# NOVINKY Z LETOŠNÍHO NEJVÝZNAMNĚJŠÍHO SETKÁNÍ ONKOLOGŮ

## Shrnutí ze sekce nádorů plic

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# Trocha čísel

- **Rakovina plic:** **533 abstraktů**
- Přednášky: 33
- Poster discussion: 30
- Poster: 167
- E-publikace abstraktů: 303

- **Imunoterapie checkpoint inhibitory**
- Atezolizumab: 34
- Durvalumab: 34
- Nivolumab: 56
- Pembrolizumab: 62
- ----------

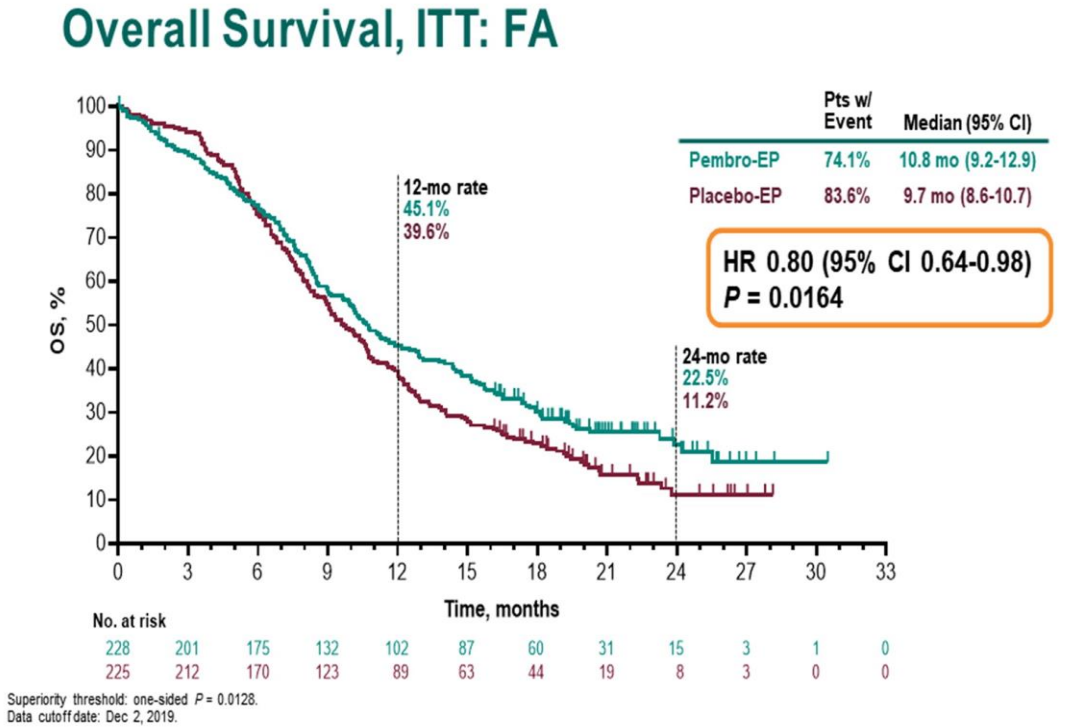
**186 = 35 %**

# 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)

- 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.

Rudin KN604 ASCO 2020




# IO + EP – upevnění standardu u SCLC ES:

**IMpower133**

**CASPIAN**

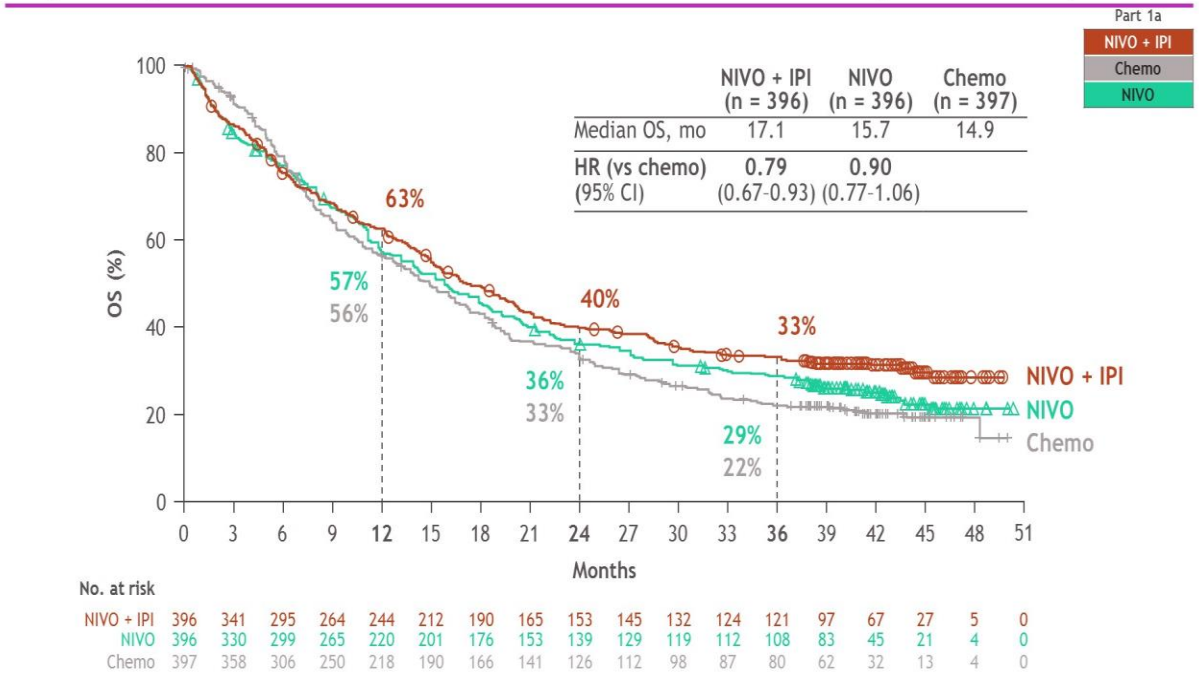
**KEYNOTE-604**


Rudin CM, et al. J Clin Oncol 38: 2020 (suppl; abstr 9001)
Horn L, et al. N Engl J Med. 2018;379:2220-9; Paz-Ares L, et al. Lancet. 2019;398:1929–39

# 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



## 3-year update: OS with NIVO + IPI vs chemo vs NIVO (PD-L1 ≥ 1%)

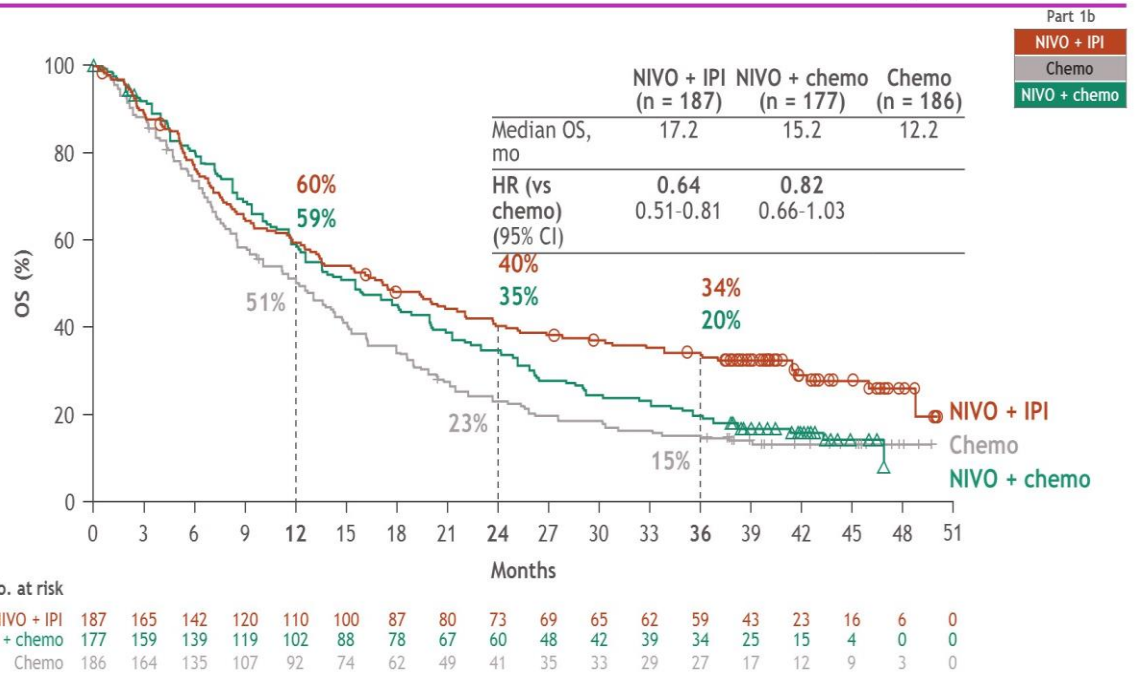



Database lock: February 28, 2020; minimum follow-up for OS: 37.7 months.
Dosages were NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W) and NIVO (240 mg Q2W). Among patients who were alive at 3 years, subsequent systemic therapy was received by 35% in the NIVO + IPI arm, 45% in the NIVO arm, and 76% in the chemo arm; subsequent immunotherapies were received by 13%, 21%, and 71%; and subsequent chemotherapy was received by 28%, 33% and 30%, respectively.



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.



