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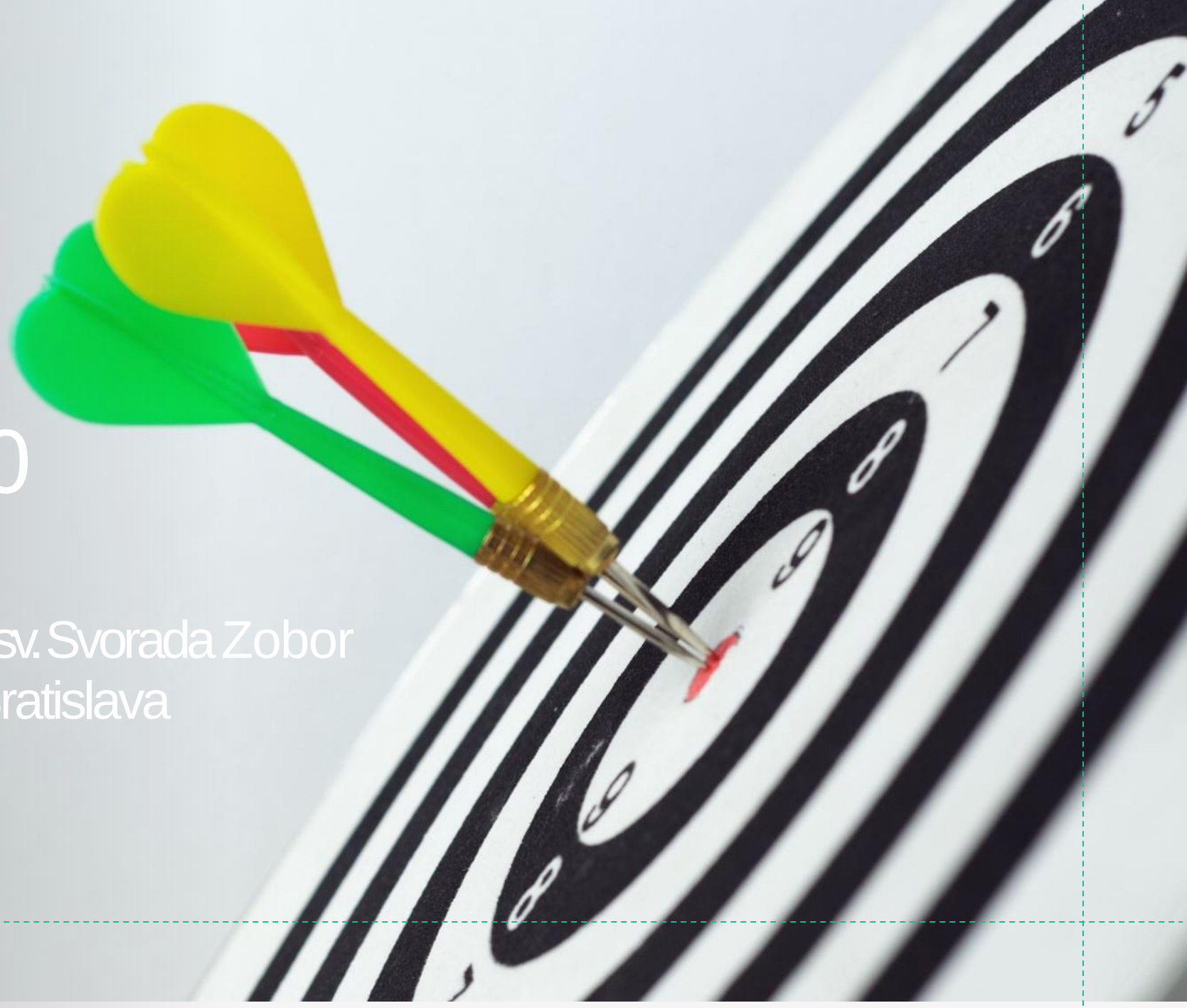
Nitra



Vyhlásenie o konflikte záujmov autora

□ Nemám potenciálny konflikt záujmov

x Deklarujem nasledujúci konflikt záujmov

Forma finančného prepojenia	Spoločnosť
Participácia na klinických štúdiách/firemnom grante	Roche
Nepeňažné plnenie (v zmysle zákona)	Angelini, Boehringer Ingelheim, MSD, Pfizer, Roche
Prednášajúci	Astra-Zeneca, Boehringer Ingelheim, MSD, Pfizer, Roche
Akcionár	
Konzultant/odborný poradca	MSD
Ostatné príjmy (špecifikovať)	

Podľa UEMS (upravené v zmysle slovenskej legislatívy)

