Symposium Post-ASCO : NSCLC – Stades précoces et localement avancés

AFBOT
Association francophone belge d'oncologie thoracique

Docteur Rodolphe Durieux

2022 ASCO ANNUAL MEETING

NSCLC

Stades précoces et localement avancés

- Nivolumab + chemotherapy (CT) versus CT as neoadjuvant treatment for resectable IIIA-B non small cell lung carcinoma (NSCLC) : NADIM II trial

  Mariano Provencio – Madrid, Spain

- Two cycles versus three cycles of neoadjuvant sintilimab plus platinum-doublet chemotherapy in patients with resectable non-small-cell lung cancer (neoSCORE): A randomized, single center, two-arm phase II trial

  Fuming Qiu – Hangzhou, China

- Intraoperative quality metrics and association with survival following lung cancer resection

  Brendan Heiden – St. Louis, USA

Nivolumab + chemotherapy (CT) vs CT as neoadjuvant treatment for resectable stage IIIA-B non-small cell lung cancer (NSCLC): NADIM II trial

Primary endpoint results of pathological complete response (pCR)

Mariano Provencio[1], Ernest Nadal[2], José Luis González-Larriba[3], Alex Martínez[4], Reyes Bernabé[5], Joaquim Bosch-Barrera[6], Joaquín Casal-Rubio[7], Virginia Calvo[1], Amelia Insa[8], Santiago Ponce[9], Noemí Reguart[10], Javier de Castro[11], Joaquín Mosquera[12], Raquel Benítez[13], Carlos Aguado de la Rosa[3], Ramón Palmero[2], Florentino Hernando-Trancho[3], Atocha Romero[1], Alberto Cruz-Bermúdez[1] & Bartomeu Massuti[14]

[1]Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain; [2]Institut Català d'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain; [3]Hospital Universitario Clínico San Carlos, Madrid, Spain; [4]Hospital Universitario e Instituto de Oncología Vall d´Hebron (VHIO), Barcelona, Spain; [5]Hospital Universitario Virgen del Rocio, Seville, Spain; [6]Institut Català d'Oncologia, Girona, España; [7]Hospital Universitario de Vigo, Pontevedra, Spain; [8]Fundación INCLIVA, Hospital Clínico Universitario de Valencia, Valencia, Spain; [9]Hospital Universitario 12 de Octubre, Madrid, Spain; [10]Hospital Clínic de Barcelona, Spain; [11]Hospital Universitario La Paz, Madrid, Spain; [12]Complejo Hospitalario Universitario A Coruña, A Coruña, Spain; [13]Genetic and Molecular Epidemiology Group, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; [14]Hospital General Universitario de Alicante, Alicante, Spain.

NADIM II (NCT03838159) is a randomized, phase 2, open-label, multicentre study evaluating nivolumab + chemotherapy vs chemotherapy as neoadjuvant treatment for potentially resectable NSCLC

2022 ASCO ANNUAL MEETING

#ASCO22

PRESENTED BY: **Mariano Provencio MD, PhD.**
Hospital Puerta de Hierro Majadahonda-Madrid, SPAIN
Spanish Lung Cancer Group

NADIM II Introduction (I)

- NSCLC accounts for 80–85% of all lung cancer cases[1]
- Approximately 20% of patients with NSCLC are diagnosed with stage IIIA (N2) disease[1]
- Multimodality treatment is necessary in this group of patients
- Outcomes remain poor for these patients, with a 5-year overall survival of around 36%[2,3]
- Preoperative CT have been shown to significantly improve overall survival in resectable NSCLC (HR for survival, 0.87, 95% CI 0.78–0.96, p=0.007). However, the absolute 5-year survival improvement is 5%[4]
- A strong association between pathological complete response (pCR) and survival following neoadjuvant CT has been shown across studies (HR for survival, 0.49; 95% CI 0.43-0.56)[5]
- However, the median rate of pCR after neoadjuvant CT is low, 4% (range 0–16%)[6]

HR, hazard ratio; NSCLC, non-small cell lung cancer; pCR, pathological complete response

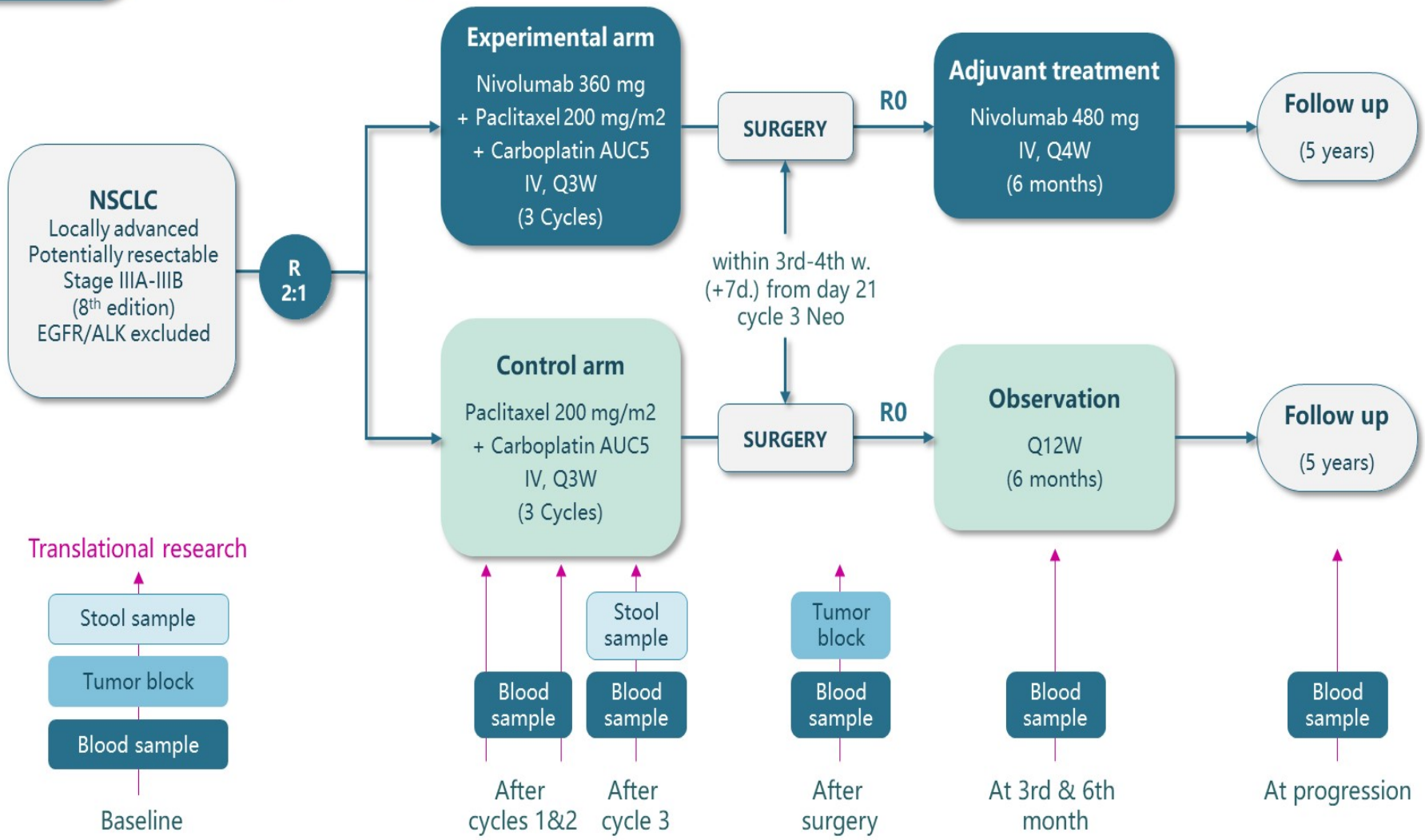
1. Siegel RL, et al. Cancer statistics, 2020. CA Cancer J Clin 2020; 70: 7-30; 2. Ramnath N, et al. Chest 2013; 143 (suppl 5): e314S-340S; 3. Goldstraw P, et al. J. Thorac. Oncol. 2016, 11, 39–51; 4. NSCLC Meta-analyses Collaborative Group. Lancet 2014;383:1561–1571; 5. Waser N, et al. Poster presentation at ESMO 2020; Sept 19-21; Virtual; P1243; 6. Hellmann, MD, et al. Lancet Oncol 2014;15:e42–e50.

