University of Colorado Cancer Center

University of Colorado Hospital

University of Colorado Health Sciences Center

Lung Cancer Immuno-Therapy 2023

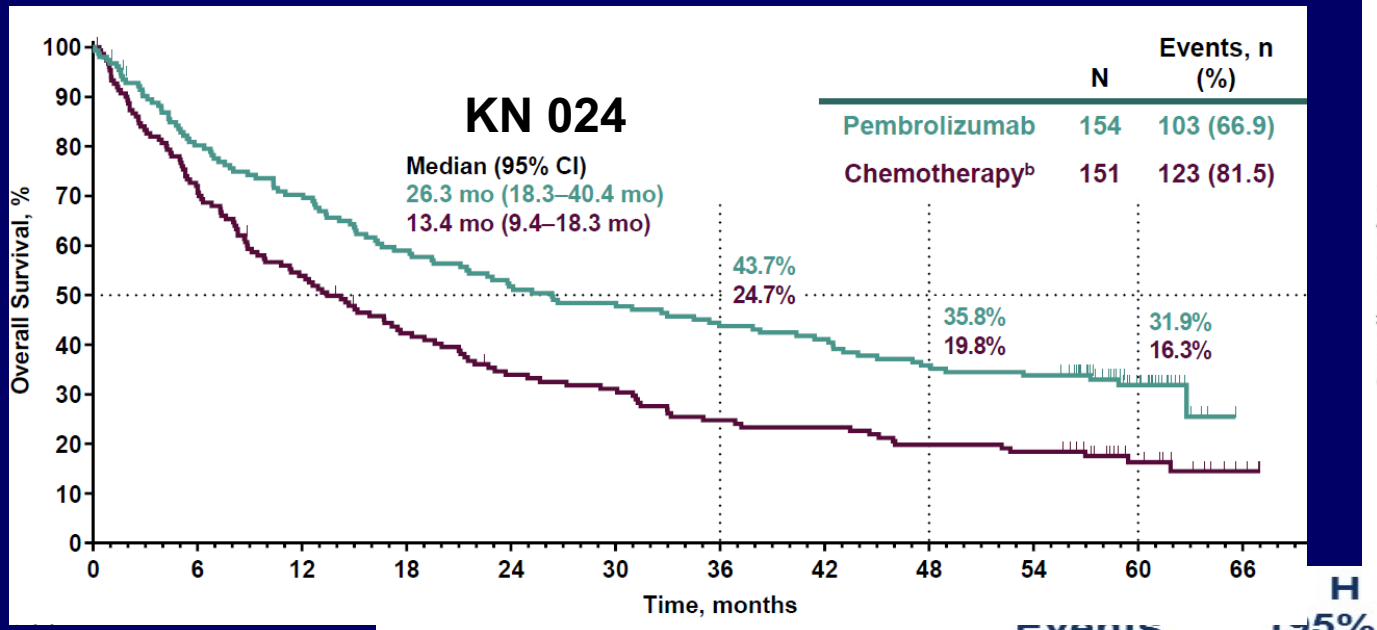
Paul A. Bunn, Jr, MD, Distinguished Professor and Dudley Endowed Chair, Univ. of Colorado Cancer Center, Aurora, CO, USA

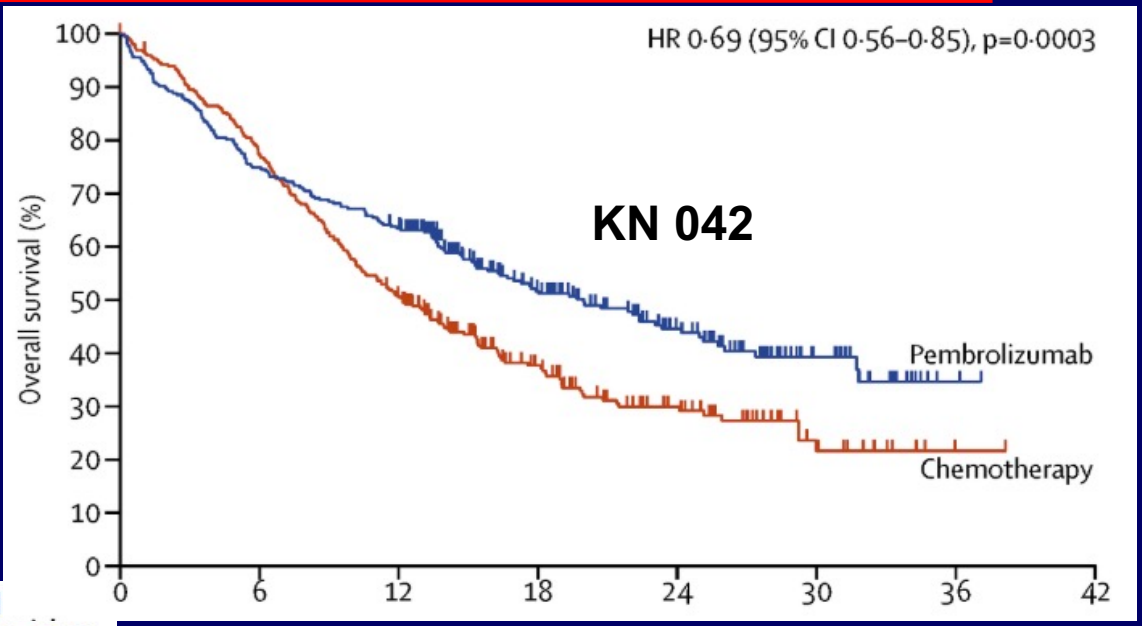
Consultant: AstraZeneca, Bayer, BMS, Daiichi-Sankyo, Eli Lilly, Merck, Roche, Ascentage, Cstone Verastem,

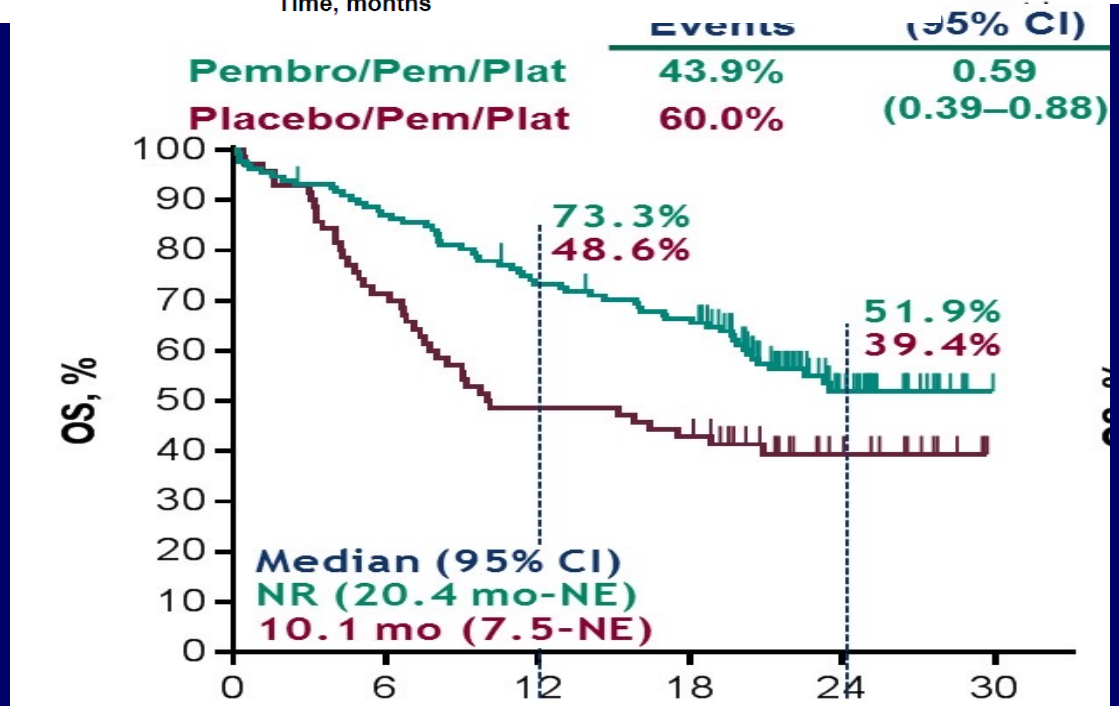
IO and CT/IO in stage 4 NSCLC & no Driver Alteration: TPS>49

- Approved single agents: pembrolizumab, atezolizumab, durvalumab, cemiplimab, (Chinese CPIs)
- Approved CT+IO (for highly symptomatic disease): Pembro, Nivo, Atezo/bev, Durva, cemiplimab, sug, tiz
- Ongoing Randomized trials: EVOKE -02 (Sacituzumab/Trop-2 ADC), AVANZAR (Dato-Dxd Trop-2 ADC)

KEYNOTE-024, 042 and 189 (TPS>49): 3-5-Year OS Update

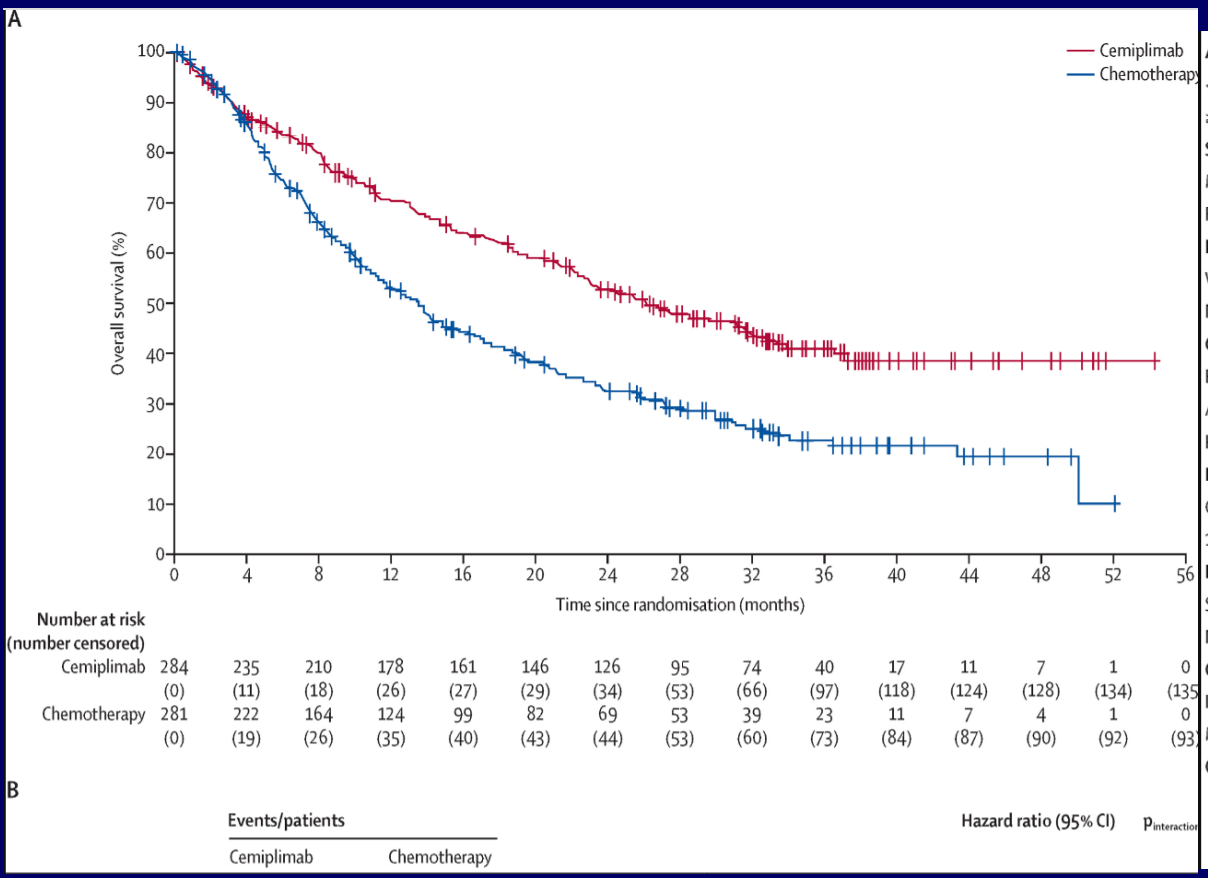


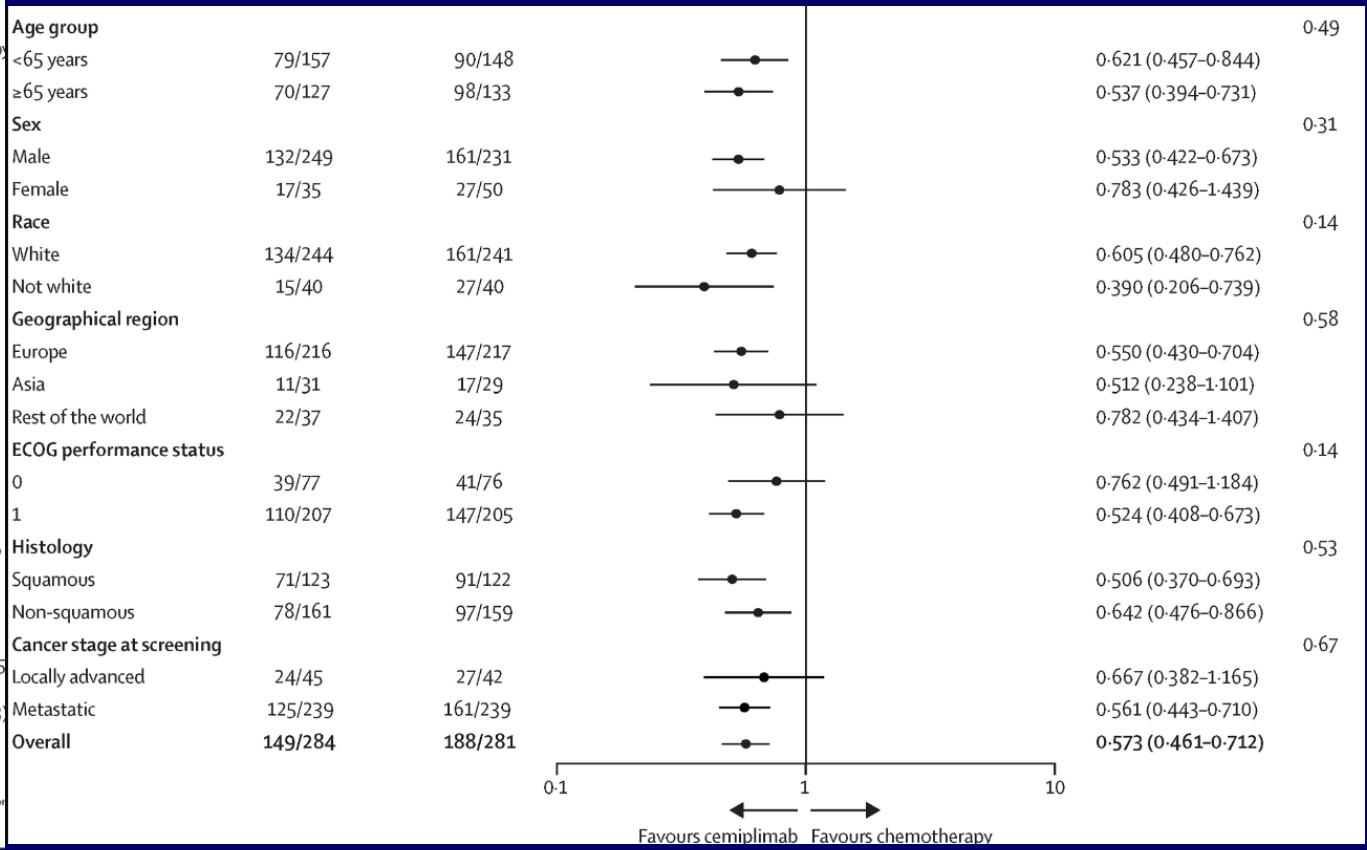




Conclusion: Checkpoint inhibitors alone or with chemotherapy produce 5 year survival rates of about 30% in stage 4 adenoca of lung with TPS>49

