Lung Cancer UPDATES
ASCO HIGHLIGTHS
02-06 JUNIO 2023
Chicago, USA

Iniciativa científica de:
GECP
lung cancer research

CPNM Driver Negativo

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Conflictos de interés

Iniciativa científica de: GECP lung cancer research

Research funding: Roche, Pfizer, Merck-Serono, Bristol Myers Squibb

Advisory board or lectures: Roche, Bristol Myers Squibb, Merck Sharp Dohme, Merck-Serono, Sanofi, Pfizer, Lilly, Amgen, Boehringer-Ingelheim, AstraZeneca, Takeda, Sanofi, Pierre Fabre, Qiagen, Mirati, Janssen and Bayer.

CheckMate 9LA 4-year clinical update

Iniciativa científica de: GECP lung cancer research

Key eligibility criteria
- Stage IV or recurrent NSCLC
- No prior systemic therapy
- No sensitizing *EGFR* mutations or known *ALK* alterations
- ECOG PS 0 or 1

Stratified by PD-L1[b] (< 1%[c] vs ≥ 1%) sex, and histology (SQ vs NSQ)

N = 719 → R 1:1

- n = 361: NIVO 360 mg Q3W + IPI 1 mg/kg Q6W + Chemo[d] Q3W (2 cycles)
- n = 358: Chemo[d] Q3W (4 cycles) with optional pemetrexed maintenance (NSQ)

Until disease progression, unacceptable toxicity, *or* for 2 years for immunotherapy

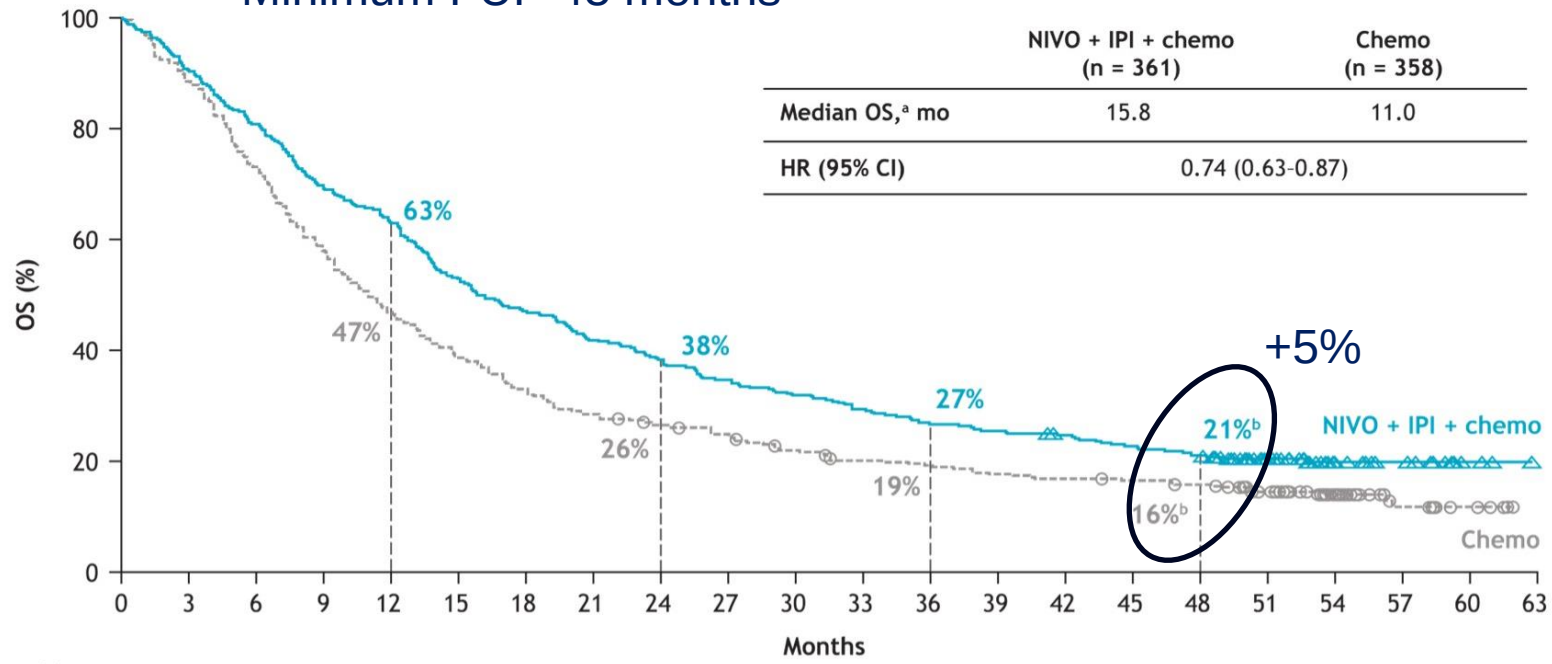
Primary endpoint
- OS

Secondary endpoints
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

Exploratory analyses
- OS by tumor histologic subtype

Minimum FUP 45 months

	NIVO + IPI + chemo (n = 361)	Chemo (n = 358)
Median OS,[a] mo	15.8	11.0
HR (95% CI)	0.74 (0.63-0.87)	



No. at risk

NIVO + IPI + chemo	361	326	292	250	227	191	170	151	138	125	115	106	96	92	87	80	74	47	21	14	4	0
Chemo	358	319	260	208	168	139	115	102	93	86	74	66	63	58	55	53	50	38	22	10	5	0

Clinical trial	4y OS
Keynote-189 (Non-SQ)	23.6%
Keynote-407 (SQ)	21.9%
CheckMate-9LA (both)	21%
CheckMate-9LA (Non-SQ)	22%
CheckMate-9LA (SQ)	20%

