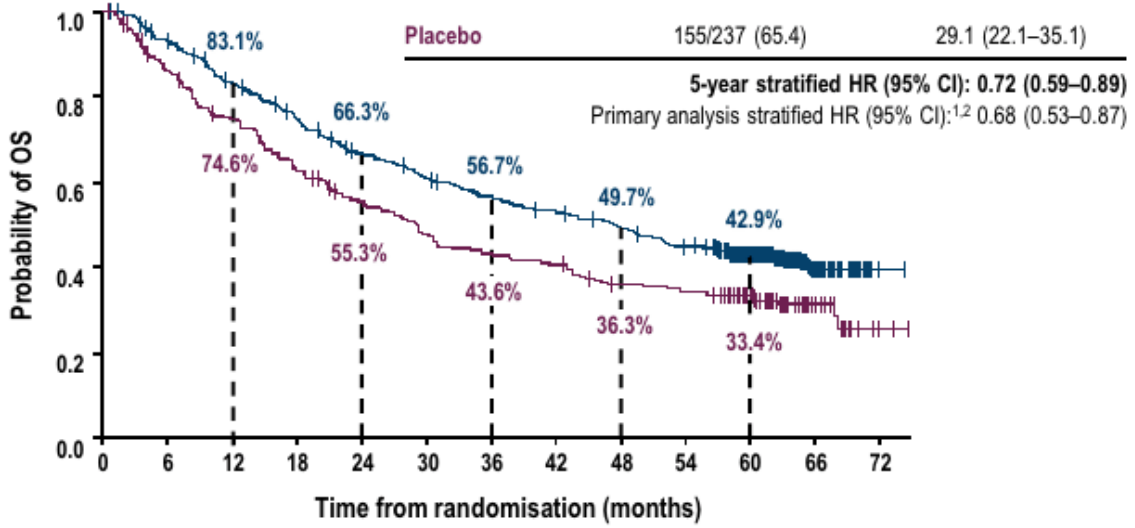


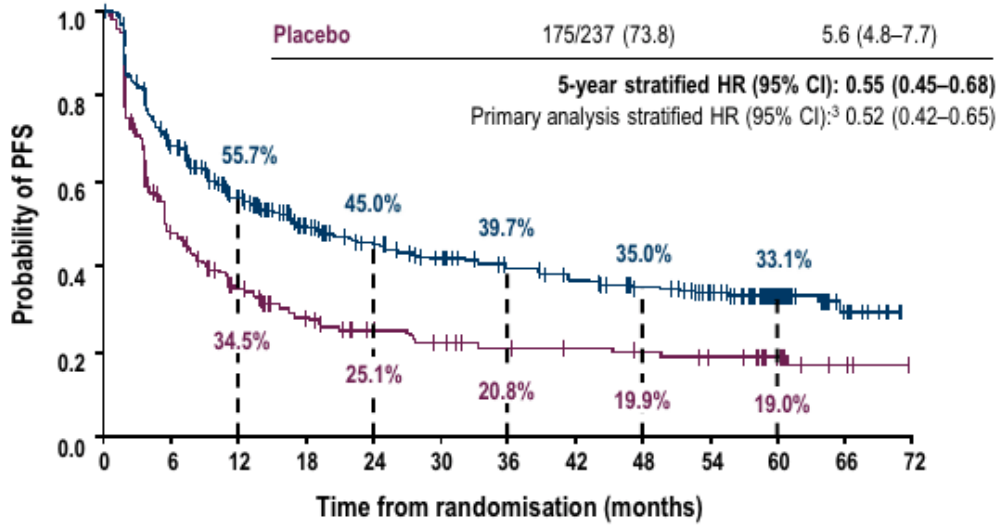
Non-small Cell Lung Cancer Collaborative Group. BMJ 311:899-909, 1995
Aupérin A, et al. J Clin Oncol 28:2181-2190, 2010
Rosenzweig KE, et al. J Clin Oncol 35:6-10, 2017

