CAMPUS SEOM

Área de formación virtual SEOM

CNMP metastásico sin mutaciones

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SEOM
Sociedad Española de Oncología Médica

Disclosure

- ✓ I have received education grants, provided consultation, attended advisory boards and/or provided lectures from the following organizations:

  AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Roche, Eli Lilly, MSD, Takeda, GSK, Sanofi, Amgen, Janssen, Novartis, Merck & Pfizer.

- ✓ I declare no conflict of interest.

Background

1. Introduction: Stage IV NSCLC wt
2. Clinical Guidelines: Squamous NSCLC wt
3. Clinical Guidelines: Non-Squamous NSCLC wt
4. Conclusions: Take-home messages

Background

1. Introduction: Stage IV NSCLC wt
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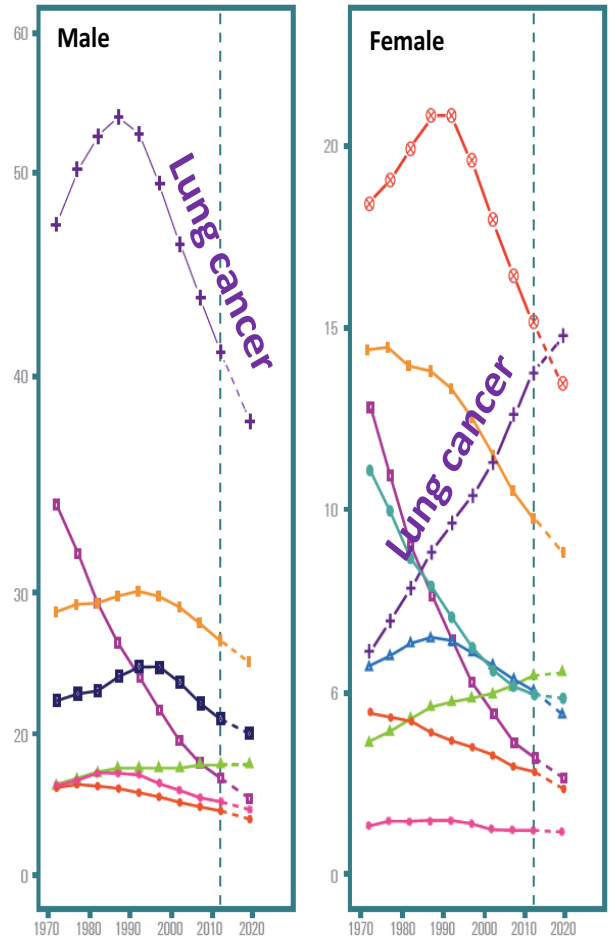
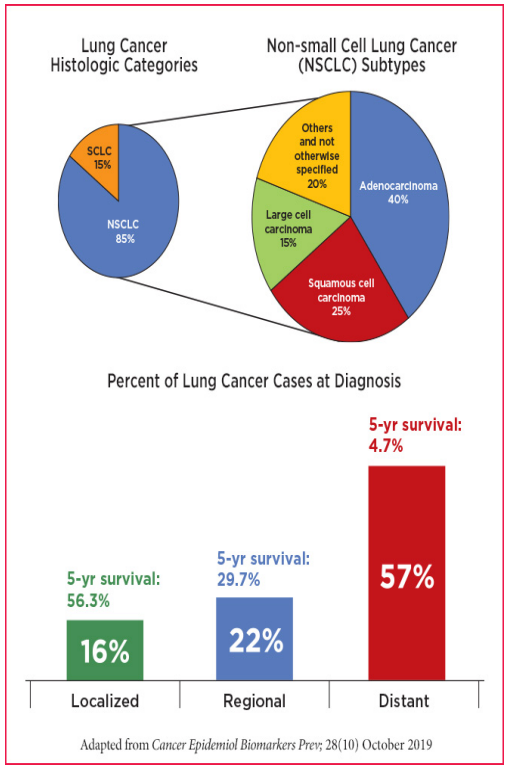
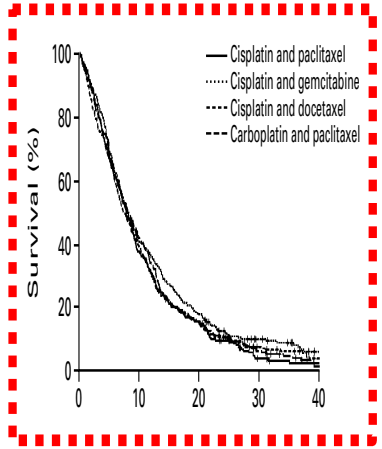
Stage IV NSCLC wt

Introduction: Historical approach



Standarized Mortality by age, Lung Cancer

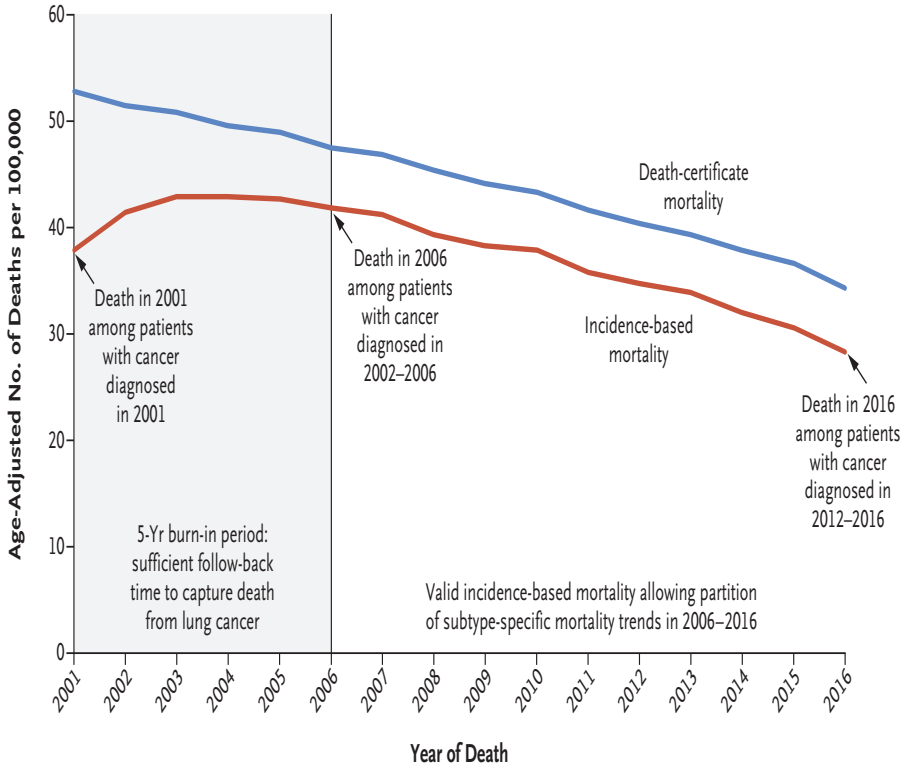


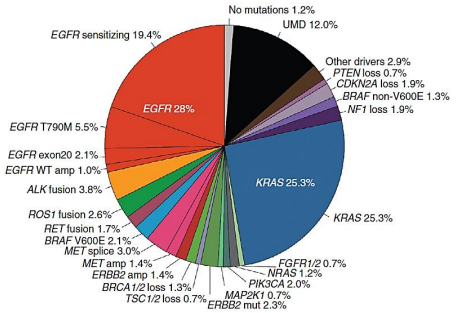


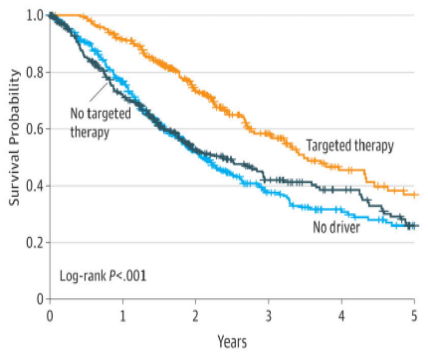
Malvezzi M, et al. Ann Oncol 2015; Schiller J, et al. NEJM 2002

