Lung Cancer UPDATES
ESMO HIGHLIGTHS
09-13 SEPTIEMBRE 2022
Paris, France

Iniciativa científica de:
GECP lung cancer research

Enfermedad avanzada sin diana

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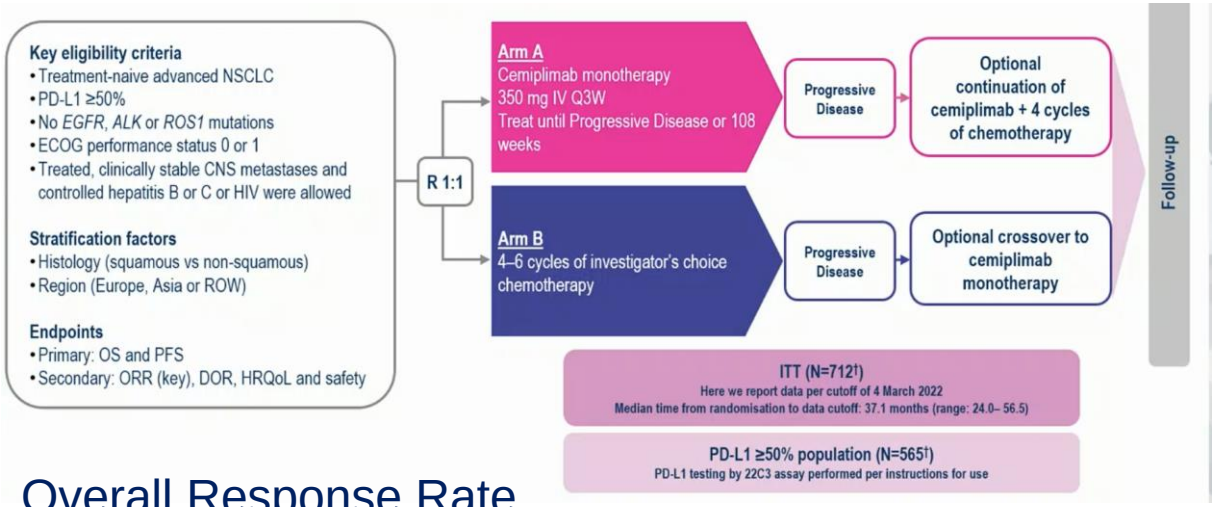
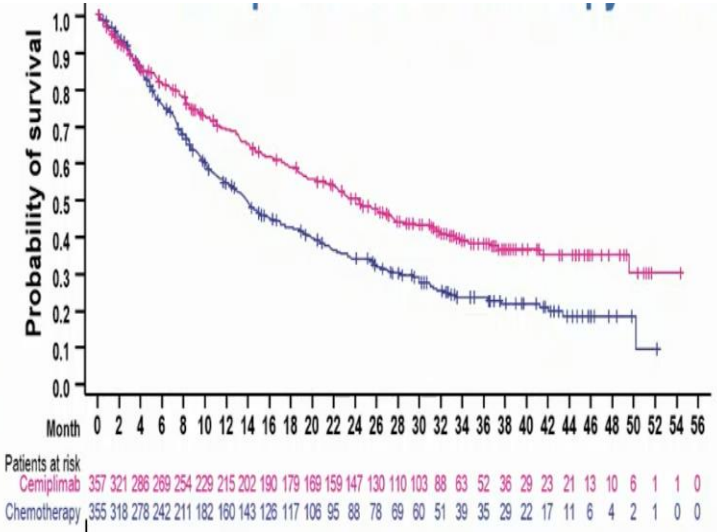
EMPOWER-Lung1 3 Years Survival and Continued Cemiplimab Beyond Progression plus Chemotherapy

Study Design



Progression Free Survival



ITT: 3-year outcomes	Patients, n	Median OS, months
Cemiplimab	357	23.4 (95% CI, 19.4, 27.4)
Chemotherapy	355	13.7 (95% CI, 11.2, 16.2)

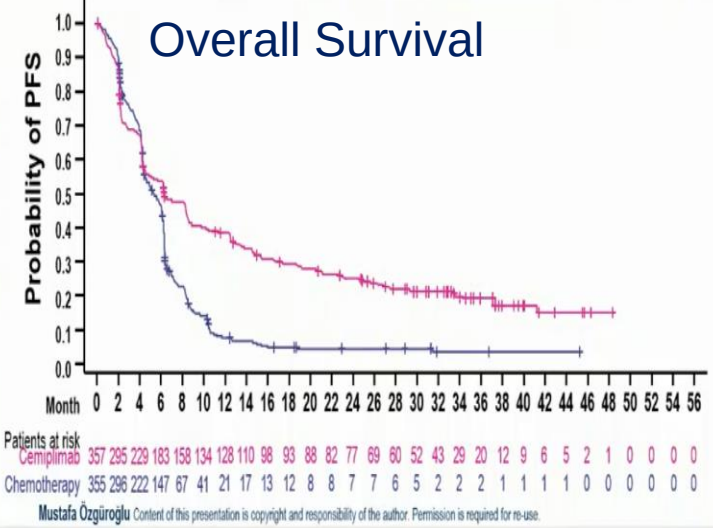
HR, 0.63 (95% CI, 0.52–0.77); *P*=0.0001

Overall Response Rate

	ITT		PD-L1 ≥50%	
	Cemiplimab (n=357)	Chemotherapy (n=355)	Cemiplimab (n=284)	Chemotherapy (n=281)
Objective Response Rate (ORR: CR+PR)	**151 (42.3)**	**76 (21.4)**	**132 (46.5)**	**59 (21.0)**
95 CI for ORR (n%)	(37.1, 41.8)	(17.3, 26.0)	(40.6, 52.5)	(16.4, 26.2)
Odds ratios (range), two-sided p-value	2.691 (1.936, 3.740) p <0.0001		3.264 (2.255, 4.724) p <0.0001	
Best Overall Tumor Response, n (%)				
Complete Response (CR)	29 (8.1)	7 (2.0)	23 (8.1)	6 (2.1)
Partial Response (PR)	122 (34.2)	69 (19.4)	109 (38.4)	53 (18.9)
Stable Disease (SD)	90 (25.2)	175 (49.3)	65 (22.9)	142 (50.5)
Non-CR/Non-PD	2 (0.6)	4 (1.1)	2 (0.7)	2 (0.7)
Progressive Disease (PD)	76 (21.3)	56 (15.8)	60 (21.1)	45 (16.0)
Not Evaluable (NE)	38 (10.6)	44 (12.4)	25 (8.8)	33 (11.7)
Median DOR, months (95% CI)	23.6 (18.6, 33.0)	5.9 (4.3, 6.3)	23.6 (16.8, 33.0)	5.9 (4.3, 6.5)

CI, confidence interval; ITT, intention-to-treat; PD-L1, programmed cell death-ligand 1; ORR, objective response rate; DOR, duration of response

Overall Survival



ITT: 3-year outcomes	Patients, n	Median PFS, months
Cemiplimab	357	6.3 (95% CI, 4.6, 8.3)
Chemotherapy	355	5.3 (95% CI, 4.3, 6.0)

HR, 0.56 (95% CI, 0.47, 0.67); *P*=0.0001

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival; PFS, progression free survival

Data cutoff date: 4 March 2022

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EMPOWER-Lung1 3 Years Survival and Continued Cemiplimab Beyond Progression plus Chemotherapy

Demographic Characteristics

n (%), unless stated otherwise	ITT Cemiplimab (n=357)	Beyond Progression Cemiplimab (N=64)
Age		
Median (Q1 : Q3)	63.0 (58.0 : 69.0)	62.5 (57.5 : 69.0)
≥65, n (%)	157 (44.0)	28 (43.8)
Sex		
Male	313 (87.7)	55 (85.9)
Female	44 (12.3)	9 (14.1)
Region of enrolment		
Europe	276 (77.3)	51 (79.7)
Asia	39 (10.9)	7 (10.9)
Rest of the world	42 (11.8)	6 (9.4)
ECOG performance status score		
0	96 (26.9)	20 (31.3)
1	261 (73.1)	44 (68.8)
Histology/Cytology, n (%)		
Squamous	160 (44.8)	37 (57.8)
Non-squamous	197 (55.2)	27 (42.2)
Cancer stage at screening n (%)		
Stage III	63 (17.6)	12 (18.7)
Stage IV	294 (82.4)	52 (81.3)

ECOG, Eastern Cooperative Oncology Group; ITT, intention-to-treat; Data cutoff date: Left column – March 4, 2022; Right column – March 1, 2020

Objective Response Rate

	Cemiplimab Beyond Progression N=64	
	Period 1	Period 2
Objective Response Rate (ORR: CR+PR), n (%)	**19 (29.7)**	**20 (31.3)**
95% CI for ORR (range %)	(18.9, 42.4)	(20.2, 44.1)
Best Overall Tumor Response, n (%)		
Complete Response (CR)	0	3 (4.7)
Partial Response (PR)	19 (29.7)	17 (26.6)
Stable Disease (SD)	28 (43.8)	35 (54.7)
Non-CR/Non-PD	0	0
Progressive Disease (PD)	13 (20.3)	9 (14.1)
Not Evaluable (NE)	4 (6.3)	0

CI, confidence interval

Data cutoff date: March 1, 2020 – Left Column; Oct 1, 2021 – Right column

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EMPOWER-Lung1 3 Years Survival and Continued Cemiplimab Beyond Progression plus Chemotherapy

Survival Continued Cemiplimab Beyond Progression plus Chemotherapy

	Cemiplimab Beyond Progression N=64	
OS	Period 1+2 Randomization to Death	Period 2 Day 1 of Continued Treatment to Death
Median (95% CI, months)	27.4 (23.0, 31.8)*	15.1 (11.3, 18.7)
Estimated Survival Probability, % (95% CI)		
6 months	100 (NE, NE)	91.9 (81.6, 96.5)
12 months	91.8 (81.4, 96.5)	56.8 (43.0, 68.5)
24 months	60.5 (46.6, 71.8)	26.2 (14.3, 39.8)
36 months	32.3 (20.1, 45.1)	NE (NE, NE)

*Includes the 15.1 months of survival beyond progression. CI, confidence interval; OS, overall survival; NE, non-evaluable

