BELGIAN RESPIRATORY SOCIETY

BTOS 2023

Belgian Thoracic Oncology Symposium

15th Edition

"Where is the highest unmet medical need in 1L mNSCLC?"

- What do the real-world data tell ?
- What do new approaches bring ?

Dr. Deschepper
VITAZ

FRIDAY, MARCH 17, 2023

16:40 - 17:00 (15' + 5' Q&A)

Van der Valk Hotel Diegem

Bristol Myers Squibb™

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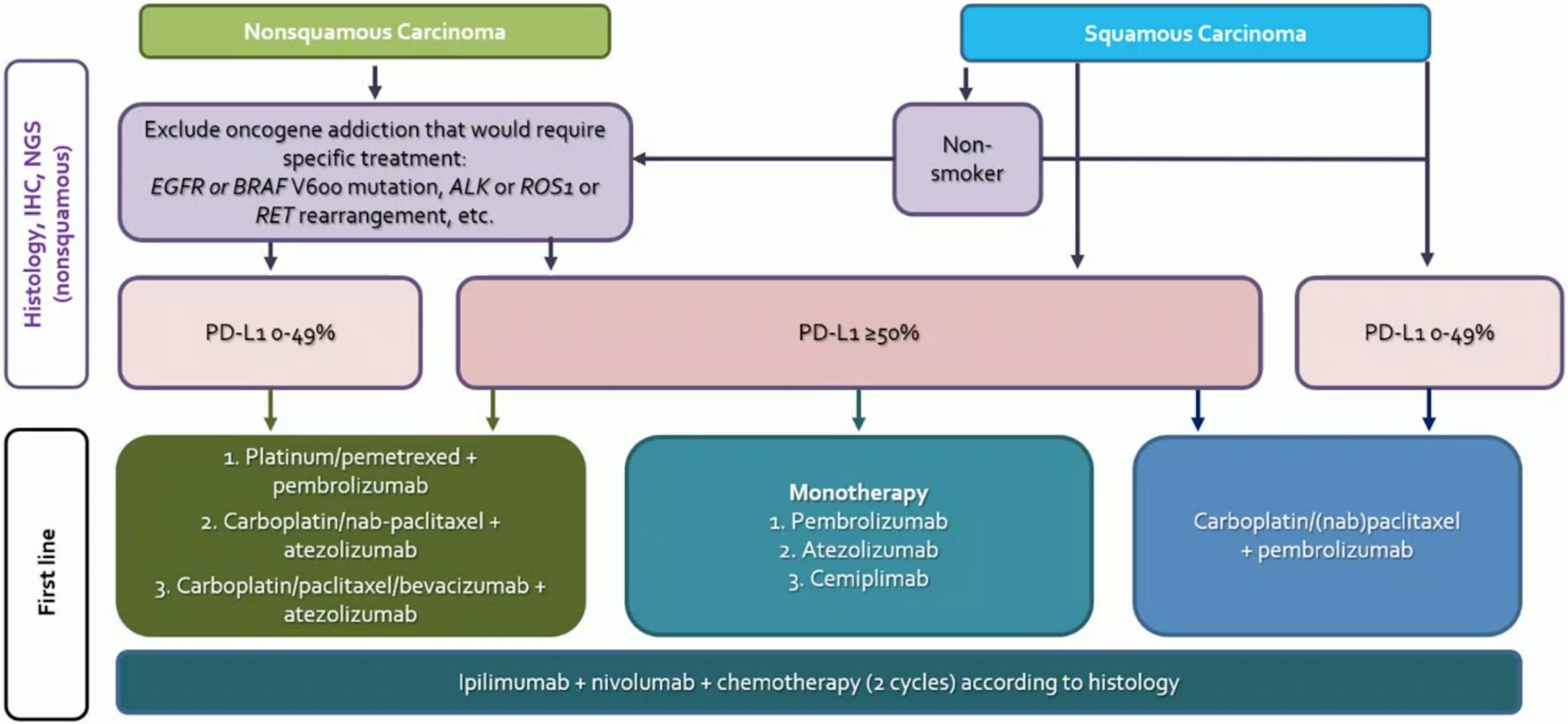
STERK IN ZORG

Immunotherapy Belongs to a Frontline Standard Treatment Strategy in Metastatic NSCLC



1. Adapted from Perol ELCC 2022

Acta Oncologica

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lonc20

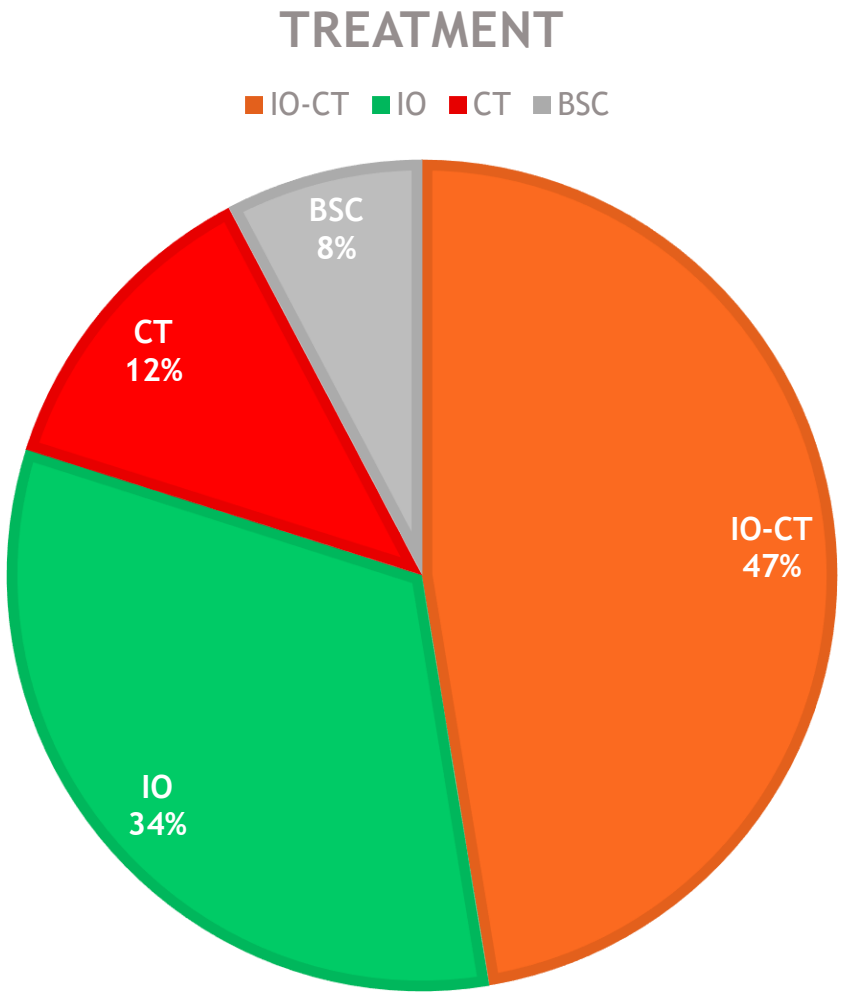
A prospective, multicenter, noninterventional study of decision factors in the first-line treatment of metastatic non–small cell lung cancer

Anne Sibille, Frederique Bustin, Luciano Carestia, Gaetan Catala, Christophe Compère, Kristof Cuppens, Benoit Colinet, Stephanie Coulon, Nele De Brucker, Lore Decoster, Lynn Decoster, Ingel Demedts, Sofie Derijcke, Koen Deschepper, Danny Galdermans, Annelies Janssens, Sebahat Ocak, Christel Oyen, Karin Pat, Thierry Pieters, Vincent Pruniau, Veerle Surmont, Saar Vandekeere & Johan Vansteenkiste

Published online: 15 May 2022.