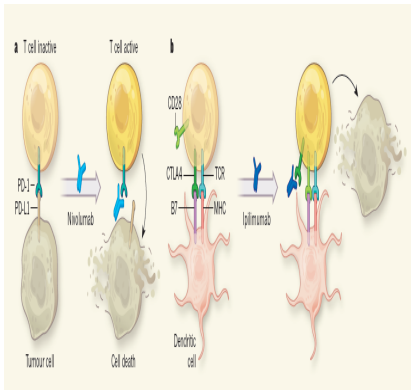
Stage IV NSCLC wt

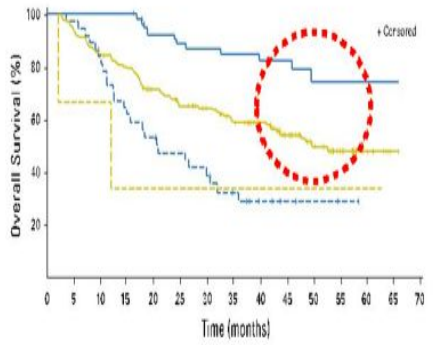
Introduction: Personalised Medicine







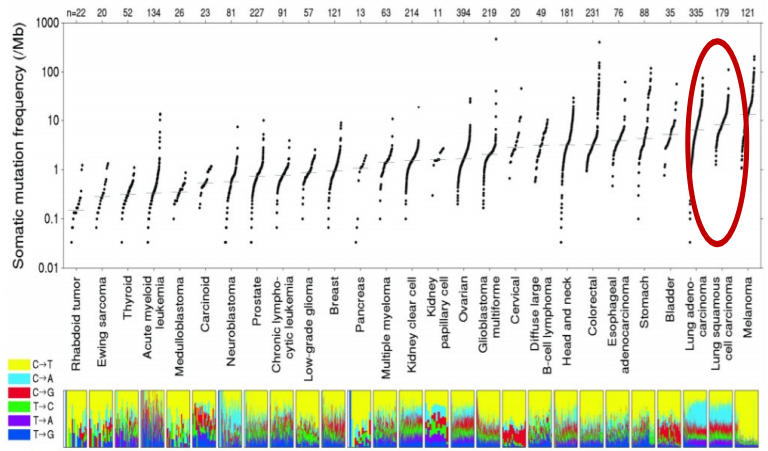




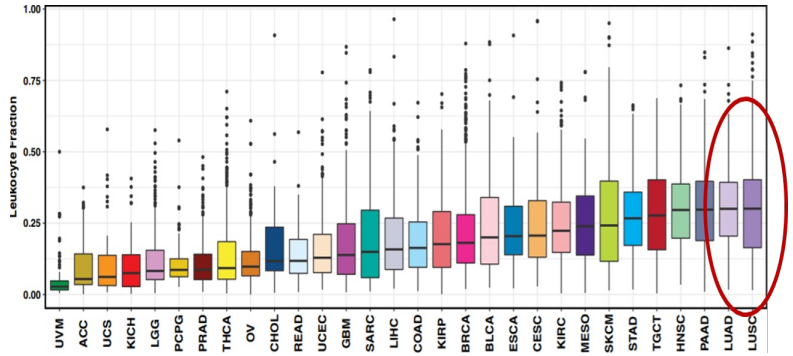
Stage IV NSCLC wt

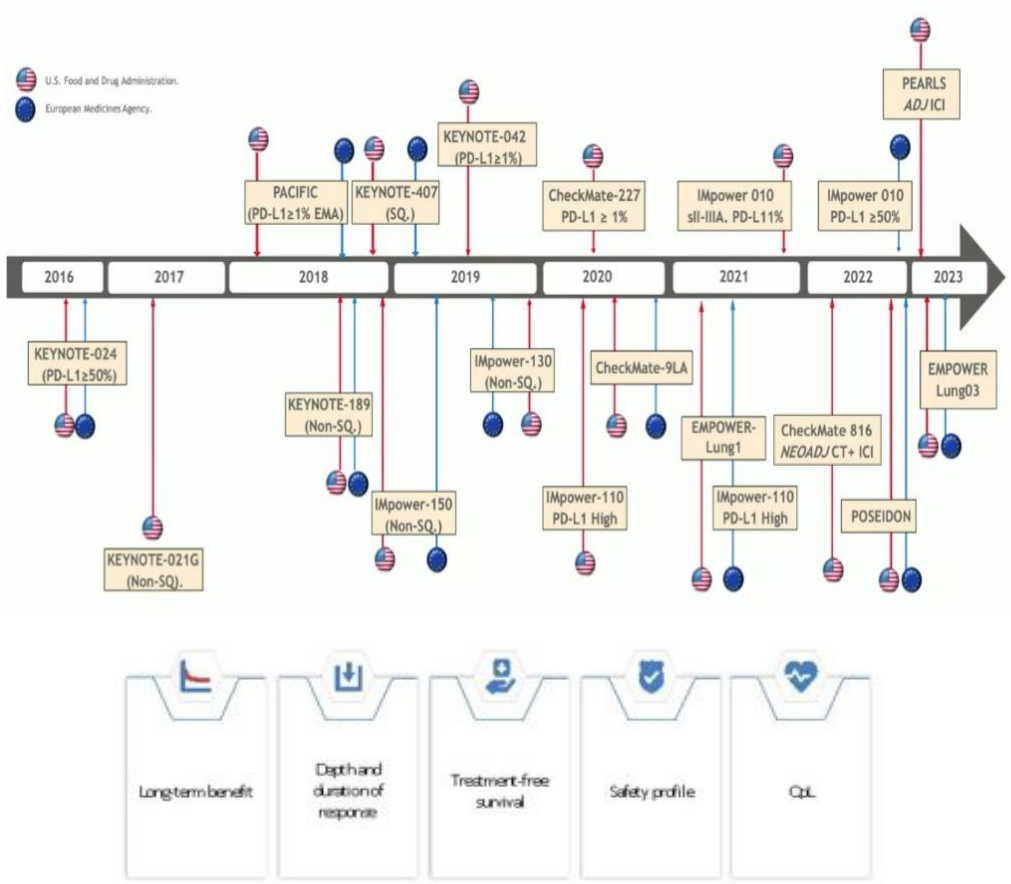
Introduction: IO target

Tumor mutational burden (TMB)