Background

In the Phase 3 PACIFIC trial, durvalumab significantly improved the primary endpoints of OS and PFS in patients with unresectable Stage III NSCLC and no disease progression after concurrent CRT

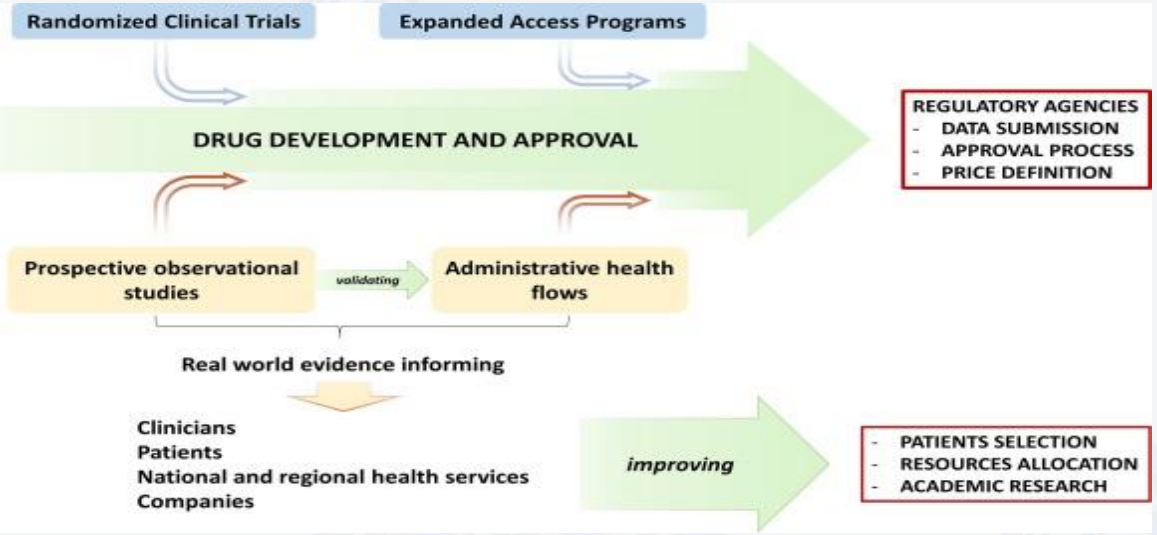
Updated results at ~5 years demonstrate sustained OS and PFS benefit with the PACIFIC regimen, which has become standard of care in this patient population

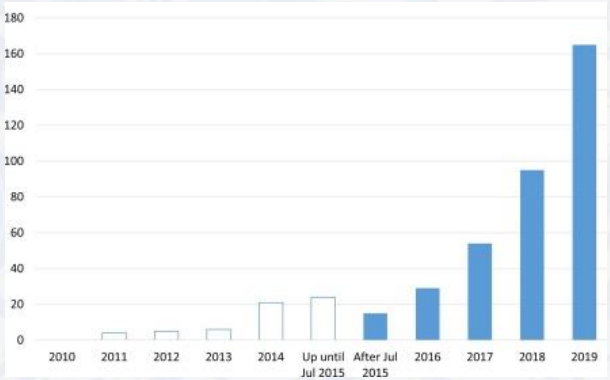




Antonia SJ, et al. New Engl J Med 2018;379:2342–50;
Antonia SJ, et al. New Engl J Med 2017;377:1919–29;
Spigel DR, et al. J Clin Oncol 2021;39(15_suppl):8511

Background





- **Randomized controlled trials and RWD remain complementary forms of medical evidence; studies using RWD should not be used as substitutes for clinical trials.**
- **The comparison of outcomes between nonrandomized groups of patients who have received different treatments in routine practice remains problematic.**
- **With due diligence, RWD can be used to identify and close gaps in health care, offering the potential for short-term improvement in health-care systems by enabling them to achieve the achievable.**