Data cutoff date: March 4, 2022

Continued cemiplimab with addition of chemotherapy beyond progression appears superior to historical data for chemotherapy in the 2nd line setting where median OS is 8.4 months (range: 5.6 - 11.2) (Bersanelli et al., Lung Cancer, 2020)

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Sintilimab plus anlotinib versus platinum-based chemotherapy as first-line therapy in metastatic NSCLC (SUNRISE)

Study Design

An Open Label, Multi-center, Randomized, Phase 2 Study

Key Eligibility Criteria

- Metastatic NSCLC* (Stage IV)
- EGFR/ALK/ROS1 negative
- No prior systemic treatment for metastatic disease
- ECOG PS 0 or 1
- 18 to 75 years

R 1:1

N=98

- Sintilimab (Sint) 200mg iv D1 + Anlotinib (Anlo) 12mg PO D1-14 Q3W
- Platinum-Doublet Chemotherapy Q3W, 4-6 Cycle† pemetrexed maintenance (NSQ) → Crossover permitted after PD → Sintilimab 200mg iv D1 Q3W

Treatment until PD, intolerable toxicity, patient withdrawal, or death

Stratification Factors
- Histology (Squamous vs non-Squamous)
- PD-L1 expression(≥1% vs <1%) §

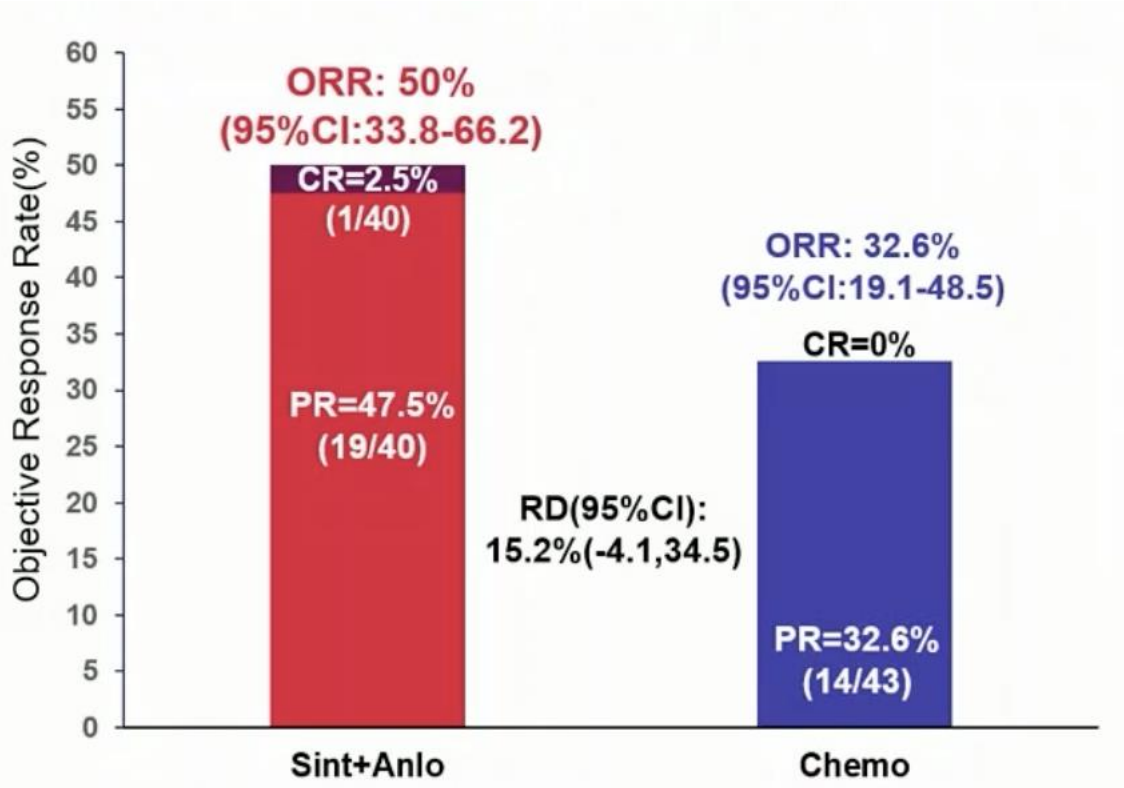
Endpoints
- Primary: ORR
- Secondary: DCR、PFS、OS、Safety

* Patients with asymptomatic brain metastases are eligible
† NSQ: pemetrexed + carboplatin; SQ: gemcitabine + carboplatin;
§ Assessed using the PD-L1 IHC 22C3 pharmDx assay

Statistical Consideration

- A sample size of 87 patients was required under the assumption of an ORR improved from 25% (Platinum-Doublet Chemotherapy) to 50% (Sintilimab+Anlotinib) with a power of 80% and one-sided α=0.05. With an expected drop-out rate of 10%, a total of 98 patients to be enrolled for 49 participants in each arm.
- A preliminary interim analysis was conducted when 89 participants were enrolled. (Data cut off: Jul. 15th, 2022)

Overall Response Rate



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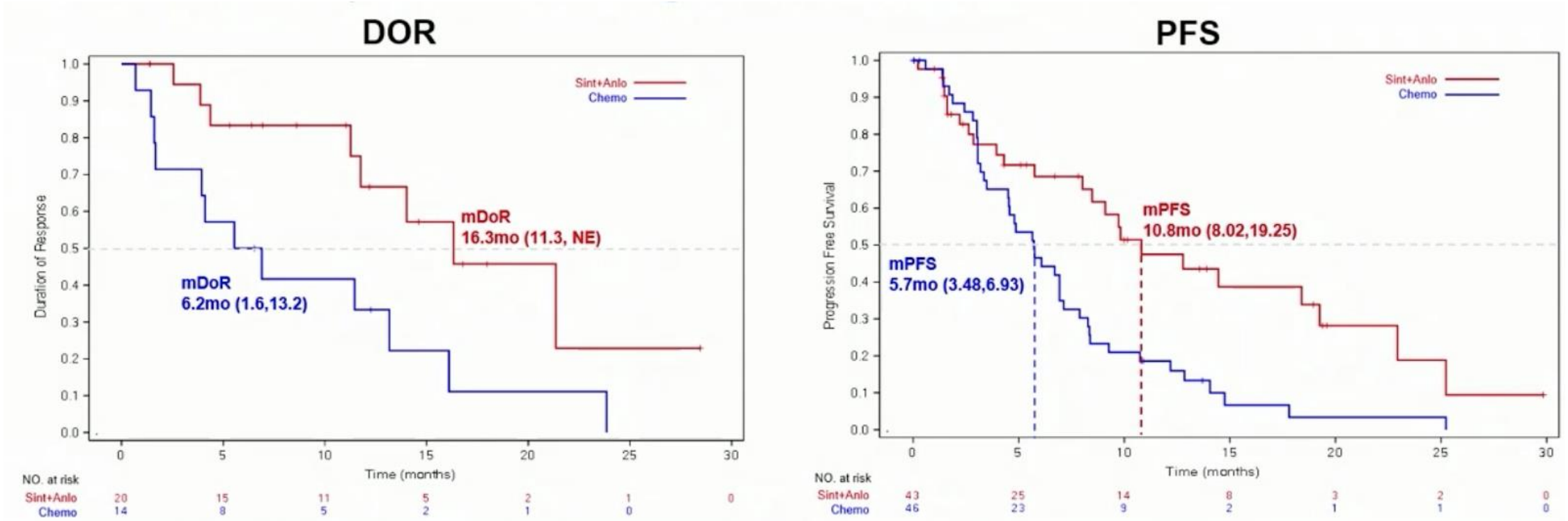
Sintilimab plus anlotinib versus platinum-based chemotherapy as first-line therapy in metastatic NSCLC (SUNRISE)



	Patients	Events	median DOR (95%CI)
Sint+Anlo	20	8 (40.0)	16.3 (11.3, NE)
Chemo	14	12 (85.7)	6.2 (1.6,13.2)

	Patients	Events	HR (95%CI)	P
Sint+Anlo	43	24 (55.8)	0.4 (0.25,0.74)	0.002
Chemo	46	41 (89.1)		

HR was calculated with stratified Cox model, and was stratified by Histology(Squamous vs non-Squamous) PD-L1 expression(≥1% vs <1%)
P value was calculated with stratified log rank test); Data cutoff : Jul. 15th 2022 ; Median follow-up 13.1 months

