

ASCO[®]20 Virtual

Novinky v léčbě nádorů plic
výběr z přednášek

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Trocha čísel

- **Rakovina plic: 533 abstraktů**

- Přednášky: 33
- Poster discussion: 30
- Poster: 167
- E-publikace abstraktu: 303

- **Imunoterapie check-point inhibitory**

- Atezolizumab: 34
- Durvalumab: 34
- Nivolumab: 56
- Pembrolizumab: 62

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186 = 35 %

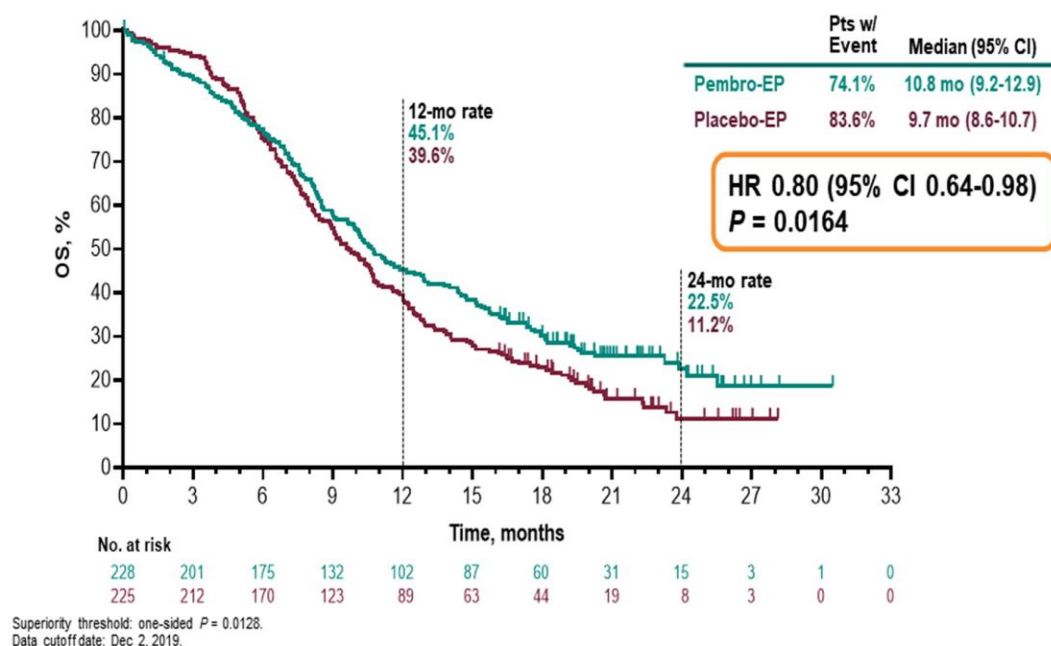
Imunoterapie v 1. linii léčby metastazujícího nádoru plic

KEYNOTE-604: Pembrolizumab (pembro) or placebo plus etoposide and platinum (EP) as first-line therapy for extensive-stage (ES) small-cell lung cancer (SCLC)

Rudin KN604 ASCO 2020

- Pembrolizumab + EP významně zlepšily PFS (HR 0,75 [95% CI: 0,61–0,91], $p = 0,0023$; medián 4,5 vs. 4,3 měsíce) a prodloužily OS (HR 0,80 [95% CI: 0,64–0,98], $p = 0,0164$; medián 10,8 vs. 9,7 měsíce) ve srovnání s placebem + EP v 1. linii nemocných s ED-SCLC; bez nových bezpečnostních signálů.

Overall Survival, ITT: FA



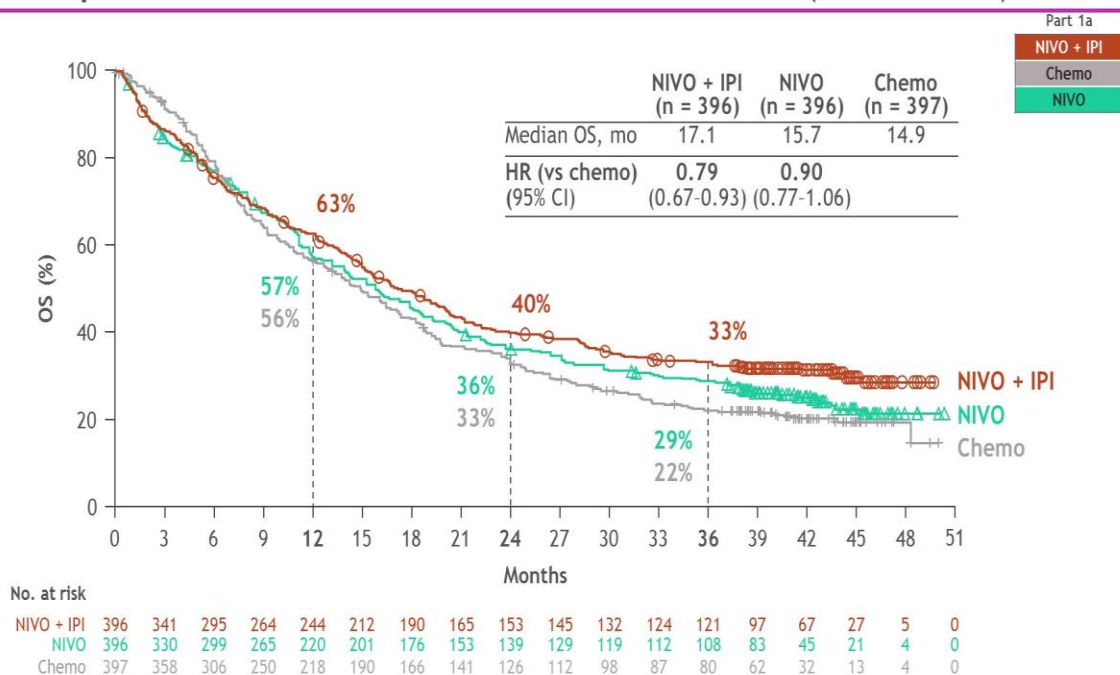
**IO + EP – upevnění
standardu u SCLC ES:**

**IMpower133
CASPIAN
KEYNOTE-604**

Nivolumab + ipilimumab versus platinum-doublet chemotherapy as first-line treatment for advanced non-small cell lung cancer: Three-year update from CheckMate 227 Part 1

CheckMate 227: 3-year update

3-year update: OS with NIVO + IPI vs chemo vs NIVO (PD-L1 $\geq 1\%$)



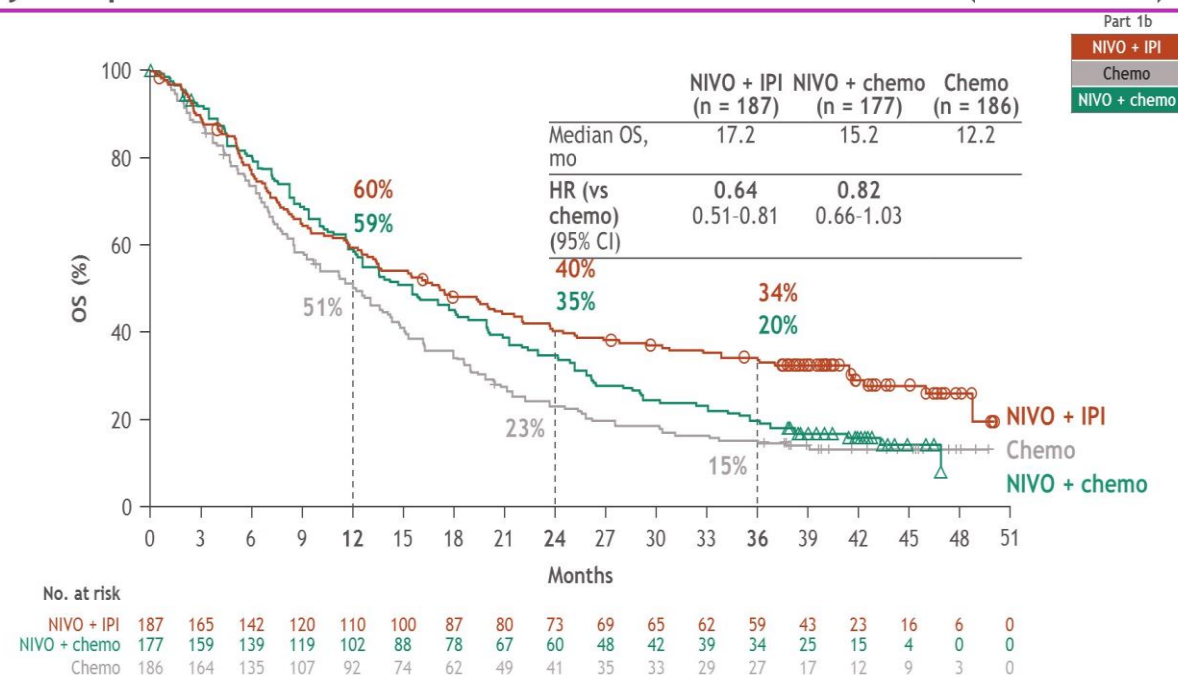
Database lock: February 28, 2020; minimum follow-up for OS: 37.7 months.

Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W) and NIVO (240 mg Q2W). Among patients who were alive at 3 years, subsequent systemic therapy was received by 35% in the NIVO + IPI arm, 45% in the NIVO arm, and 76% in the chemo arm; subsequent immunotherapies were received by 13%, 21%, and 71%; and subsequent chemotherapy was received by 28%, 33% and 30%, respectively.

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CheckMate 227: 3-year update

3-year update: OS with NIVO + IPI vs Chemo vs NIVO + Chemo (PD-L1 $< 1\%$)



Database lock: February 28, 2020; minimum follow-up for OS: 37.7 months.

Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W), and NIVO (360 mg Q3W) plus chemo. Among patients who were alive at 3 years, subsequent systemic therapy was received by 49% in the NIVO + IPI arm, 38% in the NIVO + chemo arm, and 78% in the chemo arm; subsequent immunotherapies were received by 12%, 12%, and 74%; and subsequent chemotherapy was received by 46%, 35% and 33%, respectively.

