Lung Cancer UPDATES
IASLC HIGHLIGHTS
08-14 SEPTIEMBRE 2021

Iniciativa científica de:
GECP
lung cancer research

Inmunoterapia en 1a linea CNMP avanzado

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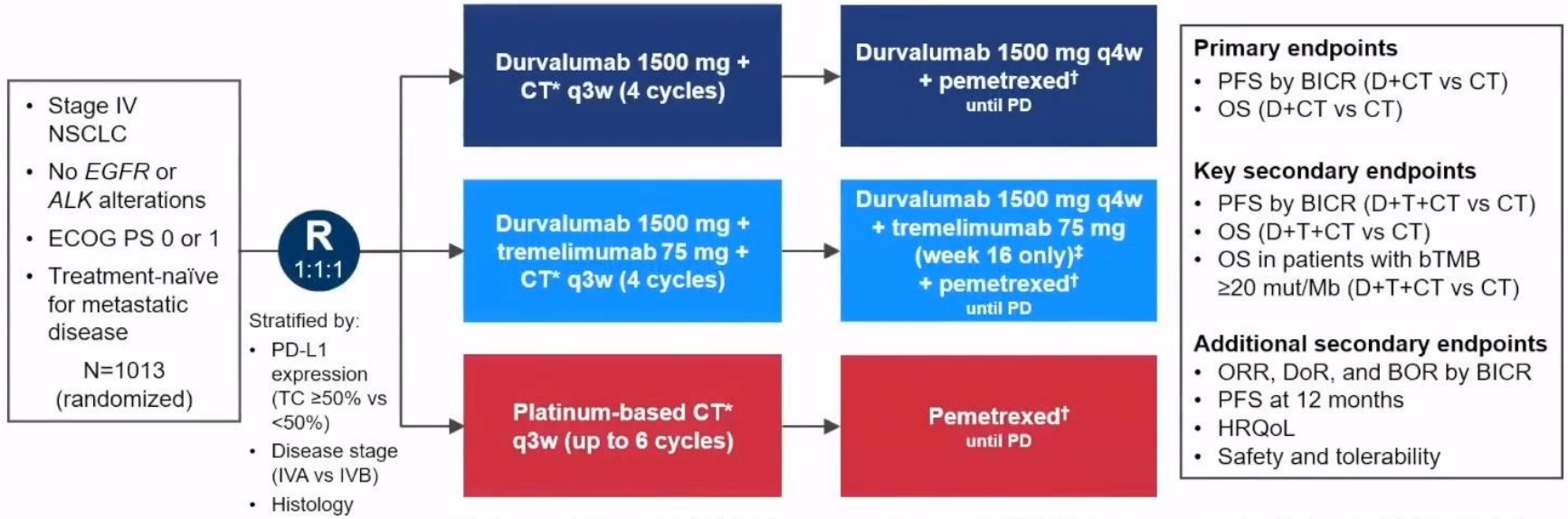
Estudio fase 3 Poseidon

Durvalumab ± Tremelimumab + Chemotherapy as First-line Treatment for mNSCLC: Results from the Phase 3 POSEIDON Study

POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study

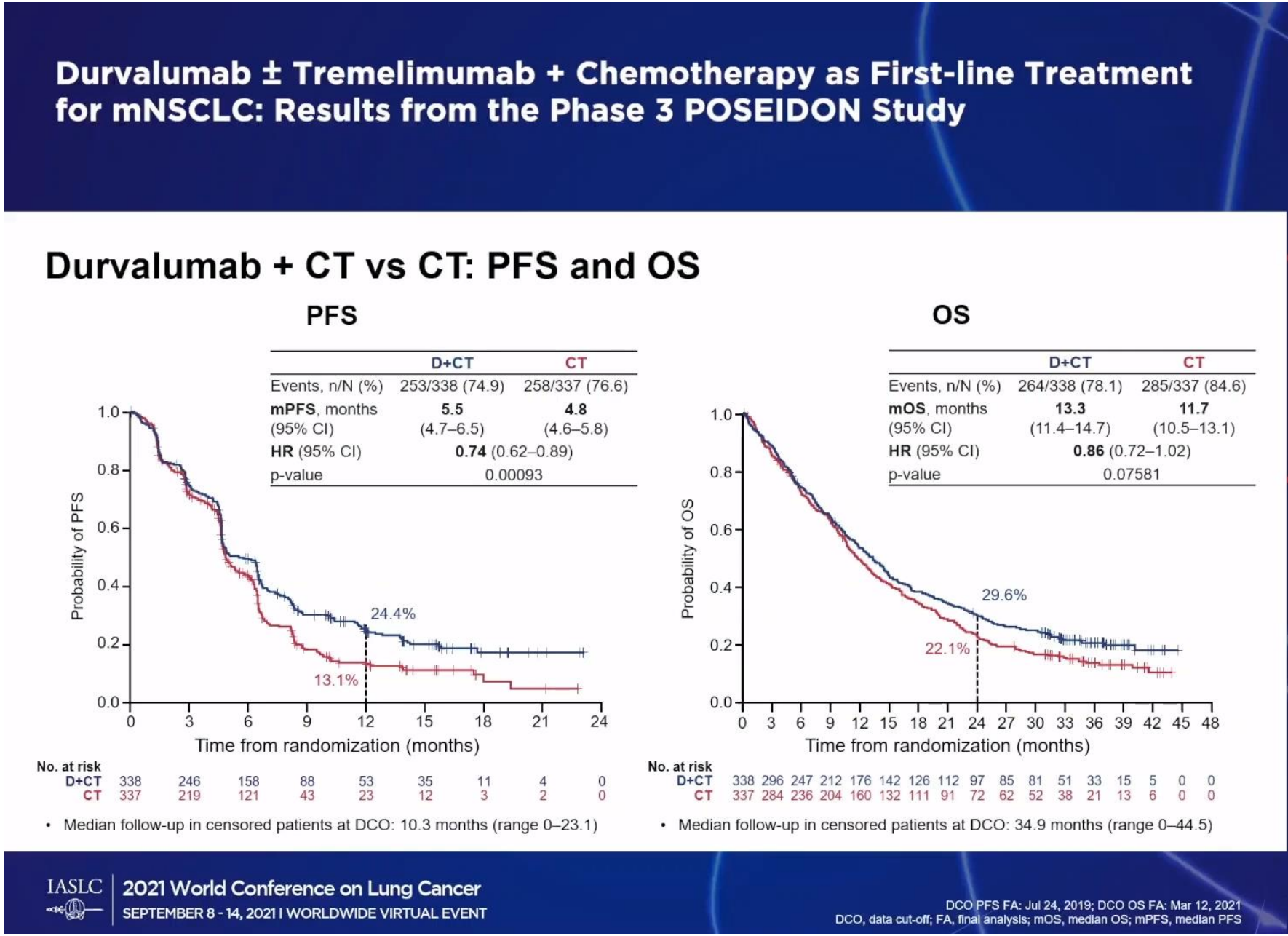


*CT options: gemcitabine + carboplatin/cisplatin (squamous), pemetrexed + carboplatin/cisplatin (non-squamous), or nab-paclitaxel + carboplatin (either histology); †Patients with non-squamous histology who initially received pemetrexed during first-line treatment only (if eligible); ‡Patients received an additional dose of tremelimumab post CT (5th dose)

BICR, blinded independent central review; BOR, best objective response; bTMB, blood tumor mutational burden; D, durvalumab; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, health-related quality of life; Mb, megabase; mut, mutations; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; q4w, every 4 weeks; T, tremelimumab; TC, tumor cell

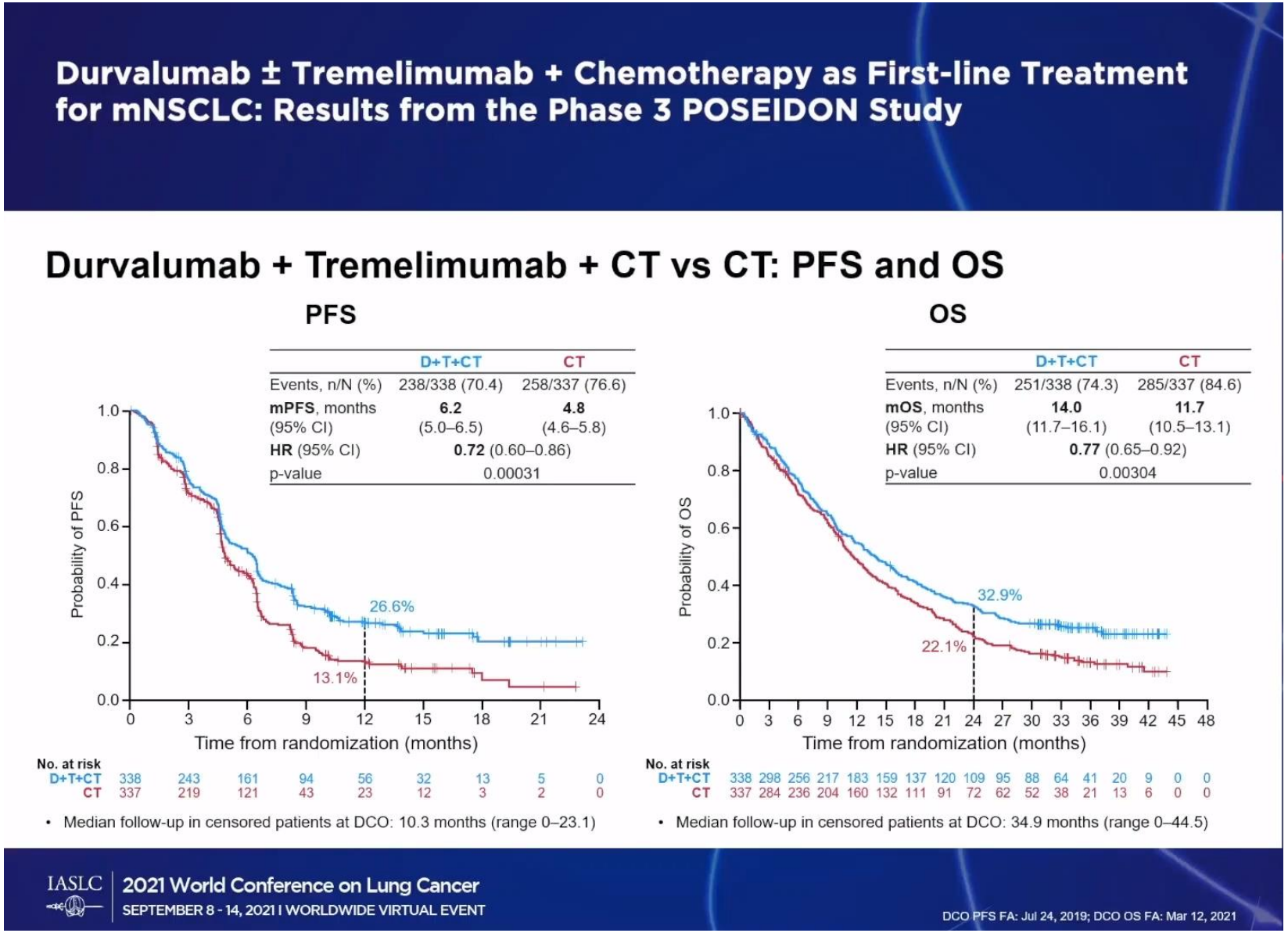
Estudio fase 3 Poseidon

- Beneficio estadísticamente significativo en PFS de añadir durvalumab a quimioterapia (HR 0.74)
- Tendencia a mejor OS (HR 0.86) -> 33% recibieron IO en brazo control en sucesivas líneas