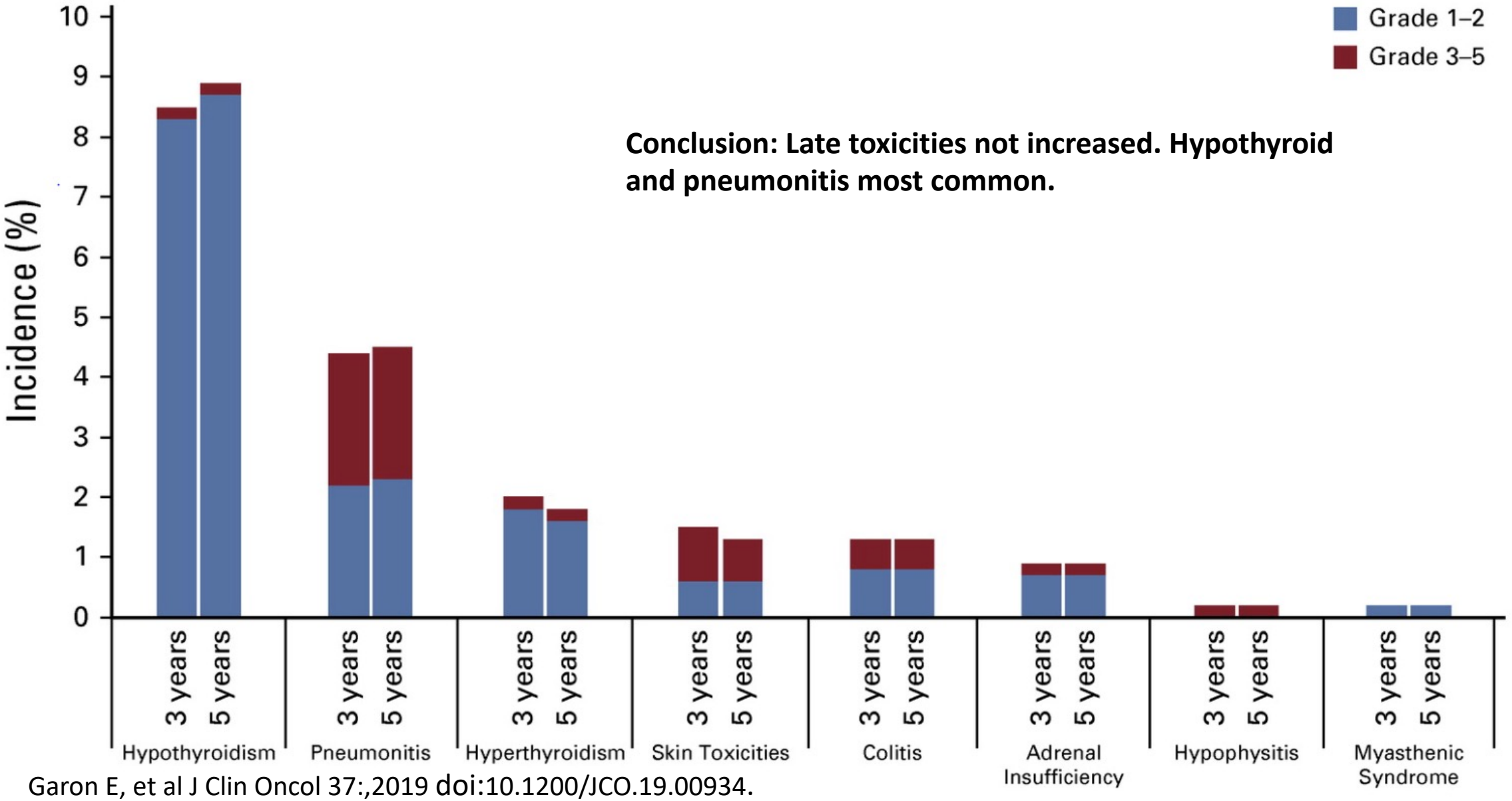
Cemiplimab EMPOWER –Lung 1:(TPS>49): 5-Year OS Update





Same conclusion with multiple PD1 and PDL1 inhibitors

Late toxicities from pembrolizumab



Conclusion: Late toxicities not increased. Hypothyroid and pneumonitis most common.

Garon E, et al J Clin Oncol 37:,2019 doi:10.1200/JCO.19.00934.

What's New:Other agents combined with CPI IO +/-CT

- Other CPIs
- ADCs
- Angiogenesis inhibitors: bev, ram, lenvatinib, anolitinib
- Parp Inhibitors: olaparib, others

CITYSCAPE: Phase II ORR and PFS

1L Stage IV NSCLC

- *EGFR/ALK* wild-type
- Tumor PD-L1 TPS ≥ 1% by 22C3 IHC by local or central assay

N=135

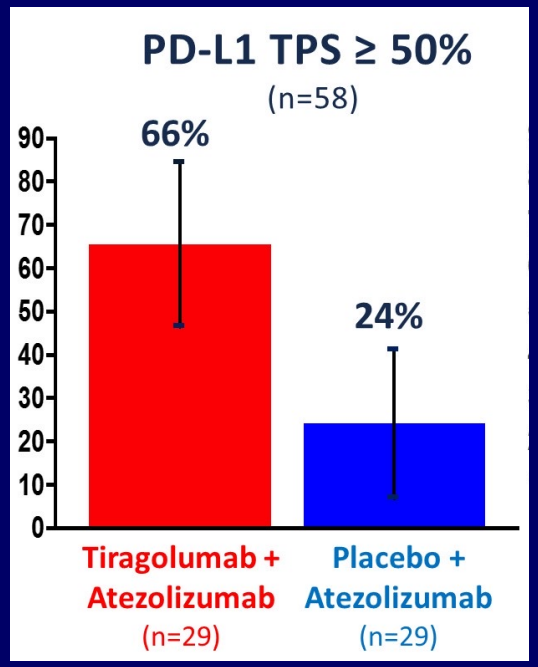
R 1:1

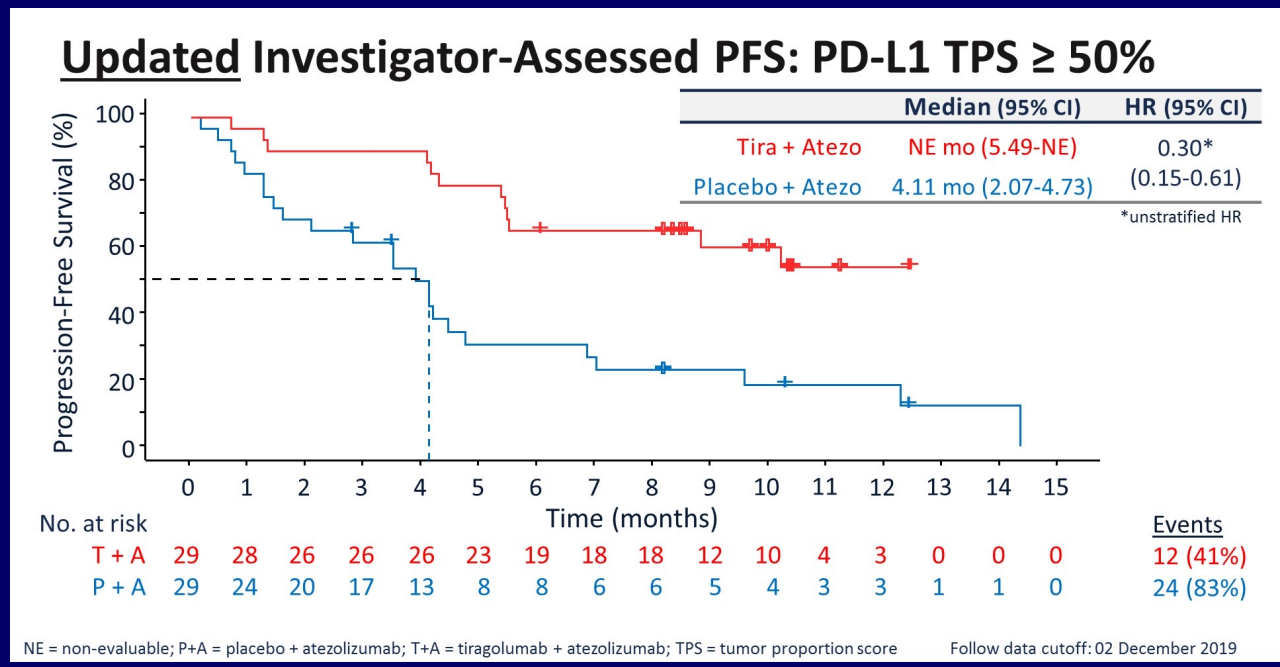
Tiragolumab 600 mg IV q3w + Atezolizumab 1200 mg IV q3w

Placebo 600 mg IV q3w + Atezolizumab 1200 mg IV q3w

No crossover

PD or loss of clinical benefit





TIGIT targeted studies

- Anti-TIGIT monotherapy resulted in ORRs ranging from 0% to 5% across several trials in advanced solid tumors
- Combination therapies are however showing promise
  - E.g.ARC-7 Ph II study with anti-TIGIT mAb, domvanalimab + anti PD1 vs anti-PD-1 (~30% reduction in risk of progression)
  - Now Ph III STAR-121 evaluating Domvanalimab + anti-PDL1 with chemo in 1st line setting

TIGIT based combinations					
NCT04672369	I	IBI939	Anti-TIGIT mAb	Pretreated	Recruiting
NCT04995523	II	AZD2936	Anti-PD-1/TIGIT bispecific mAb	Pretreated	Recruiting
NCT05102214	I/II	HLX301	Anti-PD-1/TIGIT bispecific mAb	Pretreated	Recruiting
NCT04761198	I/II	Etigilimab + Nivolumab	Anti-TIGIT mAb	Pretreated	Recruiting
NCT04738487 (KEYVIBE-003)	III	MK-7684A (Vibostolimab)/Pembrolizumab vs. Pembrolizumab	Anti-TIGIT mAb	First-Line	Recruiting
NCT04746924	III	Ociperliamab/Tislelizumab vs. Pembrolizumab	Anti-TIGIT mAb	First-Line	Recruiting
NCT04736173 (ARC-10)	III	Zimberelimab + Domvanalimab vs. Zimberelimab vs. Chemotherapy	Anti-TIGIT mAb	First-Line	Recruiting
NCT05502237 (STAR-121)	III	Zimberelimab + Domvanalimab + Chemotherapy vs. Pembrolizumab + Chemotherapy	Anti-TIGIT mAb	First-Line	Recruiting

A. Desai, S. Peters. Immunotherapy-based combinations in metastatic NSCLC. Cancer Treatment Reviews, May 2023

TROPION-Lung04 Study Design

Phase 1b, multicenter, open-label, dose escalation/confirmation and expansion study

TROPION-Lung04 is investigating Dato-DXd in combination with different immunotherapy agents ± carboplatin across 11 cohorts. This interim analysis reports the first data from Cohorts 2 and 4

Key eligibility

- Adults (≥18 years) with previously treated or treatment-naïve advanced or metastatic NSCLC[a]
- No actionable genomic alterations
- ECOG PS 0–1

	1 Part 1: Sequential dose escalation[b]	2 Part 2: Dose expansion
Cohort 1 (Doublet)	Dato-DXd 4 mg/kg + durvalumab 1120 mg, Q3W (n=5)	
Cohort 2 (Doublet)	Dato-DXd 6 mg/kg + durvalumab 1120 mg, Q3W (n=3)	Dato-DXd 6 mg/kg + durvalumab 1120 mg, Q3W (n=16)
Cohort 3[c] (Triplet)	Dato-DXd 4 mg/kg + durvalumab 1120 mg + 4 cycles carboplatin AUC 5, Q3W	
Cohort 4 (Triplet)	Dato-DXd 6 mg/kg + durvalumab 1120 mg + 4 cycles carboplatin AUC 5, Q3W (n=6)	Dato-DXd 6 mg/kg + durvalumab 1120 mg + 4 cycles carboplatin AUC 5, Q3W (n=8)

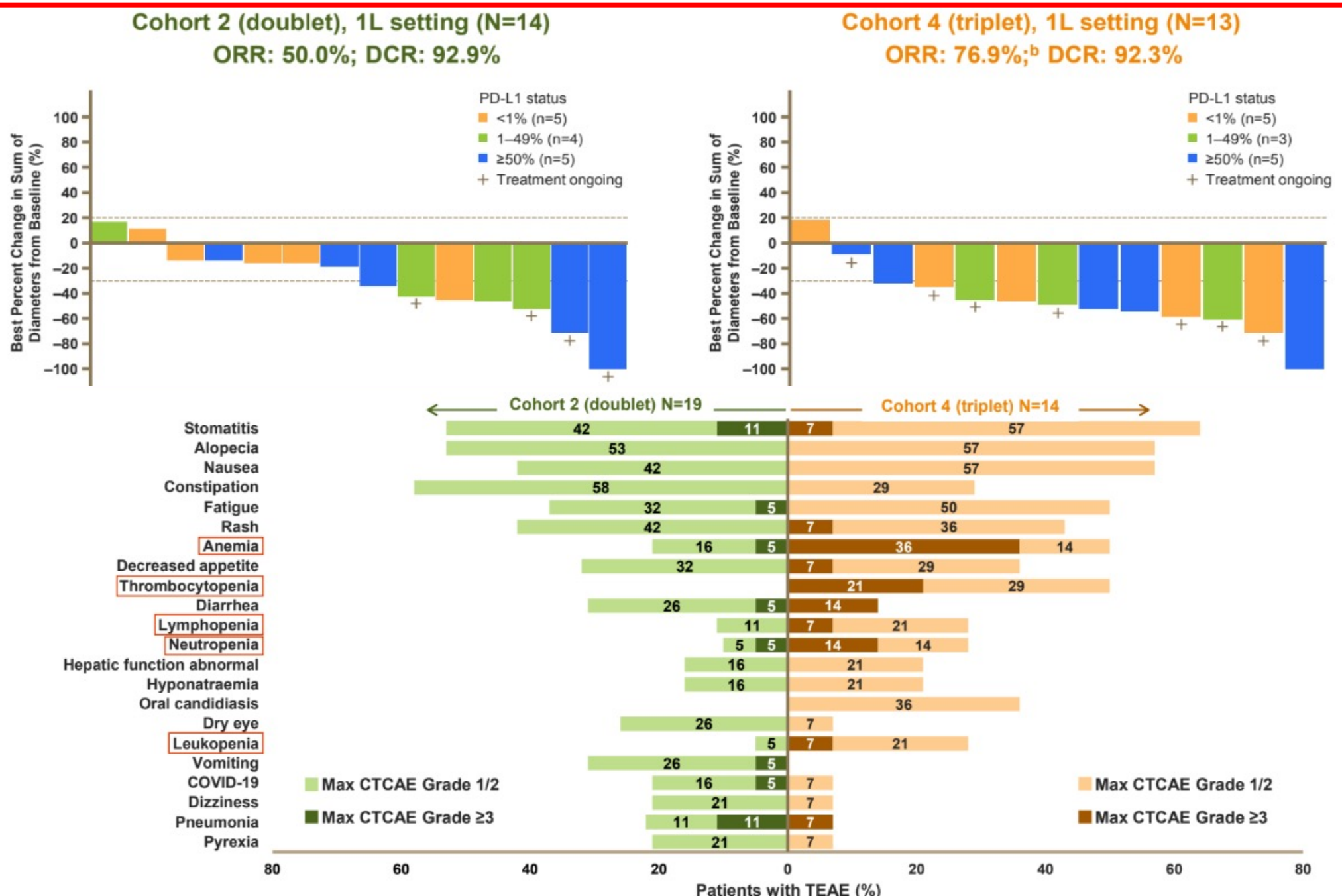
- **Primary endpoint:** Safety and tolerability
- **Key secondary endpoints:** ORR and disease control rate by investigator assessment per RECIST v1.1

Data cut-off: March 6 2023.

