Nádory hlavy a krku
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Vyhlásenie o konflikte záujmov autora

□ Nemám potenciálny konflikt záujmov

x Deklarujem nasledujúci konflikt záujmov

Forma finančného prepojenia	Spoločnosť
Participácia na klinických štúdiách/firemnom grante	Amgen
Nepeňažné plnenie (v zmysle zákona)	
Prednášajúci	MERCK
Akcionár	
Konzultant/odborný poradca	MERCK, Pierre Fabre
Ostatné príjmy (špecifikovať)	

Podľa UEMS (upravené v zmysle slovenskej legislatívy)

Prezentáciu podporila agentúra

We Make Media Slovakia s.r.o.

Abstrakt #6502: Dávky a schémy podávania cisplatiny v konkomitantnom režime s rádioterapiou v pooperačnej indikácii u high-risk pacientov

Abstrakty #6505 a #6507: Optimálna sekvencia systémovej liečby a imunoterapie (ICI) v R/M SCCHN

Abstrakty #6511 a #6504: Pokroky v liečbe zameranej na biomarkery

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Cisplatina s rádioterapiou: dávka alebo schéma?

Príklad: 55-ročný pacient s karcinómom jazyka T4N3b (ECE+) začína pooperačnú konkomitantnú liečbu RAT + CHT (cisplatina).

Aký je náš cieľ v pooperačnej intencii na základe súčasných poznatkov?

- Cisplatina á 3 týždne, nezávisle od kumulatívnej dávky
- Cisplatina v týždňovom podávaní nezávisle od kumulatívnej dávky
- Kumulatívna dávka cisplatiny > 200 mg/m2 nezávisle od schémy
- Cisplatina v kumulatívnej dávke 300 mg/m2 nezávisle od schémy podávania

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Cisplatina s rádioterapiou: dávka alebo schéma?

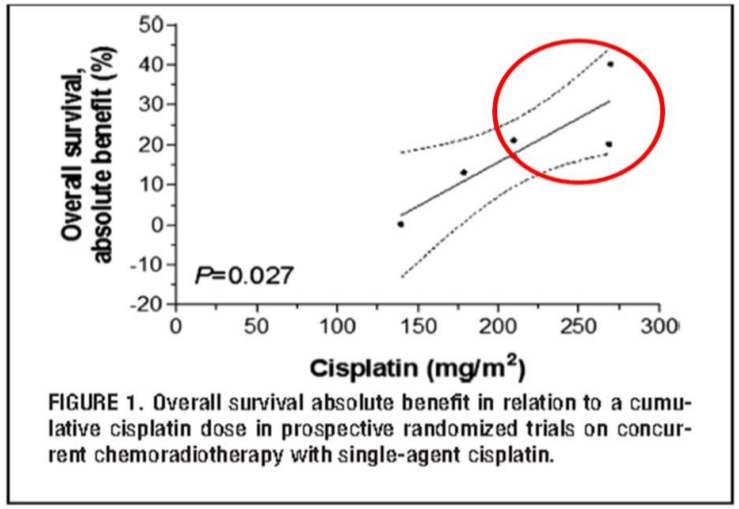


FIGURE 1. Overall survival absolute benefit in relation to a cumulative cisplatin dose in prospective randomized trials on concurrent chemoradiotherapy with single-agent cisplatin.