Belgium : 81 % of 1L mNSCLC patients are treated with IO +/- CT

N=209

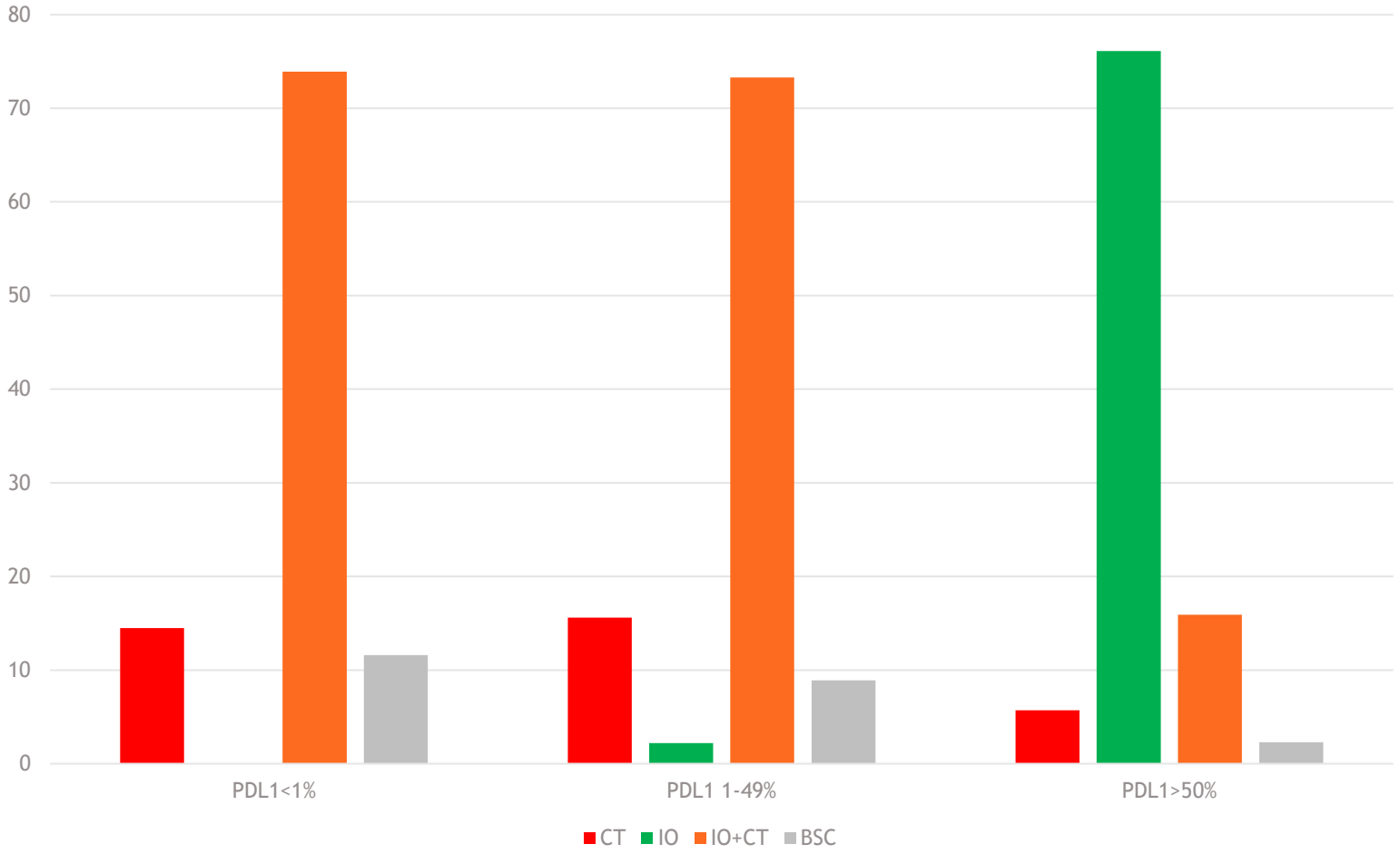


	Overall (n=209)
Age, years, mean (SD)	68.2 (9.2)
ECOG PS 0-1, n(%)	77%
Non-Squamous	66%
PD-L1<1%	33%
PD-L1 ≥50%	42%
c/f smokers	96%