Ramalingam SS, et al. J Clin Oncol 38: 2020 (suppl; abstr 9500)

Nejvýraznější prospěch u subjektů PD-L1 ≥ 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 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 for immunotherapy

**Primary endpoint**
- OS

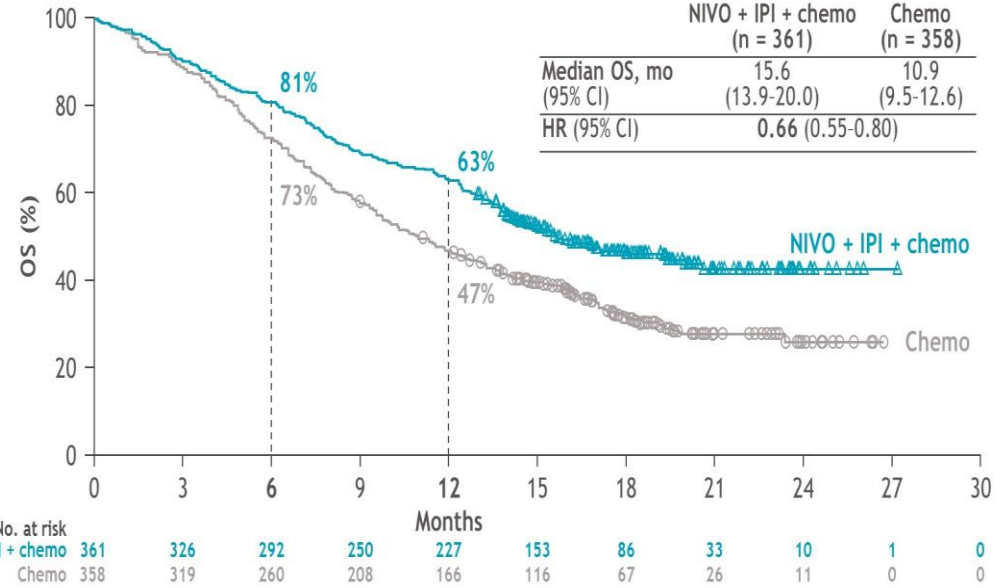
**Secondary endpoints**
- PFS by BICR[e]
- ORR by BICR[e]
- Efficacy by tumor PD-L1 expression

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.

[a]NCT03215706; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Patients unevaluable for PD-L1 were stratified to PD-L1 < 1% and capped to 10% of all randomized patients; [d]NSQ: pemetrexed + cisplatin or carboplatin; SQ: paclitaxel + carboplatin; [e]Hierarchically statistically tested.

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

## Primary endpoint (updated): Overall survival[a]




| | NIVO + IPI + chemo (n = 361) | Chemo (n = 358) |
|---|---|---|
| Median OS, mo (95% CI) | 15.6 (13.9-20.0) | 10.9 (9.5-12.6) |
| HR (95% CI) | 0.66 (0.55-0.80) | |

Minimum follow-up: 12.7 months.

[a]Patients 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

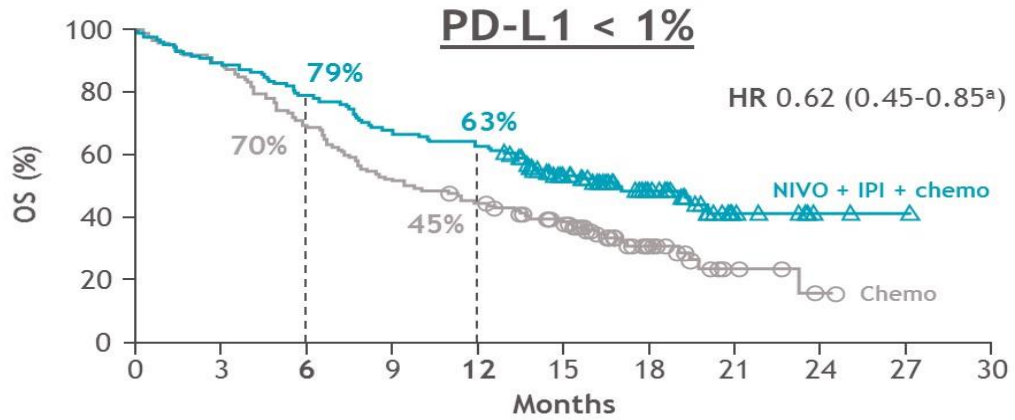


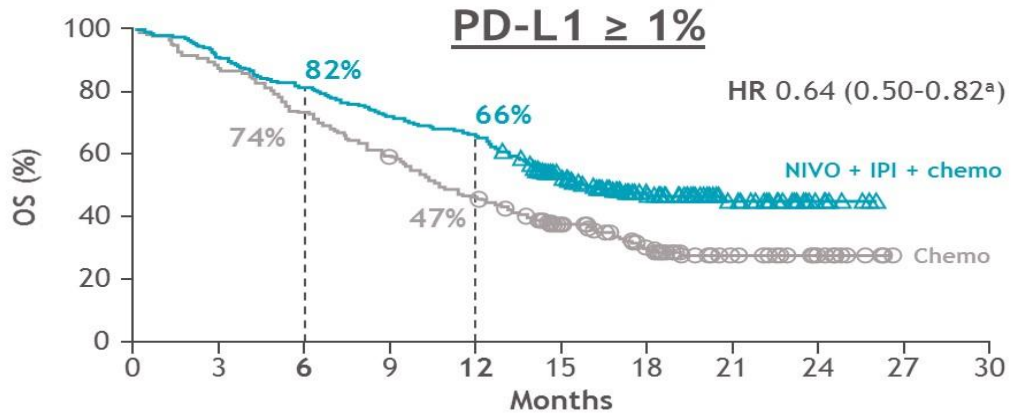
Reck M, et al. J Clin Oncol 38: 2020 (suppl; abstr 9501)

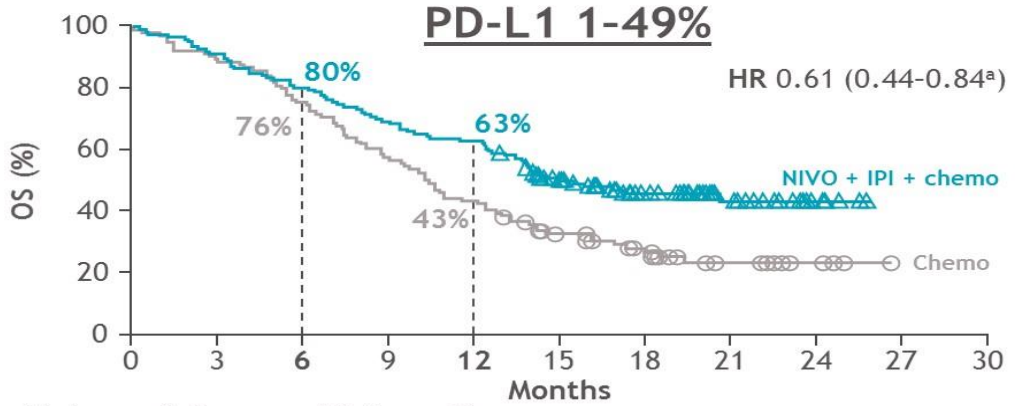
# CheckMate 9LA: krátký souběžný běh chemoterapie + IO významně zlepšuje přežití a zabraňuje rychlé progresi u části subjektů v prvních měsících léčby

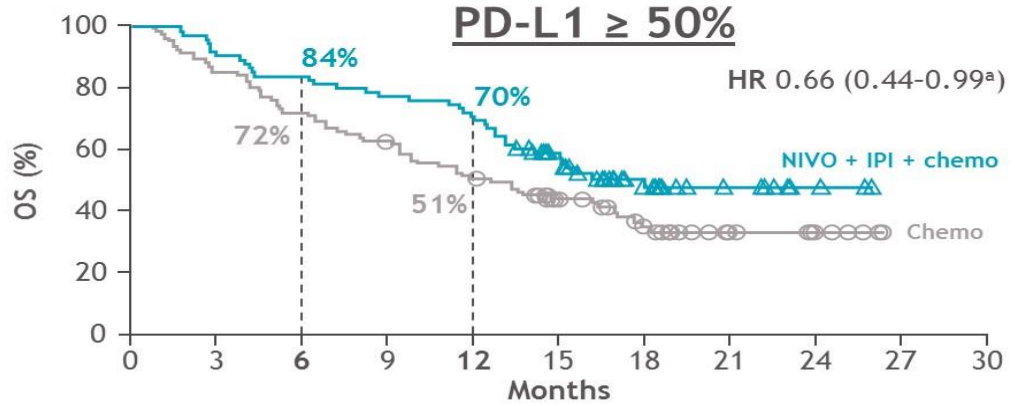
CheckMate 9LA: NIVO + IPI + 2 cycles of chemo in 1L NSCLC