PARIS ESMO congress

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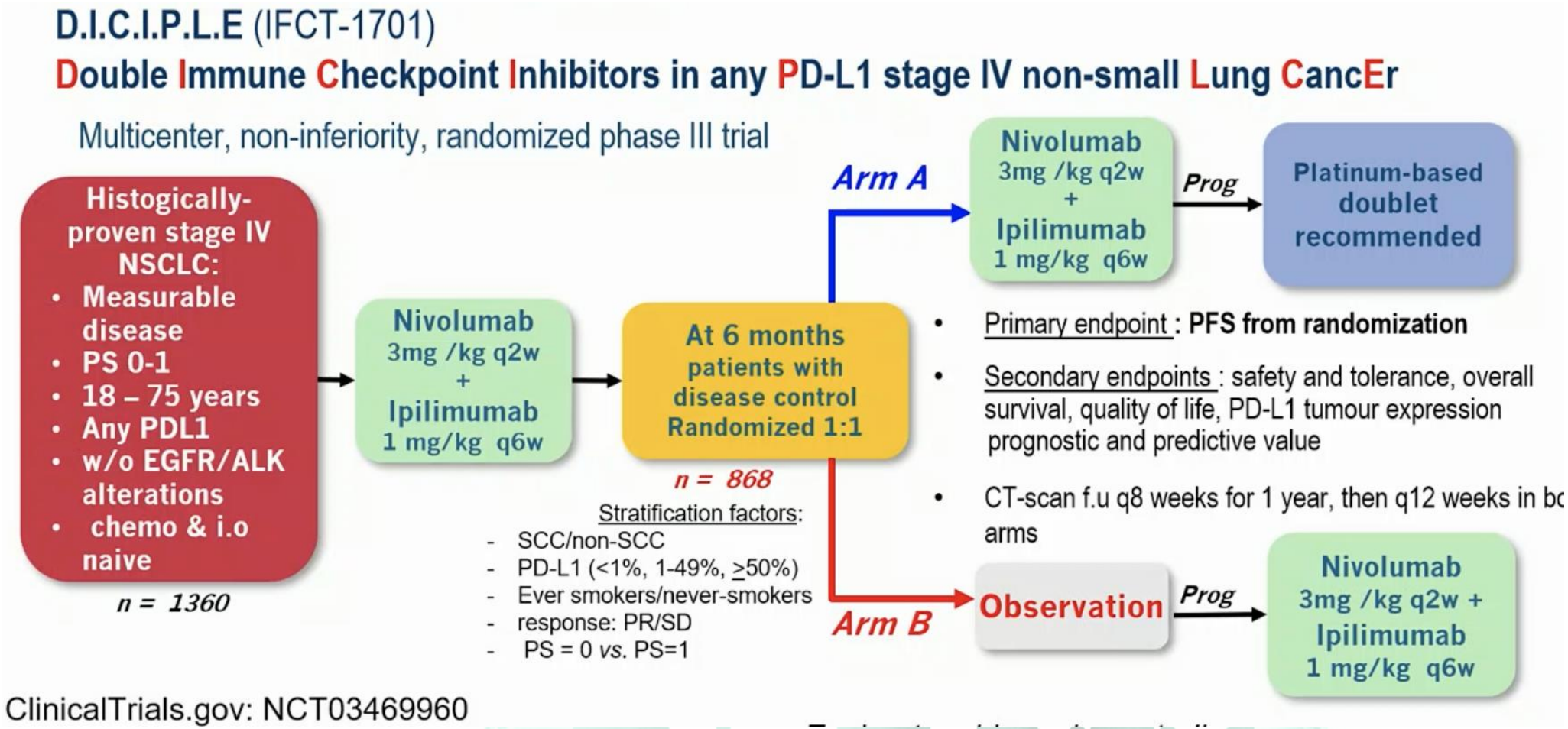
Nivolumab plus Ipilimumab 6 month Treatment Versus Continuation in Patients with Advanced NSCLC (DICIPLE)

Study Design



ClinicalTrials.gov: NCT03469960

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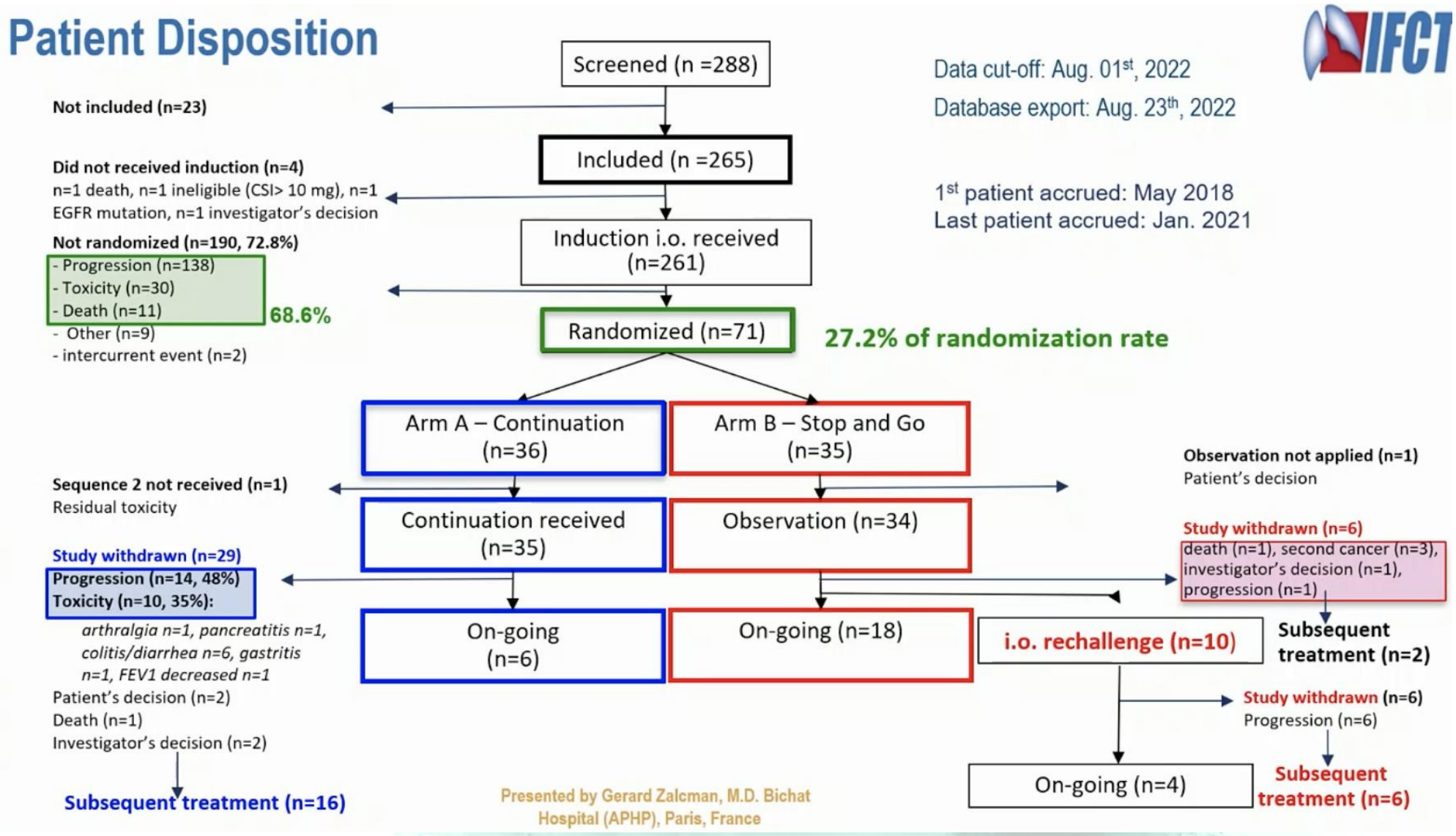
Nivolumab plus Ipilimumab 6 month Treatment Versus Continuation in Patients with Advanced NSCLC (DICIPLE)



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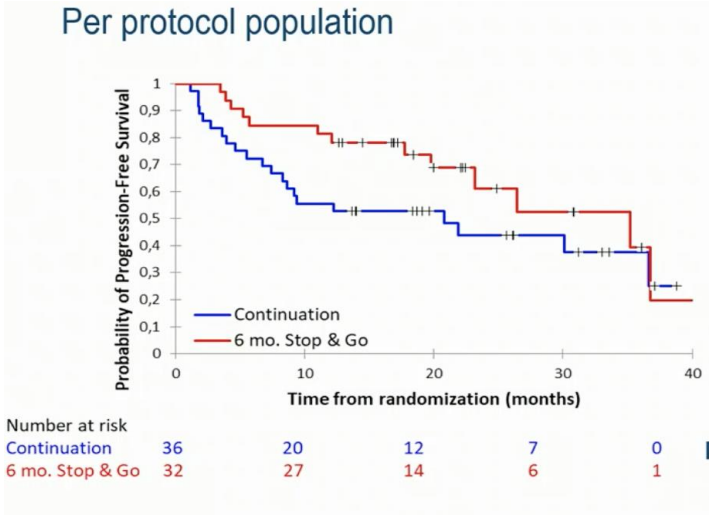
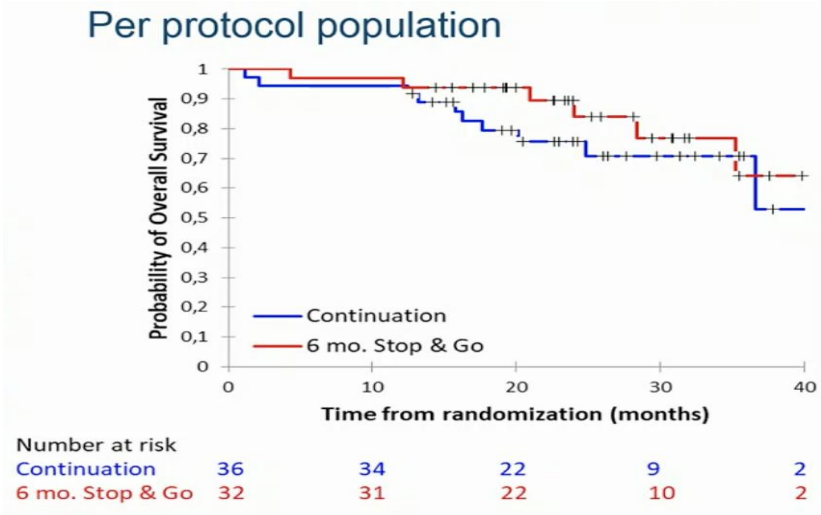
Nivolumab plus Ipilimumab 6 month Treatment Versus Continuation in Patients with Advanced NSCLC (DICIPLE)

Progression Free Survival



	Arm A Continuation (N= 36)	Arm B Stop & Go (N = 32)
Event : N (%)	21 (58.3)	13 (40.6)
Median PFS: months [95% CI]	**20.8** [7.4-36.7]	**35.2** [19.8-NR]
6-m PFS: % [95% CI]	72.2 [54.5-84.0]	84.4 [66.5-93.2]
12-m PFS: % [95% CI]	**55.6 [38.0-69.9]**	**81.2 [62.9-91.1]**
p=0.12		

Overall Survival



	Arm A Continuation (N= 36)	Arm B Stop & Go (N = 32)
Event : N (%)	10 (27.8)	6 (18.7)
Median OS: months [95% CI]	NR [36.7-NR]	NR [35.2-NR]
12-m OS: % [95% CI]	94.4 [79.6-98.6]	96.9 [79.8-99.5]
18-m OS: % [95% CI]	79.3 [61.3-89.6]	93.7 [77.2-98.4]
p=0.33		