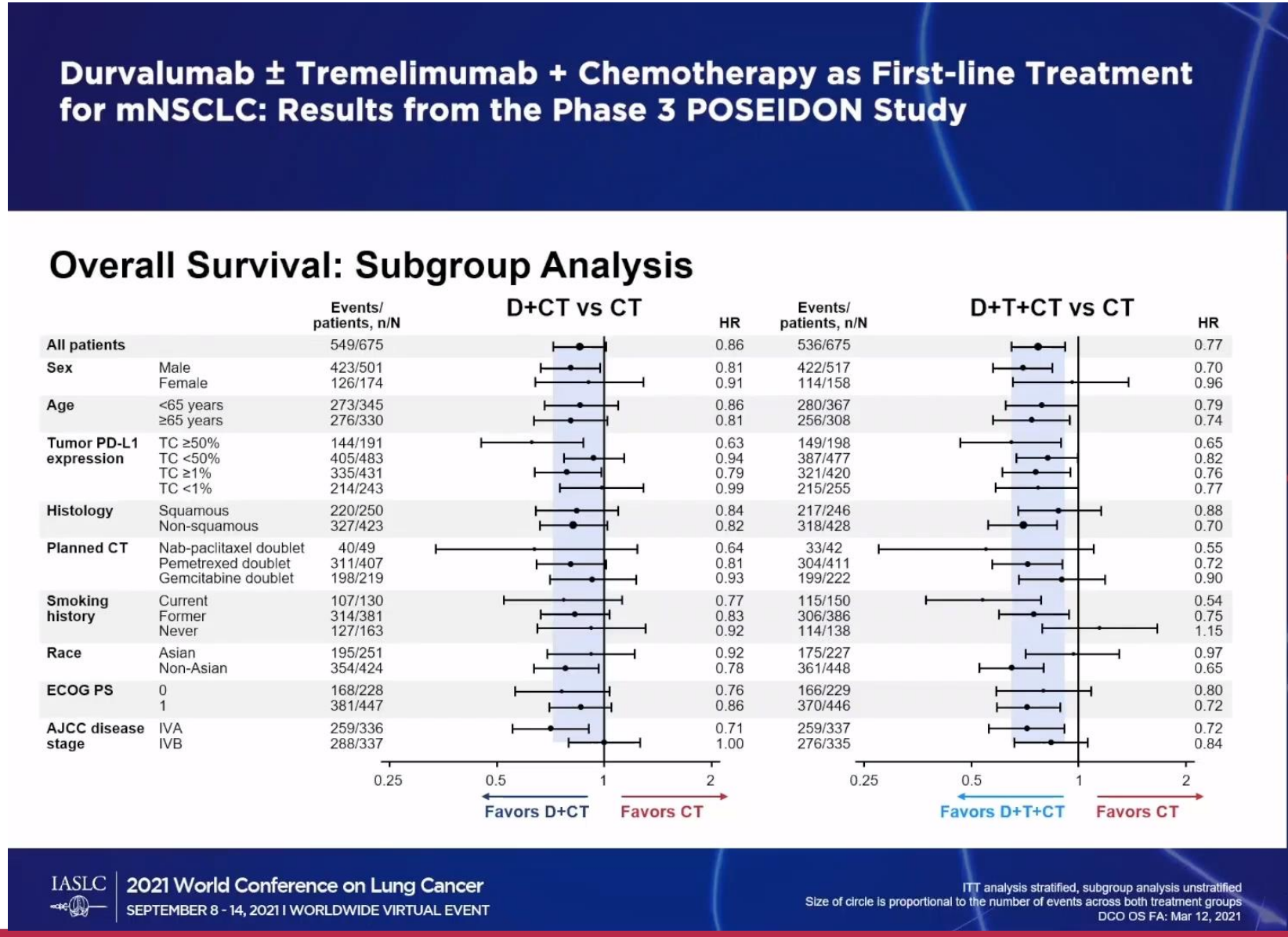
Estudio fase 3 Poseidon

- Beneficio estadísticamente significativo en PFS de añadir durvalumab + tremelimumab a quimioterapia (HR 0.72)
- Incremento de OS (HR 0.77)



Estudio fase 3 Poseidon

- Beneficio en general en todos los subgrupos.
- Beneficio en PD-L1 <1% de doble IO (HR 0.77)
- ¿Menor beneficio en pacientes tratados con gemcitabina como esquema de CT?



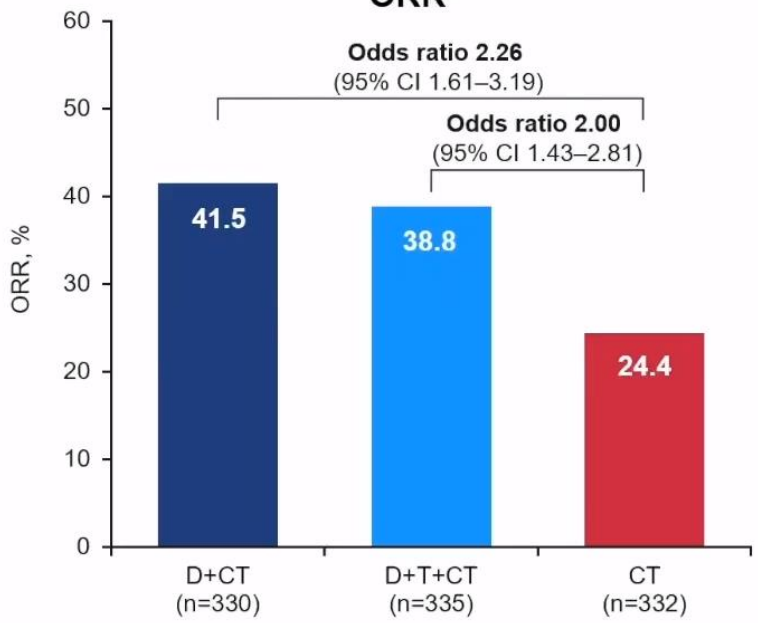
Estudio fase 3 Poseidon

- Mayor tasa de respuestas en brazos experimentales
- Mayor duración de respuesta en brazos experimentales

Durvalumab ± Tremelimumab + Chemotherapy as First-line Treatment for mNSCLC: Results from the Phase 3 POSEIDON Study

Confirmed Objective Response Rate and Duration of Response

ORR*



Duration of Response

	D+CT	D+T+CT	CT
Responders*, n	137	130	81
Median DoR, months (95% CI)	**7.0** (5.7–9.9)	**9.5** (7.2–NE)	**5.1** (4.4–6.0)
Remaining in response at 12 months, %	**38.9**	**49.7**	**21.4**

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*Confirmed objective response by BICR assessed in patients with measurable disease at baseline; confirmation was not required per protocol (post-hoc analysis)
DCO PFS FA: Jul 24, 2019
NE, not estimable

Estudio fase 3 Poseidon

- La toxicidad fue similar en los 3 grupos, aunque hubo más toxicidad inmunomediada en grupo D+T

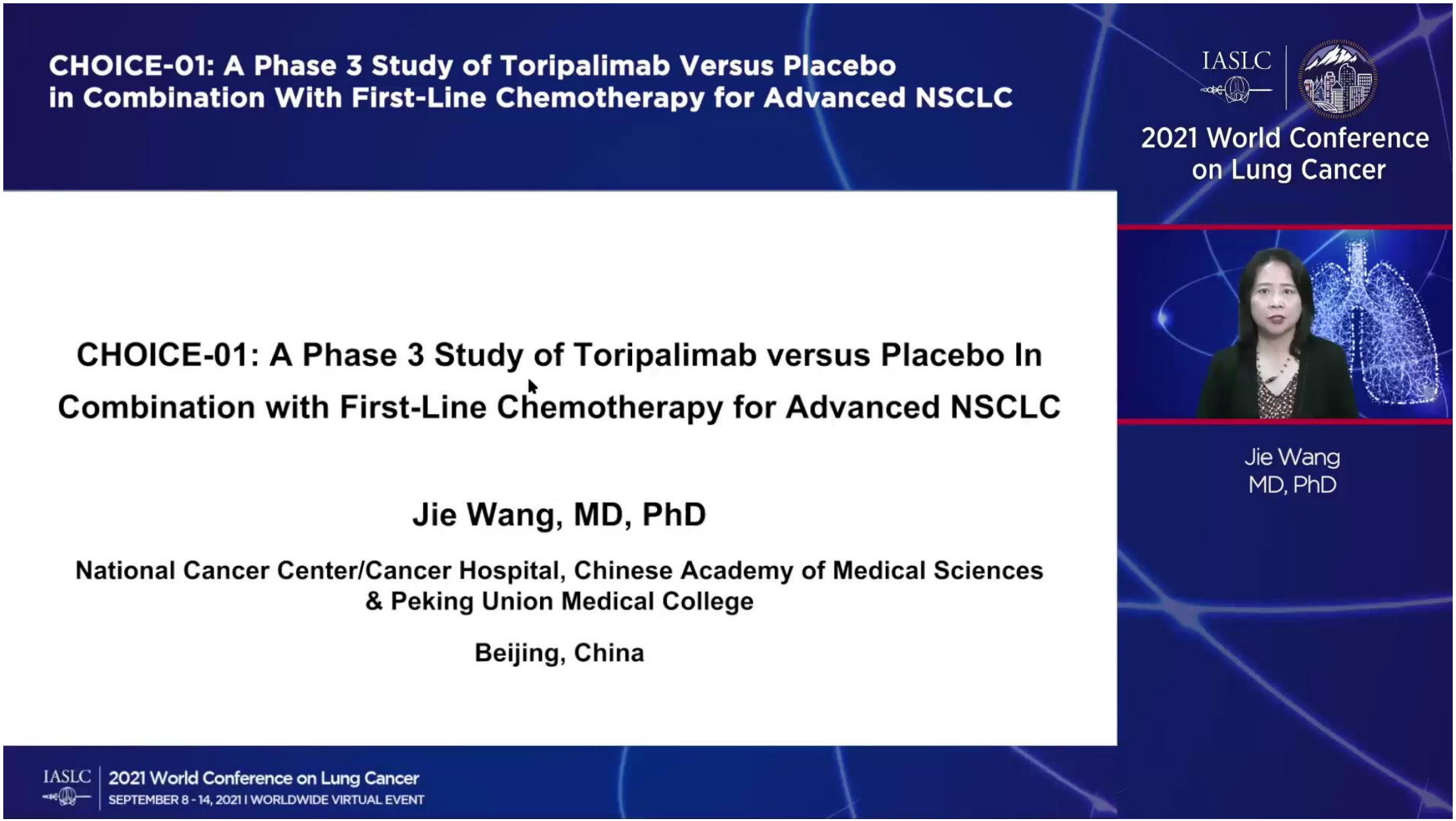
Durvalumab ± Tremelimumab + Chemotherapy as First-line Treatment for mNSCLC: Results from the Phase 3 POSEIDON Study

