ASCO©2021 – novinky v liečbe NSCLC

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Vyhlásenie o konflikte záujmov autora

☐ Nemám potenciálny konflikt záujmov

X Deklarujem nasledujúci konflikt záujmov

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2021 ASCO ANNUAL MEETING

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

Heather A. Wakelee,[1] Nasser Altorki,[2] Caicun Zhou,[3] Tibor Csőszi,[4] Ihor O. Vynnychenko,[5] Oleksandr Goloborodko,[6] Alexander Luft,[7] Andrey Akopov,[8] Alex Martinez-Marti,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Antonio Chella,[12] Shunichi Sugawara,[13] Fan Wu,[14] Jing Yi,[15] Yu Deng,[15] Mark McCleland,[15] Elizabeth Bennett,[15] Barbara J. Gitlitz,[15] Enriqueta Felip[16]

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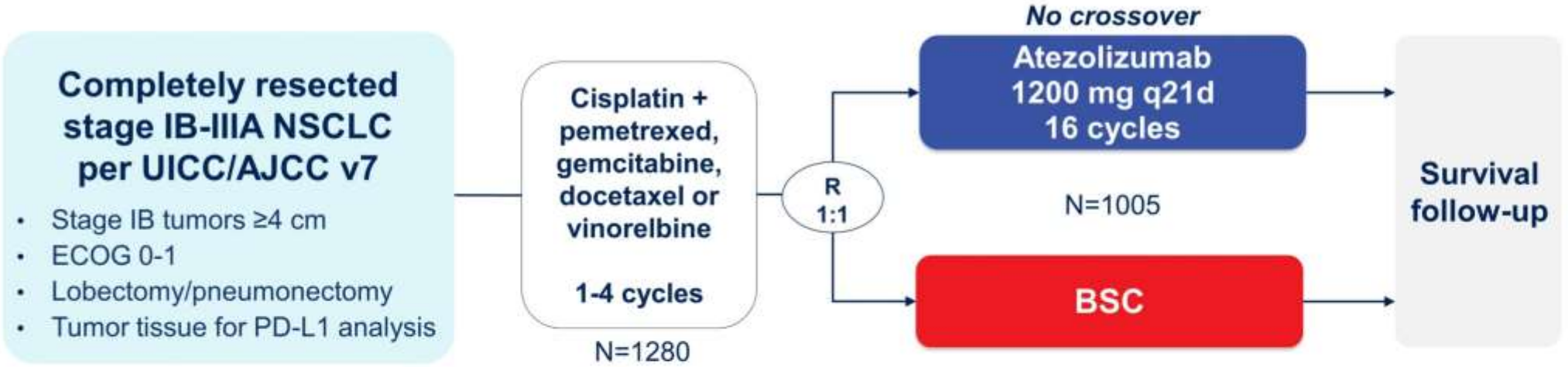
IMpower010: study design



Stratification factors

- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints

- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints

- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

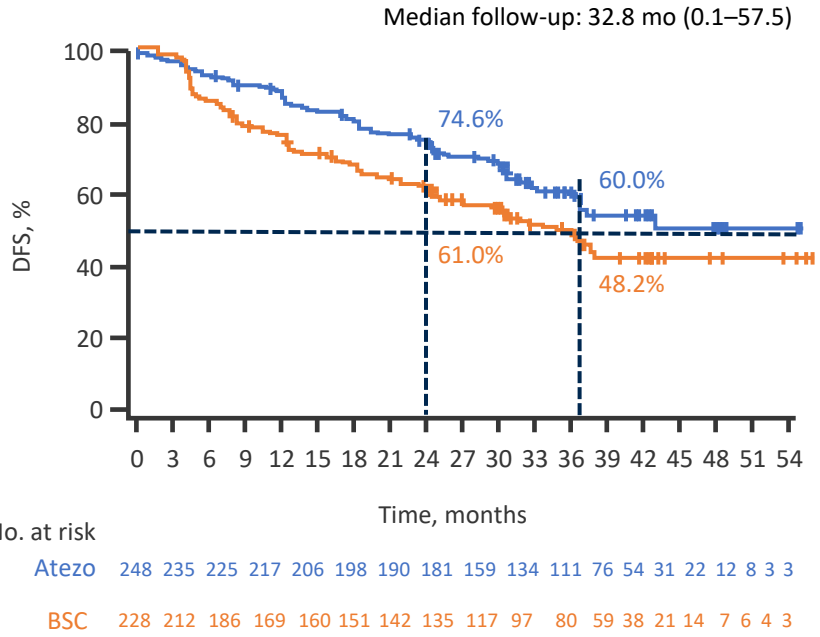
Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a] Per SP142 assay.

- # Výsledky

Disease-free survival

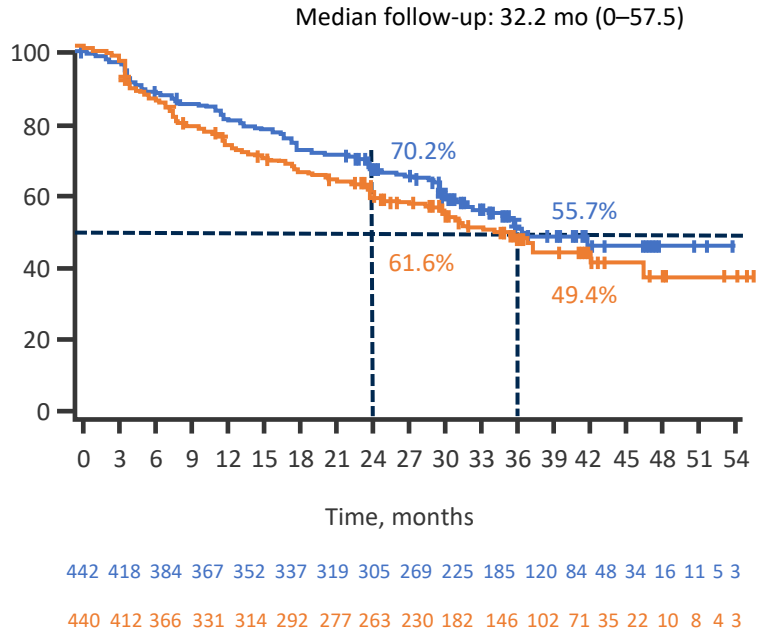
PD-L1 ≥1% stage II–IIIA population

	Atezolizumab (n=248)	BSC (n=228)
mDFS, mo (95%CI)	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95%CI)	0.66 (0.50, 0.88)	
p-value	0.004	



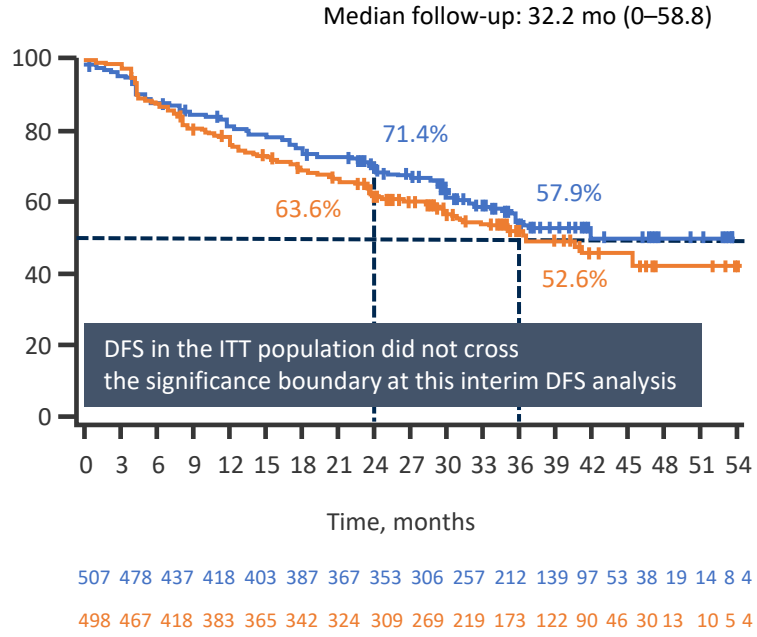
All-randomized stage II–IIIA population

	Atezolizumab (n=442)	BSC (n=440)
mDFS, mo (95%CI)	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95%CI)	0.79 (0.64, 0.96)	
p-value	0.02	



ITT population stage IB–IIIA population

	Atezolizumab (n=507)	BSC (n=498)
mDFS, mo (95%CI)	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95%CI)	0.81 (0.67, 0.99)	
p-value	0.04	



Cut-off date: Jan 21, 2021. Log-rank test

Wakelee HA, et al. J Clin Oncol 2021;39(suppl):Abstr 8500

IMpower010

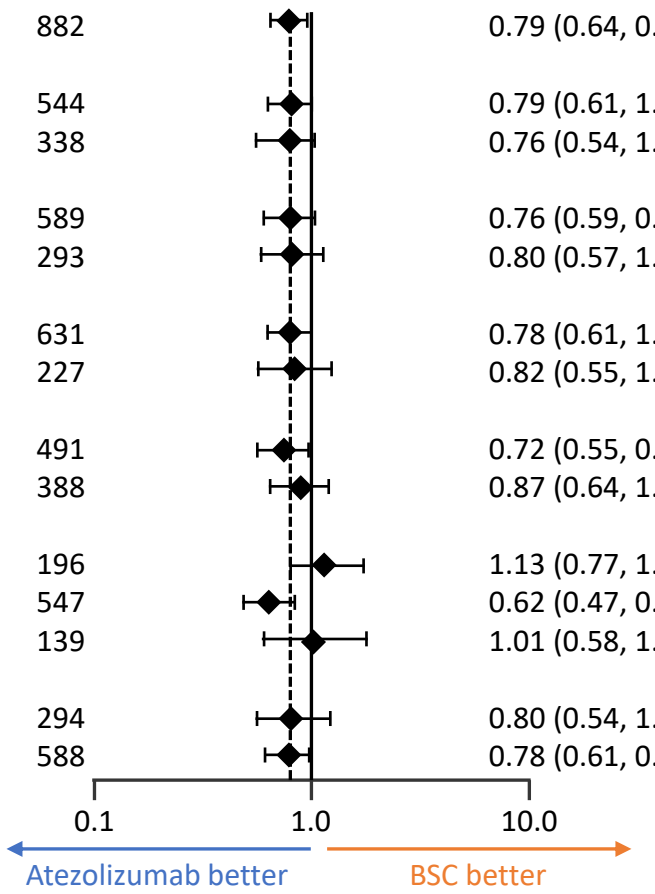
- Výsledky:
  - DFS pri **PD-L1 TC ≥ 1 % st. II – IIIA, HR 0,66** (0,50, 0,88), p = 0,0039
  - DFS pri všetkých štádiách II – IIIA: 0,79 (0,64 – 0,96), p = 0,0205
  - DFS ITT IB – IIIA: 0,81 (0,67 – 0,96), p = 0,0395

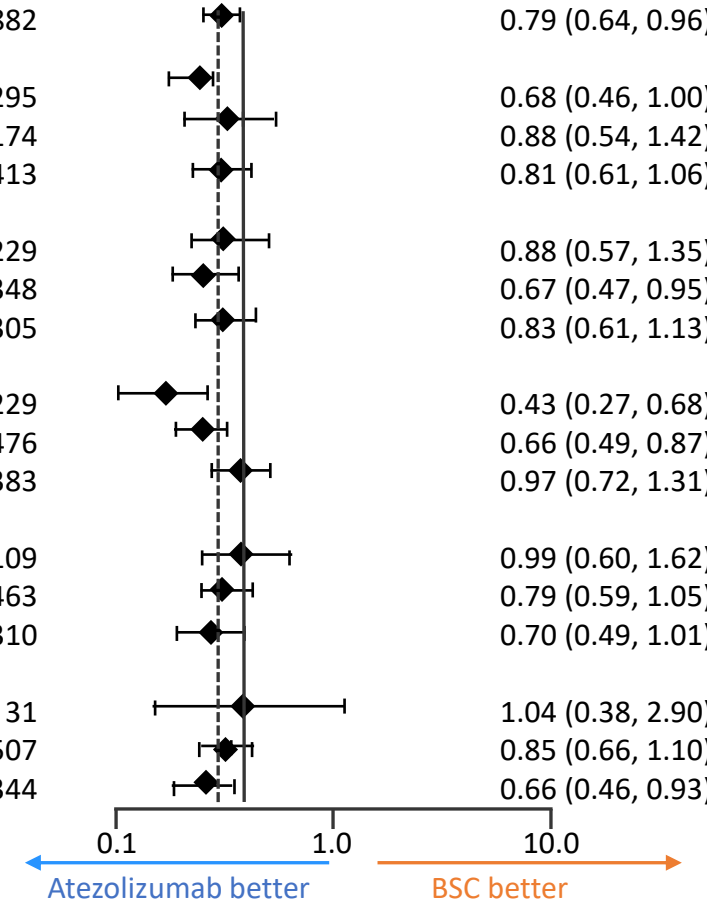
- AE vedúce k prerušeniu liečby atezolizumabom bolo 18,2 %
- Akýkoľvek stupeň toxicity v ramene s atezolizumabom bol 92,7 vs. 70,7 % v BCS
- Toxicita G¾ : 21,8 a 11,5 %