Sibille et al. Acta Oncologica 2022, vol 61, no.6, 773-776

Belgium : treatment choices across PD-L1 expression

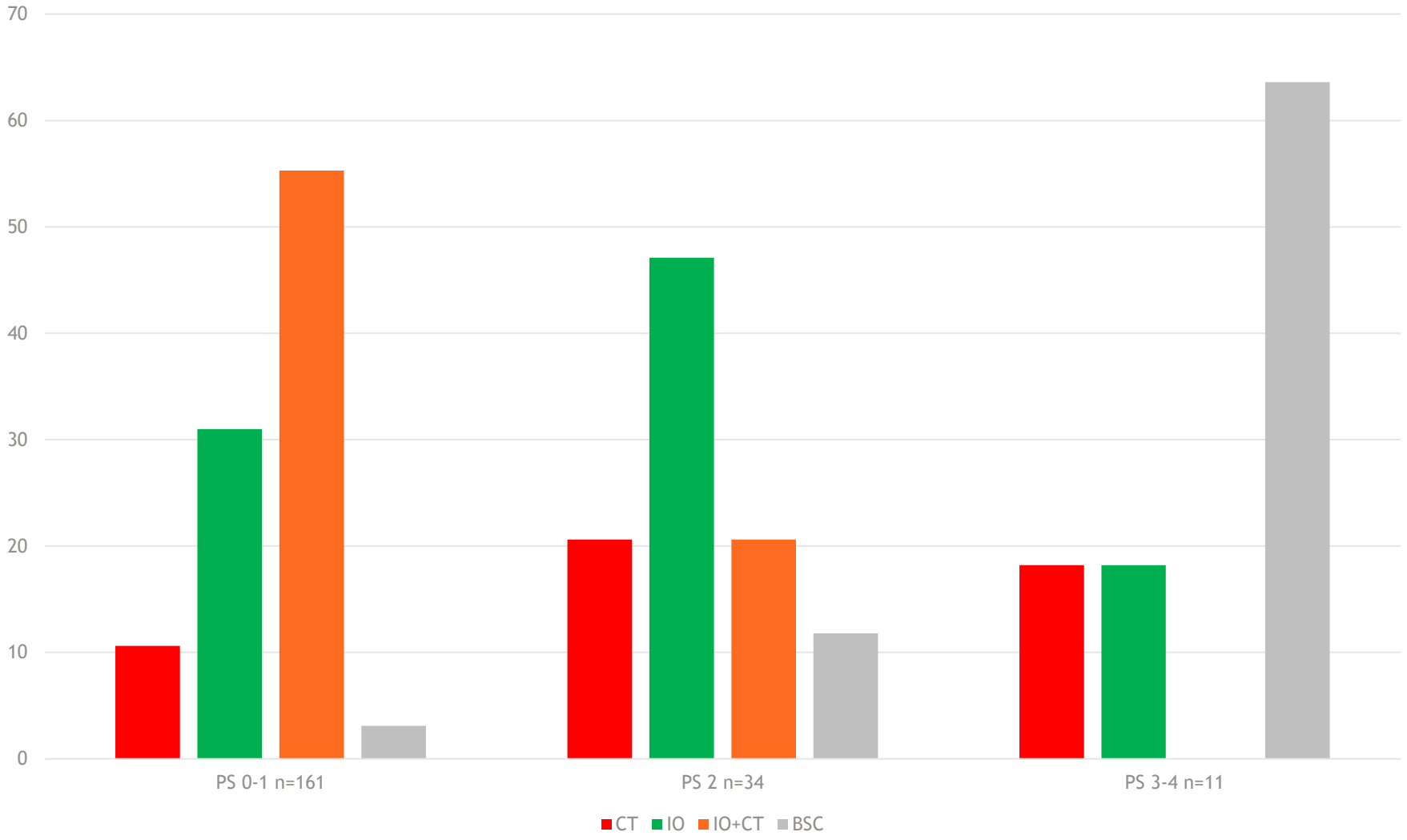
N=209



Sibille et al. Acta Oncologica 2022, vol 61, no.6, 773-776

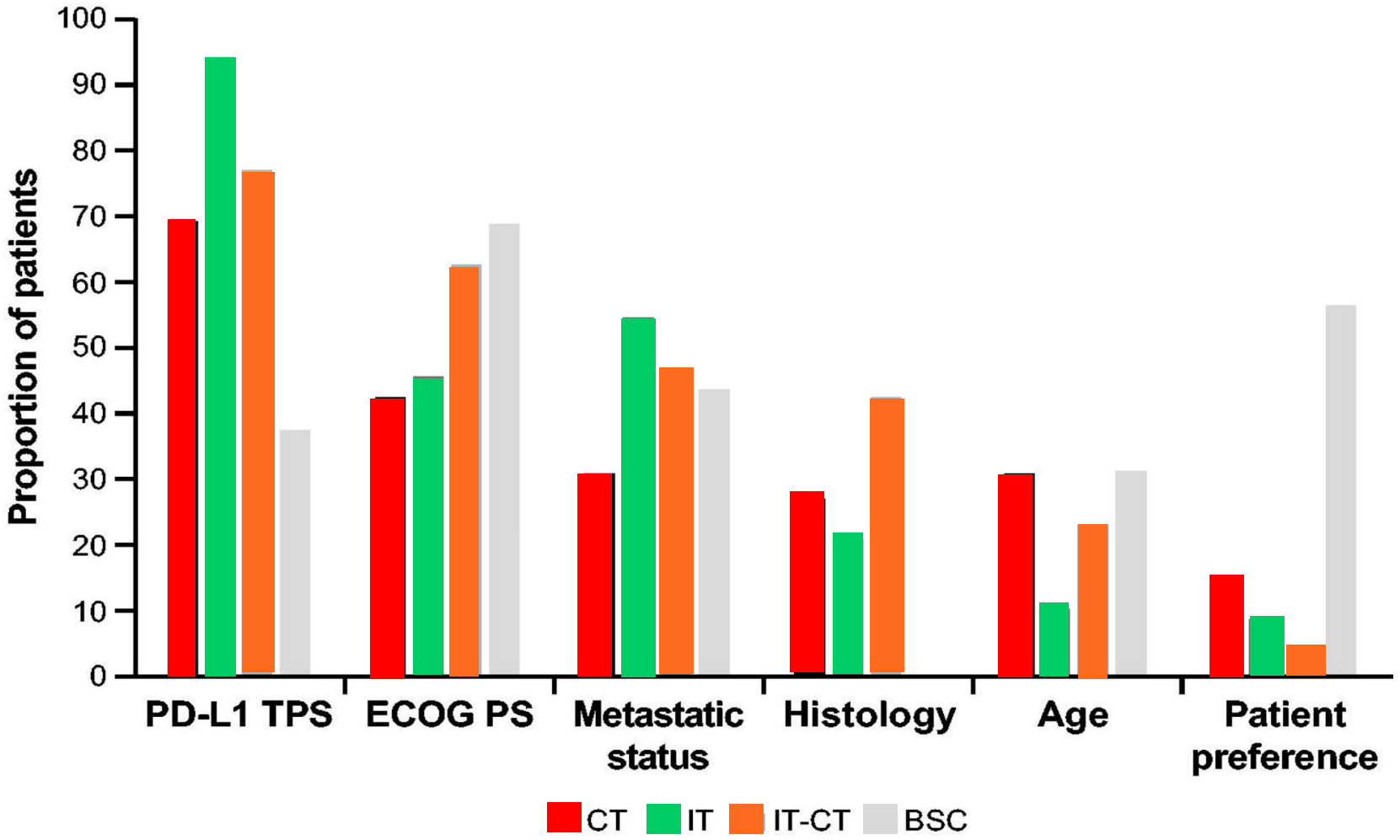
Belgium : treatment choices across ECOG Performance status

N=209



Sibille et al. Acta Oncologica 2022, vol 61, no.6, 773-776

Belgium : most important treatment decision factors in 1L mNSCLC



Sibille et al. Acta Oncologica 2022, vol 61, no.6, 773-776

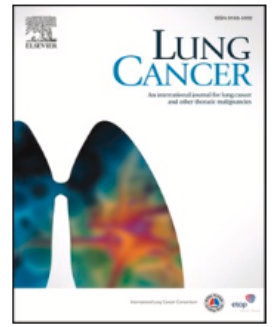
	RCT	Real World Data
Type of trial	Experimental	Observational
Primary focus	Efficacy, safety	Effectiveness
Patient population	Small and restricted	Large and unrestricted
Patient characteristics	Younger, healthier, stable	Older, comorbid.
Monitoring	Intense	Not required
Cost	High	Less expensive
Comparisons	Valid due to randomization	Invalid due to confounding
Data quality	High	Low
Purpose	Regulatory approval	Drug performance in real world

Lung Cancer 156 (2021) 41–49

Contents lists available at ScienceDirect

Lung Cancer

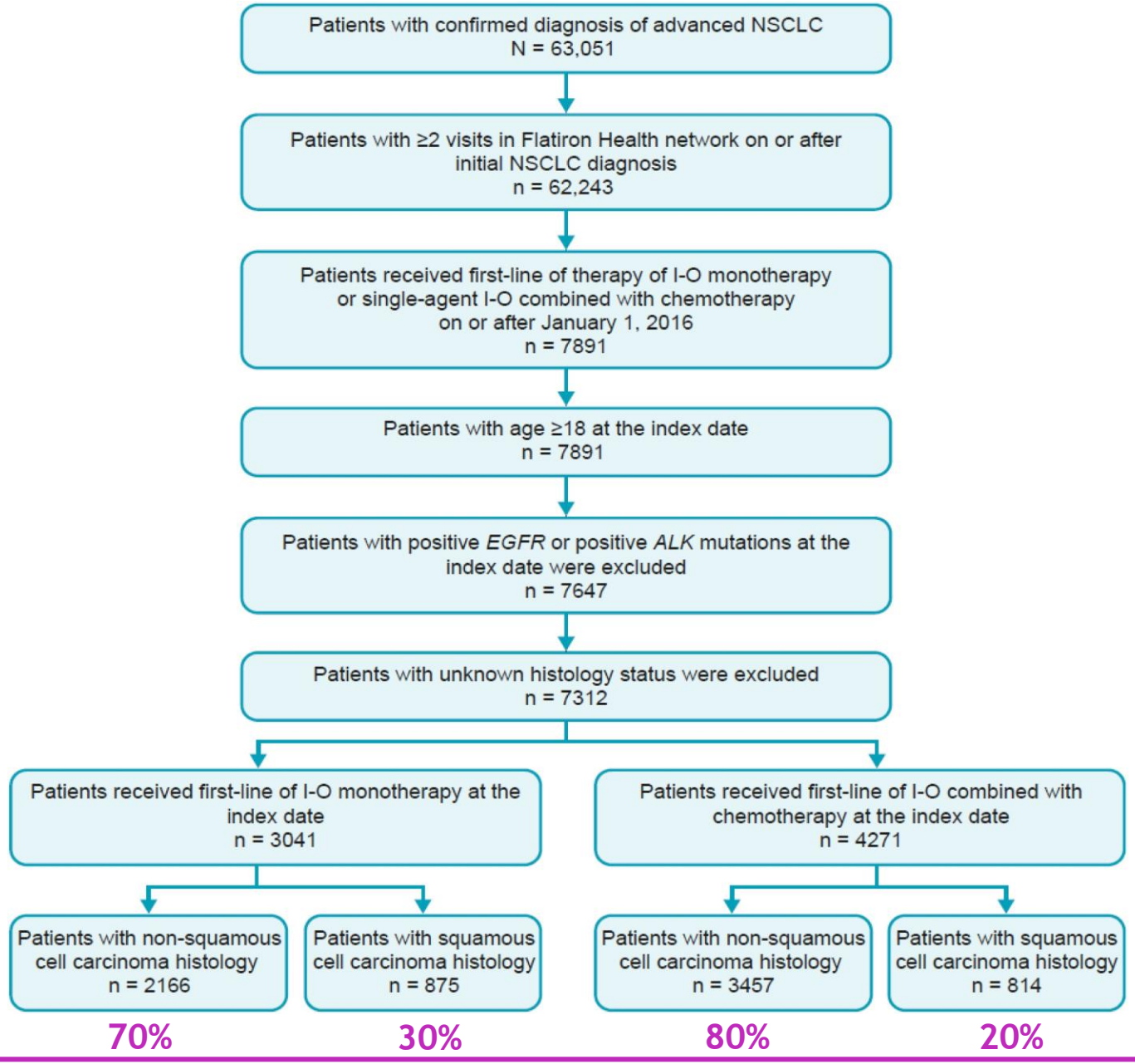
journal homepage: www.elsevier.com/locate/lungcan