[a] Patients in Cohort 1 and one patient in Cohort 2 had received ≥1 platinum-based chemotherapy regimen and anti-PD-1/PD-L1 therapy as per an earlier version of the clinical study protocol. Subsequent patients were treatment-naïve or had ≤1 prior line of systemic chemotherapy without concomitant immune checkpoint inhibitors. [b] Dose escalation was guided by a mTPI-2 design and conducted sequentially from Cohort 1 to 2 (Dato-DXd 4 mg/kg to 6 mg/kg) and Cohort 2 to 4 (doublet to triplet combination). [c] Cohort 3 was skipped as there were sufficient data available from the Dato-DXd development program to conclude that 4 mg/kg Dato-DXd in combination with immunotherapy and carboplatin has an acceptable safety profile.

AUC, area under the curve; ECOG PS, Eastern Cooperative Oncology Group performance status; mTPI-2, modified toxicity probability interval-2; Q3W, once every 3 weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Dato-Dxd in 1L NSCLC



Dato-Dxd in 1L NSCLC: ONGOING AVANZAR Trial

Cohort 2 (Doublet)	**Dato-DXd 6 mg/kg + durvalumab 1120 mg, Q3W (n=3)**
Cohort 4 (Triplet)	**Dato-DXd 6 mg/kg + durvalumab 1120 mg + 4 cycles carboplatin AUC 5, Q3W (n=6)**

Response in patients in the 1L setting,[a] n (%)		Cohort 2 (doublet) N=14	Cohort 4 (triplet) N=13
Objective response rate (confirmed)		**7 (50.0)**	**10 (76.9)[b]**
[95% CI]		[23.0, 77.0]	[46.2, 95.0]
Best objective response	Complete response	0	0
	Partial response	7 (50.0)	10 (76.9)[b]
	Stable disease	6 (42.9)	2 (15.4)
	Progressive disease	1 (7.1)	1 (7.7)
Disease control rate		**13 (92.9)**	**12 (92.3)**
[95% CI]		[66.1, 99.8]	[64.0, 99.8]

- In the 1L setting, ORRs were **50.0%** for Cohort 2 and **76.9%**[b] for Cohort 4
- In the overall population (1L/2L+), ORRs were **47.4%** for Cohort 2 (N=19) and **71.4%**[b] for Cohort 4 (N=14)
- Responses were numerically higher with the triplet versus doublet combination and were observed across all PD-L1 expression levels

Data cut-off: March 6 2023.
All subjects must have had at least one scan (6 weeks of follow-up) to be included in the ORR interim analysis set. The 2-sided 95% CIs are exact Clopper-Pearson intervals. [a] As assessed by investigator per RECIST v1.1. [b] One of the 10 partial responses in Cohort 4 was confirmed after data cut-off.
CI, confidence interval.

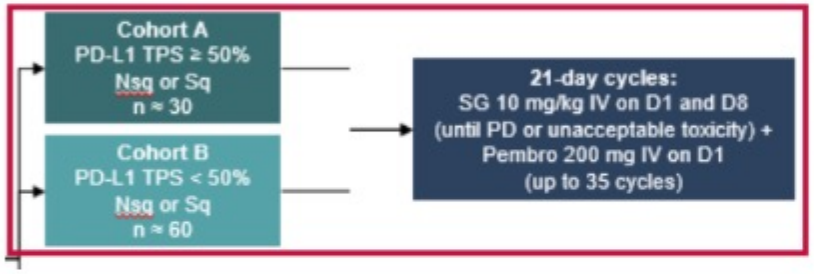
Safety

No new safety signals were observed in Cohort 2 and Cohort 4 investigating Dato-DXd in combination with durvalumab ± carboplatin, throughout dose escalation and dose expansion

The most frequent TEAEs of any grade were stomatitis, alopecia and nausea. In general, Grade ≥3 TEAEs were more frequently observed with the triplet versus the doublet combination, which was mainly driven by more hematological events. There were four cases of ILD adjudicated as drug-related, three of which were Grade 1 or 2

The Phase 3 AVANZAR trial in 1L is ongoing

EVOKE-02: An Open-Label, Multicohort Phase 2 Study, 1st Line

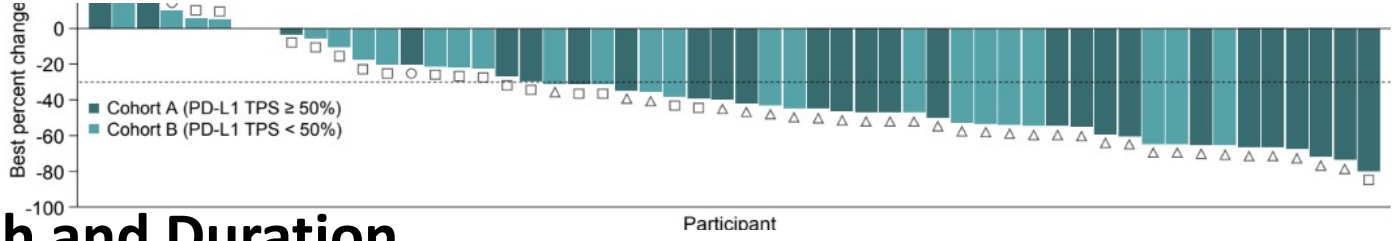


Efficacy by Investigator Assessment

Efficacy by INV[a]	Cohort A (PD-L1 TPS ≥ 50%) SG + Pembro n = 29	Cohort B (PD-L1 TPS < 50%) SG + Pembro n = 32	Total SG + Pembro n = 61
ORR[b] (95% CI), %	69 (49-85)	44 (26-62)	56 (42-69)
PR, n (%) – confirmed and unconfirmed	20 (69)	14 (44)	34 (56)
Confirmed PR, n (%)	18 (62)	12 (38)	30 (49)
SD, n (%)	5 (17)	11 (34)	16 (26)
PD, n (%)	3 (10)	2 (6)	5 (8)
DCR[c] (95% CI), %	86 (68-96)	78 (60-91)	82 (70-91)
Median DOR[d,e] (95% CI), months	NR (5.6-NR)	NR (3.5-NR)	NR (7.9-NR)
DOR rate at 6 months[d,e] (95% CI), %	88 (39-98)	88 (39-98)	87 (58-97)

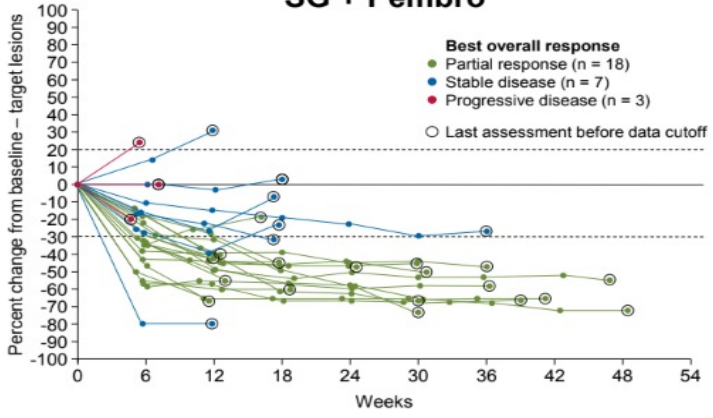
KEYNOTE 189: ORR: 62.1% (TPS≥50%), 50% (TPS 1-49%), 48.3% all comers

Waterfall Plot of Response

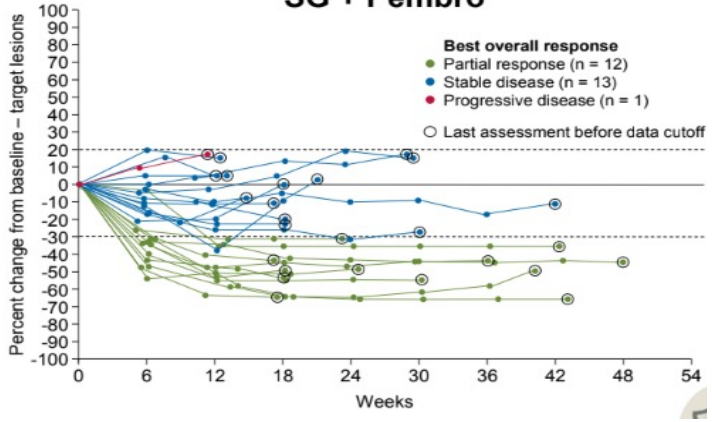


Depth and Duration

Cohort A (PD-L1 TPS ≥ 50%) SG + Pembro



Cohort B (PD-L1 TPS < 50%) SG + Pembro



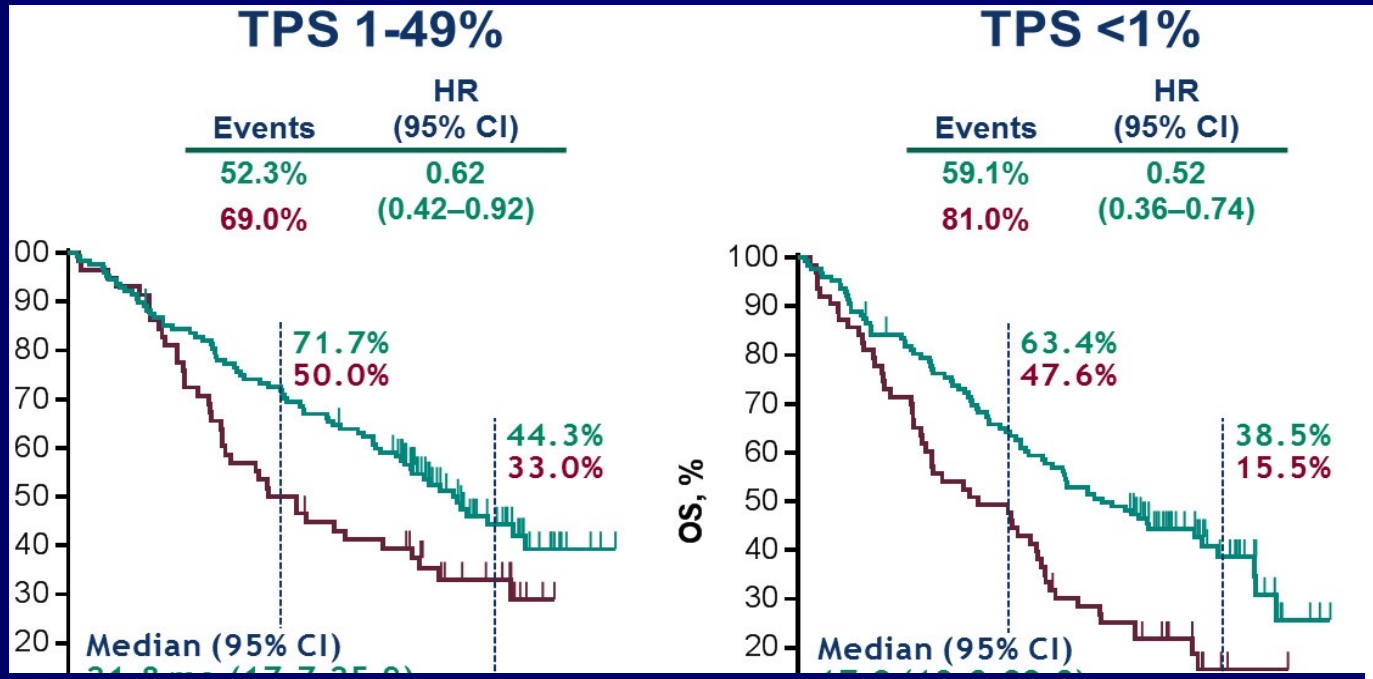
- SG + Pembro demonstrated encouraging antitumor activity in patients with 1L mNSCLC across PD-L
  - ORR was 69% and DCR was 86% in Cohort A
  - ORR was 44% and DCR was 78% in Cohort B
  - Median DOR was not reached, and DOR rate at 6 months was 88% in both cohorts
- The safety profile of SG + Pembro was manageable and consistent with the known safety of each ag
  - The most common any-grade TEAEs were diarrhea, anemia, and asthenia
  - TEAEs leading to treatment discontinuation were low (18%)

IO and CT/IO in stage 4 NSCLC No Driver Alteration: TPS1-49

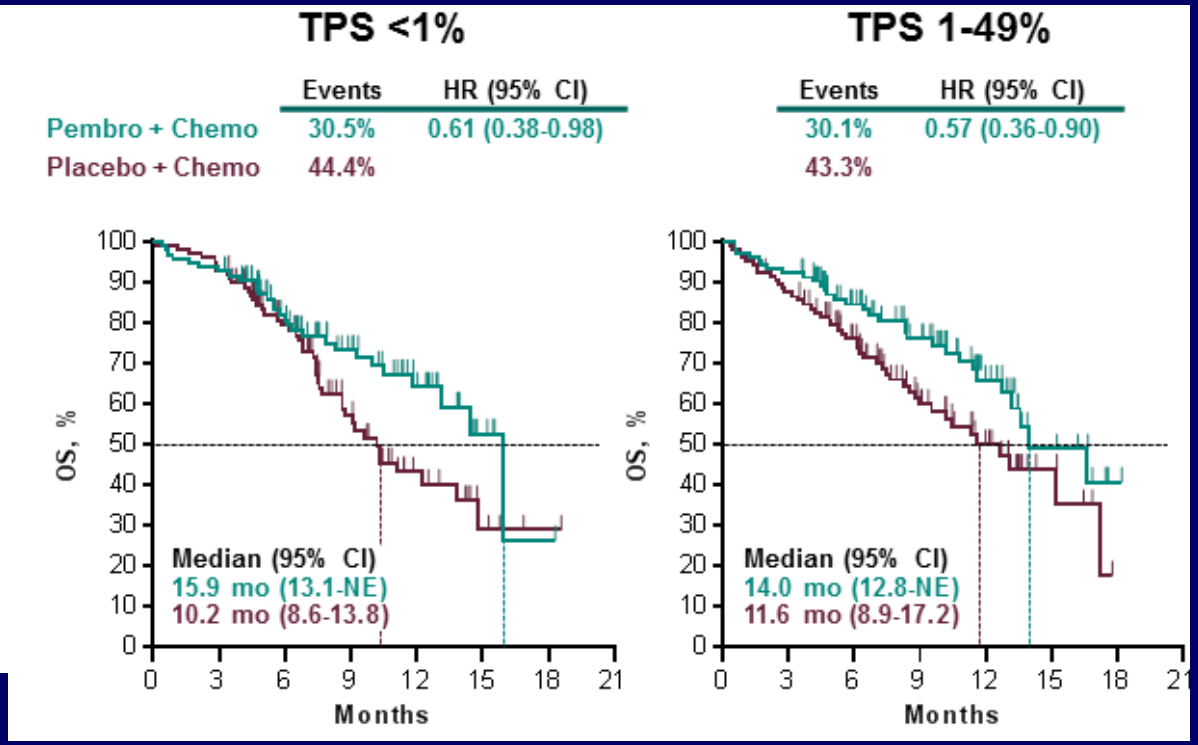
- Approved CT + IO: pembrolizumab, atezolizumab, nivolumab, durvalumab, cemiplimab, Tislelizumab, Sintilimab;Sugemalimab,toripalimab,camrelizumab
- Approved CT + IO combos: nivo+ipi, durva+tremi
- Approved IO combos: Nivo+Ipi; durva+tremi
- Investigational IO/IO combos anti-Tigit,
- Investigational:Duration of Therapy?