Prezentáciu podporila agentúra

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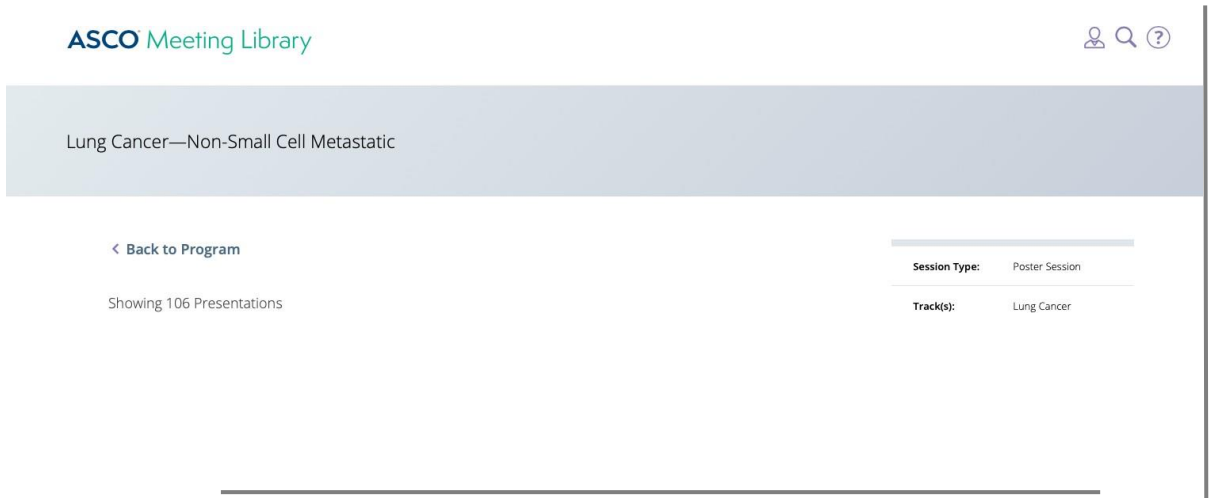
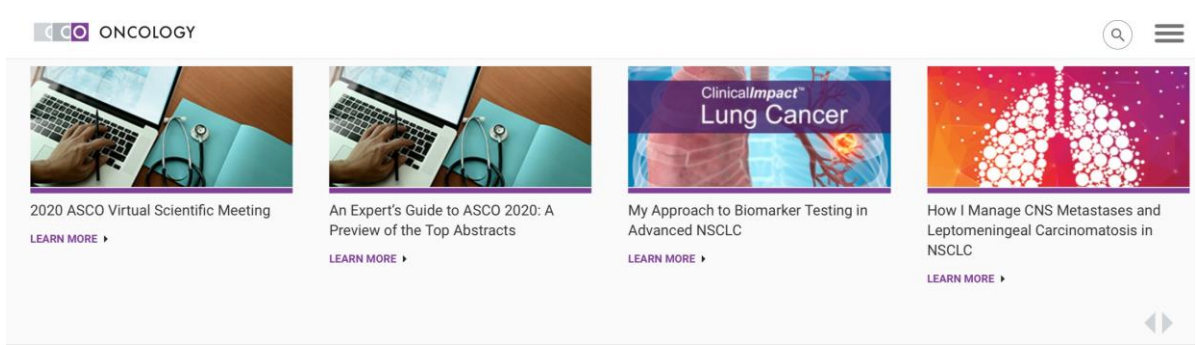
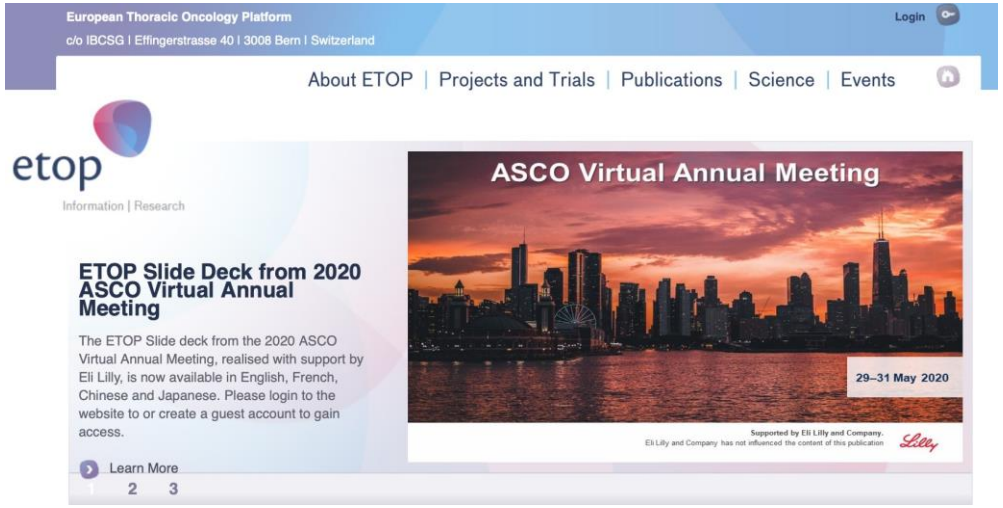






Čo ma najviac zaujalo

1. Cielená liečba - klinicky (veľmi) významné pokroky pri NSCLC
2. Duálna imunoterapia NSCLC (blokáda PD-1, PD-L1 + CTLA-4)