Real-world outcomes of immunotherapy–based regimens in first-line advanced non-small cell lung cancer

David Waterhouse [a,*], Jenny Lam [b], Keith A. Betts [c], Lei Yin [c], Sophie Gao [c], Yong Yuan [b], John Hartman [b], Sumati Rao [b], Solomon Lubinga [b], David Stenehjem [d]

[a] *OHC Cincinnati, Cincinnati, OH, USA*
[b] *Bristol Myers Squibb, Lawrenceville, NJ, USA*
[c] *Analysis Group, Los Angeles, CA, USA*
[d] *University of Minnesota, Minneapolis, MN, USA*



Waterhouse et al. Lung Cancer 156 (2021) 41-49

IO + chemo group

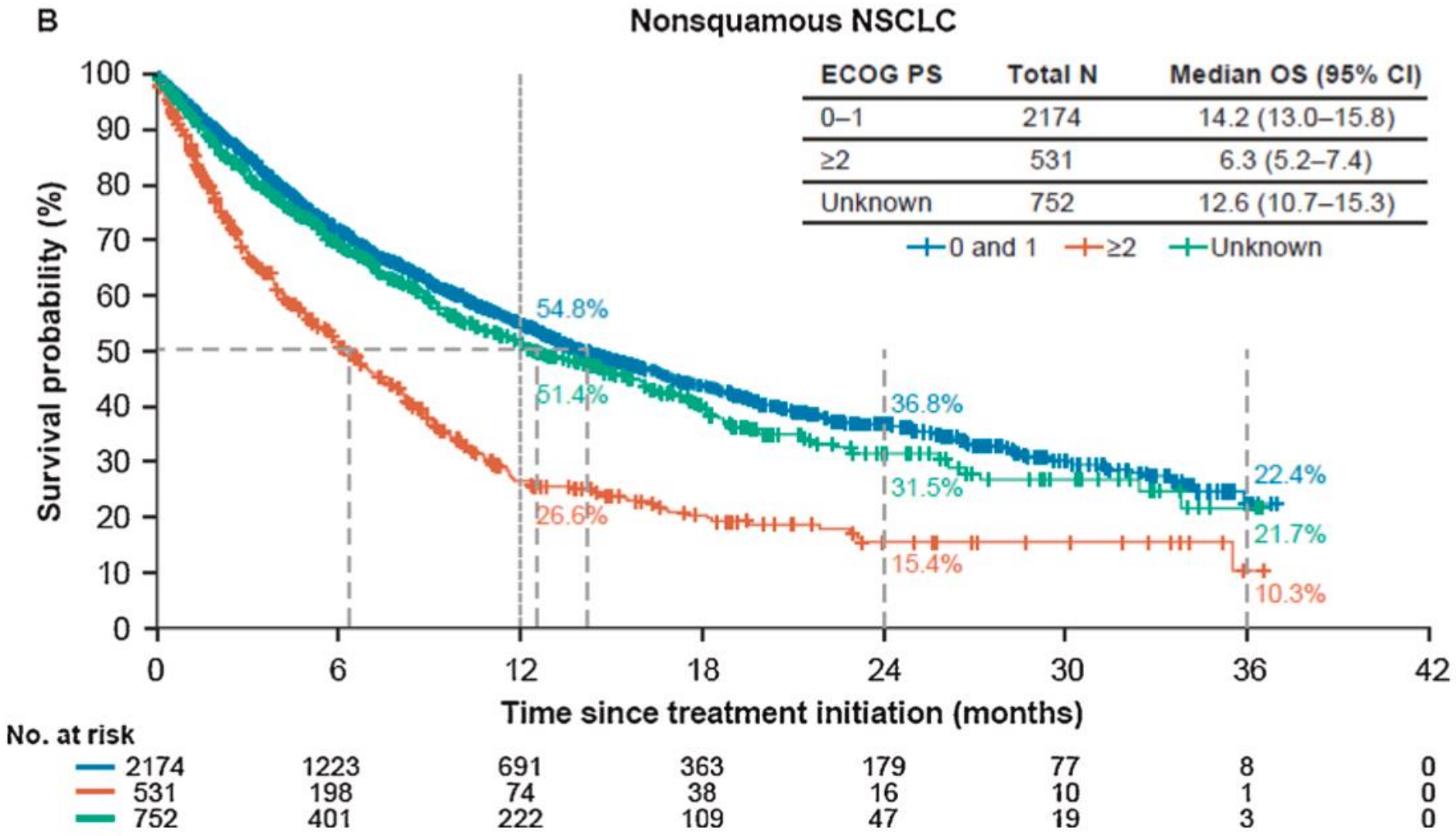
	Squamous n=814	Non-SQ n=3457	All n=4271
Age	69,6	67,8	68,1
Male	68	55	57
PS 0-1	64	63	63
PS ≥ 2	18	15	16
PDL1 <1%	26	31	30
PDL1 1-49%	31	28	29
PDL1 >50%	15	20	19
ALK EGFR UnK	42/40	18/17	22/21
Pembro+tax/plat Pembro+pem/plat	94	92	
Brain mets	5	14	12

IO monotherapy

	Squamous n=875	Non-SQ n=2166	All n=3041
Age	72,5	71,3	71,7
Male	61	46	51
PS 0-1	54	52	53
PS ≥ 2	25	23	24
PDL1 <1%	6	5	13
PDL1 1-49%	18	11	13
PDL1 >50%	61	73	70
ALK EGFR UnK	48/47	17/14	26/23
Atezolizumab Pembrolizumab	7 93	4 96	5 95
Brain mets	5	15	12