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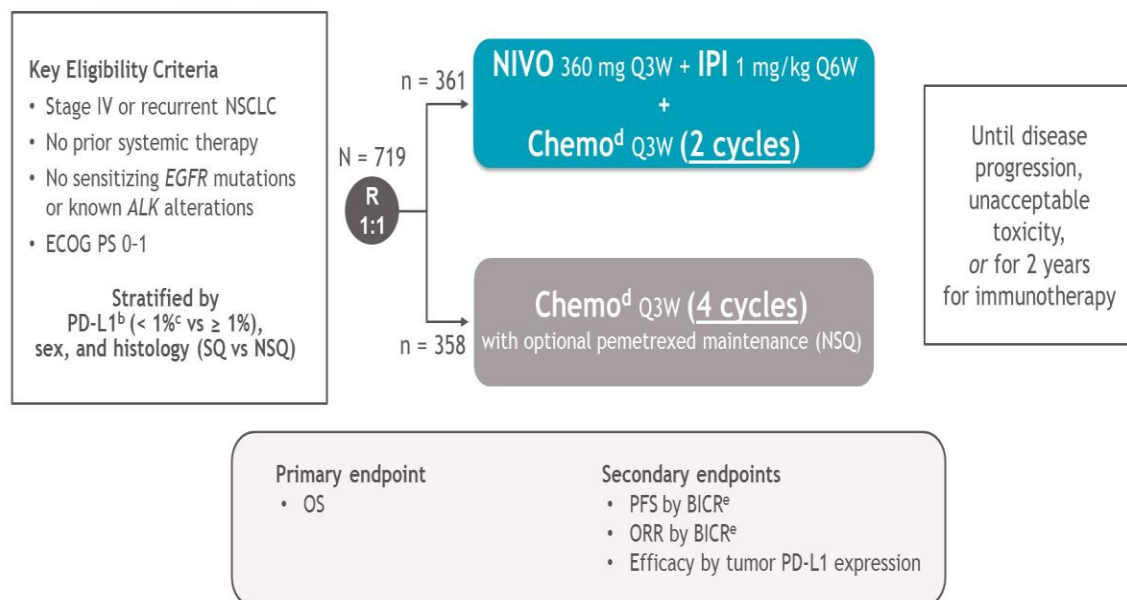
Nejvýraznější prospěch u subjektů PD-L1 $\geq 1\%$, kteří měli do šesti měsíců CR nebo PR: tříleté OS 70 %

Nivolumab (NIVO) + ipilimumab (IPI) + 2 cycles of platinum-doublet chemotherapy (chemo) vs 4 cycles chemo as first-line (1L) treatment (tx) for stage IV/recurrent non-small cell lung cancer (NSCLC): CheckMate 9LA

CheckMate 9LA: NIVO + IPI + 2 cycles of chemo in 1L NSCLC

CheckMate 9LA: NIVO + IPI + 2 cycles of chemo in 1L NSCLC

CheckMate 9LA study design^a



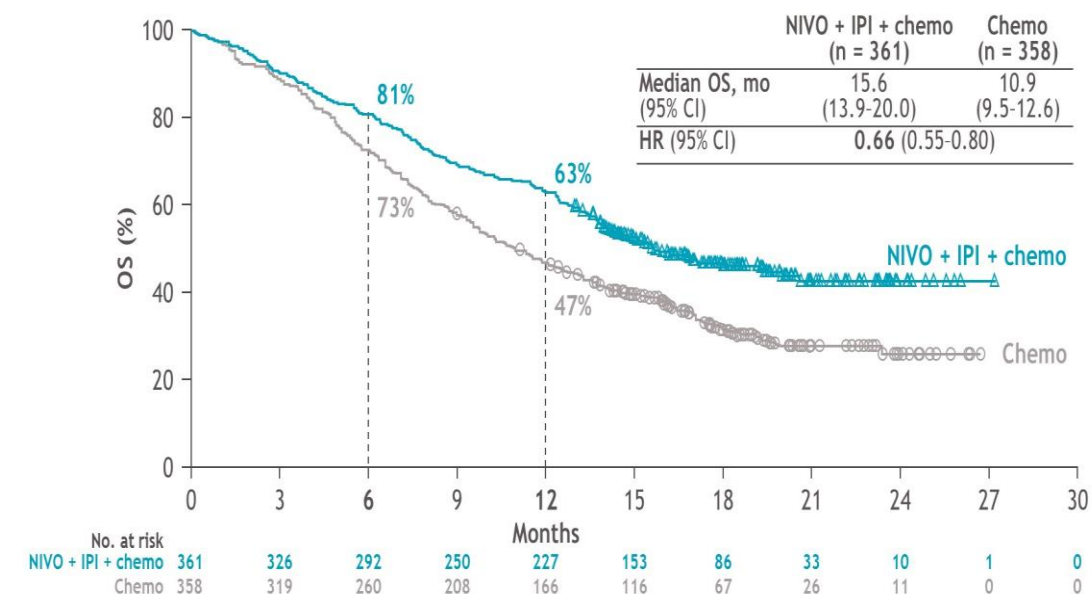
Interim database lock: October 3, 2019; minimum follow-up: 8.1 months for OS and 6.5 months for all other endpoints.

Updated database lock: March 9, 2020; minimum follow-up: 12.7 months for OS and 12.2 months for all other endpoints.

^aNCT03215706; ^bDetermined by the PD-L1 IHC 28-8 pharmDx assay (Dako); ^cPatients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients;

^dNSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; ^eHierarchically statistically tested.

Primary endpoint (updated): Overall survival^a



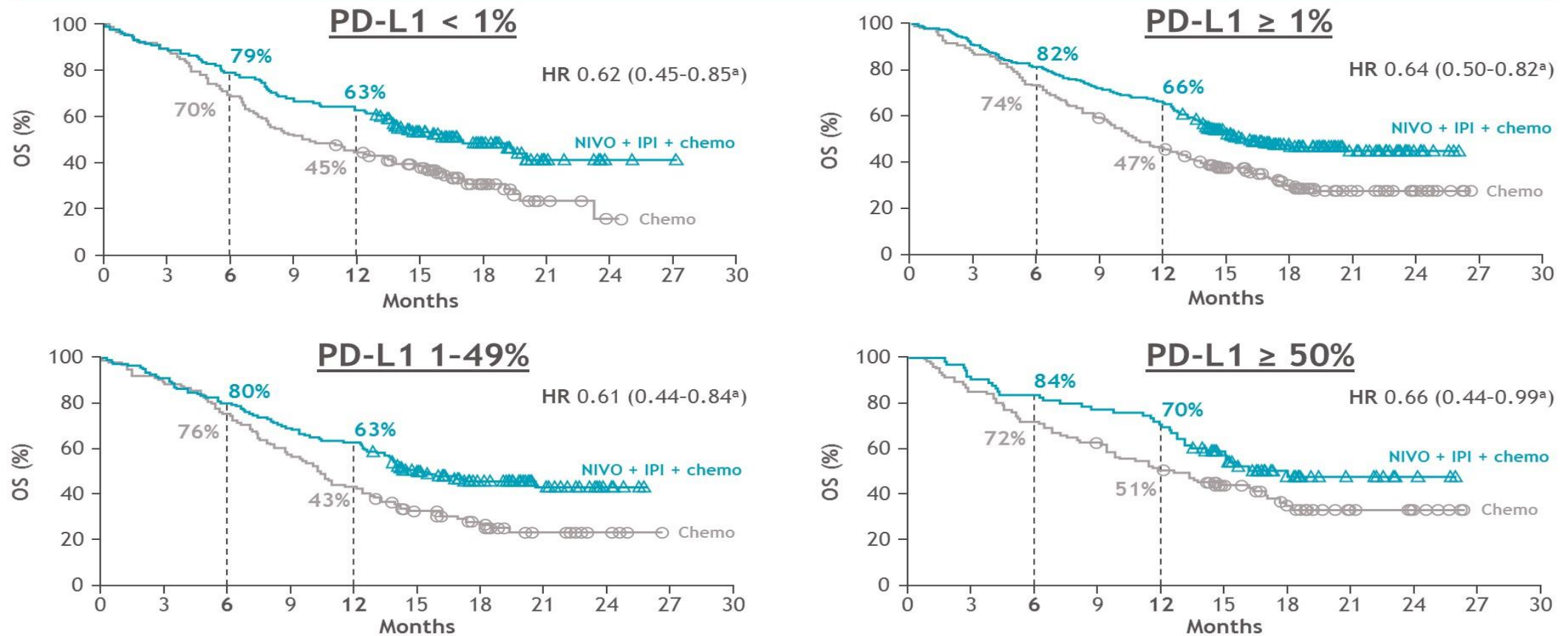
Minimum follow-up: 12.7 months.

^aPatients remaining in follow-up were censored on the last date they were known to be alive; 47% of patients in the NIVO + IPI + chemo arm and 32% of patients in the chemo arm were censored. Subsequent systemic therapy was received by 31% of patients in the NIVO + IPI + chemo arm and 40% in the chemo arm; subsequent immunotherapy was received by 5% and 30%, and subsequent chemotherapy by 29% and 22%, respectively. Among patients with BICR-confirmed disease progression on study, subsequent systemic therapy was received by 40% in the NIVO + IPI + chemo arm and 44% in the chemo arm; subsequent immunotherapy was received by 7% and 34%, and subsequent chemotherapy by 38% and 24%, respectively

CheckMate 9LA: krátký souběžný běh chemoterapie + IO významně zlepšuje přežití a zabraňuje rychlé progresi u části subjektů v prvních měsících léčby

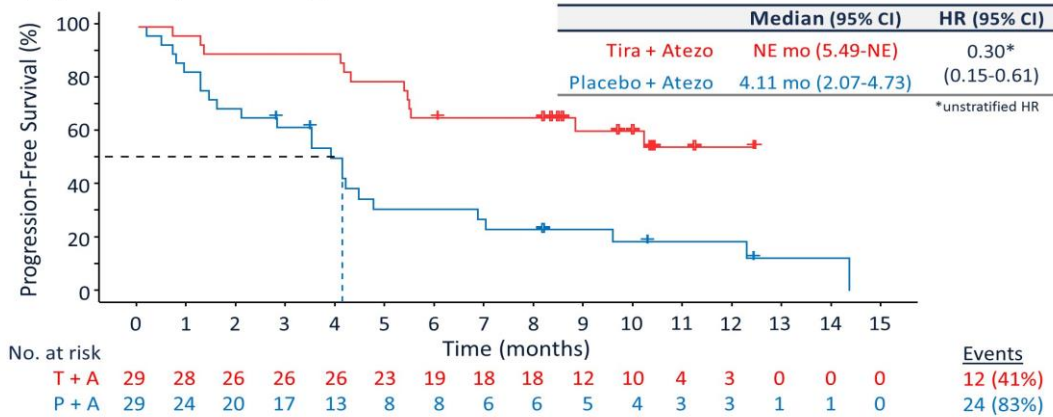
CheckMate 9LA: NIVO + IPI + 2 cycles of chemo in 1L NSCLC