NADIM II Introduction (II)

- Neoadjuvant immunotherapy for resectable NSCLC have shown promising activity in several single-arm, phase II studies.
- Phase III CM816, showed a higher rate of pathological complete response (pCR) on tumor resection and improved EFS compared to that seen with neoadjuvant chemotherapy [6]
- NADIM II is a randomized, phase 2, open-label study evaluating nivolumab + CT versus CT as neoadjuvant treatment for resectable stage IIIA-B (AJCC 8th edition) NSCLC. It is an Investigator Sponsored Research Study.
- Here we present the primary endpoint results on pCR, as well as key safety data

Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

NADIM II Study design



Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

NADIM II Endpoints

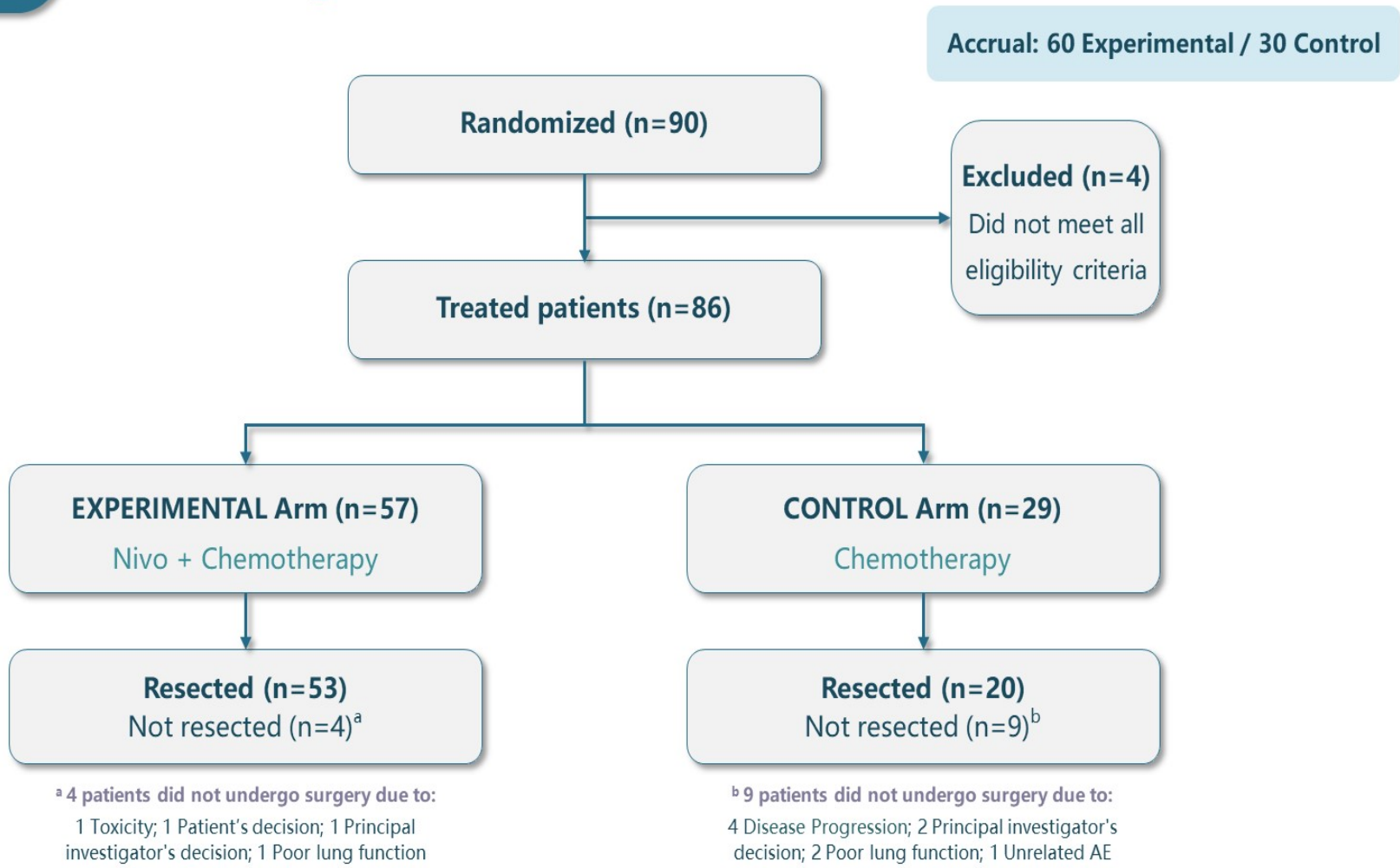
Primary endpoint

- Pathological complete response in the intention-to-treat population (ITT)

Secondary endpoints

- Major pathological response (MPR)
- Portion of delayed/canceled surgeries, length of hospital stays, surgical approach, incidence of AE/SAE related to surgery
- Safety and tolerability: Adverse events graded according to CTCAE v5.0
- Potential predictive biomarkers (ctDNA, TCR)
- Other: (i) OS at 12, 18 and 24 months; (ii) PFS at 12, 18 and 24 months; (iii) Down-staging; (iv) Mortality at 90 days after surgery; (v) Association between clinical baseline characteristics and ORR, pathological response, AEs, PFS and OS; (vi) Association between pathological response and PFS or OS; (vii) Association between MPR and histology; (viii) Association between histology and PFS at 18 months

NADIM II Flow diagram



NADIM II Baseline characteristics (I)

Baseline characteristics - ITT population		
Characteristic	**NIVO + Chemo (n = 57)**	**Chemo (n = 29)**
Age – median (range), years	63 (58-70)	62 (57-66)
Female – No. (%)	21 (36.8)	13 (44.8)
History of tobacco use – No. (%)		
Never smoker	5 (8.7)	0 (0.0)
Former smoker	23 (40.4)	10 (34.5)
Current smoker	29 (50.9)	19 (65.5)
ECOG PS – No. (%)		
0	31 (54.4)	16 (55.2)
1	26 (45.6)	13 (44.8)
Histology – No. (%)		
Adenocarcinoma	25 (43.9)	11 (37.9)
Adenosquamous	1 (1.8)	0 (0.0)
Squamous	21 (36.8)	14 (48.3)
Large Cell Carcinoma	2 (3.5)	1 (3.5)
NOS / Undifferentiated	7 (12.3)	2 (6.9)
Other	1 (1.8)	1 (3.5)

Baseline characteristics - ITT population		
Characteristic	**NIVO + Chemo (n = 57)**	**Chemo (n = 29)**
TNM classification (AJCC 8th edition)		
T1N2M0	12 (21.1)	4 (13.8)
T2N2M0	16 (28.1)	7 (24.1)
T3N1M0	2 (3.5)	1 (3.5)
T3N2M0	13(22.8)	5 (19.3)
T4N0M0	6 (10.5)	9 (31.0)
T4N1M0	8 (14.0)	3 (10.3)
Tumor size – Median (range), mm	43 (29-54)	52 (39-75)
Nodal stage – No. (%)		
N0	6 (10.5)	9 (31.0)
N1	10 (17.5)	4 (13.8)
N2	41 (71.9)	16 (55.2)
N2 multiple station	21(36.8)	10 (34.5)