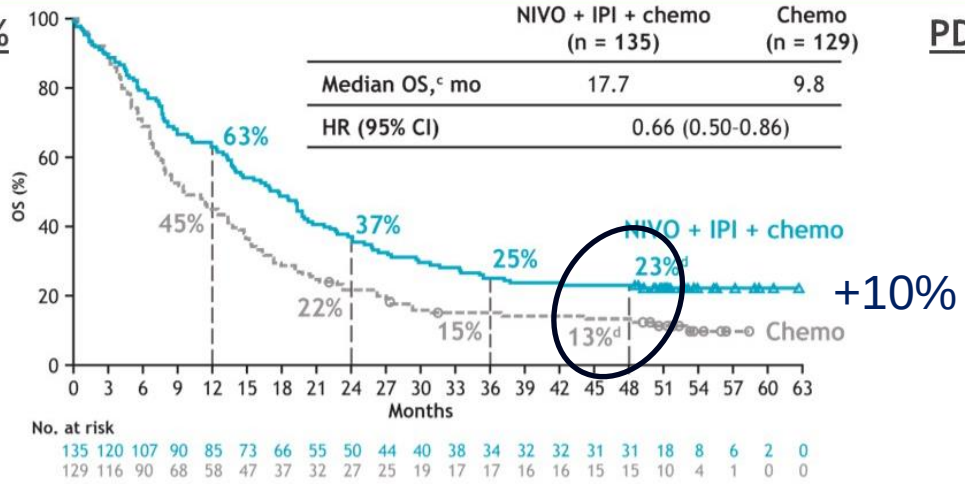
Carbone et al. Poster LBA023

CheckMate 9LA 4-year clinical update

Exploratory analysis by tumor PD-L1 expression or histology

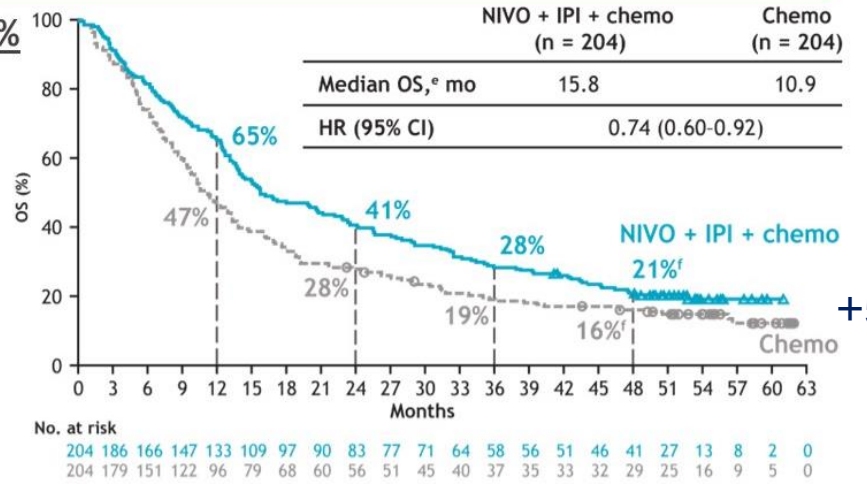
Iniciativa científica de: GECP lung cancer research