Overall survival by PD-L1 expression level



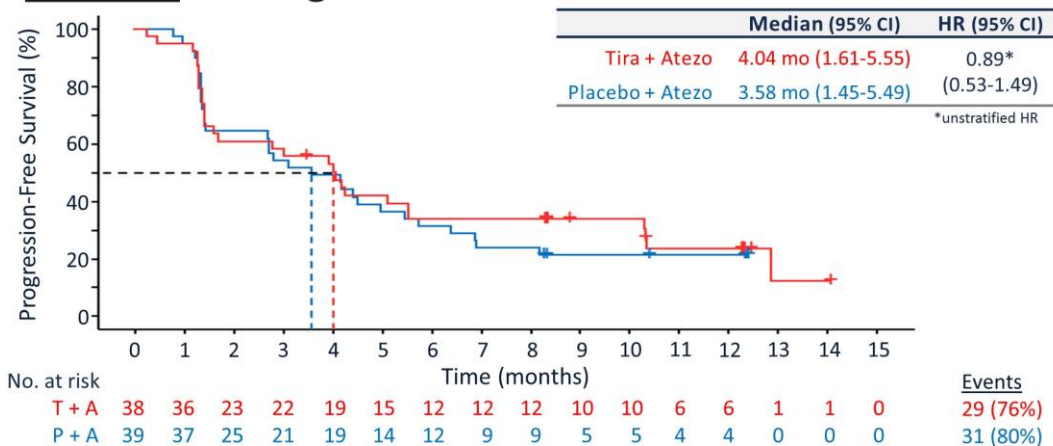
Primary analysis of a randomized, double-blind, phase II study of the anti-TIGIT antibody tiragolumab (tira) plus atezolizumab (atezo) versus placebo plus atezo as first-line (1L) treatment in patients with PD-L1-selected NSCLC (CITYSCAPE)

Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%



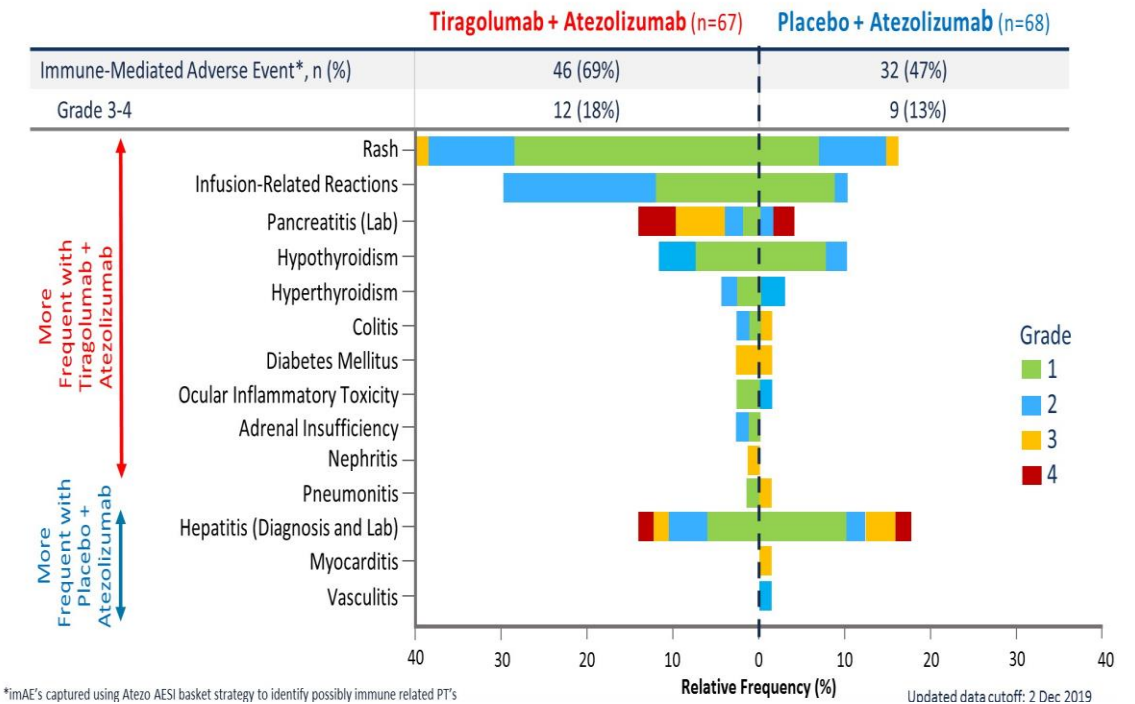
NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score Follow data cutoff: 02 December 2019

Updated Investigator-Assessed PFS: PD-L1 TPS 1-49%



NE = non-evaluable; P+A = placebo + atezolizumab; T+A = tiragolumab + atezolizumab; TPS = tumor proportion score Follow data cutoff: 02 December 2019

Updated Immune-Mediated Adverse Events



Posílení účinnosti IO – jen pro PD-L1 TPS ≥ 50 %?

- IMpower150: Exploratory analysis of brain metastases development

- V IMpower 150 kombinace ABCP (atezolizumab + bevacizumab + chemo) prokázala významně lepší PFS a OS oproti BCP. Bevacizumab může oddálit vznik mozkových metastáz (Fu Y, et al. J Chemother. 2016)

- Data prokazují, že přidání atezo k beva-CP nemůže redukovat četnost vzniku nových mozkových metastáz, ale může prodloužit období před jejich objevením.

- Nemocní s „bulky“ postižením mají příznivější HR pro kombinaci ABCP.

- IMpower150: Exploratory efficacy analysis in patients (pts) with bulky disease

Burden	3rd Quartile SLD ^a				No. of Met Sites ^b			
	High		Low		High		Low	
	ABCP n = 91	BCP n = 85	ABCP n = 266	BCP n = 252	ABCP n = 210	BCP n = 190	ABCP n = 149	BCP n = 148
OS, HR (95% CI)	0.70 (0.5-0.97)		0.83 (0.68-1.02)		0.72 (0.58-0.90)		0.89 (0.67-1.17)	
mOS, mo	15.5 vs 10.7		20.3 vs 17.1		17.6 vs 12.5		22.5 vs 21.5	
PFS, HR (95% CI)	0.52 (0.37-0.72)		0.59 (0.49-0.71)		0.56 (0.45-0.69)		0.56 (0.43-0.72)	
mPFS, mo	7.3 vs 5.8		9.6 vs 7.1		7.7 vs 6.0		11.0 vs 7.9	
ORR, % ^c	62 vs 41		53 vs 40		57 vs 40		53 vs 40	
TTR, mo	1.5 vs 1.6		1.8 vs 1.5		1.6 vs 1.5		1.7 vs 1.5	

^a High = SLD $\geq$ 3rd quartile; low = SLD < 3rd quartile; 3rd quartile = 108 mm

^b High = no. of met sites $\geq$ median; low = no. of met sites < median; median = 2

^c Pts with BI measurable disease

IMpower110: Clinical safety in a phase III study of atezolizumab (atezo) monotherapy (mono) vs platinum-based chemotherapy (chemo) in first-line non-small cell lung cancer (NSCLC)

n (%)	Atezo N = 286	Chemo N = 263	Atezo mono pooled ^a N = 3178
Gr 3-4 AE ^b	86 (30.1)	138 (52.5)	1482 (46.6)
Related Gr 3-4 AE ^b	37 (12.9)	116 (44.1)	496 (15.6)
Gr 5 AE	11 (3.8)	11 (4.2)	119 (3.7)
Related Gr 5 AE	0	1 (0.4)	11 (0.3)
AE leading to any tx withdrawal	18 (6.3)	43 (16.3)	226 (7.1)
imAE	115 (40.2)	44 (16.7)	1097 (34.5)
Gr 3-4 imAE ^b	19 (6.6)	4 (1.5)	248 (7.8)
imAE requiring corticosteroids use	30 (10.5)	3 (1.1)	247 (7.8)

^a Pooled atezo mono-treated pts (cross indications and therapy lines).

^b Gr 3-4 AE/imAE: number of pts whose highest grades of AE/imAE are 3 or 4

Atezolizumab: dobrá tolerance bez nových bezpečnostních signálů

Možnosti 1. linie léčby NSCLC

Study	Selection	Design	PFS	OS
KN024 ¹	ADENO AND SCC PD-L1 > 50%	Pembro vs Chemo	10.3 vs 6.1 HR = 0.62	30 vs 14.2 HR = 0.63
KN042 ²	ADENO AND SCC PD-L1 > 1%	Pembro vs Chemo	7.1 vs 6.4 HR: 1.07	20 vs. 12 HR: 0.81
CHKMTE 227 ³	ADENO AND SCC PD-L1 > 1% PD-L1 < 1%	Ipilimumab + Nivo vs chemo	>1% HR 0.82 <1% HR 0.75	>1% 17.1 vs 14.9 HR: 0.79 <1% 17.2 vs 12.2 HR: 0.62
KN189 ⁴	ADENO PD-L1 0%-100%	Chemo/pembro vs chemo	8.8 vs 4.9 HR = 0.52	22 vs 11.3 HR = 0.49
IMpower150 ⁵	ADENO[Bev elig] PD-L1 0%-100%	Chemo/bev/atezo vs chemo/bev	8.3 vs 6.8 HR = 0.62	19.2 vs 14.7 HR = 0.78
KN407 ⁶	SCC PD-L1 0%-100%	Chemo/pembro vs chemo	6.4 vs 4.8 HR = 0.56	15.9 vs 11.3 HR = 0.64
IMpower130 ⁷	ADENO PD-L1 0%-100%	Nab-pacl/atezo vs chemo	7.0 vs 5.5 HR = 0.64	18.6 vs 13.9 HR = 0.79
Impower 110 ⁸	ADENO AND SCC PD-L1 > 50% (or IC >10%)	Atezolizumab v Chemo	8.1 vs 5.0 HR: 0.63	20.2 vs 13.1 HR 0.59

Cílená léčba metastazujících NSCLC

Abstract 9518: Updated overall survival (OS) and safety data from the randomized, phase III ALEX study of alectinib (ALC) versus crizotinib (CRZ) in untreated advanced *ALK*+ NSCLC

Overall survival

- The median duration of follow-up was 48.2 months (range 0.5–62.7) with alectinib and 23.3 months (range 0.3–60.6) with crizotinib.
- OS data remain immature with 37% of events recorded (stratified HR 0.67, 95% CI 0.46–0.98) (**Figure 1**).
- At the updated data cut-off, the median OS was NR with alectinib vs 57.4 months with crizotinib (95% CI 34.6–NR) (**Figure 1**).