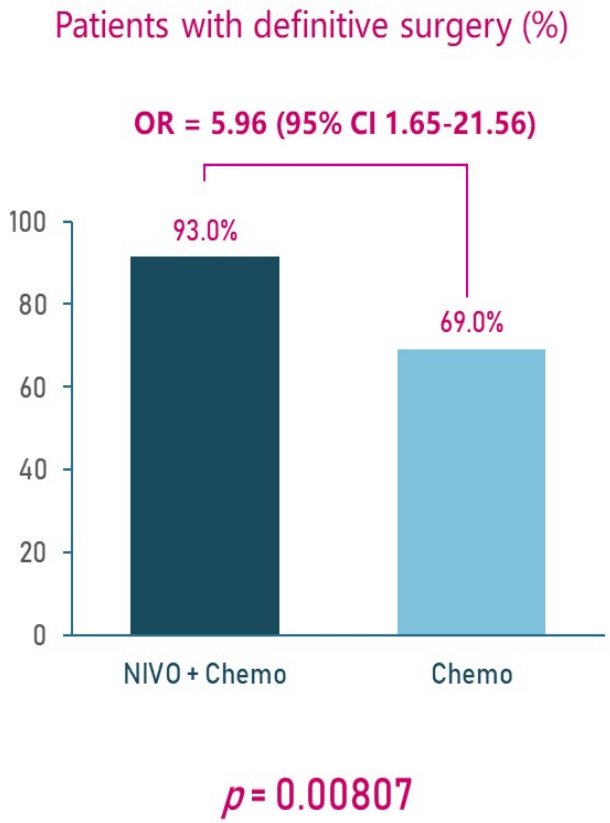
Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

AFBOT
Association francophone belge d'oncologie thoracique

2022 ASCO ANNUAL MEETING

NADIM II Surgery summary

Surgery summary			
Patients, No. (%)	**NIVO + chemo (n = 57)**	**Chemo (n = 29)**	**Total**
Patients with definitive surgery	53 (93.0)	20 (69.0)	73
Patients with cancelled definitive surgery	4 (7.0)	9 (31.0)	13
Due to adverse events	1 (1.7)	0 (0.0)	1
Due to disease progression	0 (0.0)	4 (13.7)	4
Not suitable for surgery	3 (5.2)	5 (17.2)	8



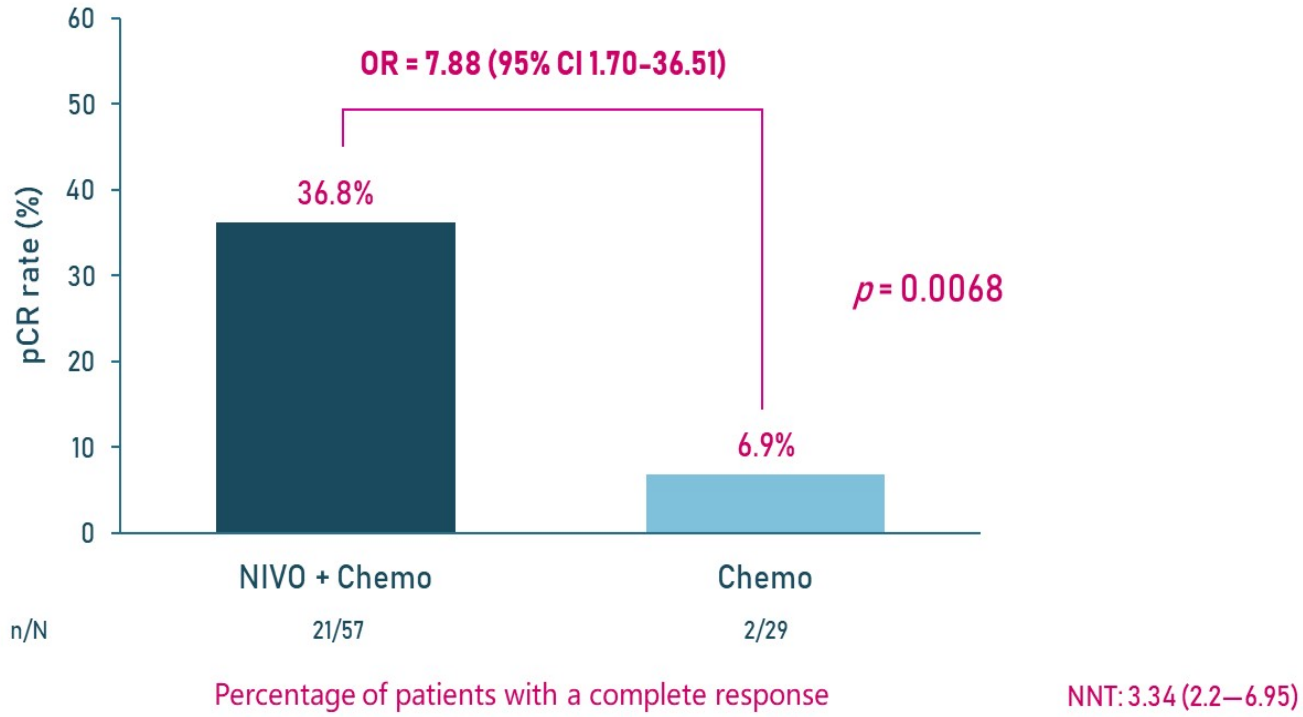
Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

AFBOT
Association francophone belge d'oncologie thoracique

2022 ASCO ANNUAL MEETING

NADIM II Primary endpoint - pCR

pCR[a] rate with neoadjuvant NIVO + CT vs CT in the ITT population[b]



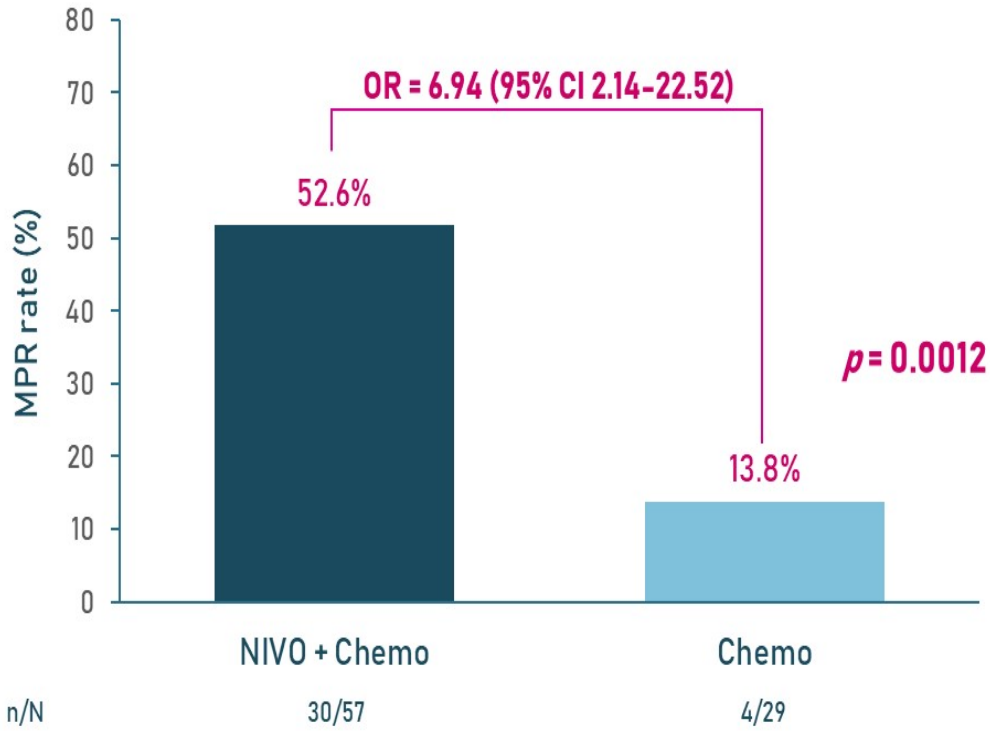
Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