Immune-Mediated Adverse Events (Grouped Terms)

	D+CT (n=334)		D+T+CT (n=330)		CT (n=333)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any imAE*, n (%)	64 (19.2)	23 (6.9)	111 (33.6)	33 (10.0)	17 (5.1)	5 (1.5)
Hypothyroid events	20 (6.0)	0	27 (8.2)	0	3 (0.9)	0
Pneumonitis	10 (3.0)	4 (1.2)	12 (3.6)	3 (0.9)	2 (0.6)	2 (0.6)
Rash	5 (1.5)	2 (0.6)	13 (3.9)	3 (0.9)	6 (1.8)	2 (0.6)
Hepatic events	11 (3.3)	8 (2.4)	12 (3.6)	7 (2.1)	0	0
Dermatitis	4 (1.2)	1 (0.3)	14 (4.2)	1 (0.3)	1 (0.3)	0
Colitis	4 (1.2)	1 (0.3)	13 (3.9)	5 (1.5)	0	0
Hyperthyroid events	4 (1.2)	1 (0.3)	9 (2.7)	0	1 (0.3)	0
Adrenal insufficiency	4 (1.2)	1 (0.3)	8 (2.4)	2 (0.6)	0	0
Rare/miscellaneous	1 (0.3)	1 (0.3)	11 (3.3)	3 (0.9)	2 (0.6)	1 (0.3)

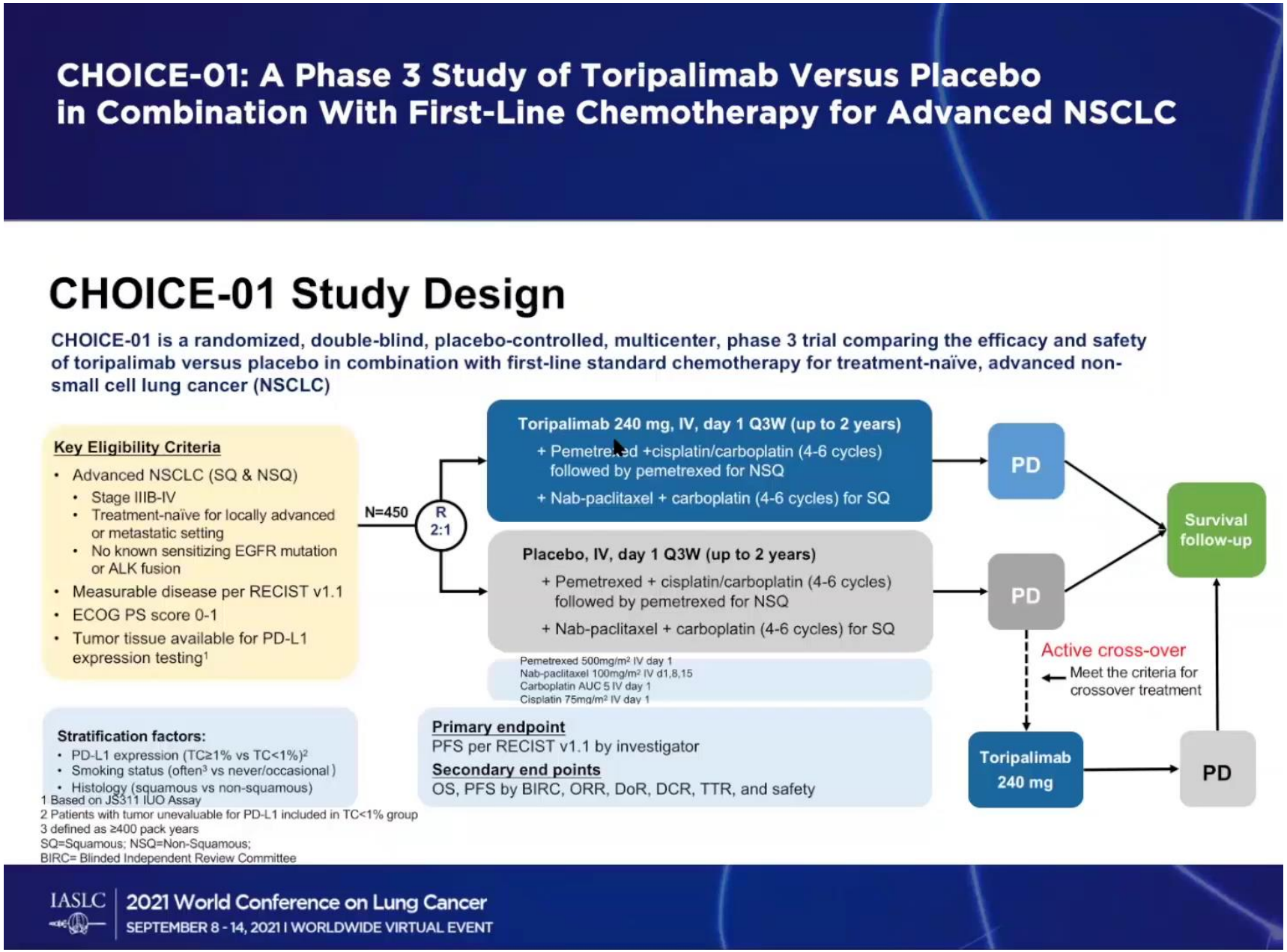
imAEs leading to death occurred in 1 patient receiving D+CT (myocarditis) and in 2 patients receiving D+T+CT (pneumonitis in 1 patient; and hepatic, renal, and pancreatic events and myocarditis in 1 patient)

Estudio fase 3 CHOICE-1: toripalimab (anti-Pd1)



Estudio fase 3 CHOICE-1: toripalimab (anti-Pd1)

- Histología escamosa y no escamosa
- Cross-over en grupo control
- PFS endpoint principal



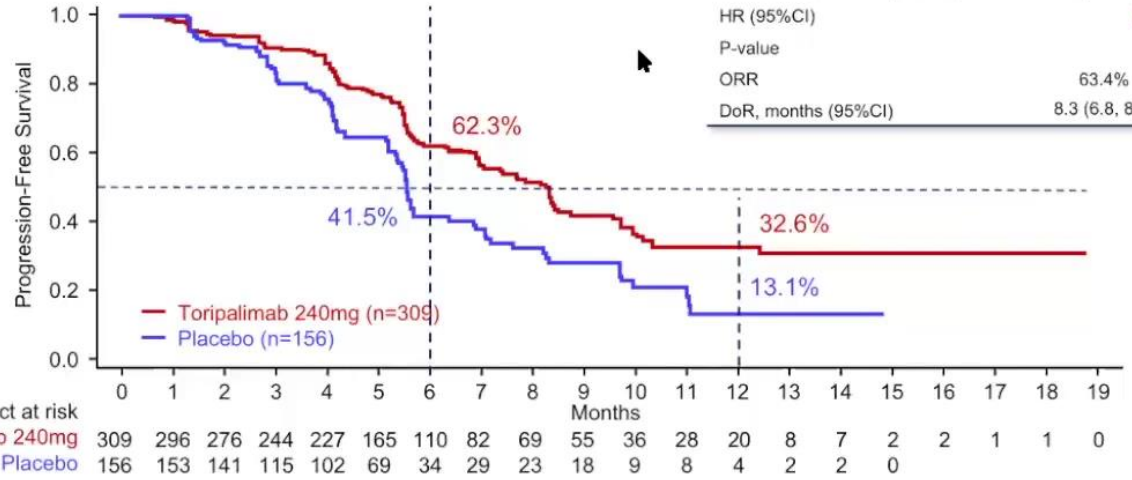
Estudio fase 3 CHOICE-1: toripalimab (anti-Pd1)

- Incremento significativo de PFS (HR 0.58)

CHOICE-01: A Phase 3 Study of Toripalimab Versus Placebo in Combination With First-Line Chemotherapy for Advanced NSCLC

Efficacy

PFS per RECIST v1.1 by Investigator



	Toripalimab +chemo (n=309)	Placebo + chemo (n=156)
Events (%)	130 (42.1)	88 (56.4)
Median PFS, months (95% CI)	8.3 (6.9-8.7)	5.6 (5.4-6.4)
HR (95%CI)	0.58 (0.442-0.769)	
P-value	0.0001	
ORR	63.4%	41.7%
DoR, months (95%CI)	8.3 (6.8, 8.7)	4.2 (4.0, 5.7)

- PFS in squamous subgroup HR=0.55 (95% CI: 0.38-0.83); non-squamous subgroup HR=0.59 (95% CI: 0.40-0.87)
- IRC-assessed PFS for squamous and non-squamous patients was consistent with Investigator's assessed PFS

Data cut-off date: November 17th, 2020

Estudio fase 3 GEMSTONE-302: Sugemalimab (anti-PDL1)

GEMSTONE-302: A Phase 3 Study of Platinum-Based Chemotherapy with Placebo or Sugemalimab, a PD-L1 mAb, for metastatic NSCLC

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GEMSTONE-302: Randomized, Double-Blind, Phase 3 Study of Sugemalimab or Placebo Plus Platinum-Based Chemotherapy as First-Line Treatment for Metastatic NSCLC