## Overall survival by PD-L1 expression level



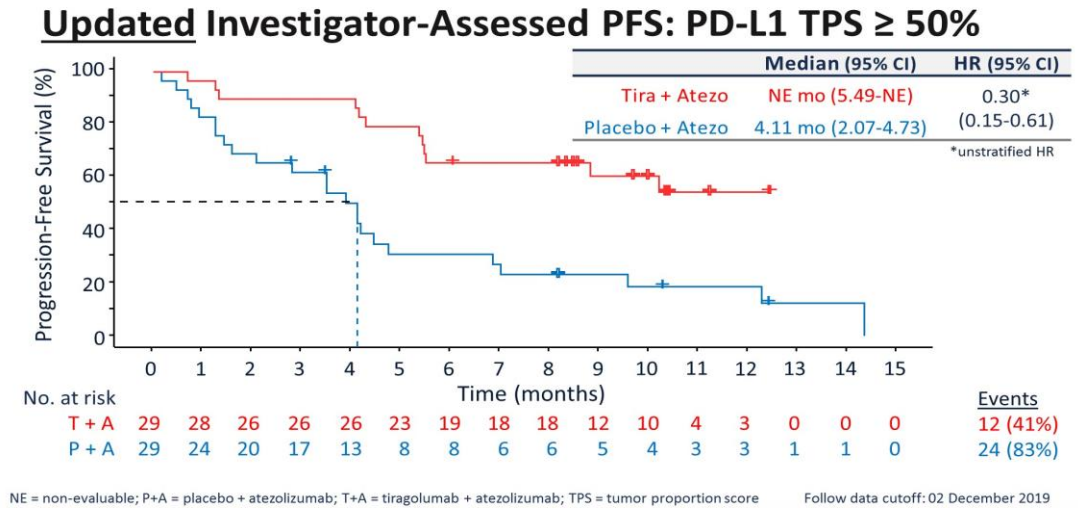



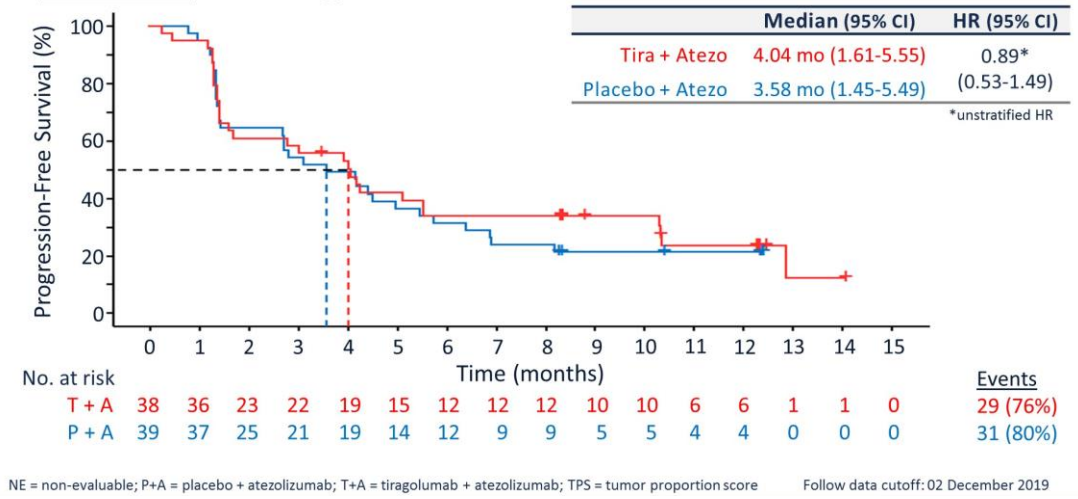

Minimum follow-up: 12.7 months.
ª95% CI.

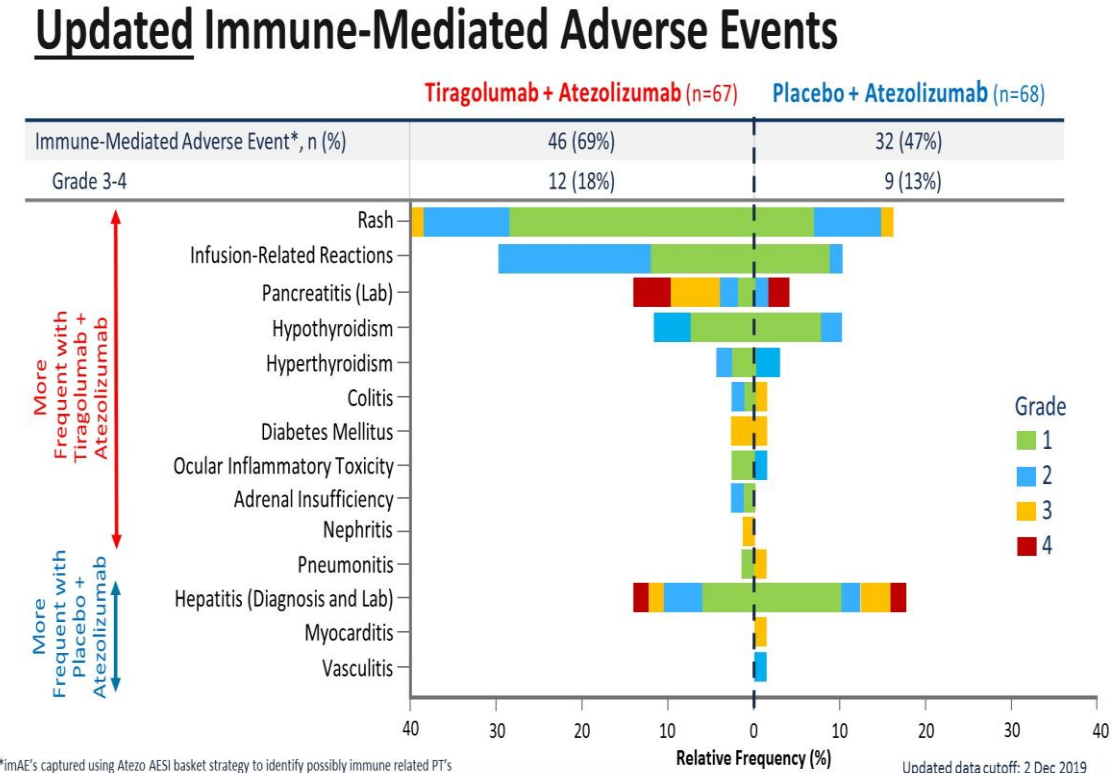
13

Reck M, et al. J Clin Oncol 38: 2020 (suppl; abstr 9501)

# 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)




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

Rodrygez-Abreu D, et al. J Clin Oncol 38: 2020 (suppl; abstr 9503)

- # IMpower150: Exploratory analysis of brain metastases development
  - Ve studii IMpower150 prokázala kombinace ABCP (atezolizumab + bevacizumab + chemo) 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

| | 3rd Quartile SLD[a] | | | | No. of Met Sites[b] | | | |
|---|---|---|---|---|---|---|---|---|
| | High | | Low | | High | | Low | |
| Burden | 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 ≥ 3rd quartile; low = SLD < 3rd quartile; 3rd quartile = 108 mm

[b] High = no. of met sites ≥ median; low = no. of met sites < median; median = 2

[c] Pts with BL measurable disease

Socinski MA, et al. N Engl J Med. 2018; Capuzzo F, et al. J Clin Oncol 38: 2020 (suppl; abstr 9587); Jotte RM, et al. J Clin Oncol 38: 2020 (suppl; abstr e21637)

# 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**

Jassem J, et al. J Clin Oncol 38: 2020 (suppl; abstr e21623)

# Možnosti 1. linie léčby NSCLC

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

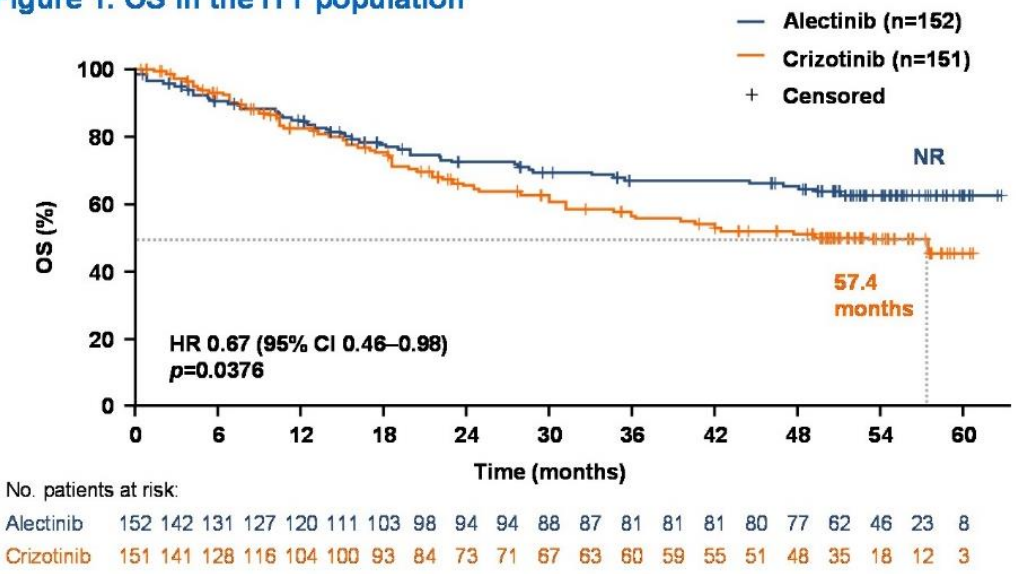
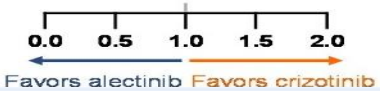



**Figure 3. OS benefit in different patient subgroups (unstratified analysis)**

| 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) | |




## 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

Peters S, et al. J Clin Oncol 38: 2020 (suppl; abstr 9518)