AFBOT
Association francophone belge d'oncologie thoracique

2022 ASCO ANNUAL MEETING

NADIM II Secondary endpoints - MPR

MPR[a] rate with neoadjuvant NIVO + CT vs CT in the ITT population [b]



Percentage of patients with a complete response or a major response

NNT: 2.57 (1.76-4.81)

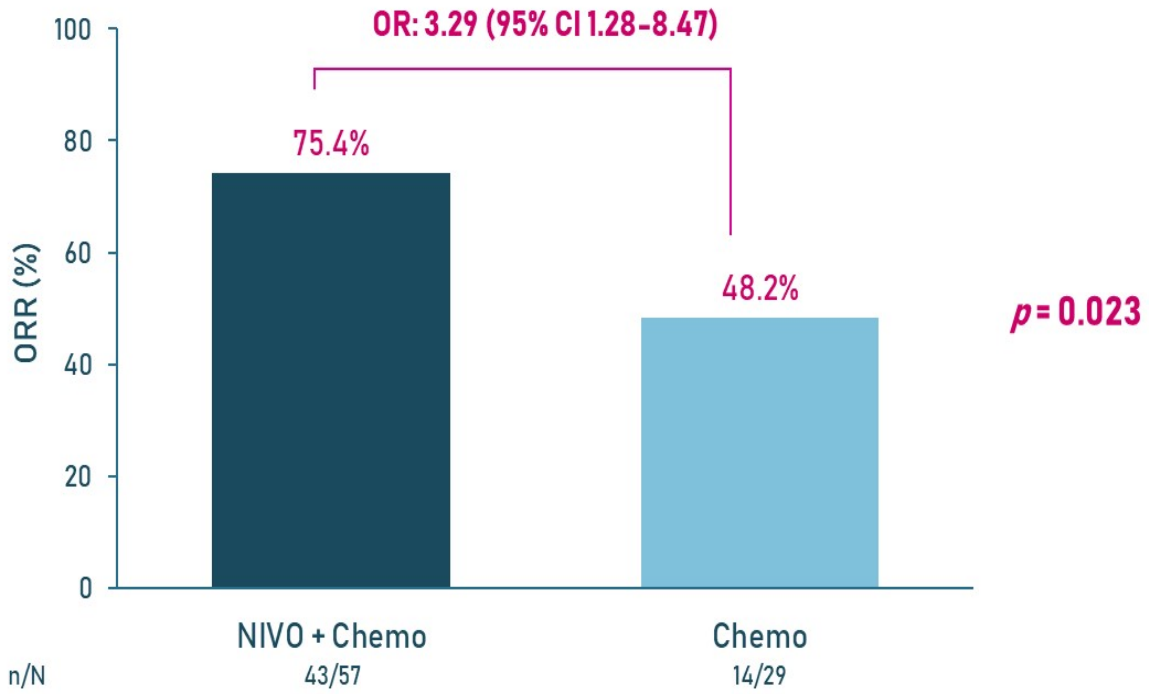
Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

AFBOT
Association francophone belge d'oncologie thoracique

2022 ASCO ANNUAL MEETING

NADIM II Secondary endpoints - ORR

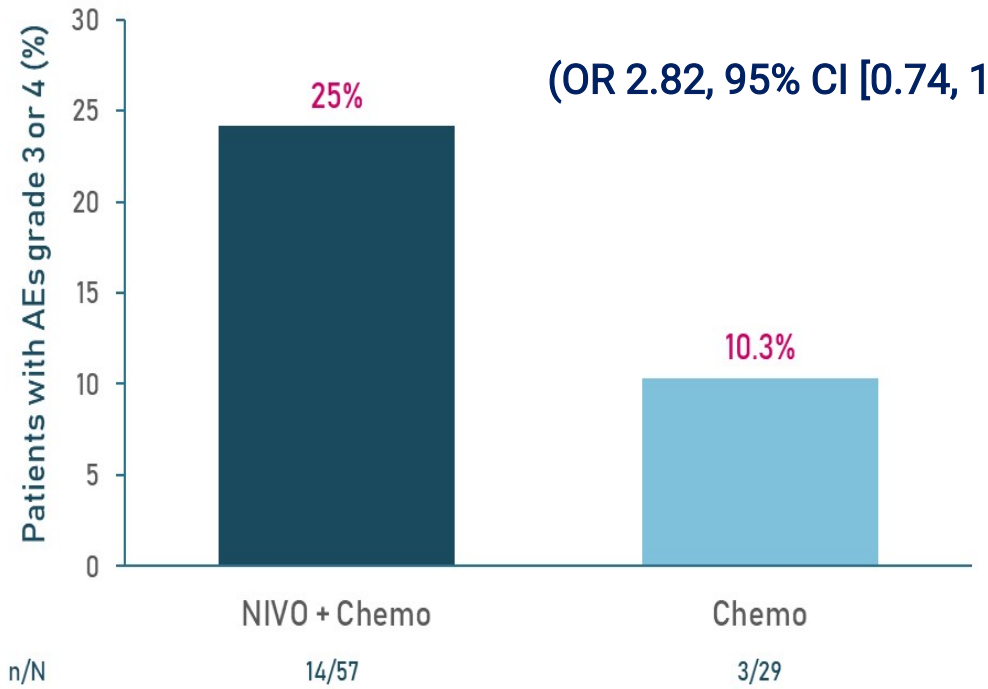
ORR[a] with neoadjuvant NIVO + Chemo vs Chemo in the ITT population [b]



Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

Secondary endpoints – Safety (I)

Adverse events G 3-4 summary (ITT population)



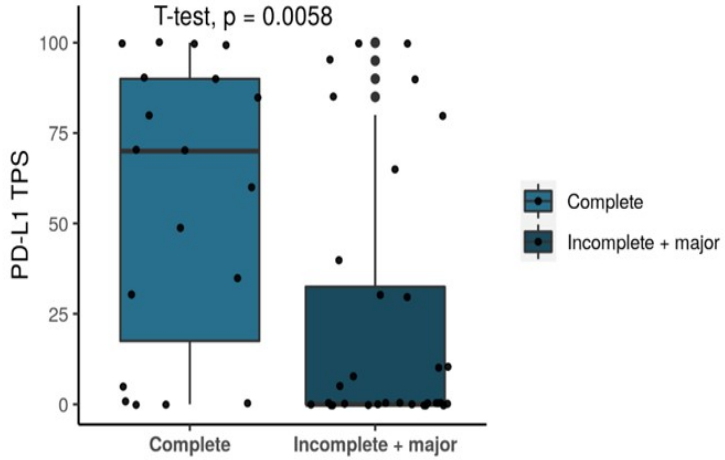
(OR 2.82, 95% CI [0.74, 10.76]; P = .201)

No grade 5 treatment-related adverse events were observed

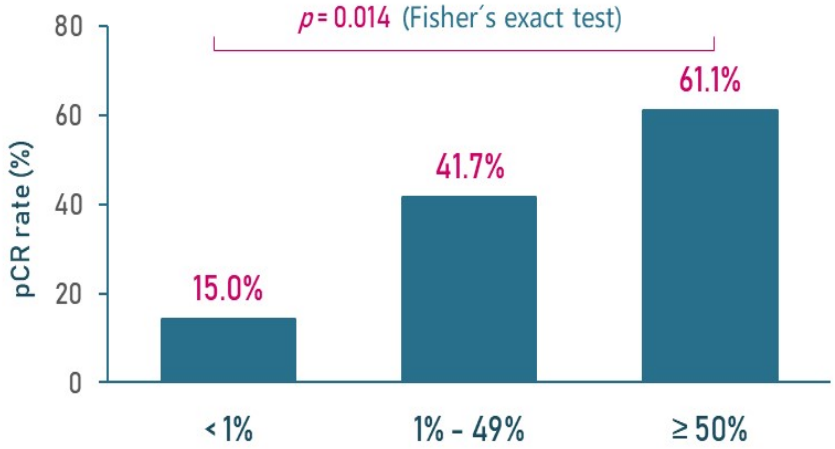
NADIM II Secondary endpoints – Predictive biomarkers