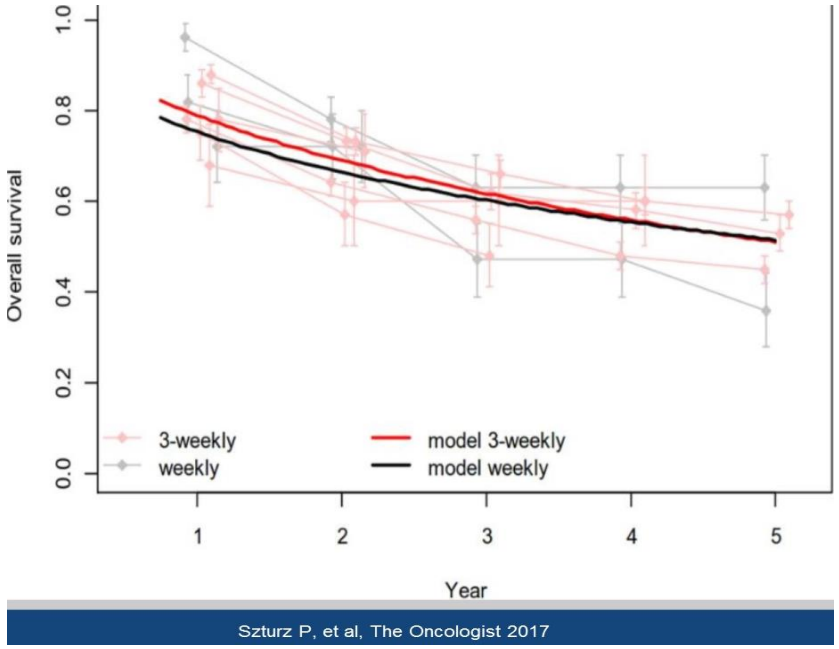
Strojan P, Head Neck, 2016

So zvyšujúcou sa kumulatívnou dávkou cisplatiny sa zlepšuje OS

Absolútny benefit 2,2 % v OS na každých 10 mg cisplatiny

(Dávkovanie od 140 mg/m2 do 270 mg/m2)
Model dosiahol štatistickú signifikanciu, p = 0,027

Komparatívna analýza medzi týždňovým a 3-týždňovým podávaním cisplatiny



Szturz P, et al, The Oncologist 2017

Je kumulatívna dávka cisplatiny hlavným determinantom efektivity?

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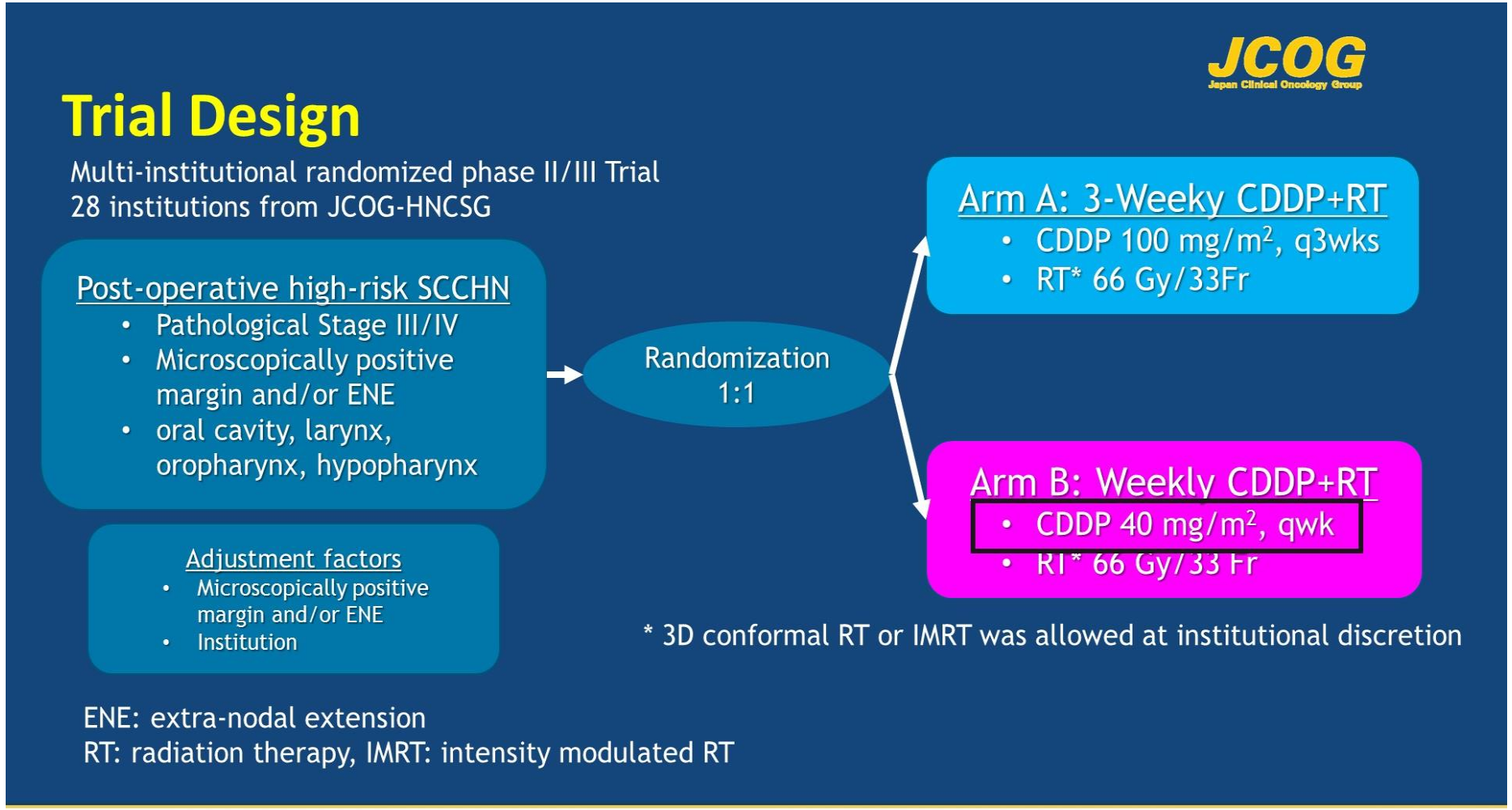
Abstrakt 6502 – JCOG1008 štúdia, fázy II/III, pooperačná RAT + CHT u high risk pacientov so SCCHN – týždňová verzus 3-týždňová cisplatina