Registrované skupiny cielených liekov

- **EMA**
- EGFR-TKI
- ALK-TKI
- ROS1-TKI
- BRAF-TKI
- NTRK-TKI

- **FDA**
- EGFR-TKI
- ALK-TKI
- ROS1-TKI
- BRAF-TKI
- NTRK-TKI
- MET-TKI
- RET-TKI

EGFR-TKI v adjuvantnej liečbe

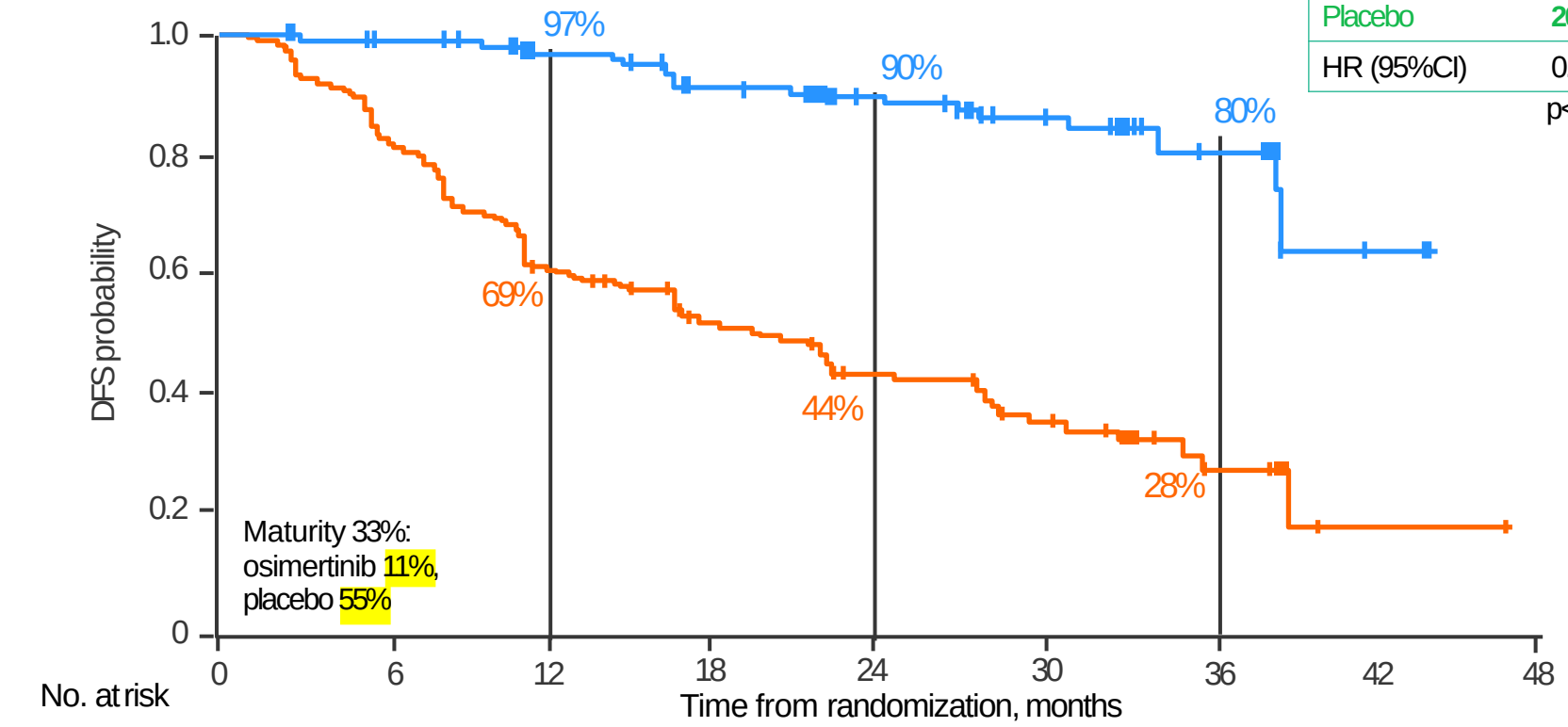
Štúdia (cit.)	NSCLC	Rameno	N	DFS medián, mes. (95%CI)	HR (95%CI)	OS medián, mes. (95%CI)	HR (95%CI)
ADAURA (1)	II -IIIA*, Ex19del, L858R ± adjuvantná cht	Osimertinib	233	**NR** (**38,8** - NC)	**0,17** (0,12 - 0,23) p<0,0001	NR	0,40** (0,18 - 0,90)
		Placebo	237	20,4 (**16,6** - 24,5)		NR	
	IB - II- IIIA Ex19del, L858R ± adjuvantná cht	Osimertinib	339	**NR** (NC - NC)	**0,21** 0,16 - 0,28 p<0,0001	NR	NR
		Placebo	343	28,1 (22,1 - 35,8)		NR	
CTONG 1104 (2)	II-IIIA, Ex19del, L858R	Gefitinib	111	**30,8** (26,7 - 36,6)	**0,56** (0,40 - 0,79) p = 0,001	75,5 (44,6 - NC)	**0,92** (0,62 - 1,36) p = 0,674
		Chemo VP	111	19,8 (15,4 – 23,0		62,8 (45,8 - NC)	

*Primárny cieľ štúdie: DFS pri št. II - IIIA, **Nezrelé údaje, mortalita 5%

1. Herbst RS, et al. J Clin Oncol 2020; 38(suppl): Abstr LBA5.
2. WU YL, et al. J Clin Oncol 2020; 38(suppl): Abstr 9005.

ADAURA - DFS u pacientov so štádiom II/IIIA

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



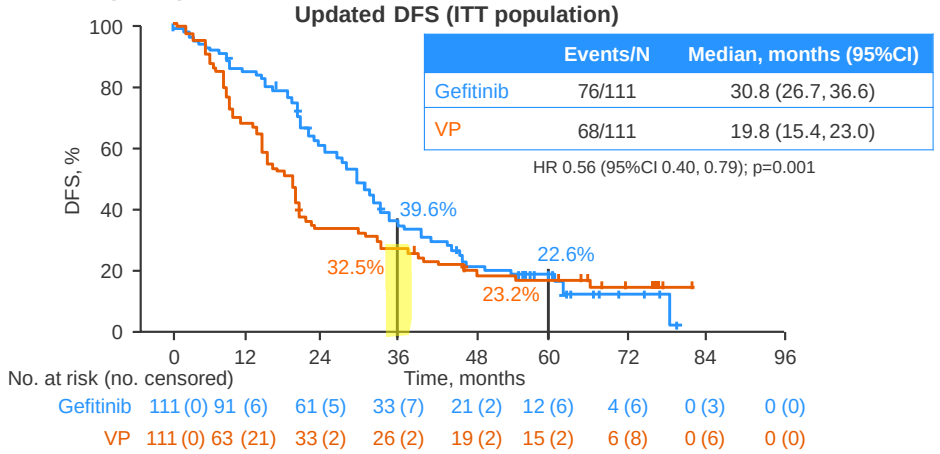
No. at risk									
Osimertinib	233	219	189	137	96	51	17	2	0
Placebo	237	190	128	82	51	27	9	1	0