Predictive biomarkers of response (pCR)[a] to neoadjuvant NIVO + CT (ITT population)[b]

- Patients who achieved pCR had higher PD-L1 expression than patients who did not
- pCR rate raised across increasing categories of PD-L1 TPS
- Predictive value of PD-L1 TPS for pCR was AUC 0.728 (95% CI 0.58-0.87; p = 0.001)
- **OR** for pCR in the PD-L1 positive group (**≥1%**): **16.0** (95% CI 1.86-137.61; ***p* = 0.007**)



Pathological response



PD-L1 Tumor Proportion Score

[a]pCR was defined as 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]Patients who did not undergo surgery were considered as non-responders
IQR, interquartile range; ITT, intention-to-treat; pCR, pathological complete response; TPS, tumor proportion score, RR, risk ratio; PD-L1 positive group defined as ≥1% TPS.

NADIM II Conclusions

- NADIM II confirms superiority of neoadjuvant nivolumab plus chemotherapy combination in patients with resectable stage IIIA-B NSCLC
- The addition of neoadjuvant nivolumab to chemotherapy:
  - → Significantly improved pCR (OR = 7.88 [95% CI 1.70-36.5]) (Chi-squared test: p = 0.0068)
  - → Maintained a tolerable safety profile, with a moderate increase in grade 3-4 toxicity
  - → Did not impede the feasibility of surgery
- PD-L1 TPS has a predictive value for pCR (AUC 0.728 [95% CI 0.59-0.87]); (Chi-squared test: $p = 0.002$)

Nadim II : Nivolumab + CT vs CT as neoadjuvant treatment for resectable IIIA-B NSCLC

2022 ASCO® ANNUAL MEETING

Two cycles versus three cycles of neoadjuvant sintilimab plus platinum-doublet chemotherapy in patients with resectable non-small-cell lung cancer (neoSCORE): a randomized, single center, two-arm phase II trial

Fuming Qiu, MD

Department of Medical Oncology, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

June 5, 2022

On behalf of Junqiang Fan, Miner Shao, Jie Yao, Lufeng Zhao, Ling Zhu, Baizhou Li, Yanbiao Fu, Lili Li, Yunben Yang, Yunke Wang, Mengyao Chen, Wanglan Xie, Xinyi Zhang, Jinglian Tu, Xiaoke Chen, Zuqun Wu, Zexin Chen

Background

- Neoadjuvant immune checkpoint inhibitors (ICIs) plus chemotherapy have shown promising efficacy in resectable NSCLC[1,2].
- Two to four cycles of neoadjuvant immuno-chemotherapy were generally used in most clinical trials [1-4].
- Currently, the consensus of the optimal period remained unestablished.
- Sintilimab, a monoclonal antibody against PD-1, has exhibited a favorable MPR rate in single-agent neoadjuvant setting[5].
- This phase II study compared the efficacy and safety of two cycles versus three cycles of neoadjuvant sintilimab plus chemotherapy in resectable stage IB-IIIA NSCLC.

NSCLC, non-small-cell lung cancer; PD-1, programmed cell death protein 1; MPR, major pathological response.

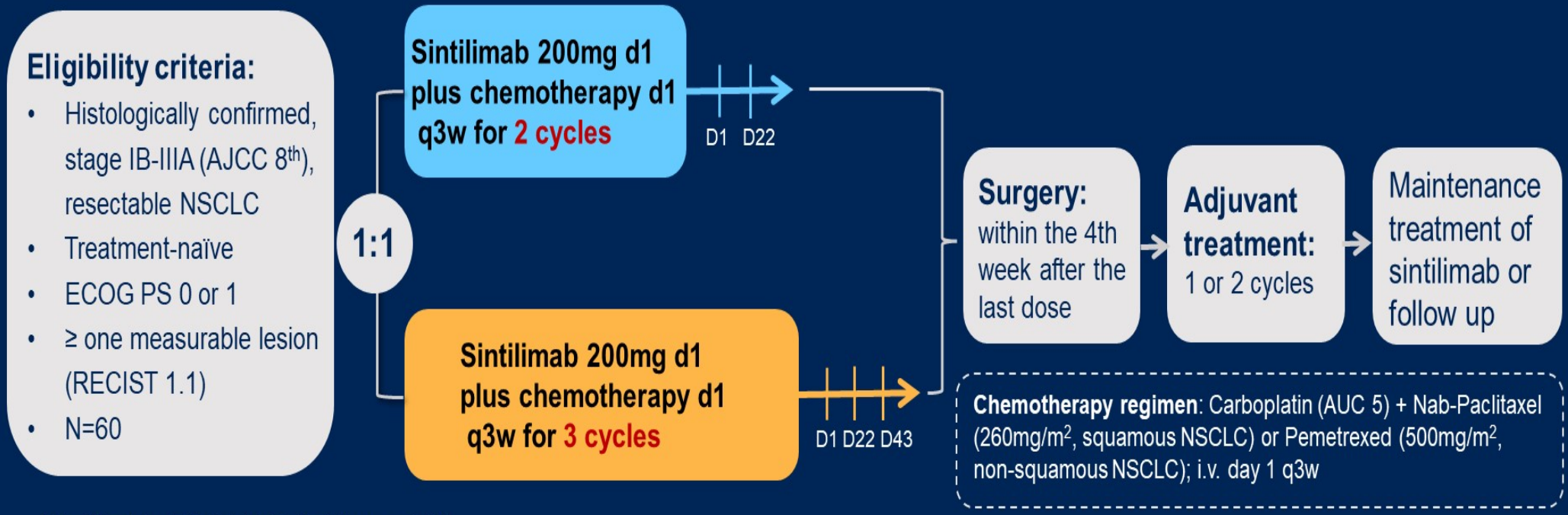
1. Provencio M, et al., Lancet Oncol. 2020. 21(11):1413-1422.
2. Forde PM, et al., N Engl J Med. 2022. online.
3. Rothschild SI , et al., J Clin Oncol. 2021. 39(26):2872-2880.
4. Shu CA, et al. Lancet Oncol. 2020. 21(6):786-795.
5. Gao S, et al. J Thorac Oncol. 2020. 15(5):816-826.

Neoadjuvant immuno-chemotherapy clinical trials

Trial	Phase	Enrollment	Stage	Neoadjuvant treatment	MPR	pCR
NCT02716038	II	30	IB-IIIA*	Atezolizumab + platinum doublet × 4 cycles	57%	33%
NADIM	II	46	IIIA*	Nivolumab + platinum doublet × 3 cycles	83%	63%
NCT04304248	II	33	IIIA, T3-4N2 IIIB**	Toripalimab + platinum doublet × 3 cycles	67%	50%
SAKK16/14	II	68	T1-3N2M0, IIIA(N2)*	Platinum doublet × 3 cycles, followed by durvalumab × 2 cycles	62%	18%
CheckMate816	III	358	IB-IIIA*	Nivolumab + platinum doublet vs platinum doublet × 3 cycles	36.9% vs 8.9%	24% vs 2.2%

*, per American Joint Committee on Cancer 7th edition
**, per American Joint Committee on Cancer 8th edition
pCR, complete pathology response.