Figure 1. OS in the ITT population

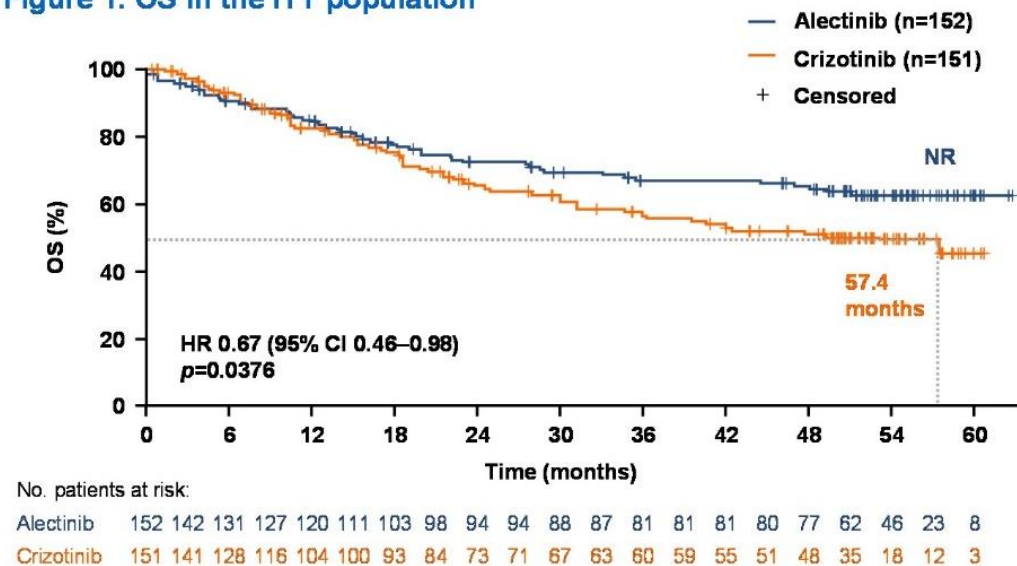


Figure 3. OS benefit in different patient subgroups (unstratified analysis)

Subgroup	Log-rank p-value	HR	95% CI	Interaction test p-value (likelihood ratio)
All	0.0609	0.70	(0.48–1.02)	
Age group (years)				
<65	0.1481	0.73	(0.48–1.12)	0.6768
≥65	0.2189	0.63	(0.30–1.33)	
Sex				
Female	0.3020	0.76	(0.45–1.28)	0.6923
Male	0.1155	0.66	(0.39–1.11)	
Race				
Asian	0.3298	0.74	(0.40–1.36)	0.8575
Non-Asian	0.1161	0.69	(0.43–1.10)	
Smoking status				
Active smoker	n=17 0.4126	1.97	(0.38–10.20)	0.5471
Non-smoker	0.1181	0.68	(0.42–1.11)	
Past smoker	0.1339	0.62	(0.33–1.17)	
ECOG PS				
0	0.1266	0.52	(0.22–1.22)	0.4636
1	0.0960	0.68	(0.44–1.07)	
2	n=20 0.6440	1.30	(0.43–3.90)	
CNS mets at baseline (IRC)				
Yes	0.0477	0.58	(0.34–1.00)	0.4677
No	0.2851	0.76	(0.45–1.26)	
Prior brain radiation				
Yes	0.0889	0.39	(0.13–1.19)	0.2064
No	0.1956	0.77	(0.52–1.14)	

0.0 0.5 1.0 1.5 2.0
Favors alectinib Favors crizotinib

Safety

- Median treatment duration was 28.1 months with alectinib vs 10.8 months with crizotinib.
- No new safety signals were observed in this updated analysis of the ALEX data with almost three-times longer median treatment duration with alectinib vs crizotinib (**Table 1**).

Table 1. Safety summary

Event, n (%)	Alectinib (n=152)	Crizotinib (n=151)
All grade AEs	147 (97)	147 (97)
Serious AEs	59 (39)	48 (32)
Grade 3–5 AEs	79 (52)	85 (56)
Fatal AEs	7 (5)	7 (5)
AEs leading to treatment discontinuation	22 (15)	22 (15)
AEs leading to dose reduction	31 (20)	30 (20)
AEs leading to dose interruption	40 (26)	40 (27)

AE, adverse event

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic NSCLC: Interim results of DESTINY-Lung01



DESTINY-Lung01 Study Design

An open-label, multicenter, phase 2 study (NCT03505710)

Patients

- Unresectable/metastatic nonsquamous NSCLC
- Relapsed/refractory to standard treatment
- HER2-expressing or HER2-activating mutation^a
- No prior HER2-targeted therapy, except pan-HER TKIs



Cohort 1 (n = 42)

HER2 expressing (IHC 3+ or IHC 2+)

Cohort 2 (n = 42)

HER2 mutated

T-DXd 6.4 mg/kg q3w

Primary endpoint

- Confirmed ORR by independent central review

Data cutoff: November 25, 2019

- 45.2% of patients (19/42) in Cohort 2 remained on treatment
- 54.8% discontinued, primarily for progressive disease and adverse events (21.4% each)

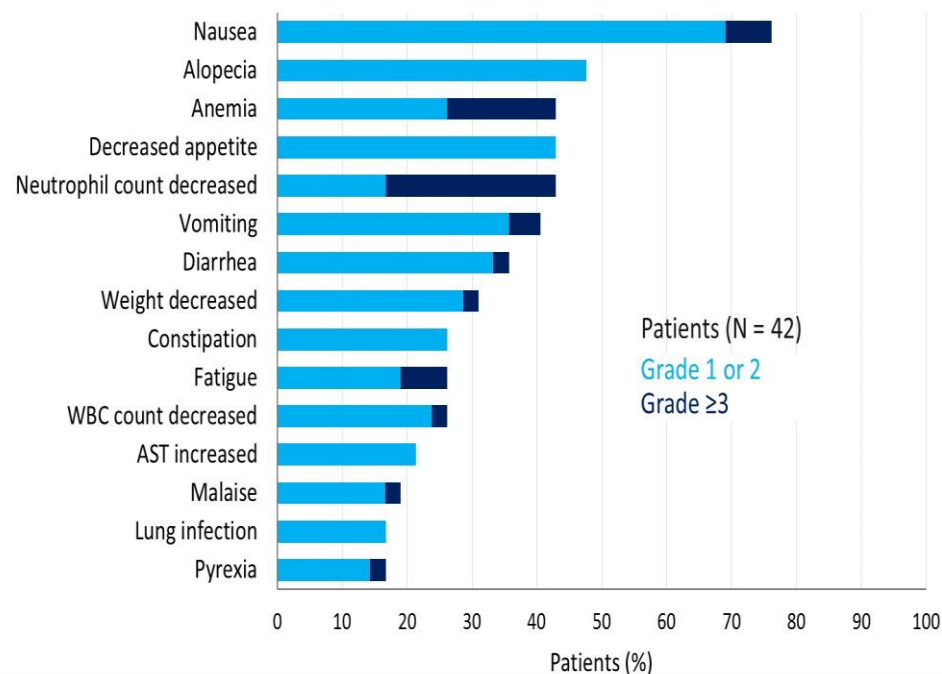
^a Based on local assessment of archival tissue.

DESTINY-Lung01 – výsledky

DESTINY-Lung01 HER2-Mutated NSCLC



Treatment-Emergent Adverse Events in >15% of Patients



Select phase II trials in HER2 altered NSCLC

Drug	Phase	N	RR	PFS
TKIs				
Afatinib ¹	II	13	7.7%	4 mos
Dacomitinib ²	II	30	11.5%	3 mos
Pozotinib ³	II	12	50%	5.6 mos
Pyrotinib ⁴	II	15	53.3%	6.4 mos
Monoclonal Antibodies/ ADC				
Ado-Trastuzumab emtasine ⁵	II	18	44%	5.0 mos
Trastuzumab Deruxtecan ⁶	II	42	61%	14 mos

Nové možnosti posílení účinnosti anti-EGFR terapie

EGFR TKI + Anti-VEGF

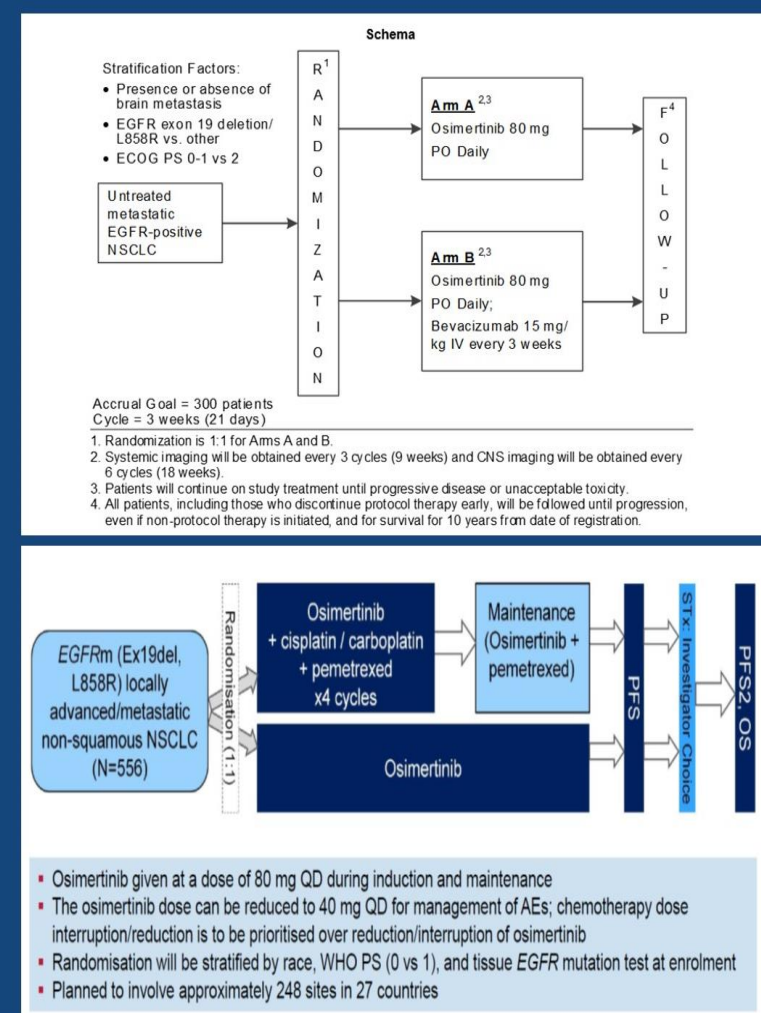
Trial	Phase	n	EGFR TKI	Anti-VEGF	PFS	OS
JO25567 ^{1,2}	Phase 2	154	Erlotinib	Bevacizumab	16 vs 9.7 (HR: 0.54; p=0.005)	47 vs 47.4 (HR: 0.81, p=0.32)
NEJ026 ³	Phase 3	228	Erlotinib	Bevacizumab	16.9 vs 13.3 (HR: 0.605; p=0.015)	50.7 vs 46.2 (HR: 1.00)
ALLIANCE ⁴	Phase 2	88	Erlotinib	Bevacizumab	17.9 vs 13.5 (HR: 0.81, p= 0.39)	32 vs 50.6 (HR : 1.41; p = 0.33)
RELAY ⁵	Phase 3		Erlotinib	Ramucirumab	19.4 vs 12.4 (HR: 0.591; p<0.0001)	Immature

EGFR TKI +Chemotherapy

Trial	Phase	n	EGFR TKI	Chemotherapy	PFS	OS
NEJ009 ⁶	Phase 3	345	Gefitinib	Carboplatin + Pemetrexed	20 vs 11.2 (HR: 0.494; p =0.001)	52 vs 38.8 (HR: 0.65, p=0.013)
Noronha ⁷	Phase 3	350	Gefitinib	Carboplatin + Pemetrexed	16 vs 8 (HR: 0.51; p=0.001)	NR vs 17 (HR 0.45; p=0.001)