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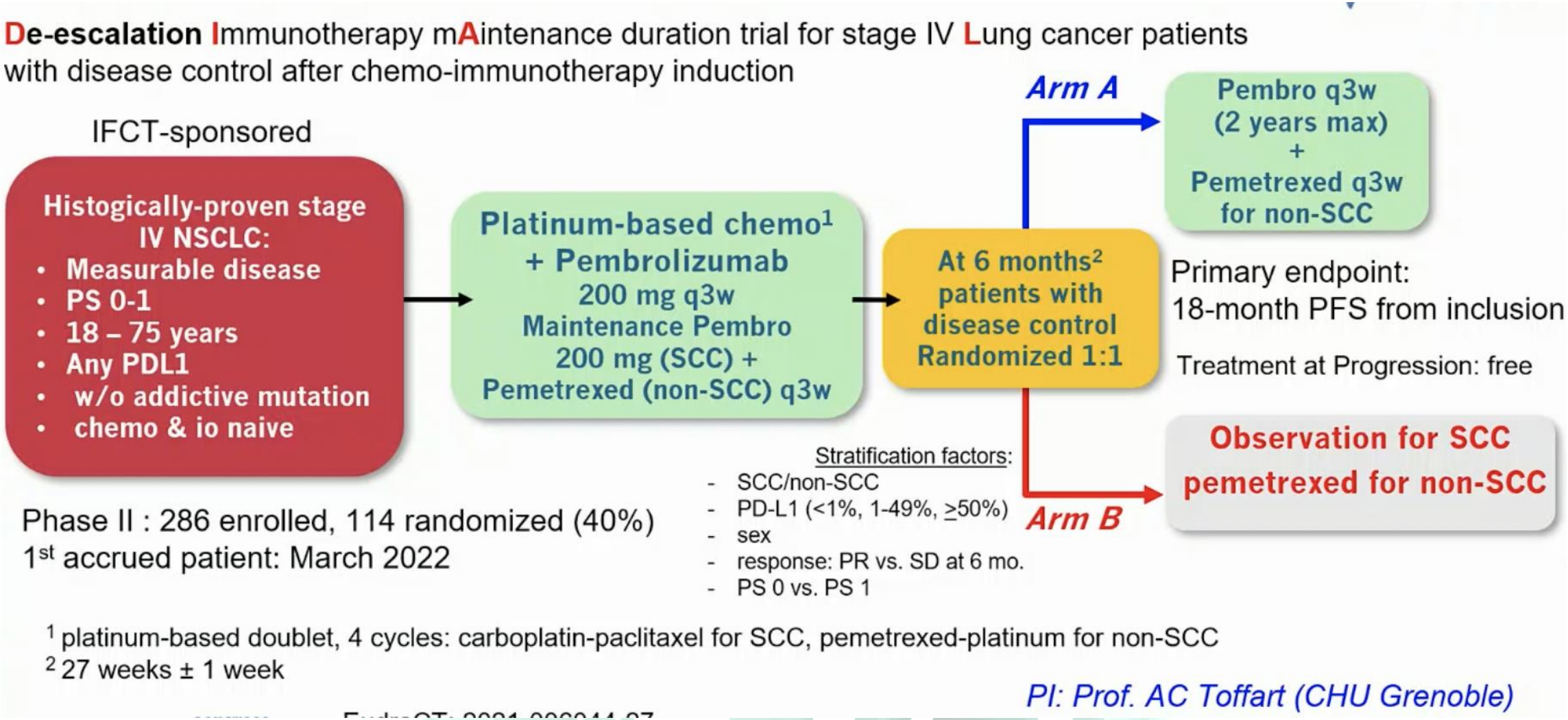
Nivolumab plus Ipilimumab 6 month Treatment Versus Continuation in Patients with Advanced NSCLC (DICIPLE)

Adverse Events

	Arm A Continuation (N=35)				Arm B Stop and Go (N=34)			
	Any Grade	Grade 3	Grade 4	Grade 5	Any Grade	Grade 3	Grade 4	Grade 5
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Any adverse event	32 (91.4%)	15 (42.9%)	4 (11.4%)	0 (0%)	23 (67.6%)	6 (17.6%)	0 (0%)	1 (2.9%)
Immune-related adverse event (irAE)	24 (68.6%)	**10 (28.6%)**	0 (0%)	0 (0%)	17 (50%)	**1 (2.9%)**	0 (0%)	0 (0%)
Serious Adverse Event (SAE)	14 (40%)	**9 (25.7%)**	1 (2.9%)	0 (0%)	7 (20.6%)	**4 (11.8%)**	0 (0%)	1 (2.9%)

Enfermedad avanzada sin diana

Nivolumab plus Ipilimumab 6 month Treatment Versus Continuation in Patients with Advanced NSCLC (DICIPLE)



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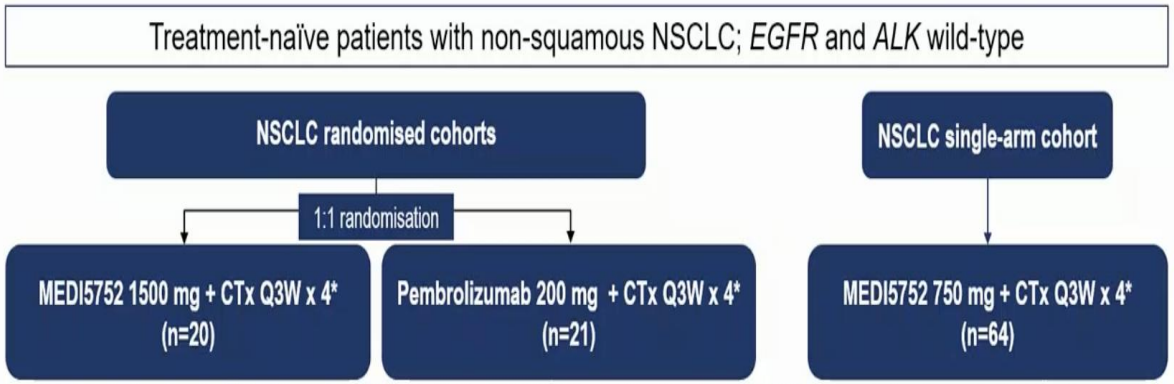
MEDI5752 or pembrolizumab (P) plus carboplatin/pemetrexed (CP) in treatment-naïve (1L) non-small cell lung cancer (NSCLC): A phase Ib/II trial

Study Design

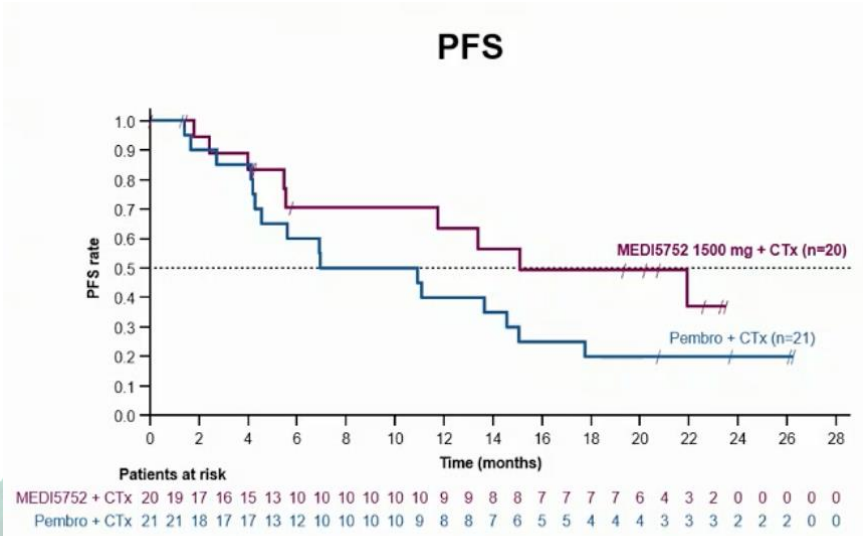


*MEDI5752 or pembrolizumab + carboplatin AUC 5 + pemetrexed 500 mg/m^2 as initial treatment IV Q3W x 4 cycles, followed by maintenance with MEDI5752 or pembrolizumab + pemetrexed IV Q3W until unacceptable toxicity, disease progression, or withdrawal of consent.

- As of 12 July 2022, 105 patients were enrolled in two 1L non-squamous NSCLC dose expansion cohorts
- Results from 91 patients are presented:
  - 41 patients in the randomised cohorts (MEDI5752 1500 mg + CTx, n=20; pembrolizumab 200 mg + CTx, n=21)
  - First 50 patients in the single-arm cohort (MEDI5752 750 mg + CTx) who had at least 8 weeks of follow-up

Efficacy Data MEDI5752 1500 mg

1L Non-squamous NSCLC	Randomised cohort (N=41)	
	MEDI5752 1500 mg + CTx (n=20)	Pembrolizumab + CTx (n=21)
Median follow-up, months (range)	22.8 (0.8–26.9)	14.5 (1.6–27.9)
ORR, n (%)	10 (50.0)	10 (47.6)
Disease control rate, n (%)	17 (85.0)	20 (95.2)
Median DOR, months (95% CI)	20.5 (4.1–NE)	9.9 (2.8–NE)
Median PFS, months	15.1	8.9
Median OS, months	NR	16.5
ORR, PD-L1 <1%, n/N (%) (95% CI)	5/9 (55.6) (21.2–86.3)	3/10 (30.0) (6.7–65.2)
Median PFS, PD-L1 <1%, months	13.4	9