PD-L1 < 1%



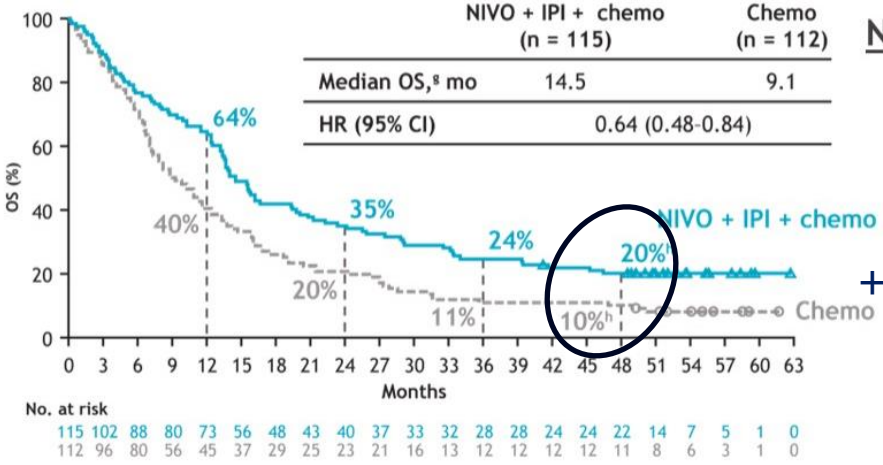
+10%

PD-L1 ≥ 1%



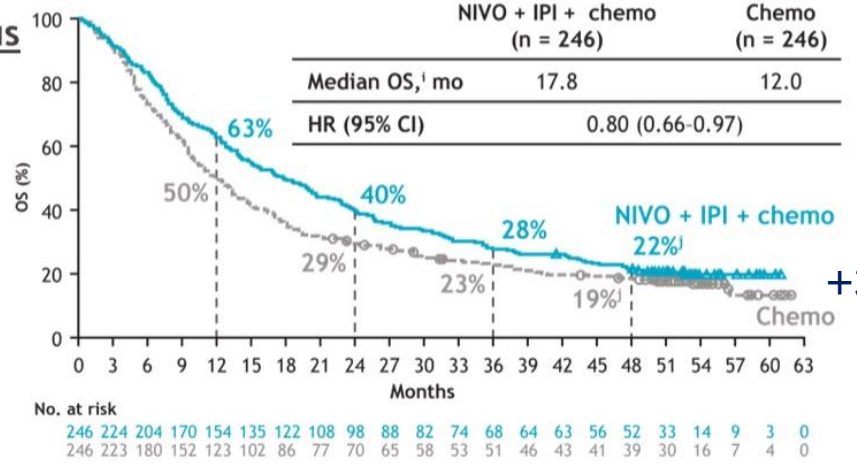
+5%

Squamous



+10%

Non-squamous

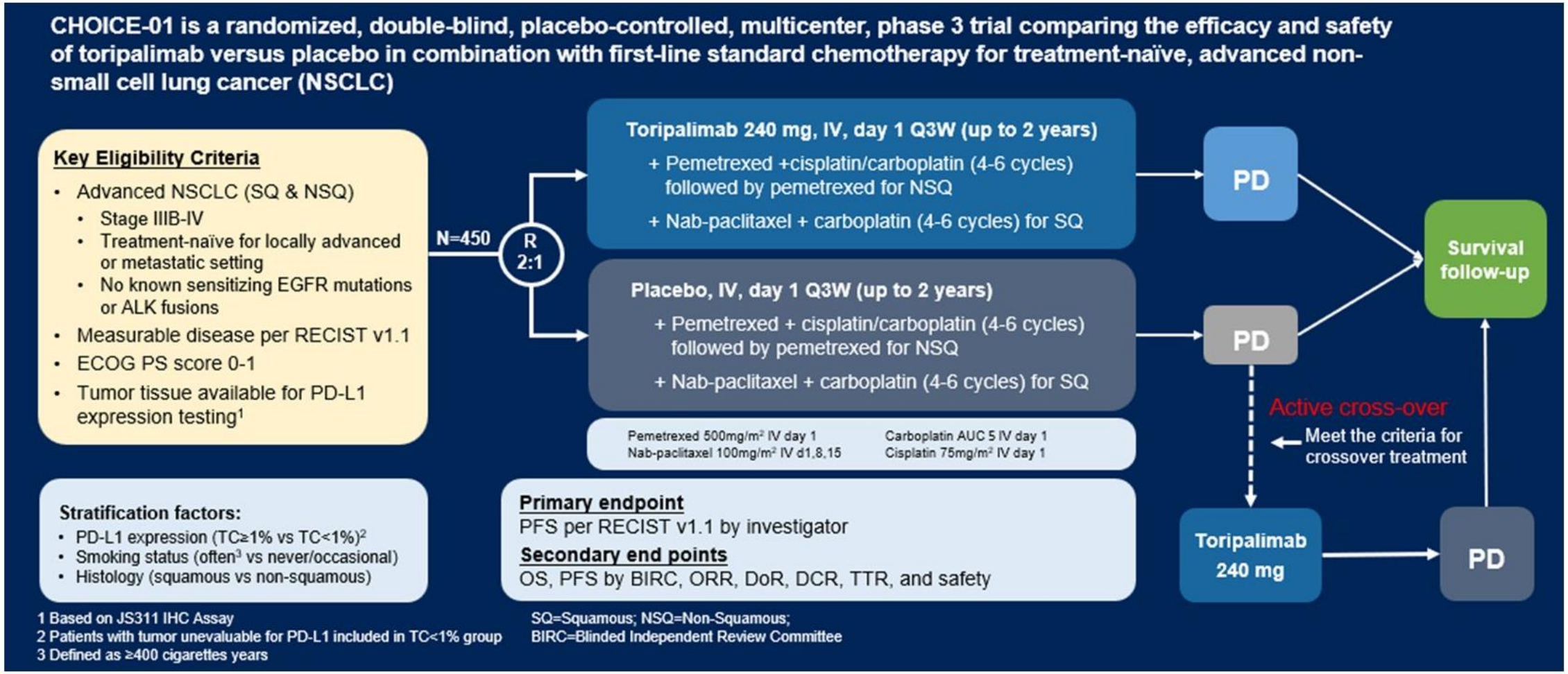


+3%

Carbone et al. Poster LBA023

CHOICE-01: Toripalimab vs placebo plus chemotherapy in adavanced EGFR/ALK negative NSCLC (both histologies)

Iniciativa científica de: GECP lung cancer research

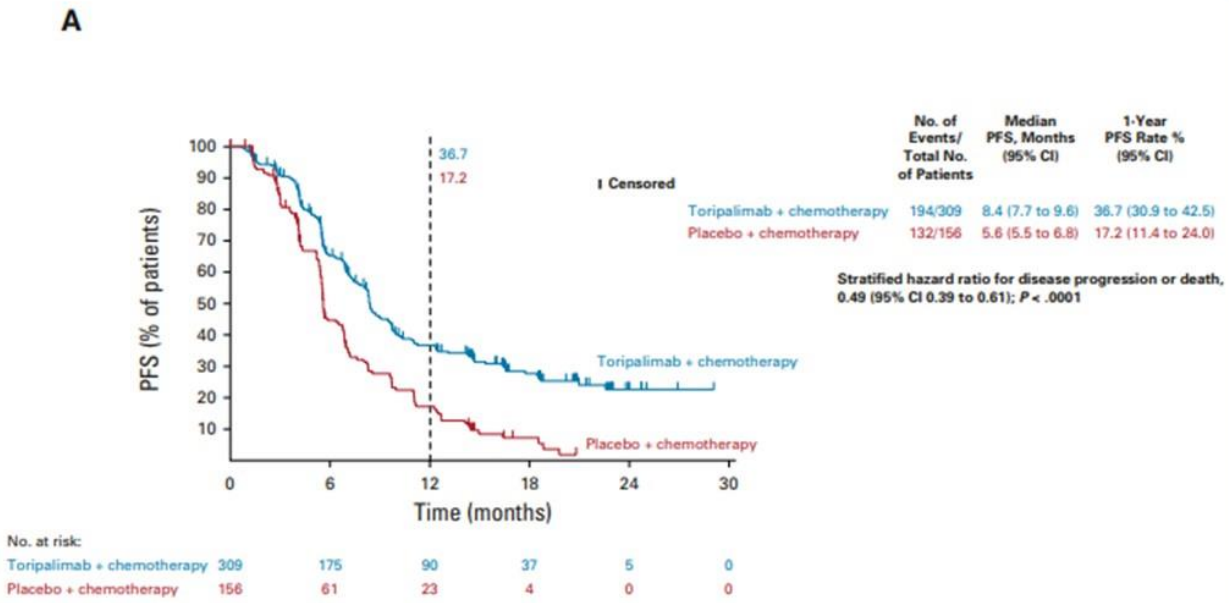


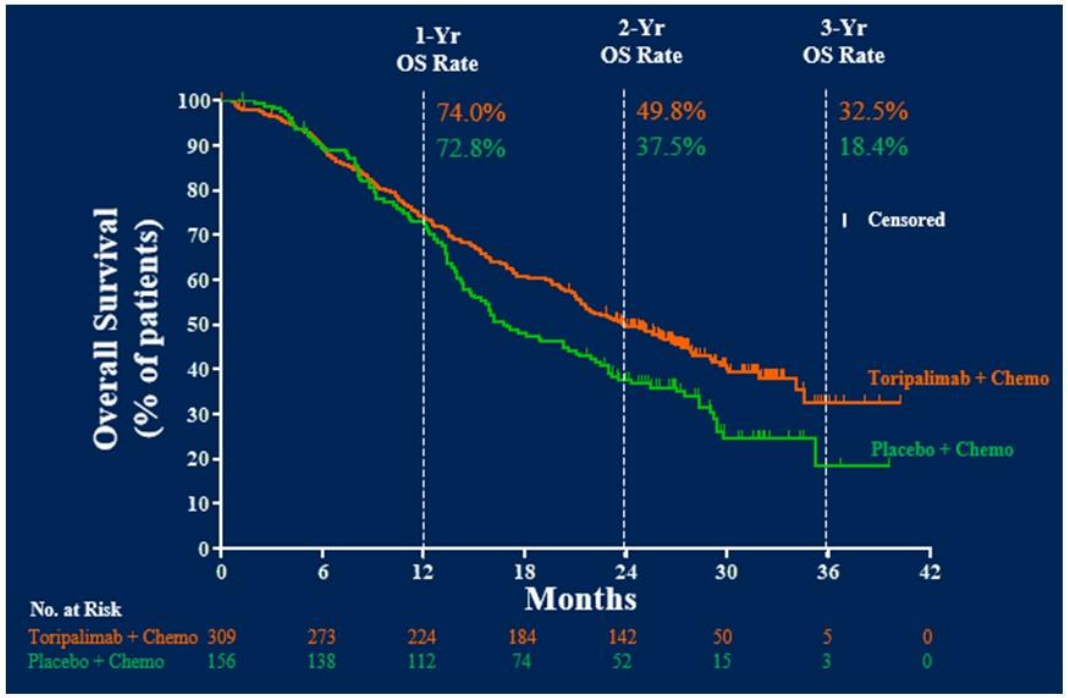
Wu et al. Oral Presentation.