Leukocyte infiltration

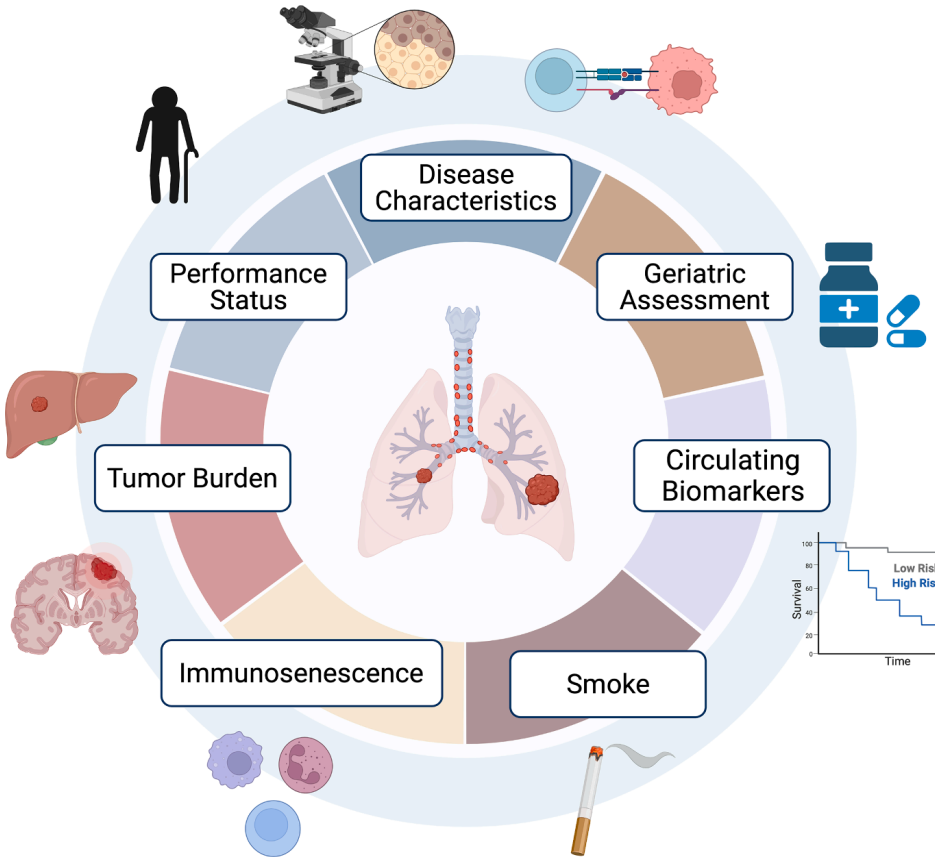


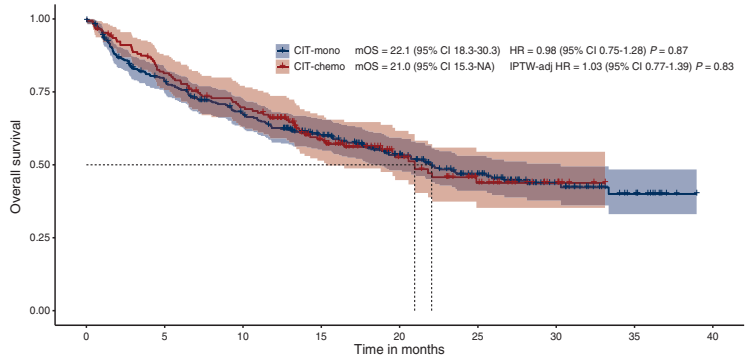


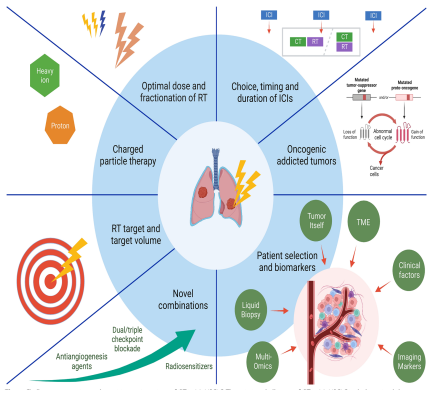
Lawrence MS, et al. Nature 2013; Thorsson, et al. Immunity 2018; Hendriks L, et al. ESMO 2023; Peters S, et al. JITC 2021

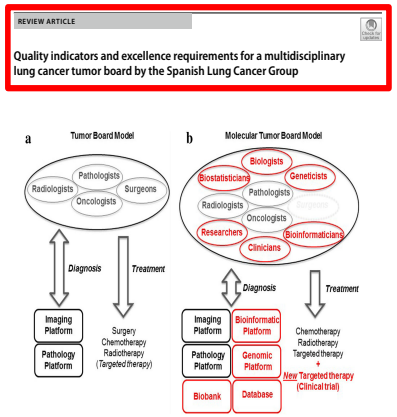
Stage IV NSCLC

Introduction: Transforming lives








REVIEW ARTICLE

Quality indicators and excellence requirements for a multidisciplinary lung cancer tumor board by the Spanish Lung Cancer Group

Background

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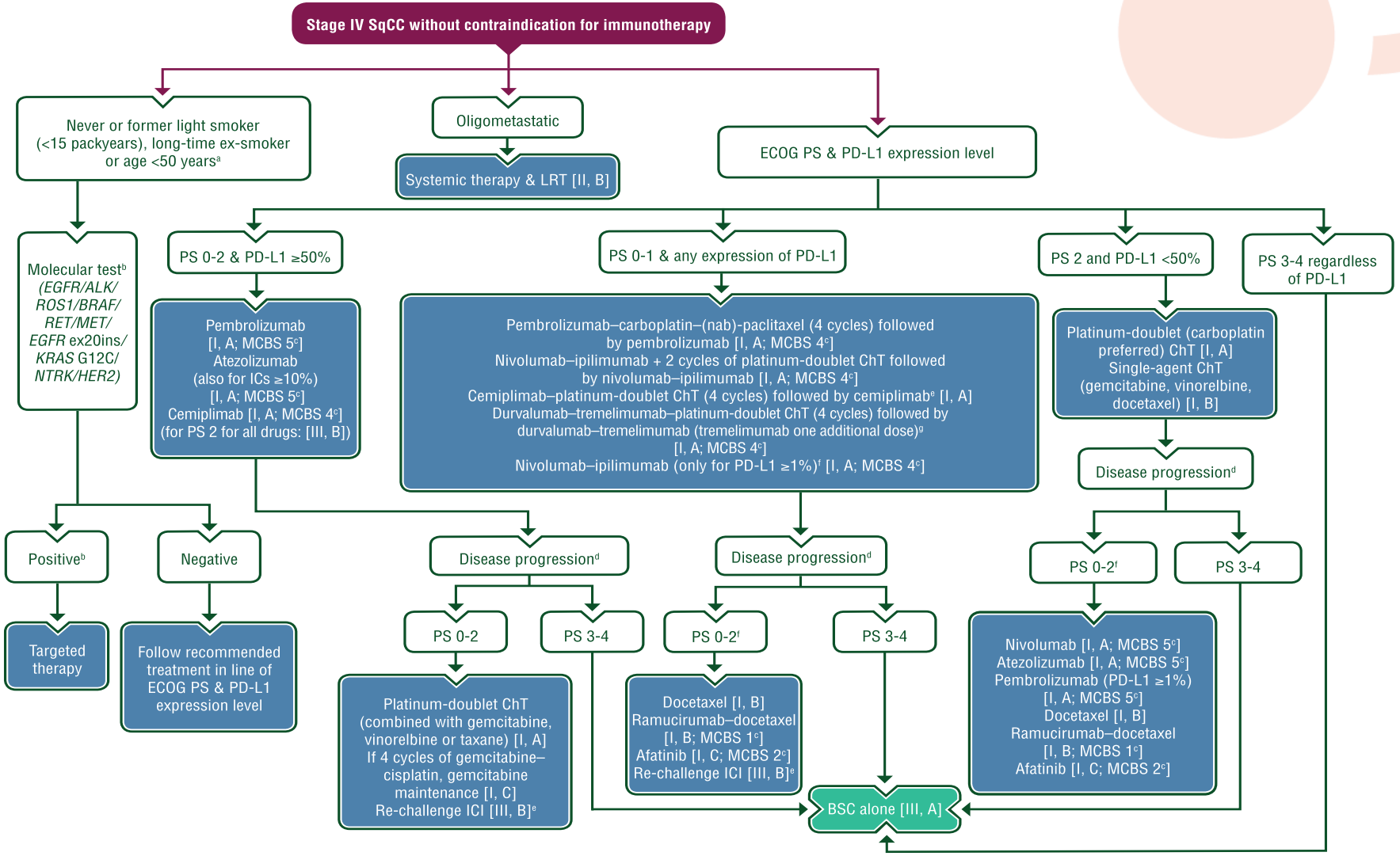
1L Sq-NSCLC wt

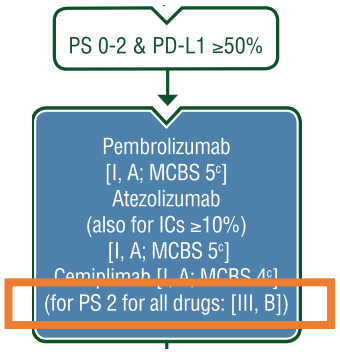
Clinical Guidelines



Hendriks LE, et al. Ann Oncol 2023

1L Sq-NSCLC

ECOG 0-2 & PD-L1 high



	N	Squamous Histology	Dose & Comparator	Time IO	ORR	OS median	OS (follow-up)	G3-4 Tox
Pembrolizumab (KN024)	305	18.8%	200 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	46.1% 31.1%	26.3 m 13.4 m	HR=0.62 5y	31.2% 53.3%
Atezolizumab (IMPower 110)	205	25.2%	1200 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	40.2% 28.6%	20.2 m 14.7 m	HR=0.76 32m	33.9% 53.2%
Cemiplimab (EMPOWER-Lung 1)	710	45%	350 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	39% 20%	26.1 m 13.3 m	HR=0.57 3y	28% 39%

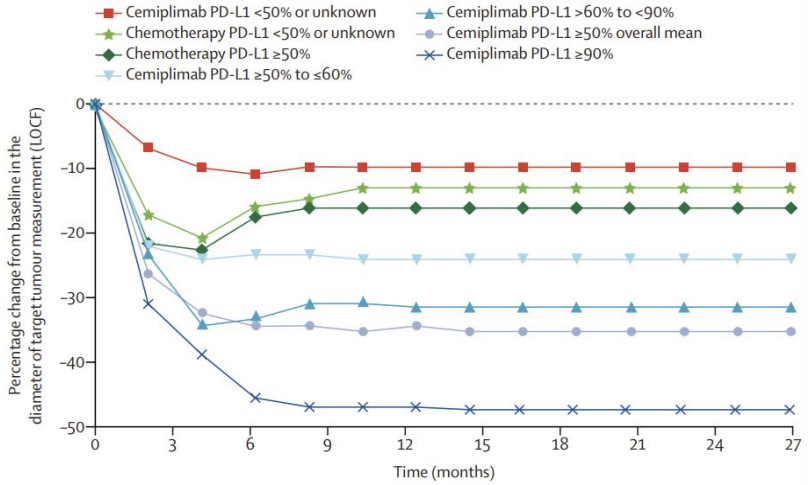
Hendricks L, et al. Ann Oncol 2023; Reck M, et al. JCO 2021; Ozguroglu M, et al. Lancet Oncol 2023; Jassem J, et al. JTO 2021