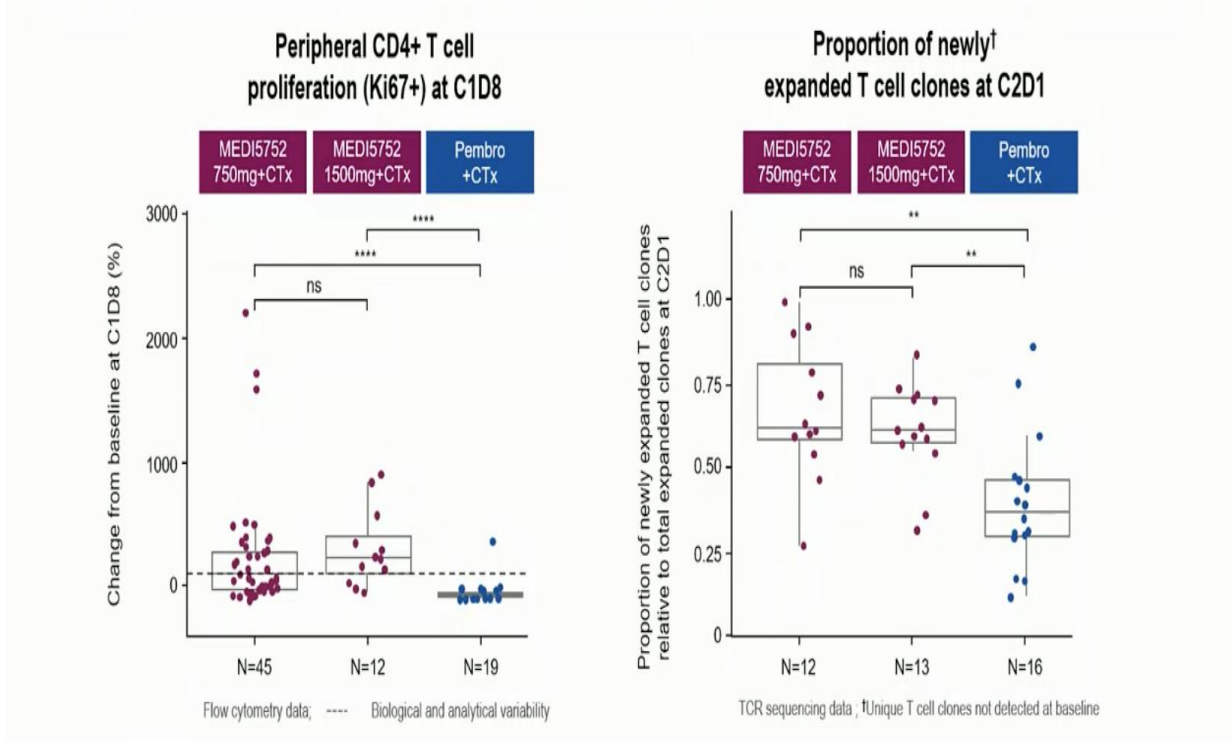
Enfermedad avanzada sin diana

MEDI5752 or pembrolizumab (P) plus carboplatin/pemetrexed (CP) in treatment-naïve (1L) non-small cell lung cancer (NSCLC): A phase Ib/II trial

Safety Profile

	Randomised cohort (N=41)				Single-arm cohort	
	MEDI5752 1500 mg + CTx (n=20)		Pembrolizumab + CTx (n=21)		MEDI5752 750 mg + CTx (n=50)	
Median duration of exposure to MEDI5752, cycles (range)	4.5 (1–32)		NA		4.0 (1–12)	
Any TEAE, n (%)	20 (100.0)		21 (100.0)		49 (98.0)	
TEAE leading to treatment discontinuation	14 (70.0)		6 (28.6)		10 (20.0)	
Any TRAE*, n (%)	20 (100.0)		21 (100.0)		46 (92.0)	
Grade 3/4 TRAE	16 (80.0)		13 (61.9)		25 (50.0)	
TRAE leading to death	0		1 (4.8)†		1 (2.0)‡	
Select AEs (preferred term), %	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**	**All Grade**	**Grade 3/4**
Rash	55	10	9.5	0	24	2
ALT increase	55	30	14.3	0	10	2
AST increase	55	20	9.5	0	8	2
Hyperthyroidism	40	0	0	0	12	0
Pneumonitis	20	5	9.5	4.8	0	0
Diarrhea	10	5	4.8	0	4	2

T cell Proliferation and Clonal Expansion



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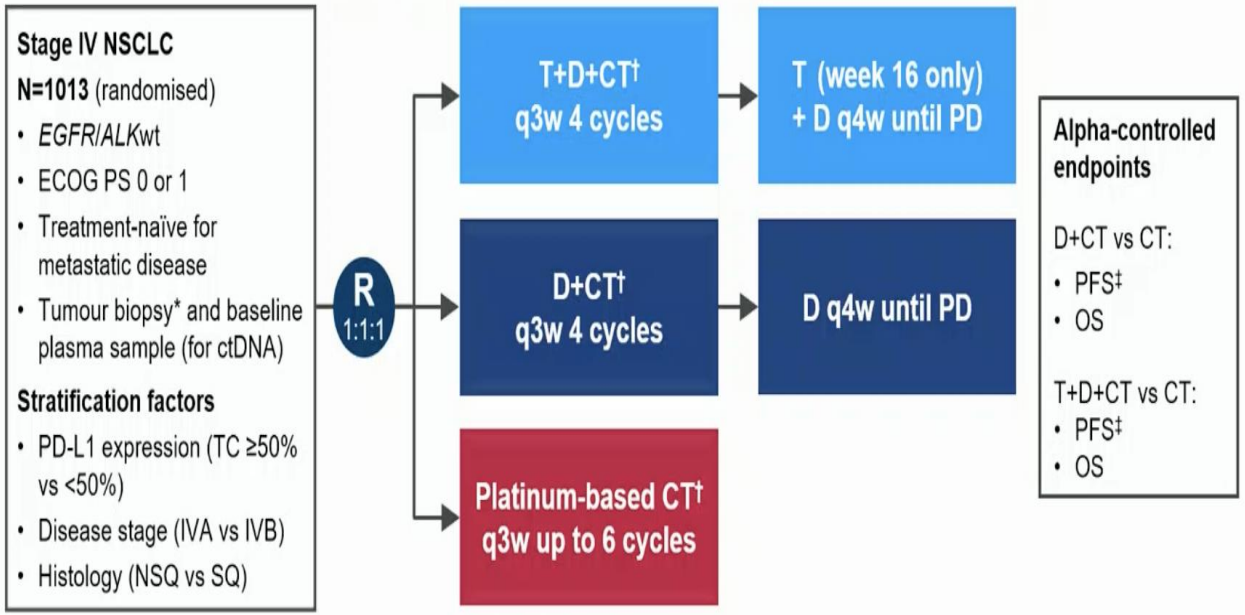
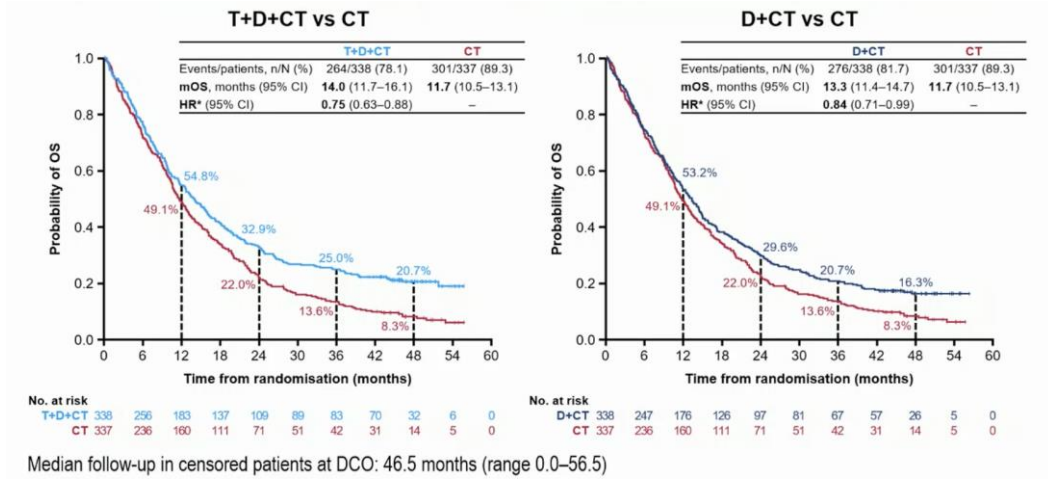
Durvalumab (D) ± tremelimumab (T) + chemotherapy (CT) in 1L metastatic (m) NSCLC: Overall survival (OS) update from POSEIDON after median follow-up (mFU) of approximately 4 years (y)

Study Design



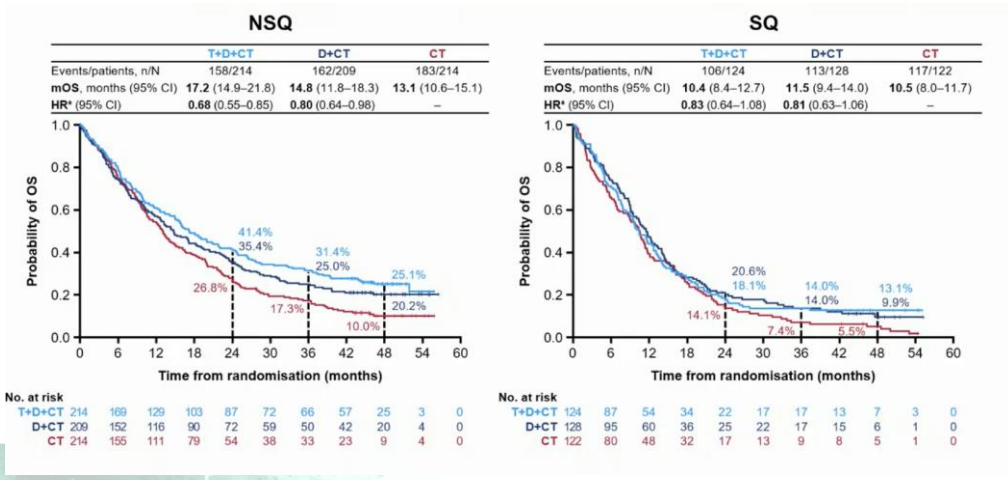
- **Durvalumab** 1500mg ± **limited-course tremelimumab** 75mg + **CT** q3w for **4 cycles**
  - One additional dose of tremelimumab post-CT (week 16; 5th dose)
- Followed by **durvalumab q4w maintenance** until PD, and optional pemetrexed q4w§

Overall Survival



Median follow-up in censored patients at DCO: 46.5 months (range 0.0–56.5)