Herbst RS, et al. J Clin Oncol 2020;38(suppl):Abstr LBA5.
Obrázok ETOP Slide Deck from ASCO© 2020. http://www.etop-eu.org/index.php?option=com_content&view=article&id=115649:etop-slide-deck-from-2020-asco-annual-meeting-7&catid=13:news&Itemid=557

DFS v CTONG -1104 av ADAURA

9005: CTONG1104: Adjuvant gefitinib versus chemotherapy for resected N1-N2 NSCLC with EGFR mutation—Final overall survival analysis of the randomized phase III trial 1 analysis of the randomized phase III trial – Wu Y-L, et al

- **Key results (cont.)**



	Events/N	Median, months (95%CI)
Gefitinib	76/111	30.8 (26.7, 36.6)
VP	68/111	19.8 (15.4, 23.0)

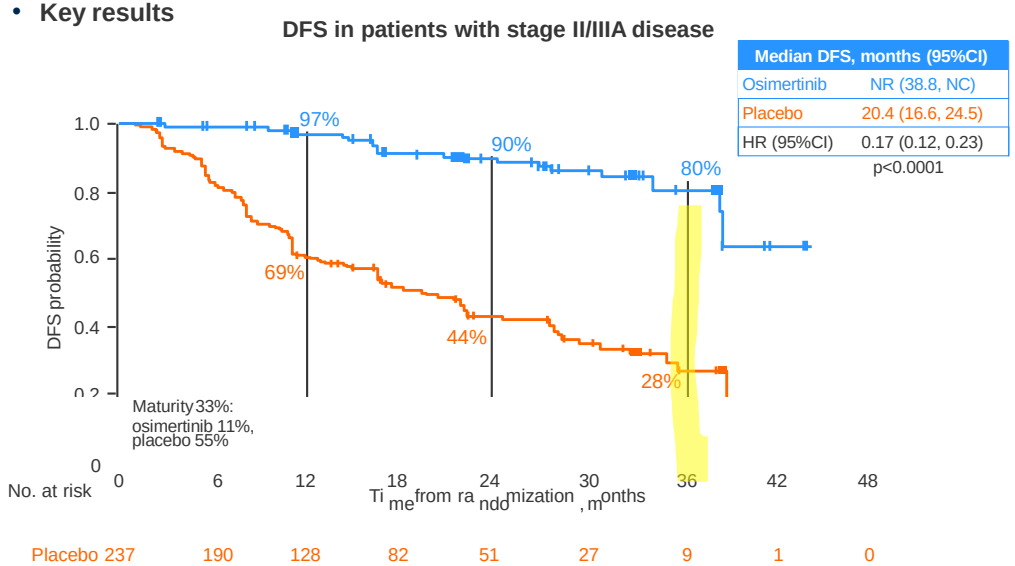
HR 0.56 (95%CI 0.40, 0.79); p=0.001

- **Conclusio**
  - In**n** gefitinib did not translate to a significant OS difference

Wu Y-L, et al. J Clin Oncol 2020;38(suppl):Abstr 9005

LBA5: Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA – Herbst RS, et al

- **Key results**



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

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

Obrázky : ETOP Slide Deck from ASCO© 2020. http://www.etop-eu.org/index.php?option=com_content&view=article&id=115649:etop-slide-deck-from-2020-asco-annual-meeting-7&catid=13:news&Itemid=557

„What would I do if it were me or one of my family members?"

Despite "the questions that remain regarding survival and limited follow-up,
I would choose osimertinib."

David Spigel, MD, FASCO
Director, Lung Cancer Research Program, Sarah Cannon Research Institute