• Výsledky – pokračovanie

Disease-free survival in all-randomized stage II–IIIA population subgroups

Subgroup	N	HR (95%CI)*
All patients	882	0.79 (0.64, 0.96)
Age, years		
<65	544	0.79 (0.61, 1.03)
≥65	338	0.76 (0.54, 1.05)
Sex		
Male	589	0.76 (0.59, 0.99)
Female	293	0.80 (0.57, 1.13)
Race		
White	631	0.78 (0.61, 1.00)
Asian	227	0.82 (0.55, 1.22)
ECOG PS		
0	491	0.72 (0.55, 0.95)
1	388	0.87 (0.64, 1.18)
Tobacco use history		
Never	196	1.13 (0.77, 1.67)
Previous	547	0.62 (0.47, 0.81)
Current	139	1.01 (0.58, 1.75)
Histology		
Squamous	294	0.80 (0.54, 1.18)
Nonsquamous	588	0.78 (0.61, 0.99)
All patients	882	0.79 (0.64, 0.96)
Stage		
IIA	295	0.68 (0.46, 1.00)
IIB	174	0.88 (0.54, 1.42)
IIIA	413	0.81 (0.61, 1.06)
Regional lymph node stage (pN)		
N0	229	0.88 (0.57, 1.35)
N1	348	0.67 (0.47, 0.95)
N2	305	0.83 (0.61, 1.13)
SP263 PD-L1 status		
TC ≥50%	229	0.43 (0.27, 0.68)
TC ≥1%	476	0.66 (0.49, 0.87)
TC <1%	383	0.97 (0.72, 1.31)
EGFR mutation status		
Yes	109	0.99 (0.60, 1.62)
No	463	0.79 (0.59, 1.05)
Unknown	310	0.70 (0.49, 1.01)
ALK re-arrangement status		
Yes	31	1.04 (0.38, 2.90)
No	507	0.85 (0.66, 1.10)
Unknown	344	0.66 (0.46, 0.93)





Cut-off date: Jan 21, 2021. *Stratified for all patients, unstratified for all other subgroups

Wakelee HA, et al. J Clin Oncol 2021;39(suppl):Abstr 8500

IMpower010: závery

- U pacientov po kompletnej resekcii NSCLC, atezolizumab podaný po adjuvantnej chemoterapii signifikantne predlžuje DFS v štádiách II – IIIA a má bezpečný profil konzistentný s predchádzajúcimi dátami

- Najväčší benefit bol pozorovaný u pacientov s PD-L1 TC ≥ 1 %

Wakelee HA, et al. J Clin Oncol 2021;39(suppl):Abstr 8500

2021 ASCO ANNUAL MEETING

Surgical outcomes from the phase 3 CheckMate 816 trial: nivolumab + platinum-doublet chemotherapy vs chemotherapy alone as neoadjuvant treatment for patients with resectable non-small cell lung cancer

Jonathan Spicer,[1] Changli Wang,[2] Fumihiro Tanaka,[3] Gene B. Saylors,[4] Ke-Neng Chen,[5] Moishe Liberman,[6] Everett Vokes,[7] Nicolas Girard,[8] Shun Lu,[9] Mariano Provencio,[10] Tetsuya Mitsudomi,[11] Mark M. Awad,[12] Enriqueta Felip,[13] Patrick M. Forde,[14] Scott J. Swanson,[12] Julie R. Brahmer,[14] Keith Kerr,[15] Cécile Dorange,[16] Junliang Cai,[16] Stephen Broderick[14]

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Abstract Number 8503

CheckMate 816, štúdia fázy III

- Cieľ štúdie: neoadjuvatne nivo + chemo vs. chemo pri resekabilnom NSCLC – chirurgické výsledky

Key patient inclusion criteria
- Stage IB (≥4 cm)–IIIA NSCLC
- No known sensitizing EGFR or ALK alterations
- ECOG PS 0–1

(n=358)

R
1:1

Nivolumab 360 mg + platinum-doublet chemotherapy q3w (n=179) 3cycles

Stratification
- Stage IIB/II vs. IIIA)
- PD-L1 (≥1% vs. <1%)*
- Sex

Chemotherapy q3w for 3 cycles (n=179)

S U R G E R Y

Optional adjuvant chemotherapy ± radiotherapy

Primary endpoints
- pCR (0% viable tumor cells in lung and lymph nodes), EFS

Secondary endpoints
- MPR, OS, safety

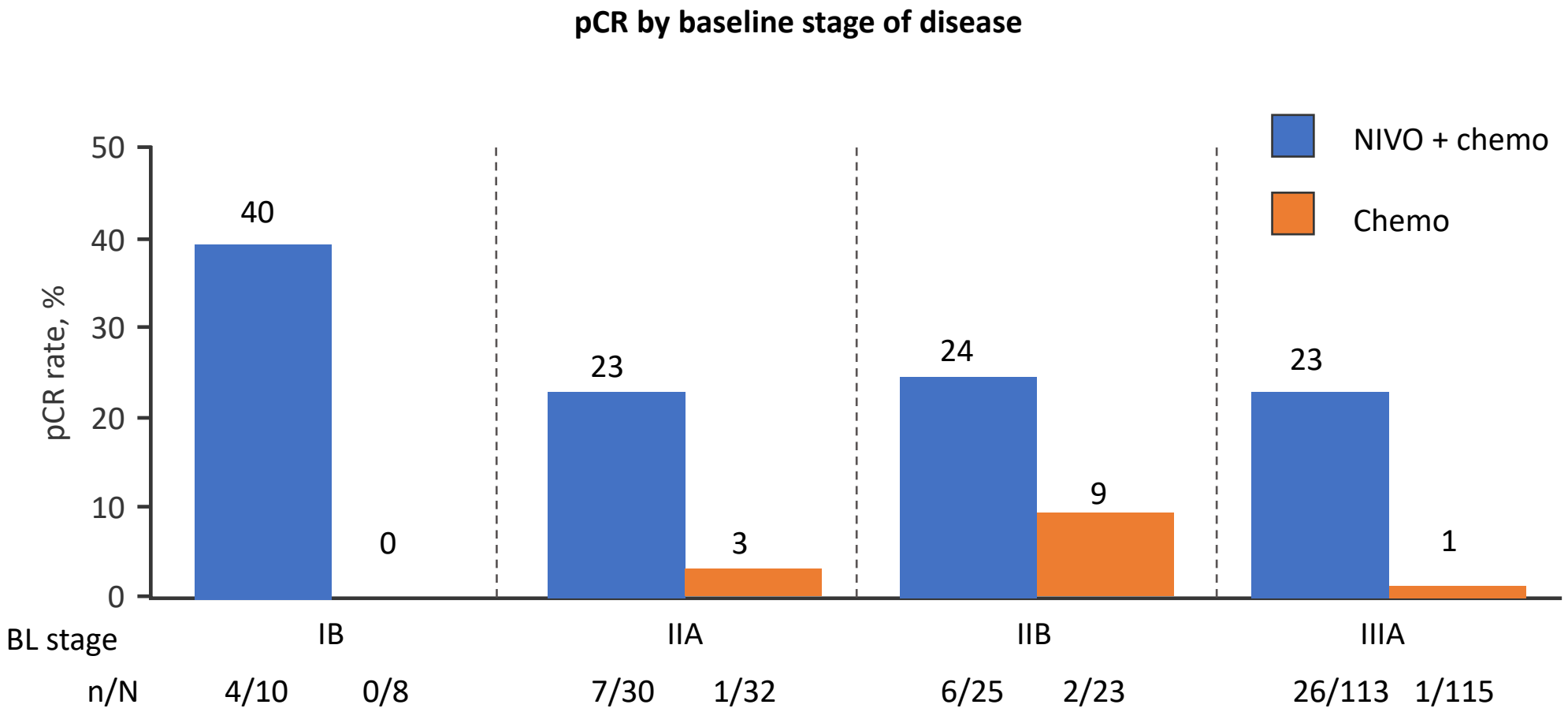
*Determined using IHC 28-8 pharmDx assay

Spicer J, et al. J Clin Oncol 2021;39(suppl):Abstr 8503

Výsledky

- Primárny cieľ: počet pCR/MPR: 24/36,9 % vs. 2,2/8,9 %
- Operácia 83 vs. 75 %
- Minimálna invazívna chirurgia: 30 vs. 22 %, konverzia 11 vs. 16 %
- Lobektómia/PE: 77/17 % vs. 61/25 %
- RO resekcia: 83 vs. 78 %
- Medián reziduálnych buniek: 10 vs. 74 %
- Trvanie operácie: 184 vs. 217

- # Výsledky



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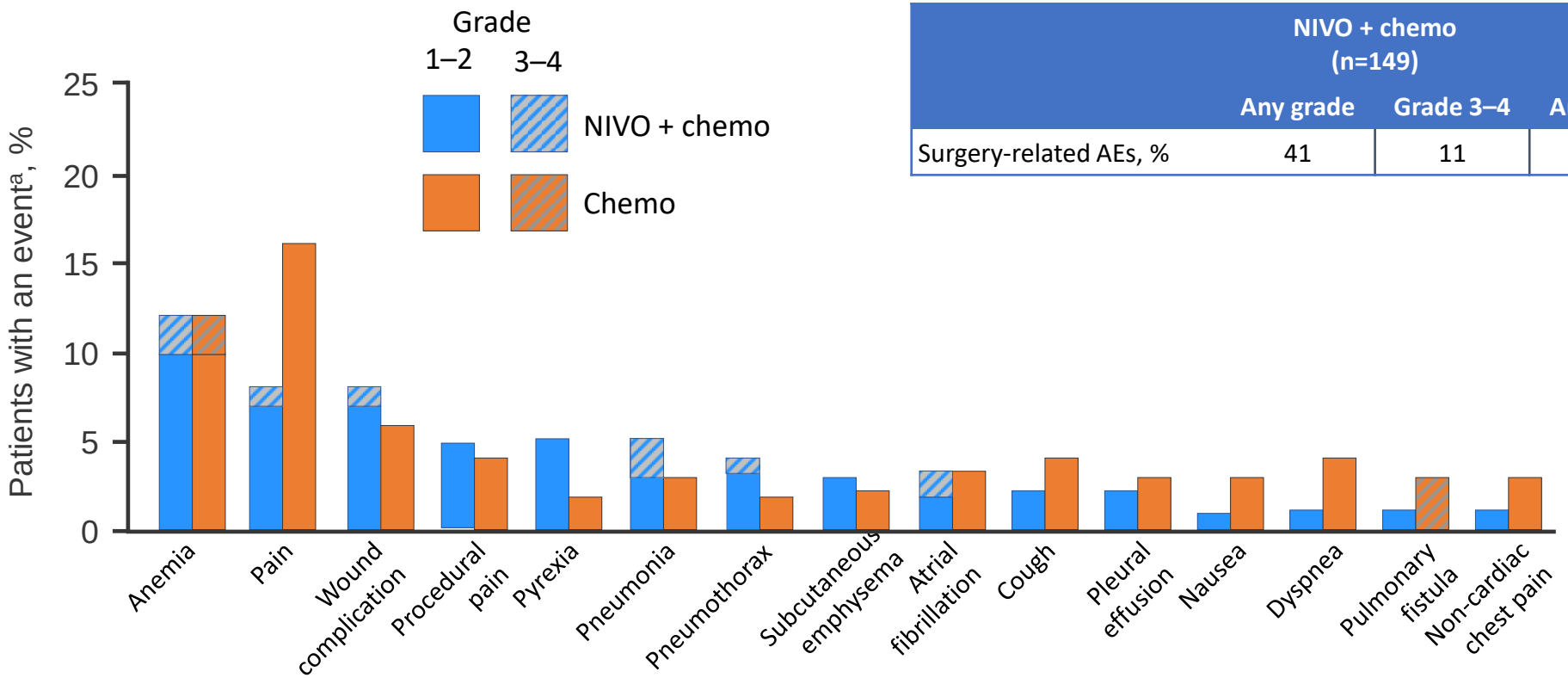

	NIVO + chemo (n=149)		Chemo (n=135)	
	Any grade	Grade 3–4	Any grade	Grade 3–4
Surgery-related AEs, %	41	11	47	15

- **Závery:**
  - U pacientov s resekabilným NSCLC, neoadjuvantne nivolumab + chemoterapia preukázali signifikantne zlepšenie v pCR pomere a hĺbke patologickej odpovede v porovnaní so samotnou chemoterapiou, liečba bola dobre tolerovaná bez zvýšenia pooperačných komplikácií.