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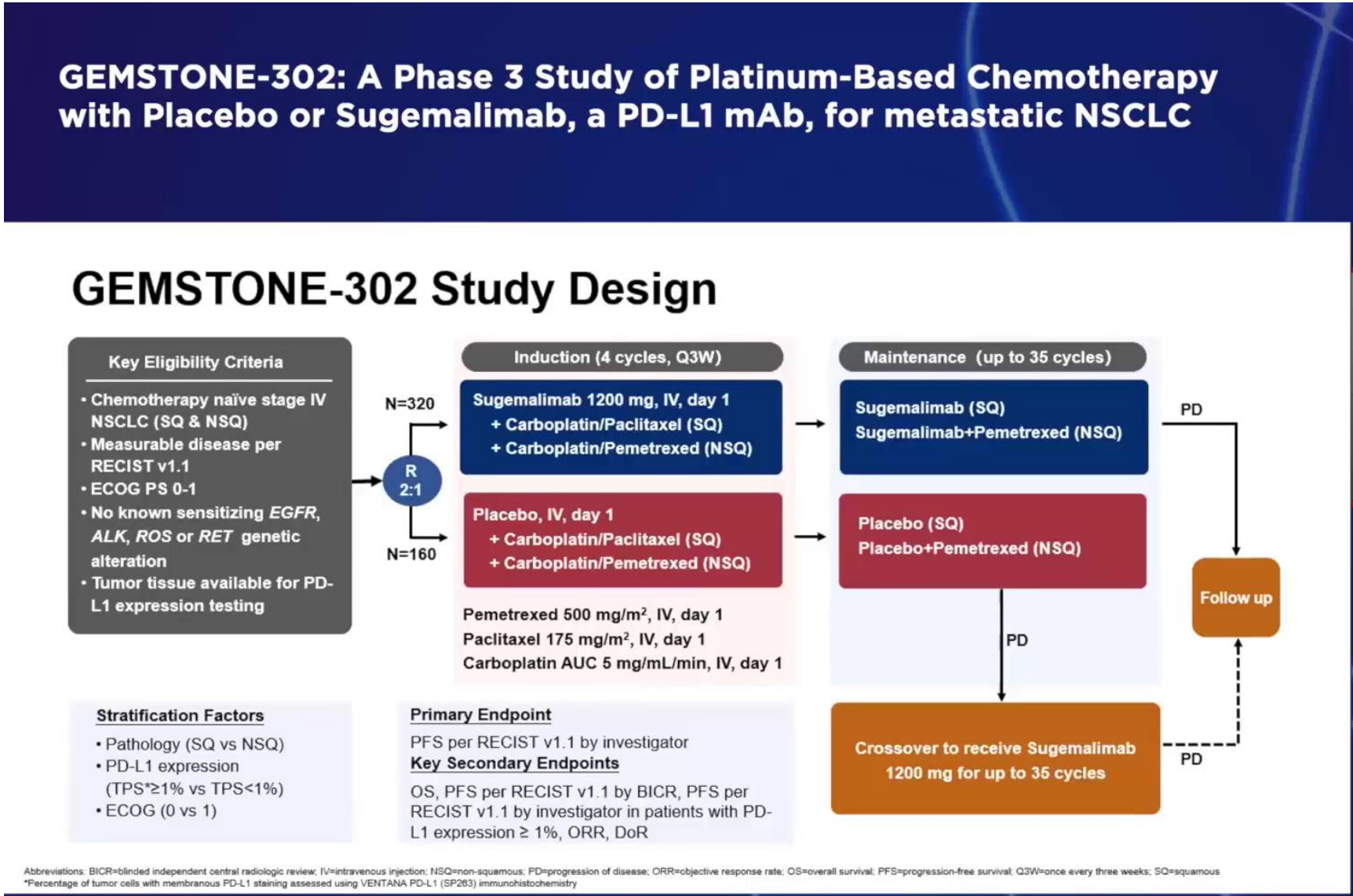
Estudio fase 3 GEMSTONE-302: Sugemalimab (anti-PDL1))

- Histología escamosa y no escamosa
- PFS como endpoint principal.
- Permite cross-over en brazo control

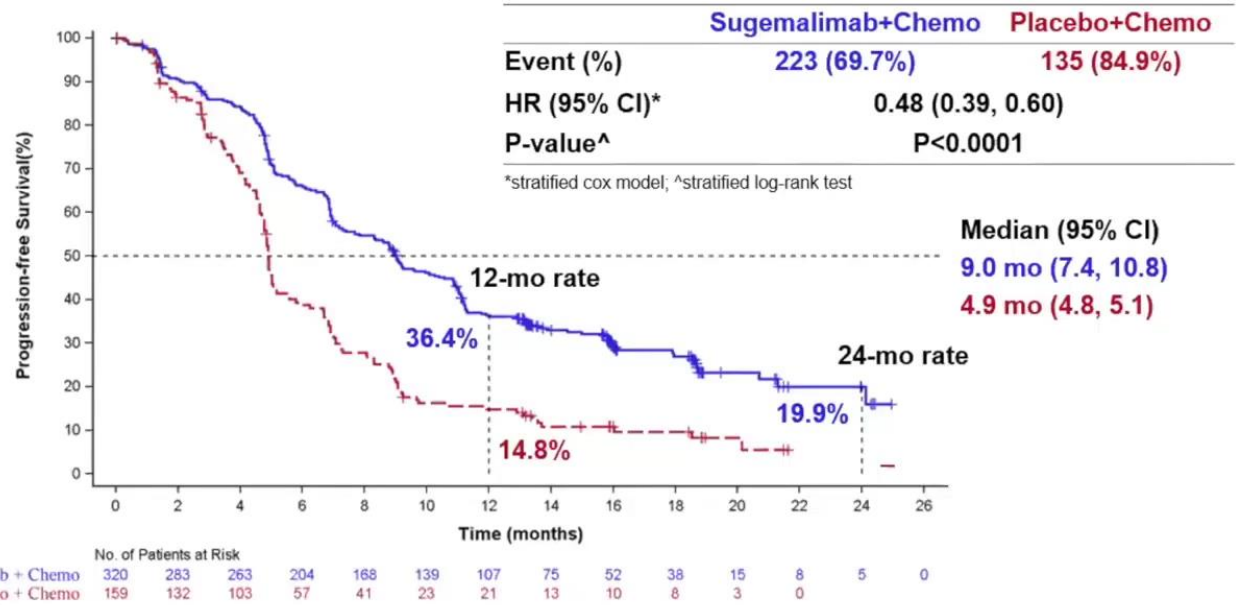


Estudio fase 3 GEMSTONE-302: Sugemalimab (anti-PDL1))

- Beneficio en PFS con HR 0.48

GEMSTONE-302: A Phase 3 Study of Platinum-Based Chemotherapy with Placebo or Sugemalimab, a PD-L1 mAb, for metastatic NSCLC

Investigator-Assessed PFS (RECIST v1.1, ITT)



	Sugemalimab+Chemo	Placebo+Chemo
Event (%)	223 (69.7%)	135 (84.9%)
HR (95% CI)*	0.48 (0.39, 0.60)	
P-value^	P<0.0001	

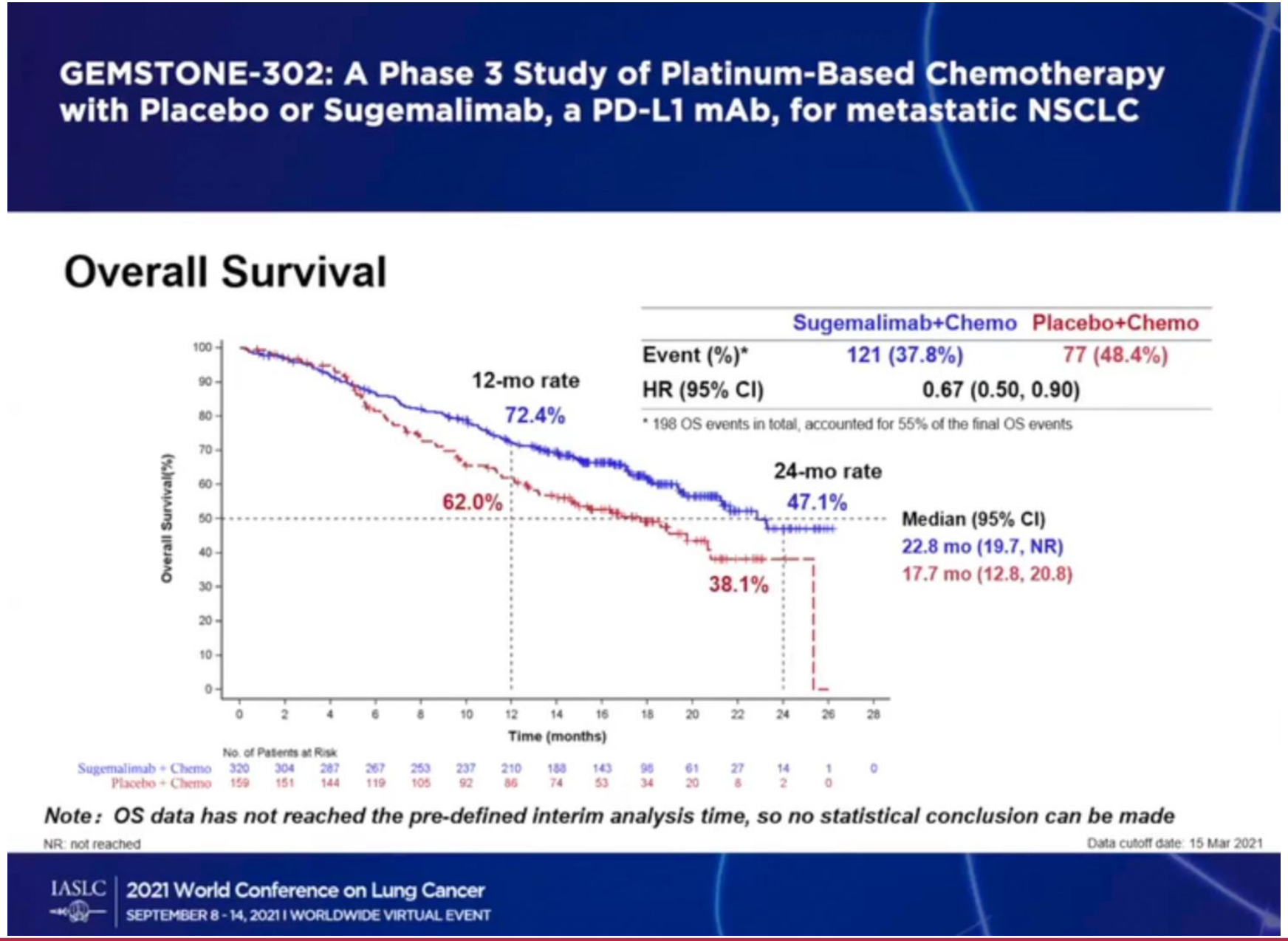
*stratified cox model; ^stratified log-rank test

Median (95% CI)
9.0 mo (7.4, 10.8)
4.9 mo (4.8, 5.1)

Data cutoff date: 15 Mar 2021

Estudio fase 3 GEMSTONE-302: Sugemalimab (anti-PDL1))

- Datos inmaduros para OS, pero HR 0.67



Estudio fase 3 9LA (Brain Metastases)

First-line Nivolumab + Ipilimumab + Chemotherapy in Patients with Advanced NSCLC and Brain Metastases: Results From CheckMate 9LA

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First-line nivolumab + ipilimumab + chemotherapy in patients with advanced NSCLC and brain metastases: results from CheckMate 9LA

David Paul Carbone,[1] Tudor-Eliade Ciuleanu,[2] Manuel Cobo,[3] Michael Schenker,[4] Bogdan Zurawski,[5] Juliana Menezes,[6] Eduardo Richardet,[7] Jaafar Bennouna,[8] Enriqueta Felip,[9] Oscar Juan-Vidal,[10] Aurelia Alexandru,[11] Hiroshi Sakai,[12] Emmanuel de la Mora Jimenez,[13] Luis Paz-Ares[14], Martin Reck,[15] Thomas John,[16] Nan Hu,[17] Xiaoqing Zhang,[17] Phuong Tran,[17] Diederik Grootendorst,[17] Shun Lu[18]