Nyberg K. ASCO© Daily News, May 31, 2020

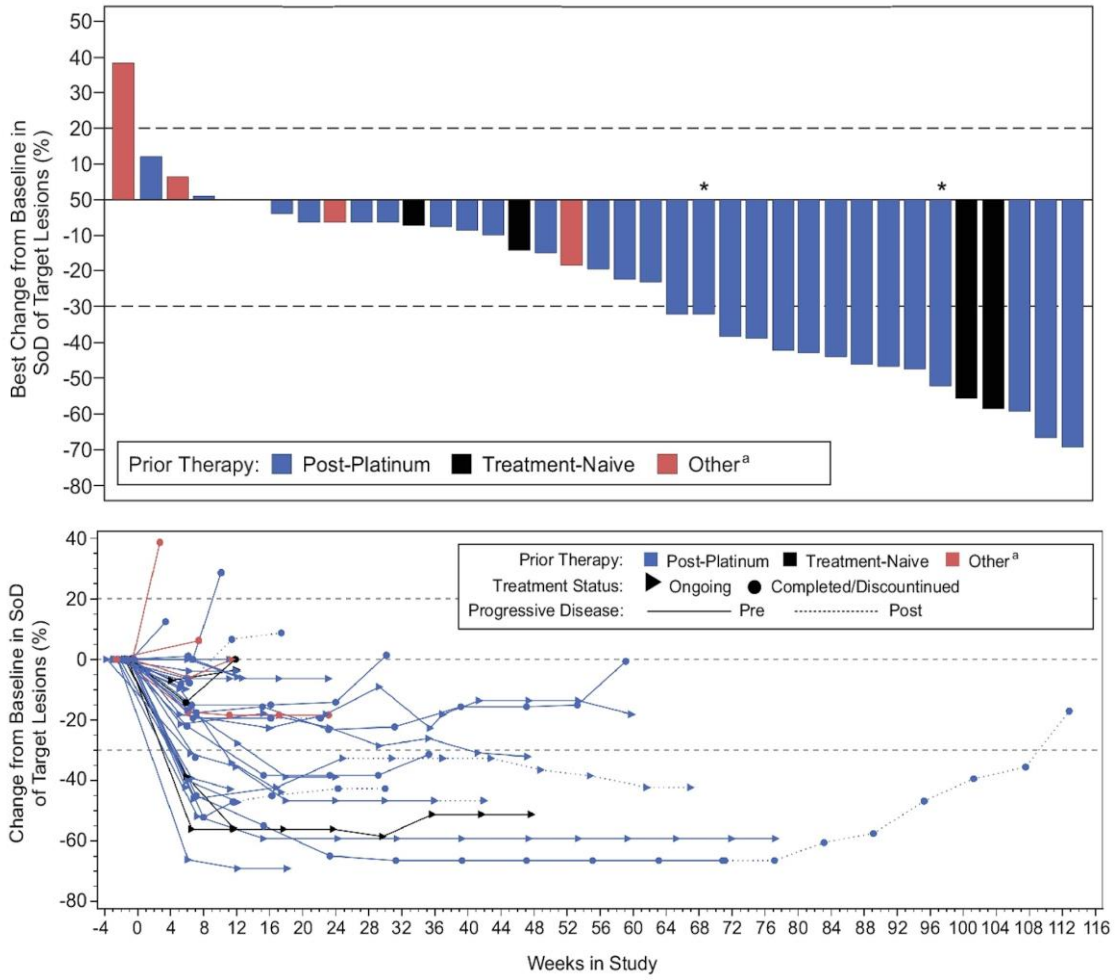
EGFRM+ NSCLC - inzercie v exóne 20

Štúdia, fáza (cit.)	Liek	Línia liečby	N	ORR % (95%CI)	DCR (%) (95%CI)	PFS medián, mes. (95%CI)
ECOG-AGRIN 5162, II, (1)	Osimertinib ↑D: 160 mg	**1.**	20	**25** (NR)	**85** (NR)	**9,7** (4,1 - NA)
ZENITH20-1, II (2)	Poziotinib -ITT	**3.** (medián) 2. - 9.	115	**14,8** (8,9 - 22,6)	**68,7** (59,4 - 77,0)	**4,2** (NR)
	-Evaluable		88	19,3 (11,7 - 29,1)	80,7 (70,9 - 88,3)	4,1 (3,7 - 5,5)
CHRYZALIS, I (3)	Amivantanab	**2.** (medián) 1. - 8.	39	**36** (21 - 53)	67%*	8,3 (3,0 - 14,8)

*Benefit z liečby - aspoň 12 týždňov trvajúca odpoveď alebo stabilizované ochorenie

1. Piotrovska Z, et al. JClin Oncol 2020; 38(suppl):Abstr 9513.
2. Le X, et al. JClin Oncol 2020; 38(suppl):Abstr 9514.
3. Park K, et al. JClin Oncol 2020; 38(suppl):Abstr 9512.

Odpoveď na amivantanab v štúdii CHRYZALIS



Overall Response Rate:
Total 36% (95%CI: 21-53)
Post-platinum 41% (95%CI: 24 - 61)

Clinical benefit:
Total 67% (95%CI: 50-81)
Post-platinum 72% (95%CI: 53 - 87)

Median duration of response:
Total: 10 months (range: 1- 16)
Post-platinum: 7 months (1 -16)

Obrázky : Halmos B. 2020 ASCO© Update on EGFR+ NSCLC . https://www.vumedi.com/video/2020-asco-update-on-egfr-nsclc-new-data-on-the-efficacy-toxicity-and-dosing-of-osimertinib-poziotini/

MET-inhibítory

Štúdia (cit.)	Liečba	MET	N	Línia liečby	ORR, % (95%CI)	DCR ,% (95%CI)	PFS medián, mes. (95%CI)
GEOMETRY mono-1 K 6 (1)	Capmatinib	*MET ex14-mut*	31	2.	48,4 (30,2 - 66,9)	90,3 (74,2 - 98,0)	8,11 (4,17 - 9,86)
GEOMETRY mono-1 K 1a (2)	Capmatinib	↑*MET* amplifikácia*	69	2.-3.	29 (18,7 - 41,2)	71 (58,8 - 81,3)	4,07 (2,86 - 4,83)
K 5a (2)			15	1.	40 (16,3 - 67,7)	66,7 (38,4 - 88,2)	4,17 (1,45 - 6,87)
NCT 02897479	Savolitinib	*MET ex14-mut*	70	1. - 2.	42,9 (31,1 - 55,3)	82,9 (71,2 - 90,8)	6,9
VISION Liquid biopsy	Tepotinib	*MET ex14-mut*	66	1. - ≥2	44 (32 - 57)	64 (51 - 75)	8,5 (5,1 - 11,0)
Tissue biopsy			60	1. - ≥2	47 (34 - 60)	70 (57 - 81)	11,0 (7,8 - 17,1)

*GCN (gene copy number) ≥ 10

1. Groen HJM, et al. JClin Oncol 2020; 38(suppl):Abstr 9520.
2. Wolf J,et al. JClin Oncol 2020; 38(suppl):Abstr 9509.
3. Lu S,et al. JClin Oncol 2020; 38(suppl):Abstr 9519.