Waterhouse et al. Lung Cancer 156 (2021) 41-49

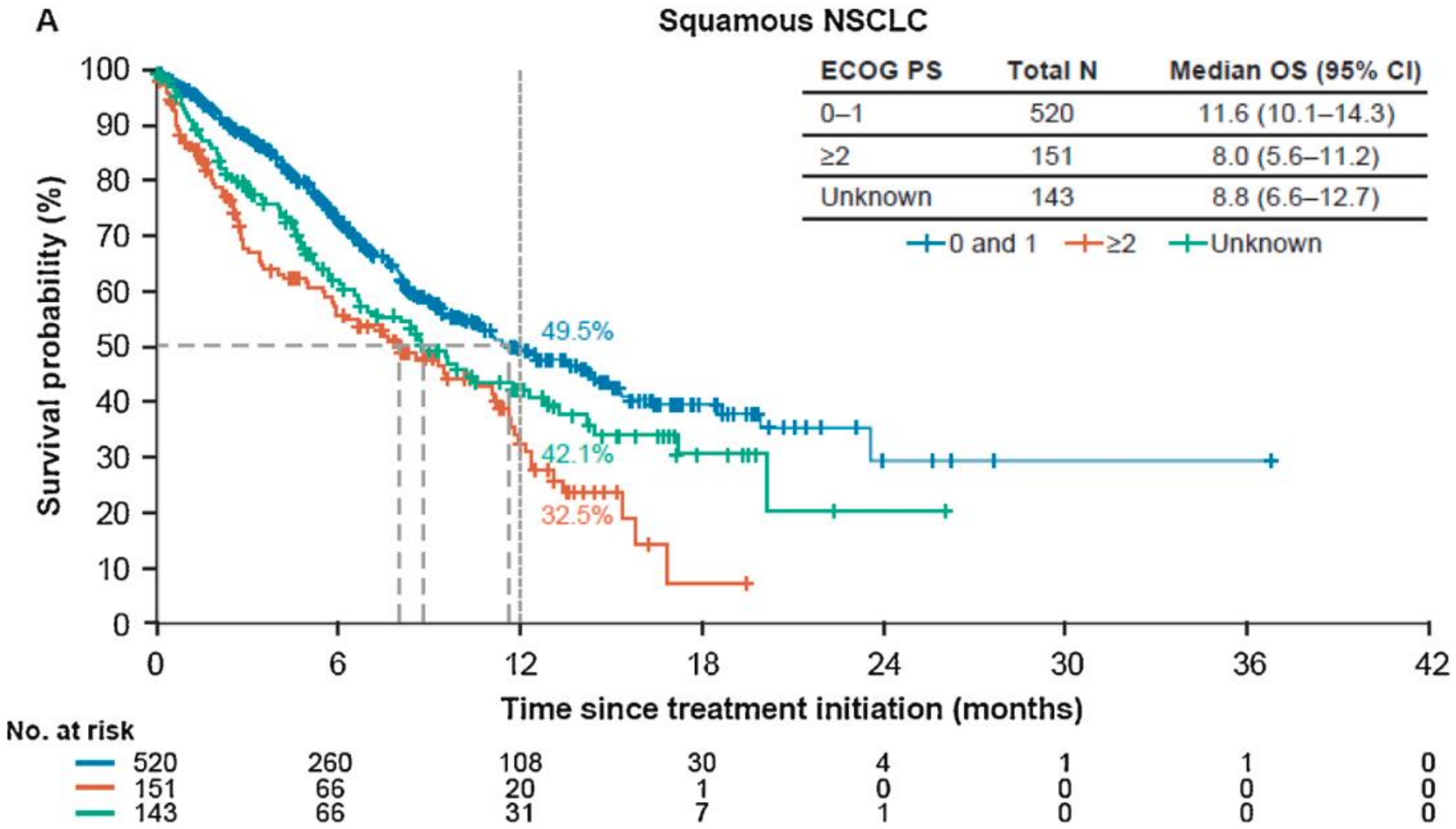
IO + chemo group (NSQ): OS by ECOG



Keynote-189
Median OS 22m
12m-OS 69,8 %

Waterhouse et al. Lung Cancer 156 (2021) 41-49; Garassino et al. JCO 2023

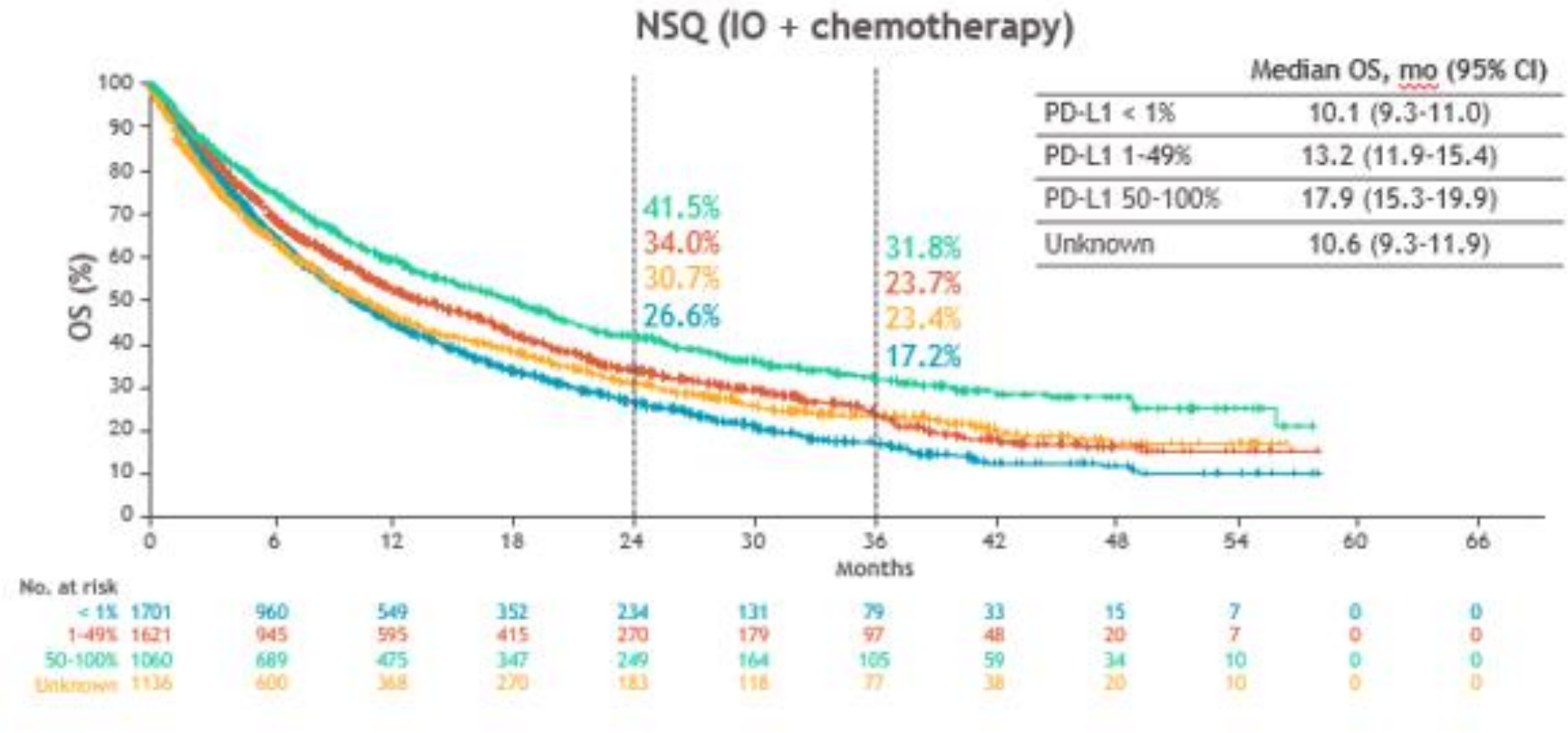
IO + chemotherapy (SQ): OS by ECOG



Keynote-407
Median OS 17,2m
12m-OS 64,7 %

Waterhouse et al. Lung Cancer 156 (2021) 41-49; Novello S. et al. JCO 2023

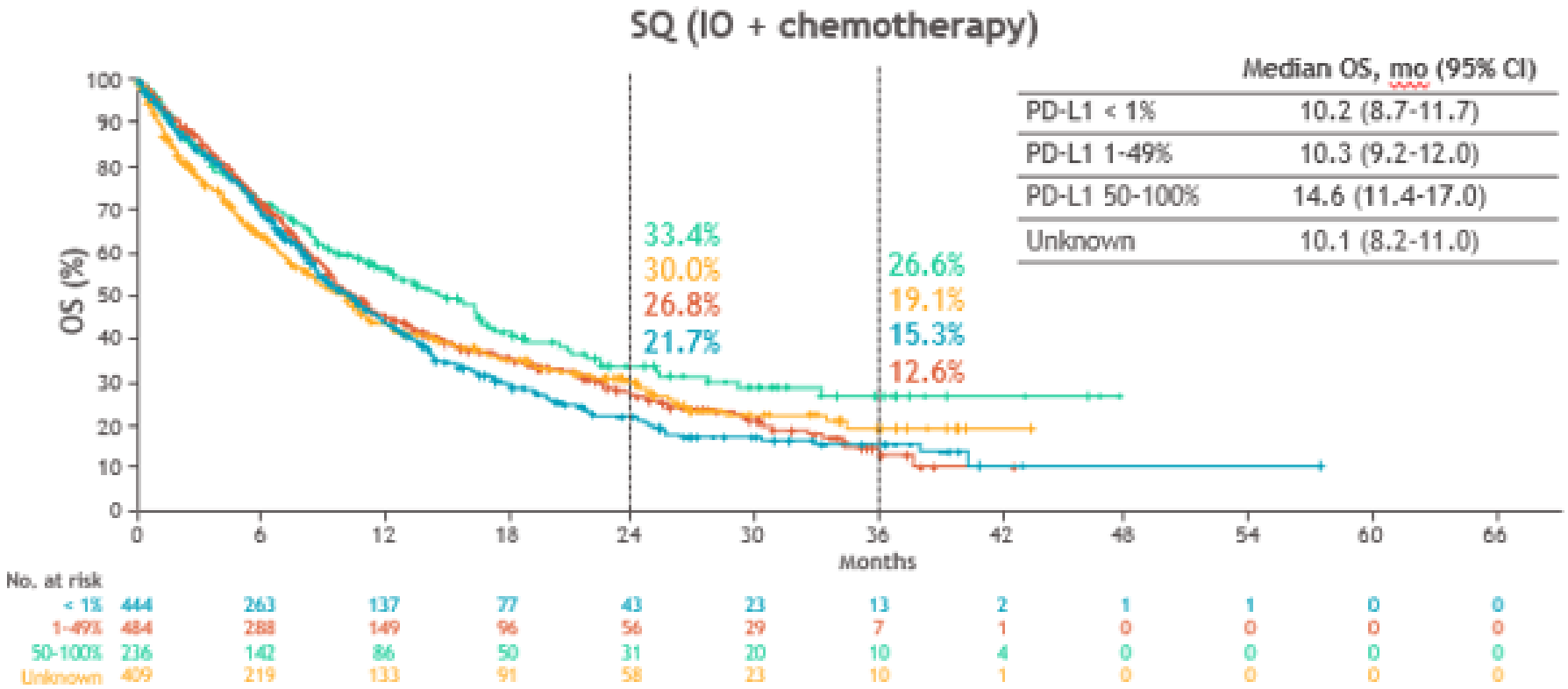
IO + chemotherapy (NSQ): OS by PD-L1



Keynote-189 (PD-L1<1%)
Median OS 17.2m
36m-OS 23,3%

Waterhouse et al. Lung Cancer 156 (2021) 41-49; Garassino et al. JCO 2023

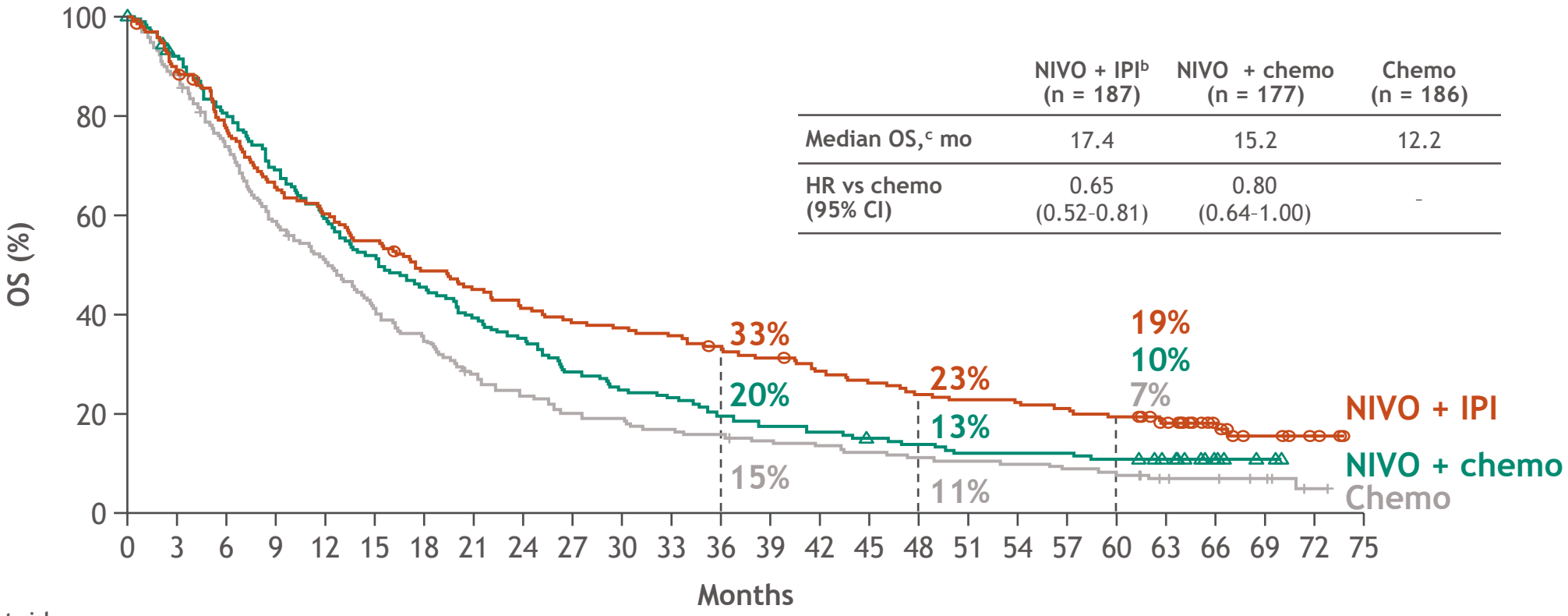
IO + chemotherapy (SQ): OS by PD-L1



Keynote-407 (PD-L1<1%)
Median OS 15m
36m-OS 22,1%

Waterhouse et al. Lung Cancer 156 (2021) 41-49; Novello S. et al. JCO 2023

CheckMate 227*: OS in patients with tumor PD-L1 < 1%



	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)	0.80 (0.64-1.00)	-

No. at risk																										
NIVO + IPI	187	165	142	120	110	100	88	81	74	69	67	64	59	55	49	45	41	39	38	36	33	27	15	8	3	0
NIVO + chemo	177	159	139	119	102	88	78	67	60	48	42	39	34	29	27	24	22	19	19	19	17	14	7	2	0	0