[a]Includes events reported up t0 days after definitive surgery

Spicer J, et al. J Clin Oncol 2021;39(suppl):Abstr 8503

2021 ASCO ANNUAL MEETING

Abstract number: 8511

5-YEAR SURVIVAL OUTCOMES WITH DURVALUMAB AFTER CHEMORADIOTHERAPY IN UNRESECTABLE STAGE III NSCLC – AN UPDATE FROM THE PACIFIC TRIAL

David R. Spigel,[1] Corinne Faivre-Finn,[2] Jhanelle E. Gray,[3] David Vicente,[4] David Planchard,[5] Luis Paz-Ares,[6] Johan F. Vansteenkiste,[7] Marina C. Garassino,[8,9] Rina Hui,[10] Xavier Quantin,[11] Andreas Rimner,[12] Yi-Long Wu,[13] Mustafa Özgüroğlu,[14] Ki H. Lee,[15] Terufumi Kato,[16] Maike de Wit,[17] Euan Macpherson,[18] Michael Newton,[19] Piruntha Thiyagarajah,[20] Scott J. Antonia[3]

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June 4th, 2021

5-ročné výsledky prežívania s durvalumabom po chemorádioterapii v neresekabilnom štádiu III NSCLC: PACIFIC štúdia

Key patient inclusion criteria

- Unresectable, stage III NSCLC
- No progression after ≥2 cycles of platinum-based CRT*
- Any tumor PD-L1 status
- WHO PS 0–1

(n=713)

R
2:1

Durvalumab 10 mg/kg q2w for up to 12 months (n=476)

Placebo (n=237)

Stratification

- Age (<65 vs. ≥65 years)
- Sex
- Smoking history (current/former smoker vs. never smoked)

Primary endpoints

- OS, PFS (RECIST v1.1, BICR)

Secondary endpoints

- ORR, DoR and TTDM (BICR), safety, PROs

*60–66 Gy in 30–33 fractions

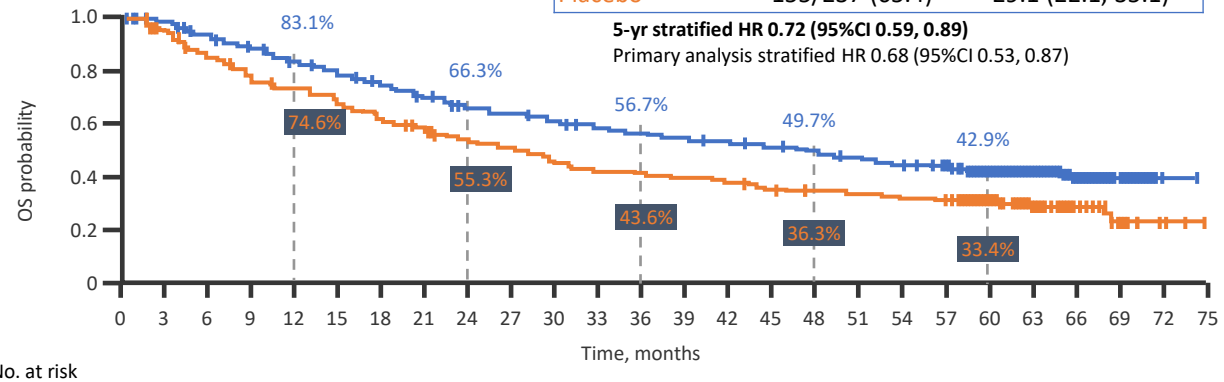
Spigel Dr, et al. J Clin Oncol 2021;39(suppl):Abstr 8511

- # Výsledky

Overall survival

	No. events/total patients, %	mOS, mo (95%CI)
Durvalumab	264/476 (55.5)	47.5 (38.1, 52.9)
Placebo	155/237 (65.4)	29.1 (22.1, 35.1)

5-yr stratified HR 0.72 (95%CI 0.59, 0.89)
Primary analysis stratified HR 0.68 (95%CI 0.53, 0.87)



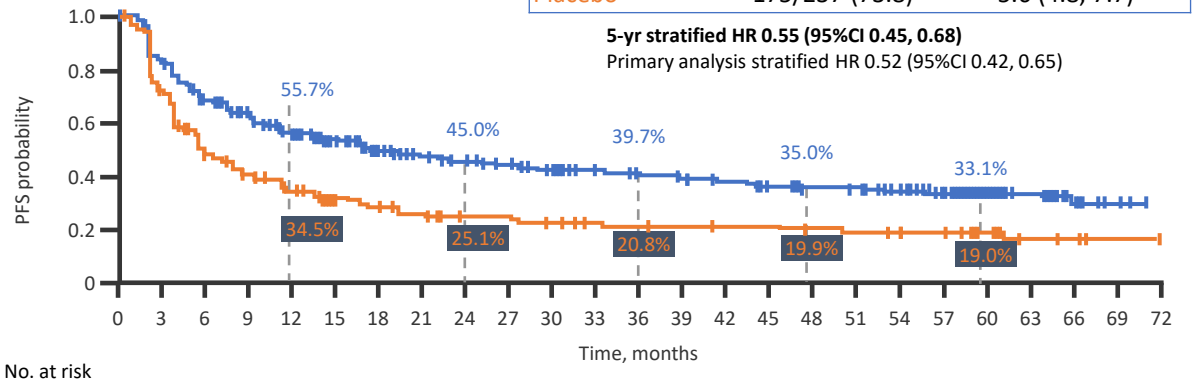
No. at risk

Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

Progression-free survival

	No. events/total patients, %	mPFS mo (95%CI)
Durvalumab	268/476 (56.3)	16.9 (13.0, 23.9)
Placebo	175/237 (73.8)	5.6 (4.8, 7.7)

5-yr stratified HR 0.55 (95%CI 0.45, 0.68)
Primary analysis stratified HR 0.52 (95%CI 0.42, 0.65)



No. at risk

Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

- **Záver**
  - U pacientov s neresekabilným štádiom III NSCLC, 5 ročný follow-up potvrdil pokračujúci benefit v OS a PFS durvalumabu voči placebo, pričom 42,9% pacientov stale žije v durvalumabovom ramene.

Spigel Dr, et al. J Clin Oncol 2021;39(suppl):Abstr 8511

2021 ASCO ANNUAL MEETING

First-line nivolumab + ipilimumab + 2 cycles of chemotherapy versus chemotherapy alone (4 cycles) in patients with advanced non-small cell lung cancer: 2-year update from CheckMate 9LA

Martin Reck,[1] Tudor-Eliade Ciuleanu,[2] Manuel Cobo,[3] Michael Schenker,[4] Bogdan Zurawski,[5] Juliana Menezes,[6] Eduardo Richardet,[7] Jaafar Bennouna,[8] Enriqueta Felip,[9] Oscar Juan-Vidal,[10] Aurelia Alexandru,[11] Hiroshi Sakai,[12] Arnaud Scherpereel,[13] Shun Lu,[14] Luis G. Paz-Ares,[15] David P. Carbone,[16] Arteid Memaj,[17] Sathiya Marimuthu,[17] Phuong Tran,[17] Thomas John[18]

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Abstract Number 9000

CheckMate 9LA – dizajn štúdie

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

(n=719)

R
1:1

Nivolumab 360 mg q3w + ipilimumab 1 mg/kg q6w + chemotherapy q3w (2 cycles)
(n=361)

PD/toxicity/
2 years

Stratification
- PD-L1 (<1% vs. ≥1%)
- Sex
- Histology (SQ vs. NSQ)

Chemotherapy q3w (4 cycles) with optional pemetrexed maintenance (NSQ)
(n=358)

PD/toxicity/
2 years

Primary endpoint
- OS

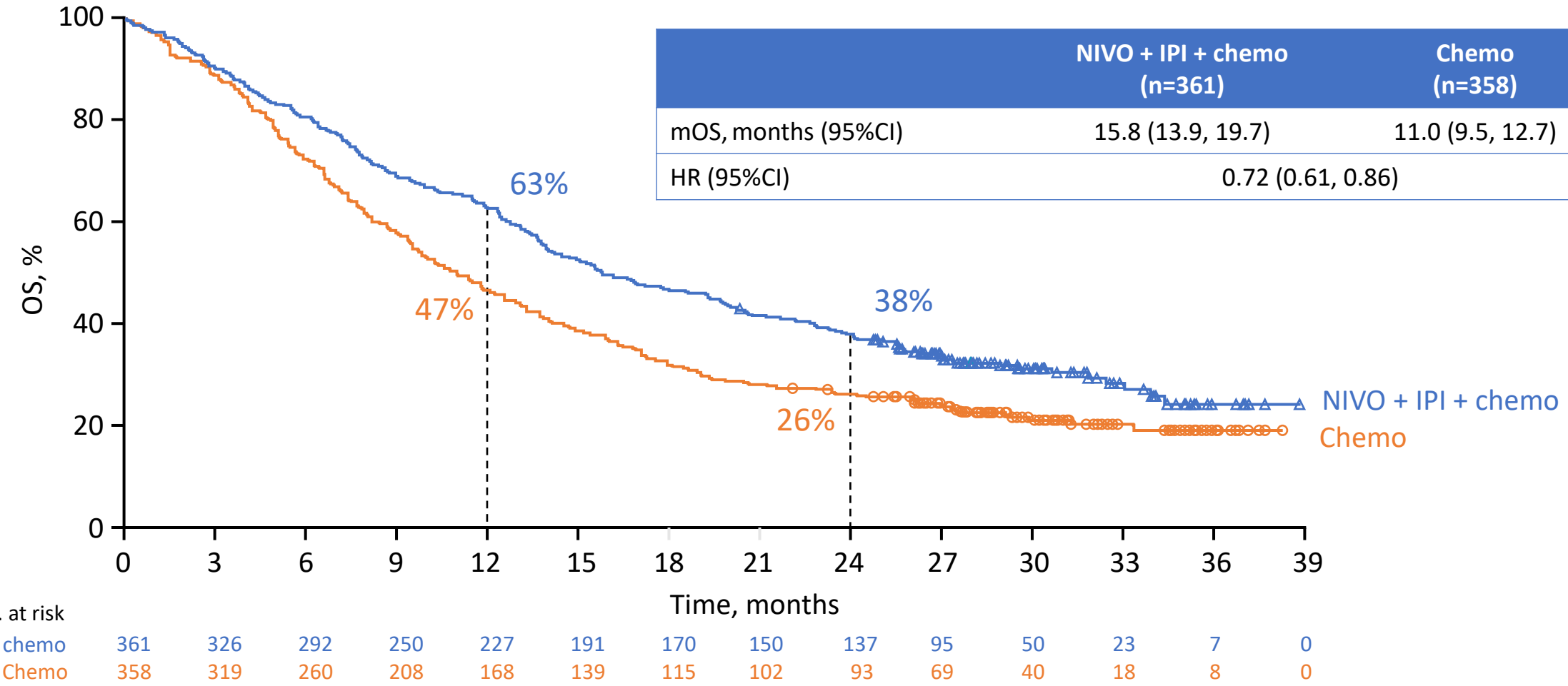
Secondary endpoints
- PFS and ORR (BICR), safety

Reck M, et al. J Clin Oncol 2021;39(suppl):Abstr 9000

- # Výsledky

Overall survival (2 years)