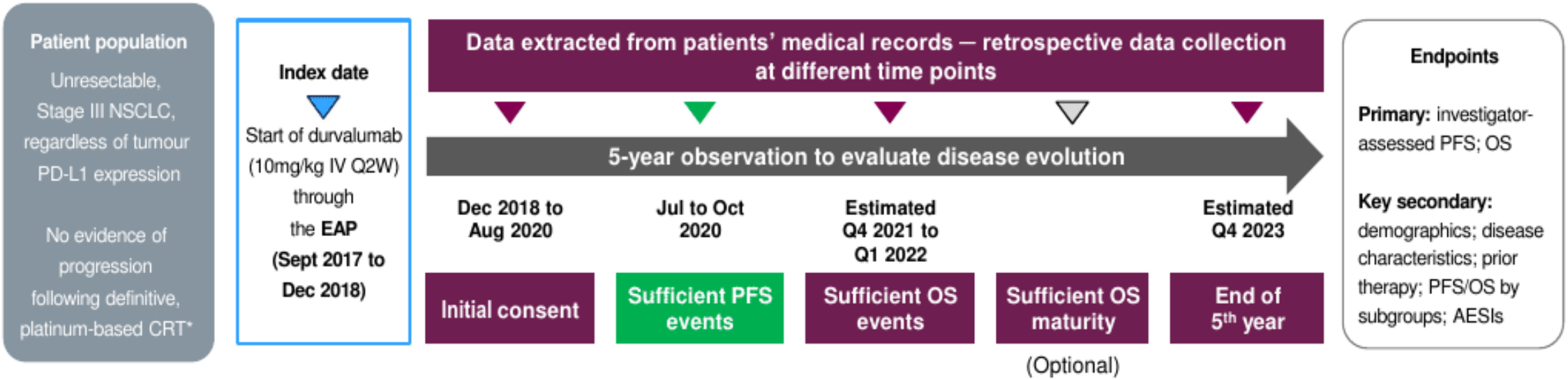
Booth, C.M. . *Nat Rev Clin Oncol* **16,** 312–325 (2019)

Pasello, G et al. Cancer Treatment Reviews, Volume 87,2020

RWD

PACIFIC-R: An International, Observational Study

Study design



1,399 patients included in the full analysis set (FAS) from 290 active sites in 11 participating countries – France (n=342), Spain (244)† , Australia (165), Netherlands (155), Belgium (118), Italy (116), Israel (92), Germany (62), UK (54), Norway (36), and Switzerland (15)

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PACIFIC-R: An International, Observational Study
Patients characteristics

Characteristics		FAS (N=1,399)
Age at EAP inclusion (years)	Median (range)	66.0 (26–88)
Age categories, %	≤75 years / >75 years	89.6 / 10.4
Sex, %	Male / Female	67.5 / 32.5
Smoking status at EAP inclusion, %	Never / Current / Former	7.9 / 32.6 / 59.5
Stage at diagnosis, %*[A]	Stage IIIA	43.2
	Stage IIIB/C	51.0
Histological subtype, %*[B]	Squamous	35.5
	Non-squamous	63.1
	Unknown	1.4
ECOG/WHO PS at EAP inclusion, %	0 / 1 / 2 / 3	51.4 / 46.6 / 1.9 / 0.1
CRT type, %*[C]	Concurrent	76.6
	Sequential	14.3
	Other	9.1
PD-L1 expression, %*[D] (Based on n=967 tested patients)	≥1%	72.5
	<1%	17.9
	Inconsistent†	9.6

- Median time to durvalumab initiation from the end of RT = **56 days**
- Overall median durvalumab treatment duration = **335 days (~11 months)** – >12 months' treatment: 20.1% – >14 months' treatment: 4.4%
- Patients received a median of **22** durvalumab infusions – 7.1% received >26 infusions

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RWD

PACIFIC-R: An International, Observational Study
Real-world PFS

	PACIFIC-R FAS	PACIFIC trial (durva. arm)[1]
PFS	N=1,399	N=476
Total events, N (%)	737 (52.7)	268 (56.3)†
Progression per RECIST	456 (32.6)	
Progression per physician assessment	170 (12.2)	
Progression, assessment unknown	30 (2.1)	
Deaths in absence of progression	81 (5.8)	
Median PFS, months	**21.7**	**16.9**
95% CI	19.2–24.5	13.0–23.9
PFS rate, %		
12 months	62.4	55.7
24 months	48.2	45.0