Overall Survival by histology



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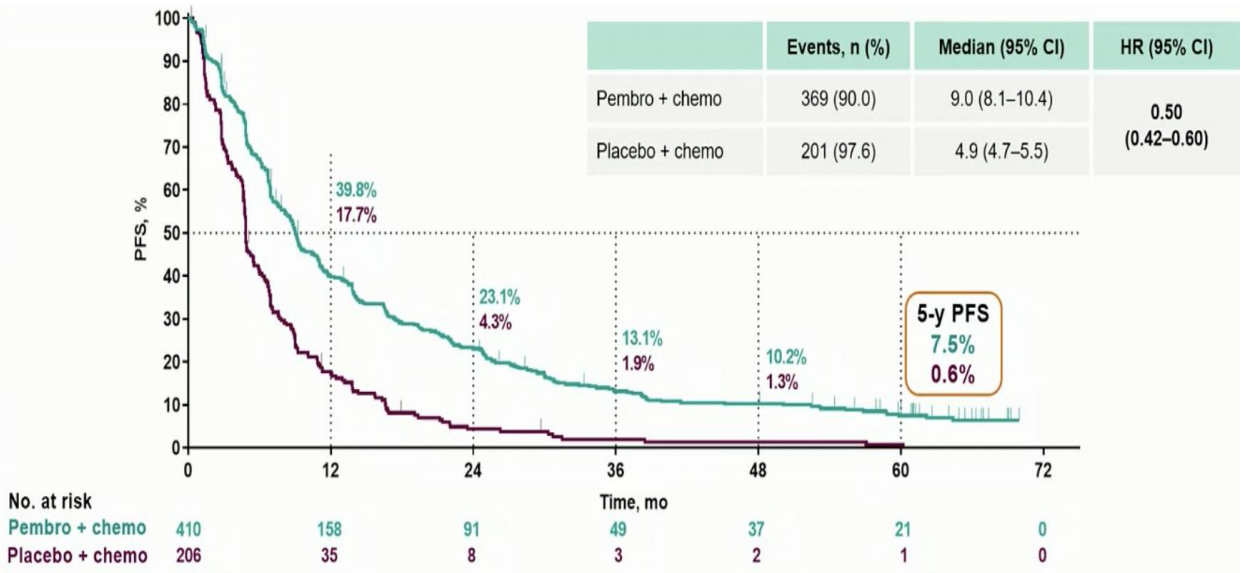
KEYNOTE-189 5-year update

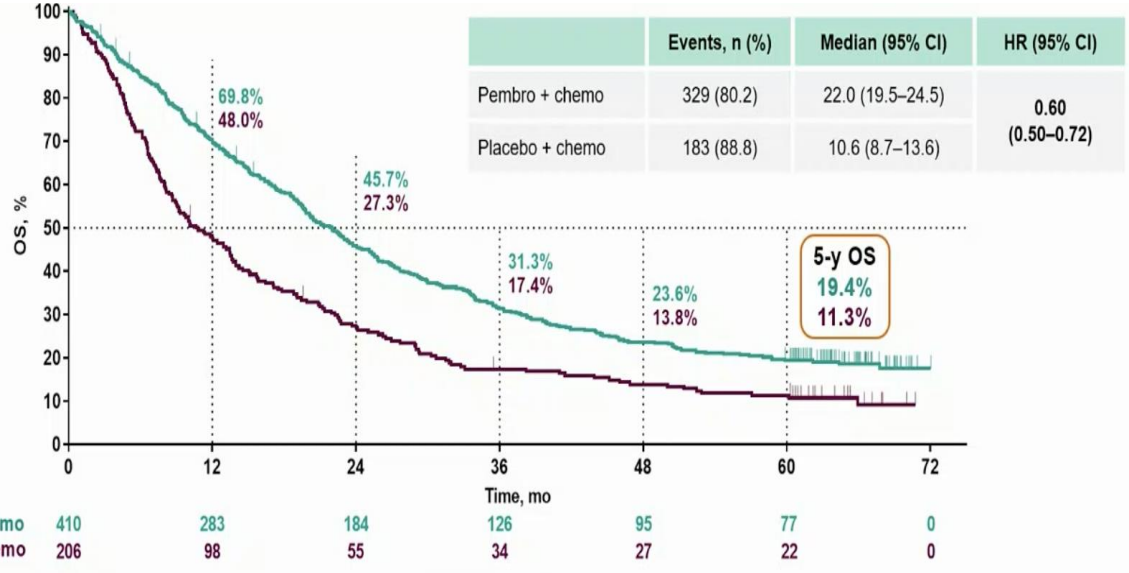
5 y Progression Free Survival



	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	369 (90.0)	9.0 (8.1–10.4)	0.50 (0.42–0.60)
Placebo + chemo	201 (97.6)	4.9 (4.7–5.5)	

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
PFS HR (95% CI)	0.35 (0.25–0.49)		0.57 (0.41–0.80)		0.67 (0.49–0.92)	
5-y PFS rate,[b] %	12.8	0	6.5	1.9	2.4	0

5 y Overall Survival



	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	329 (80.2)	22.0 (19.5–24.5)	0.60 (0.50–0.72)
Placebo + chemo	183 (88.8)	10.6 (8.7–13.6)	

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
OS HR (95% CI)	0.68 (0.49–0.96)		0.65 (0.46–0.90)		0.55 (0.39–0.76)	
5-y OS rate,[a] %	29.6	21.4	19.8	7.7	9.6	5.3

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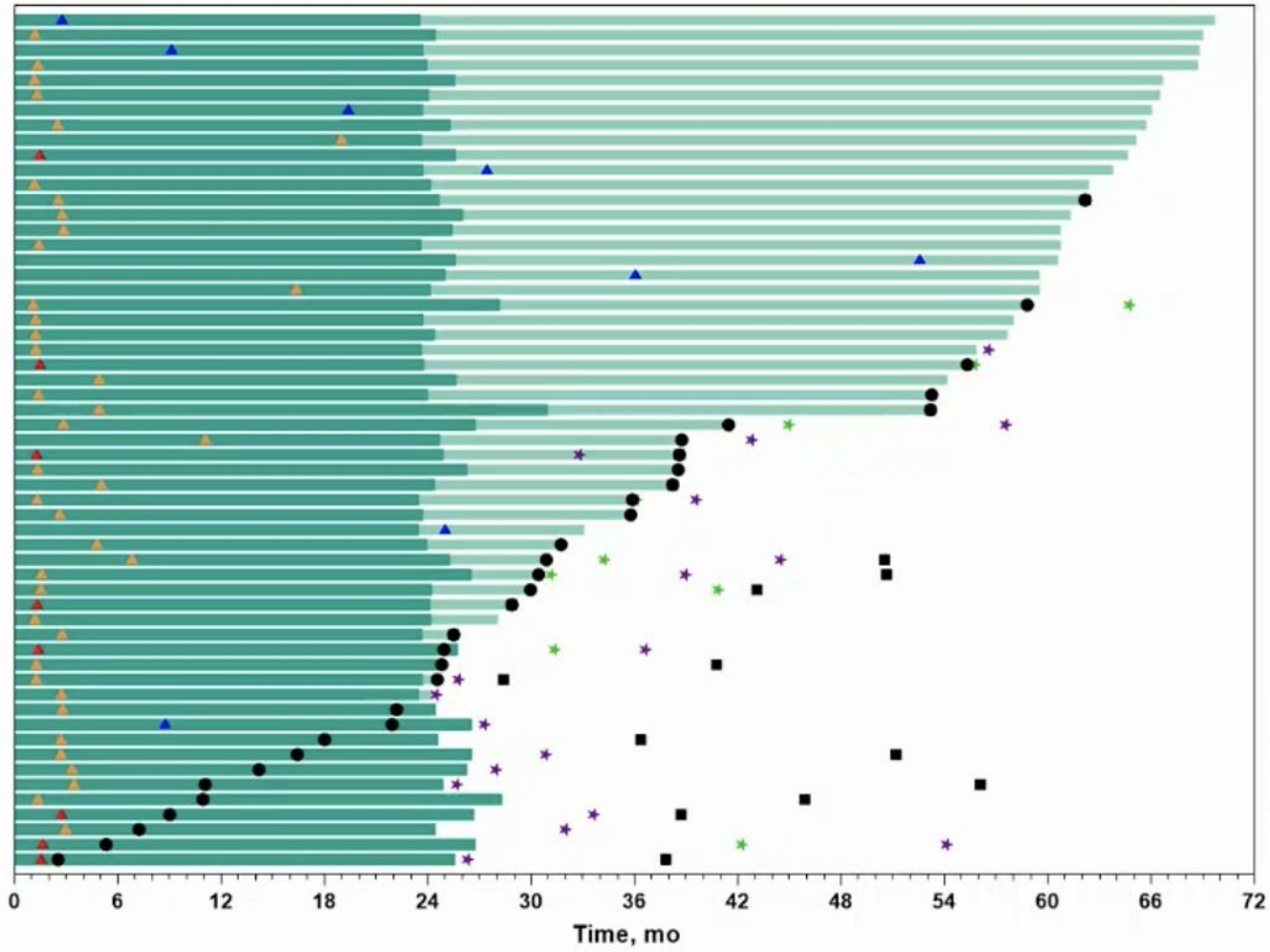
KEYNOTE-189 5-year update

Update Patients Completed 35 cicles



	n = 57
ORR (95% CI),[a] %	86.0 (74.2–93.7)
Best overall response, n (%)	
CR	8 (14.0)
PR	41 (71.9)
Median DOR (range),[b] mo	57.7 (4.2 to 68.3+)
3-y OS rate after completing 35 cycles[c]	71.9%
Alive without PD or subsequent therapy, n (%)	23 (40.4)

r RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. [c]Approximately 5 years after randomization. Data cutoff date: March 8, 2022.