CHOICE-01: Toripalimab vs placebo plus chemotherapy in adavanced EGFR/ALK negative NSCLC

Iniciativa científica de: GECP lung cancer arch

CHOICE-01 PFS and OS



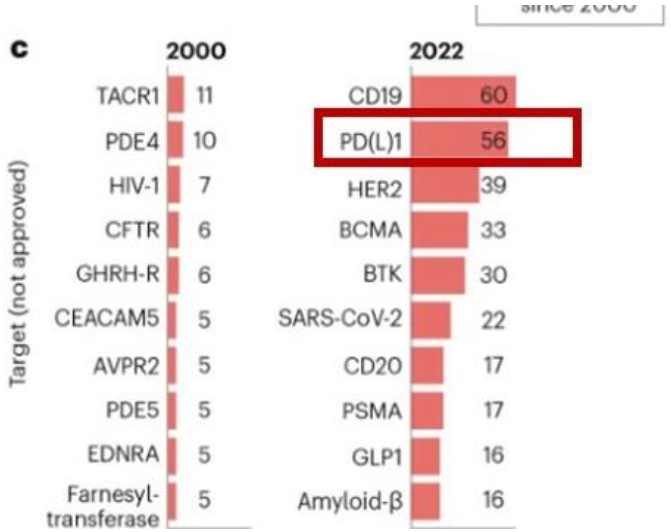


Wu et al. Oral Presentation.

The ”me too” in the PD1/PD-L1 world

- Innovation
- Combinations with novel targets
- Earlier lines of therapy

- Redundancy
- Divert resources from new discovery
- Trial designs with control arms of an obsolete standard of care



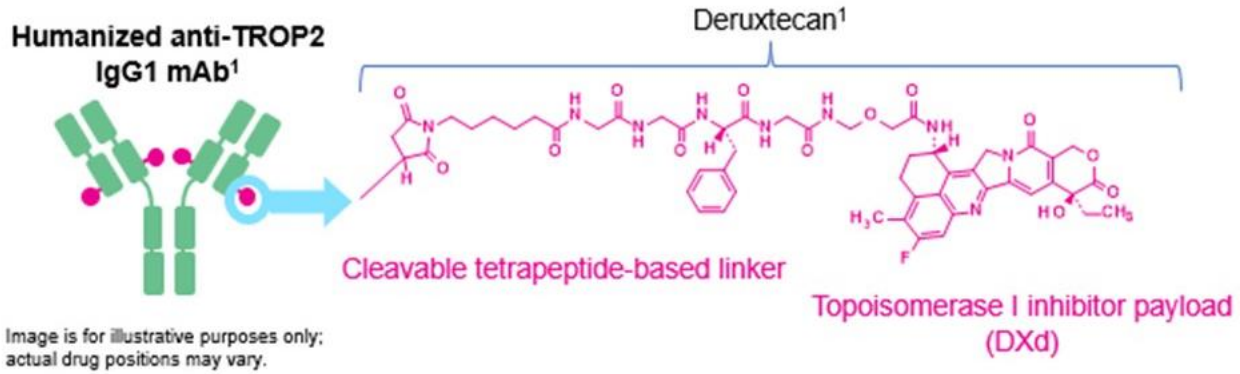
PD-1/PD-L1: 56 assets

“the number of assets in clinical development is outpacing the number of biological approaches”

Heist R. Discussant.

TROPION-Lung02: Dato-Dxd plus pembro +/- chemotherapy

Iniciativa científica de: GECP lung cancer research



Dato-DXd

Previously treated NSCLC monotherapy RR 25%

No selection by TROP2 expression

Key eligibility criteria

- **Advanced/metastatic NSCLC**
- **Dose escalation**[c]: ≤2 lines of prior therapy[d]
- **Dose expansion**
  - ≤1 line of platinum-based CT (cohorts 1 and 2)[d]
  - Treatment naive (cohort 2, enrollment after Jun 30, 2022)[d]
  - Treatment naive (cohorts 3-6)[d]

	Dato-DXd IV Q3W	+	pembro IV Q3W	+	platinum CT IV Q3W	
Cohort 1 (n=20):	4 mg/kg	+	200 mg			Doublet
Cohort 2 (n=32):	6 mg/kg	+	200 mg			
Cohort 3 (n=20):	4 mg/kg	+	200 mg	+	carboplatin AUC 5	Triplet
Cohort 4 (n=26):	6 mg/kg	+	200 mg	+	carboplatin AUC 5	
Cohort 5 (n=12):	4 mg/kg	+	200 mg	+	cisplatin 75 mg/m²	
Cohort 6 (n=10):	6 mg/kg	+	200 mg	+	cisplatin 75 mg/m²	

- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and antidrug antibodies

Goto et al. ASCO 2023.