Trial design

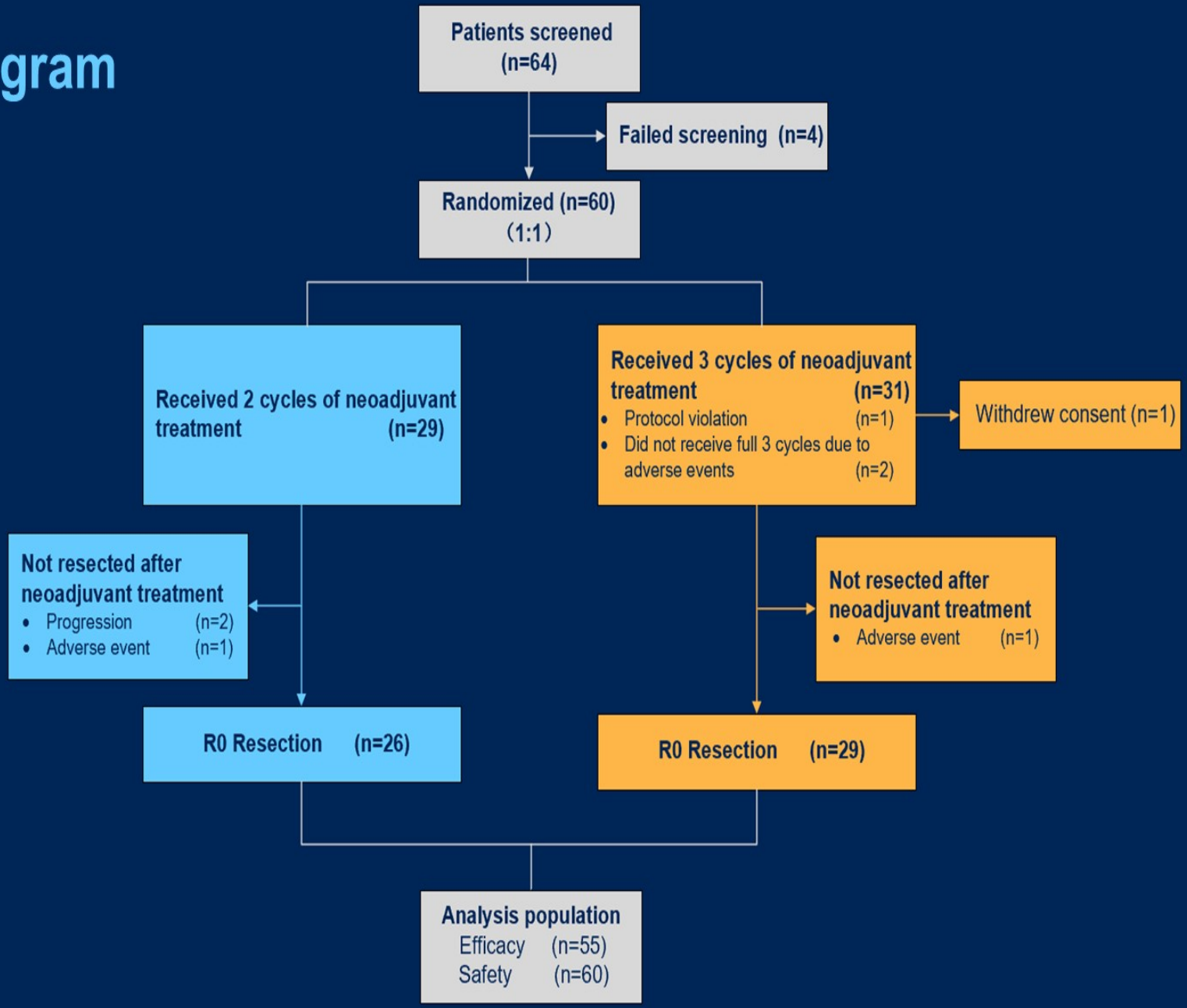


Stratified by PD-L1 TPS (≥1% vs < 1%)

- **Primary endpoint:** MPR rate
- **Secondary endpoints:** pCR rate, ORR, 2-year DFS rate, 2-year OS rate, safety
- **Exploratory endpoints:** novel immune biomarkers and the impact of sintilimab maintenance on 2-year DFS and OS

AJCC, American Joint Committee on Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; RECIST, Response Evaluation Criteria in Solid Tumors; PD-L1, programmed cell death ligand-1; TPS, tumor proportion score; i.v., intravenously; q3w, every 3 weeks; AUC, area under curve; ORR, objective response rate; DFS, disease-free survival; OS, overall survival.

Flow diagram

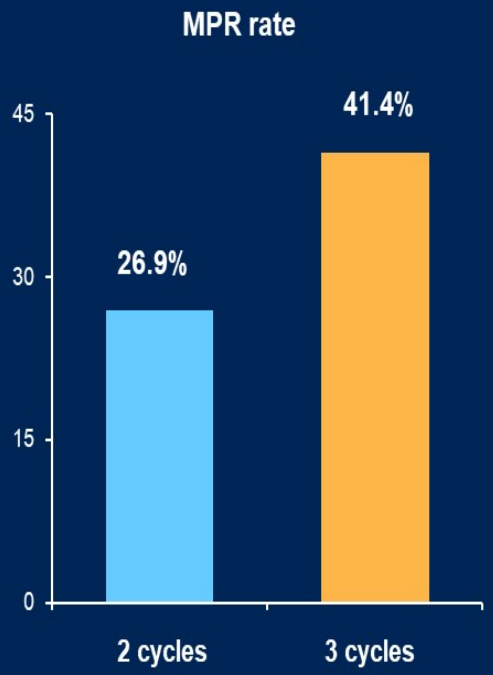


Baseline Characteristics

Characteristic	Overall (n=60)	2 cycles (n=29)	3 cycles (n=31)	*P* value*
Age, median (range), y	64.5 (38-75)	66 (50-75)	63 (38-74)	0.711
Sex, n (%)				
Male	48 (80.0)	25 (86.2)	23 (74.2)	0.245
Female	12 (20.0)	4 (13.8)	8 (25.8)	
ECOG PS, n (%)				
0	23 (38.3)	12 (41.4)	11 (35.5)	0.639
1	37 (61.7)	17 (58.6)	20 (64.5)	
Smoking status, n (%)				
Never	23 (38.3)	10 (34.5)	13 (41.9)	0.553
Current/Former	37 (61.7)	19 (65.5)	18 (58.1)	
Clinical stage, AJCC8th, n (%)				
IB-IIB	28 (46.7)	11 (37.9)	17 (54.8)	0.190
IIIA	32 (53.3)	18 (62.1)	14 (45.2)	
Histology, n (%)				
Adenocarcinoma	23 (38.3)	10 (34.5)	13 (41.9)	0.513
Squamous	36 (60.0)	19 (65.5)	17 (54.8)	
NOS	1 (1.7)	0 (0.0)	1 (3.2)	
PD-L1 TPS, n (%)				
<1%	29 (48.3)	15 (51.7)	14 (45.2)	0.611
≥1%	31 (51.7)	14 (48.3)	17 (54.8)	

NOS, not otherwise specified; *, the two-sided *P* values were from the Mann-Whitney U tests for the continuous factors, $\chi 2$ tests and Fisher's exact tests for the categorical factors.