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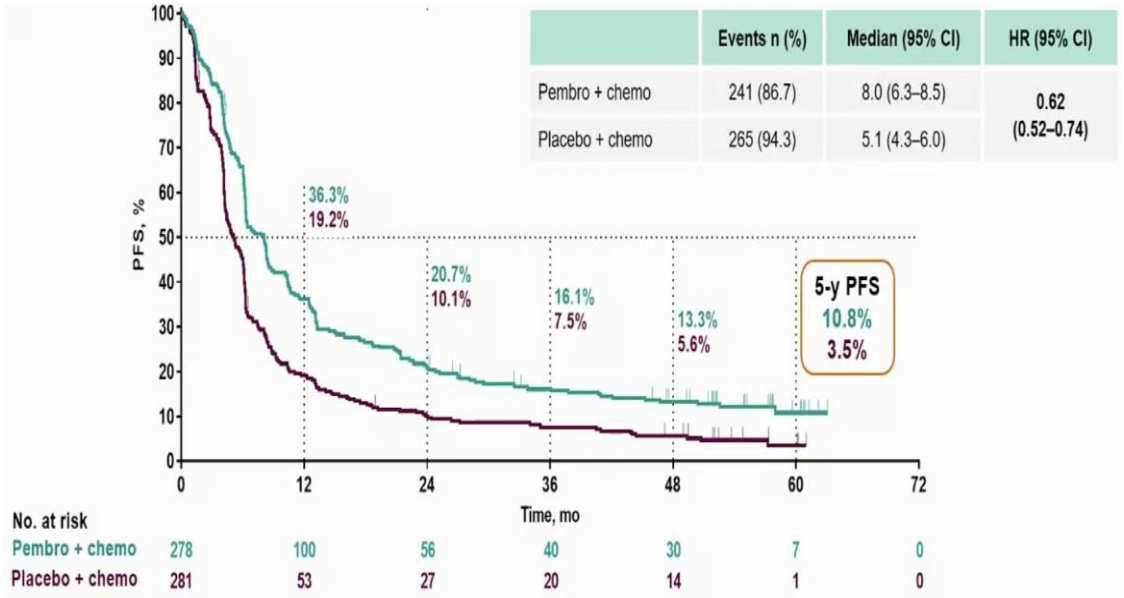
KEYNOTE-407 5-year update

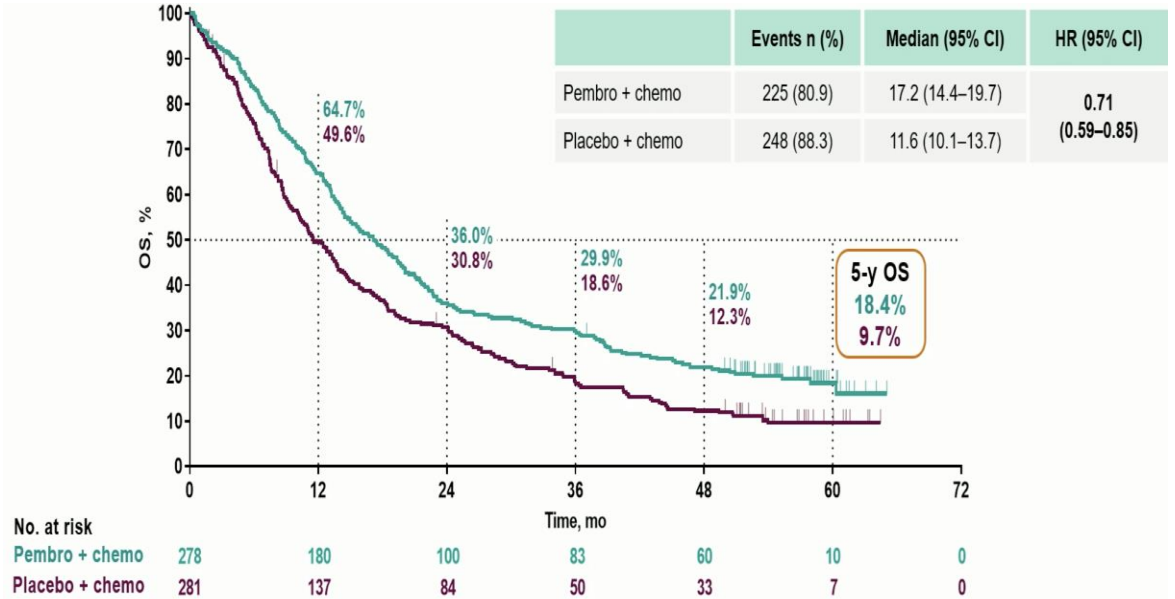
5 y Progression Free Survival



	Events n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	241 (86.7)	8.0 (6.3–8.5)	0.62 (0.52–0.74)
Placebo + chemo	265 (94.3)	5.1 (4.3–6.0)	

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
PFS HR (95% CI)	0.48 (0.33–0.69)		0.60 (0.45–0.81)		0.70 (0.52–0.95)	
5-y PFS rate[b], %	15.0	NR	11.8	NR	7.1	6.7

5 y Overall Survival



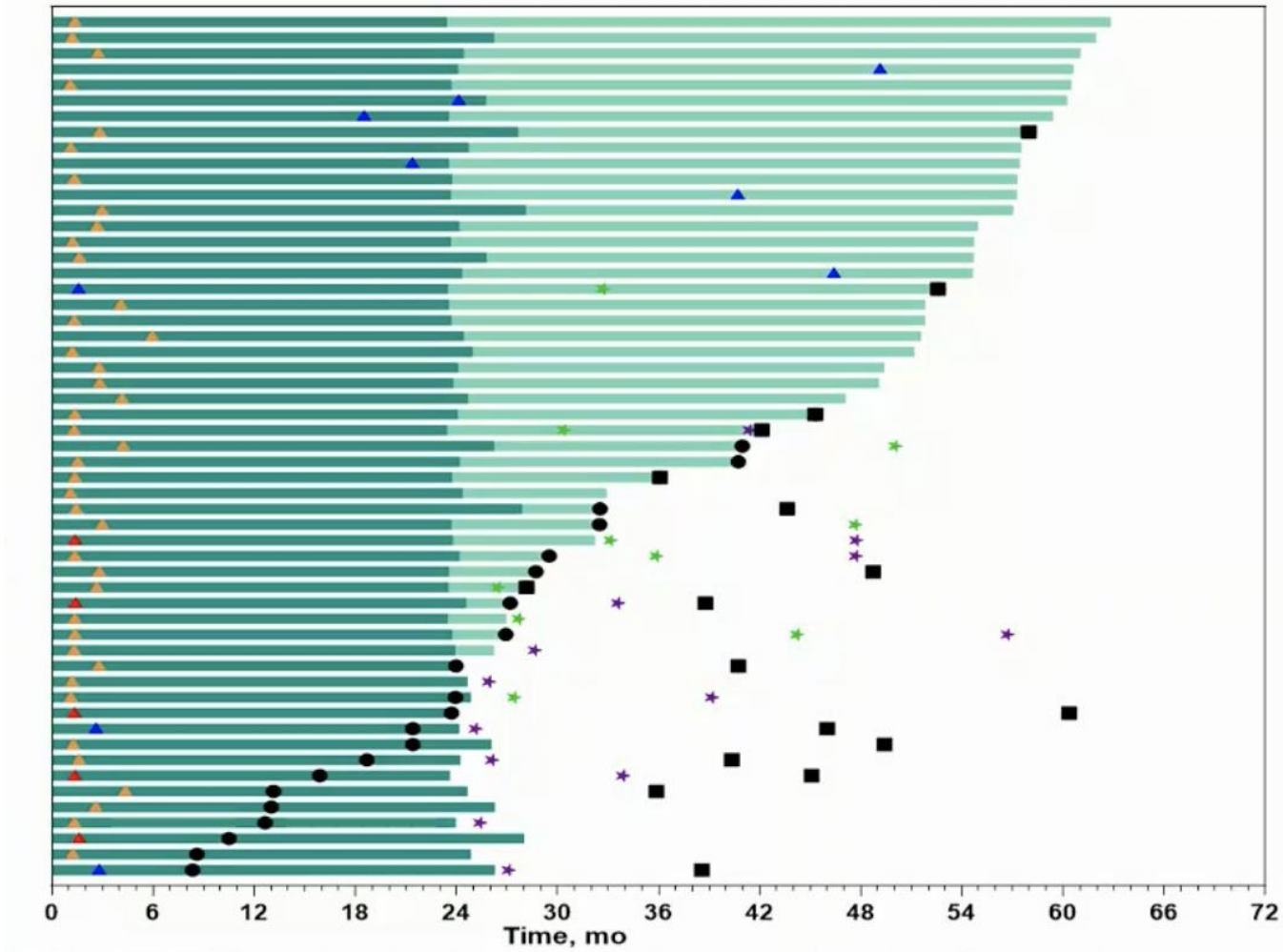
	Events n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	225 (80.9)	17.2 (14.4–19.7)	0.71 (0.59–0.85)
Placebo + chemo	248 (88.3)	11.6 (10.1–13.7)	

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
OS HR (95% CI)	0.68 (0.47–0.97)		0.61 (0.45–0.83)		0.83 (0.61–1.13)	
5-y OS rate,[a] %	23.3	8.3	20.6	7.6	10.7	13.1

Enfermedad avanzada sin diana

KEYNOTE-407 5-year update

Update Patients Completed 35 cicles



	n = 55
ORR (95% CI),[a] %	90.9 (80.0–97.0)
Best overall response, n (%)	
CR	9 (16.4)
PR	41 (74.5)
Median DOR (range),[b] mo	NR (7.1 to 61.5+)
3-y OS rate after completing 35 cycles[c]	69.5%
Alive without PD or subsequent therapy, n (%)	24 (43.6)

[a]Per RECIST v1.1 by BICR. [b]Kaplan-Meier estimate. [c]Approximately 5 years after randomization. Data cutoff date: February 23, 2022.

Enfermedad avanzada sin diana

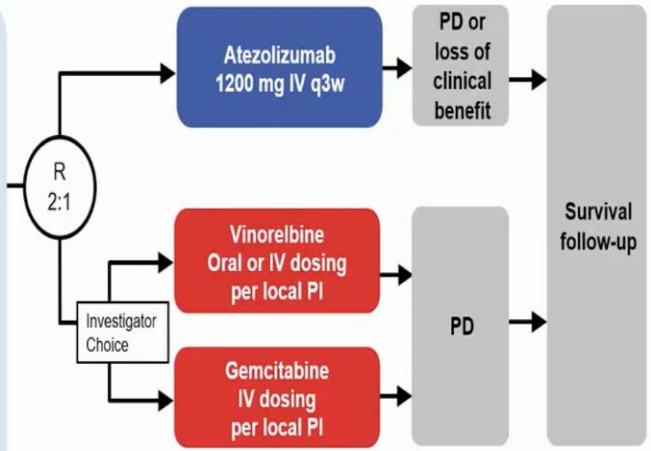
IPSOS: Results from a phase III study of first-line (1L) atezolizumab (atezo) vs single-agent chemotherapy (chemo) in patients (pts) with NSCLC not eligible for a platinum-containing regimen