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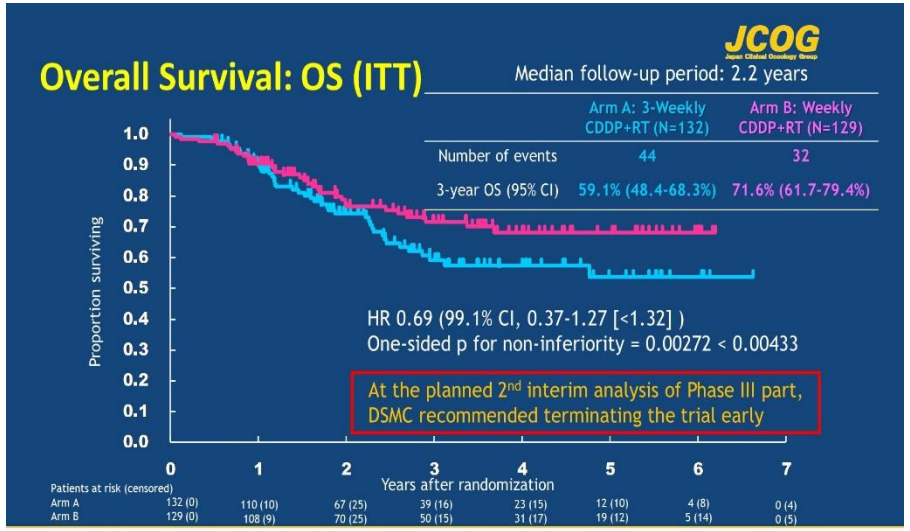
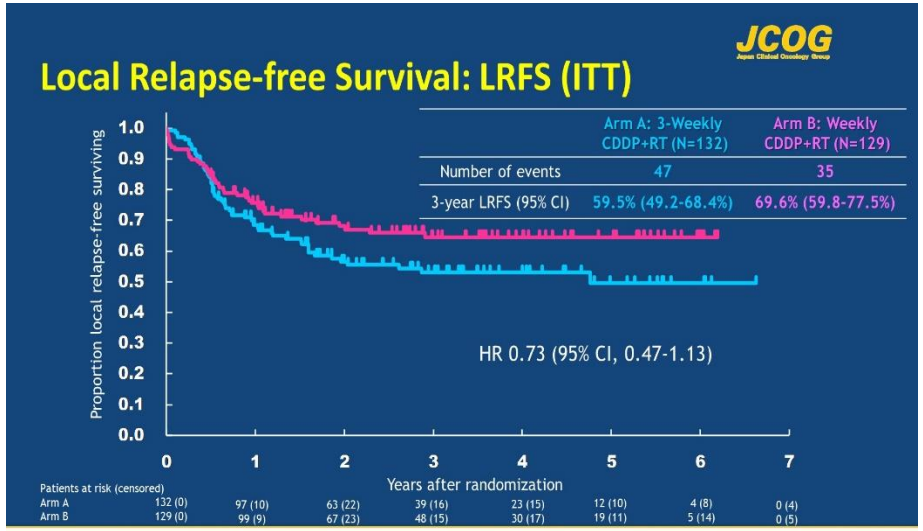
Abstrakt 6502 – JCOG1008 štúdia, fázy II/III, pooperačná RAT + CHT u high risk pacientov so SCCHN – týždňová verzus 3-týždňová cisplatina