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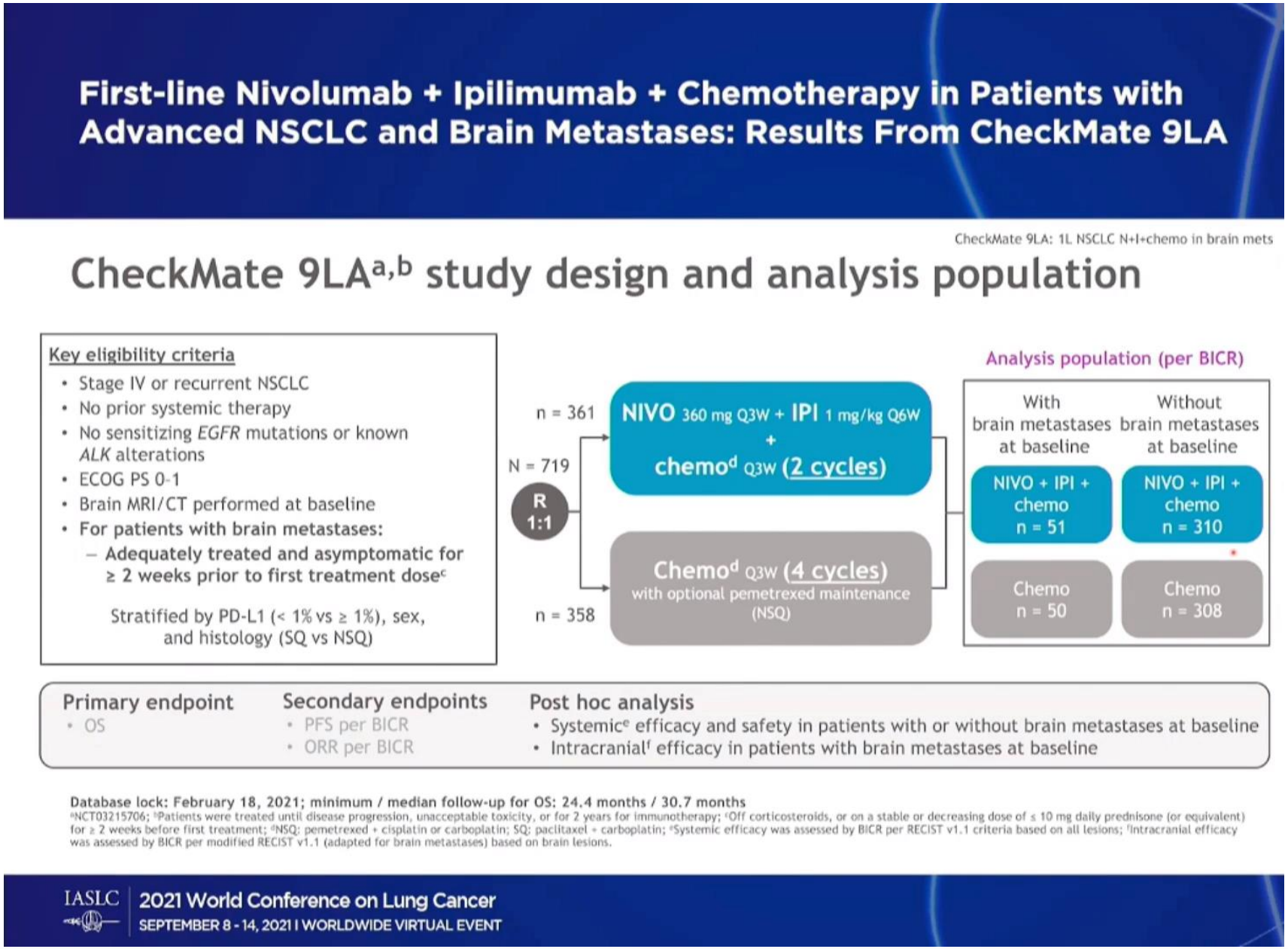
David Carbone
MD, PhD

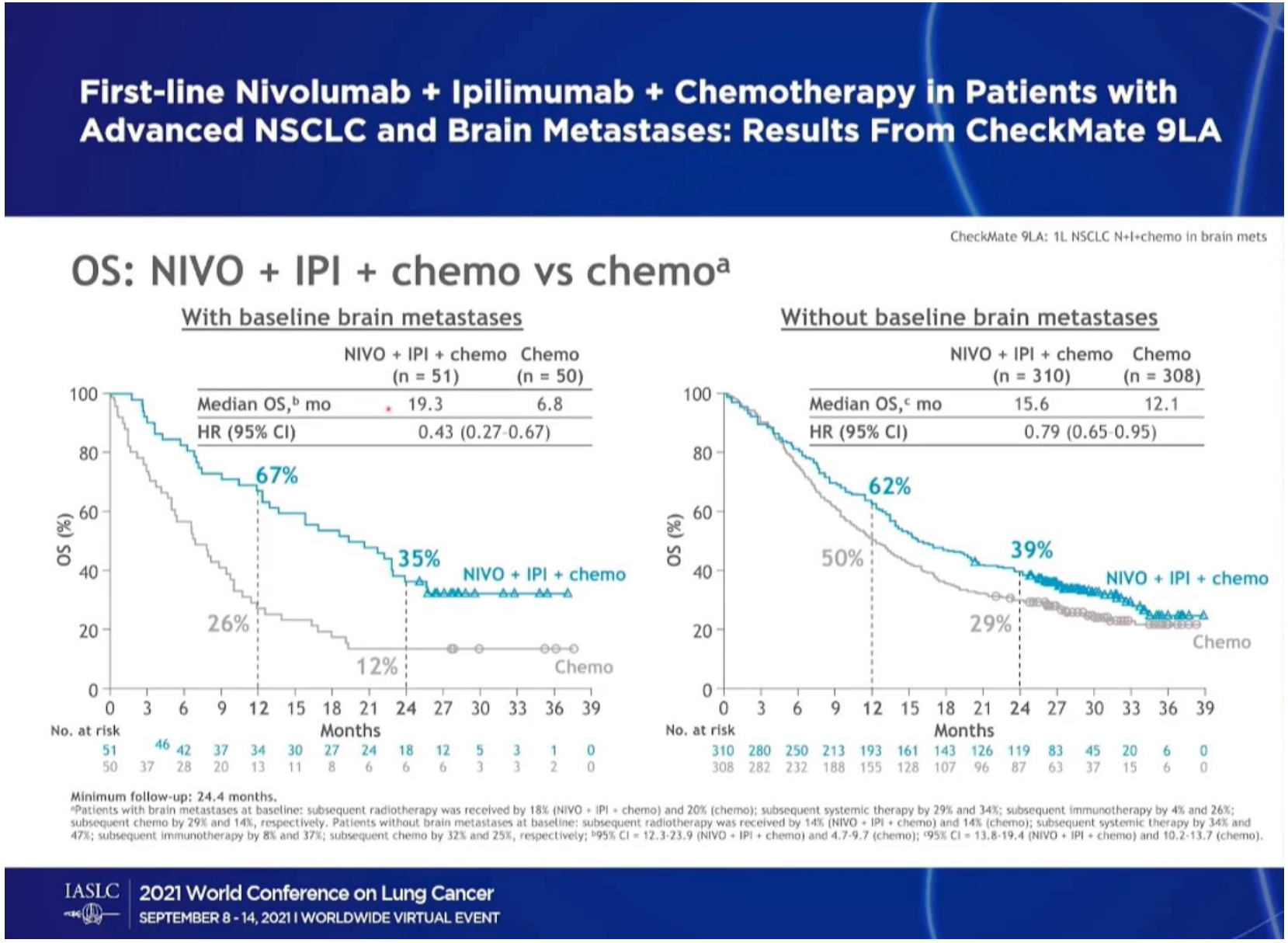
Estudio fase 3 9LA (Brain Metastases)

- Diseño del estudio 9LA.
- Unos 50 pacientes por brazo tenían M1 cerebrales, **tratadas y asintomáticas**



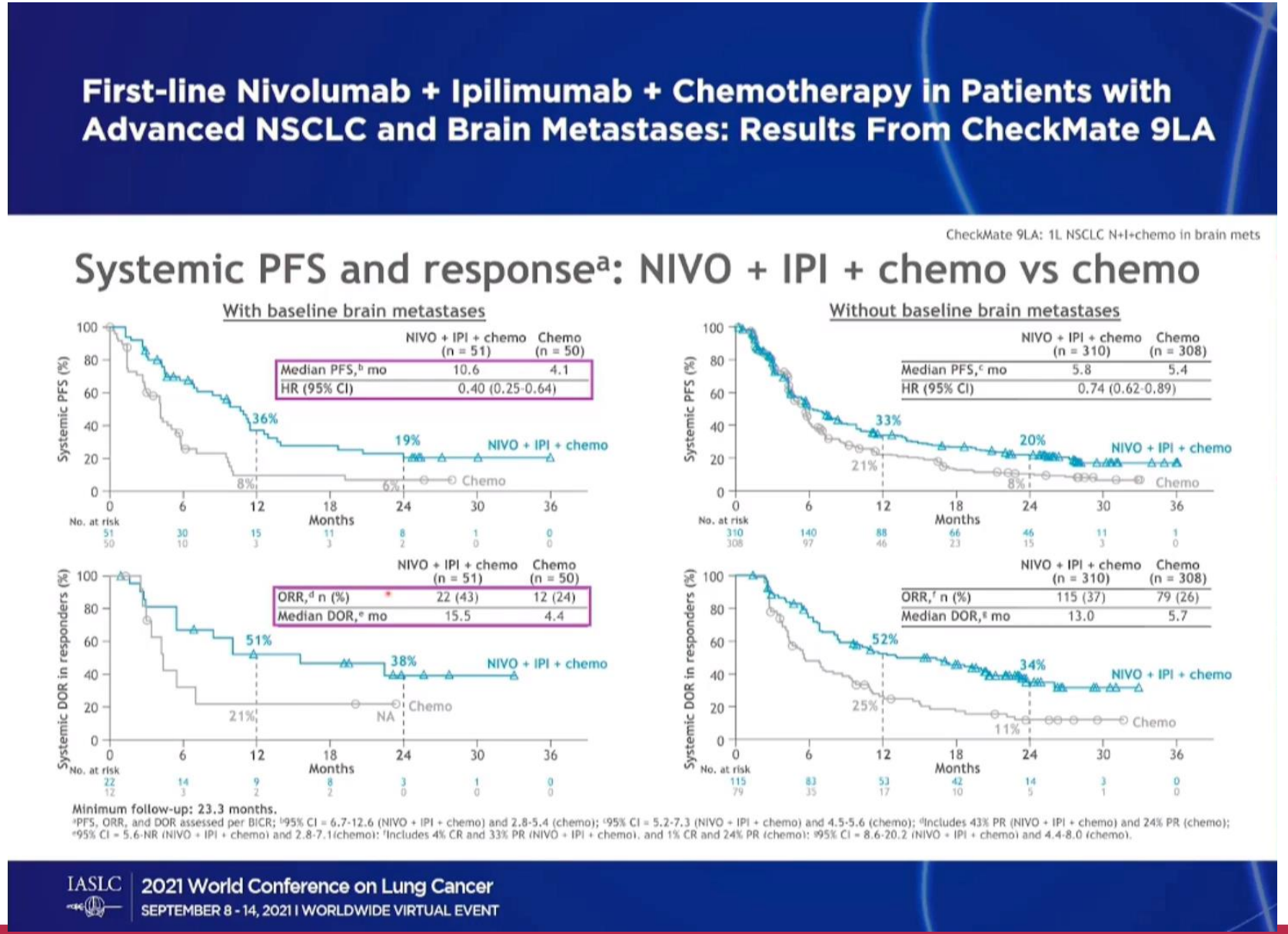
Estudio fase 3 9LA (Brain Metastases)