Primary endpoint



- Three cycles treatment presented a **14.5%** increase in MPR rate in comparison to two cycles

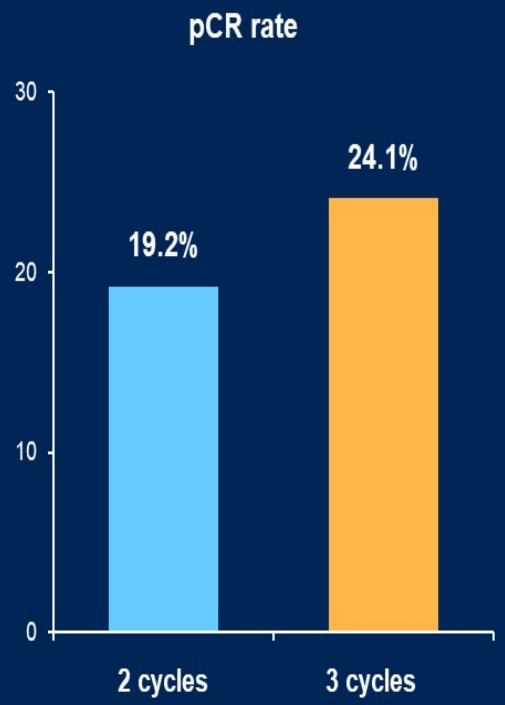
Pathological response, n(%)	Total, n=55	2 cycles, n=26	3 cycles, n=29	*P* value*
MPR	19（34.5%） (95% CI：22.2-48.6%)	7（26.9%） (95% CI：11.6-47.8%)	12（41.4%） (95% CI：23.5-61.1%)	0.260

- Narrow cycle difference of treatment
- Small sample size

*, the two-sided *P* value was from the χ2 test, the exact two-sided 95% CIs were calculated by use of the Clopper-Pearson method.

NOS, not otherwise specified; *, the two-sided *P* values were from the Mann-Whitney U tests for the continuous factors, χ2 tests and Fisher's exact tests for the categorical factors.

Secondary endpoints



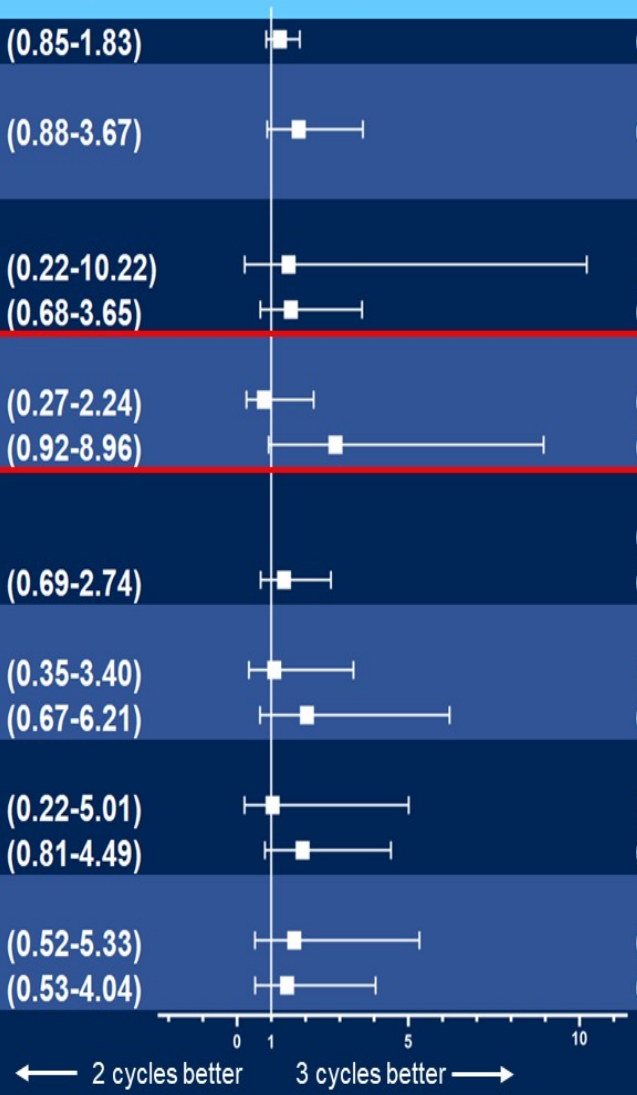
- Three cycles treatment presented a **4.9%** increase in pCR rate in comparison to two cycles

Pathological response, n(%)	Total, n=55	2 cycles, n=26	3 cycles, n=29	*P* value*
pCR	12（21.8%） (95% CI：11.8-35.0%)	5（19.2%） (95% CI：6.6-39.4%)	7（24.1%） (95% CI：10.3-43.5%)	0.660

*, the two-sided *P* value was from the $\chi 2$ test, the exact two-sided 95% CIs were calculated by use of the Clopper-Pearson method.

Subgroup analysis of MPR

Subgroups	2 cycles, n(%)	3 cycles, n(%)	RR (95%CI)	*P* value*
Overall	7/26 (26.9)	12/29 (41.4)	1.25 (0.85-1.83)	0.26
Sex				
Male	7/22 (31.8)	12/21 (57.1)	1.80 (0.88-3.67)	0.095
Female	0/4	0/8		
Age				
<60	1/4 (25.0)	3/8 (37.5)	1.50 (0.22-10.22)	1
≥60	6/22 (27.3)	9/21 (42.9)	1.57 (0.68-3.65)	0.284
Clinical stage				
IB-IIB	4/10 (40.0)	5/16 (31.3)	0.78 (0.27-2.24)	0.692
IIIA	3/16 (18.8)	7/13 (53.8)	2.87 (0.92-8.96)	0.064
Histology				
Non-squamous	0/10	3/14 (21.4)		0.239
Squamous	7/16 (43.8)	9/15 (60.0)	1.37 (0.69-2.74)	0.366
PD-L1 TPS				
<1%	4/13 (30.8)	4/12 (33.3)	1.08 (0.35-3.40)	1
≥1%	3/13 (23.1)	8/17 (47.1)	2.04 (0.67-6.21)	0.259
Smoking status				
Never	2/9 (22.2)	3/13 (23.1)	1.04 (0.22-5.01)	1
Current/Former	5/17 (29.4)	9/16 (56.3)	1.91 (0.81-4.49)	0.119
ECOG PS				
0	3/11 (27.3)	5/11 (45.5)	1.67 (0.52-5.33)	0.659
1	4/15 (26.7)	7/18 (38.9)	1.46 (0.53-4.04)	0.458

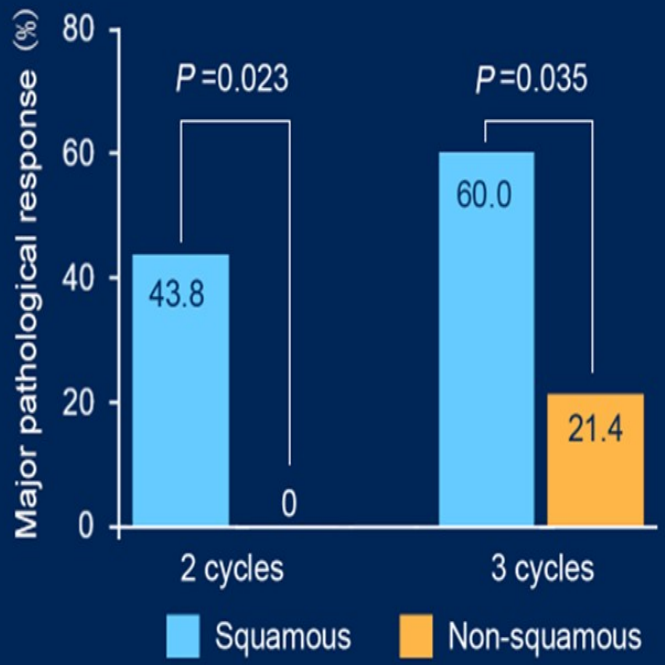


*, the two-sided *P* values and relative risks (RRs) were from $\chi 2$ tests and Fisher's exact tests.

Tumor response by histology

- Patients with squamous NSCLC achieved a significantly higher MPR rate compared with non-squamous subtype in both groups.
- Similar trends were observed in pCR rate and ORR.