– Median Follow-up Duration = **23.0** Months

- Median rwPFS in PACIFIC-R was higher than the median PFS reported for the durvalumab arm of the PACIFIC trial
- Challenges with collecting rwPFS data limit comparisons between PACIFIC-R and PACIFIC
- RwPFS is likely overestimated as:
  - Germany and UK sites did not collect deaths that occurred prior to study enrolment‡ (50 early deaths not counted)
  - RECIST criteria for tumour assessments is used heterogeneously across countries
  - Assessments for progression in the real world may not occur as frequently or consistently as in clinical trials; the COVID-19 pandemic may also have resulted in fewer hospital visits

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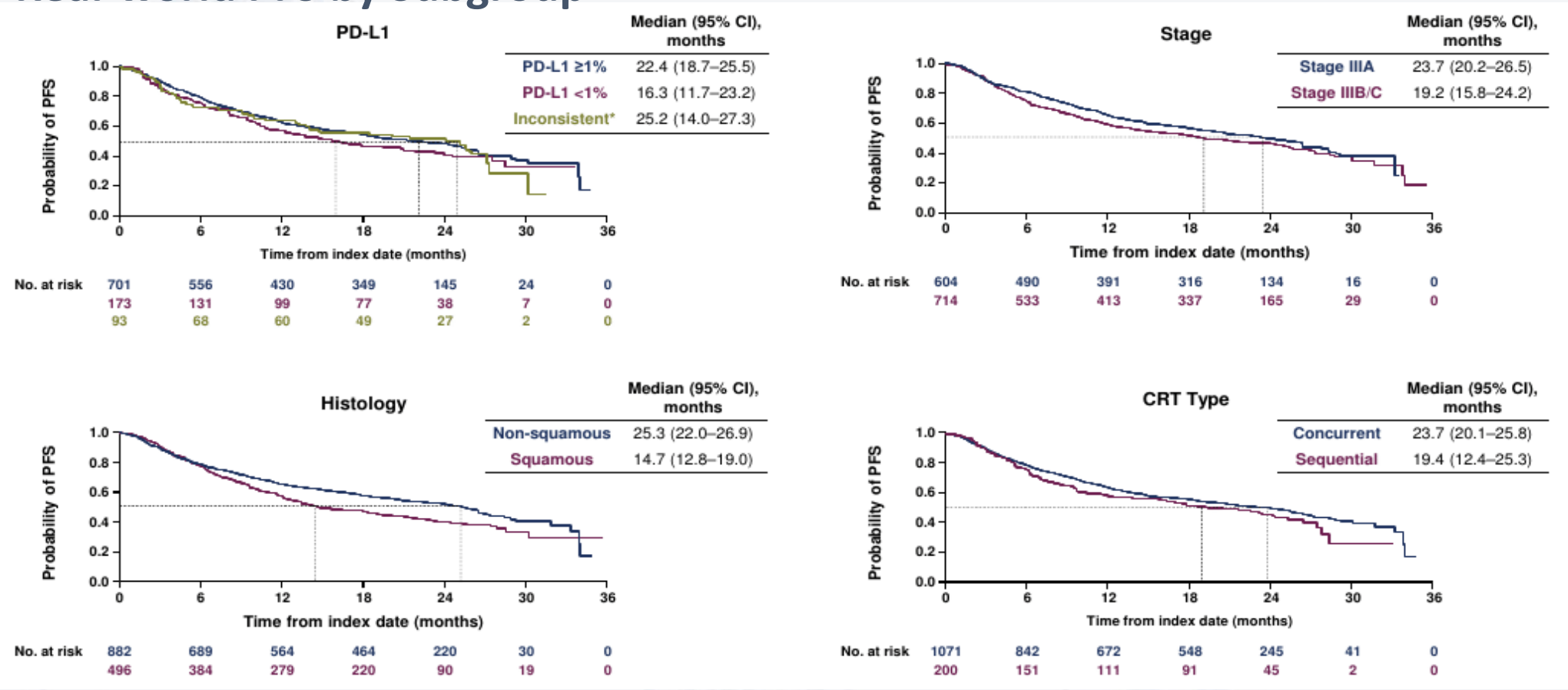
RWD