Chemo	186	164	135	107	92	74	62	49	41	35	33	29	27	24	22	20	18	17	16	14	12	8	7	5	1	0

Database lock: February 15, 2022; minimum/median follow-up for OS: 61.3/66.7 months.

[a]In patients with PD-L1 < 1% with a PFS event (per BICR), subsequent systemic therapy was received by 44% in the NIVO + IPI arm, 39% in the NIVO + chemo arm, and 48% in the chemo arm; subsequent immunotherapies by 8%, 5%, and 33%; subsequent chemo by 43%, 37%, and 33%, respectively. [b]NIVO + IPI vs NIVO + chemo HR was 0.80 (95% CI, 0.63-1.00). [c]Median OS 95% CI are 13.21-22.05 (NIVO + IPI), 12.29-19.78 (NIVO + chemo), and 9.17-14.32 (chemo). NA, not available (no patients at risk at 5 years).

Brahmer et al. ASCO 2022

*** not EMA approved**

CheckMate 9LA study design[a]

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

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 of immunotherapy

Primary endpoint
- OS

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

Exploratory analysis
- Efficacy by histology (NSQ vs SQ) or by baseline brain metastases status[f] in patients with tumor PD-L1 < 1%

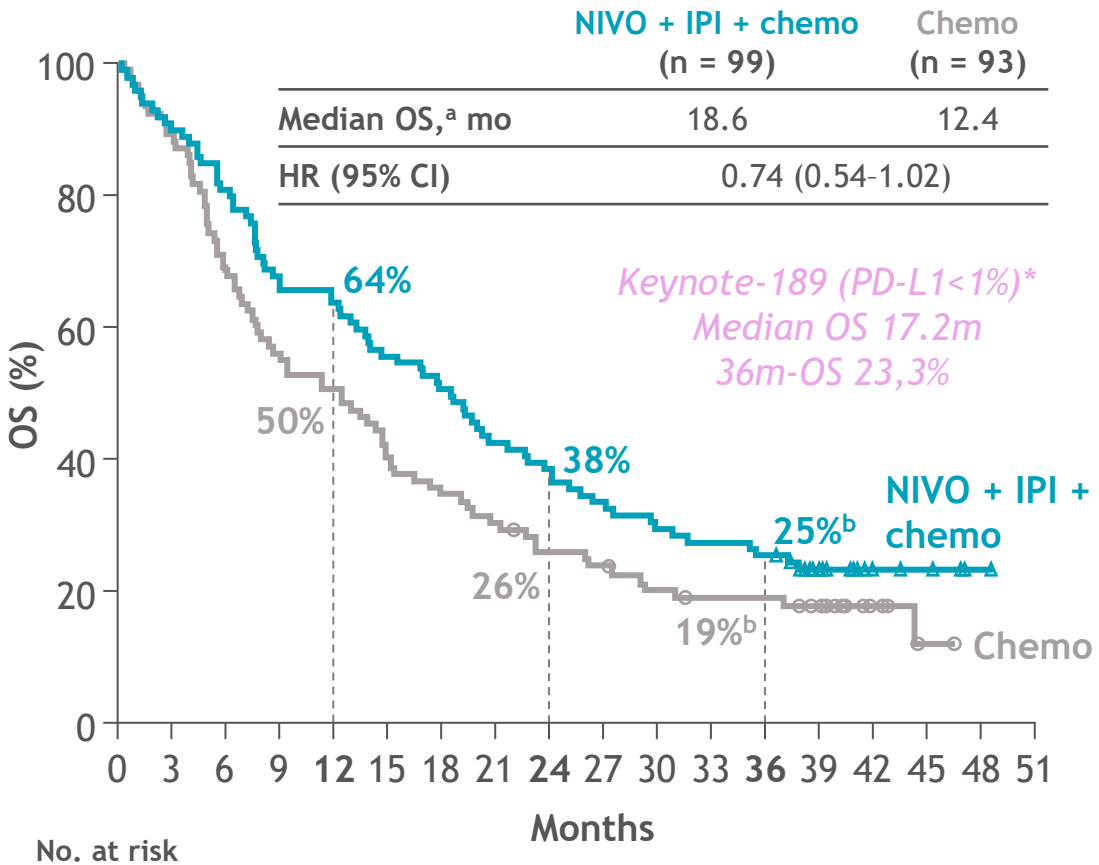
Database lock: February 15, 2022; minimum/median follow-up for OS: 36.1/42.6 months.