- Los pacientes con M1 cerebrales tratadas se benefician del brazo experimental (HR 0,43)



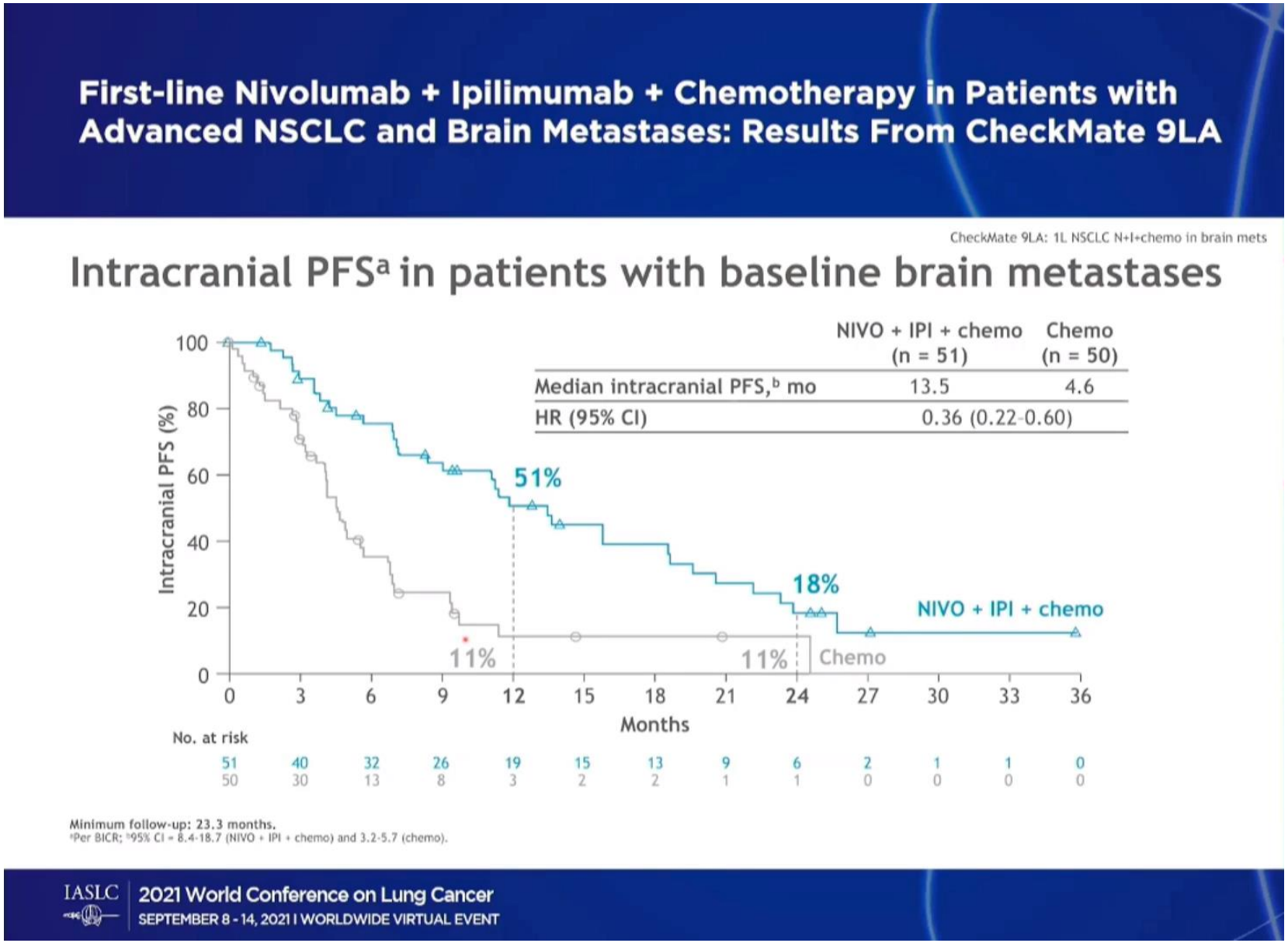
Estudio fase 3 9LA (Brain Metastases)

- Hay beneficio a favor del brazo experimental en PFS y respuesta.



Estudio fase 3 9LA (Brain Metastases)

- La PFS intracraneal es claramente superior en el brazo experimental (HR 0,36)



Estudio fase 3 9LA (Brain Metastases)

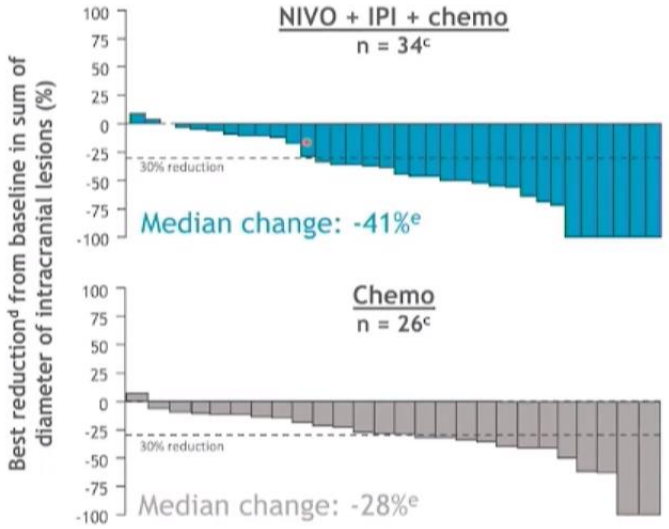
- Casi doble de tasa de respuesta intracraneal en los pacientes en el brazo experimental, y con un incremento en el porcentaje medio de reducción.

First-line Nivolumab + Ipilimumab + Chemotherapy in Patients with Advanced NSCLC and Brain Metastases: Results From CheckMate 9LA

CheckMate 9LA: 1L NSCLC N+I+chemo in brain mets

Intracranial response[a] in patients with baseline brain metastases

Intracranial response	NIVO + IPI + chemo (n = 51)	Chemo (n = 50)
ORR, n (%)	20 (39)	10 (20)
BOR,[b] n (%)		
CR	5 (10)	4 (8)
PR	15 (29)	6 (12)
SD	18 (35)	18 (36)
PD	1 (2)	3 (6)
DCR, n (%)	38 (74)	28 (56)
Median time to response, mo (range)	2.8 (1.3-11.4)	2.2 (1.3-5.8)
Median DOR, mo (95% CI)	22.3 (9.7-NR)	18.9 (1.8-NR)



Minimum follow-up: 23.3 months.

[a]Per BICR; [b]Unable to be determined or not reported in 4% and 20% of the NIVO + IPI + chemo arm, and 10% and 28% of the chemo arm, respectively; [c]Patients with measurable intracranial lesion(s) at baseline and at least one on-treatment brain lesion assessment per BICR (modified RECIST v1.1 [adapted for brain metastases]); [d]Best reduction is based on evaluable intracranial target lesions measurements up to progression or start of subsequent anticancer therapy; [e]Range of best reduction from baseline: −100% to 9% (NIVO + IPI + chemo) and −100% to 7% (chemo).

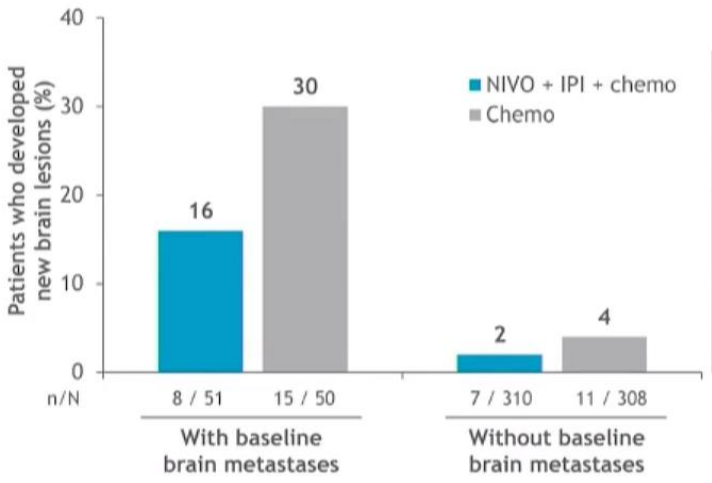
Estudio fase 3 9LA (Brain Metastases)

- Menos aparición de nuevas lesiones cerebrales en el brazo experimental.
- Mayor tiempo de aparición de nuevas lesiones en el cerebro en brazo experimental.

First-line Nivolumab + Ipilimumab + Chemotherapy in Patients with Advanced NSCLC and Brain Metastases: Results From CheckMate 9LA

CheckMate 9LA: 1L NSCLC N+I+chemo in brain mets

Development of new brain lesions[a]



	With baseline brain metastases		Without baseline brain metastases	
	NIVO + IPI + chemo (n = 51)	Chemo (n = 50)	NIVO + IPI + chemo (n = 310)	Chemo (n = 308)
Median time to development of new brain lesions, mo (range)	9.0 (2.3-19.6)	4.6 (1.9-9.5)	6.9 (1.4-18.8)	5.3 (1.2-26.7)
Tumor burden in patients who developed new brain lesions, mm,[b,c] range	13-19	10-38	4-74	6-37

[a]By initial PD; [b]Sum of longest diameter in brain lesions; [c]Number of patients with measurable new brain lesions in NIVO + IPI + chemo vs chemo: 2 vs 5 (with baseline brain metastases); 7 vs 10 (without baseline brain metastases).