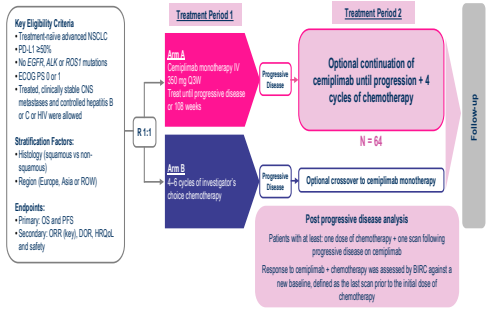
2L Sq-NSCLC

ECOG 0-2 & PD-L1 high

PS 0-2 & PD-L1 ≥50%

Pembrolizumab
[I, A; MCBS 5[c]]
Atezolizumab
(also for ICs ≥10%)
[I, A; MCBS 5[c]]
Cemiplimab [I, A; MCBS 4[c]]
(for PS 2 for all drugs: [III, B])





OS	Cemiplimab Beyond Progression N=64	
	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)

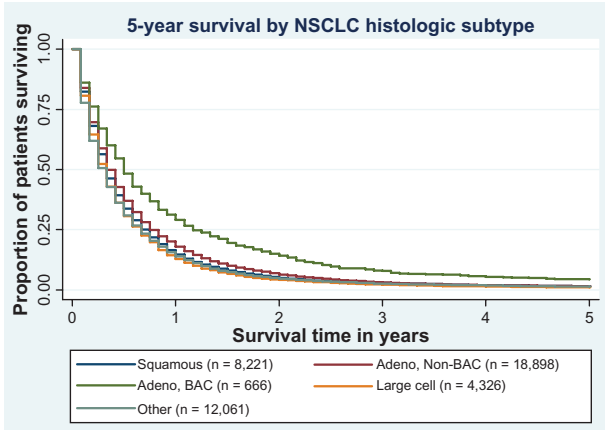
Disease progression[d]

PS 0-2

PS 3-4

Platinum-doublet ChT
(combined with gemcitabine, vinorelbine or taxane) [I, A]
If 4 cycles of gemcitabine–cisplatin, gemcitabine maintenance [I, C]
Re-challenge ICI [III, B][e]

BSC alone [III, A]

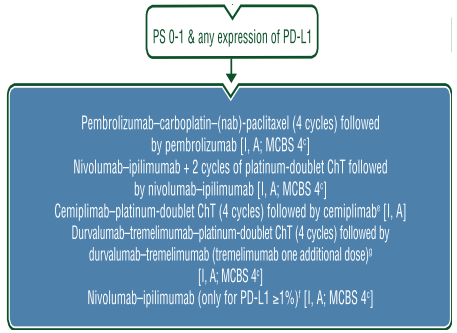


	Cohort 1
	Pembrolizumab Monotherapy
	n = 58
OS, median (95% CI), mo[a]	27.5 (21.7-NR)
6-mo OS rate, % (95% CI)	*85.4 (72.9-92.4)*
PFS,[a,b] median (95% CI), mo	8.2 (5.3-14.0)
6-mo PFS[b] rate, % (95% CI)	*59.6 (45.0-71.5)*
ORR,[b] % (95% CI)	19.0 (9.9-31.4)
SD, n (%)	31 (53.4)
DCR, n (%)	42 (72.4)

Ozguroglu M, et al. Lancet 2021; Ozguroglu M, et al. Lancet Oncol 2023; Cetin K, et al. Clin Epid 2011; Rodríguez-Abreu D, et al. IASLC 2022

1L Sq-NSCLC

ECOG 0-1 & any PD-L1



	N	Squamous histology	Dose & Comparator	Time IO	ORR	OS median	OS follow-up	G3-4 Tox
KN407 (Pembrolizumab)	559	100%	200 mg 3w Cb/Taxol or Nab-Pacl 4-6c	2y	62.2% 38.8%	18.4m 9.7m	HR=0.71 5y	69.8% 68.2%
EMPOWER-Lung 3 (Cemiplimab)	466	42.9%	350 mg 3w Platinum-CT 4-6c	2y	43.6% 22.1%	22.3m 13.8m	HR=0.61 3y	48.7% 32.7%
CM9LA (Nivo+Ipi)	719	31,6%	N 360 mg 3w Ipi 1 mg/Kg 6w Platinum-CT 4c	2y or until PD/tox	38.2% 24.9%	15.8m 11m	HR=0.72 4y	47% 38%
POSEIDON (Durva+Treme)	675	36.6%	D 1500 mg 3w T 75 mg 3w Platinum-CT 4-6c	Until PD/tox	46.3% 33.4%	17.2m 13.1m	HR=0.70 5y	51.8% 44.4%
CM227 (Nivo+Ipi)	793	29.5%	N 3 mg/Kg 2w Ipi 1 mg/Kg 6w Platinum-CT 4c	Until PD/tox	35.9% 30%	17.1m 14.9m	HR=0.79 5y	36% 32.8%

Novello S, et al. JCO 2023; Makharadze T, et al. JTO 2023; Carbone DP, et al. ASCO 2023; Peters S, et al. ESMO 2023; Brahmer J, et al. JCO 2023

1L Sq-NSCLC

ECOG 0-1 & any PD-L1

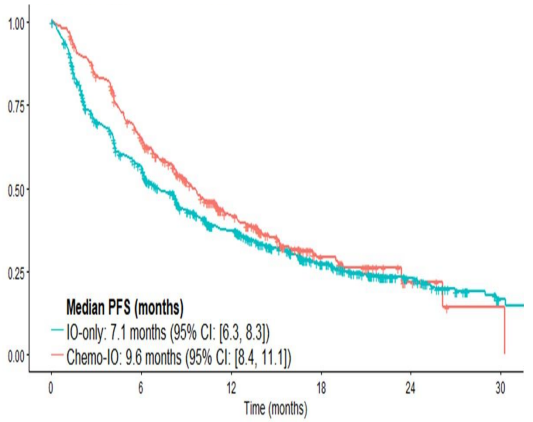
PS 0-1 & any expression of PD-L1

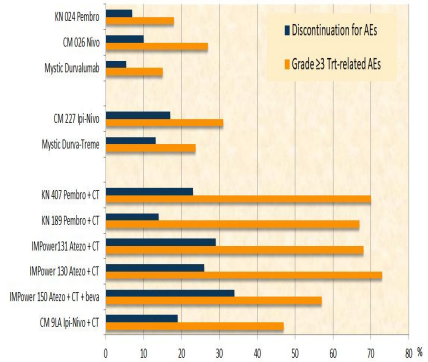
Pembrolizumab–carboplatin–(nab)-paclitaxel (4 cycles) followed by pembrolizumab [I, A; MCBS 4[c]]
Nivolumab–ipilimumab + 2 cycles of platinum-doublet ChT followed by nivolumab–ipilimumab [I, A; MCBS 4[c]]
Cemiplimab–platinum-doublet ChT (4 cycles) followed by cemiplimab[e] [I, A]
Durvalumab–tremelimumab–platinum-doublet ChT (4 cycles) followed by durvalumab–tremelimumab (tremelimumab one additional dose)[g] [I, A; MCBS 4[c]]
Nivolumab–ipilimumab (only for PD-L1 ≥1%)[i] [I, A; MCBS 4[c]]

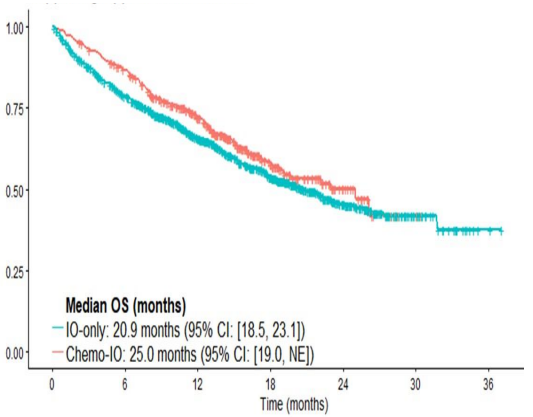
Disease
- PD-L1 expression
- Histology
- Metastatic sites (brain)
- Tumor kinetic
- TMB
- Mutations (*KRAS*, *TP53*, *STK11*, *KEAP1* ...)