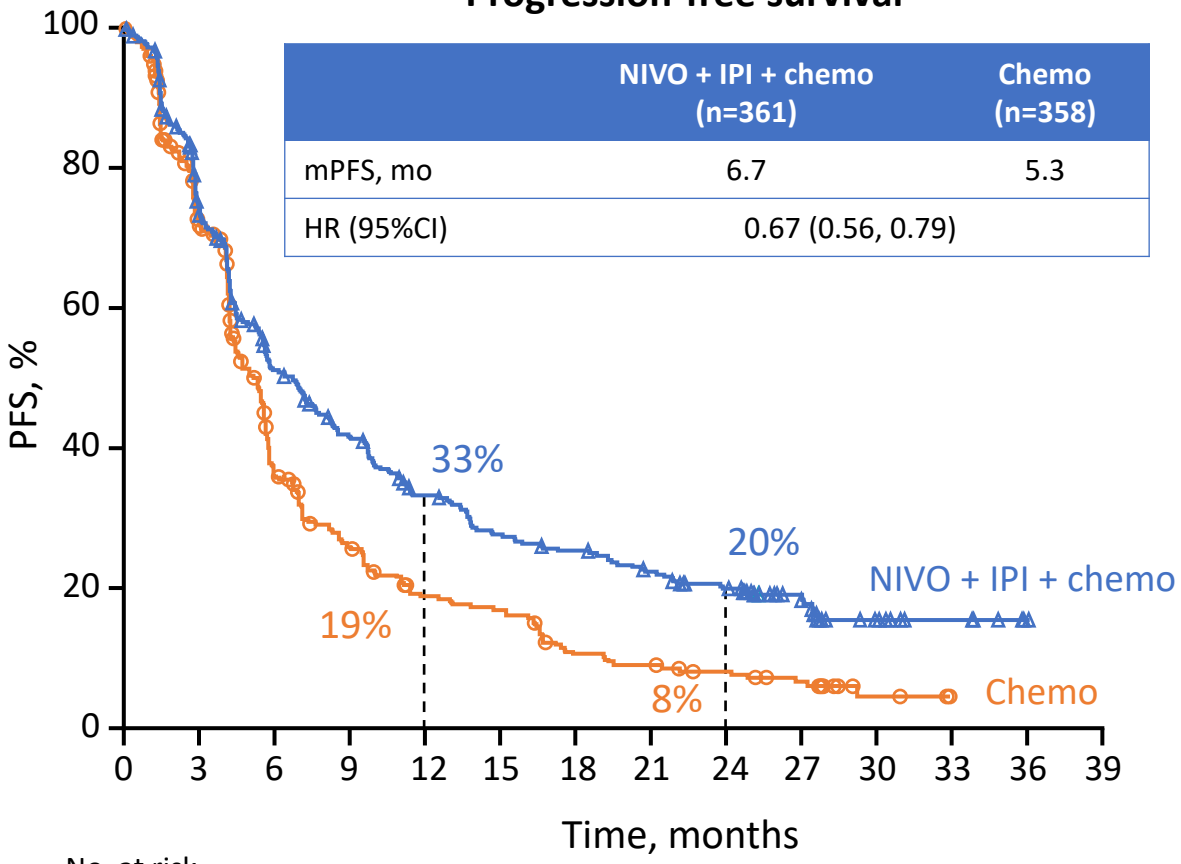
	NIVO + IPI + chemo (n=361)	Chemo (n=358)
mOS, months (95%CI)	15.8 (13.9, 19.7)	11.0 (9.5, 12.7)
HR (95%CI)	0.72 (0.61, 0.86)	



Reck M, et al. J Clin Oncol 2021;39(suppl):Abstr 9000

Progression-free survival

	NIVO + IPI + chemo (n=361)	Chemo (n=358)
mPFS, mo	6.7	5.3
HR (95%CI)	0.67 (0.56, 0.79)	

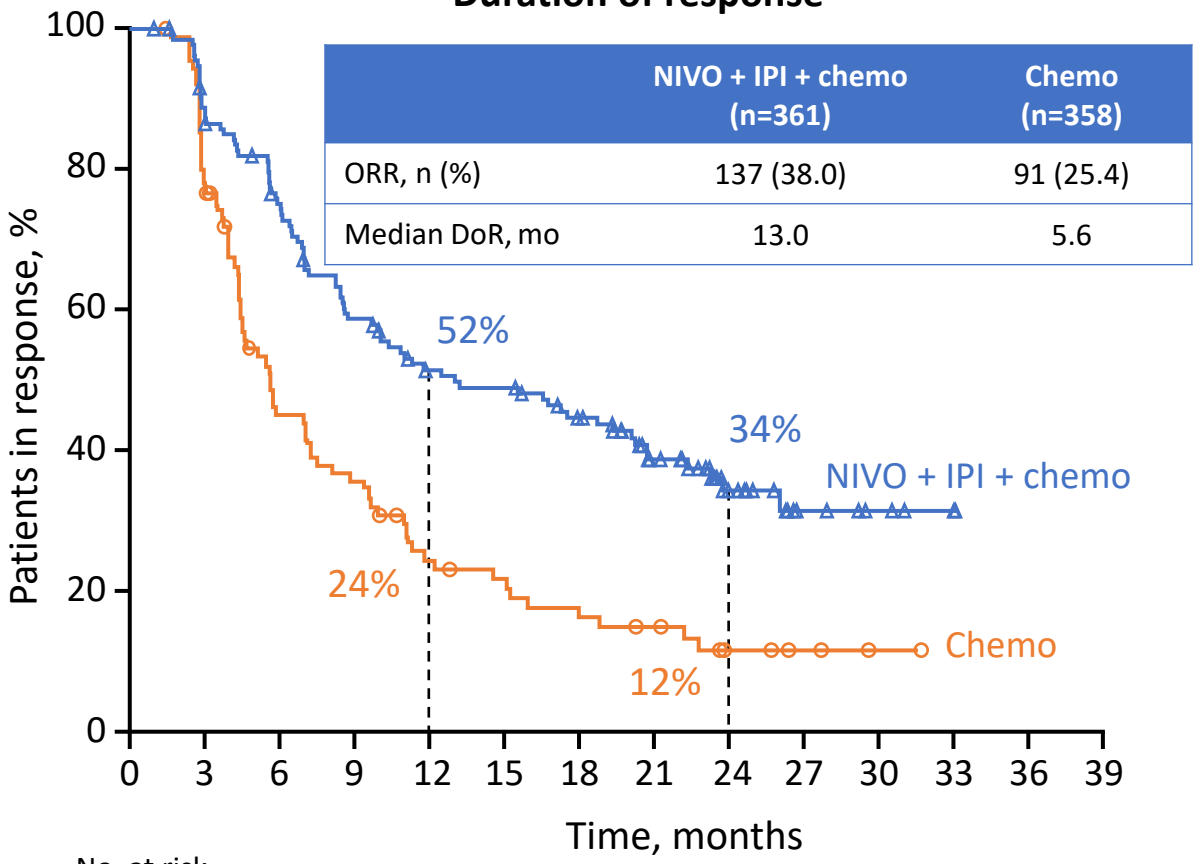


No. at risk

361	252	170	134	103	85	77	66	54	29	12	6	1	0
358	232	107	72	49	44	26	22	17	12	3	0	0	0

Duration of response

	NIVO + IPI + chemo (n=361)	Chemo (n=358)
ORR, n (%)	137 (38.0)	91 (25.4)
Median DoR, mo	13.0	5.6



No. at risk

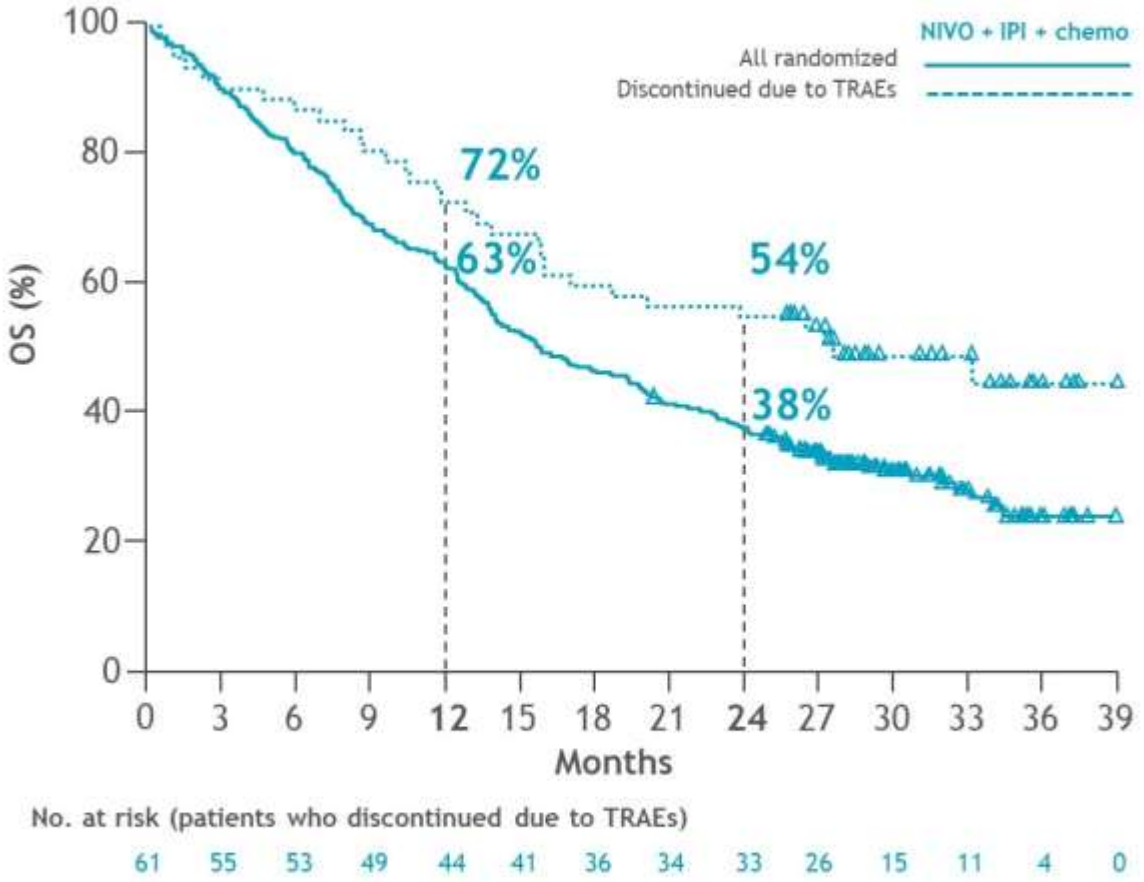
137	116	97	75	62	59	50	35	17	7	4	2	0	0
91	70	38	30	19	16	12	10	5	3	1	0	0	0

Reck M, et al. J Clin Oncol 2021;39(suppl):Abstr 9000

	PD-L1 ≥1%		PD-L1 ≥50%		PD-L1 <1%	
	NIVO + IPI + chemo (n=204)	Chemo (n=204)	NIVO + IPI + chemo (n=76)	Chemo (n=98)	NIVO + IPI + chemo (n=135)	Chemo (n=129)
mOS, months	15.8	10.9	18.9	12.9	17.7	9.8
HR (95%CI)	0.70 (0.56, 0.89)		0.67 (0.46, 0.97)		0.67 (0.51, 0.88)	
mPFS, months	7.0	5.0	7.5	4.5	5.8	4.9
HR (95%CI)	0.67 (0.53, 0.84)		0.59 (0.41, 0.84)		0.68 (0.51, 0.89)	
ORR, n (%)	87 (42.6)	57 (27.9)	38 (50.0)	31 (31.6)	42 (31.1)	26 (20.2)
mDoR, months	11.8	5.6	26.0	5.4	17.5	4.3

Reck M, et al. J Clin Oncol 2021;39(suppl):Abstr 9000

Efficacy in patients who discontinued NIVO + IPI + chemo due to TRAEs[a]



Patients who discontinued all components of NIVO + IPI + chemo due to TRAEs

	NIVO + IPI + chemo (n = 61)
Median OS,[b] mo	27.5
2-year OS rate, %	54
ORR, n (%)	31 (51)
Median DOR after discontinuation,[c] mo	14.5
Ongoing response for ≥ 1 year after discontinuation,[c] %	56

Among patients who discontinued all components of NIVO + IPI + chemo due to TRAEs:

- Median (range) number of doses was 7 (1–33) for NIVO and 3 (1–17) for IPI
- Median (range) duration of treatment was 4.4 (0–23.3) months

[a]Post hoc analysis and includes patients with TRAEs (reported between first dose and 30 days after last dose of study treatment) that were considered leading to discontinuation of all components of study treatment; [b]95% CI = 15.8-NR; [c]2 responders (among patients who discontinued due to TRAEs) in the NIVO + IPI + chemo arm had their responses ended before treatment end date and therefore were excluded from the analysis of duration of response after discontinuation.