EA5182

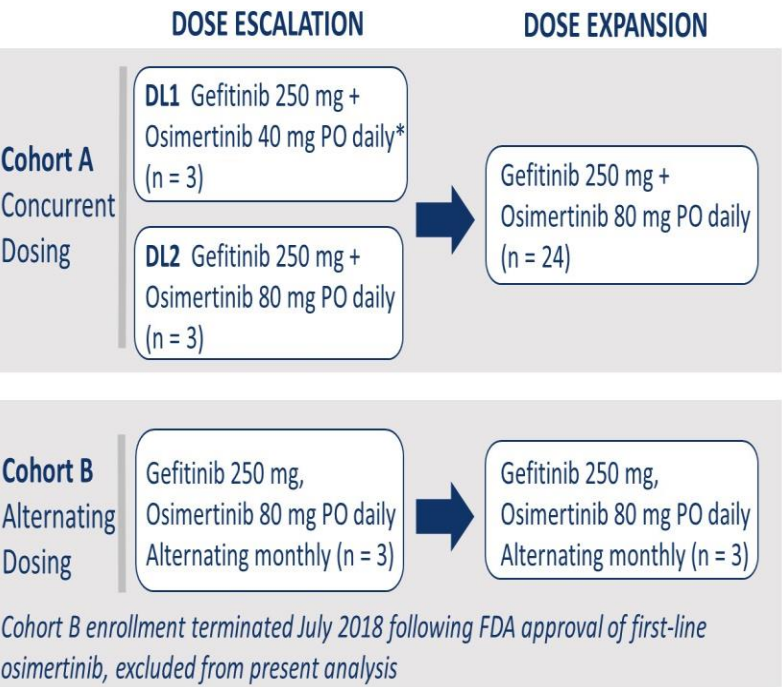
FLAURA 2



Concurrent osimertinib plus gefitinib for first-line treatment of EGFR-mutated NSCLC

Study Schema

Phase I/II study, EGFR-mutated stage IV NSCLC without prior treatment



*Inpatient dose escalation to osimertinib 80 mg po daily following study amendment

Primary Endpoints

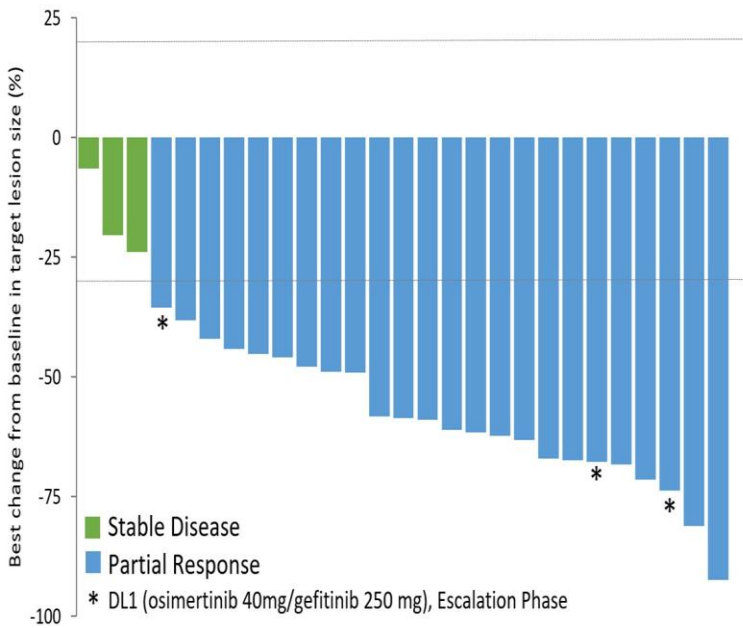
- Dose Escalation: MTD
- Dose Expansion: Feasibility, defined as receipt of combination therapy for ≥ 6 28-day cycles

Secondary Endpoints

- Rate of G3-5 TRAEs
- ORR per RECIST 1.1
- Progression free survival
- Overall survival
- cfDNA clearance
- Genomic alterations at progression

NCT03122717

Radiographic Response, RECIST 1.1



Endpoint (n=27)	
Objective Response rate - % of patients (95% CI)*	88.9% (71.9% - 96.1%)
Disease Control Rate - % of patients (95% CI)	100% (87.5% - 100.0%)
Type of Response - n(%)	
Complete	0 (0%)
Partial	24 (88.9%)
Stable Disease	3 (11.1%)
Progression	0 (0%)
Median Depth of Response - % (range)	58.6% (6.5% - 94.2%)

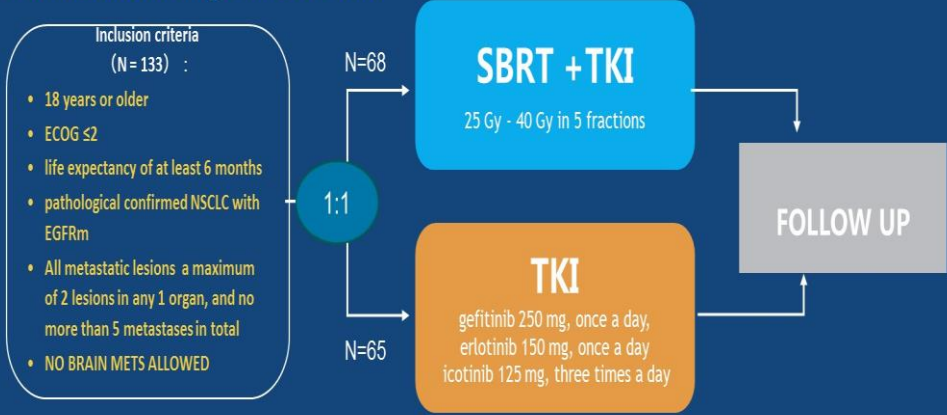
*All responses confirmed

Kombinace zabraňuje tvorbě rezistentních mutací, bezpečnost léčby je zachována.

First-line tyrosine kinase inhibitor with or without aggressive upfront local radiation therapy in patients with EGFRm oligometastatic non-small cell lung cancer: Interim results of a randomized phase III, open-label clinical trial (SINDAS)

Study Design and Enrollment

2016.1—2019.6, Investigator-initiated, multicenter, open label, parallel-group, phase 3 randomized clinical trial from 5 centers located indifferent provinces of China



Statistical Analysis

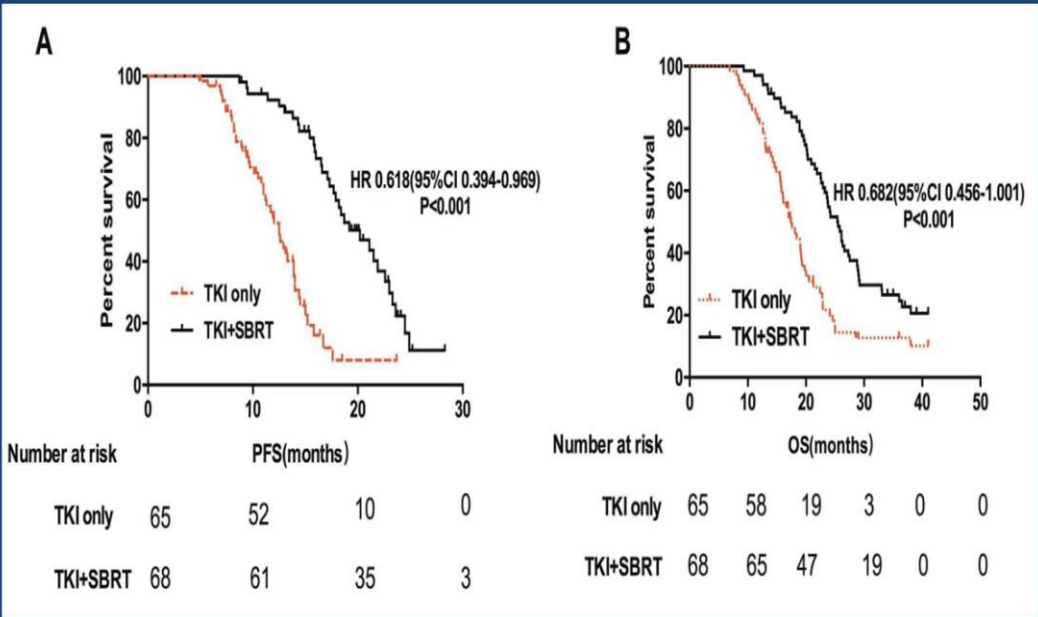
- Descriptive statistics
- Chi-square test
- Kaplan-Meier method and log-rank test
- Multivariate analyses using Cox regression models

The primary endpoint : PFS
The secondary endpoint : OS
Safety

Randomization and Blinding

- Computer-generated randomization
- Open-label study not blinded to the treatment arm
- Randomization assignment

Kaplan-Meier plot of PFS (A) and OS (B)



SBRT=stereotactic body radiotherapy. HR=hazard ratio. (A) PFS and (B) OS. PFS,=progression-free survival; OS,=overall survival; C= confidence interval

Kombinace lokální + systémové léčby u metastazujících NSCLC??

Questions?

What is the definition of oligometastatic?

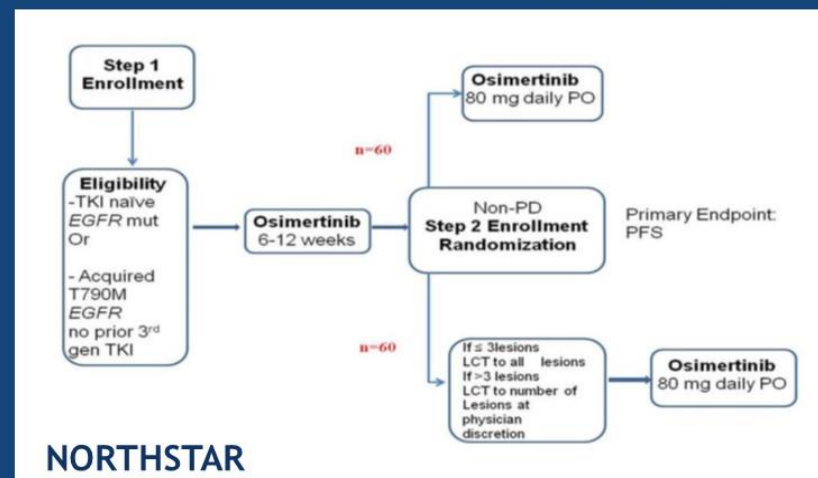
What is the optimal timing of LAT?

Concurrently? After induction? At the time of oligoprogression?