# 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)

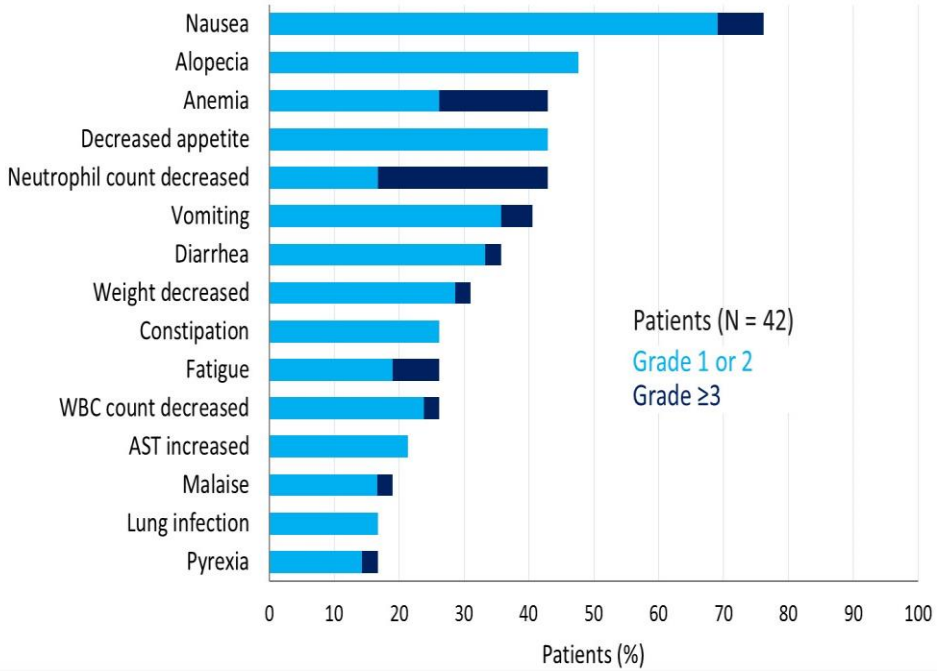
[a] Based on local assessment of archival tissue.

Smit EF, et al. J Clin Oncol 38: 2020 (suppl; abstr 9504)

# 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 |
| Poziotinib[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 |

Smit EF, et al. J Clin Oncol 38: 2020 (suppl; abstr 9504)

# Nové možnosti posílení účinnosti anti-EGFR terapie

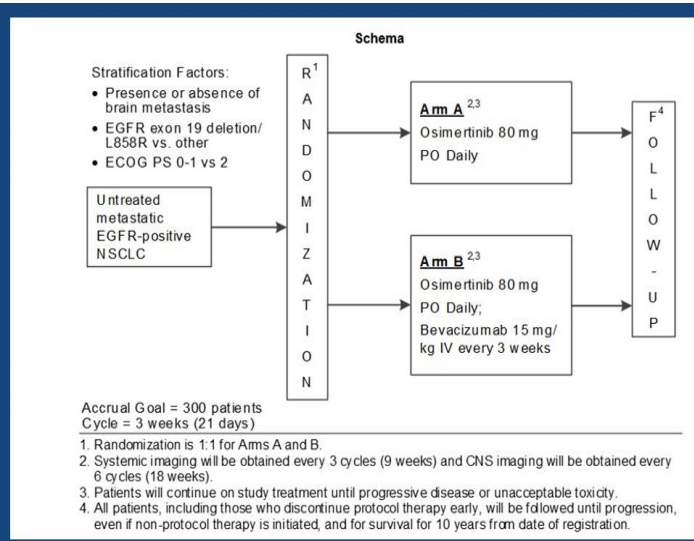
## EGFR TKI + Anti-VEGF

| 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 |

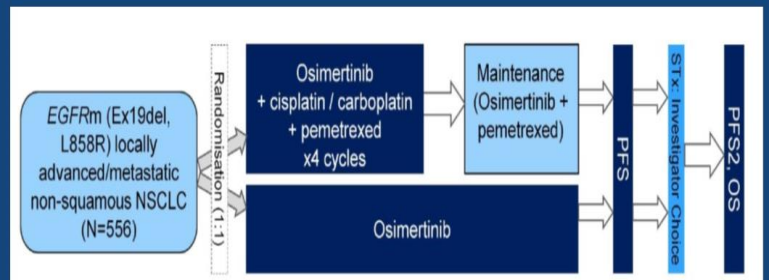
## EGFR TKI +Chemotherapy

| 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

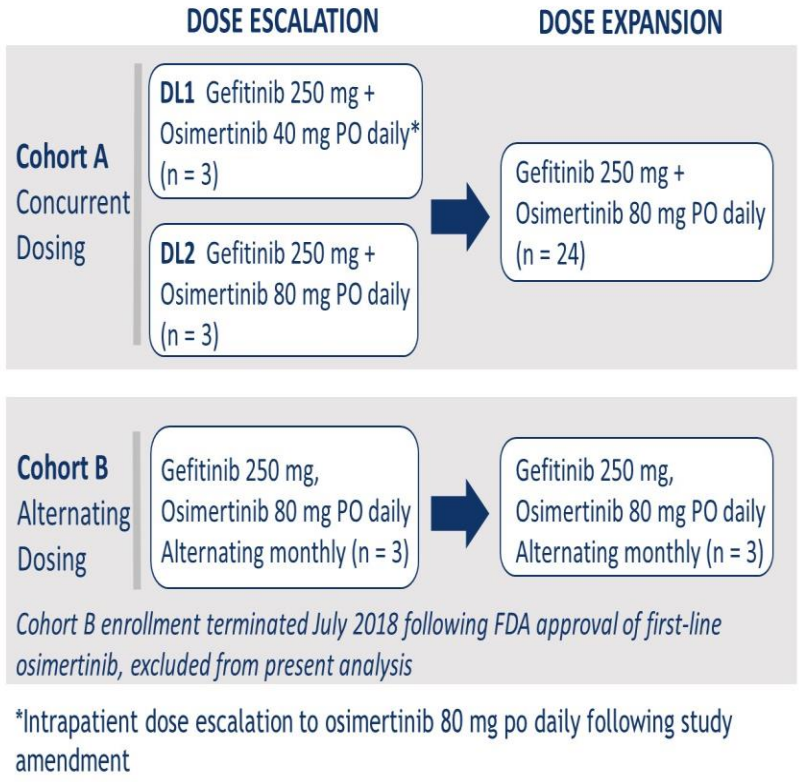



- Osimertinib given at a dose of 80 mg QD during induction and maintenance
- The osimertinib dose can be reduced to 40 mg QD for management of AEs; chemotherapy dose interruption/reduction is to be prioritised over reduction/interruption of osimertinib
- Randomisation will be stratified by race, WHO PS (0 vs 1), and tissue *EGFR* mutation test at enrolment
- Planned to involve approximately 248 sites in 27 countries

# 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




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

**Primary Endpoints**

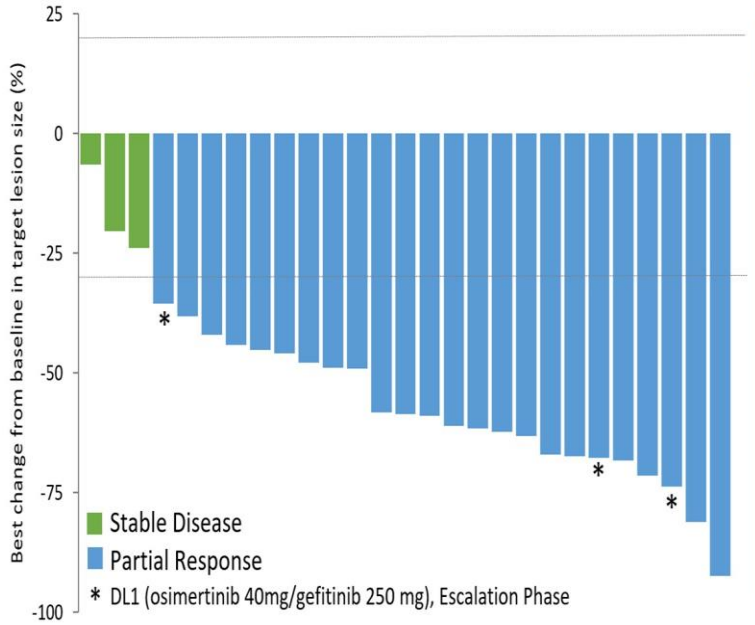
- Dose Escalation: MTD
- Dose Expansion: Feasibility, defined as receipt of combination therapy for ≥ 6 28-day cycles

**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**

Rotow JK, et al. J Clin Oncol 38: 2020 (suppl; abstr 9507)

# 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

Inclusion criteria (N = 133) :

- 18 years or older
- ECOG ≤2
- life expectancy of at least 6 months
- pathological confirmed NSCLC with EGFRm
- All metastatic lesions a maximum of 2 lesions in any 1 organ, and no more than 5 metastases in total
- NO BRAIN METS ALLOWED

1:1

N=68 **SBRT +TKI** 25 Gy - 40 Gy in 5 fractions

N=65 **TKI** gefitinib 250 mg, once a day, erlotinib 150 mg, once a day icotinib 125 mg, three times a day