IO and CT/IO in stage 4 NSCLC & no Driver Alteration: TPS 0-49

Non-sq Ca

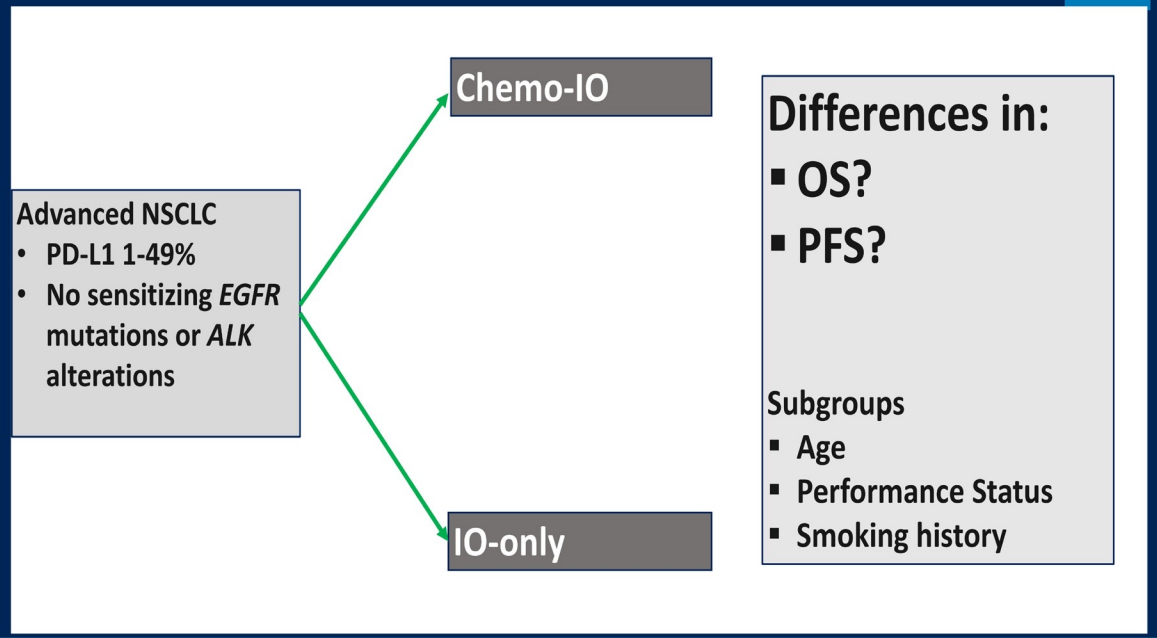


Squamous Ca



FDA Pooled Analysis of Trials in TPS 1-49: ?Role of IO alone vs IO+CT

Exploratory Questions: NSCLC PD-L1 1-49%



Trials supporting FDA approval of first-line Chemo-IO and IO-only regimens

Trial*	Active treatment
Immunotherapy-only (PD-L1 ≥1%)	
KEYNOTE-042	**Pembrolizumab**
CHECKMATE-227	**Nivolumab plus Ipilimumab**
Chemo-immunotherapy	
KEYNOTE-189	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-407	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-021 (cohort G)	**Pembrolizumab** plus Platinum-doublet chemo
IMPOWER-150**	**Atezolizumab** plus Bevacizumab plus Platinum-doublet chemo
IMPOWER-130	**Atezolizumab** plus Platinum-doublet chemo
CA2099LA	**Nivolumab plus Ipilimumab** plus Platinum-doublet chemo

*Control arms: Platinum-doublet chemotherapy
**Control arm in IMPOWER-150: Bevacizumab plus Platinum-doublet chemotherapy

Presented By:
Oladimeji Akinboro; June 4, 2021

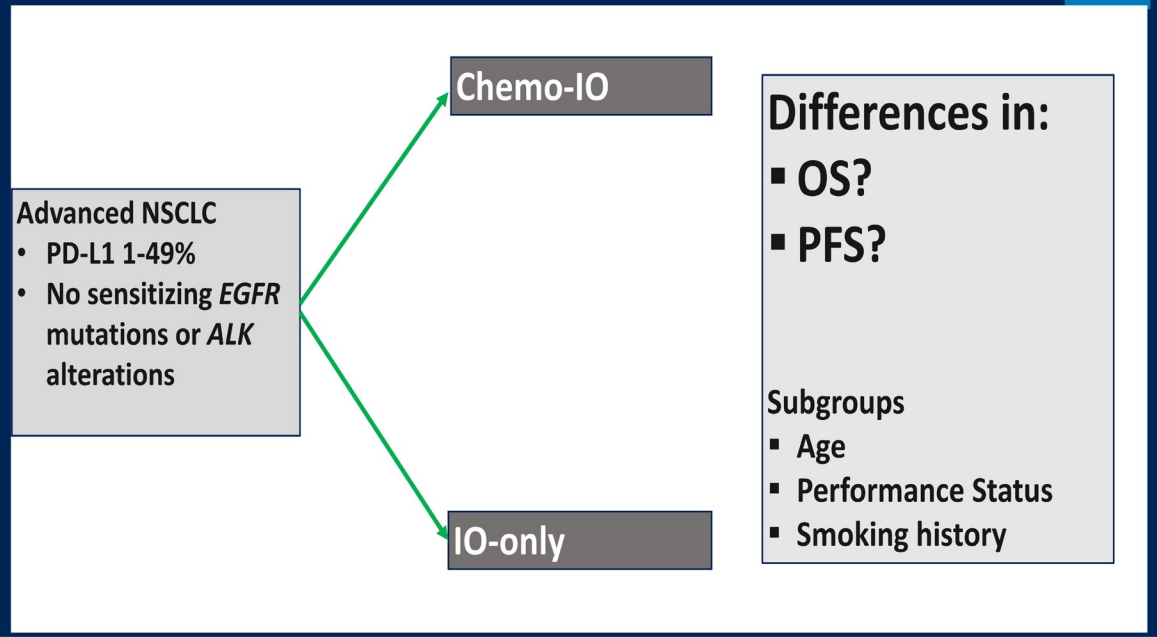
#ASCO21 | Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

2021 ASCO ANNUAL MEETING

FDA Pooled Analysis

Exploratory Questions: NSCLC PD-L1 1-49%

FDA



Trials supporting FDA approval of first-line Chemo-IO and IO-only regimens

FDA

Trial*	Active treatment
Immunotherapy-only (PD-L1 ≥1%)	
KEYNOTE-042	**Pembrolizumab**
CHECKMATE-227	**Nivolumab plus Ipilimumab**
Chemo-immunotherapy	
KEYNOTE-189	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-407	**Pembrolizumab** plus Platinum-doublet chemo
KEYNOTE-021 (cohort G)	**Pembrolizumab** plus Platinum-doublet chemo
IMPOWER-150**	**Atezolizumab** plus Bevacizumab plus Platinum-doublet chemo
IMPOWER-130	**Atezolizumab** plus Platinum-doublet chemo
CA2099LA	**Nivolumab plus Ipilimumab** plus Platinum-doublet chemo

*Control arms: Platinum-doublet chemotherapy
**Control arm in IMPOWER-150: Bevacizumab plus Platinum-doublet chemotherapy

Presented By:
Oladimeji Akinboro; June 4, 2021

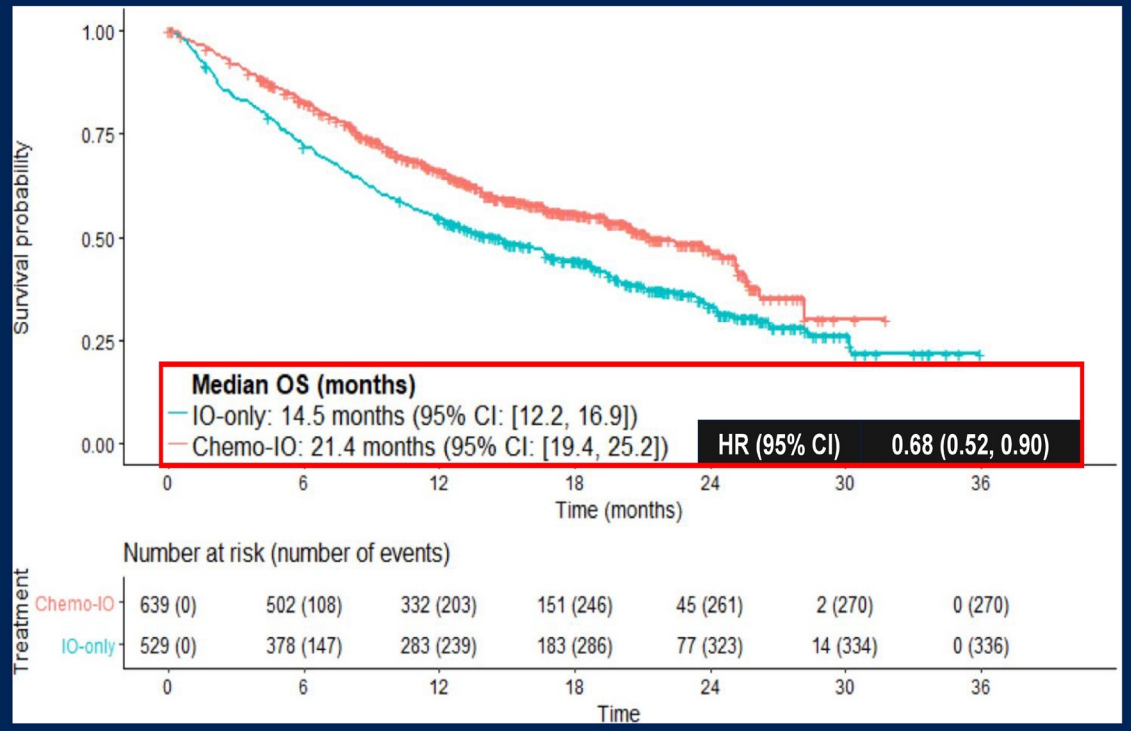
#ASCO21 | Content of this presentation is the property of the author, licensed by ASCO. Permission required for reuse.