Grade 3–4 TRAEs, %	NIVO + IPI + chemo (n=358)	Chemo (n=349)
Any	48	38
Led to discontinuation of any component	18	5
Led to discontinuation of all components	14	3
Serious	26	15
Led to death	2	2

- **Závery:**
  - U pacientov s pokročilým NSCLC: prvá línia nivolumab + ipilimumab + chemoterapia prináša pokračujúci dlhotrvajúci benefit vo všetkých skupinách s PD-L1 expresiou, bez objavenia nových nežiaducich účinkov.
  - Prerušenie v dôsledku TRAE nemá negatívny vplyv na dlhotrvajúci benefit
    - 56 % respondentov malo viac ako 1 rok liečebnú odpoveď

Reck M, et al. J Clin Oncol 2021;39(suppl):Abstr 9000

2021 ASCO ANNUAL MEETING

OUTCOMES OF ANTI-PD-(L)1 THERAPY IN COMBINATION WITH CHEMOTHERAPY VS. IMMUNOTHERAPY (IO) ALONE FOR FIRST-LINE (1L) TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) WITH PD-L1 SCORE 1-49%: FDA POOLED ANALYSIS

Oladimeji Akinboro[1], Jonathon Vallejo[1], Pallavi Mishra-Kalyani[1], Erin Larkins[1], Nicole Drezner[1], Shenghui Tang[1], Richard Pazdur[1,2], Julia A. Beaver[1,2], Harpreet Singh[1,2]

[1]Center for Drug Evaluation and Research, U.S. Food and Drug Administration.

[2]Oncology Center of Excellence, U.S. Food and Drug Administration.

- **Cieľ štúdie**
  - Vyhodnotenie účinnosti a bezpečnosti imunoterapie v kombinácii s chemoterapiou v prvej línii liečby pri pokročilom NSCLC s PD-L1 skóre 1 – 49 %

- **Metódy**
  - Údaje z 8 RCTs* predtým neliečených pacientov s pokročilým NSCLC (EGFR/ALK WT) a PD-L1 skóre 1 – 49 % (n = 2 108) boli zhromaždené na porovnanie OS a PFS medzi tými, ktorí dostávali imunoterapiu s platinovým dubletom v prvej línii (n = 639), a tými, ktorí dostávali samotnú imunoterapiu (n = 529)

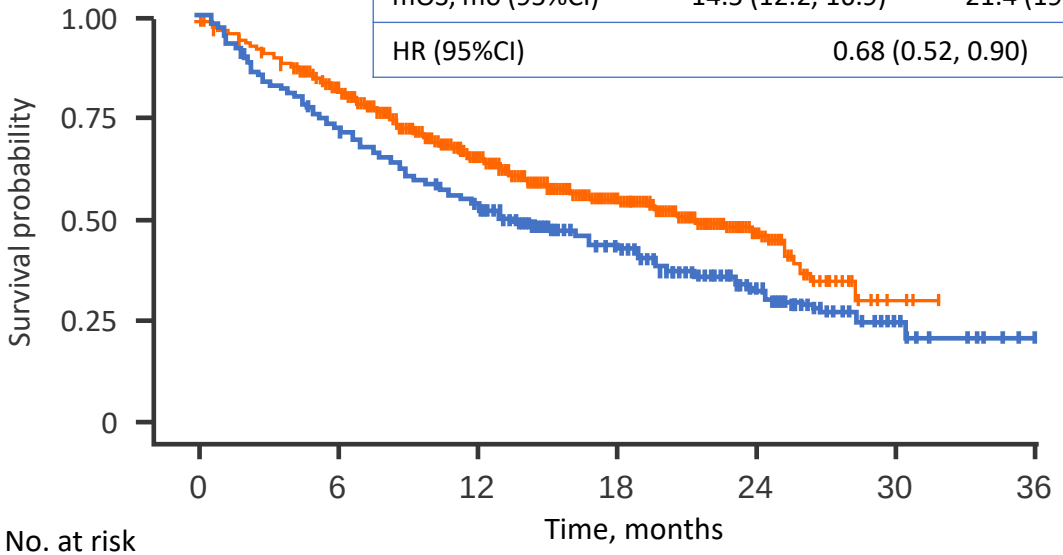
*KEYNOTE-042, CheckMate 227, KEYNOTE-189, KEYNOTE-407, KEYNOTE-021 (cohort G), IMpower150, IMpower130, CA2099LA; †atezolizumab, nivolumab + ipilimumab or pembrolizumab

Akinboro O, et al. J Clin Oncol 2021;39(suppl):Abstr 9001

- # Výsledky

Overall survival

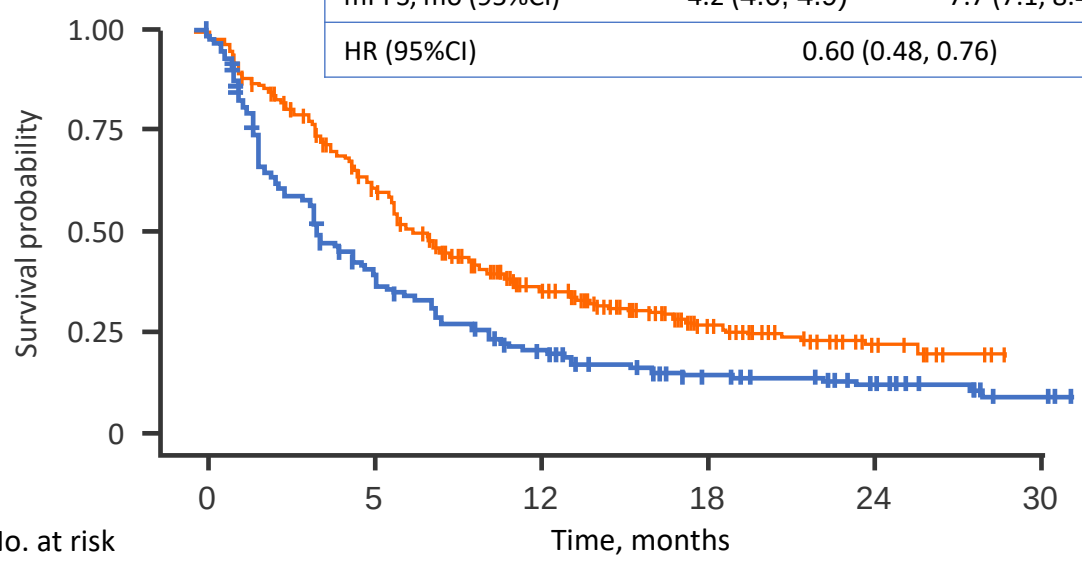
	IO-only (n=639)	Chemo-IO (n=529)
mOS, mo (95%CI)	14.5 (12.2, 16.9)	21.4 (19.4, 25.2)
HR (95%CI)	0.68 (0.52, 0.90)	



No. at risk (no. events)							
Chemo-IO	639 (0)	502 (108)	332 (203)	151 (246)	45 (261)	2 (270)	0 (270)
IO-only	529 (0)	378 (147)	283 (239)	183 (286)	77 (323)	14 (334)	0 (336)

Progression-free survival

	IO-only (n=639)	Chemo-IO (n=529)
mPFS, mo (95%CI)	4.2 (4.0, 4.9)	7.7 (7.1, 8.4)
HR (95%CI)	0.60 (0.48, 0.76)	

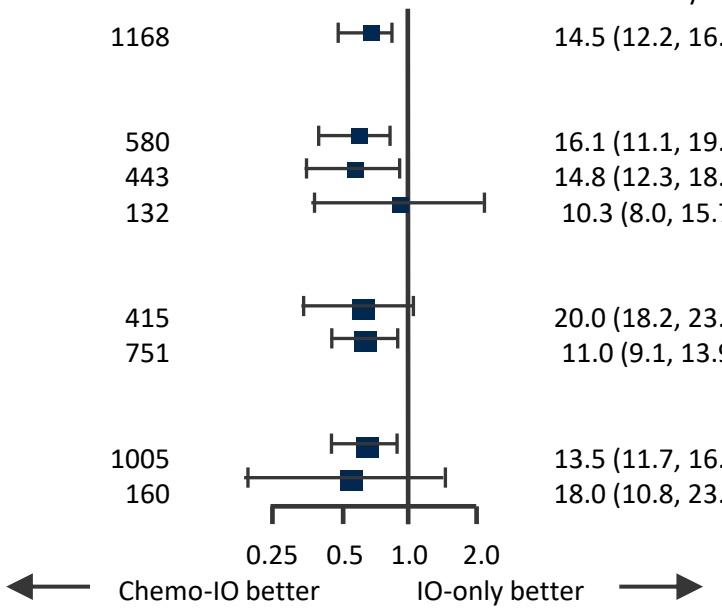


No. at risk (no. events)							
Chemo-IO	639 (0)	360 (224)	158 (368)	49 (397)	11 (404)	0 (405)	
IO-only	529 (0)	200 (308)	93 (407)	49 (432)	19 (438)	1 (440)	

Akinboro O, et al. J Clin Oncol 2021;39(suppl):Abstr 9001

Overall survival subgroup analysis

Subgroup	N	mOS (95%CI)	
		IO-only	Chemo-IO
Overall	1168	14.5 (12.2, 16.9)	21.4 (19.4, 25.2)
Age			
<65 years	580	16.1 (11.1, 19.6)	23.7 (18.1, 25.6)
65–74 years	443	14.8 (12.3, 18.2)	22.5 (20.5, NE)
≥75 years	132	10.3 (8.0, 15.7)	13.9 (10.2, NE)
ECOG PS			
0	415	20.0 (18.2, 23.9)	25.2 (23.7, NE)
1+	751	11.0 (9.1, 13.9)	16.8 (13.8, 22.3)
Smoking status			
Current / former smokers	1005	13.5 (11.7, 16.6)	20.8 (17.4, 25.1)
Never smokers	160	18.0 (10.8, 23.8)	28.2 (20.3, NE)



- **Záver:** U pacientov s pokročilým NSCLC: kombinácia anti-PD-L1 s chemoterapiou môže zlepšiť OS a PFS v porovnaní so samotnou IO napriek limitáciám spôsobeným povahou tejto analýzy. Výsledky sú konzistentné vo všetkých podskupinách.

Akinboro O, et al. J Clin Oncol 2021;39(suppl):Abstr 9001

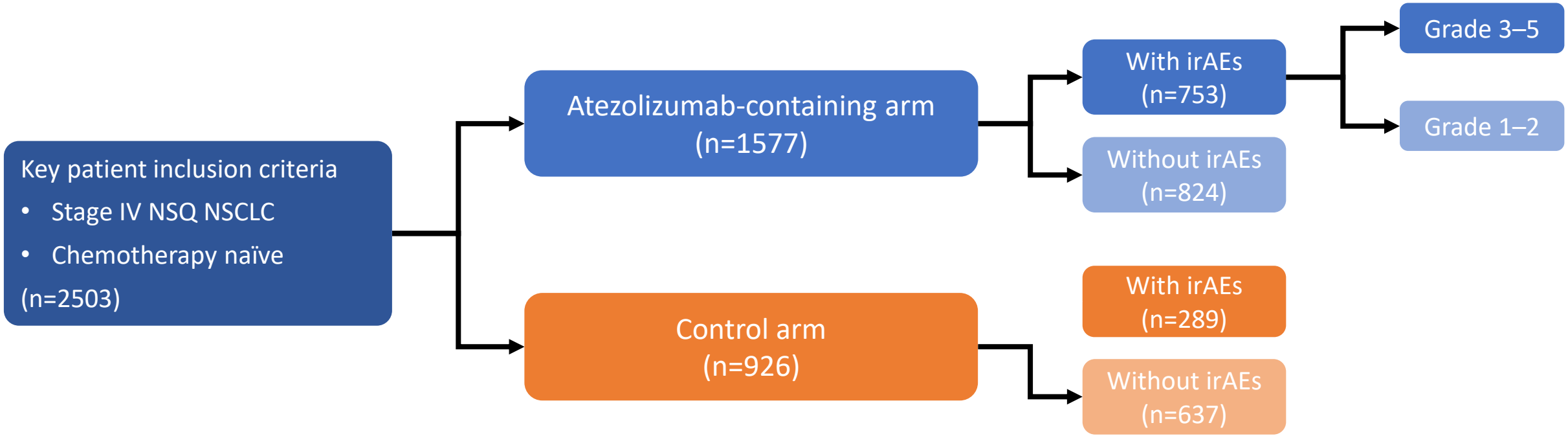
2021 ASCO ANNUAL MEETING

Pooled Analyses of Immune-Related Adverse Events and Efficacy From the Phase 3 Trials IMpower130, IMpower132 and IMpower150

Mark A. Socinski,[1] Robert M. Jotte,[2] Federico Cappuzzo,[3] Makoto Nishio,[4] Tony S. K. Mok,[5] Martin Reck,[6] Gene Finley,[7] Wei Yu,[8] Hina Patel,[8] Nindhana Paranthaman,[8] Ilze Bara,[8] Howard West[9]