FOLLOW UP

Statistical Analysis

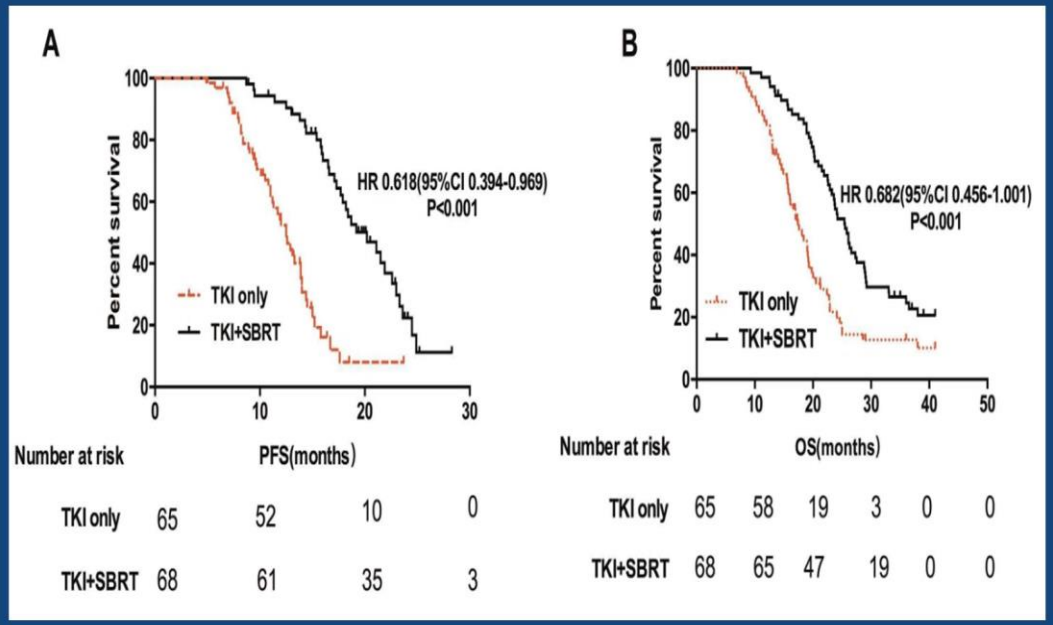
- Descriptive statistics
- Chi-square test
- Kaplan-Meier method and log-rank test
- Multivariate analyses using Cox regression models

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)




| Number at risk | | | | | |
|---|---|---|---|---|---|
| TKI only | 65 | 52 | 10 | 0 | |
| TKI+SBRT | 68 | 61 | 35 | 3 | |

| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| TKI only | 65 | 58 | 19 | 3 | 0 | 0 |
| TKI+SBRT | 68 | 65 | 47 | 19 | 0 | 0 |

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

Wang X, et al. J Clin Oncol 38: 2020 (suppl; abstr 9508)

# Kombinace lokální + systémové léčby u metastazujících NSCLC??

## Questions?

What is the definition of oligometastatic?

What is the optimal timing of LAT?

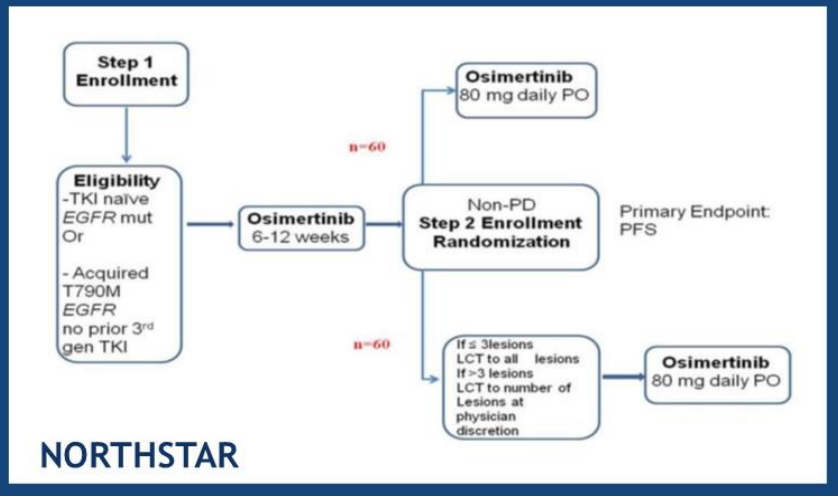
Concurrently? After induction? At the time of oligoprogression?

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<br><br>Restaging studies reveal no evidence of progression and limited (≤ 3 discrete sites) metastatic disease, all of which must be amenable to SBRT +/- Surgery | **S T R A T I F Y** | **Histology:**<br>Squamous vs. Non-squamous<br><br>**Systemic Therapy:**<br>Immunotherapy* vs Cytotoxic Chemotherapy | **R A N D O M I Z E** | **Arm 1**:<br>Maintenance systemic therapy alone**<br><br>**Arm 2:**<br>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.**<br><br>** **As noted in Section 5** |