2021 ASCO ANNUAL MEETING

FDA Pooled Analysis of Trials in TPS 1-49: ?Role of CT

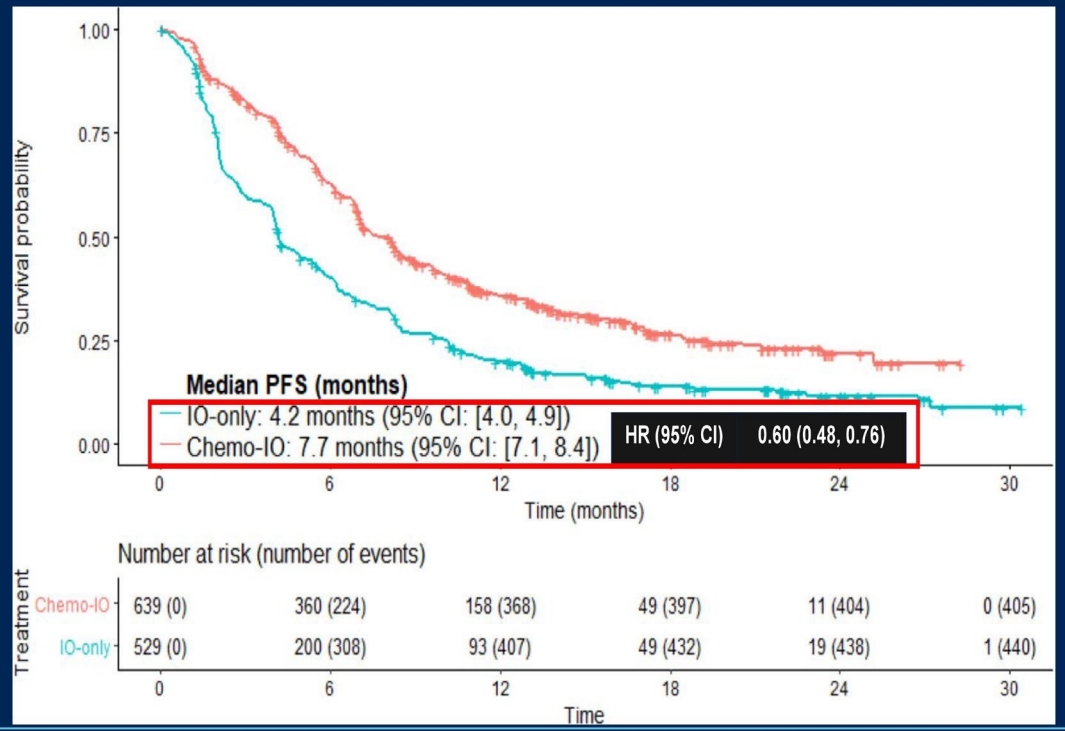
Exploratory OS: NSCLC PDL1 1-49%

FDA



Exploratory PFS: NSCLC PDL1 1-49%

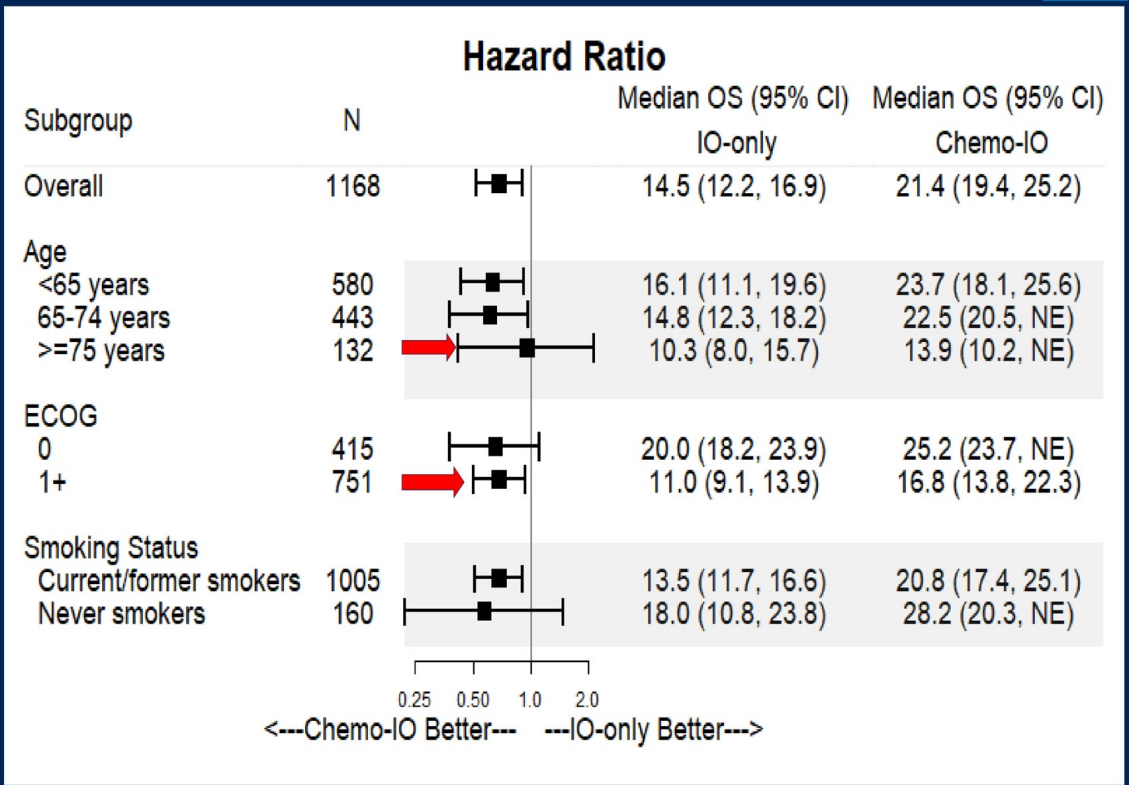
FDA



IO vs CT/IO in stage 4 NSCLC & no Driver Alteration: TPS 1-49

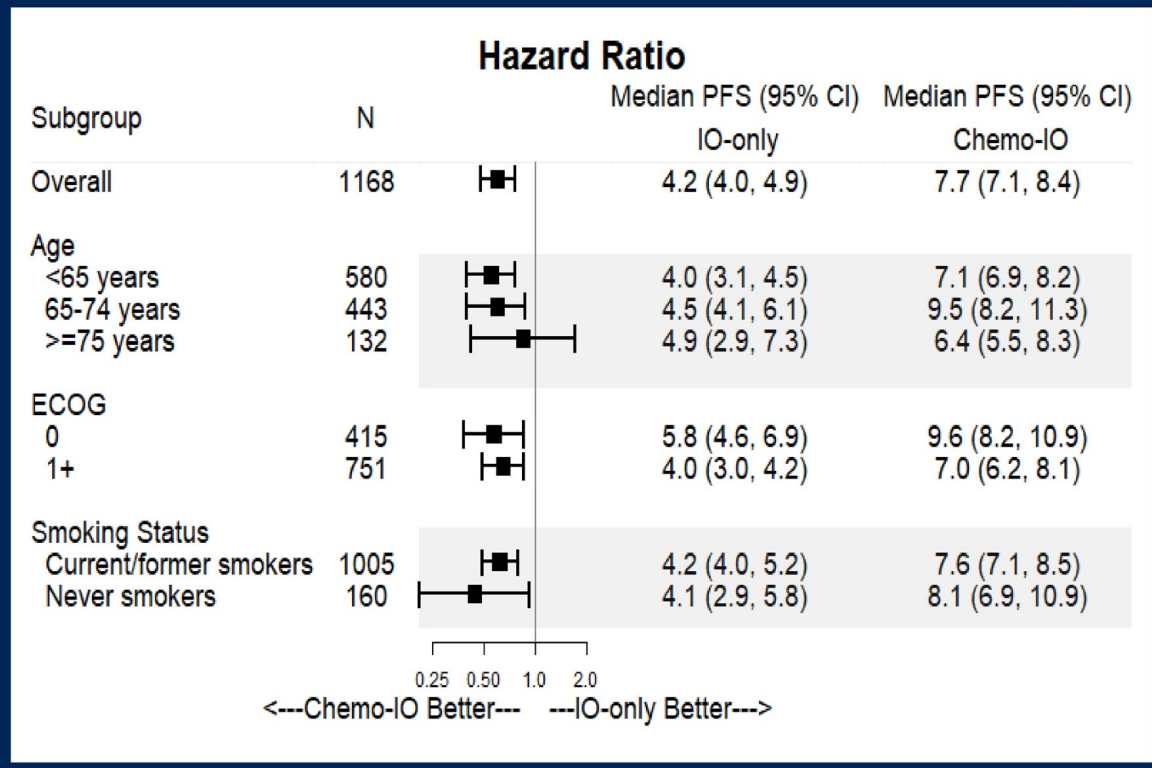
OS in PDL1 1-49%: Subgroup analyses

FDA



PFS in PDL1 1-49%: Subgroup analyses

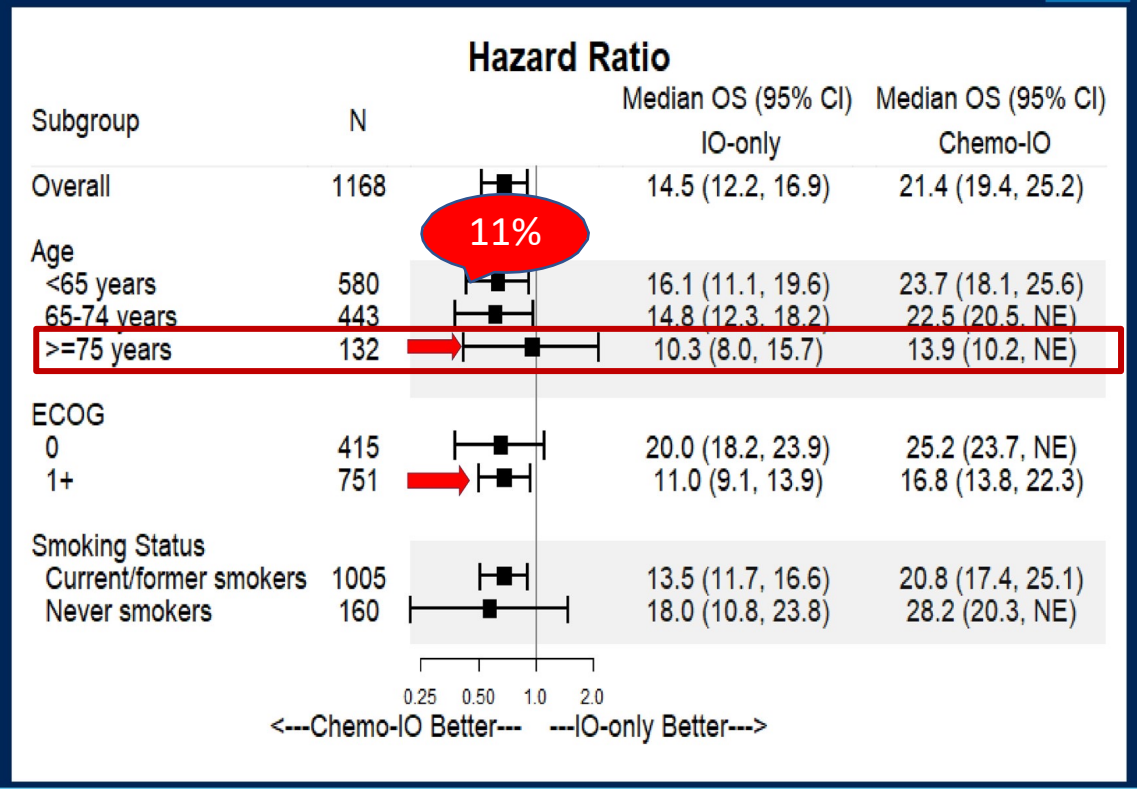
FDA



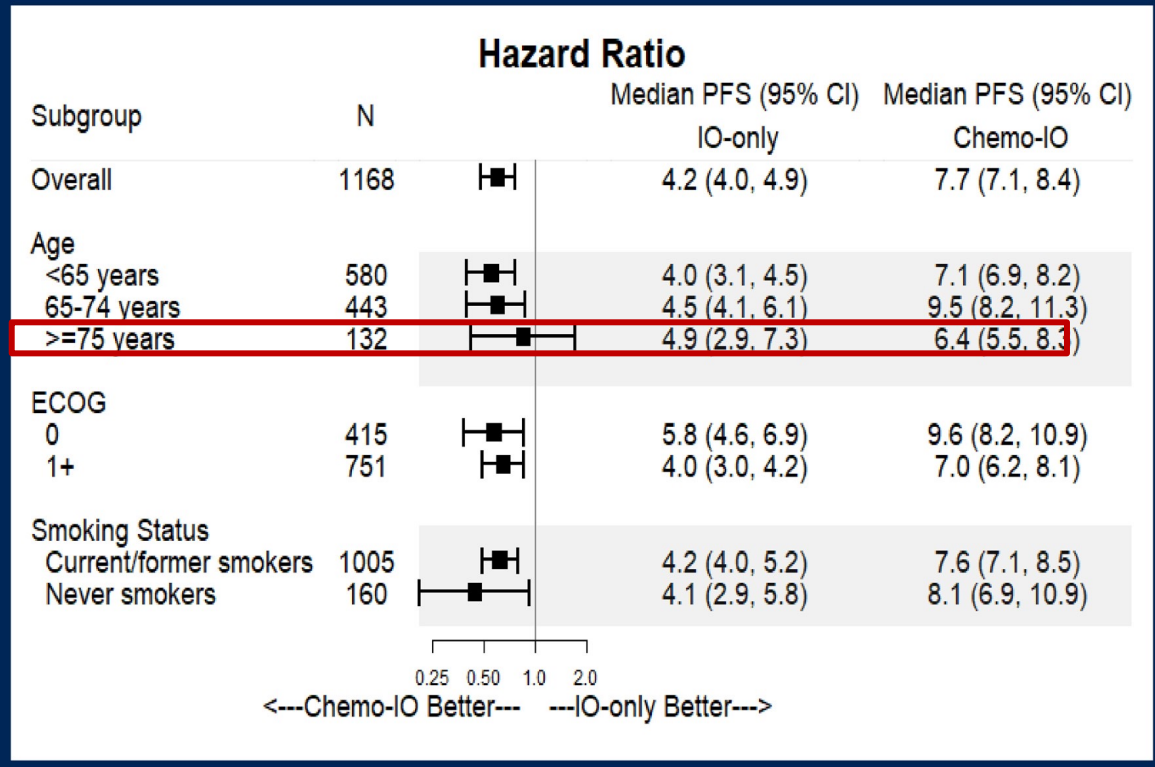
Conclusion: IO equivalent in elderly patients

Is there an elderly subgroup of patients that would be appropriate for monotherapy?

OS in PDL1 1-49%: Subgroup analyses



PFS in PDL1 1-49%: Subgroup analyses



IO + LAG-3 Trials, Lung Cancer

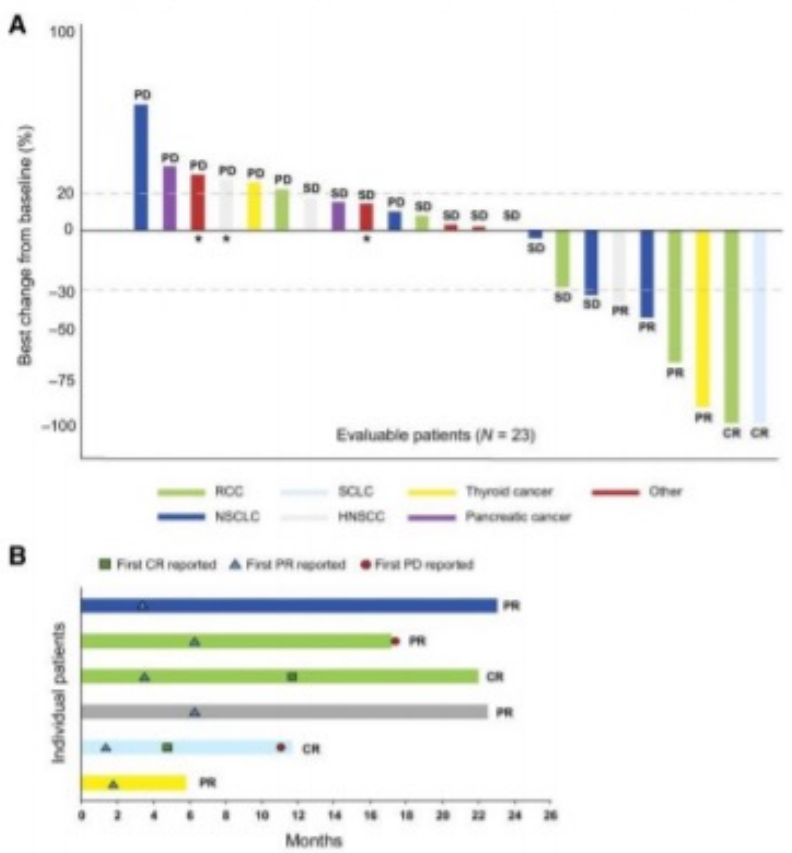
Investigational Agents	Tumor types	Status
MP321 (Soluble LAG-3 fusion protein) + Pembro	IO-naïve or refractory NSCLC	Enrolling
LAG525 (Anti-LAG-3) +/- Spartalizumab (Anti-PD-1)	Multiple Tumor types, Including NSCLC	Active, not recruiting
ym021 (Anti-PD-1) + Sym022 Anti-LAG-3) or Sym023 (Anti-TIM-3)	Multiple tumor types, Including **SCLC**	Enrolling
REGN3767 (Anti-LAG-3) +/- Cemiplimab	Multiple tumor types	Enrolling
XmAb22841 (Bispecific Ab LAG-3/CTLA-4) + Pembrolizumab	Multiple tumor types, Including NSCLC and SCLC	Enrolling
RO7247669 (PD-1/LAG-3 bispecific Ab)	Multiple tumor types, including NSCLC	Enrolling

IO + Anti-OX40 Trials

Study Agent	Tumor Type	Enrollment
MOXR0916 + Atezolizumab	Multiple	Completed ASCO 2016* Further development terminated
BBV-927 (OX40 agonist) +CD 40 agonist +/- anti-PD1	Multiple Including NSCLC	Ongoing
PF-04518600 (OX40 agonist) +/- 4-1BB (CD137) agonist	Multiple	Recruitment completed
INHBRX-106 (Hexavalent OX40 agonist) +/- Pembrolizumab	Multiple Including NSCLC	Ongoing
SL-279252 (PD1-Fc-OX40L =Fc domain linked fusion protein)	Multiple Including NSCLC	Ongoing
ATOR-1015 CTLA-4 x OX40 bispecific Ab)	Multiple	Ongoing
HS-130 (OX40L fusion protein) + Viagenpumatucel-L	Multiple	Ongoing