TROPION-Lung02: Dato-Dxd plus pembro +/- chemotherapy

Iniciativa científica de: GECP lung cancer research

	All patients		Patients in 1L	
Response[a]	**Doublet (n=61)[b]**	**Triplet (n=71)[b]**	**Doublet (n=34)[b]**	**Triplet (n=53)[b]**
Confirmed + pending ORR, n (%)[c,d] [95% CI]	23 (38) [26-51]	35 (49) [37-61]	17 (50) [32-68]	30 (57) [42-70]
Confirmed + pending BOR, n (%)[d,e]				
Confirmed CR	0	1 (1)	0	1 (2)
Pending CR[d]	0	0	0	0
Confirmed PR	21 (34)	34 (48)	15 (44)	29 (55)
Pending PR[d]	2 (3)	0	2 (6)	0
SD, n (%)[f]	30 (49)	27 (38)	16 (47)	18 (34)
DCR, n (%)[g]	51 (84)	62 (87)	31 (91)	48 (91)
Median DOR, months [95% CI]	NE [8.8-NE]	NE [5.8-NE]	NE [5.5-NE]	NE [5.7-NE]

Preliminary PFS in all patients, median (95% CI), months: doublet, 8.3 (6.8-11.8); triplet 7.8 (5.6-11.1)[h]

- In the 1L setting, the ORR (confirmed and pending)[d] was 50% in patients receiving doublet therapy and 57% in those receiving triplet therapy
- Among all patients, the DCR was 84% (doublet) and 87% (triplet); in the 1L setting, the DCR was 91% in both therapy subgroups

Goto et al. ASCO 2023.

TROPION-Lung02: Dato-Dxd plus pembro +/- chemotherapy

Iniciativa científica de: GECP lung cancer research

Safety Summary

Event, n (%)	Doublet (n=64)	Triplet (n=72)
TEAEs[a]	62 (97)	72 (100)
Study treatment related[b]	58 (91)	72 (100)
Grade ≥3 TEAEs	34 (53)	55 (76)
Study treatment related[b]	20 (31)	42 (58)
Serious TEAEs	20 (31)	29 (40)
Study treatment related	6 (9)	16 (22)
TEAEs associated with:		
Death[f]	3 (5)	5 (7)
Dose reduction of any drug	14 (22)	14 (19)
Dose reduction of Dato-DXd	14 (22)	11 (15)
Discontinuation of any drug	18 (28)	27 (38)
Discontinuation of Dato-DXd[g]	15 (23)	20 (28)

- During the dose-finding phase, 2 patients receiving Dato-DXd + pembrolizumab + platinum CT had DLTs[c,d,e]
- TEAEs (treatment-emergent adverse events) associated with discontinuation of Dato-DXd occurred in 23% of patients receiving the doublet regimen and in 28% of patients receiving the triplet regimen

Goto et al. ASCO 2023.

TROPION-Lung02: Dato-Dxd plus pembro +/- chemotherapy

Iniciativa científica de: GECP lung cancer research

Adverse Events of Special Interest

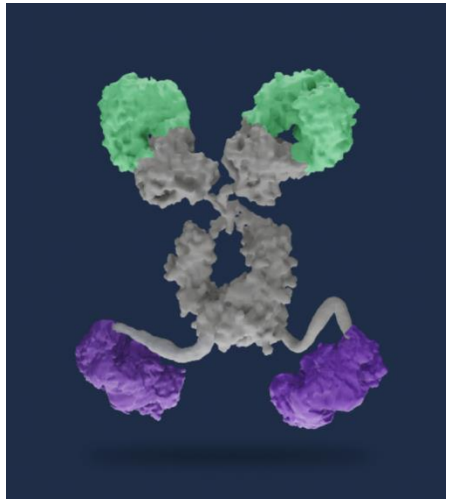
AESI, n (%)[a,b]	Doublet (n=64)		Triplet (n=72)	
	All grades	Grade ≥3	All grades	Grade ≥3
Oral mucositis/stomatitis	37 (58)	5 (8)	31 (43)	4 (6)
ILD/pneumonitis adjudicated as drug related[c]	11 (17)	2 (3)	16 (22)	2 (3)
Ocular surface toxicity[d]	10 (16)	1 (2)	17 (24)	2 (3)
IRR[e]	15 (23)	0	10 (14)	0

- Oral mucositis/stomatitis was the most common AESI and was predominantly grade 1/2
- No grade 5 AESIs have occurred
- There were no grade 4 or 5 adjudicated ILD/pneumonitis events[f]

Goto et al. ASCO 2023.

SI-B001 plus docetaxel in previously treated patients with advanced EGFR/ALK negative NSCLC

Iniciativa científica de: GECP lung cancer research



SI-B001 = Bi-specific antibody directed against EGFR & ERBB3

Study Design

2

Key Eligibility criteria

- Locally advanced or metastatic EGFR/ALK wild-type NSCLC
- Previously treated with anti-PD-1/L1 therapy
- Docetaxel-Naïve
- Eastern Cooperative Oncology Group performance status of 0-1
- At least one measurable lesion per RECIST v1.1
- No autoimmune, inflammatory illnesses
- Adequate organ and marrow function
- Either no brain metastases or stable brain metastases at screening

Cohorts

- **Cohort A: SI-B001 + PBC（2L）** first-line anti-PD-1/L1 antibody monotherapy
- **Cohort B: SI-B001 + docetaxel（2L）** first-line anti-PD-1/L1 therapy plus PBC
- **Cohort C: SI-B001 + docetaxel（≥3L）** first-line anti-PD-1/L1 therapy and PBC

Schedules

- **Schedule 1: 16+9mg/kg QW**
- **Schedule 2: 14mg/kg D1D8 Q3W**
- **Schedule 3: 21+12mg/kg QW**

Primary endpoints: ORR, optimal dose for combination
Secondary endpoints: PFS, DCR, DOR, safety

Zhao et al. Poster abstract 9025

SI-B001 plus docetaxel in previously treated patients with advanced EGFR/ALK negative NSCLC

Iniciativa científica de: GECP lung cancer research

Safety in all three cohorts: A) 2L + PBC; B) 2L + doce; C) 3L + docetaxel

- The most common Grade ≥3 treatment-related adverse events (TRAEs) were neutropenia (15%), myelosuppression (13%), and leukopenia (9%).
- No drug-related death was observed.