RET-TKI pri pokročilom RET+ NSCLC

Štúdia (cit.)	Liek	Línia liečby	N	ORR % (95%CI)	DOR, medián (mes.) (95%CI)	PFS, medián, mes. (95%CI)
Libretto-001	Selpercatinib	2.*	105	**64** (54 - 73)	**18** (12 - NE)	**17** (14 - NE)
		1.	39	**85** (70 - 94)	NE (12 - NE)	NE (14 - NE)
ARROW	Pralsetinib	2.*	80	**61** (50 - 72)	NE (11,3 - NE)	-
		1.	26	**73** (52 - 88)		-

+ Preukázaná aktivita pri MTS do CNS.
+ V ARROW aj kompletné odpovede : 5% po chemo splatinou, 12% v 1. línii.

*2. línia po chemo v kombinácii scisplatinou

1. Subbiah V, et al. J Clin Oncol 2020; 38(suppl):Abstr 9516.
2. Gainor JF, et al. J Clin Oncol 2020; 38(suppl):Abstr 9016.

Registrované možnosti IT pri pokročilom NSCLC

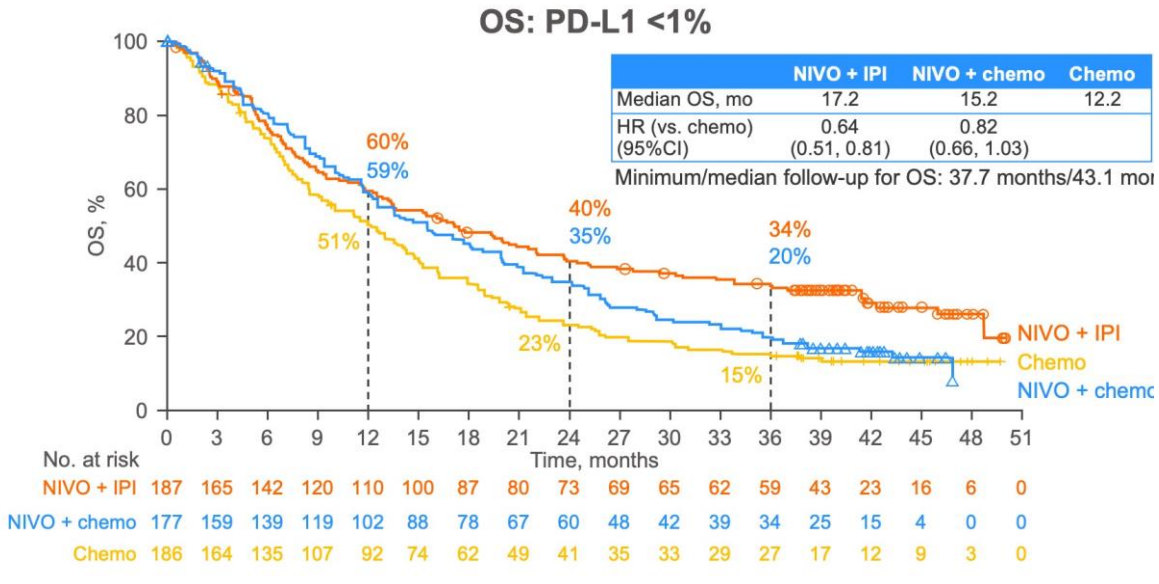
- **EMA**
  - 2.línia: anti PD1, anti PD-L1 monoterapia
  - 1. línia: anti PD1 monoterapia
  - 1. línia: anti PD-1, anti PDL1 a chemoterapia
- **FDA**
  - 2.línia: anti PD1, anti PD-L1 monoterapia
  - 1. línia: anti PD1 monoterapia
  - 1. línia: anti PD-1, anti PDL1 a chemoterapia
  - 1. línia: anti PD-1+ anti CTLA-4
  - 1. línia: chemo + anti PD-1+ anti CTLA-4