4-1BB (CD137) Combinations
Advanced NSCLC

Ph I Utomilumab + Pembrolizumab



ORR 26%; durable responses in NSCLC

Anti-CD137 + Anti-PD-1	
Utomilumab + Avelumab (JAVELIN medley)	Ph I trial (Active multiple sites)
Utomilumab + OX40 Agonist (PF0458600)	Ph I/II trial: completed (28 sites, NSCLC included)
Anti-CD137 + SBRT	
Urelumab (cohort) + SBRT	Ph I trial (U Chicago, NSCLC cohort)
Anti-CD137 intratumoral injection + Anti-PD-1	
IT Urelumab + Nivolumab	Ph I/II trial (U Navarra, solid tumors)
Anti-CD137/PD-L1 Bi-specific	
INBRX-105	FIH trial in solid tumors (1/90 accrued)

Tolcher et al, Clin Cancer Res 2017
Etxeberria et al, ESMO Open 2020

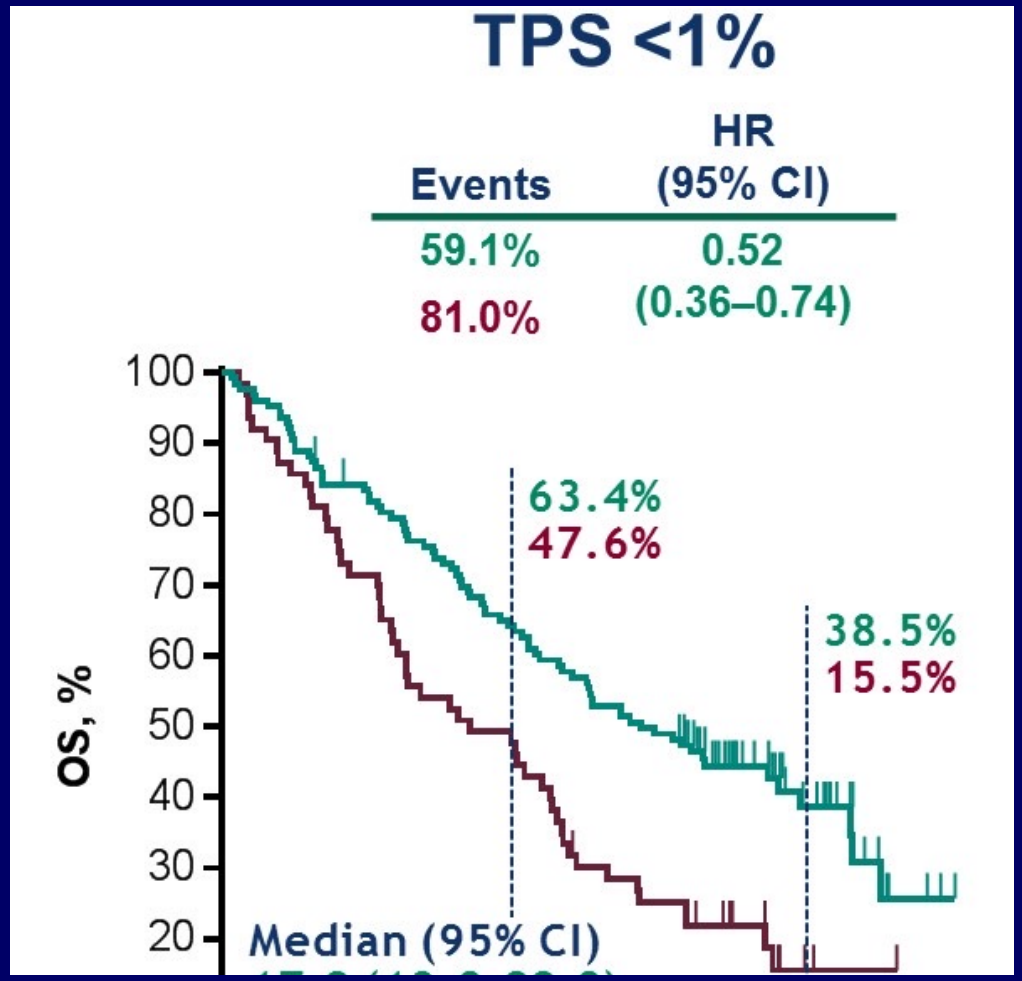
IO and CT/IO in stage 4 NSCLC: TPS <1

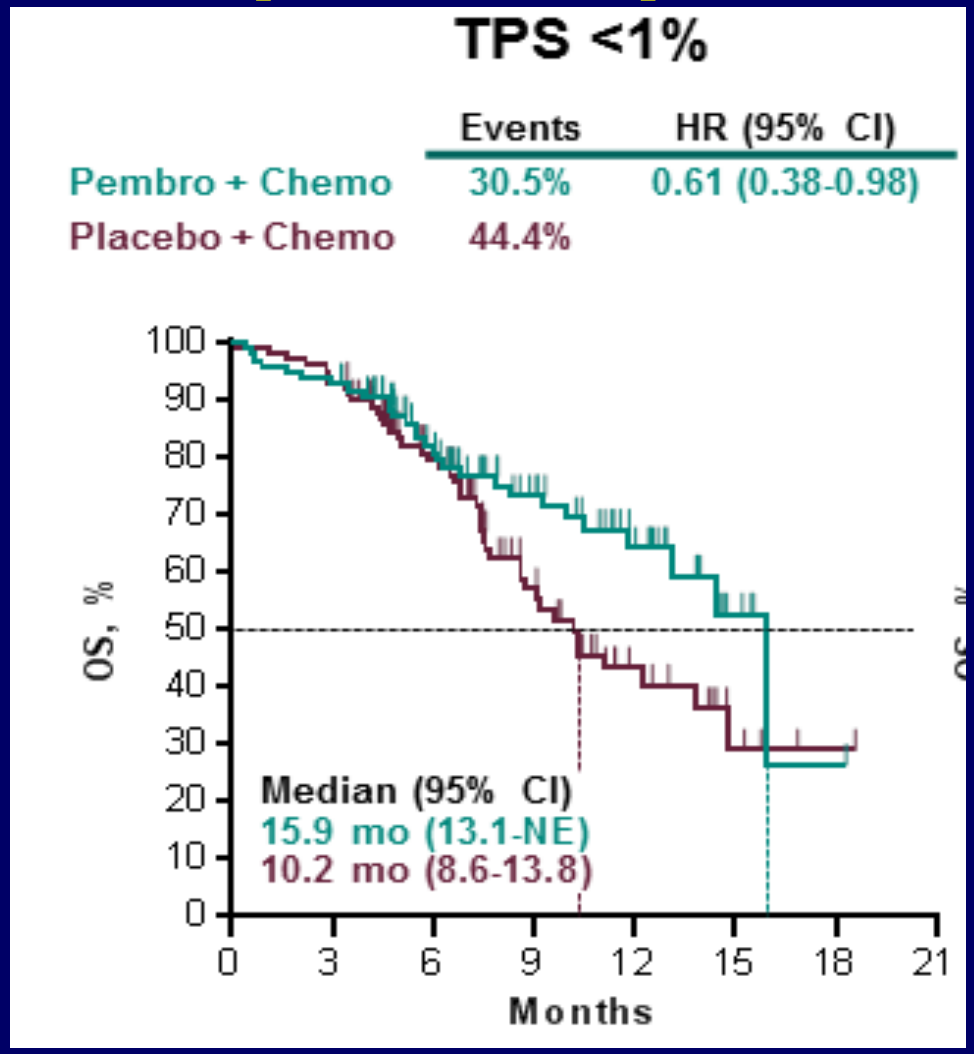
- Approved CT + IO: pembrolizumab, atezolizumab, nivolumab, durvalumab, cemiplimab, tos
- Approved IO combos: nivo+ipi, durva+tremi
- Approved CT+IO combos

Investigational IO/IO combos

Investigational: Duration of Therapy?

OS in TPS <1 in Non Sq and Sq CA





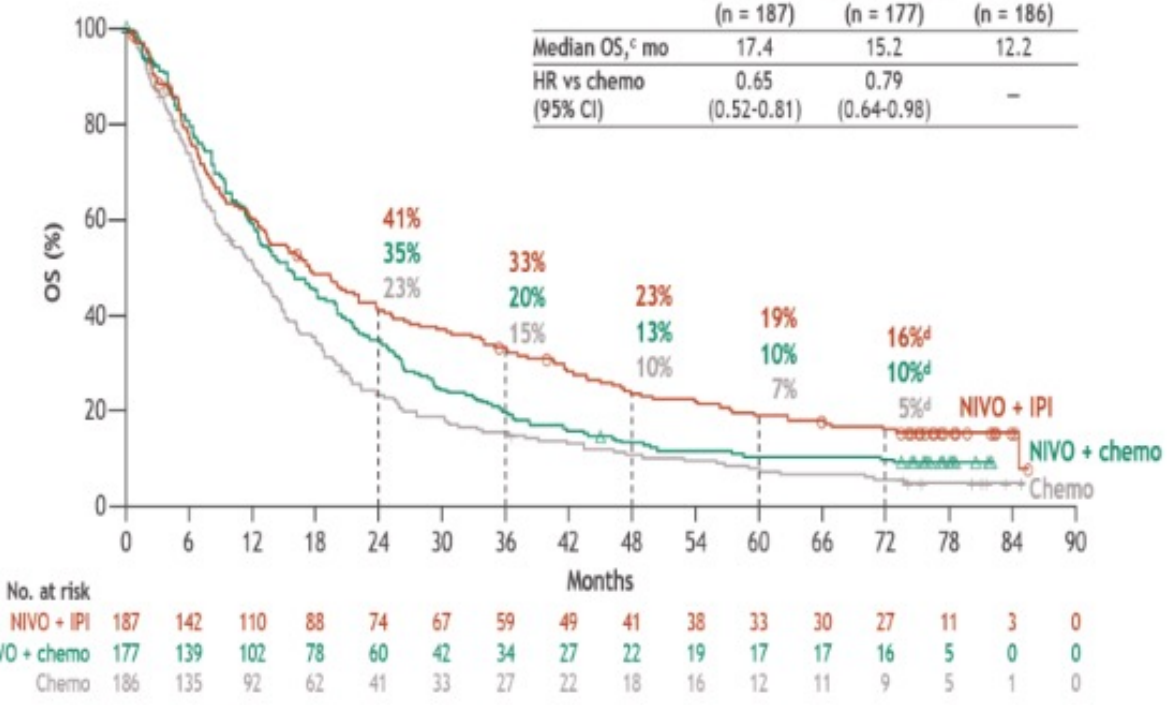
Conclusion: CT+IO produces some long-term survivors but fewer than in patients with higher TPS

Do individual patients benefit selectively from distinct immunotherapies? Which patients need CTLA-4 blockade?

CM227, PD-L1 ≤ 1%

OS

	NIVO + IPI[b] (n = 187)	NIVO + chemo (n = 177)	Chemo (n = 186)
Median OS,[c] mo	17.4	15.2	12.2
HR vs chemo (95% CI)	0.65 (0.52-0.81)	0.79 (0.64-0.98)	–

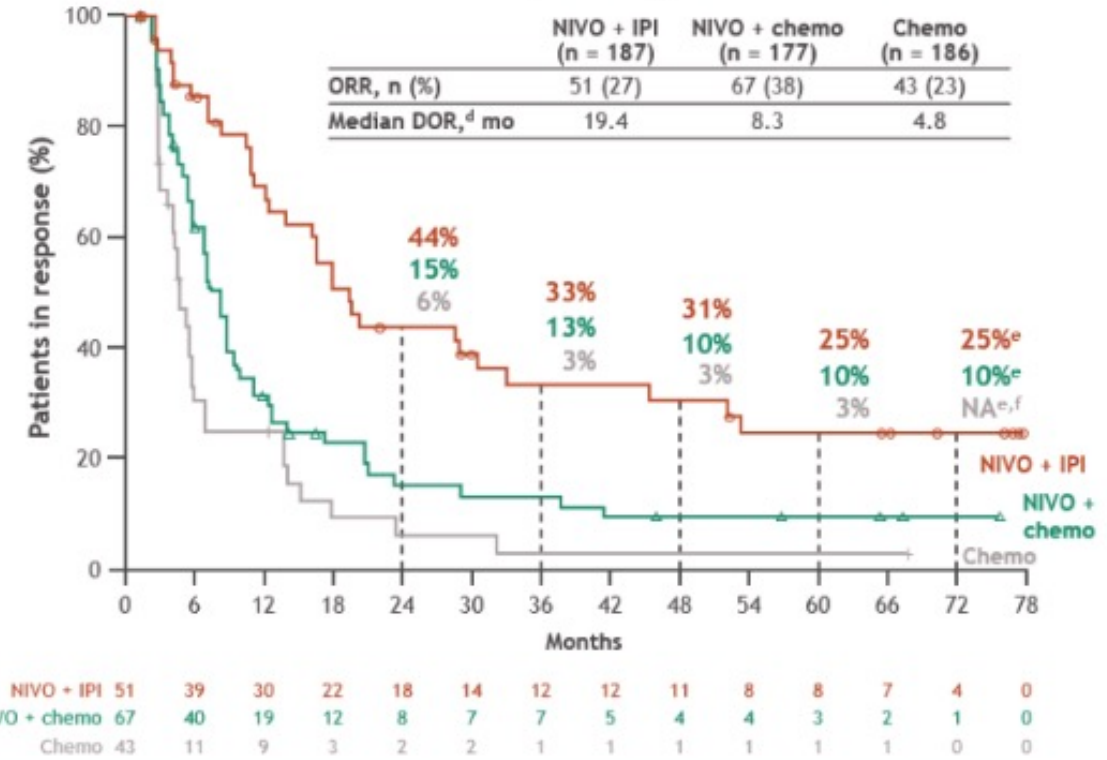


No. at risk

NIVO + IPI	187	142	110	88	74	67	59	49	41	38	33	30	27	11	3	0
NIVO + chemo	177	139	102	78	60	42	34	27	22	19	17	17	16	5	0	0
Chemo	186	135	92	62	41	33	27	22	18	16	12	11	9	5	1	0

DoR

	NIVO + IPI (n = 187)	NIVO + chemo (n = 177)	Chemo (n = 186)
ORR, n (%)	51 (27)	67 (38)	43 (23)
Median DOR,[d] mo	19.4	8.3	4.8



NIVO + IPI	51	39	30	22	18	14	12	12	11	8	8	7	4	0
NIVO + chemo	67	40	19	12	8	7	7	5	4	4	3	2	1	0
Chemo	43	11	9	3	2	2	1	1	1	1	1	1	0	0

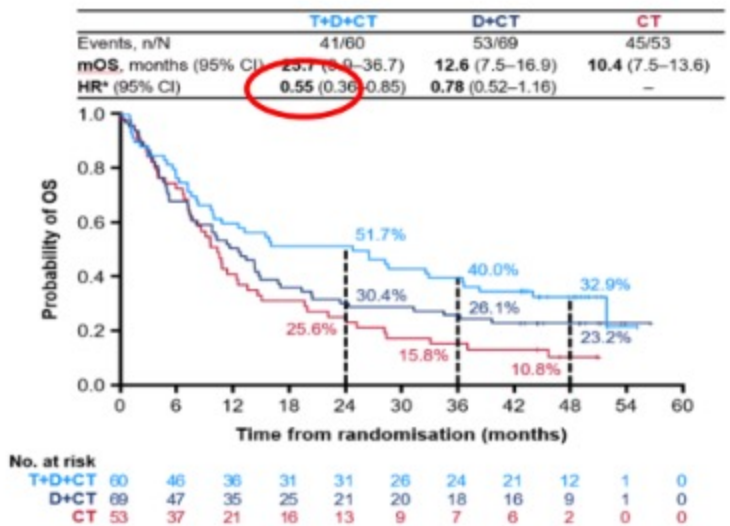
- In patients with SQ NSCLC and PD-L1 < 1% the 6 year OS rate with ipi/nivo vs chemo was 18% vs 4%