Záver:
Konkomitantná RAT + CHT s týždennou cisplatinou 40 mg/m2 je akceptovateľný štandard v pooperačnej intencii

Ako je to v primárnej RAT + CHT?

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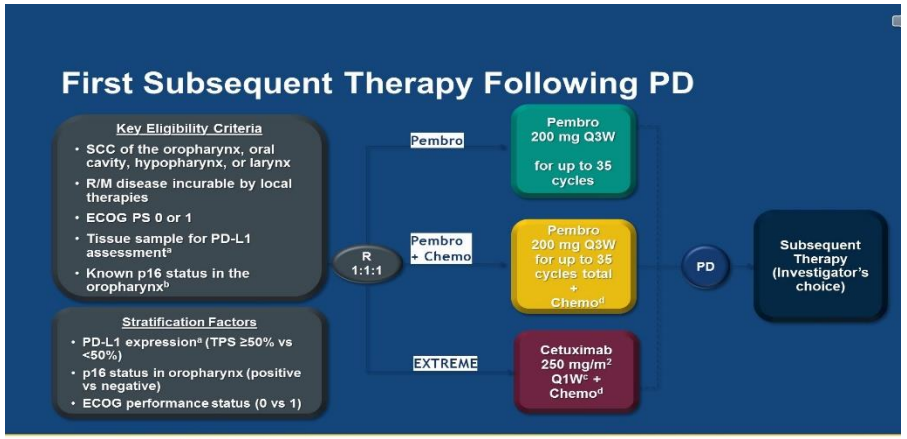
Optimálna sekvencia systémovej liečby a imunoterapie v liečbe R/M SCCHN?
Abstrakt 6505: KN048 – progresia po ďalšej línii liečby

Abstract # 6505

KEYNOTE-048: Progression After the Next Line of Therapy Following Pembrolizumab or Pembrolizumab Plus Chemotherapy vs EXTREME as First-Line Therapy for Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Kevin Harrington,[1] Danny Rischin,[2] Richard Greil,[3] Denis Soulieres,[4] Makoto Tahara,[5] Gilberto Castro,[6] Amanda Psyrri,[7] Neus Baste,[8] Prakash C. Neupane,[9] Åse Bratland,[10] Thorsten Fuereder,[11] Brett G. M. Hughes,[12] Ricard Mesia Sr.,[13] Nuttapong Ngamphaiboon,[14] Tamara Rordorf,[15] Wan Zamaniah Wan Ishak,[16] Yayan Zhang,[17] Burak Gumuscu,[17] Ramona F. Swaby,[17] Barbara Burtness[18]

[1]The Institute of Cancer Research/The Royal Marsden NHS Foundation Trust National Institute of Health Research Biomedical Research Centre, London, UK; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Paracelsus Medical University, Salzburg Cancer Research Institute, and Cancer Cluster Salzburg, Salzburg, Austria; [4]Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada; [5]National Cancer Center Hospital East, Kashiwa, Japan; [6]Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Brazil; [7]National Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece; [8]Vall d'Hebron University Hospital, Barcelona, Spain; [9]University of Kansas Medical Center, Kansas City, KS, USA; [10]Oslo University Hospital, Oslo, Norway; [11]Medical University of Vienna, Vienna, Austria; [12]Royal Brisbane and Women's Hospital and University of Queensland, Brisbane, Australia; [13]Catalan Institute of Oncology, Hospitalet de Llobregat, Barcelona, Spain; [14]Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [15]University Hospital, Zurich, Switzerland; [16]University of Malaya, Kuala Lumpur, Malaysia; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA



First Subsequent Therapy

n (%)	Pembro Monotherapy n = 301	Pembro + Chemotherapy n = 281	EXTREME n = 300
Any new anticancer treatment[a]	148 (49.2)	115 (40.9)	159 (53.0)
Chemotherapy	135 (44.9)	88 (31.3)	102 (34.0)
EGFR inhibitor	59 (19.6)	37 (13.2)	19 (6.3)
Immune checkpoint inhibitor	6 (2.0)	12 (4.3)	50 (16.7)
Other immunotherapy	1 (0.3)	0 (0.0)	6 (2.0)
Kinase inhibitor	1 (0.3)	7 (2.5)	1 (0.3)
Other	2 (0.7)	1 (0.4)	2 (0.7)

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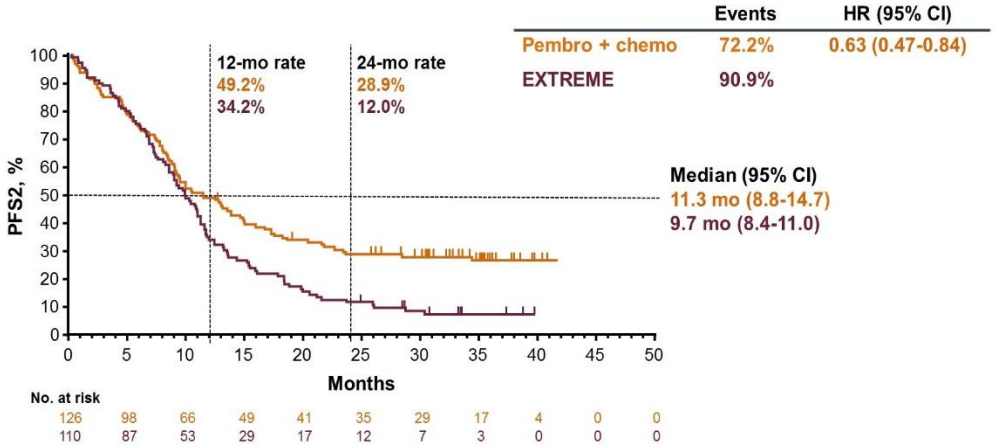
PFS2: Initially Randomized, Pembro + Chemotherapy vs EXTREME, CPS ≥20 Population



- PFS2 analysis involved patients in the ITT population with PD-L1 CPS≥20 (Pembro + Chemotherapy vs EXTREME

Data cutoff: February 25, 2019 (final analysis).

Abstrakt 6505

- potvrdil, že „včasné" zavedenie ICI je štandardom v liečbe R/M SCCHN

- je sekvencia ICI → chemo lepšia ako CHT → ICI?

- KN048 nebola dizajnovaná na zodpovedanie otázky optimálnej sekvencie

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Optimálna sekvencia systémovej liečby a imunoterapie v liečbe R/M SCCHN?
Abstrakt 6507: TPEx – analýza prežívania podľa 2. línie liečby

(Abstract # 6507)

TPExtreme randomized trial:
Quality of Life (QoL) and survival according to second-line treatments in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC)

Joël Guigay, Jerome Fayette, Ricard Mesia Sr., Esma Saada-Bouzid, Cedrik Lafond, Lionnel Geoffrois, Laurent Martin, Olivier Capitain, Didier Cupissol, Helene Castanie, Alison Claire Johnson, D Sire, Raissa Kapso, Melissa Delhommeau, Cecile Chevassus-Clement, Ulricl
GORTEC - AIO Studien gGmbH - TTCC - Unicancer H&N

Centre Antoine Lacassagne, FHU OncoAge, Université Côte d'Azur, Nice, France; Centre Léon Bérard, Medical Oncology, Lyo Antoine Lacassagne, Université Côte d'Azur, Nice, France; Clinique Victor Hugo, Le Mans, France; Centre Alexis Vautrin, Van Havre, France; Institut de Cancerologie de l'Ouest, Site Paul Papin, Angers, France; Centre Val d'Aurelle, Montpellier, France Caen, France; Institut de Cancerologie de l'Ouest–René Gauducheau, Nantes, France; Gustave Roussy, Villejuif, France; CH d Gustave Roussy, Villejuif, France; GORTEC, Tours, France; Charité Comprehensive Cancer Center, Berlin, Germany; Centre H