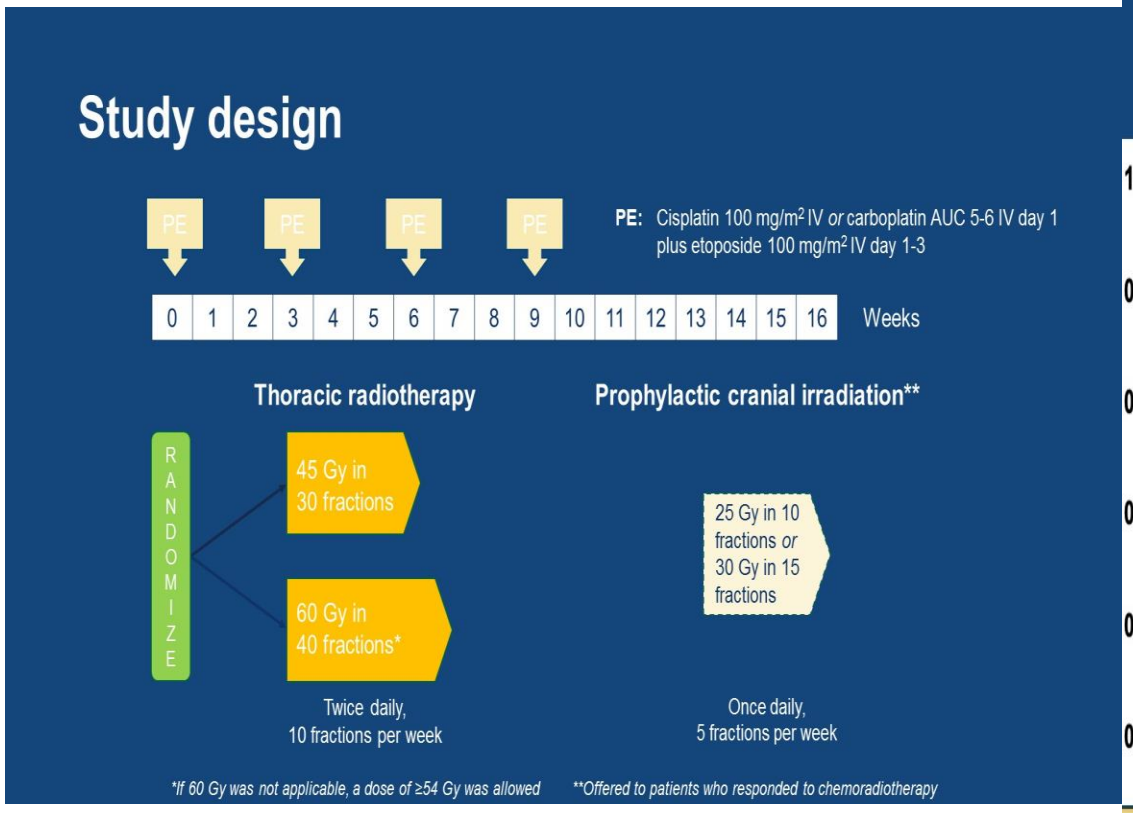
**NRG-LU002**

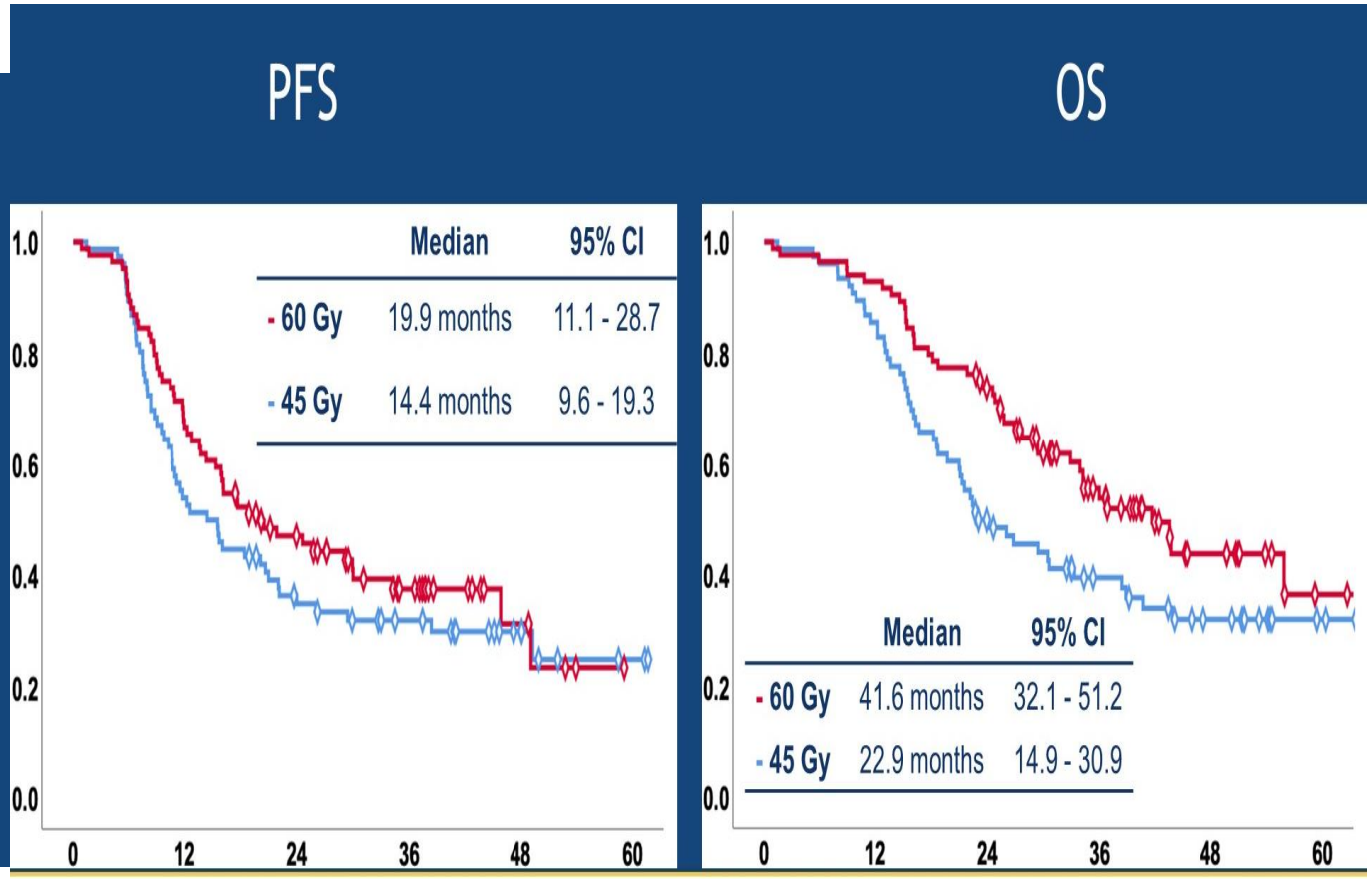



**NORTHSTAR**

# 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)



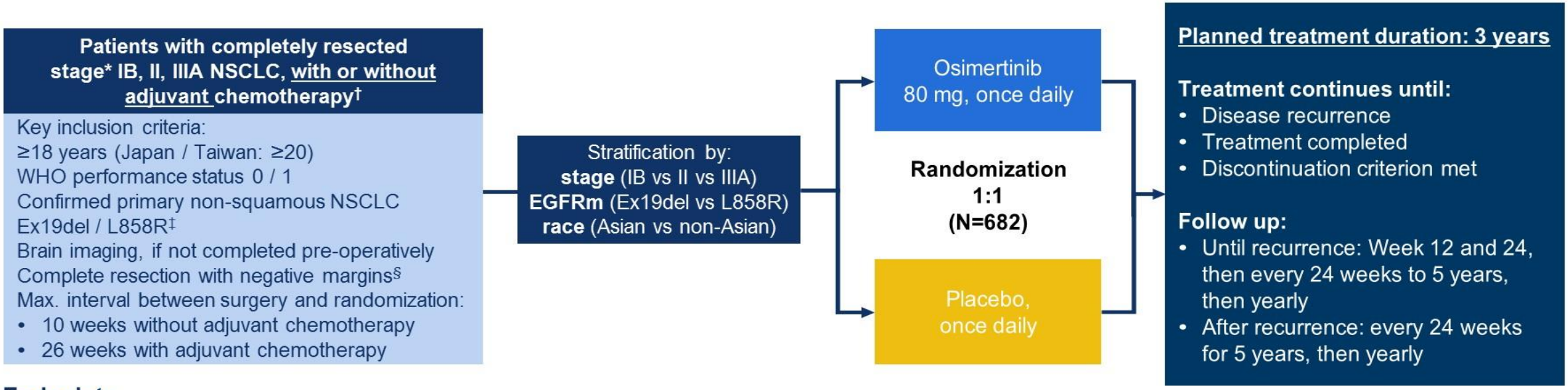




Gronberg BJ, et al. J Clin Oncol 38: 2020 (suppl; abstr 9007)

# 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




**Endpoints**

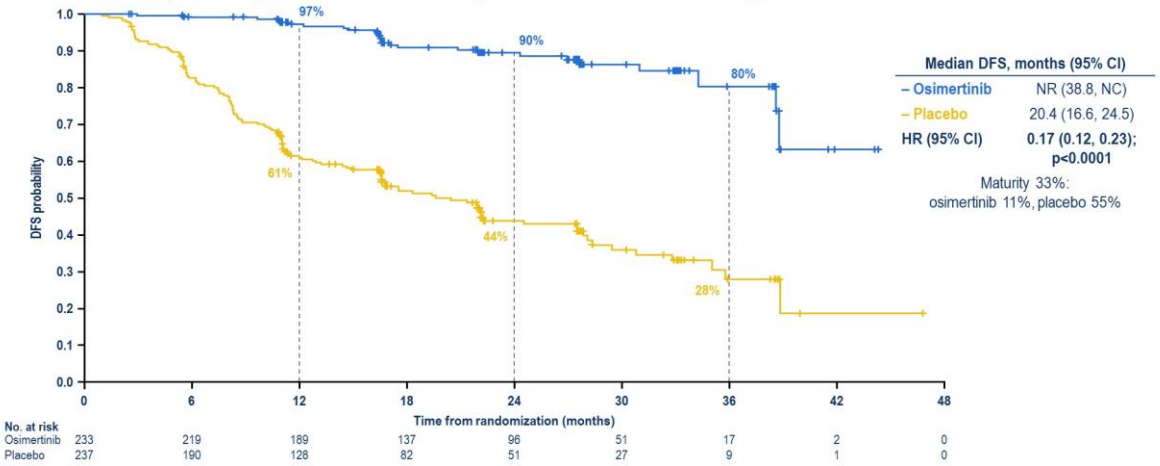
- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

Herbst R, et al. J Clin Oncol 38: 2020 (suppl; abstr LBA5)

# ADAURA – účinnost

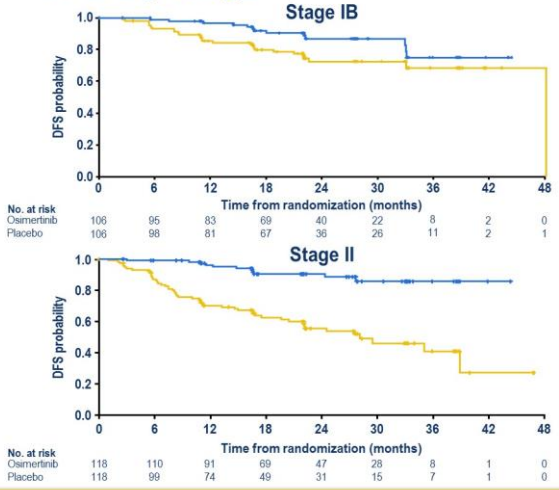
## Primary endpoint: DFS in patients with stage II/IIIA disease




| Median DFS, months (95% CI) | |
|---|---|
| – Osimertinib | NR (38.8, NC) |
| – Placebo | 20.4 (16.6, 24.5) |
| HR (95% CI) | 0.17 (0.12, 0.23); p<0.0001 |

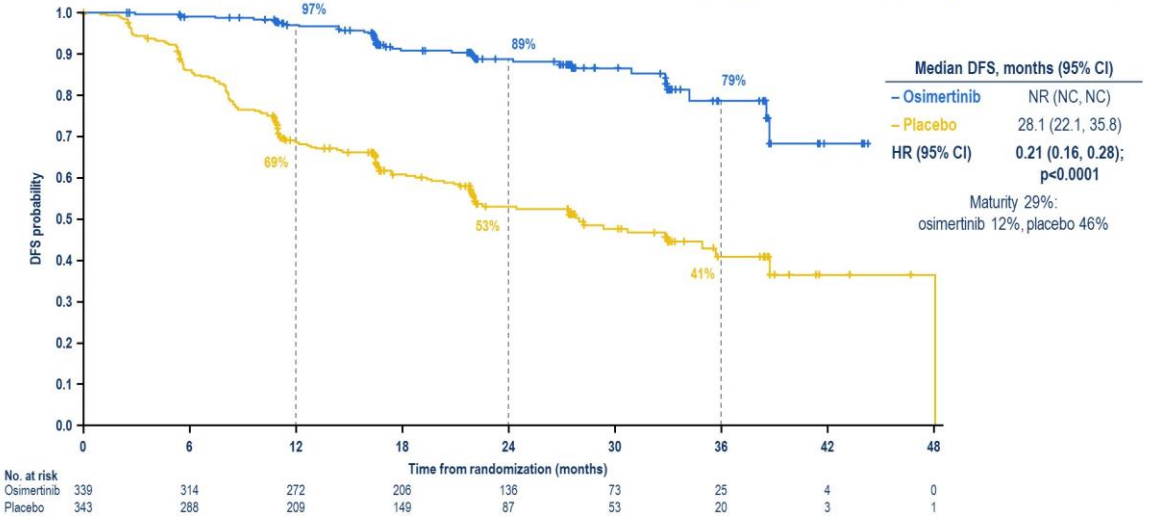
Maturity 33%:
osimertinib 11%, placebo 55%

## DFS by stage




| | Stage IB | Stage II | Stage IIIA |
|---|---|---|---|
| 2 year DFS rate, % (95% CI) | | | |
| – Osimertinib | 87 (77, 93) | 91 (82, 95) | 88 (79, 94) |
| – Placebo | 73 (62, 81) | 56 (45, 65) | 32 (23, 42) |
| Overall HR (95% CI) | 0.50 (0.25, 0.96) | 0.17 (0.08, 0.31) | 0.12 (0.07, 0.20) |