Ramalingam SS….Peters S et al, WCLC 2023

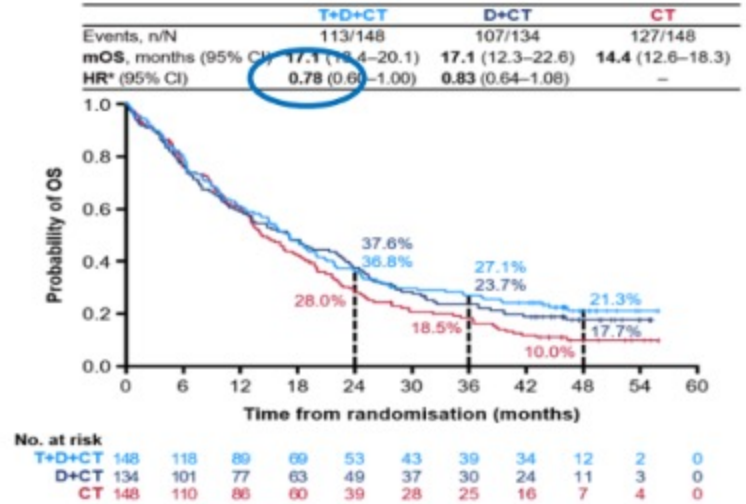
Patients with *KRAS*^{MUT} NSCLC may also benefit from dual ICB

POSEIDON

KRAS-mut

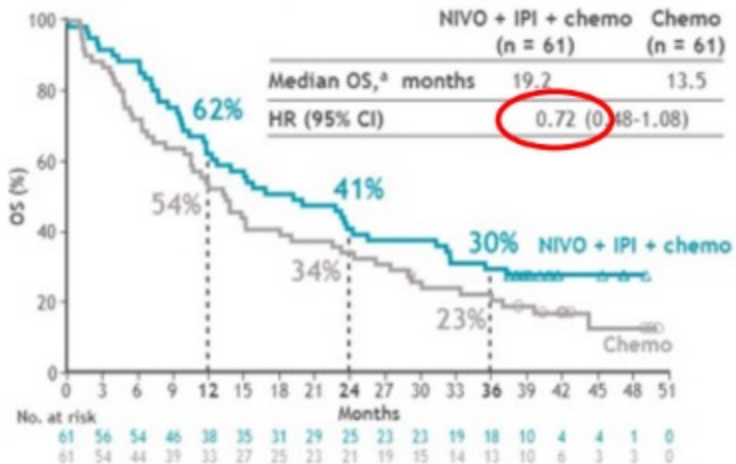


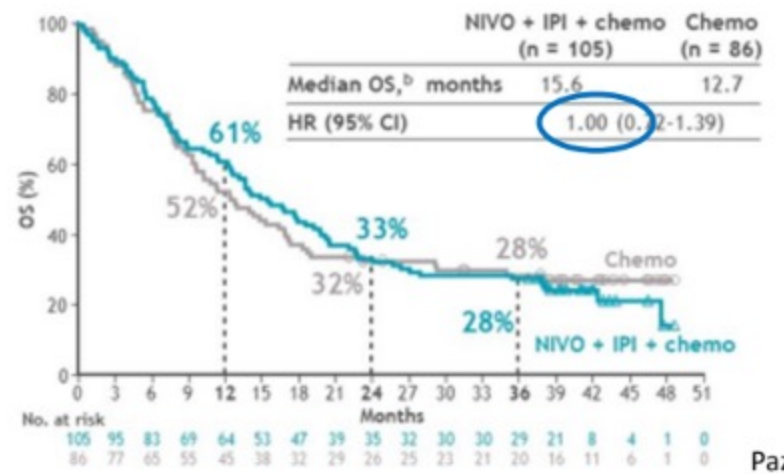
KRAS-wt



Johnson ML et al., ESMO, 2022

9-LA





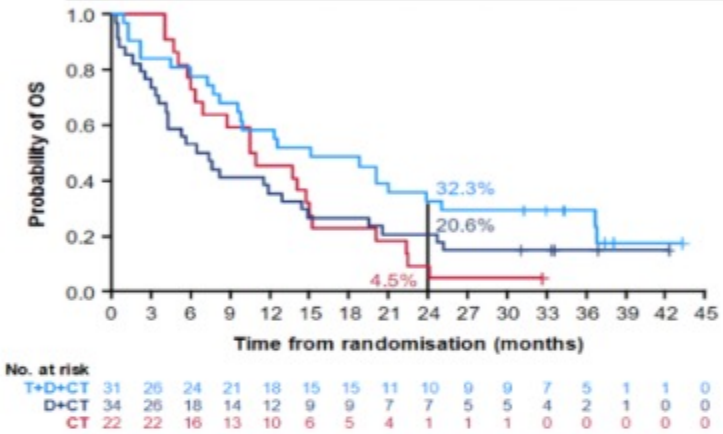
Paz-Ares L et al., ASCO, 2022

Patients with *STK11*^{MUT} and/or *KEAP1*^{MUT} nsNSCLC may benefit from dual ICB

POSEIDON

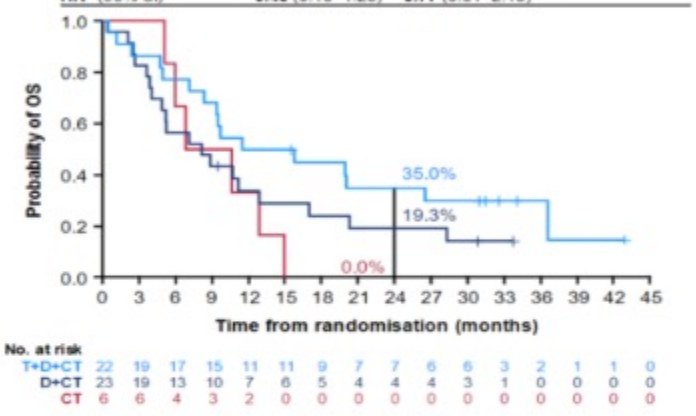
STK11-mut

	T+D+CT	D+CT	CT
Events, n/N	24/31	29/34	21/22
mOS, mo (95% CI)	**15.0** (8.2–23.8)	**6.9** (3.6–12.9)	**10.7** (6.0–14.9)
HR* (95% CI)	**0.56** (0.30–1.03)	**1.03** (0.59–1.84)	–



KEAP1-mut

	T+D+CT	D+CT	CT
Events, n/N	16/22	19/23	6/6
mOS, mo (95% CI)	**13.7** (7.2–26.5)	**8.1** (4.0–12.9)	**8.7** (5.1–NE)
HR* (95% CI)	**0.43** (0.16–1.25)	**0.77** (0.31–2.15)	–



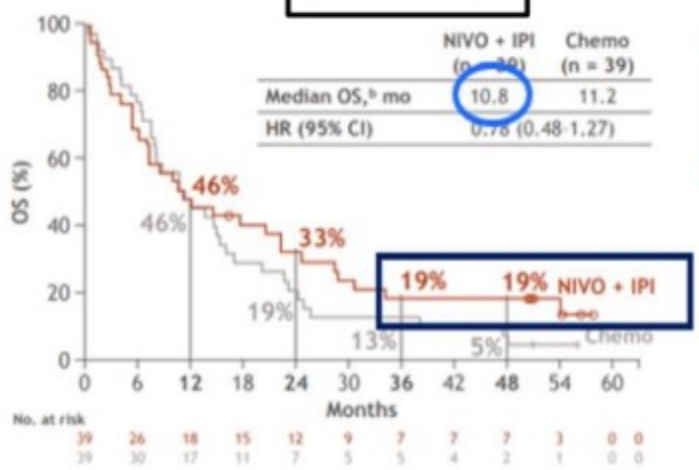
HR (95% CI) vs CT in NSQ *KEAP1*m was 0.33 (0.10–1.15) with T+D+CT and 0.67 (0.23–2.17) with D+CT

Peters S et al., WCLC, 2022

CM227

STK11-mut

	NIVO + IPI (n = 39)	Chemo (n = 39)
Median OS,[b] mo	10.8	11.2
HR (95% CI)	0.78 (0.48-1.27)	



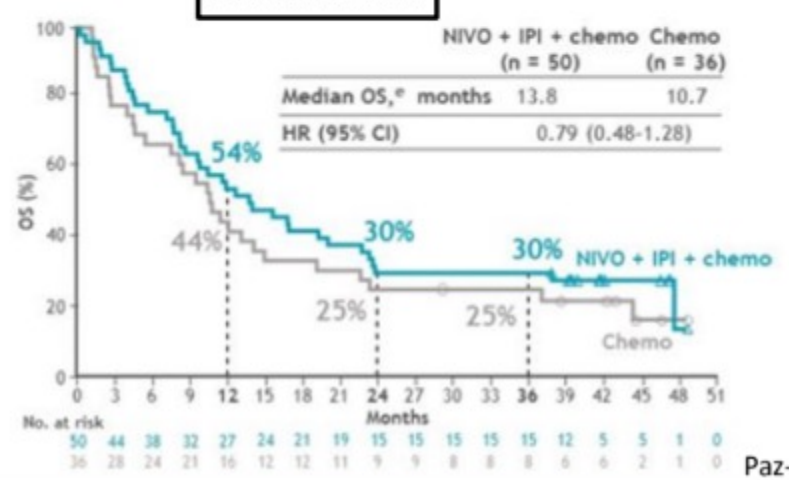
KEAP1^{MUT}(N=38)
Ipi/Nivo: mOS 24.4m
Chemo: mOS 8.9m

Ramalingam S et al.,
ESMO IO Congress,2021

9-LA

STK11-mut

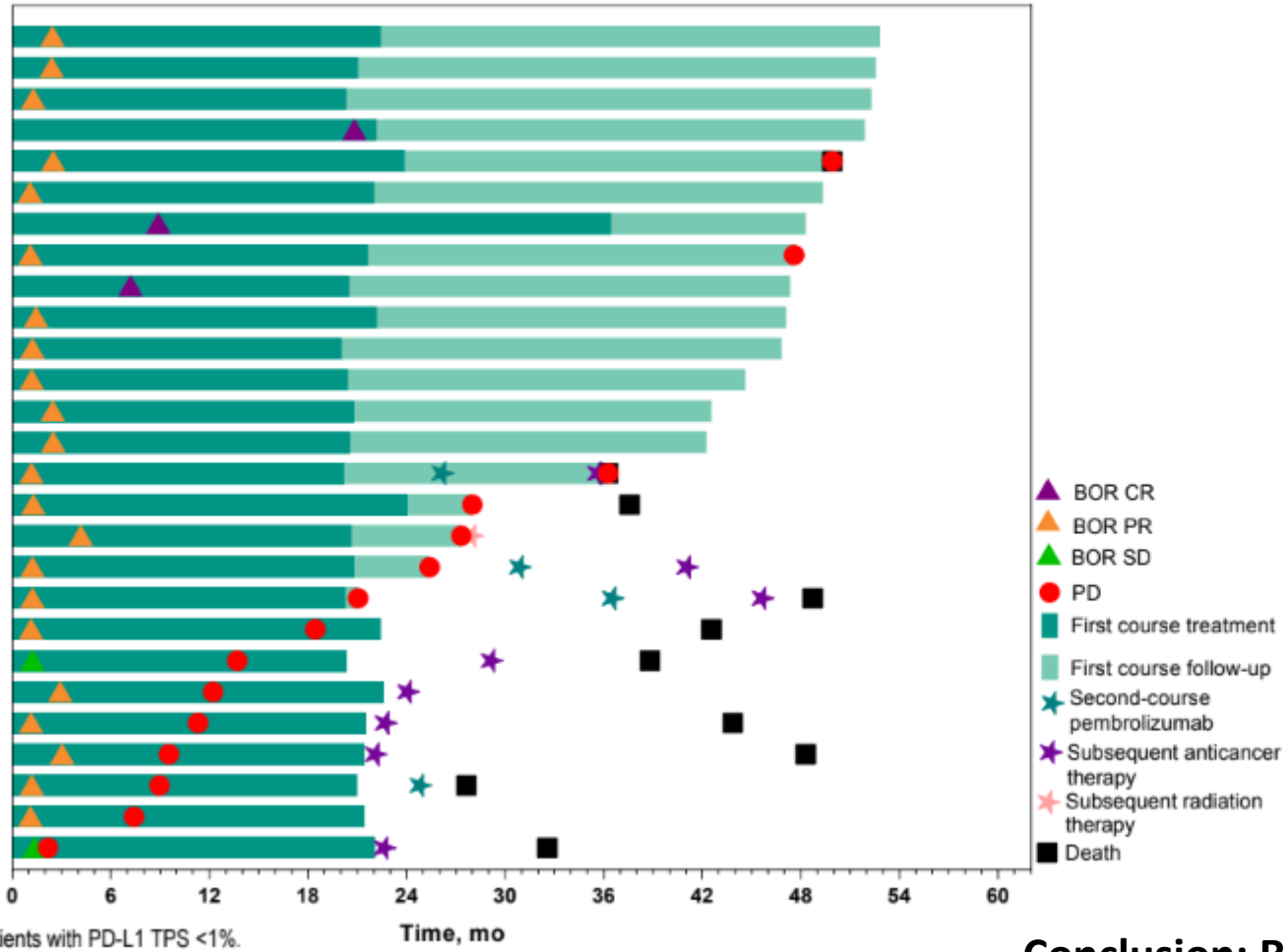
	NIVO + IPI + chemo (n = 50)	Chemo (n = 36)
Median OS,[c] months	13.8	10.7
HR (95% CI)	0.79 (0.48-1.28)	



Paz-Ares L et al., ASCO, 2022

Outcome of patients who discontinue IO and then later progress?