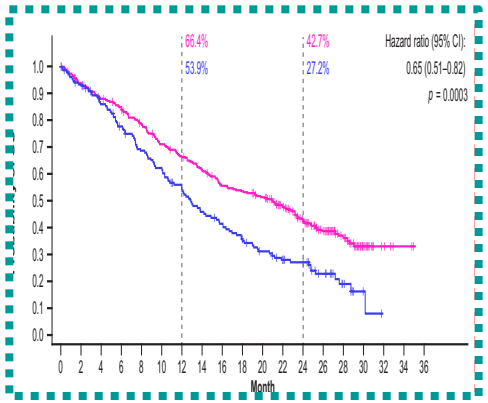
Patient
- PS
- Age
- Comorbidities
- CI immunotherapy
- Smoking habits
- Lympho./neutro. ratio

Co-medications
- Corticosteroids
- Antibiotics
- PPI





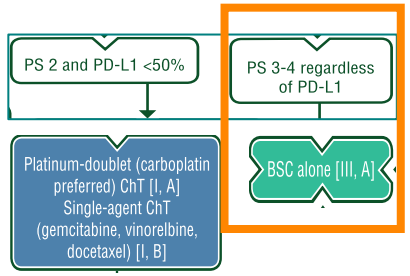




Perol M, et al. Ann Oncol 2022; Akinboro O, et al. JCO 2022; Li L, et al. BMJ Open 2020; Liu L, et al. JTO 2021; Makharadze T, et al. JTO 2023

1L Sq-NSCLC

ECOG ≥2 regardless PD-L1



Preferred option

Single-agent chemotherapy with a third generation drug (e.g. gemcitabine, vinorelbine, taxanes)

Alternative options

Carboplatin-based doublets

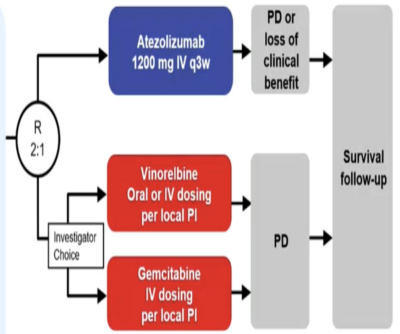
Cisplatin-based doublets with attenuated doses of cisplatin

Reference	Chemotherapy	All patients			PS2 patients		
		n	Survival (CT *vs.* BSC)	QoL gain for CT	*n*	Survival (CT *versus* BSC)	QoL gain for CT
NSCLC group [12]	Meta-analysis of CDDP-based CT	778	HR 0.73 (*P* <0.0001)	NA	NA	Advantage for CT both in good and poor PS	NA
Cullen et al. [26]; Billingham and Cullen [29]	MMC + Ifo + CDDP	797	CT > BSC (*P* = 0.01)	Yes	159	HR 0.98, NS	Yes
Stephens et al. [30]	CDDP-based	725	HR 0.77 (*P* = 0.0015)	No	147	Advantage for CT, NS	NA
ELVIS [32]	Vinorelbine	161	HR 0.65 (*P* = 0.03)	Yes	41	6.4 *versus* 1.9 months[a]	NA
Roszkowski et al. [34]	Docetaxel	207	CT > BSC (*P* = 0.026)	Yes	41	NA	NA
Ranson et al. [33]	Paclitaxel	157	CT > BSC (*P* = 0.037)	Yes	26	4.1 *versus* 2.9 months[b]	NA
Anderson et al. [31]	Gemcitabine	300	5.7 *versus* 5.9 months (*P* = 0.84)	Yes	108	3.2 *versus* 2.6 months[b]	NA

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



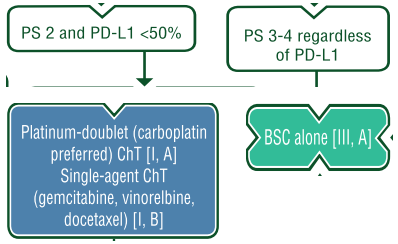
10.3 vs 9.2 m (HR=0.78)

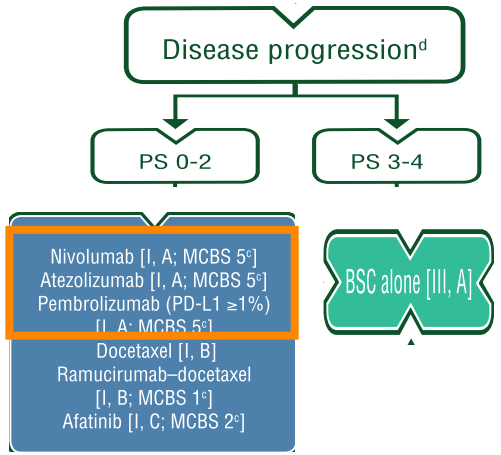
Reference	P-based arm	P-free arm	Total No. of pts	Overall survival (months) (P-based *versus* P-free)	PS2 pts (% of total pts)	Outcome in PS2 patients(P-based *versus* P-free)
Georgoulias et al. [38]	CDDP/Doc	Gem/Doc	406	10 *versus* 9.5 (*P* = 0.98)	12	Comparable survival
Kosmidis et al. [39]	CBDCA/Ptx	Gem/Ptx	479	10.4 *versus* 9.8 (*P* = 0.32)	13	Comparable survival
Giaccone [40]	CDDP/Ptx (A) or CDDP/Gem (B)	Gem/Ptx	480	8.1 (A), 8.8 (B) *versus* 6.9 (*P* = NA)	12	Comparable survival
Alberola et al. [41]	CDDP/Gem (A) or CDDP/Gem/Vin (B)	Gem/Vin followed by Ifo/Vin	557	9.3 (A), 8.2 (B) *versus* 8.1 (*P* = NA)	15	NA
Gridelli et al. [42]	CDDP/Gem or CDDP/Vin	Gem/Vin	501	8.8 *versus* 7.4 (*P* = 0.08)	13	Comparable survival

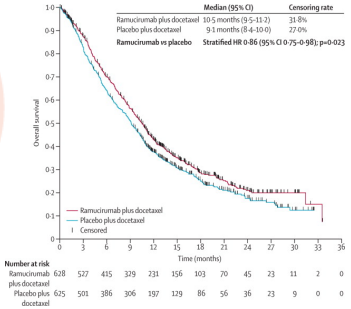
Gridelli C, et al. Ann Oncol 2004; Lee SM, et al. Lancet 2023

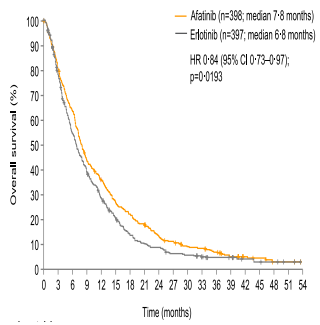
2L Sq-NSCLC

ECOG ≥2 regardless PD-L1









	CheckMate-017	CheckMate 057	KeyNote 010	OAK
Study Design	Nivolumab vs Docetaxel	Nivolumab vs Docetaxel	Pembrolizumab vs Docetaxel	Atezolizumab vs Docetaxel
N	272	582	1034	1225
Dose schedule	3 mg/Kg 2w until PD/tox	3 mg/Kg 2w until PD/tox	2 mg/kg 3w 2y	1200 mg 3w until PD/tox
Histology	Squamous	Non-Sq	Both	Both
PD-L1 status	+/-	+/-	≥1%	+/-
OS (m)	9.2 vs 6 HR=0.59	12.2 vs 9.4 HR=0.73	10.4 vs 8.6 HR=0.71	13.8 vs 9.6 HR=0.73
ORR (%)	20 vs 9	19 vs 12	18 vs 9	14 vs 13
G3-4 Tox (%)	7 vs 55	10 vs 54	13-16 vs 35	15 vs 43

Borghaei H, et al. JCO 2021; Herbst R, et al. JTO 2021; Mazieres J, et al. JTO 2021; Garon E, et al. Lancet 2014; Goss GD, et al. Eclinical Medicine 2021