[1]AdventHealth Cancer Institute, Orlando, FL, USA; [2]Rocky Mountain Cancer Centers, Denver, CO, USA and US Oncology, Houston, TX, USA; [3]Istituto Nazionale Tumori "Regina Elena," Rome, Italy; [4]The Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [5]State Key Laboratory of Translational Oncology, The Chinese University of Hong Kong, Hong Kong; [6]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany; [7]Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA; [8]Genentech, Inc., South San Francisco, CA, USA; [9]City of Hope Comprehensive Cancer Center, Duarte, CA, USA

- **Cieľ:** Zhodnotenie vzťahu medzi imunitne súvisiacimi AES a účinnosťou v prvej línii atezolizumabu + chemoterapie s alebo bez bevacizumabu pri pokročilom NSCLC v IMpower130, IMpower132 a IMpower150

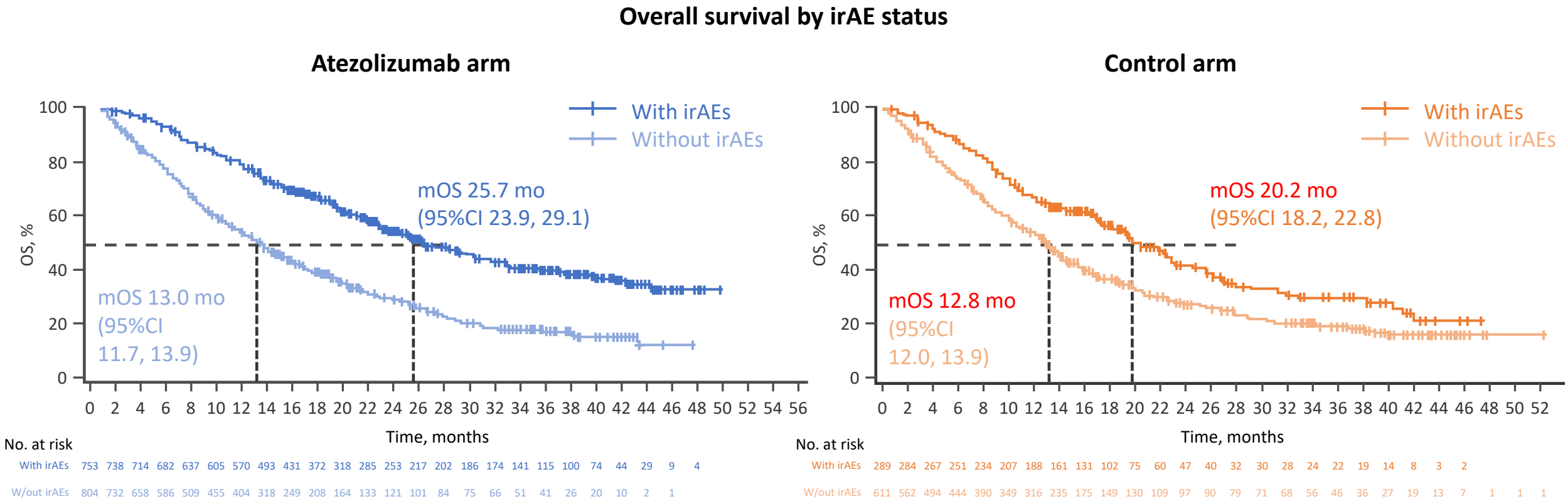


Exploratory analysis

- Association between OS and irAEs

Socinski MA, et al. J Clin Oncol 2021;39(suppl):Abstr 9002

Celkové prežívanie podľa irAE



Time dependent Cox model: HR 0.69 (95%CI 0.60, 0.78)

Time dependent Cox model: HR 0.82 (95%CI 0.68, 0.99)

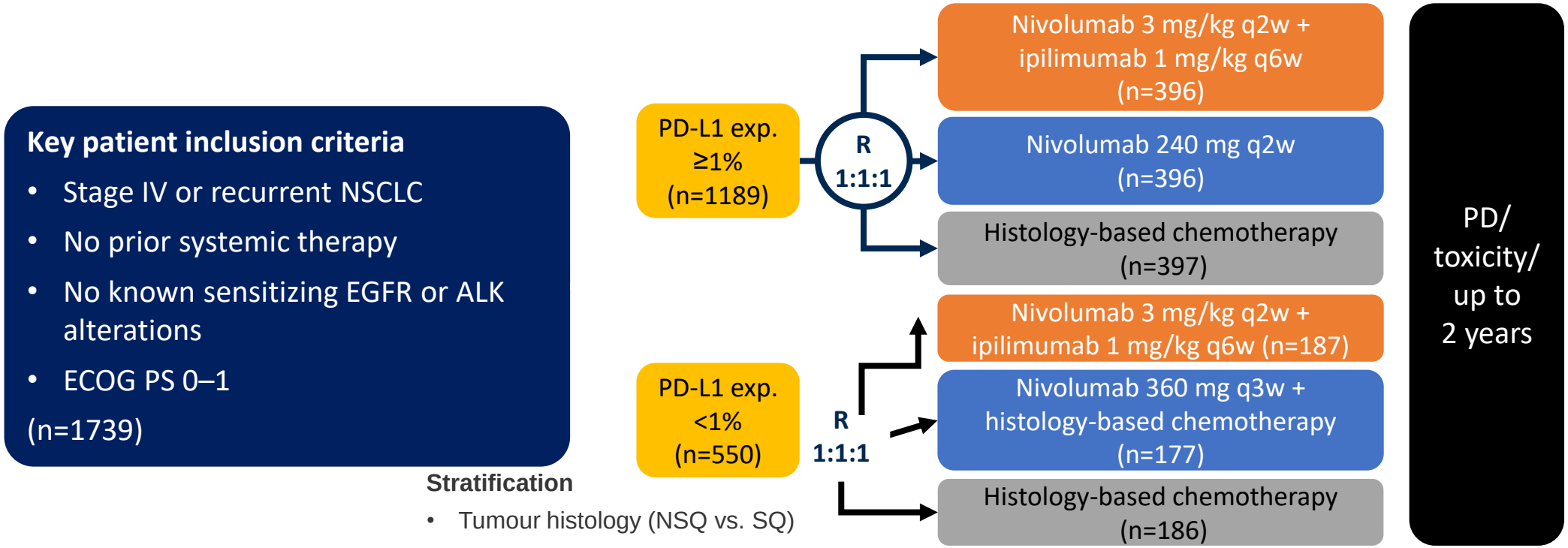
Pacienti s irAE stupňov 1 a2 mali najdlhšie OS v ramene obsahujúcom atezolizumab a pacienti s irAE stupňov 3 až 5 mali najkratšie OS, pravdepodobne v dôsledku prerušenia alebo prerušenia liečby.

Pacienti s neskvamóznym NSCLC v štádiu IV, ktorí mali irAEs, mali dlhšie OS v porovnaní s pacientmi, ktorí nemali irAEs v oboch ramenách.

Socinski MA, et al. J Clin Oncol 2021;39(suppl):Abstr 9002

CheckMate 227 – 4-ročné aktualizované dáta

- **Cieľ:**
  - Nivolumab + ipilimumab v prvej línii pri pokročilom NSCLC vs. chemo



Primary endpoints

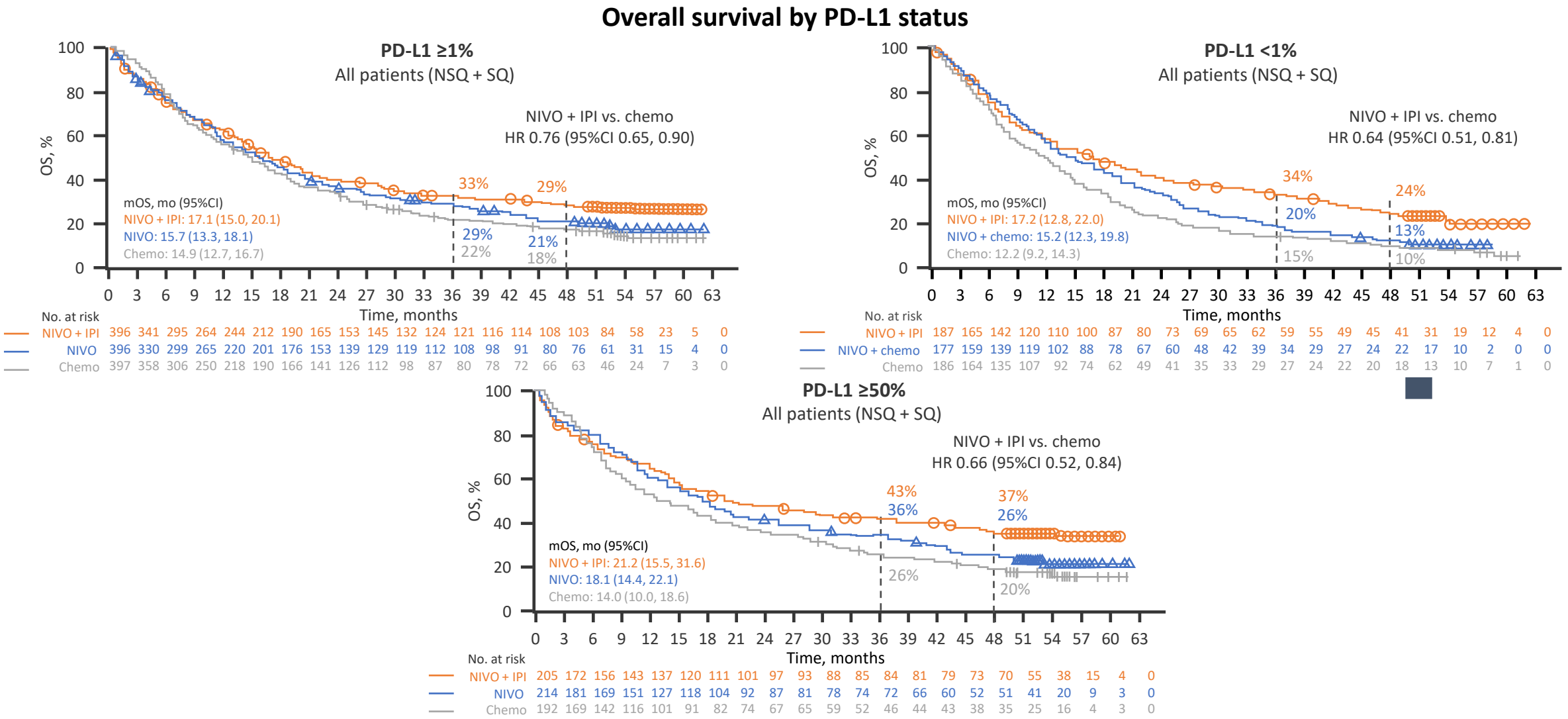
- OS in PD-L1 ≥1% population
- PFS in high TMB (≥10 mut/Mb) population

Secondary endpoints

- OS and PFS in patients with PD-L1 expression <1%, OS in patients with PD-L1 ≥50%