Treatment related AE (≥G3 occurred) of SI-B001 plus chemotherapy (N=55)

PT Term	G1	G2	G3	G4	All Grade
Rash	20 (36%)	10 (18%)	3 (5%)		33 (60%)
Mouth ulceration	6 (11%)	7 (13%)	1 (2%)		14 (25%)
Leukopenia	6 (11%)	2 (4%)	5 (9%)		13 (24%)
Anemia	6 (11%)	5 (9%)	2 (4%)		13 (24%)
Pyrexia	9 (16%)	3 (5%)	1 (2%)		13 (24%)
Neutropenia	4 (7%)		7 (13%)	1 (2%)	12 (22%)
Diarrhea	8 (15%)	3 (5%)	1 (2%)		12 (22%)
Myelosuppression	1 (2%)	2 (4%)	2 (4%)	5 (9%)	10 (18%)
Paronychia	5 (9%)	2 (4%)	1 (2%)		8 (15%)
Hypokalemia	3 (5%)	2 (4%)	2 (4%)		7 (13%)
Dermatitis acneiform	6 (11%)		1 (2%)		7 (13%)
Pneumonia		2 (4%)	4 (7%)		6 (11%)
Asthenia	3 (5%)	2 (4%)	1 (2%)		6 (11%)
Lymphopenia	3 (5%)		2 (4%)		5 (9%)
Chest discomfort	2 (4%)	2 (4%)	1 (2%)		5 (9%)
Hypersensitivity			4 (7%)		4 (7%)
Hypoaesthesia	1 (2%)		1 (2%)		2 (4%)
Respiratory failure	1 (2%)		1 (2%)		2 (4%)
Cardiomyopathy			1 (2%)		1 (2%)
Gastritis			1 (2%)		1 (2%)
Soft tissue infection			1 (2%)		1 (2%)
Heart rate increased			1 (2%)		1 (2%)
Interstitial lung disease			1 (2%)		1 (2%)
Tachypnoea			1 (2%)		1 (2%)
Cardiac failure				1 (2%)	1 (2%)
Septic shock				1 (2%)	1 (2%)

Zhao et al. Poster abstract 9025

SI-B001 plus docetaxel in previously treated patients with advanced EGFR/ALK negative NSCLC

Iniciativa científica de: GECP lung cancer research

Efficacy in 23 evaluable patients from cohort B (SI-B001 16 + 9 mg/kg QW + docetaxel)

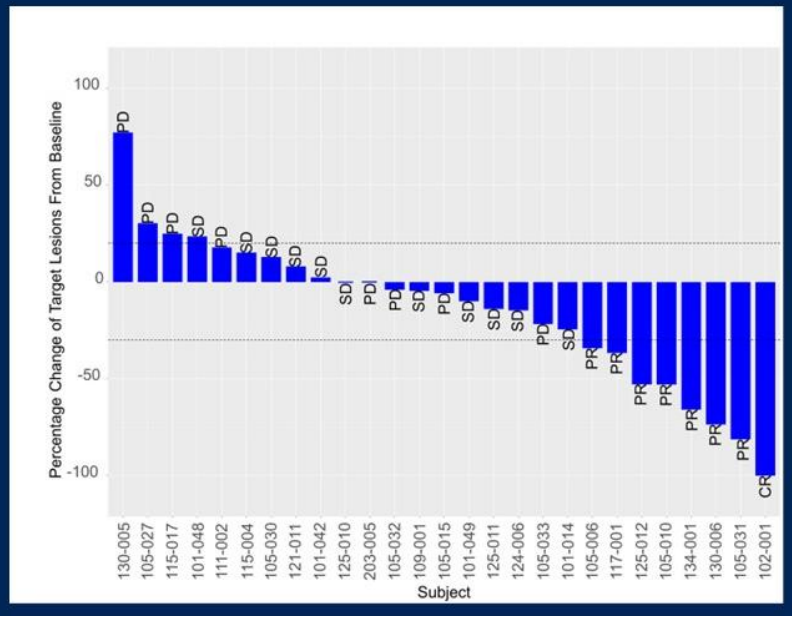
	No AGA (N=19)	With AGA (N=4)	Total (N=23)
BOR			
CR	0	0	0
PR	9	1	10
SD	5	1	6
PD	2	2	4
NE	3	0	3
ORR % (95%CI)	47.4% (24.5~71.1)	25.0% (0.6~80.6)	43.5% (23.2~65.5)
DCR % (95%CI)	73.7% (48.8~90.9)	50.0% (6.8~93.2)	69.6% (47.1~86.8)
DoR (m) (median, range)	NR (0.2~13.1+)	3.8	NR (0.2~13.1+)
PFS (m) (median, 95% CI)	7.2 (4.3, NR)	3.0 (1.4, NR)	5.6 (4.1, NR)

Zhao et al. Poster abstract 9025

ONC-392/BNT316 (IgG1 anti-CTLA-4 mAb) in previously treated driver negative advanced NSCLC

Iniciativa científica de: GECP lung cancer research

- Metastatic NSCLC patients without targetable driver mutations
- Progressed on anti-PD-(L)1 therapy
- Dose escalation cohort (10 mg/kg, Q3W, N=2)
- Expansion cohort Arm I and treated with 2 cycles at 10 mg/kg, followed by 6 mg/kg, q3w (N=33)



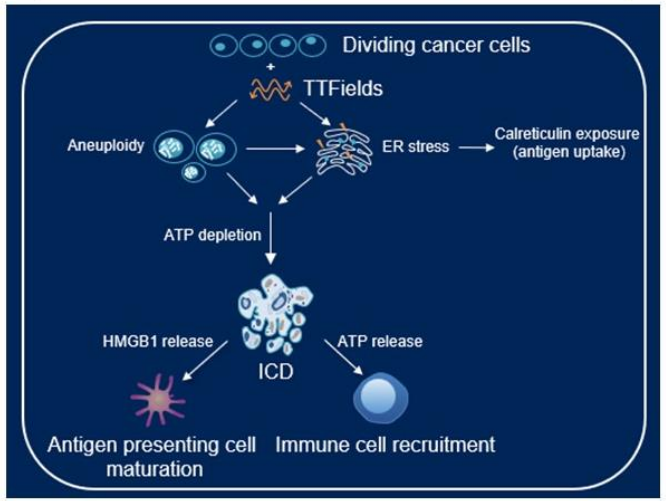
- Response rate among evaluable patients - 29.6%
- Grade 3-4 TRAEs - 13 (39%)
- Gr 3-4 irAEs - 10 (30%)
- Significant irAEs - 2 colitis, intestinal perforation, immune hepatitis, adrenal insufficiency, tubulointerstitial nephritis

He et al. Poster abstract

LUNAR: TTFields in advanced NSCLC

Iniciativa científica de: GECP lung cancer research

Tumor Treating Fields: Mechanism of Action



- Electric fields delivered by transducer arrays placed on skin close to tumor
- Initial mechanism of action centered on effect of TTFields on disruption of mitosis because of effects of cell charge and polarity
- Also proposed MOA effects on cell migration; cell membrane permeability; autophagy; replication stress; immunologic cell death