TPExtreme study design (NCT 02268695)

KEY ELIGIBILITY CRITERIA
- → R/M HNSCC not suitable for locoregional treatment
- → Age 18-70 years
- → PS 0-1
- → Creatinine clearance >60 mL/min
- → Prior cisplatin ≤300 mg/m²
- → No Anti-EGFR for 1 year

MINIMIZATION FACTORS
- → PS
- → Metastatic status
- → Previous cetuximab
- → Country

R 1:1

N = 270

EXTREME
(Reference arm)
6 cycles Q3W CT
CISPLATIN → 100 mg/m² IV
5FU → 4000 mg/m² 96h continuous infusion
CETUXIMAB → 400 mg/m² (loading dose), then 250 mg/m² IV weekly

→ Maintenance cetuximab 250 mg/m²
→ WEEKLY
→ until progression or unacceptable toxicity

N = 269

TPEx
(Experimental arm)
4 cycles Q3W CT
CISPLATIN → 75 mg/m² IV
DOCETAXEL → 75 mg/m² IV
CETUXIMAB → 400 mg/m² (loading dose), then 250 mg/m² IV weekly
+ G CSF after each cycle

→ Maintenance cetuximab 500 mg/m²
→ EVERY 2 WEEKS
→ until progression or unacceptable toxicity

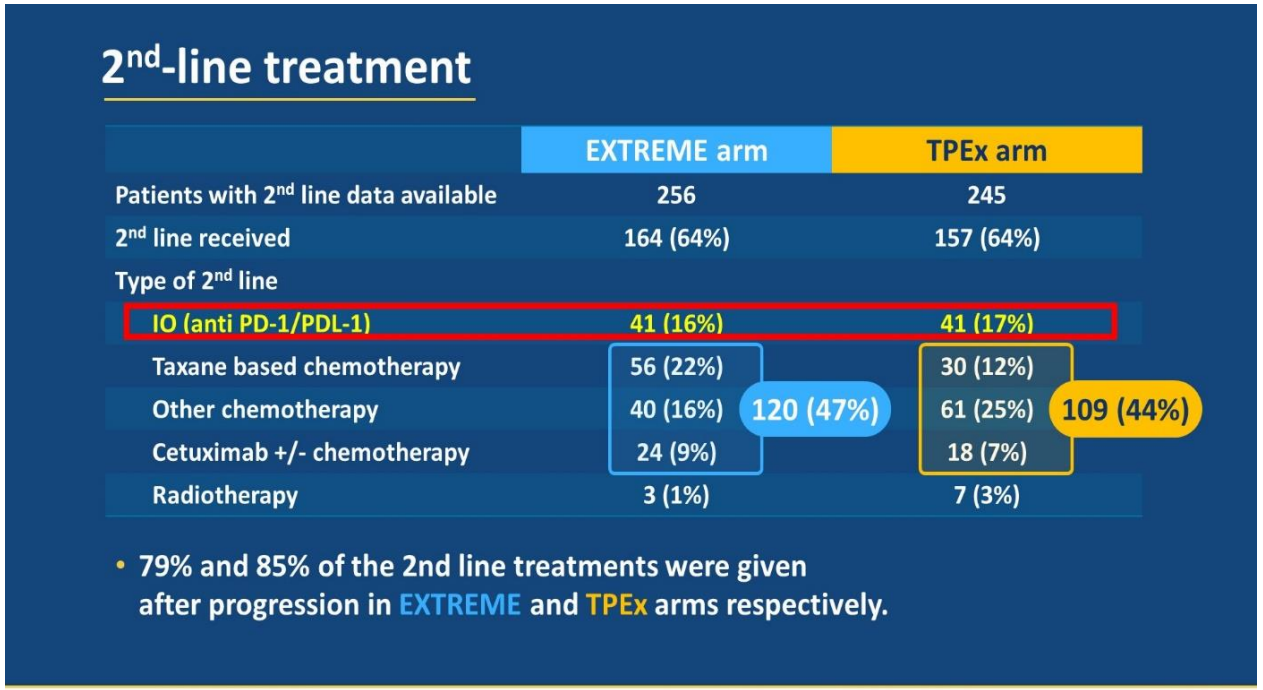
Prezentované na ASCO© 2020, Guigay, J., Abstract No. 6507