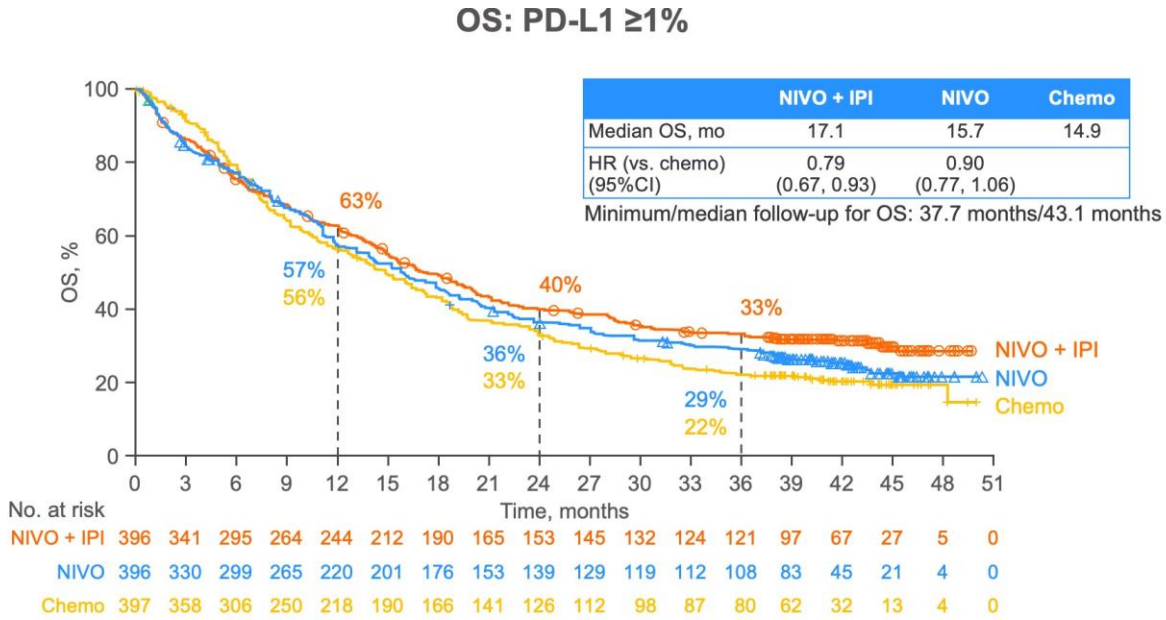
Nivolumab + ipilimumab pri pokročilom NSCLC

CheckMate 227	Rameno	N	ORR %	Medián DOR, mes. (95%CI)	Medián PFS, mes.	Medián OS, mes.	HR (95%CI) Nivo + Ipi vs chemo
PD-L1 ≥ 1%	**Nivo + IPI**	**396**	**36,4**	**23,2 (15,2 - 32,2)**	**5,1**	**17,1**	**0,79** (0,67 - 0,93)
	Chemo	**397**	**30,2**	**6,7 (5,6 - 7,6)**	**5,6**	**14,9**	
	Nivo	396	27,5	15,5 (12,7 - 23,5)	4,2	15,7	
PD-L1< 1%	**Nivo + IPI**	187	27,3	18,0 (12,4 - 33,2)	5,1	17,2	**0,64** (0,51 - 0,81)
	Chemo	186	23,1	4,8 (3,7 - 5,8)	4,7	12,2	
	Nivo + chemo	177	37,9	8,3 (5,9 - 9,4)	5,6	15,2	

Ramalingam SS,et al. JClin Oncol 2020; 38(suppl):Abstr 9500

OS v CheckMate 227





Obrázky : ETOP Slide Deck from ASCO© 2020.
http://www.etop-eu.org/index.php?option=com_content&view=article&id=115649:etop-slide-deck-from-2020-asco-annual-meeting-7&catid=13:news&Itemid=557

CheckMate 227 a EMA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/CHMP/193977/2020
Committee for Medicinal Products for Human Use (CHMP)

Withdrawal assessment report

OPDIVO	nivolumab
Yervoy	ipilimumab

Procedure No. EMEA/H/C/xxxx/WS/1372

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 February 2020
EMA/92336/2020
EMEA/H/C/WS/1372

Withdrawal of application to change the marketing authorisation for Opdivo (nivolumab) and Yervoy (ipilimumab)

Bristol-Myers Squibb Pharma EEIG withdrew its application for the use of Opdivo and Yervoy in the treatment of metastatic non-small cell lung cancer that has not been treated previously.

The company withdrew the application on 30 January 2020.

What are Opdivo and Yervoy and what are they used for?

Opdivo and Yervoy are cancer medicines. They contain the active substances nivolumab and ipilimumab, respectively.

Opdivo has been authorised in the EU since June 2015. It is already used on its own to treat non-small cell lung cancer in patients who have previously been treated with other cancer medicines. It is also used to treat the following other cancers: melanoma (a skin cancer), renal cell carcinoma (a kidney cancer), Hodgkin's lymphoma (a blood cancer), squamous cell cancer of the head and neck, and urothelial (bladder) cancer.

Yervoy has been authorised in the EU since July 2011. It is used to treat melanoma and renal cell carcinoma.

Further information on current uses of Opdivo and Yervoy can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/opdivo and ema.europa.eu/medicines/human/EPAR/yervoy.

What change had the company applied for?

The company applied for an extension of indication to add the use of Opdivo and Yervoy together in patients with previously untreated non-small cell lung cancer that has spread to other parts of the body (metastatic) and where the cancer does not have mutations (changes) in genes called EGFR and ALK.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