Outcomes in Patients Who Completed 35 Cycles of Pembrolizumab[a]

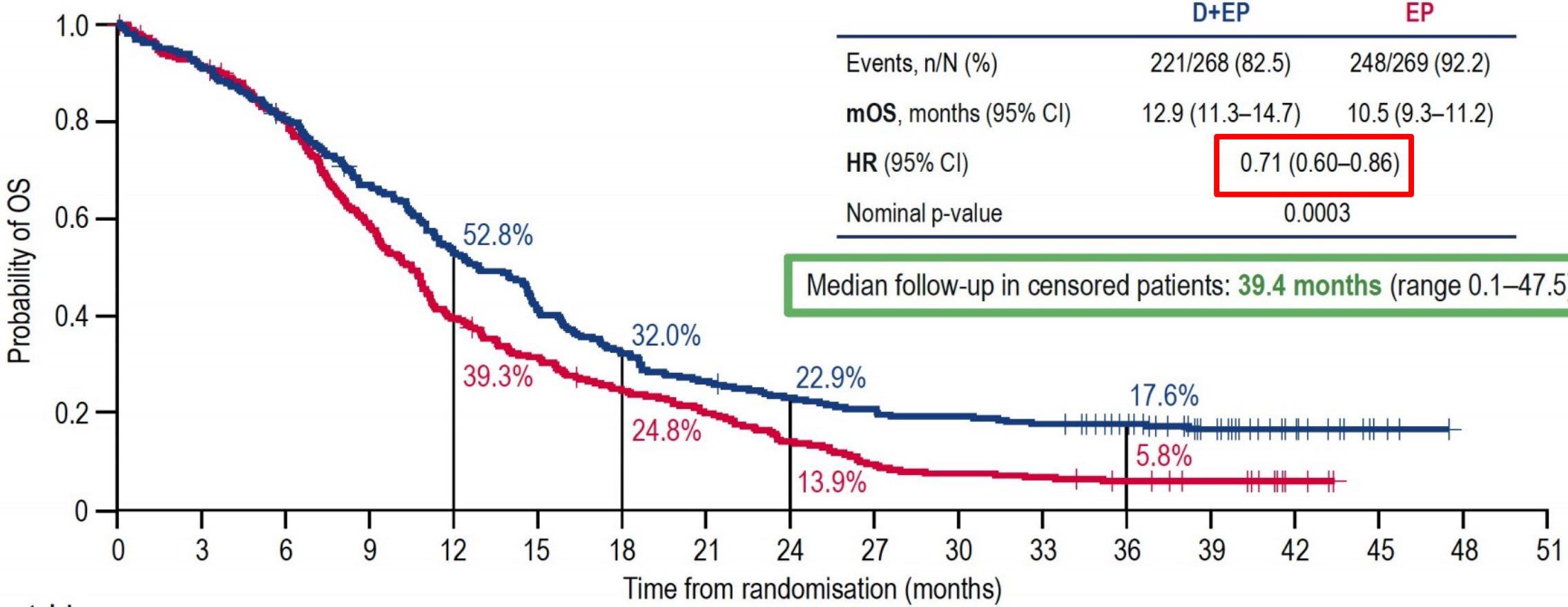


Outcome	Patients who completed 35 cycles[a] n = 27
ORR[b] (95% CI), %	92.6 (75.7–99.1)
Best overall response, n (%)	
Complete response	3 (11.1)
Partial response	22 (81.5)
Stable disease[c]	2 (7.4)
Median DOR (range), mo	55.1 (7.4 to 59.3+)
3-year OS rate after completing 35 cycles, %	56.7
Alive without subsequent therapy or PD, n (%)	12 (44.4)

[a]Patients with PD-L1 TPS <1%.
[b]Response assessed per RECIST v1.1 per blinded independent central review.
[c]Includes SD and non-CR/non-PD.
Data cutoff dates: KN189 Global, March 8, 2022; KN189 Japan Extension, February 7, 2023; KN407 Global, February 23, 2022; KN407 China Extension, February 10, 2023.

Conclusion: Retreatment can be highly effective

CASPIAN 3-Year OS Update: Durvalumab + EP vs EP[1]



	D+EP	EP
Events, n/N (%)	221/268 (82.5)	248/269 (92.2)
mOS, months (95% CI)	12.9 (11.3–14.7)	10.5 (9.3–11.2)
HR (95% CI)	0.71 (0.60–0.86)	
Nominal p-value	0.0003	

Median follow-up in censored patients: **39.4 months** (range 0.1–47.5)

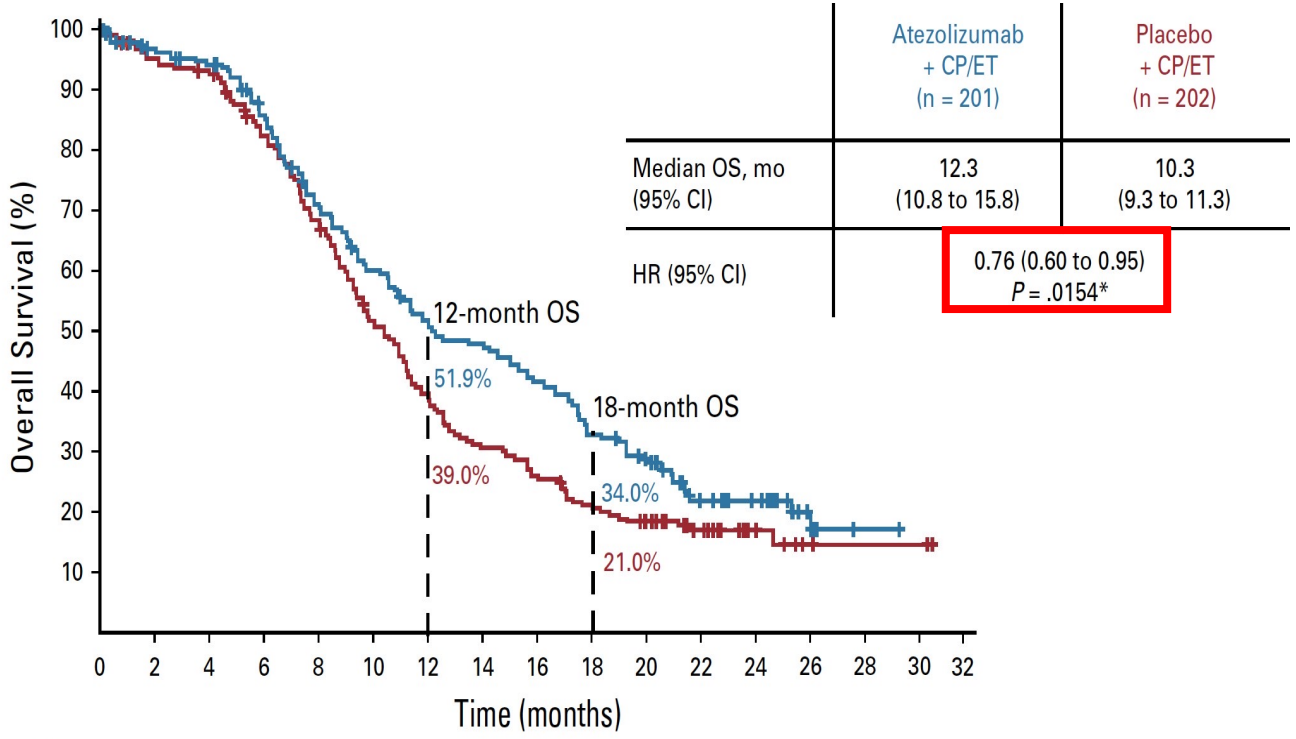
No. at risk

D+EP	268	244	214	177	140	109	85	70	60	54	50	46	39	25	13	3	0	0
EP	269	243	212	156	104	82	64	51	36	24	19	17	13	10	3	0	0	0

Data cutoff: March 22, 2021. Size of circle is proportional to the number of events across both treatment groups.

1. Paz-Ares LG et al. ESMO 2021. Abstract LBA61.

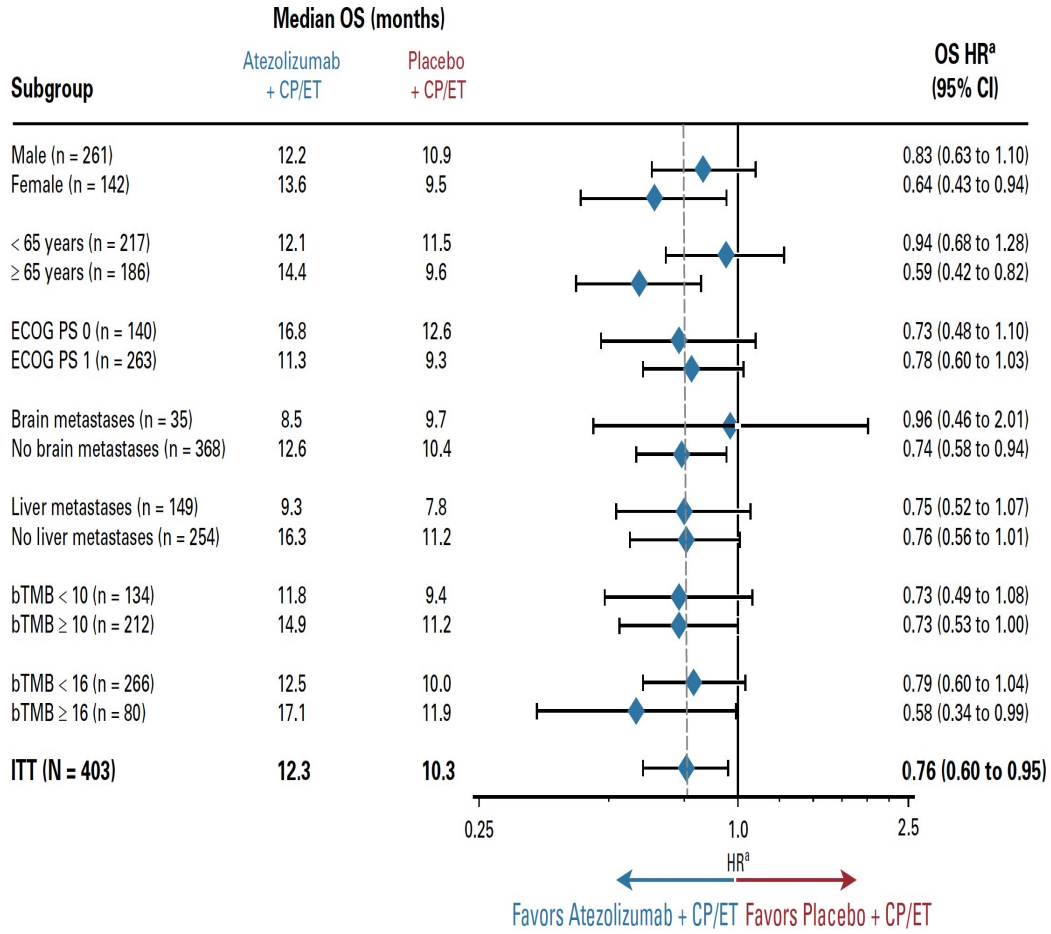
IMpower 133: Chemo +/- Atezolizumab



	Atezolizumab + CP/ET (n = 201)	Placebo + CP/ET (n = 202)
Median OS, mo (95% CI)	12.3 (10.8 to 15.8)	10.3 (9.3 to 11.3)
HR (95% CI)	0.76 (0.60 to 0.95) *P* = .0154*	

No. of Patients at Risk

Atezolizumab + CP/ET	201	187	180	159	130	109	93	86	75	61	51	28	21	8	1
Placebo + CP/ET	202	189	183	160	131	97	74	58	49	39	33	20	8	3	2	2

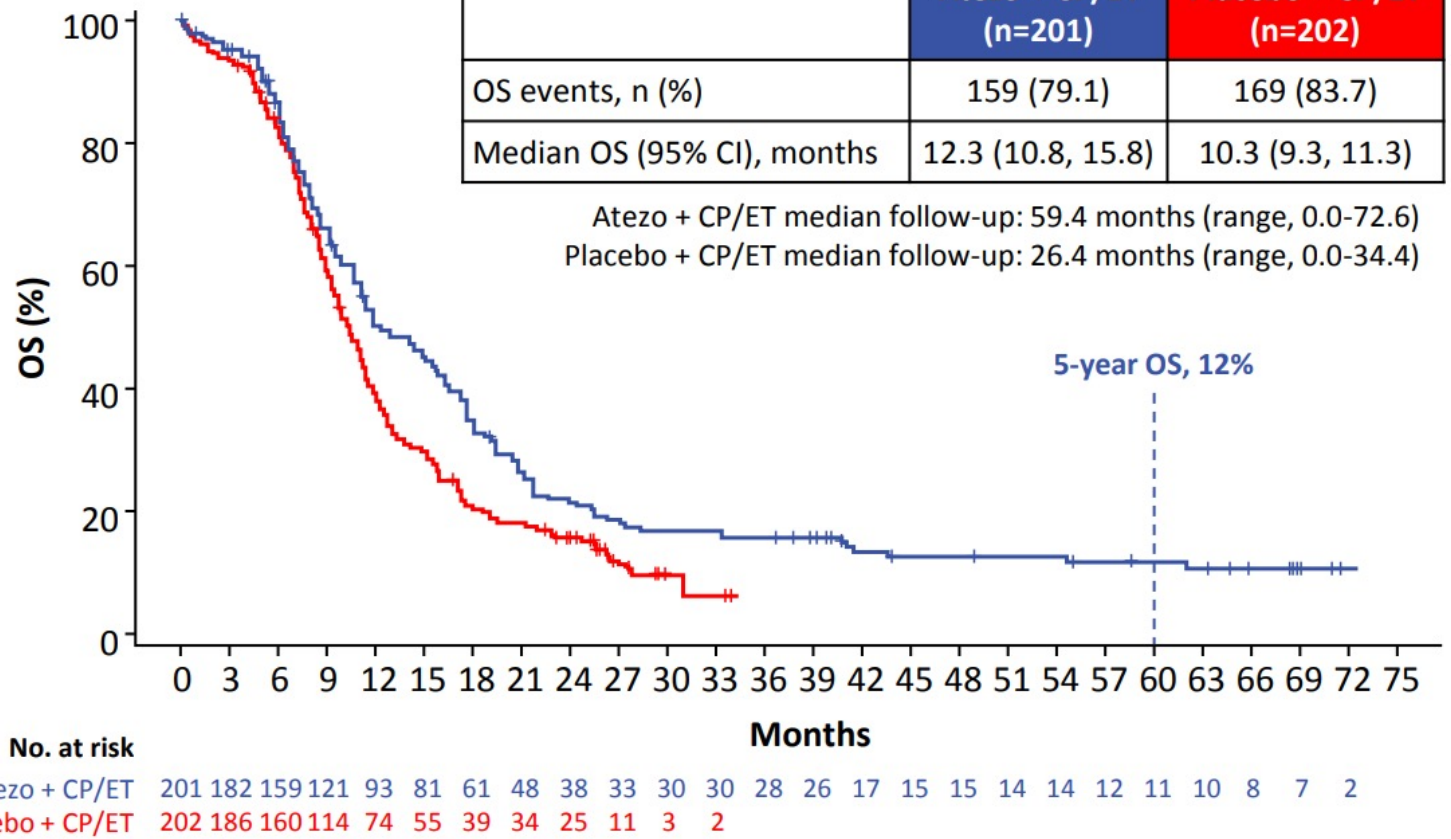


Liu et al, JCO 2021

IMpower133 and IMbrella A: long-term OS

	Atezo + CP/ET (n=201)	Placebo + CP/ET (n=202)
OS events, n (%)	159 (79.1)	169 (83.7)
Median OS (95% CI), months	12.3 (10.8, 15.8)	10.3 (9.3, 11.3)

Atezo + CP/ET median follow-up: 59.4 months (range, 0.0-72.6)
Placebo + CP/ET median follow-up: 26.4 months (range, 0.0-34.4)



OS rate (95% CI), %	IMpower133 and IMbrella A Atezo + CP/ET (n=201)	IMpower133 only Placebo + CP/ET (n=202)
1-year	52% (45-59)	39% (32-46)
2-year	22% (16-28)	16% (11-21)
3-year	16% (11-21)	NE[a]
4-year	13% (8-18)	NE[a]
5-year	12% (7-17)	NE[a]

Clinical cutoff date: 16 March 2023. NE, not estimable. [a] OS rates were NE in the control arm as rollover to IMbrella A was not permitted.