Estudio fase 2 ATEZO-BRAIN

Atezo-Brain: Single Arm Phase II Study of Atezolizumab Plus Chemotherapy in Stage IV NSCLC With Untreated Brain Metastases

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ATEZO-BRAIN (GECP 17/05): NON-RANDOMIZED PHASE II CLINICAL TRIAL OF ATEZOLIZUMAB COMBINED WITH CARBOPLATIN PLUS PEMETREXED IN CHEMOTHERAPY-NAÏVE PATIENTS WITH ADVANCED NON-SQUAMOUS NSCLC WITH UNTREATED BRAIN METASTASES

Ernest Nadal (1), Delvys Rodríguez-Abreu (2), Bartomeu Massutí (3), Oscar Juan (4), Gerardo Huidobro (5), Rafael López (6), Javier De Castro (7), Anna Estival (8), Rosario Garcia-Campelo (9), Ivana Sullivan (10), Enriqueta Felip (11), Ana Blasco (12), Maria Guirado (13), Marta Simó (14), Eva Pereira (15), Valentín Navarro (1), Jordi Bruna (14)

(1) Institut Català d'Oncologia – L'Hospitalet, Spain; (2) Hospital Insular de Gran Canaria, Spain; (3) Hospital General de Alicante, Spain; (4) Hospital Universitari La Fe, Spain; (5) Complejo Hospitalario Universitario de Vigo, Spain; (6) Hospital Clínico de Valladolid, Spain; (7) Hospital Universitario La Paz, Spain; (8) Institut Català d'Oncologia - Badalona, Spain; (9) Hospital Universitario A Coruña, Spain; (10) Hospital Sant Pau, Spain; (11) Hospital Universitario Vall d'Hebron, Spain; (12) Hospital General de Valencia, Spain; (13) Hospital Universitario de Elche, Spain; (14) Hospital Universitari de Bellvitge, Spain; (15) Spanish Lung Cancer Group, Spain

Ernest Nadal
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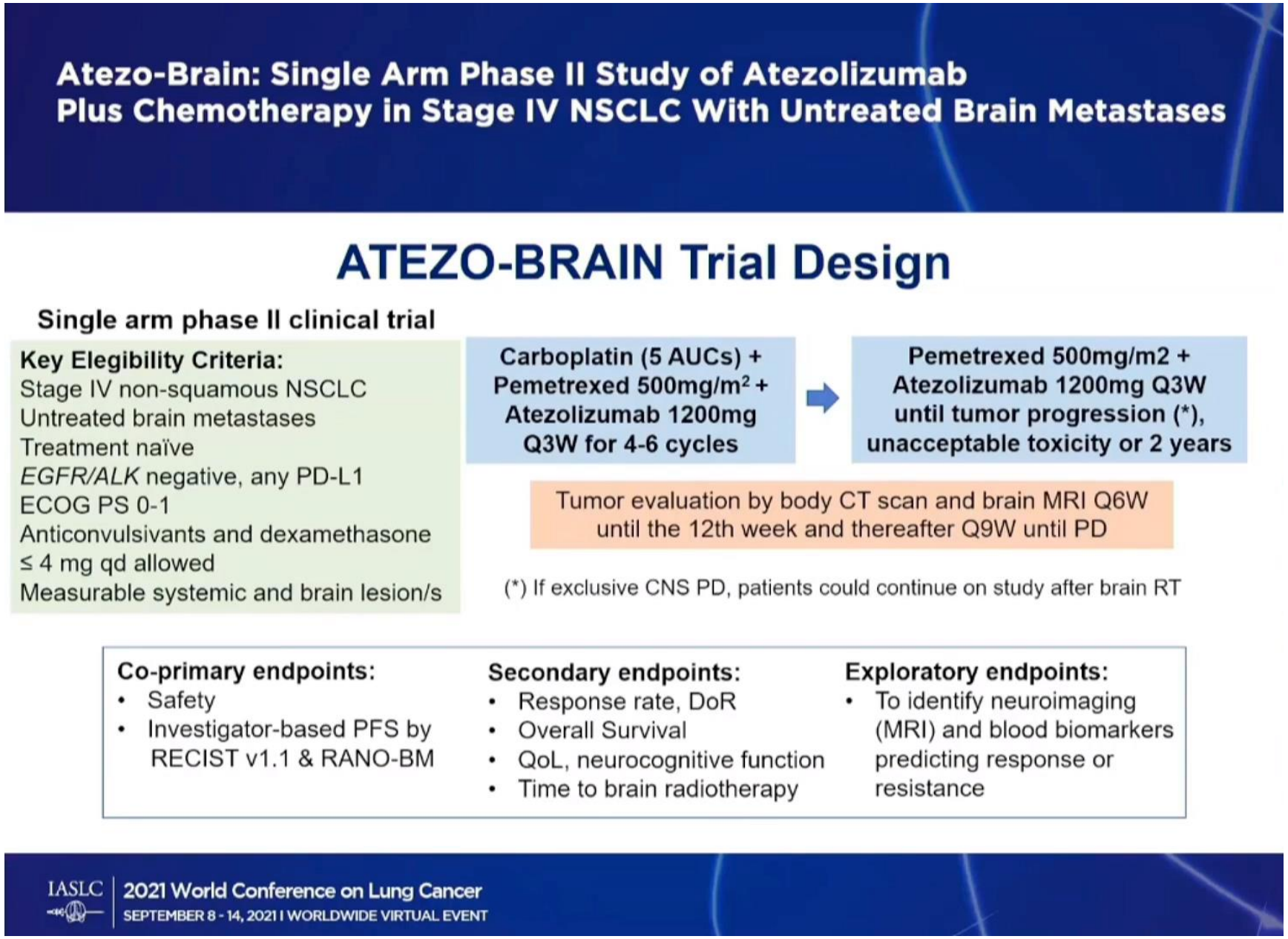
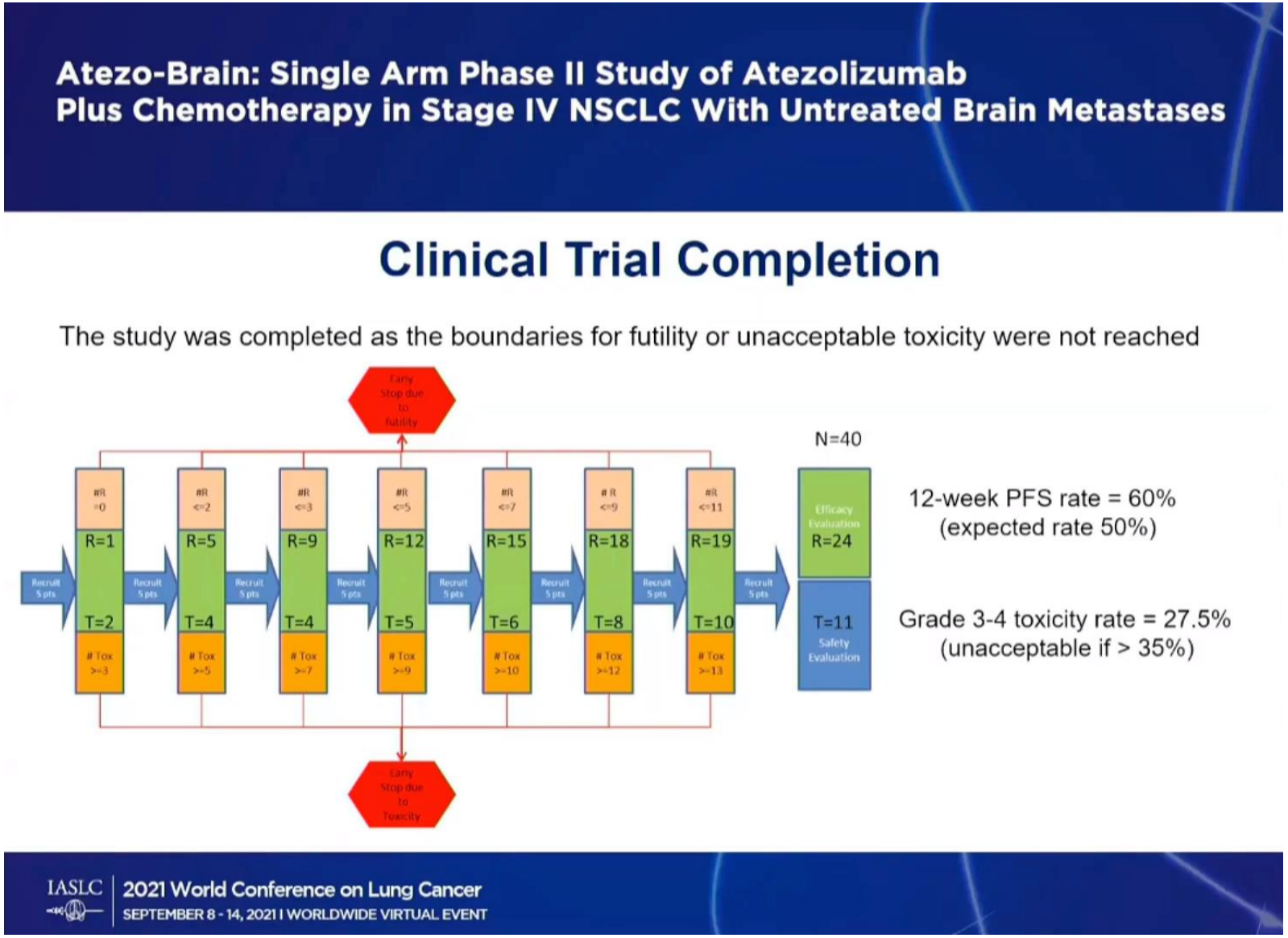
Estudio fase 2 ATEZO-BRAIN

- M1 cerebrales **no tratadas, asintomáticas** (máximo 4 mg de dexametasona)
- Añadir atezolizumab a carboplatino-pemetrexed de 1ª L.