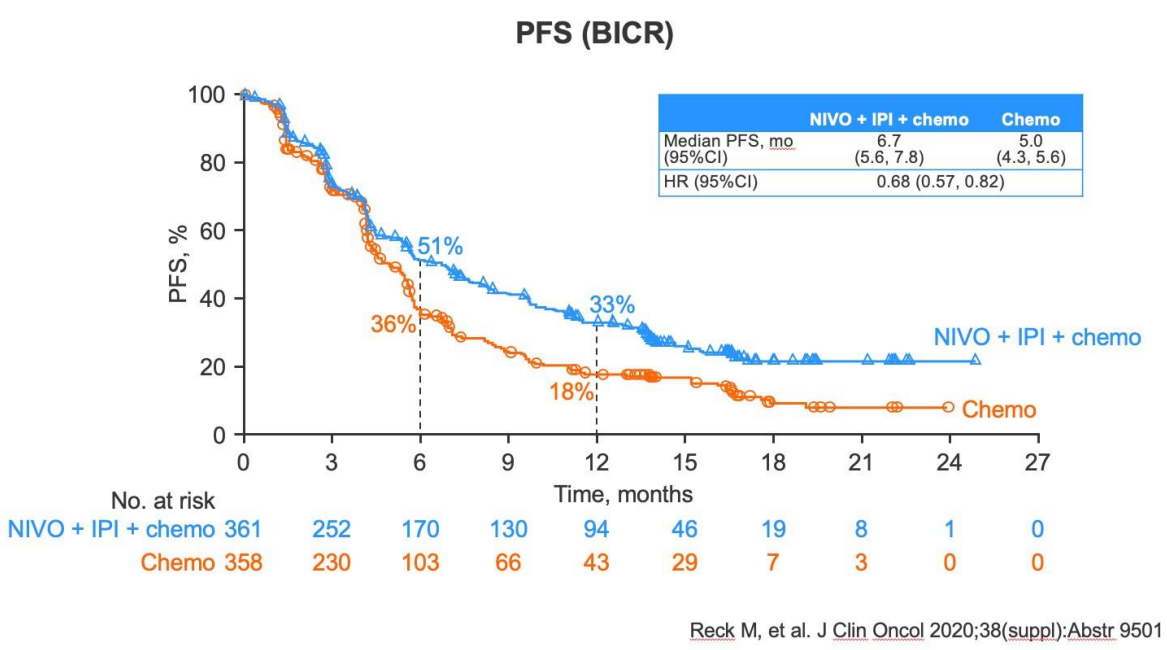
European Medicines Agency. Withdrawal assessmentreport Opdivo (nivolumab) Yervoy (ipilimumab). EMA/CHMP/193977/2020. https://www.ema.europa.eu/en/documents/withdrawal-report/withdrawal-assessment-report-opdivo-yervoy-ws/1372_en.pdf

CheckMate 9LA chemo, nivo, ipi vs chemo pri pokročilom NSCLC

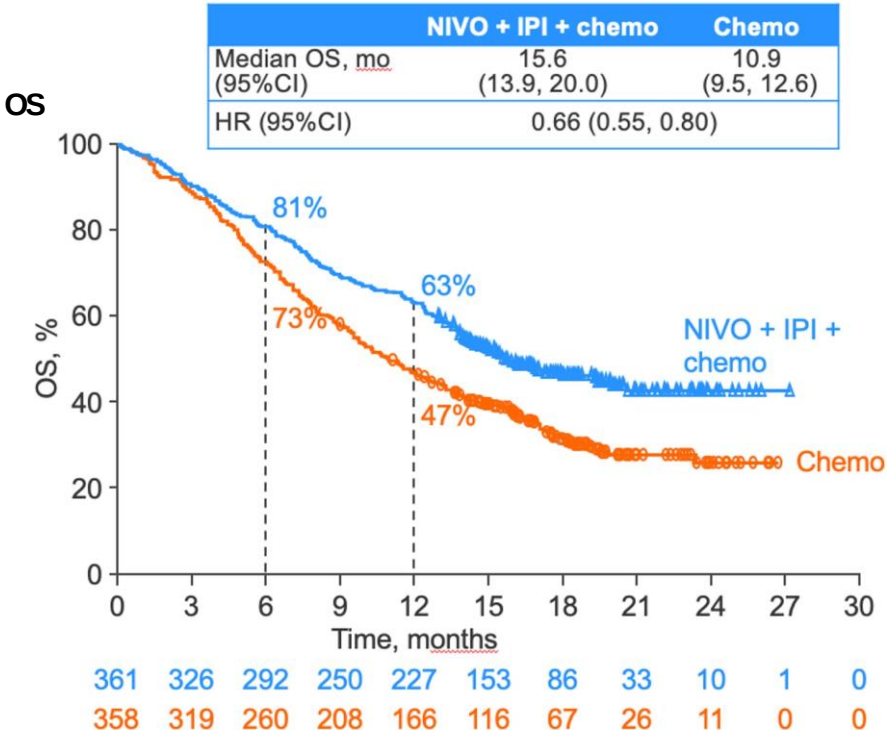
Štúdia	Rameno	N	ORR %	Medián PFS, mes. (95%CI)	HR (95%CI) Chemo + Nivo + Ipi vs chemo	Medián OS, mes.	HR (95%CI) Chemo + Nivo + Ipi vs chemo
CheckMate 9LA	Chemo 2 c. +Nivo + IPI	361	38	6,7 (5,6 - 7,8)	0,68 (0,57 - 0,82)	15,6 (13,9 - 20)	0,66 (0,55 - 0,80)
	Chemo 4 cykly	358	25	5,0 (4,3 - 5,6)		10,9 (9,5 - 12,6)	

Ramalingam SS,et al. JClin Oncol 2020; 38(suppl):Abstr 9500

CheckMate 9LA



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



Zhrnutie

- ASCO 2020 prinieslo snáď až neočakávne veľa výsledkov meniacich klinickú prax pri pokročilom NSCLC
- Osimertinib v adjuvantnjej liečbe bude novým štandardom pri resekovanom EGFRM+ NSCLC
- Prichádzajú nové MET a RET inhibítory (a ďalšie cielené lieky)
- Duálna IT nivolumab + ipilimumab s iniciálnou krátkou chemoterapiou je ďalšou liečebnou možnosťou pokročilého NSCLC