Study design

Treatment-naive stage IIIB[a]/IV (AJCC 7th edition) NSCLC

- Squamous or non-squamous histology
- Platinum ineligible because of:
  - ECOG PS 2 or 3
  - ECOG PS 0 or 1 permitted if ≥70 years of age with substantial comorbidities or other contraindictions to platinum chemotherapy
- *EGFR*+ (L858R or exon 19 deletion) or *ALK*+ excluded
- Patients with treated asymptomatic brain metastases permitted

n=453



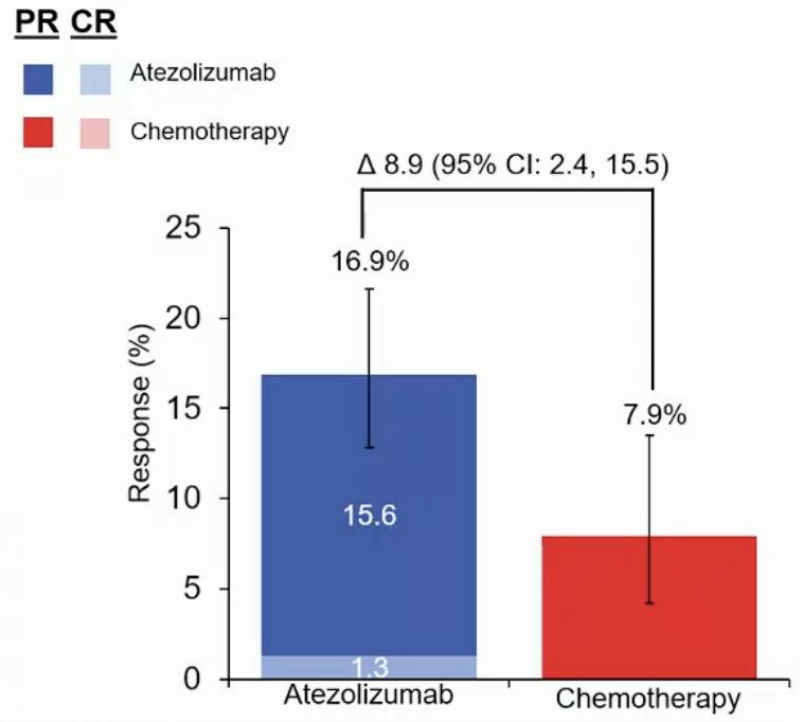
Stratification factors:
- Histology (squamous or non-squamous)
- PD-L1 expression level by SP142 IHC assay (TC3 or IC3 vs TC0/1/2 or IC0/1/2[b] vs unknown)
- Brain metastases (yes/no)

Primary endpoint:
- OS

Secondary endpoints:
- OS rates at 6, 12, 18 and 24 months
- PFS
- Objective response rate
- Duration of response
- OS and PFS in PD-L1 positive subgroup[c]

Other endpoints:
- PROs
- Safety
- Exploratory biomarker analyses

Overall Response Rate

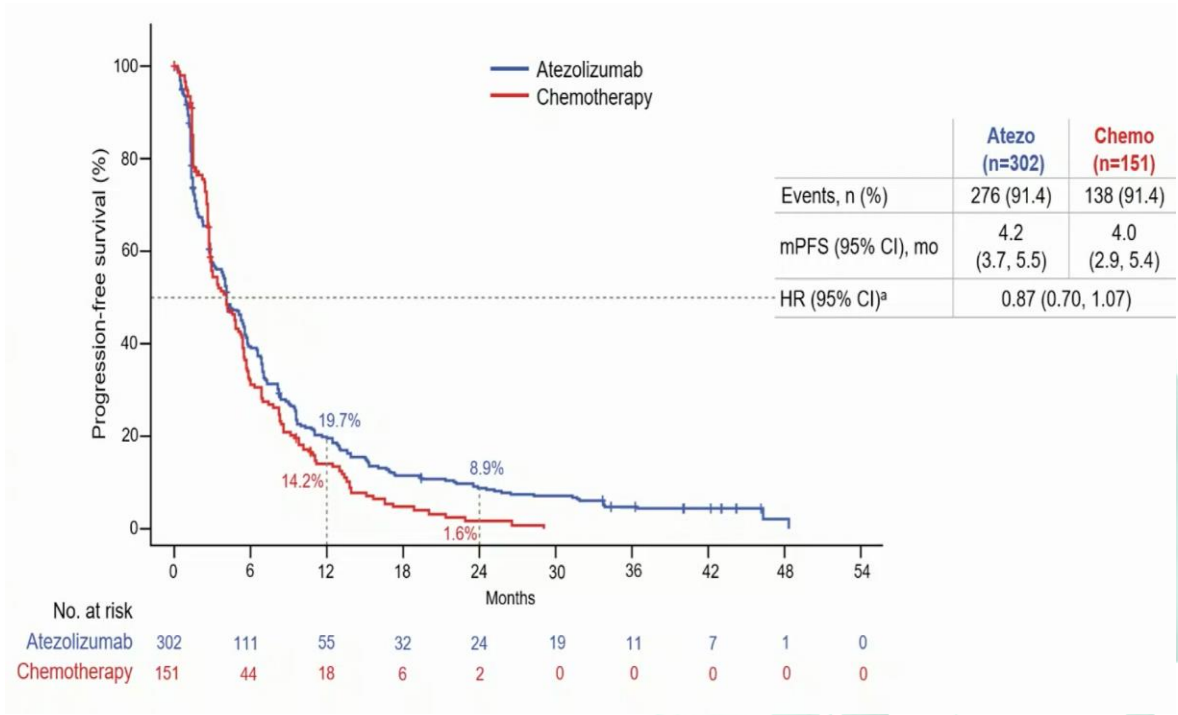


	Atezolizumab	Chemotherapy
Median DOR, months (95% CI)	14.0 (8.1, 20.3)	7.8 (4.8, 9.7)

Enfermedad avanzada sin diana

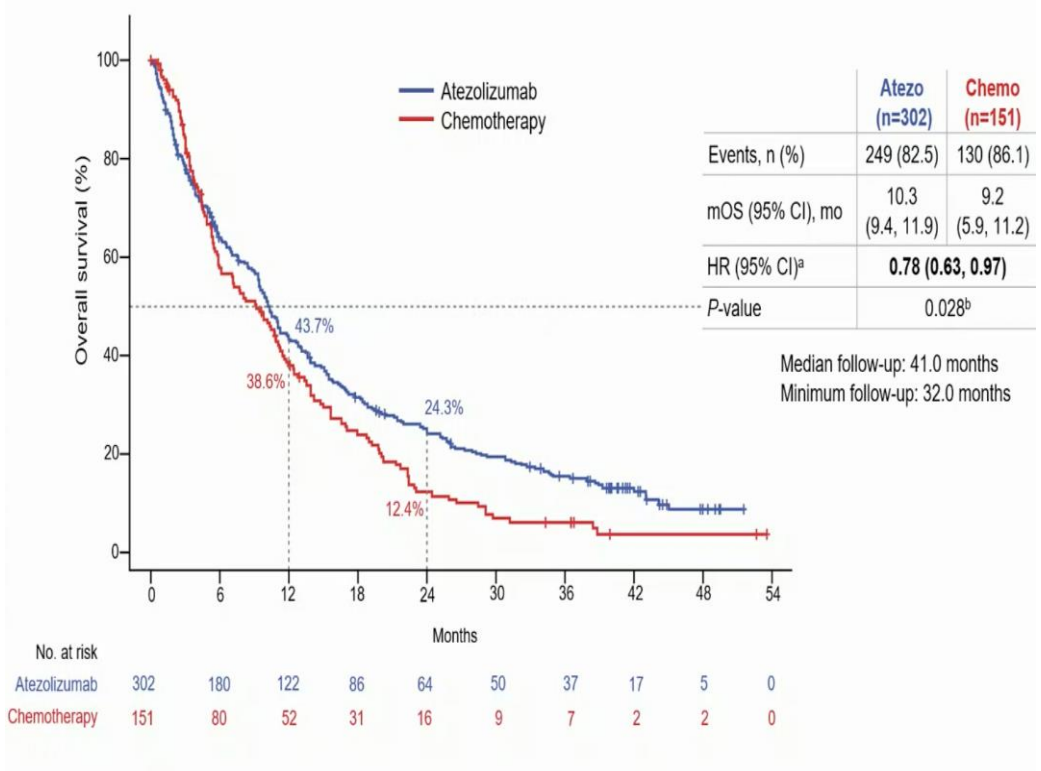
IPSOS: Results from a phase III study of first-line (1L) atezolizumab (atezo) vs single-agent chemotherapy (chemo) in patients (pts) with NSCLC not eligible for a platinum-containing regimen

Progression Free Survival



	Atezo (n=302)	Chemo (n=151)
Events, n (%)	276 (91.4)	138 (91.4)
mPFS (95% CI), mo	4.2 (3.7, 5.5)	4.0 (2.9, 5.4)
HR (95% CI)[a]	0.87 (0.70, 1.07)	

Overall Survival



	Atezo (n=302)	Chemo (n=151)
Events, n (%)	249 (82.5)	130 (86.1)
mOS (95% CI), mo	10.3 (9.4, 11.9)	9.2 (5.9, 11.2)
HR (95% CI)[a]	**0.78 (0.63, 0.97)**	
P-value	0.028[b]	

Median follow-up: 41.0 months
Minimum follow-up: 32.0 months

Enfermedad avanzada sin diana

Conclusiones

- Cemiplimab en pacientes con CPCNP con enfermedad avanzada y PD-L1 >50% demuestra beneficio a 3 anos de seguimiento.
- Mantener la inmunoterapia y añadir tratamiento con quimioterapia es una opción a al progresión a la inmunoterapia en pacientes con PD-L1 > 50% que debería ser explorada en estudios fase III aleatorizados.
- Sintilimab mas anlotinib es superior a la quimioterapia, pero desconocemos su efecto frente al tratamiento estándar.
- Aunque se cierra prematuramente, el estudio DISCIPLE, sugiera que el uso de 6 meses de tratamiento podría ser suficiente. Son necesario estudios confirmatorios.
- Pembrolizumab más quimioterapia mantiene la eficacia a 5 años de seguimiento, en pacientes con histología escamosa y no escamosa.
- El estudio IPSOS demuestra superioridad de la inmunoterapia frente a la monoterapia con quimioterapia, en pacientes no elegibles para platino. A pesar de ser un estudio positivo, no es clínicamente relevante, ya que el comparador no es el adecuado en pacientes con PD-L1 superior al 50%. Además desconocemos la eficacia en los distintos subgrupos .