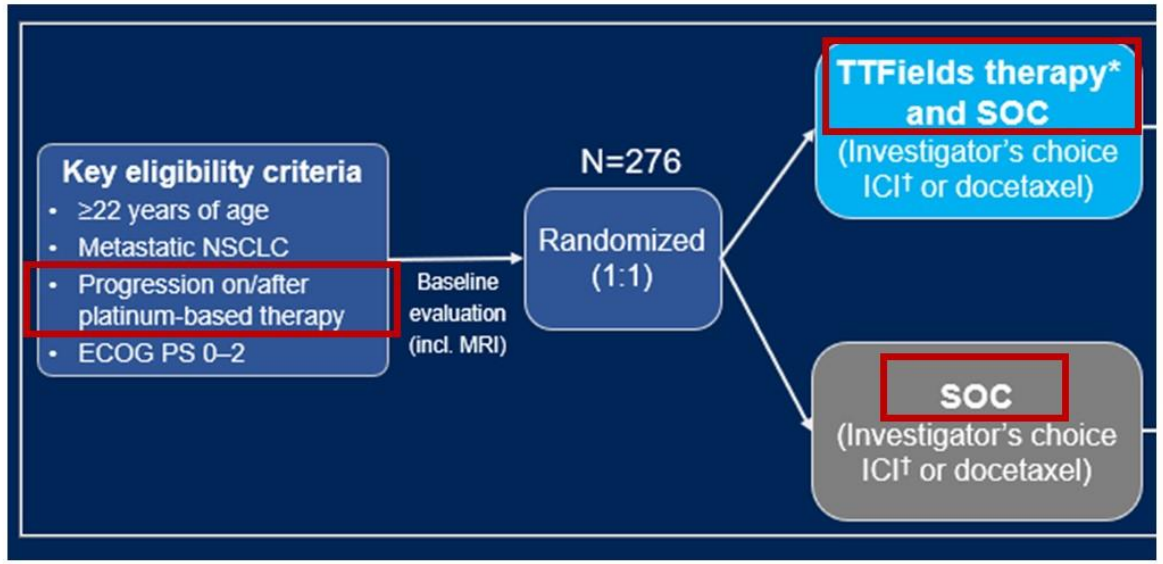
Leal et al ASCO 2023; Moser et al Cancer Res 2022 Oct 17;82(20):3650-3658.

Leal et al. Oral presentation.

LUNAR: TTFields in advanced NSCLC

Iniciativa científica de: GECP lung cancer research

Changing SOC landscape poses challenges for clinical trial design



Leal et al ASCO 2023

ClinicalTrials.gov Identifier: NCT02973789

Recruitment Status : Active, not recruiting
First Posted : November 25, 2016
Last Update Posted : May 17, 2023

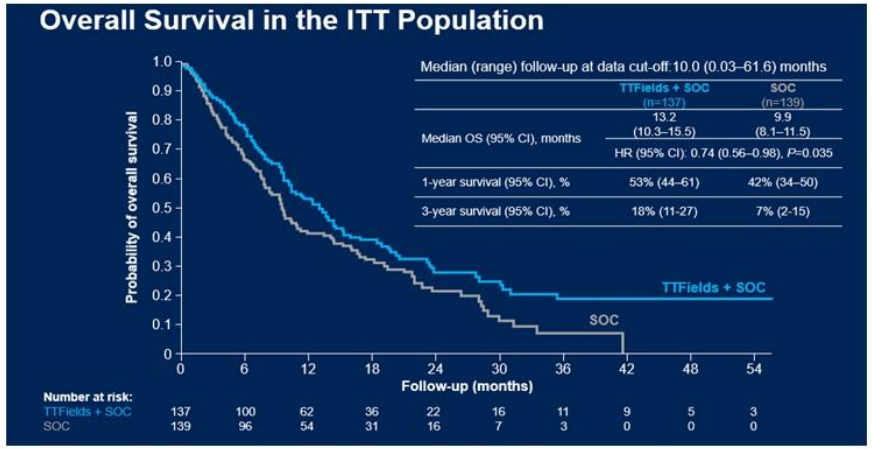
- By 2016, at time of study start, ICI superior to docetaxel in 2L
- By 2018, ICI moved to 1L NSCLC treatment
- We currently do not use ICI as used in this study

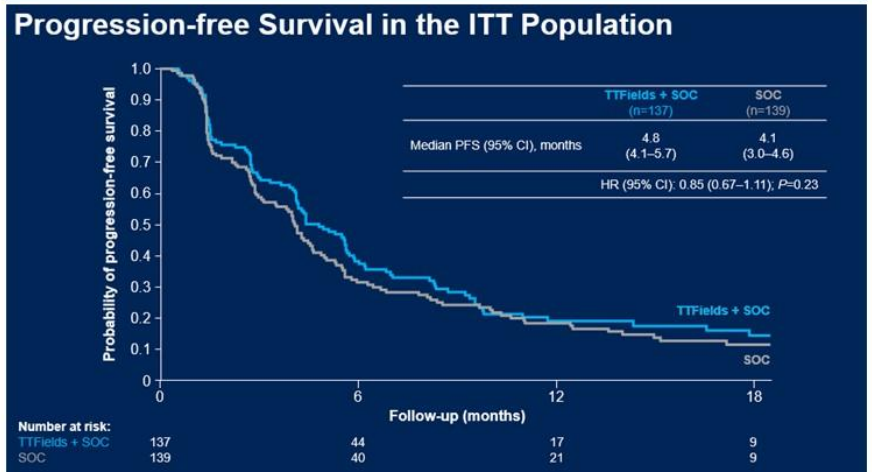
Leal et al. Oral presentation.