PACIFIC-R: An International, Observational Study
Real-world PFS by Subgroup



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PACIFIC-R: An International, Observational Study
Safety profile

Durvalumab Treatment Discontinuation

FAS (N=1,399)	Discontinuation reason, n (%)*	Median time from durva. start to discontinuation
Patient decision	20 (1.4)	6.1 months
AE	233 (16.7)	2.8 months
Completed treatment†	659 (47.1)	12.0 months
Disease progression	377 (26.9)	5.1 months
Death	21 (1.5)	1.9 months

Pneumonitis/interstitial lung disease (ILD) was the most common AE leading to (% of FAS):

- Permanent discontinuation: 133 (9.5%) ‡
- Temporary interruption: 73 (5.2%) ‡

Pneumonitis/ILD

	FAS (N=1,399)
Patients with any pneumonitis/ILD, n (%)§	250 (17.9)
Mild event¶	56 (4.0)
Moderate event¶	118 (8.4)
Severe event¶	41 (2.9)
Life-threatening or fatal event¶	5 (0.4)

Median time to onset of pneumonitis/ILD from durvalumab initiation: 2.5 months

Corticosteroid administration was required in 71.3% of events

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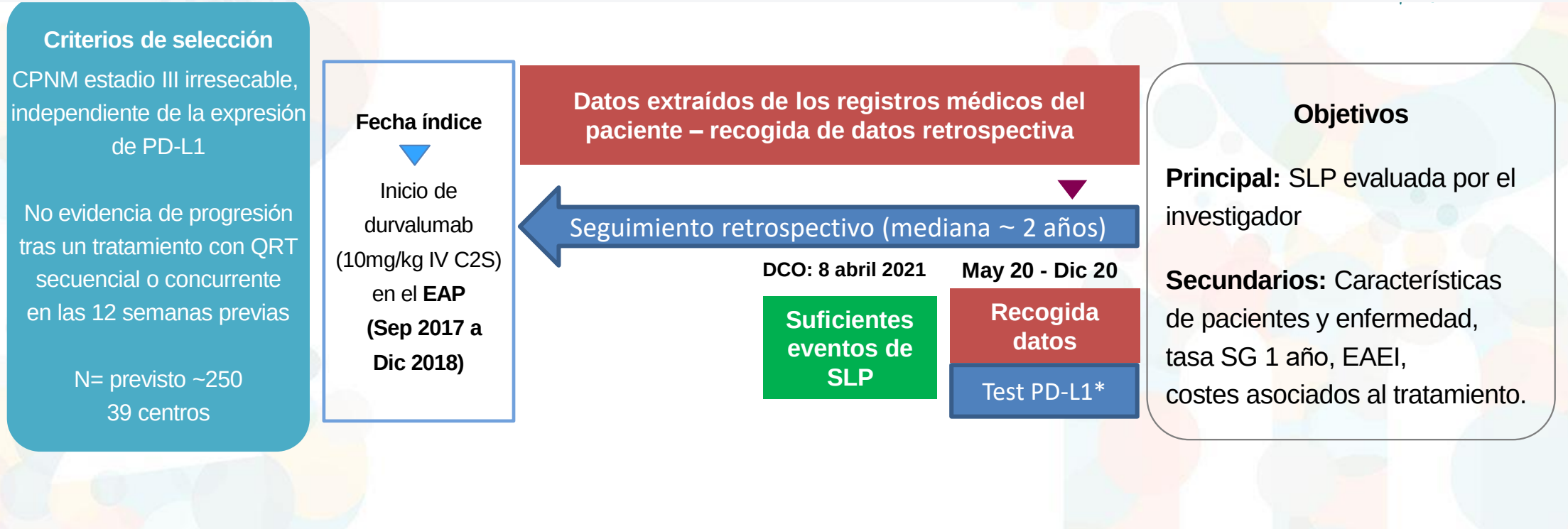
S-REAL: Estudio observacional retrospectivo