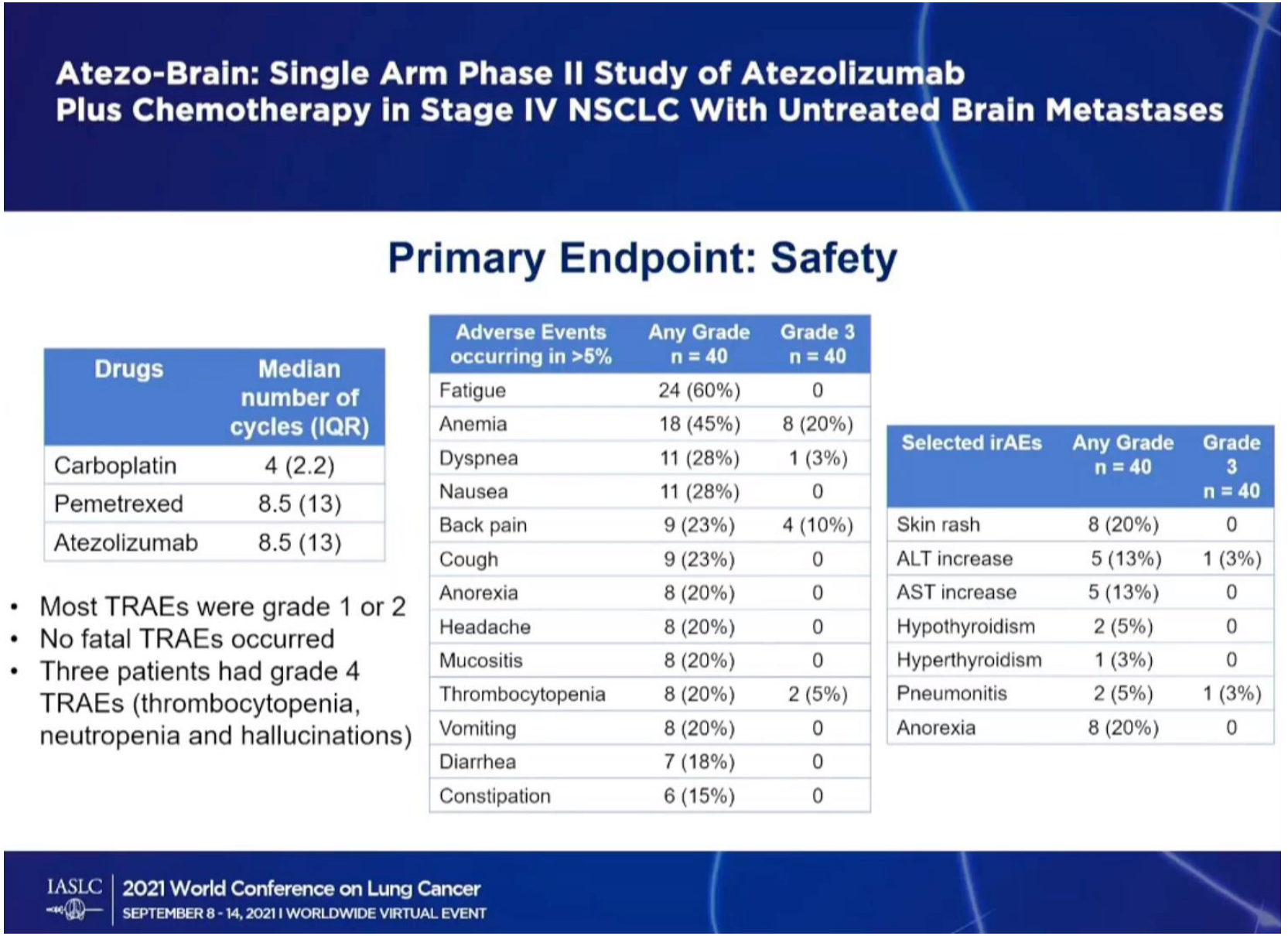
Estudio fase 2 ATEZO-BRAIN

- Se pudo completar el estudio con los 40 pacientes planificados, dado que no se detectó toxicidad inaceptable ni futilidad.



Estudio fase 2 ATEZO-BRAIN

- Perfil de seguridad aceptable.



Atezo-Brain: Single Arm Phase II Study of Atezolizumab Plus Chemotherapy in Stage IV NSCLC With Untreated Brain Metastases

Primary Endpoint: Safety

Drugs	Median number of cycles (IQR)
Carboplatin	4 (2.2)
Pemetrexed	8.5 (13)
Atezolizumab	8.5 (13)

- Most TRAEs were grade 1 or 2
- No fatal TRAEs occurred
- Three patients had grade 4 TRAEs (thrombocytopenia, neutropenia and hallucinations)

Adverse Events occurring in >5%	Any Grade n = 40	Grade 3 n = 40
Fatigue	24 (60%)	0
Anemia	18 (45%)	8 (20%)
Dyspnea	11 (28%)	1 (3%)
Nausea	11 (28%)	0
Back pain	9 (23%)	4 (10%)
Cough	9 (23%)	0
Anorexia	8 (20%)	0
Headache	8 (20%)	0
Mucositis	8 (20%)	0
Thrombocytopenia	8 (20%)	2 (5%)
Vomiting	8 (20%)	0
Diarrhea	7 (18%)	0
Constipation	6 (15%)	0

Selected irAEs	Any Grade n = 40	Grade 3 n = 40
Skin rash	8 (20%)	0
ALT increase	5 (13%)	1 (3%)
AST increase	5 (13%)	0
Hypothyroidism	2 (5%)	0
Hyperthyroidism	1 (3%)	0
Pneumonitis	2 (5%)	1 (3%)
Anorexia	8 (20%)	0

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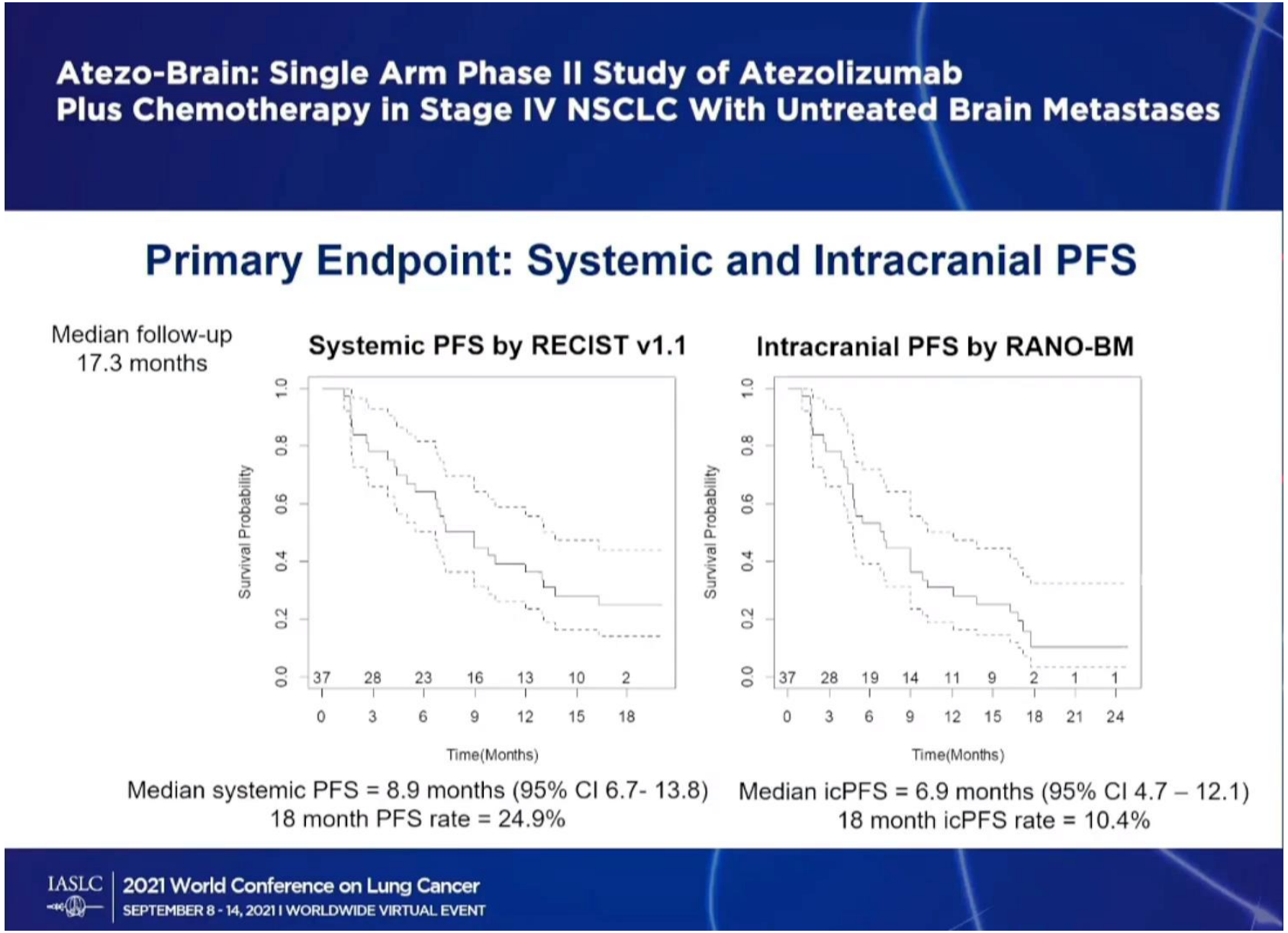
Estudio fase 2 ATEZO-BRAIN

- La PFS sistémica fue de 8,9 meses, i la PFS intracraneal de 6.9 meses.



Estudio fase 2 ATEZO-BRAIN

- La tasa de respuesta intracraneal fue del 40%, y una OS de 13.6 meses, con un 32% de tasa supervivencia a 2 años.

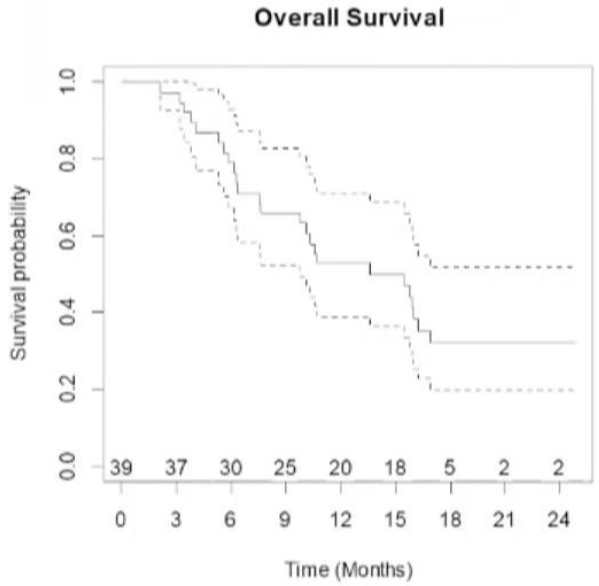
Atezo-Brain: Single Arm Phase II Study of Atezolizumab Plus Chemotherapy in Stage IV NSCLC With Untreated Brain Metastases

Secondary Endpoints: Response Rate and Overall Survival

	Best Intracranial Response (RANO-BM)	Best Systemic Response (RECIST v1.1)
CR	4 (10%)	0
PR	12 (30%)	19 (47.5%)
SD	19 (47.5%)	16 (40%)
PD	4 (10%)	3 (7.5%)
NE	1 (2.5%)	2 (5%)
ORR	**16 (40%)**	**19 (47.5%)**

Only 4 patients had discordance among systemic and CNS response:

- 2 with PD in body and SD in brain
- 2 with PD in brain and PR in body



Median OS = 13.6 months (95% CI 9.7 – NR)
2y OS rate = 32%

Principales conclusiones

- Estudio Poseidon: beneficio de añadir durvalumab + tremelimumab a la quimioterapia de 1ª línea en PFS y OS, un nuevo combo activo de quimio-inmunoterapia. Menor actividad en pacientes con gemcitabina.

- Sugemalimab (antiPDL1) y Toripalimab (anti-PD1) activos en 1ª línea al combinar-se con doblete de platino en PFS.

- Subanálisis del estudio 9LA muestra clara actividad de quimio + nivo + ipilumumab en pacientes con metástasis cerebrales tratadas y asintomáticas.

- Estudio atezobrain muestra que en pacientes con m1 cerebrales asintomáticas sin tratamiento local pueden beneficiarse de carbo-alimta-atezolizumab.