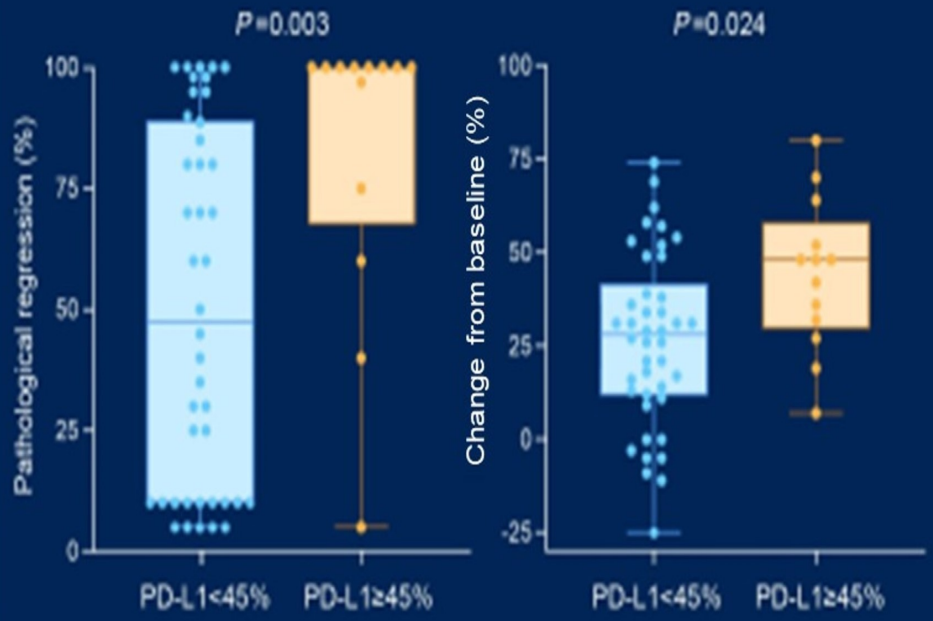
Response	Squamous (n=31) n(%)	Non-squamous (n=24) n(%)	*P* value*
MPR	16 (51.6%) 95% CI：33.1-69.8%	3（12.5%） 95% CI：2.7-32.4%	0.002
pCR	9 (29.0%) 95% CI：14.2-48.0%	3（12.5%） 95% CI：2.7-32.4%	0.141
ORR	19 (61.3%) 95% CI：42.2-78.2%	10 (41.7%) 95% CI：22.1-63.4%	0.148



*, the two-sided *P* values were from the χ2 tests and Fisher's exact tests, the exact two-sided 95% CIs were calculated by use of the Clopper-Pearson method.

PD-L1 TPS

- Better tumor responses were seen in patients with PD-L1 TPS≥45%.



Surgical details

- Planned surgery was conducted for 89.7% vs 93.5% of patients in 2-cycle arm and 3-cycle arm.
- Three cycles treatment did not increase surgical risk or postoperative complications.

Surgical parameters		Overall (n=55)	2 cycles (n=26)	3 cycles (n=29)	*P* value*
Type of resection, n (%)	Segmentectomy	1 (1.8)	0	1 (3.4)	0.281
	Lobectomy	43 (78.2)	20 (76.9)	23 (79.3)	
	Bilobectomy	9 (16.4)	6 (23.1)	3 (10.3)	
	Pneumonectomy	2 (3.6)	0	2 (6.9)	
Surgical approach, n (%)	Thoracotomy	1 (1.8)	0	1 (3.4)	1.0
	Thoracoscopy	54 (98.2)	26 (100.0)	28 (96.6)	
Timing of operation (minute)		110 (50-345)	120 (50-260)	110 (50-345)	0.946
Intraoperative blood loss (mL)		20 (10-300)	20 (10-100)	25 (10-300)	0.704
Intraoperative blood transfusion (mL)		0 (0-400)	0 (0-0)	0 (0-400)	0.095
Hospitalization time (day)		4 (2-12)	4 (2-12)	4 (2-12)	0.574

Postoperative complications** n (%)	Overall (n=55)	2 cycles (n=26)	3 cycles (n=29)
Recurrent laryngeal nerve paresis	4 (7.3)	3 (11.5)	1 (3.4)
Air leak > 5 days duration	3 (5.5)	2 (7.7)	1 (3.4)
Atrial fibrillation	3 (5.5)	0	3 (10.3)
Pneumonia	2 (3.6)	1 (3.8)	1 (3.4)
Pleural Effusion requiring drainage	2 (3.6)	1 (3.8)	1 (3.8)
Chyle leak	1 (1.8)	0	1 (3.4)
Blood transfusion	1 (1.8)	0	1 (3.4)
Bronchial haemorrhage	1 (1.8)	1 (3.8) †	0

*, the two-sided *P* values were from the Mann-Whitney U tests for the continuous factors, $\chi 2$ tests and Fisher's exact tests for the categorical factors;
**, complications were monitored during the first 30 days after surgery; †, one patient in 2-cycle arm had grade V bronchial haemorrhage (the Clavien-Dindo classification), which was considered unrelated to the study drug medication.

Treatment-related adverse events

TRAE, n (%)	2 cycles (n=29)		3 cycles (n=31)	
	Any grade	≥grade 3	Any grade	≥grade 3
Hematological toxicities				
Anemia	15 (51.7)	0	19 (61.3)	2 (6.5)
Decreased white blood cell count	8 (27.6)	2 (6.9)	6 (19.4)	2 (6.5)
Neutropenia	5 (17.2)	4 (13.8)	6 (19.4)	3 (9.7)
Thrombocytopenia	4 (13.8)	2 (6.9)	6 (19.4)	1 (3.2)
Non-hematological toxicities				
Alopecia	20 (69.0)	0	19 (61.3)	0
Paresthesia	8 (27.6)	0	11 (35.5)	0
Fatigue	11 (37.9)	0	10 (32.3)	0
Nausea	4 (13.8)	0	7 (22.6)	0
Vomiting	4 (13.8)	0	5 (12.9)	0
Rash	6 (20.7)	0	6 (19.4)	0
Constipation	2 (6.9)	0	5 (16.1)	0
Diarrhea	2 (6.9)	2 (6.9)	1 (3.2)	0
Increased alanine aminotransferase	12 (41.4)	1 (3.4)	14 (45.2)	2 (6.5)
Increased aspartate aminotransferase	5 (17.2)	0	7 (22.6)	1 (3.2)
Increased blood lactate dehydrogenase	8 (27.6)	0	5 (16.1)	0
Blood creatinine increased	3 (10.3)	0	2 (6.5)	0
Increased lipase	12 (41.4)	0	9 (29.0)	0
Immune-related colitis	0	0	1 (3.2)	1 (3.2)
Immune-related pneumonia	1 (3.4)	1 (3.4)	1 (3.2)	1 (3.2)

Shown were the treatment-related adverse events of any grade that occurred in more than 10% of patients in either group, or any treatment-related adverse events of grade≥ 3.

Conclusion

- Our study is the first randomized study comparing different treatment periods of immuno-chemotherapy in the neoadjuvant setting.
- Three cycles neoadjuvant treatment achieved a numerically higher MPR rate compared with two cycles, and was consistent across most subgroups.
  - MPR rate: 26.9% vs 41.4%.
- The MPR rate was impressively higher in patients with squamous NSCLC compared with non-squamous subtype.
  - MPR rate: 43.8% vs 0% (2 cycles); 60% vs 21.4% (3 cycles)
- PD-L1 expression had a modest predictive value for pathological response.
- The neoadjuvant regimen with an extra cycle was well tolerated.

Our data suggest that more cycles of neoadjuvant immuno-chemotherapy provide higher MPR rate for patients with resectable NSCLC, especially in the squamous subtype.