Gómez A et la SEOM 2021

RWD

S-REAL: Estudio observacional retrospectivo

Características		Total (N=244)
Edad a la fecha índice (años)	Mediana (rango) < 70 años 70 ↔75 años > 75 años	67,0 (42-86) 151 (61,9) 50 (20,5) 43 (17,6)
Sexo, n (%)	Hombre Mujer	195 (79,9) 49 (20,1)
Hábito tabáquico a la fecha índice, n (%)	Nunca Actual Exfumador	8 (3,3) 155 (63,5) 81 (33,2)
ECOG a la fecha índice, n (%)	0 1 □ 🗎 No disponible	105 (43,0) 82 (34,1) 7 (2,8) 50 (20,6)
Estadio IALSC, n (%)	IIIa IIIb IIIc Otros	97 (40,2) 107 (44,4) 22 (9,1) 18 (6,3)
Subtipo histológico, n (%)	Adenocarcinoma Carcinoma escamoso Otros	110 (45,3) 110 (45,3) 24 (9,4)
Expresión PD-L1	□🖃 <1% No valorable No testados	127 (52,1) 35 (14,3) 14 (5,7) 68 (27,9)

Variable		Total (N=244)
Quimiorradioterapia previa, n (%)	Concomitante Secuencial Otros	170 (69,7) 38 (15,6) 36 (14,8)
Dosis radioterapia total (Gy)	n Mediana (rango)	230 66,0 (0-98)
Rangos de dosis total n (%)	□ ⌛🖃 🖂 >60 - □ ⌛⌛ 🖂 > 66 Gy No disponible	78 (33,9) 125 (54,3) 27 (11,8) 14

- Mediana de **tiempo hasta inicio de Durvalumab** tras la radioterapia = **72 días**
- Mediana **duración tratamiento durvalumab =** 318 días (**10,6 meses**)
  - – >12 meses tratamiento: 18,4%
  - – >14 meses tratamiento: 3,7%
- Los pacientes recibieron una **mediana de 19 infusiones** de durvalumab
- Mediana seguimiento 22.2 meses

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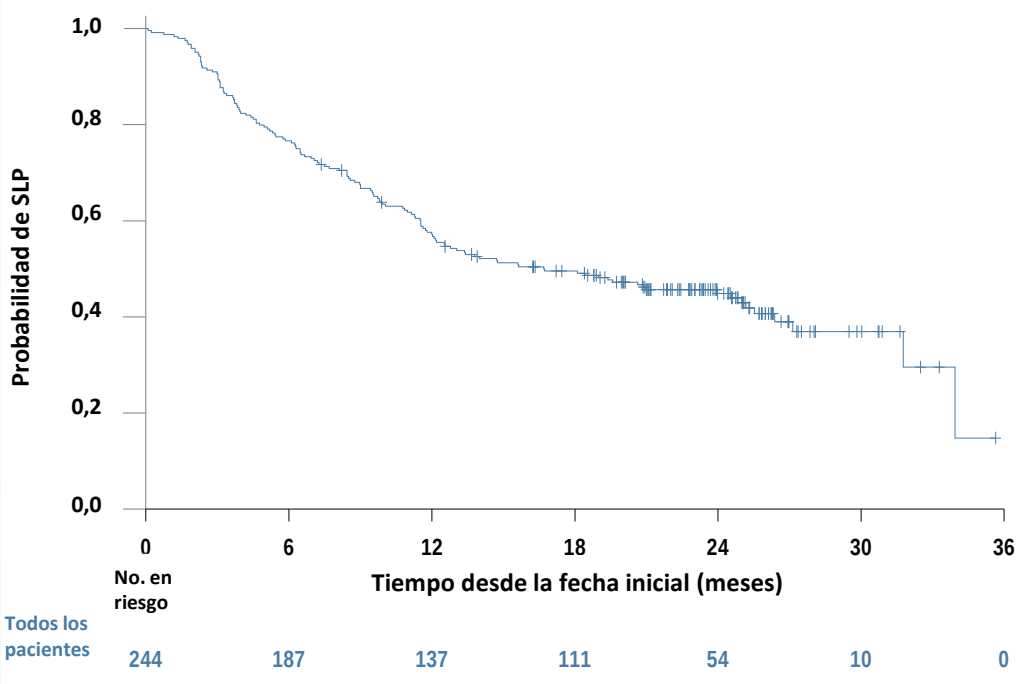
RWD