Adapted from *Lancet Oncology*, 22, Paz-Ares L, et al, First-line nivolumab plus ipilimumab combined with 2 cycles of chemotherapy in patients with non-small cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial, 198–211, Copyright 2021, with permission from Elsevier.
[a]NCT03215706. [b]Determined using the PD-L1 IHC 28-8 pharmDx assay (Dako). [c]Patients unevaluable for PD-L1 status were included in the tumor PD-L1 < 1% subgroup and capped at 10% of all randomized patients. [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin. [e]Statistically tested hierarchically. [f]Brain metastases determined by BICR at baseline. ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; ORR, objective response rate; PFS, progression-free survival; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomized.

John et al. ESMO 2022

OS by histology in patients with tumor PD-L1 < 1% expression

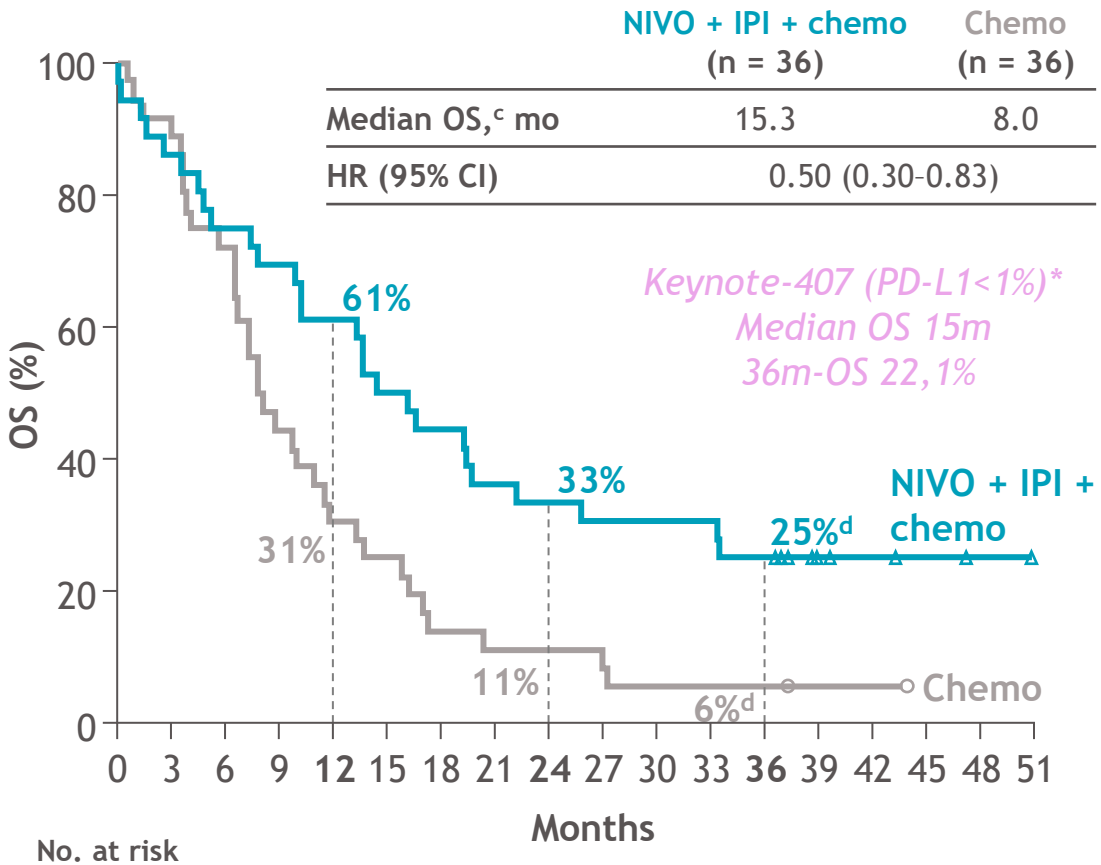
NSQ



No. at risk

NIVO + IPI + chemo	99	89	80	65	63	55	50	42	38	33	29	27	25	15	5	4	1	0
Chemo	93	83	64	52	47	38	32	28	23	21	17	15	15	12	5	1	0	0

SQ



No. at risk

NIVO + IPI + chemo	36	31	27	25	22	18	16	13	12	11	11	11	9	4	3	2	1	0
Chemo	36	33	26	16	11	9	5	4	4	4	2	2	2	1	1	0	0	0

Minimum follow-up: 36.1 months.

[a]95% CI, 13.2–22.7 (NIVO + IPI + chemo); 7.7–15.2 (chemo). [b]95% CI, 17–34 (NIVO + IPI + chemo) and 12–27 (chemo). [c]95% CI, 9.9–22.2 (NIVO + IPI + chemo) and 6.6–11.5 (chemo). [d]95% CI, 12–40 (NIVO + IPI + chemo) and 1–16 (chemo). CI, confidence interval; HR, hazard ratio.

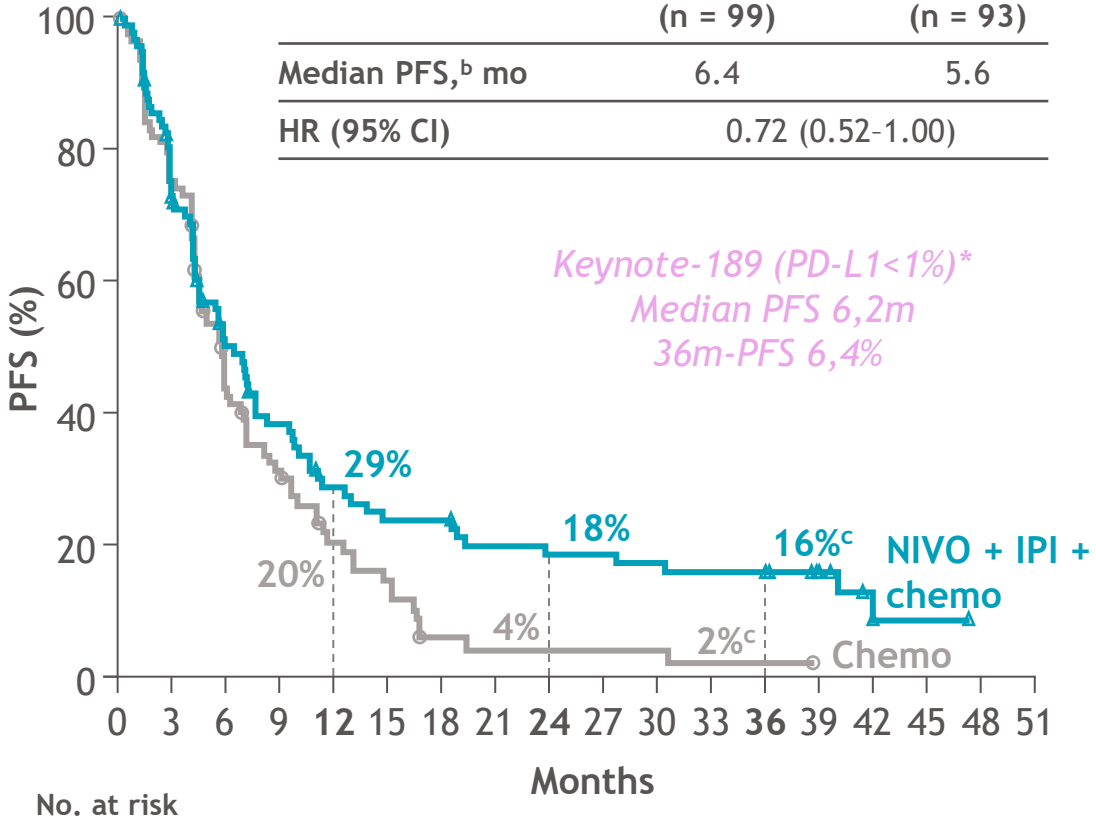
John et al. ESMO 2022; Novello et al. JCO 2023, Garassino et al. JCO 2023