Paz-Ares LG, et al. J Clin Oncol 2021;39(suppl):Abstr 9016

- Výsledky



Paz-Ares LG, et al. J Clin Oncol 2021;39(suppl):Abstr 9016

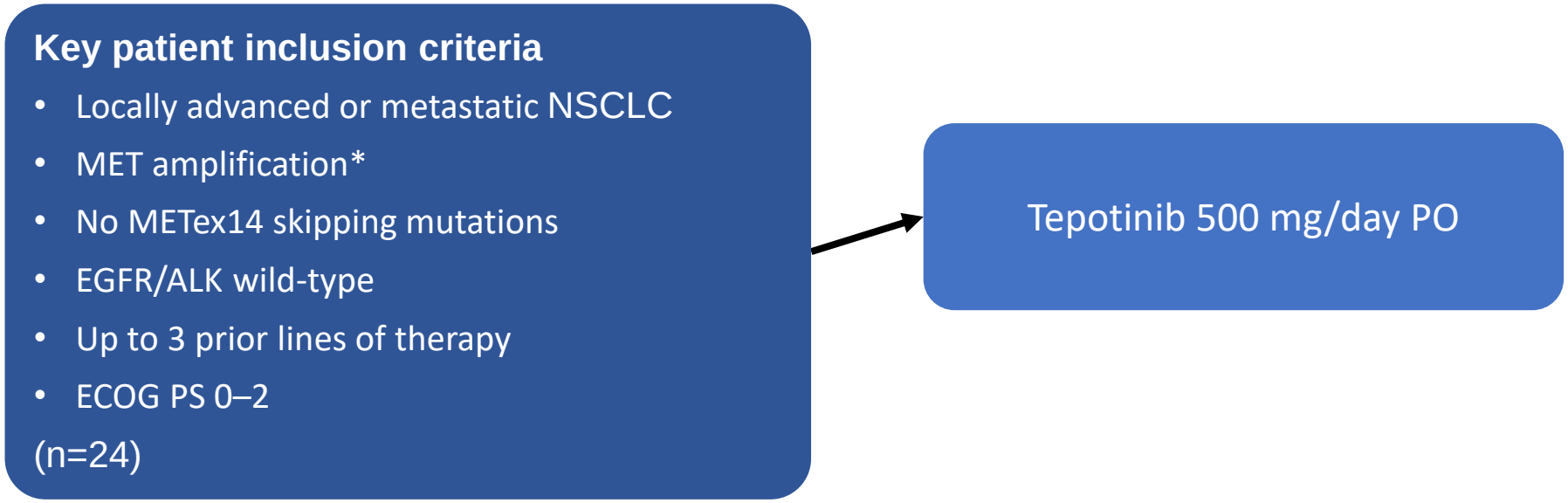
- # Výsledky

	PD-L1 ≥1%			PD-L1 ≥50%			PD-L1 <1%		
	NIVO + IPI (n=396)	NIVO (n=396)	Chemo (n=397)	NIVO + IPI (n=205)	NIVO (n=214)	Chemo (n=192)	NIVO + IPI (n=187)	NIVO (n=177)	Chemo (n=186)
ORR, %	36.4	27.5	30.0	45.4	36.9	35.4	27.3	37.9	23.1
mPFS, months (95%CI)	5.1 (4.1, 6.3)	4.2 (3.0, 5.3)	5.6 (4.6, 5.8)	6.7 (4.5, 11.1)	5.6 (4.2, 8.3)	5.6 (4.6, 6.6)	5.1 (3.5, 6.4)	5.6 (4.6, 6.9)	4.7 (4.2, 5.6)
HR vs. chemo (95%CI)	0.81 (0.68, 0.96)	0.98 (0.83, 1.15)		0.60 (0.47, 0.76)	0.72 (0.57, 0.90)		0.74 (0.58, 0.94)	0.72 (0.57, 0.91)	
4-year PFS rate, %	14	10	4	20	14	1	12	7	NA
mDoR, months (95%CI)	23.2 (15.5, 33.9)	15.5 (12.7, 20.8)	6.7 (5.6, 7.6)	31.8 (20.7, 51.2)	16.8 (13.5, 29.6)	5.8 (4.5, 6.9)	18.0 (12.4, 33.2)	8.3 (5.9, 9.4)	4.8 (3.7, 5.8)

- **Závery:**
  - U pacientov s pokročilým NSCLC pretrváva dlhodobý benefit v prvej línii nivolumab + ipilimumab nezávisle od PD-L1 expresie či histológie a neboli pozorované žiadne nové nežiaduce účinky.

Paz-Ares LG, et al. J Clin Oncol 2021;39(suppl):Abstr 9016

Tepotinib, MET inhibítor u pacientov s pokročilým NSCLC a MET amplifikáciou pri VISION Cohort B



Primary endpoint

- ORR (RECIST v1.1, IRC)

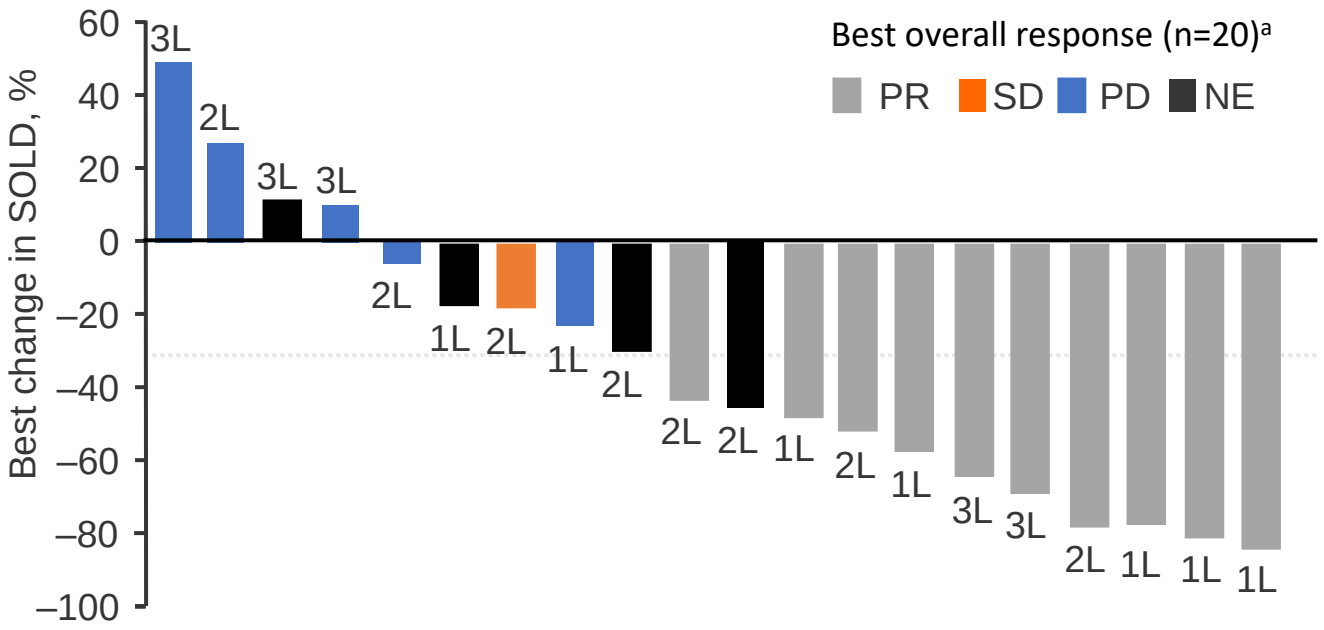
Secondary endpoints

- DoR, PFS, OS, safety

*Guardant360®, MET gene copy number ≥2.5

Le X, et al. J Clin Oncol 2021;39(suppl):Abstr 9021

• Výsledky



	Overall (n=24)	First-line (n=7)	Second-line (n=10)	Third-line (n=7)
ORR, % (95%CI)	41.7 (22.1, 63.4)	71.4 (29.0, 96.3)	30.0 (6.7, 65.2)	28.6 (3.7, 71.0)
BOR, n (%)				
PR	10 (41.7)	5 (71.4)	3 (30.0)	2 (28.6)
SD	1 (4.2)	0	1 (10.0)	0
PD	5 (20.8)	1 (14.3)	2 (20.0)	2 (28.6)
NE	8 (33.3)	1 (14.3)	4 (40.0)	3 (42.9)

[a]Four patients without baseline data and/or treatment measurement data were excluded

Le X, et al. J Clin Oncol 2021;39(suppl):Abstr 9021

TRAEs occurring in ≥5% of patients, n (%)	Tepotinib 500 mg (n=24)	
	Any grade	Grade 3
Peripheral edema	9 (37.5)	2 (8.3)
Generalized edema	4 (16.7)	2 (8.3)
Constipation	4 (16.7)	0
Transaminases increased	2 (8.3)	1 (4.2)
Diarrhea	2 (8.3)	0
Edema	2 (8.3)	0

- **Závery:**
  - U pacientov s NSCLC a MET amplifikáciou tepotinib potvrdil povzbudzujúcu antitumorovú aktivitu, obzvlášť v prvej línii s akceptabilnou toxicitou.

Le X, et al. J Clin Oncol 2021;39(suppl):Abstr 9021

2021 ASCO ANNUAL MEETING

OVERALL SURVIVAL AND EXPLORATORY SUBGROUP ANALYSES FROM THE PHASE 2 CODEBREAK100 TRIAL EVALUATING SOTORASIB IN PRETREATED *KRAS* P.G12C MUTATED NON-SMALL CELL LUNG CANCER

Presenter: Ferdinandos Skoulidis, M.D., Ph.D.[1]

[1]Department of Thoracic and Head and Neck Medical Oncology

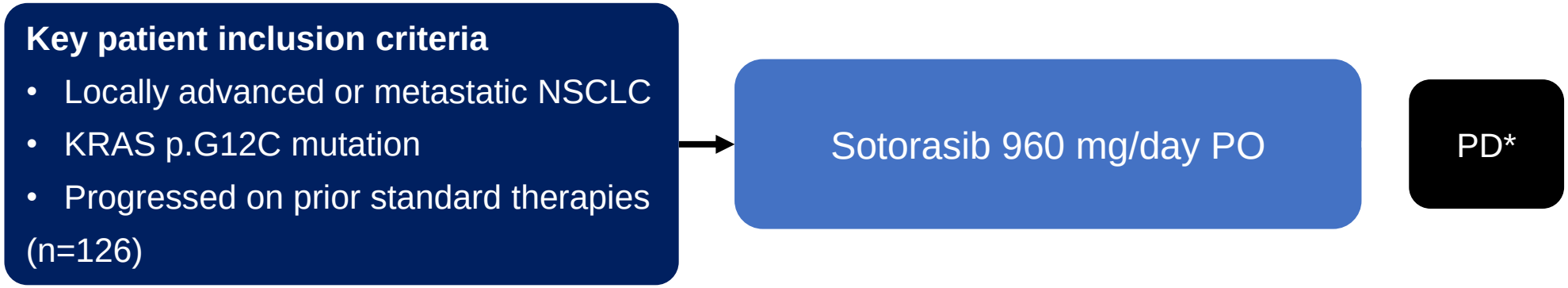
The University of Texas MD Anderson Cancer Center

On behalf of: Bob T. Li,[2] Ramaswamy Govindan,[3] Grace K. Dy,[4] Geoffrey I. Shapiro,[5] Joshua M. Bauml,[6] Martin H. Schuler,[7] Alfredo Addeo,[8] Terufumi Kato,[9] Benjamin Besse,[10] Abraham Anderson,[11] Agnes Ang,[11] Gift Ngarmchamnanrith,[11] Qui Tran,[11] Vamsidhar Velcheti[12]

[2]Memorial Sloan Kettering Cancer Center and Weill Cornell Medicine, New York, NY, USA; [3]Alvin J Siteman Cancer Center at Washington University School of Medicine, St Louis, MI, USA; [4]Roswell Park Cancer Institute, Buffalo, NY, USA; [5]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [6]University of Pennsylvania, Philadelphia, PA, USA; [7]West German Cancer Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany, German Cancer Consortium (DKTK), Heidelberg, Germany; [8]Oncology Department, University Hospital Geneva, Geneva, Switzerland; [9]Kanagawa Cancer Center, Yokohama, Japan; [10]Gustave Roussy Institute, Villejuif, South Paris, France; [11]Amgen Inc. Thousand Oaks, CA. USA; [12]Thoracic Medical Oncology, Perlmutter Cancer Center, New York University, New York, NY, USA.