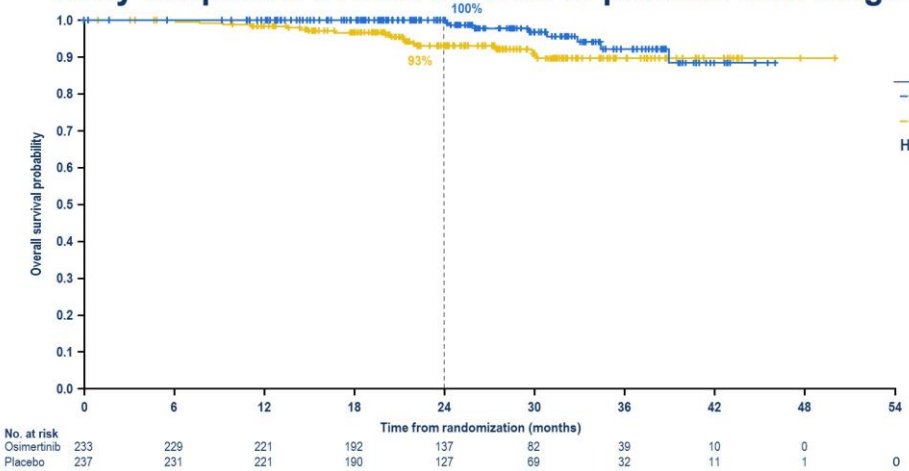
## Secondary endpoint: DFS in the overall population (stage IB/II/IIIA)




| Median DFS, months (95% CI) | |
|---|---|
| – Osimertinib | NR (NC, NC) |
| – Placebo | 28.1 (22.1, 35.8) |
| HR (95% CI) | 0.21 (0.16, 0.28); p<0.0001 |

Maturity 29%:
osimertinib 12%, placebo 46%

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

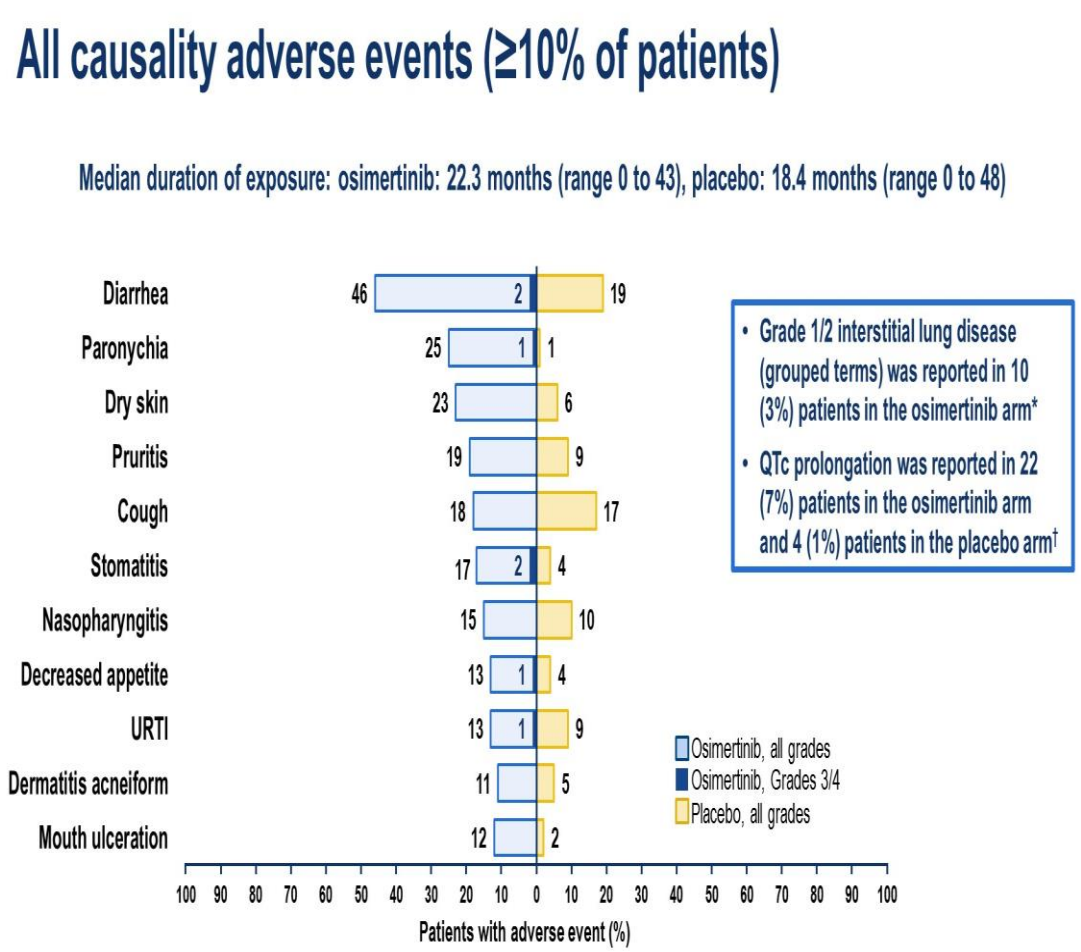



| Median OS, months (95% CI) | |
|---|---|
| – Osimertinib | NR (NC, NC) |
| – Placebo | NR (NC, NC) |
| HR (95% CI) | 0.40 (0.18, 0.90) |

Maturity 5%:
osimertinib 3%, placebo 7%

Herbst R, et al. J Clin Oncol 38: 2020 (suppl; abstr LBA5)

# ADAURA – toxicita a závěry



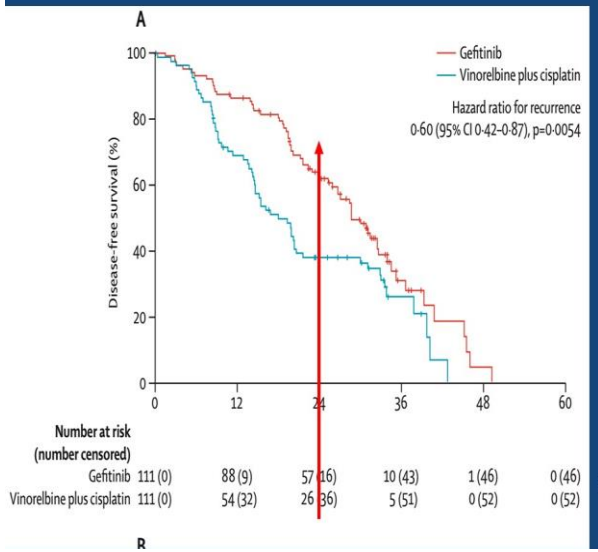

- První cílená léčba prokazující v adjuvantním podání statisticky i klinicky významné prodloužení PFS v léčbě stadia IB/II/IIIA u EGFR-mutovaného NSCLC
- 79% snížení rizika recidivy nebo úmrtí (DFS HR 0,21 [95% CI: 0,16–0,28]; p < 0,0001)
- Zlepšení DFS bez ohledu na podání adjuvantní chmt ANO/NE
- Konzistentně příznivý bezpečnostní profil

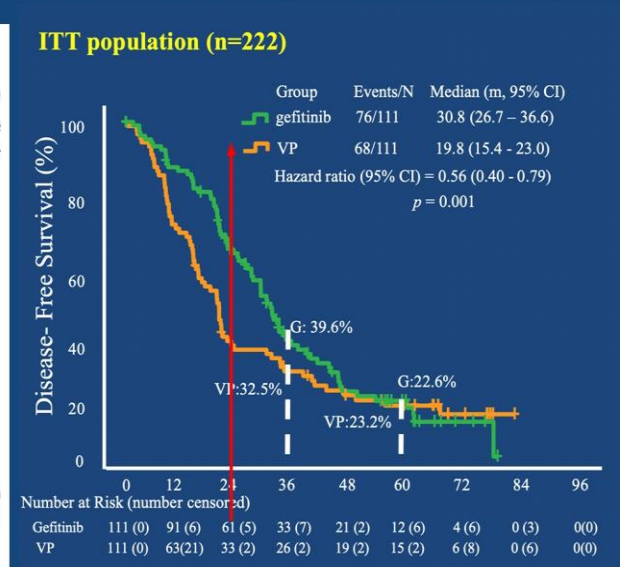
Herbst R, et al. J Clin Oncol 38: 2020 (suppl; abstr LBA5)