**cross-trial comparisons cannot be made - no conclusions can be drawn.*

PFS[a] by histology in patients with tumor PD-L1 < 1% expression

NSQ

	NIVO + IPI + chemo (n = 99)	Chemo (n = 93)
Median PFS,[b] mo	6.4	5.6
HR (95% CI)	0.72 (0.52–1.00)	

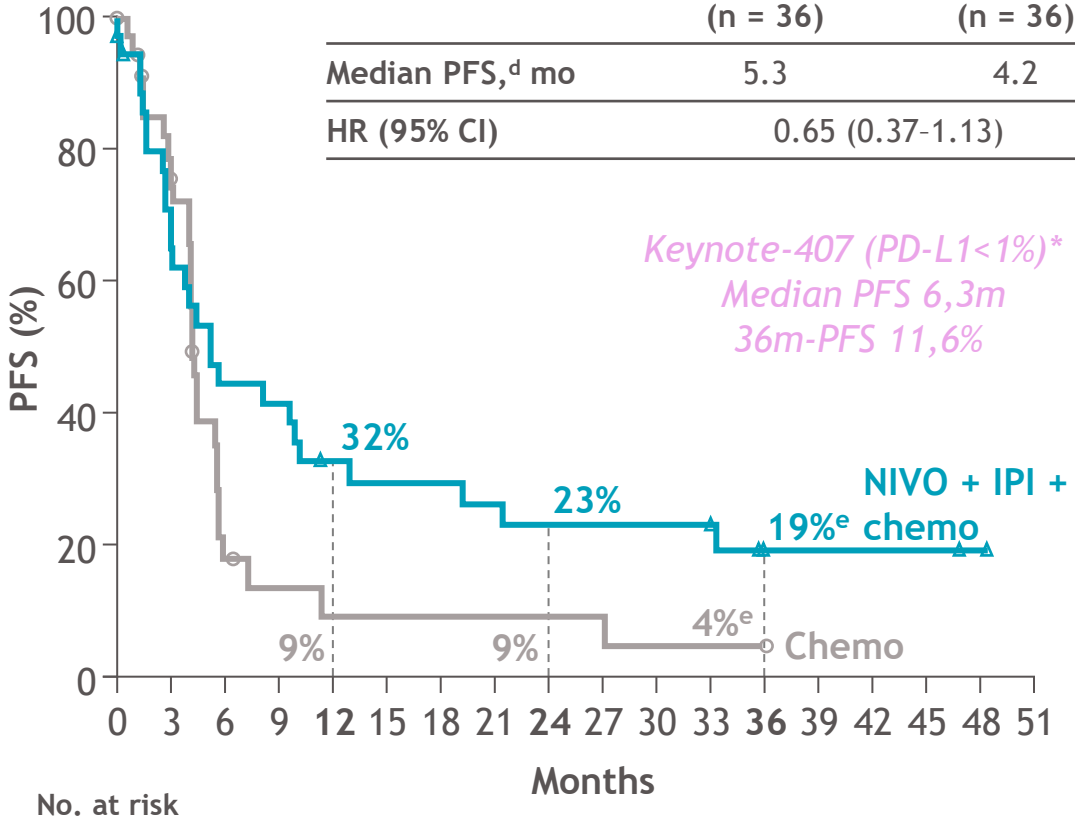


*Keynote-189 (PD-L1<1%)**
Median PFS 6,2m
36m-PFS 6,4%

No. at risk																		
NIVO + IPI + chemo	99	67	43	32	23	19	19	15	14	14	13	12	12	6	3	1	0	0
Chemo	93	67	36	24	14	10	3	2	2	2	2	1	1	0	0	0	0	0

SQ

	NIVO + IPI + chemo (n = 36)	Chemo (n = 36)
Median PFS,[d] mo	5.3	4.2
HR (95% CI)	0.65 (0.37–1.13)	



*Keynote-407 (PD-L1<1%)**
Median PFS 6,3m
36m-PFS 11,6%

No. at risk																		
NIVO + IPI + chemo	36	23	15	14	10	9	9	8	7	7	7	7	4	2	2	2	1	0
Chemo	36	25	5	3	2	2	2	2	2	2	1	1	1	0	0	0	0	0

Minimum follow-up: 35.2 months.

[a]PFS assessed per BICR. [b]95% CI, 4.2-7.7 (NIVO + IPI + chemo) and 4.2-6.9 (chemo). [c]95% CI, 9-24 (NIVO + IPI + chemo) and < 1-8 (chemo). [d]95% CI, 3.0-10.2 (NIVO + IPI + chemo) and 4.0–5.6 (chemo). [e]95% CI, 8-34 (NIVO + IPI + chemo) and < 1-18 (chemo).

John et al. ESMO 2022; Novello et al. JCO 2023, Garassino et al. JCO 2023

**cross-trial comparisons cannot be made - no conclusions can be drawn.*

Safety summary

	All treated				PD-L1 < 1%			
	NIVO + IPI + chemo (n = 358)		Chemo (n = 349)		NIVO + IPI + chemo (n = 134)		Chemo (n = 125)	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
TRAEs[a], %	92	48	88	38	90	48	87	36
Treatment-related SAEs[a], %	30	26	18	15	32	28	21	16
TRAEs leading to discontinuation[a], %	22	18	9	5	23	18	13	6
Treatment-related death[b], %	2[c]		2[c]		1[d]		4[d]	

*Keynote-189**
TRAEs gr 3-5: 52%
TRAEs leading to discont.: 27 %

*Keynote-407**
TRAEs gr 3-5 : 57%
TRAEs leading to discont.: 21 %

Minimum follow-up: 35.2 months for safety.

[a]Includes events reported between the first dose and 30 days after the last dose of study drug. [b]Includes deaths related to study drug toxicity occurring at any time. [c]Treatment-related deaths in the NIVO + IPI + chemo arm (n = 8): acute renal failure, thrombocytopenia, pneumonitis, hepatic toxicity, hepatitis, sepsis (n = 1 each), and diarrhea (n = 2); treatment-related deaths in the chemo arm (n = 6; 1 for each event): sepsis, anemia, pancytopenia, respiratory failure, pulmonary sepsis, and febrile neutropenia. [d]Treatment-related deaths in the NIVO + IPI + chemo arm (n = 2; 1 for each event): hepatitis and sepsis; treatment-related deaths in the chemo arm (n = 5; 1 for each event): sepsis, anemia, pancytopenia, respiratory failure, and pulmonary sepsis. SAE, serious adverse event.

John et al. ESMO 2022; Novello et al. JCO 2023, Garassino et al. JCO 2023

**cross-trial comparisons cannot be made - no conclusions can be drawn.*

CONCLUSIONS

- There is a high adherence in Belgium to clinical guidelines.
- Apart from PD-L1 there are other important clinical decision factors that guide clinicians to different regimens: ECOG PS, histology, metast. disease, age, patient preferences.
- Real world data show that OS is generally lower than those reported in pivotal clinical trials.
- ECOG PS has a strong association with OS regardless of histology.
- Patients with higher tumor PD-L1 TPS were associated with longer mOS regardless of histology.
- Real world data indicate there remains room for improvement in patients with metastatic NSCLC receiving 1L IO-based regimens, especially in the PD-L1<1%.

CONCLUSIONS

- With a 3-year minimum follow-up, 1L nivolumab + ipilimumab + chemotherapy for metastatic NSCLC showed long-term, durable OS benefit vs chemo in this exploratory analysis in patients with tumor PD-L1 expression < 1%, regardless of histology.
- There is evidence of added efficacy of CTLA-4 inhibition in PD-L1<1% (cold tumor)
- The safety profile was consistent with previous reports, and no new safety signals were seen in patients.
- These data further support NIVO + IPI + chemo as a 1L treatment option for patients with metastatic NSCLC, including those with a high unmet need