How will this strategy evolve as frontline treatment combinations emerge for EGFR patients

Future Trials

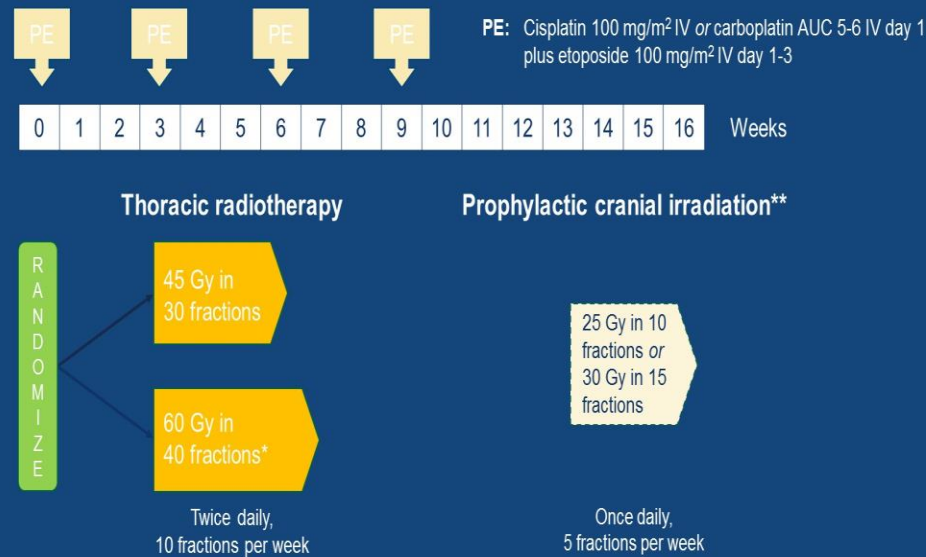
Patients with metastatic NSCLC having completed 4 cycles or courses of first-line/induction systemic therapy	S T R A T I F I C A T I O N	Histology:	R A N D O M I Z E	Arm 1: Maintenance systemic therapy alone**
Restaging studies reveal no evidence of progression and limited (≤ 3 discrete sites) metastatic disease, all of which must be amenable to SBRT +/- Surgery		Squamous vs. Non-squamous		Arm 2: SBRT or SBRT and Surgery to all sites of metastases (≤ 3 discrete sites) plus irradiation (SBRT or hypofractionated RT) of the primary site followed by maintenance systemic therapy. All Arm 2 patients, even if treated with Surgery, must have one site of disease (metastasis or primary) treated with radiation.**
		Systemic Therapy: Immunotherapy* vs Cytotoxic Chemotherapy		
NRG-LU002				
** As noted in Section 5				



Hyperfrakcionace u malobuněčného karcinomu

Randomized phase II trial comparing the efficacy of standard-dose with high-dose twice-daily thoracic radiotherapy (TRT) in limited disease small-cell lung cancer (LD SCLC)

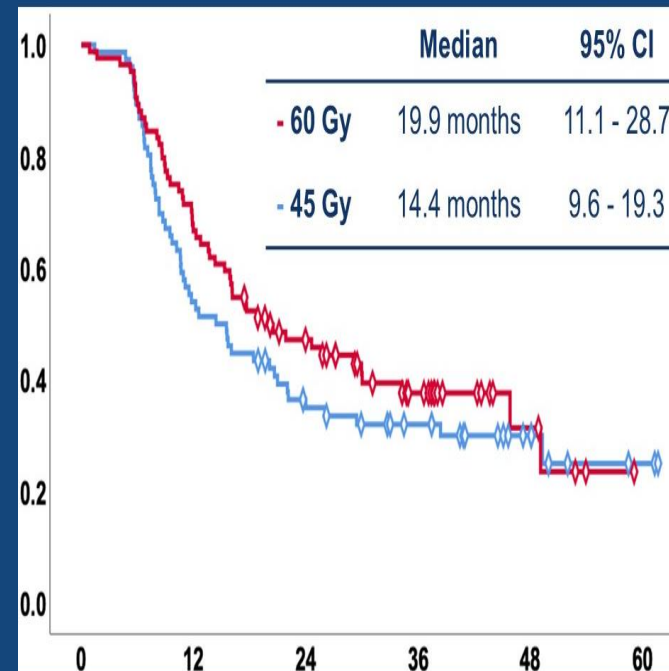
Study design



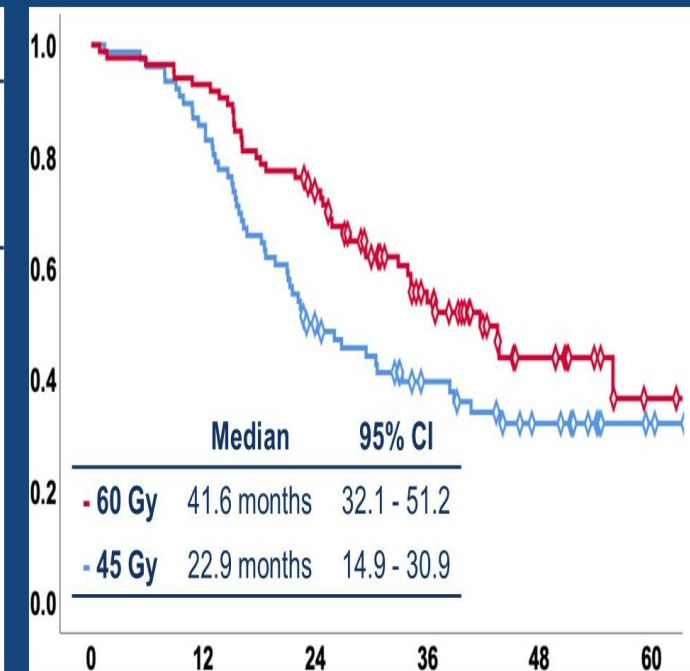
*If 60 Gy was not applicable, a dose of ≥54 Gy was allowed

**Offered to patients who responded to chemoradiotherapy

PFS



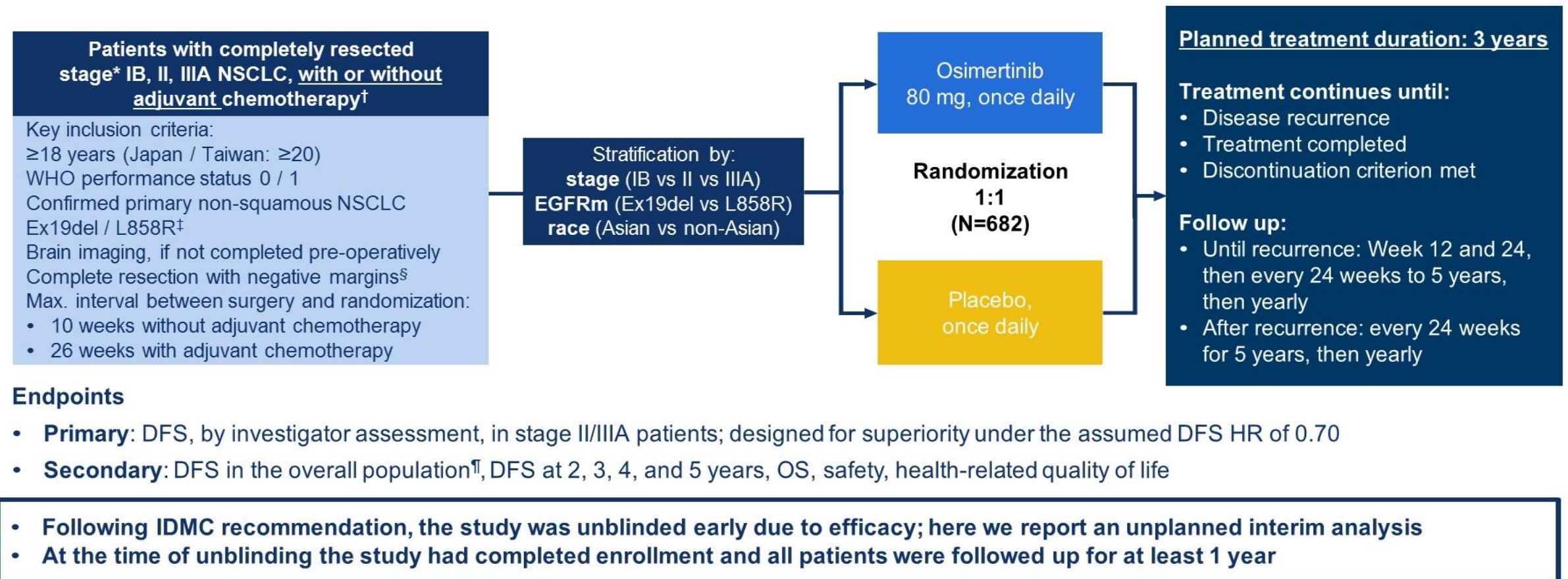
OS



Adjuvantní terapie EGFR-mutovaných NSCLC

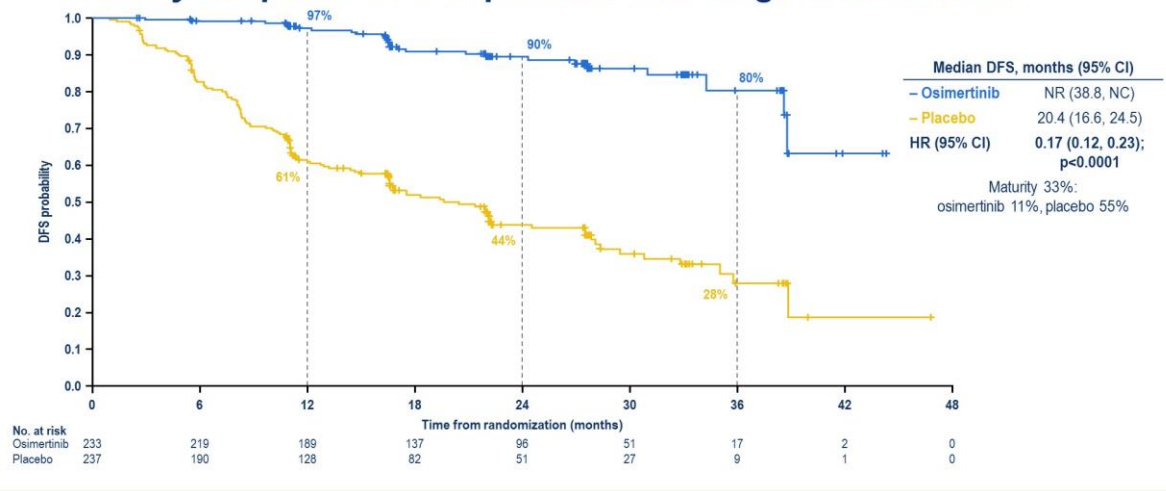
Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA

ADAURA Phase III double-blind study design

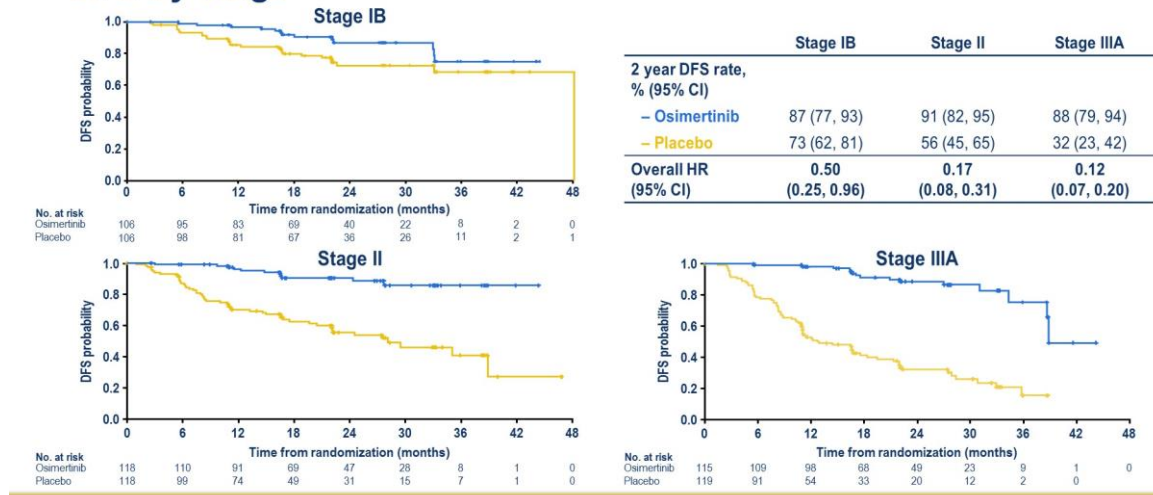


ADAURA – účinnost

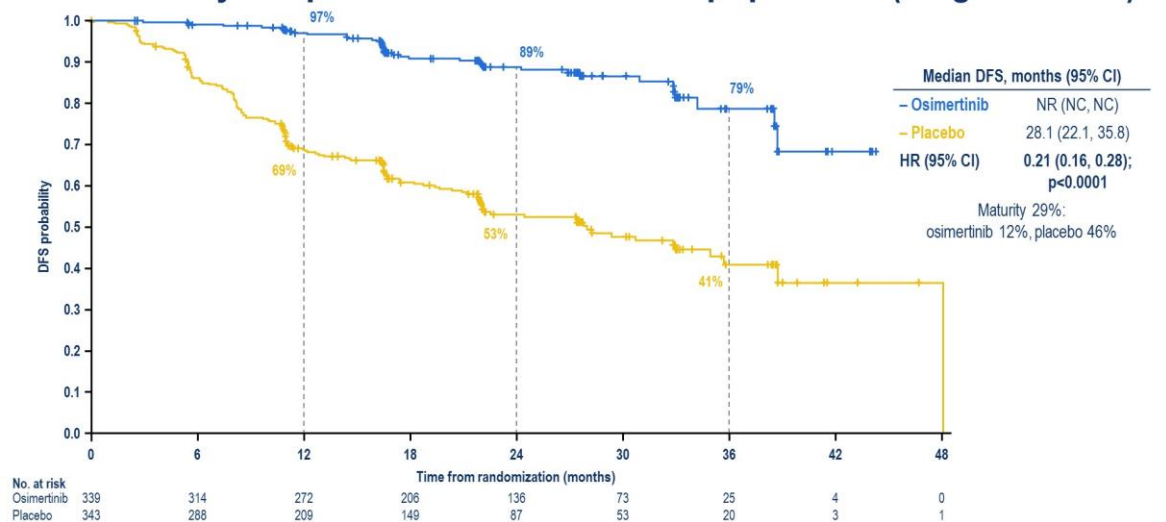
Primary endpoint: DFS in patients with stage II/IIIA disease



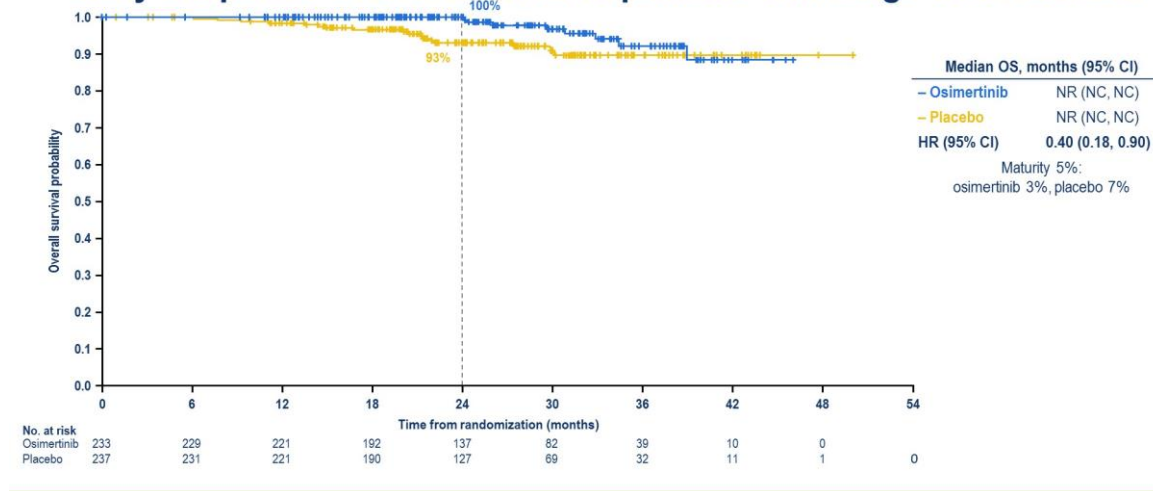
DFS by stage



Secondary endpoint: DFS in the overall population (stage IB/II/IIIA)



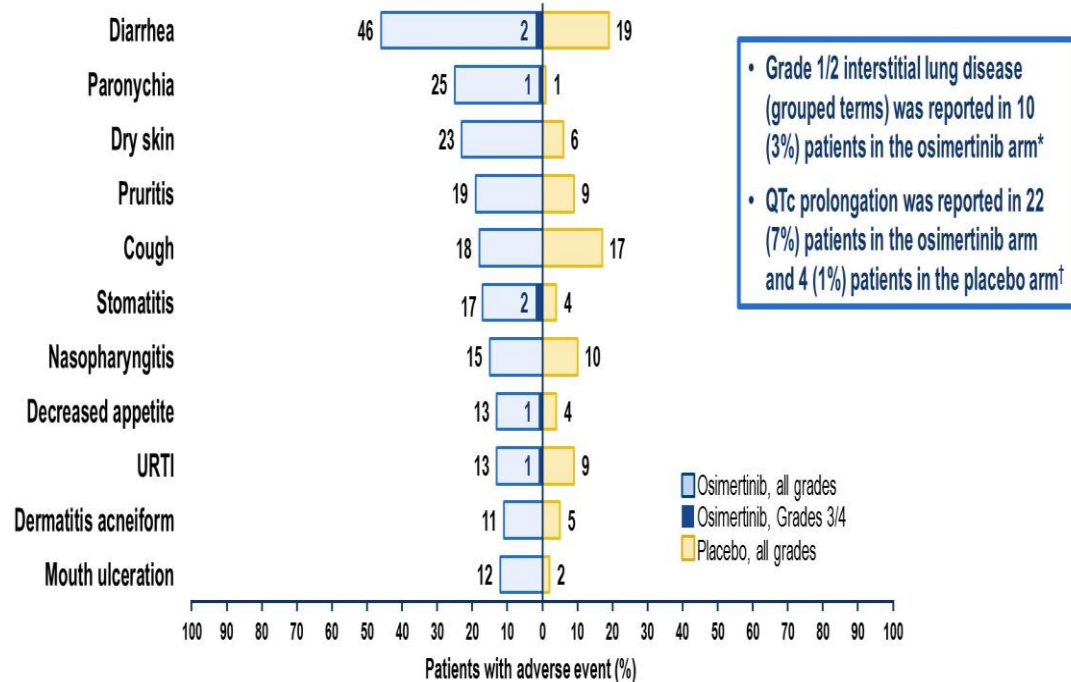
Early snapshot: overall survival in patients with stage II/IIIA disease



ADAURA – toxicita a závěry

All causality adverse events ($\geq 10\%$ of patients)

Median duration of exposure: osimertinib: 22.3 months (range 0 to 43), placebo: 18.4 months (range 0 to 48)



- První cílená léčba prokazující v adjuvantním podání statisticky i klinicky významné prodloužení PFS v léčbě stadia IB/II/IIIA u EGFR-mutovaného NSCLC

- 79% snížení rizika recidivy nebo úmrtí (DFS HR 0,21 [95% CI: 0,16–0,28; $p < 0,0001$])

- Zlepšení DFS bez ohledu na podání adjuvantní chmt ANO/NE

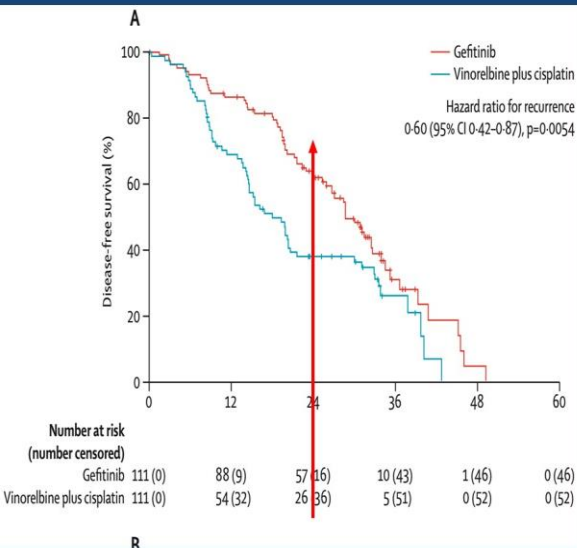
- Konzistentně bezpečnostní profil

příznivý

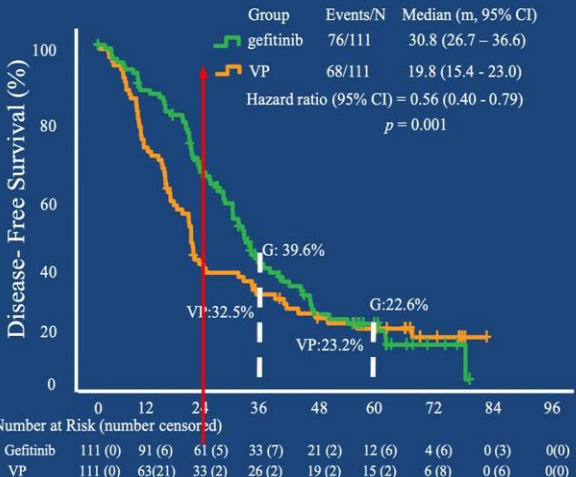
CTONG1104: Adjuvant gefitinib versus chemotherapy for resected N1-N2 NSCLC with EGFR mutation—Final overall survival analysis of the randomized phase III trial