Background

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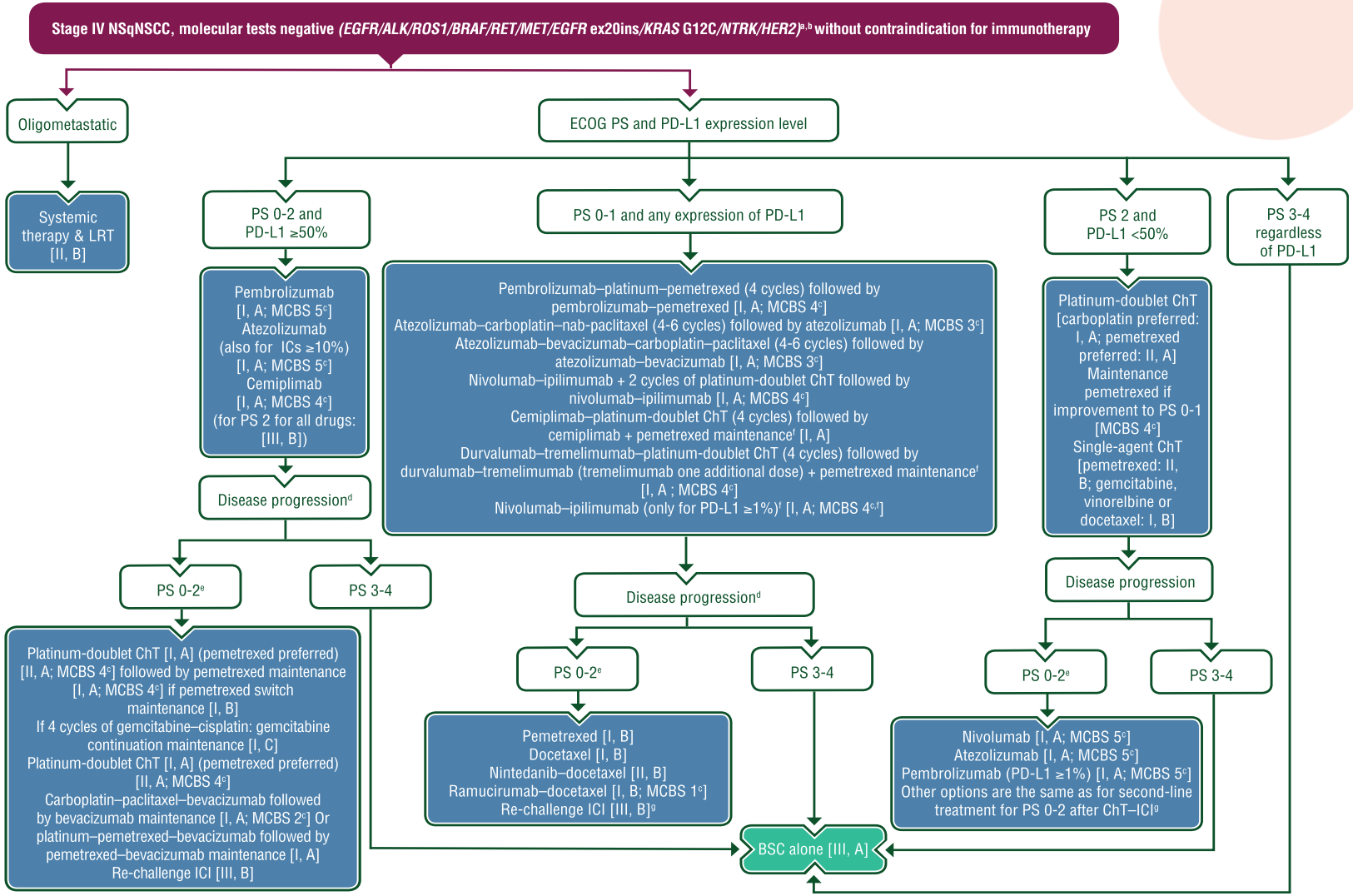
2. Clinical Guidelines: Squamous NSCLC wt
3. Clinical Guidelines: Non-Squamous NSCLC wt
4. Conclusions: Take-home messages

1L Non-Sq-NSCLC

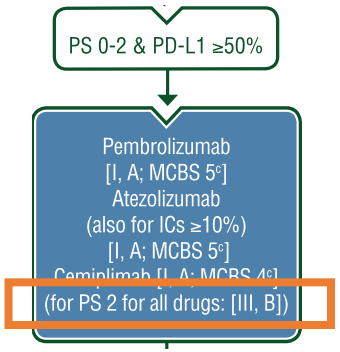
Clinical Guidelines



Hendriks LE, et al. Ann Oncol 2023

1L Sq-NSCLC

ECOG 0-2 & PD-L1 high

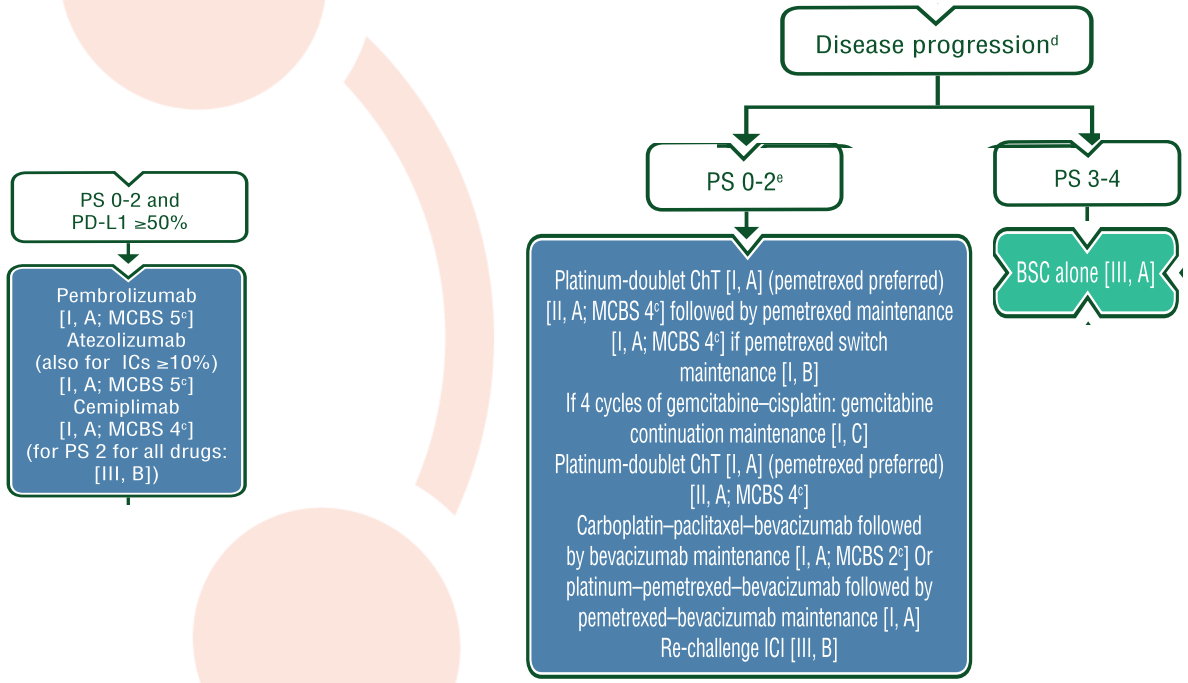


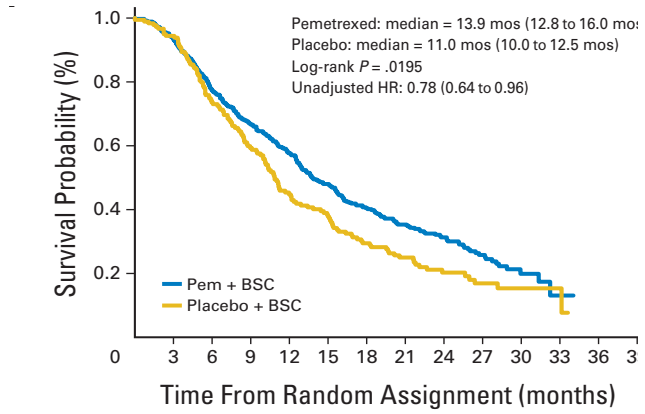
	N	Squamous Histology	Dose & Comparator	Time IO	ORR	OS median	OS (follow-up)	G3-4 Tox
Pembrolizumab (KN024)	305	81.2%	200 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	46.1% 31.1%	26.3 m 13.4 m	HR=0.62 5y	31.2% 53.3%
Atezolizumab (IMPower 110)	205	74.8%	1200 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	40.2% 28.6%	20.2 m 14.7 m	HR=0.76 32m	33.9% 53.2%
Cemiplimab (EMPOWER-Lung 1)	710	55%	350 mg 3w CT Cis/Cb + Pem/Gem/Taxol	2y 4-6c	39% 20%	26.1 m 13.3 m	HR=0.57 3y	28% 39%

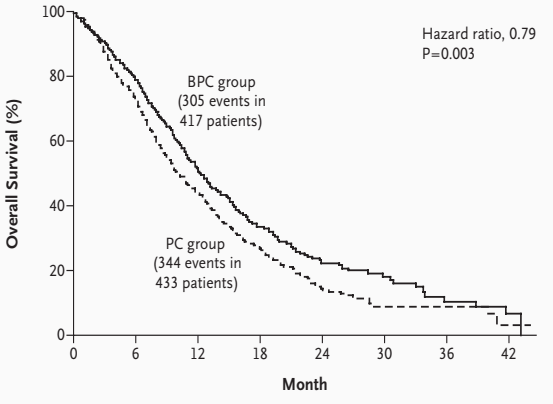
Hendricks L, et al. Ann Oncol 2023; Reck M, et al. JCO 2021; Ozguroglu M, et al. Lancet Oncol 2023; Jassem J, et al. JTO 2021