S-REAL: Estudio observacional retrospectivo



	S-REAL FAS	PACIFIC trial (durva. arm)[1]
SLP	N=244	N=476
Eventos, n (%)	105 (43,0)	268 (56,3)[†]
Libre de progresión al corte datos	104 (42,6)	
Pérdida de seguimiento	1 (0,4)	
Mediana de SLP, meses	**16,7**	**16,9**
IC del 95%	12,2–25,0	13,0–23,9
Tasa de SLP, %		
12 meses	57,2	55,7
24 meses	44,9	45,0

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RWD

S-REAL: Estudio observacional retrospectivo

EAEI	Total (N=244)
Pacientes con algún EAEI, n (%)	94 (38,5)
Diarrea/colitis y/o perforación intestinal	7 (2,9)
Neumonitis	**34 (13,9)**
Enfermedad pulmonar intersticial	3 (1,2)
Hepatitis/aumento de transaminasas	4 (1,6)
Endocrinopatías	27 (11,1)
Dermatitis	17 (7,0)
Nefritis/aumento creatinina en sangre	6 (2,5)
Neuropatía/toxicidad neuromuscular	2 (0,8)
Otros	17 (7,0)

EAEI

•Mediana de tiempo hasta el desarrollo del evento: 99 dias

•50 pacientes precisaron tratamiento con GC (53%), ninguno con IS

•En 26 (10,7%) pacientes supuso una interrupcción temporal del tratamiento y en 27 (11,1%) una discontinuación permanente

Neumonitis y/o EPI	Total (N=244)
Pacientes con neumonitis y/o EPI, n (%)	36 (14,8)
Leve	14 (5,7)
Moderado	16 (6,6)
Severo	4 (1,6)
Potencialmente mortal	1 (0,4)
Desconocido	1 (0,4)

•Limitada al tejido irradiado en el 50% de los casos.

•La mediana del **tiempo de aparición de neumonitis/EPI** desde el inicio de durvalumab fue de **73 días**.

•Se requirió la **administración de corticoides** en el **83%** de los eventos de neumonitis/EPI.