CodeBreaK 100

- **Cieľ:** Sotorasib u predliečených pacientov s KRAS p.G21C mutáciou NSCLC pri CodeBreaK 100



Primary endpoint

- ORR (RECIST v1.1, ICR)

Secondary endpoints

- DoR, DCR, TTR, PFS, OS, safety

*Treatment beyond PD permitted if certain criteria were met

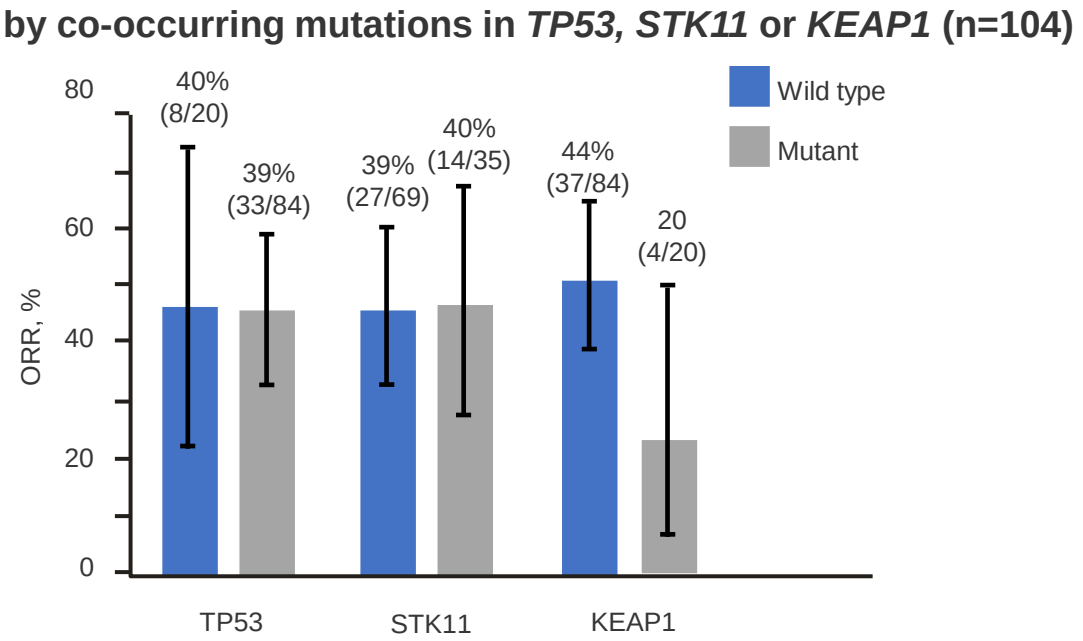
Skoulidis F, et al. J Clin Oncol 2021;39(suppl):Abstr 9003

CodeBreaK 100 – VÝSLEDKY

	Sotorasib 960 mg (n=124)
ORR, % (95%CI)	37.1 (28.6, 46.2)
BOR, n (%)	
CR	4 (3.2)
PR	42 (33.9)
SD	54 (43.5)
PD	20 (16.1)
NE/missing	4 (3.2)
Disease control rate, % (95%CI)	80.6 (72.6, 87.2)
mDoR, months (95%CI)	11.1 (6.9, NE)
Median time to response, months (95%CI)	1.35 (1.2, 10.1)
mPFS, months (95%CI)	6.8 (5.1, 8.2)
mOS, months (95%CI)	12.5 (10.0, NE)

Skoulidis F, et al. J Clin Oncol 2021;39(suppl):Abstr 9003

CodeBreaK 100 – VÝSLEDKY



- Stupeň 3 TRAEs bol u 25 (19,8 %) pacientov, najčastejšími nežiaducimi účinkami bolo zvýšenie ALT (6,3 %), AST (5,6 %) a hnačka (4 %).

- **Závery:**
  - U pacientov s KRAS p.G21C mutáciou NSCLC sotorasib potvrdil klinický benefit s priaznivým bezpečnostným profilom. Účinnosť bola pozorovaná v molekulárnych podskupinách vrátane STK11, KEAP1 a TP53 mutácií.

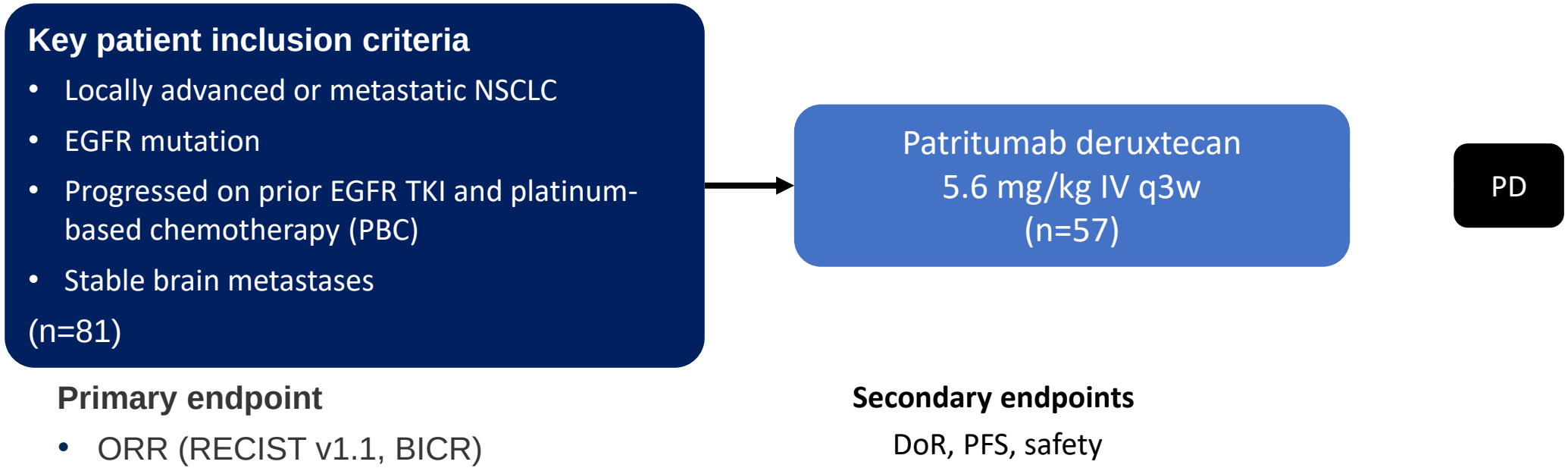
Skoulidis F, et al. J Clin Oncol 2021;39(suppl):Abstr 9003

Dve sľubné stratégie po osimertinibe

- **1. Patrimumab Deruxtecan**
  - **ILD je novou toxicitou**
  - **Mohol by byť aktívny nezávisle od rezistentného mechanizmu**

- **2. Amivantanab + lazertinib**
  - **Správna selekcia je stále nejasná**

- **Cieľ**
  - patritumab deruxtekan, HER3 ADC, u pacientov s EGFR TKI rezistentným, EGFR-mutovaným NSCLC



Jänne PA, et al. J Clin Oncol 2021;39(suppl):Abstr 9007

- Výsledky

Outcomes (BICR per RECIST 1.1) *Median follow-up 10.2 months (5.2–19.9)*	HER3-DXd 5.6 mg/kg Prior TKI ± PBC (n=57)	HER3-DXd 5.6 mg/kg Prior osimertinib, PBC (n=44)
Confirmed ORR, % (95%CI)	39 (26, 52)	39 (24, 55)
BOR, n (%)		
CR	1 (2)	1 (2)
PR	21 (37)	16 (36)
SD, non-CR/non-PD	19 (33)	13 (30)
PD	9 (16)	8 (18)
NE	7 (12)	6 (14)
DCR, % (95%CI)	72 (59, 83)	68 (52, 81)
Median time to response, months (range)	2.6 (1.2–5.4)	2.7 (1.2–5.4)
Median DoR, months (95%CI)	6.9 (3.1, NE)	7.0 (3.1, NE)
Median PFS, months (95%CI)	8.2 (4.4, 8.3)	8.2 (4.0, NE)

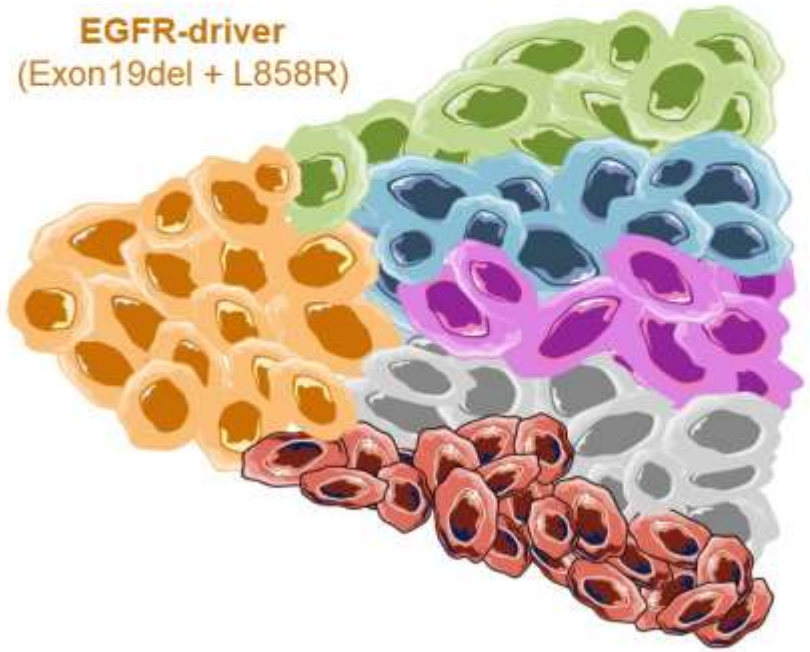
Záver: Účinnosť pri rôznych mechanizmoch rezistencie na EGFR TKI, po viacerých líniách vrátane chemoterapie. Najčastejšia toxicita G3 ≥ 3: trombocytopénia (30 %), neutropénia (19 %) a únava (14 %).

Jänne PA, et al. J Clin Oncol 2021;39(suppl):Abstr 9007

Acquired Resistance to Osimertinib in EGFRm NSCLC

Osimertinib → **Platinum Chemotherapy**

Primary Mutations → **Resistance Mutations**



EGFR-dependent
(C797S)

MET-dependent
(MET amplification)

Other Pathways
(PIK3CA, RAS/RAF, Fusions, Cell Cycle)

Unknown
(~40-50%)

Transformations

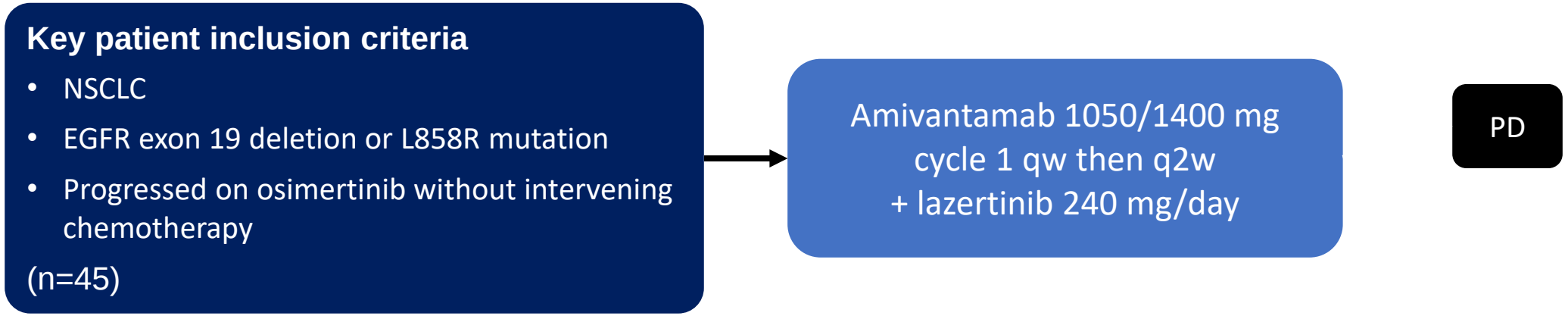
Osimertinib resistance is complex

- Heterogenous patterns of resistance
- Co-occurrence of multiple resistance mechanisms
- NGS of ctDNA has been the most frequently used method to characterize osimertinib resistance mechanisms due to difficulties in obtaining tissue[1-2]

[1]Papadimitrakopoulou *Annals of Oncol* 29:VIII741; [2]Ramalingam *Annals of Oncol* 29:VIII740. ctDNA, circulating tumor DNA; Exon19del, exon 19 deletion; NGS, next generation sequencing

CHRYSALIS štúdia

- **Cieľ štúdie:**
  - amivantamab (EGFR-MET bišpecifická protilátka) + lazertinib (a 3rd generačnýTKI) po osimertinibe u chemoterapiou nepredliečených pacientov pri EGFR-mutovanom NSCLC v CHRYSALIS + potenciálne biomarkery



Exploratory endpoints

- ORR (RECIST v1.1, investigator assessed), osimertinib resistance mutations or amplifications in EGFR/MET

Bauml J, et al. J Clin Oncol 2021;39(suppl):Abstr 9006

Výsledky

- **Investigator-assessed response (n = 45)**
- *Medián follow-up: 11 mes. (1 – 15)*
- *Medián trvania liečby: 5,6 mesiaca (0,5 – 14,8)*
- ORR (95 % CI): 36 % (22, 51)
- mDoR (95 % CI): 9,6 mes. (5,3, NR)
- DoR ≥ 6 mes.: 69 %
- CBR, % (95 % CI): 64 (49, 78)
- mPFS, (95 % CI): 4,9 mes. (3,7; 9,5)

- IHC v 20 nádorových vzorkách, z toho 10 z nich bolo EGFR/MET rezistentných (kombinované H skóre ≥ 400) a 9 respondentov na liečbu (ORR 90 %)

- EGFR/MET expresia bola asociovaná s liečebnou odpoveďou: možný biomarker

Conclusions

If we don’ t test we don’t allow for proper drug access
(EGFR, ALK, ROS1, BRAF, METex14, HER2, RET, NTRK, PD-L1)

“Equity. Every patient. Every day. Everywhere.”

Ďakujem za pozornosť!