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

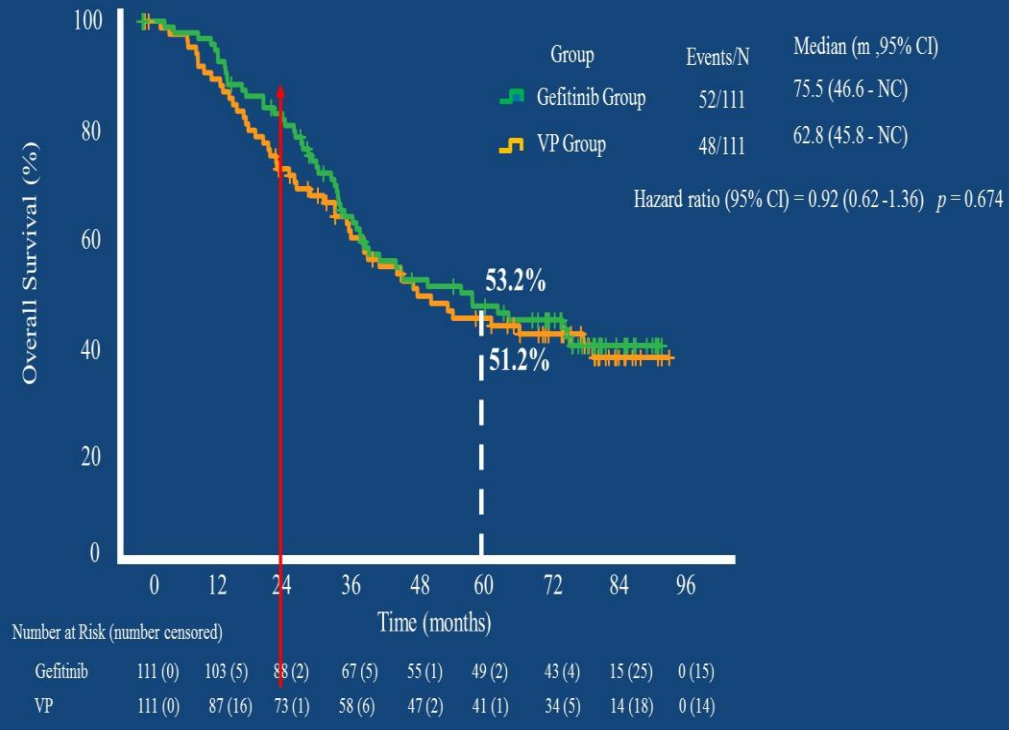
## DFS, then and now

Zhong, Lancet Oncology 2017




## Overall survival (ITT population)




Wu YL, et al. J Clin Oncol 38: 2020 (suppl; abstr 9005)

# 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

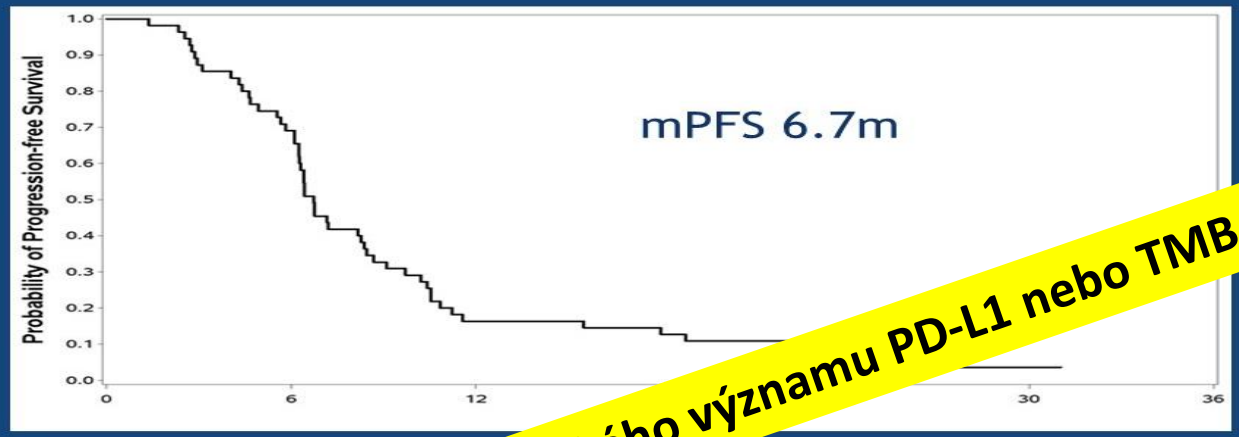
- Unresectable MPM
- No prior therapy
- ECOG 0-1
- Baseline tumor specimen

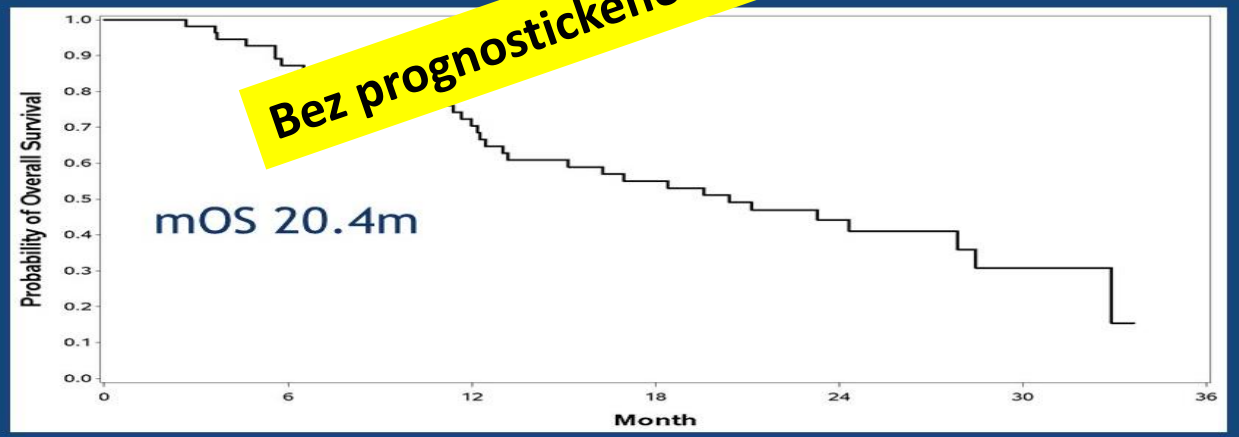
→ Durvalumab 1120 mg + Pemetrexed 500 mg/m² + Cisplatin* 75 mg/m² every 3 weeks x 6 cycles → SD or PR → Durvalumab 1120 mg every 3 weeks until PD**

- 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 PD-L1 nebo TMB**

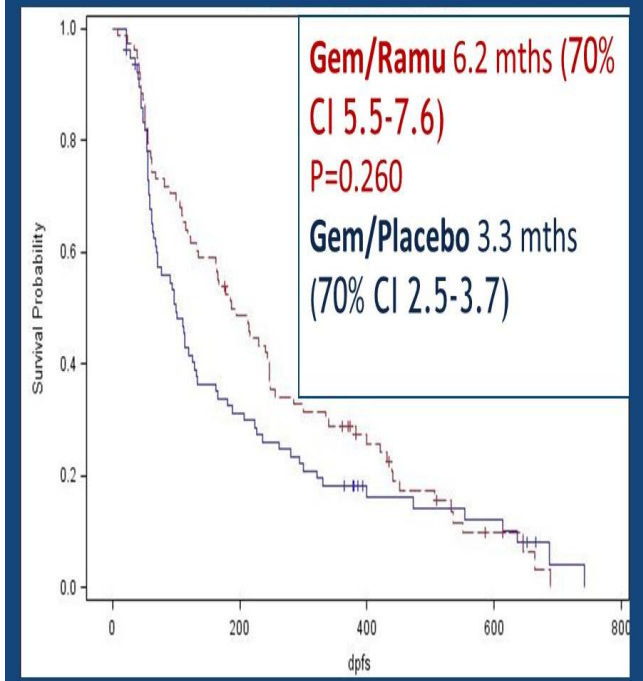
Forde PM, et al. J Clin Oncol 38: 2020 (suppl; abstr 9003)

# 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

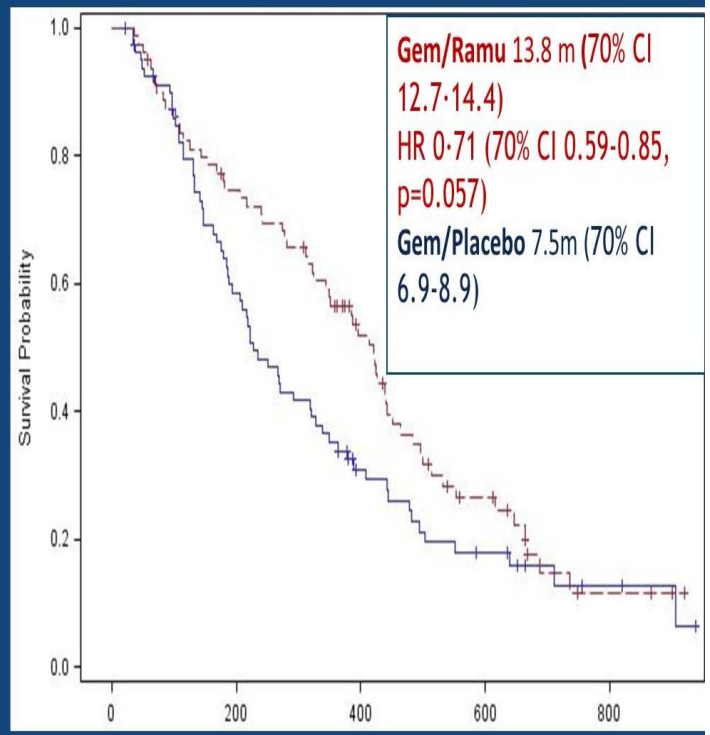
## What do we expect in 2L Mesothelioma?

| Drug | PFS | OS | Trial |
|---|---|---|---|
| Durva/Tremi | 5.7 | 16.6 | Calabrò, Lancet Resp. 2018 |
| Pembro vs.<br>Gem or Vin | 2.5<br>3.4 | 10.7<br>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




Pagano M, et al. J Clin Oncol 38: 2020 (suppl; abstr 9004)

Děkuji za pozornost!