DFS, then and now

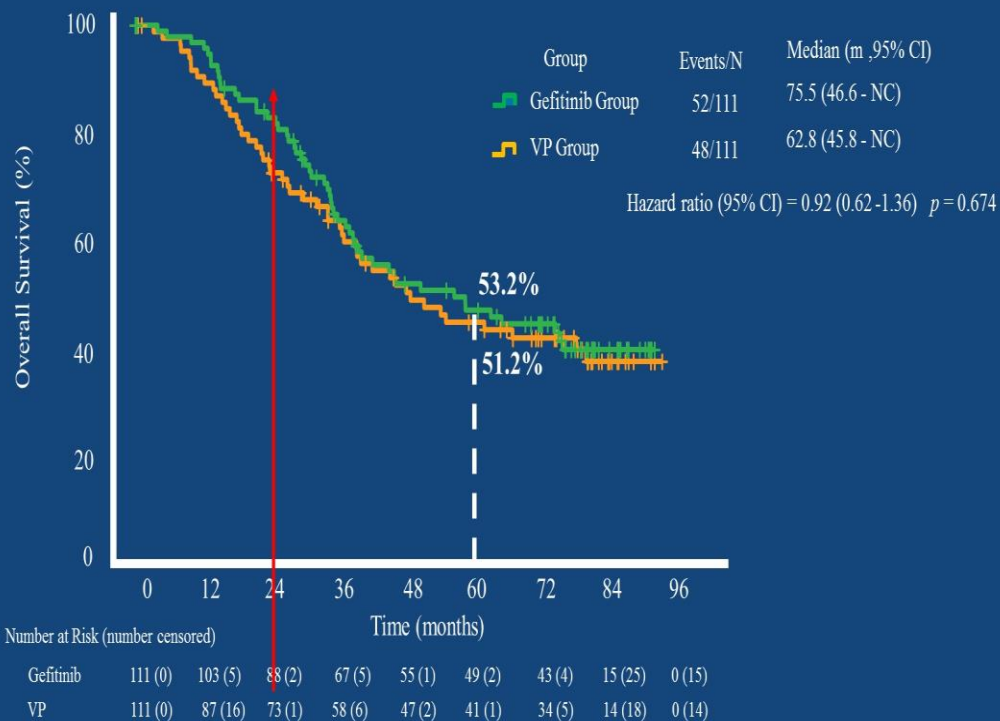
Zhong, Lancet Oncology 2017



ITT population (n=222)



Overall survival (ITT population)



Maligní mezoteliom pleury

So What is the Current SOC?

- Platinum + Pem
- Likely OK to substitute CbP
- Probably add bev
- Maybe add TTF
- Maybe do pem maintenance

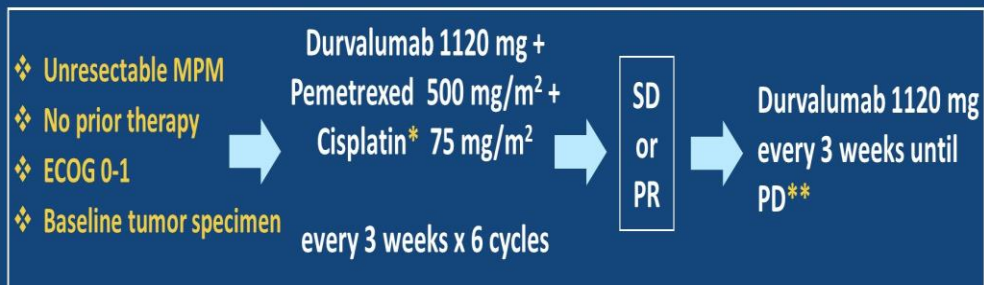
What do we expect with these options?

- PFS about 7-9m
- OS about 16-18m

PrE0505: Phase II multicenter study of anti-PD-L1, durvalumab, in combination with cisplatin and pemetrexed for the **first-line** treatment of unresectable malignant pleural mesothelioma (MPM)—A PrECOG LLC study

Patients and Methods

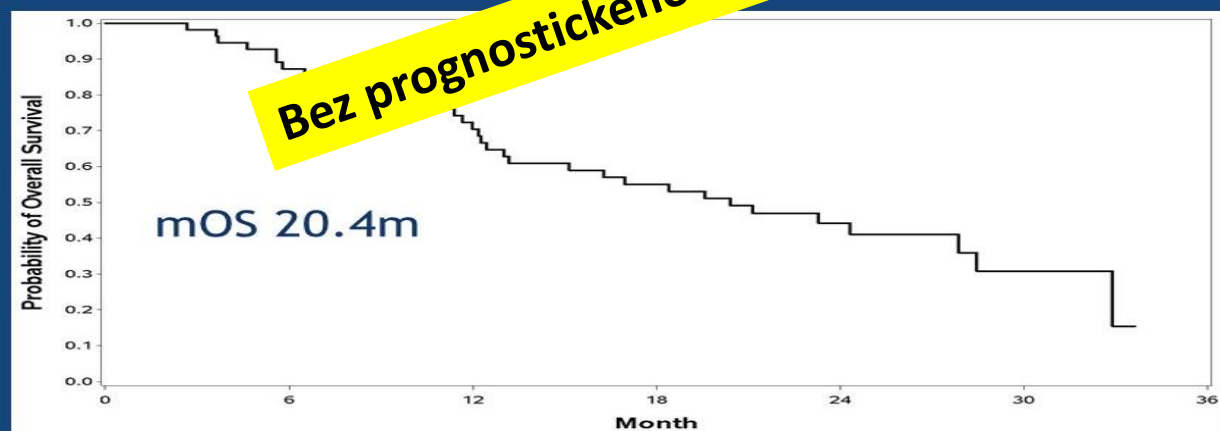
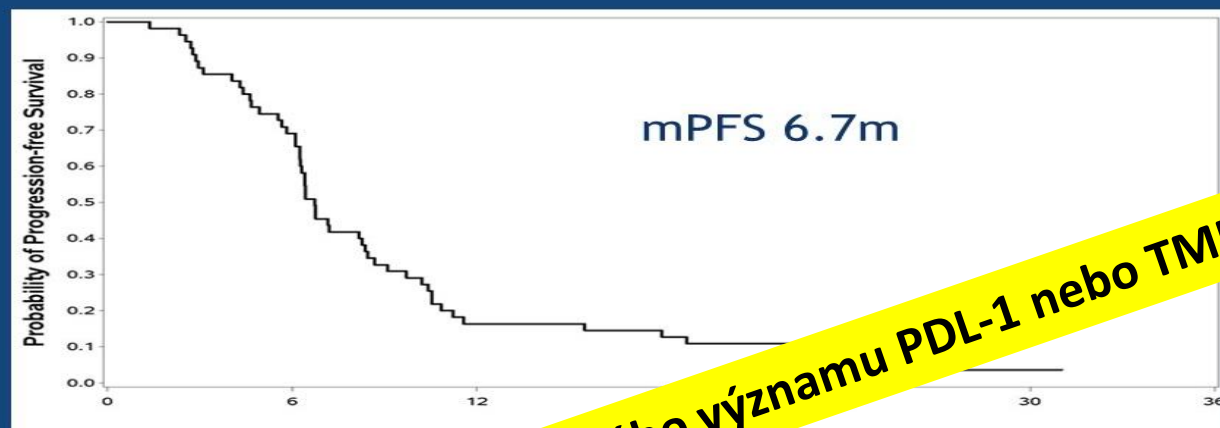
Between June 2017 and June 2018, 55 patients were enrolled at 15 US sites



- 90% power to detect a 37% reduction in the OS hazard rate of 0.058 to 0.037 based on Wald test for the log failure rate parameter (one-sided type I error rate of 10%)
- To correspond to a 58% improvement in the median OS from 12 months (historical control) to 19 months (goal)
- Pre-specified safety review after enrollment of the first 6 and 15 patients. No DLTs noted for the combination with durvalumab 1120 mg

* Carboplatin was substituted if cisplatin was contraindicated, or due to toxicity during treatment

** Max duration 1 year from start of study



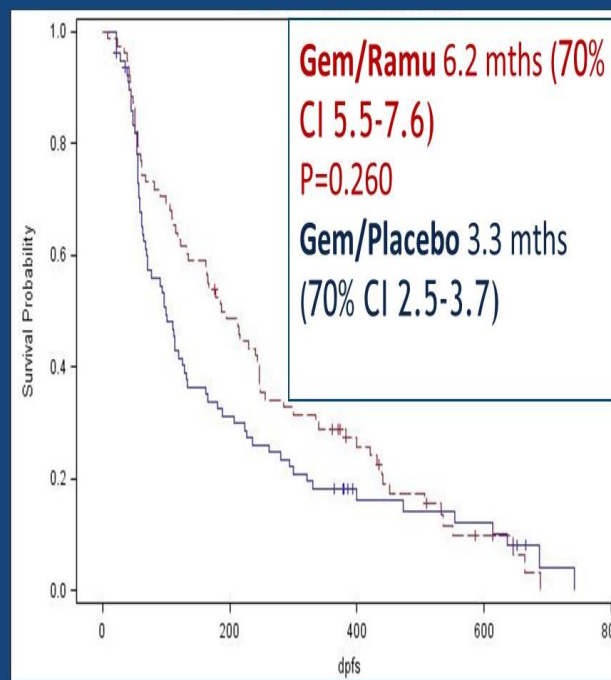
Bez prognostického významu PDL-1 nebo TMB

Randomized phase II study on gemcitabine with or without ramucirumab as second-line treatment for advanced malignant pleural mesothelioma (MPM): Results of Italian Rames Study

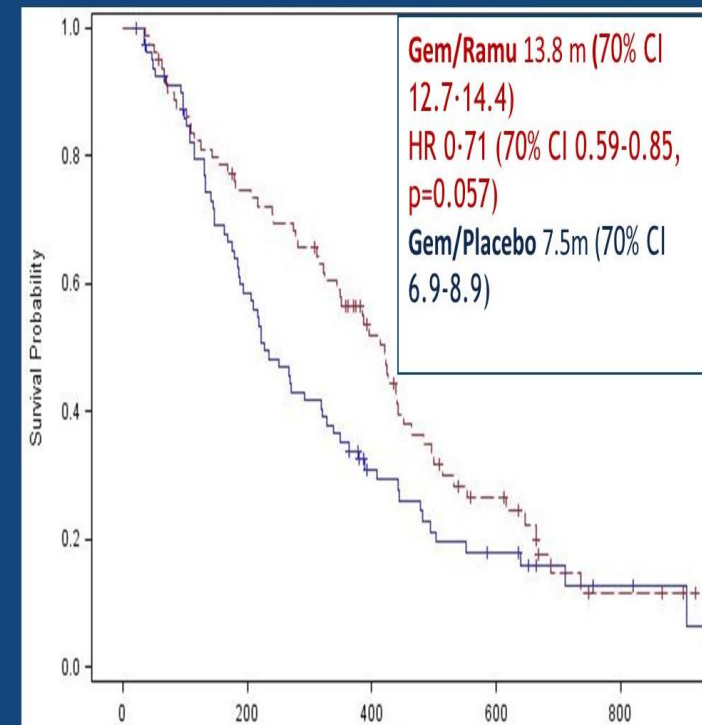
What do we expect in 2L Mesothelioma?

Drug	PFS	OS	Trial
Durva/Tremi	5.7	16.6	Calabrò, Lancet Resp. 2018
Pembro vs. Gem or Vin	2.5 3.4	10.7 11.7	Popat, ESMO 2019
Gem		8	Van Meerbeeck, Cancer 1999
Gem		4.7	Kindler, Lung Cancer 2001
Gem	6	11.2	Toyokawa, IJCO, 2014

PFS



OS



Děkuji za pozornost!