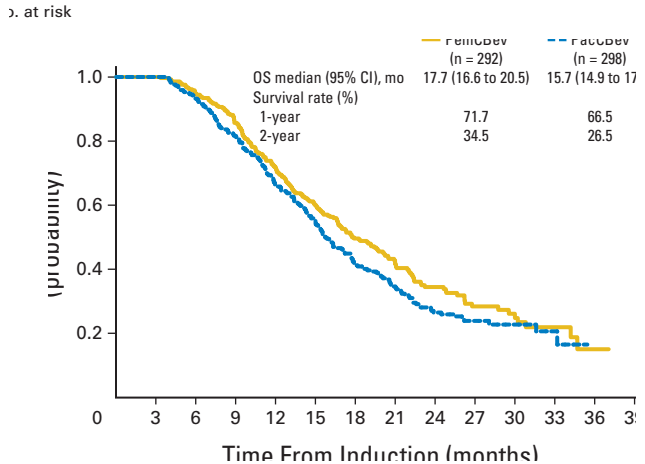
2L Non-Sq-NSCLC

ECOG 0-2 & PD-L1 high







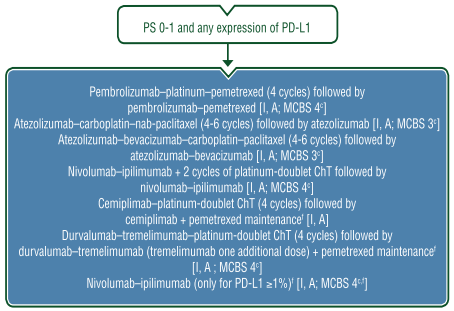


	Cohort 1
	Pembrolizumab Monotherapy
	n = 58
OS, median (95% CI), mo[a]	27.5 (21.7-NR)
6-mo OS rate, % (95% CI)	*85.4 (72.9-92.4)*
PFS,[a,b] median (95% CI), mo	8.2 (5.3-14.0)
6-mo PFS[b] rate, % (95% CI)	*59.6 (45.0-71.5)*
ORR,[b] % (95% CI)	19.0 (9.9-31.4)
SD, n (%)	31 (53.4)
DCR, n (%)	42 (72.4)

Hendriks LE, et al. Ann Oncol 2023; Paz-Ares L, et al. JCO 2013; Sandler A, et al. NEJM 2006; Patel JD, et al. JCO 2013; Rodriguez-Abreu D, et al. IASLC 2022

1L Non-Sq-NSCLC

ECOG 0-1 & any PD-L1



	N	Non-Sq histology	Dose & Comparator	Time IO	ORR	OS median	OS follow-up	G3-4 Tox
KN189 (Pembrolizumab)	616	100%	200 mg 3w Cis or Cb/Pem 4c & maintenance	2y	48.3% 19.9%	19.4m 11.3m	 HR=0.60 5y	52.3% 42.1%
EMPOWER-Lung 3 (Cemiplimab)	466	57.1%	350 mg 3w Cis or Cb/Pem 4 c & maintenance	2y	43.6% 22.1%	22.3m 13.8m	 HR=0.61 3y	48.7% 32.7%
CM9LA (Nivo+Ipi)	719	68.4%	N 360 mg 3w Ipi 1 mg/Kg 6w Cis or Cb/Pem 4c & maintenance	2y or until PD/tox	38.2% 24.9%	15.8m 11m	 HR=0.72 4y	47% 38%
IMPower150 (Atezo+Beva)	1202	100%	1200 mg 3w Cb/Paclitaxel/Beva 4-6c	Until PD/tox	55% 42%	19m 14.7m	 HR=0.84 3y	57.3% 49%
IMPower 130 (Atezolizumab)	679	100%	1200 mg 3w Cb/Paclitaxel or nab-paclitaxel 4-6c	Until PD/tox	49.2% 31.9%	18.6m 13.9m	 HR=0.79 NR	73.2% 60.3%

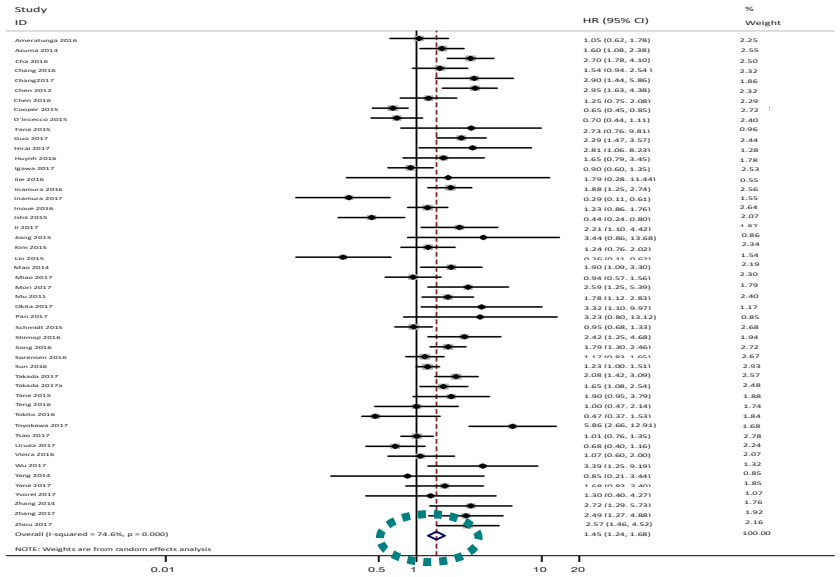
Garassino MC, et al. JCO 2023; Makharadze T, et al. JTO 2023; Carbone DP, et al. ASCO 2023; Socinski M, et al. JTO 2021; West H, et al. Lancet Oncol 2019

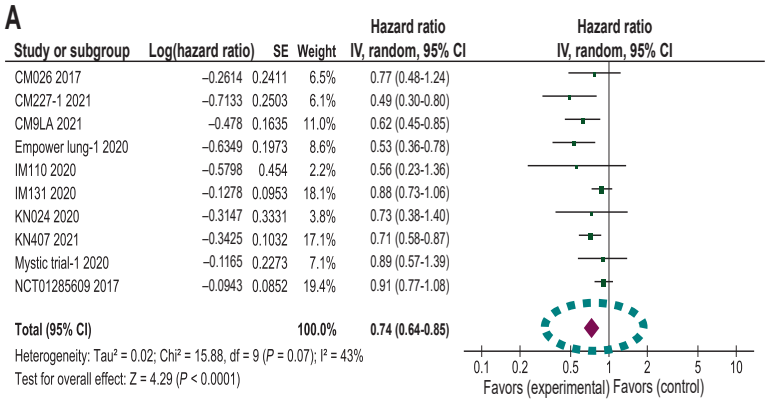
1L Non-Sq-NSCLC

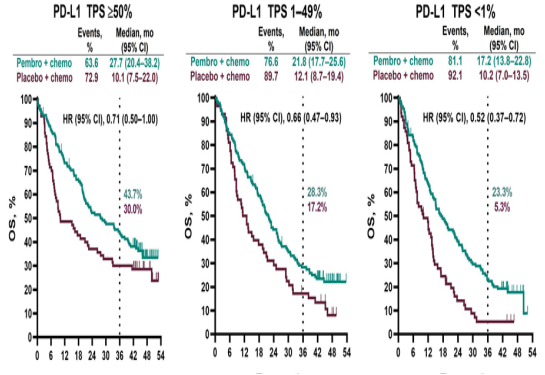
ECOG 0-1 & any PD-L1

PS 0-1 and any expression of PD-L1

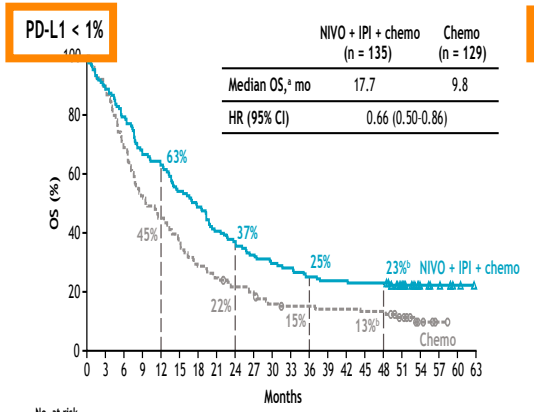
Pembrolizumab–platinum–pemetrexed (4 cycles) followed by pembrolizumab–pemetrexed [I, A; MCBS 4[2]]
Atezolizumab–carboplatin–nab-paclitaxel (4-6 cycles) followed by atezolizumab [I, A; MCBS 3[2]]
Atezolizumab–bevacizumab–carboplatin–paclitaxel (4-6 cycles) followed by atezolizumab–bevacizumab [I, A; MCBS 3[2]]
Nivolumab–ipilimumab + 2 cycles of platinum-doublet ChT followed by nivolumab–ipilimumab [I, A; MCBS 4[2]]
Cemiplimab–platinum-doublet ChT (4 cycles) followed by cemiplimab + pemetrexed maintenance[f] [I, A]
Durvalumab–tremelimumab–platinum-doublet ChT (4 cycles) followed by durvalumab–tremelimumab (tremelimumab one additional dose) + pemetrexed maintenance[f] [I, A ; MCBS 4[2]]
Nivolumab–ipilimumab (only for PD-L1 ≥1%)[f] [I, A; MCBS 4[2]]