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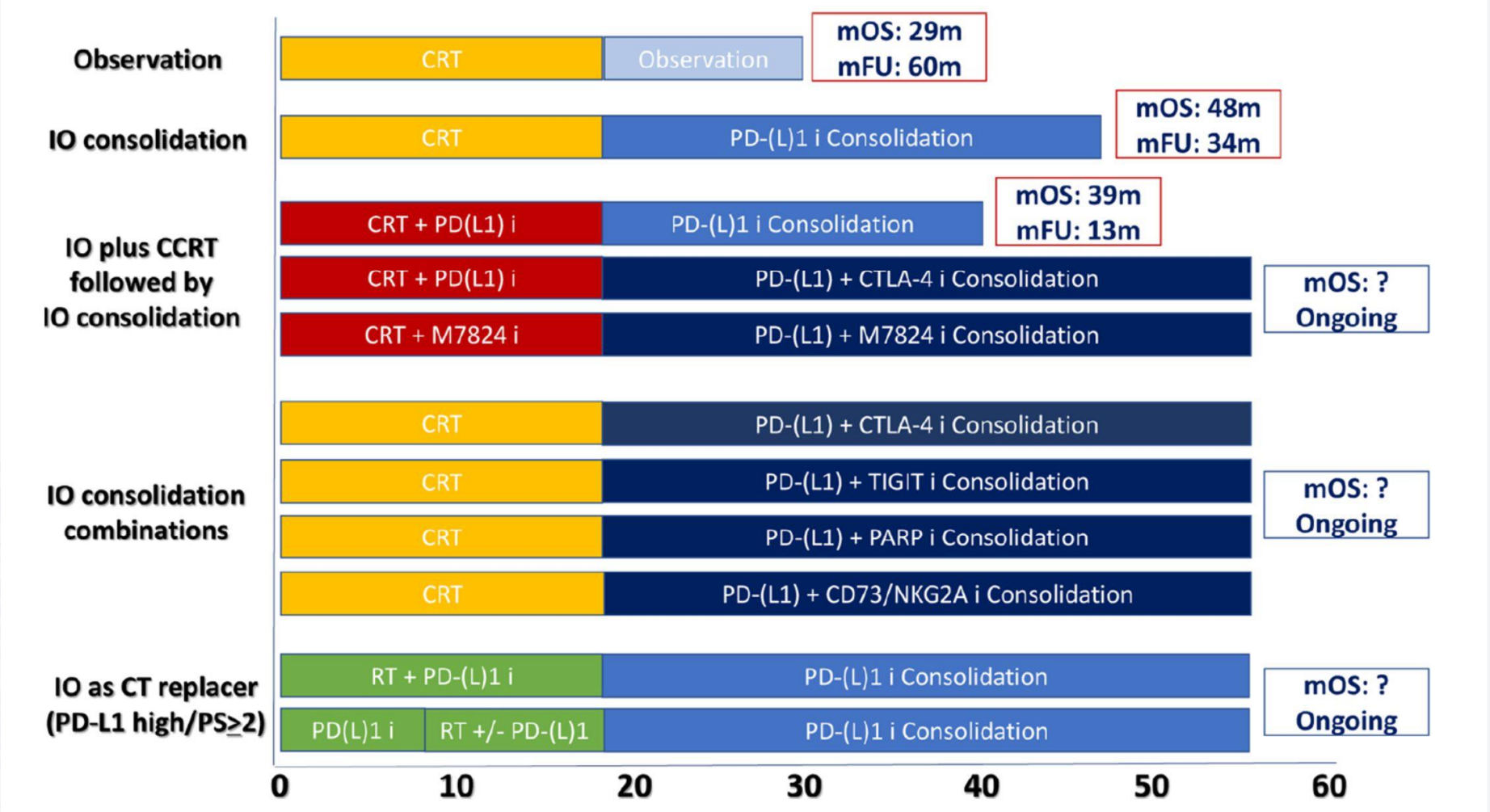
•El **4%** y el **8% de los pacientes interrumpieron o discontinuaron** el tratamiento **debido a neumonitis/EPI,**

Future directions



Passiglia F, et al. Lung Cancer 157:85-91, 2021

To wrap up…

- PACIFIC-R and PACIFIC-S demonstrates that consolidation durvalumab after CRT is effective in a large, real-world cohort of patients with unresectable Stage III NSCLC
- Median real-world PFS was higher than the median PFS reported for the durvalumab arm of the PACIFIC trial.Challenges with collecting real-world PFS data limit comparisons between PACIFIC RWD and PACIFIC
- The effectiveness of durvalumab after CRT in the analysed subgroups was generally consistent with previous analyses from the PACIFIC trial, including PD-L1 subgroups
- Rates of durvalumab treatment discontinuation due to AEs (16.7%) and disease progression (26.9%) were consistent with PACIFIC (15.4% and 31.3%, respectively)
- Pneumonitis/ILD events were manageable and mostly moderate in severity – aligned with PACIFIC

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Gracias

ARÁN