LUNAR: TTFields in advanced NSCLC

Iniciativa científica de: GECP lung cancer research

LUNAR met its Primary Endpoint





- OS benefit
- No difference in RR or PFS

- OS benefit with minimal/no RR/PFS benefit has been seen, particularly in IO studies

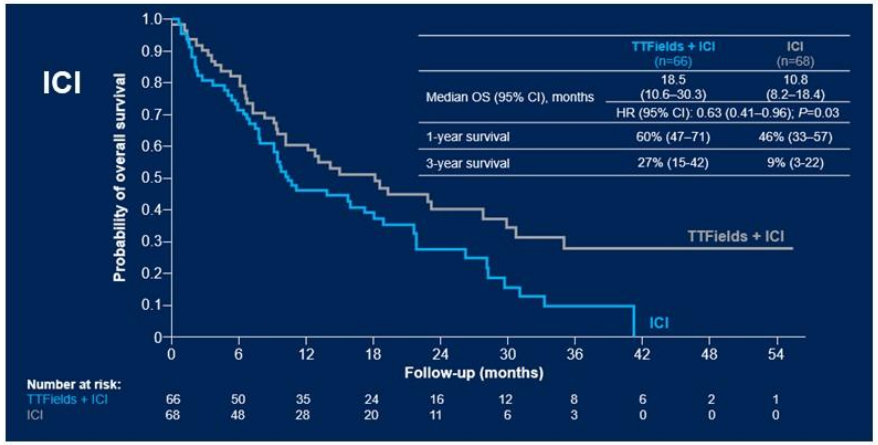
- Was there any imbalance? What were the rates of subsequent therapies?

Leal et al. Oral presentation.

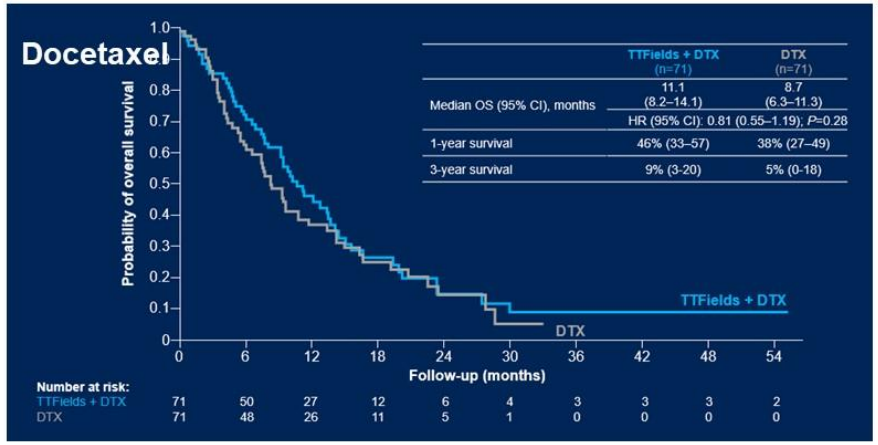
LUNAR: TTFields in advanced NSCLC

Iniciativa científica de: GECP lung cancer research

OS benefit in ICI- but not docetaxel- treated



	TTFields + ICI (n=66)	ICI (n=68)
Median OS (95% CI), months	18.5 (10.6–30.3)	10.8 (8.2–18.4)
	HR (95% CI): 0.63 (0.41–0.96); *P*=0.03	
1-year survival	60% (47–71)	46% (33–57)
3-year survival	27% (15-42)	9% (3-22)



	TTFields + DTX (n=71)	DTX (n=71)
Median OS (95% CI), months	11.1 (8.2–14.1)	8.7 (6.3–11.3)
	HR (95% CI): 0.81 (0.55–1.19); *P*=0.28	
1-year survival	46% (33–57)	38% (27–49)
3-year survival	9% (3-20)	5% (0-18)

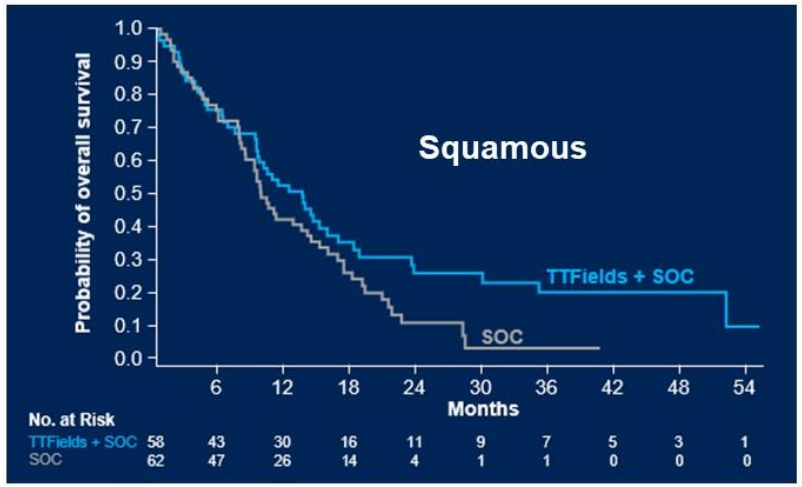
- Surprising, as proposed mechanism of action of TTFields should have effect in docetaxel treated patients as well
- Mechanism of action for activity in ICI are proposed
- ICI after platinum doublet is no longer a standard of care

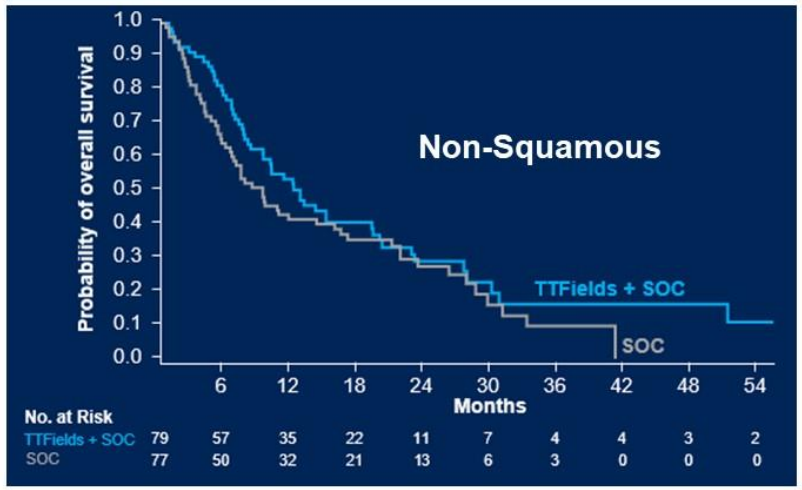
Leal et al. Oral presentation.

LUNAR: TTFields in advanced NSCLC

Iniciativa científica de: GECP lung cancer research

OS benefit in Squamous but not Non-Squamous





- Secondary outcome measure
- Based on presumed locoregional mode of action, did the patients with squamous NSCLC have more locoregional disease?

Leal et al. Oral presentation.

/Salut

ICO
Institut Català d'Oncologia

Universitat de Barcelona

IDIBELL
Oncobell program

Gracias por vuestra atención

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