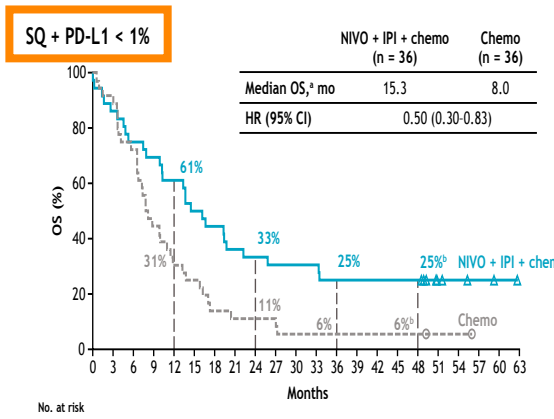






	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
OS HR (95% CI)	0.68 (0.47–0.97)		0.61 (0.45–0.83)		0.83 (0.61–1.13)	
5-y OS rate,[a] %	23.3	8.3	20.6	7.6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

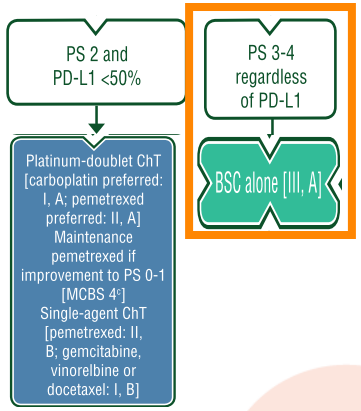


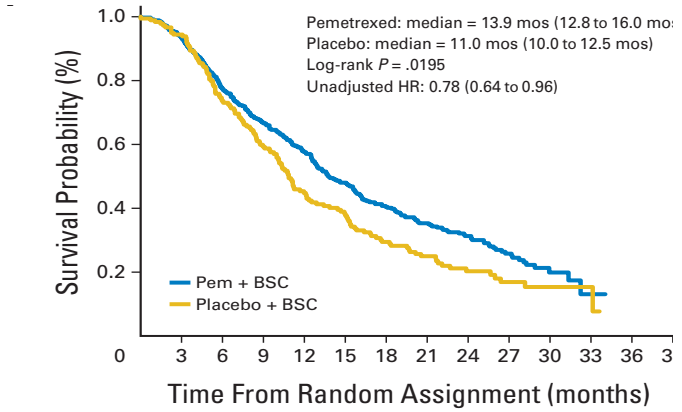


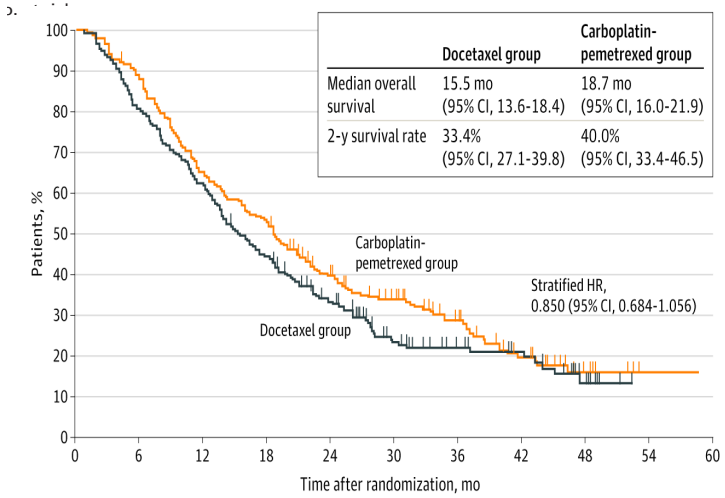
Li H, et al. Transl Lung Cancer Res 2019; Garassino MC, et al. JCO 2023; Novello S, et al. JCO 2023; Siciliano MA, et al. Ann Oncol 2022; Cobo M, et al. GECP 2023

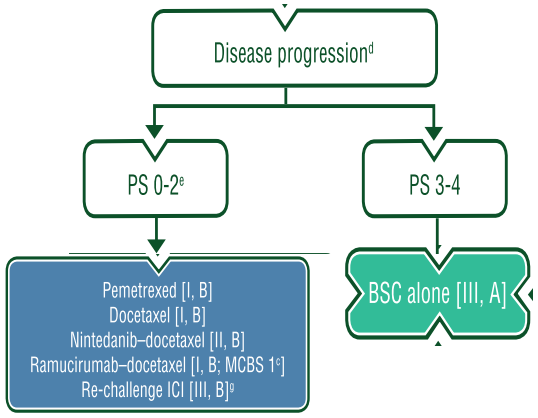
1&2L Non-Sq-NSCLC

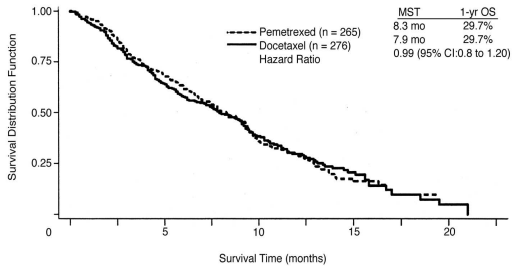
ECOG ≥2 regardless PD-L1

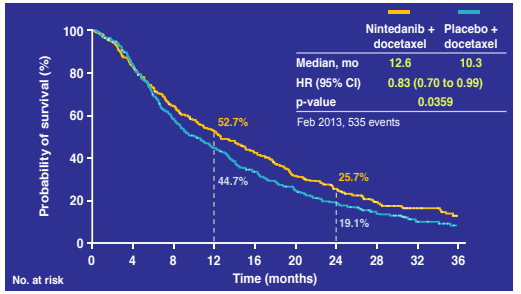












Cohort 2	
Pembrolizumab + Chemotherapy	
n = 16	
OS, median (95% CI), mo[a]	NR (NR-NR)
6-mo OS rate, % (95% CI)	*86.2 (55.0-96.4)*
PFS,[a,b] median (95% CI), mo	7.7 (1.8-NR)
6-mo PFS[b] rate, % (95% CI)	*58.3 (27.0-80.1)*
ORR,[b] % (95% CI)	6.3 (0.2-30.2)
SD, n (%)	7 (43.8)
DCR, n (%)	8 (50.0)

Paz Ares L, et al. JCO 2013; Okamoto I, et al. JAMA Oncol 2020; Hanna N, et al. JCO 2004; Reck M, et al. Lancet Oncol 2014; Rodriguez-Abreu D, et al. IASLC 2022

Background

1. Introduction: Stage IV NSCLC wt
2. Clinical Guidelines: Squamous NSCLC wt
3. Clinical Guidelines: Non-Squamous NSCLC wt
4. Conclusions: Take-home messages

Stage IV NSCLC wt

Take-home messages

- ✓ **Stage IV NSCLC WT: 1L Treatment approach by histology & PS + *PD-L1* level: IO exceptions?**
  - ➡ **PS 0-1 & *PD-L1* ≥50%: 1L monotherapy IO (vs CT+IO?-local restrictions)**
    2L Platinum-based CT (schedule by histology)
  - ➡ **PS 0-1 & any *PD-L1*: 1L Platinum-based CT + IO (several options by histology)**
    PD-L1 negative=special value of double IO +/- CT
    2L CT+/-antiangiogenics (Non-Sq histology)
  - ➡ **PS2 & any *PD-L1:* 1L Platinum-based CT vs monoCT (IO alone=III evidence level)**
    2L monotherapy IO
  - ➡ **PS3-4: BSC**
- ✓ **Clinical +/- translational ongoing research is required to support current considerations (rechallenge, IO duration, unselected population, etc)**

Muchas gracias por vuestra atención

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