Optimálna sekvencia systémovej liečby a imunoterapie v liečbe R/M SCCHN?
Abstrakt 6507: TPEx – analýza prežívania podľa 2. línie liečby

Post-hoc exploratórna analýza liečby v 2. línii (CHT +/– cetuximab verzus ICI)

Metóda: analýza OS podľa typu liečby v 1. línii

- **V obidvoch ramenách EXTREME a TPEx 64 % pacientov dostalo liečbu v 2. línii**
- 79 % režimov v 2. línii bolo podaných po progresii v ramene EXTREME a 85 % v ramene TPEx



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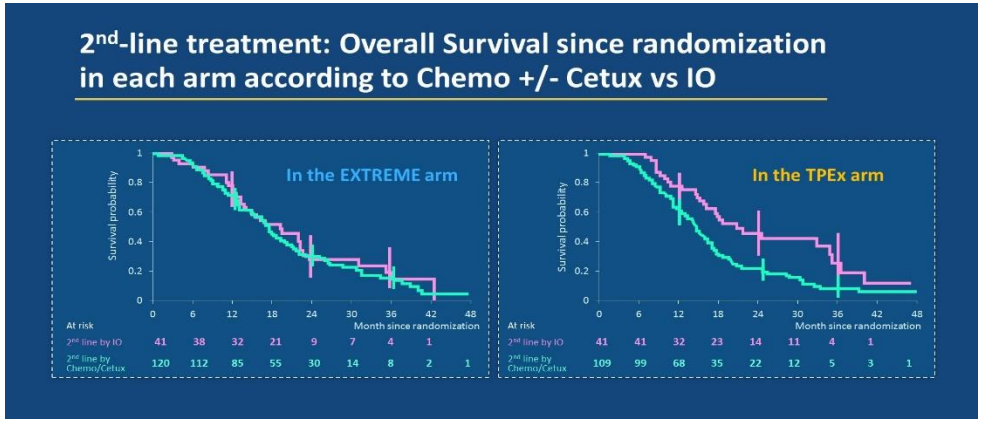
Optimálna sekvencia systémovej liečby a imunoterapie v liečbe R/M SCCHN?
Abstrakt 6507: TPEx – analýza prežívania podľa 2. línie liečby



2nd line treatment: Overall Survival since randomization in each arm according to Chemo +/- Cetux vs IO

	EXTREME arm		TPEx arm	
	2nd line with chemo/cetux	2nd line with IO	2nd line with chemo/cetux	2nd line with IO
Overall survival at 12 months	70.8%	78.1%	62.4%	78.1%
Overall survival at 24 months	29.9%	27.5%	23.2%	46.9%
Overall survival at 36 months	15.6%	18.9%	9.9%	27.5%
Median OS (95%CI)	17.6 months (15.2 – 19.5)	19.4 months (13.4 – 22.3)	14.9 months (13.0 – 16.3)	21.9 months (15.9 – 35.0)

Prezentované na ASCO© 2020, Guigay, J., Abstract No. 6507

Optimálna sekvencia systémovej liečby a imunoterapie v liečbe R/M SCCHN?
Abstrakt 6507: TPEx – analýza prežívania podľa 2. línie liečby

Závery autorov:

- Exploratórna analýza ukázala, že taxánový **TPEx režim s následnou liečbou check-point inhibítormi v 2. línii** by mohol priniesť **zaujímavý medián OS** pre pacientov, ktorí potrebujú chemoterapiu v 1. línii, **pri nižšej toxicite** ako režim EXTREME
- **Sekvencia TPEx → ICI by sa mala porovnať s prístupom, keď sa začne liečba kombináciou platina + 5-FU + pembrolizumab**

Slabé stránky:

- Pacienti v tejto štúdii neboli liečení podľa štandardov roku 2020
- Výsledky neindikujú jednoznačne posunutie ICI do neskoršej línie, lebo TPEx nie je štandard v 1. línii so silou kat. 1
- Môže byť základom pre budúce paradigmy sekvencií

Viac klinických štúdií!!!

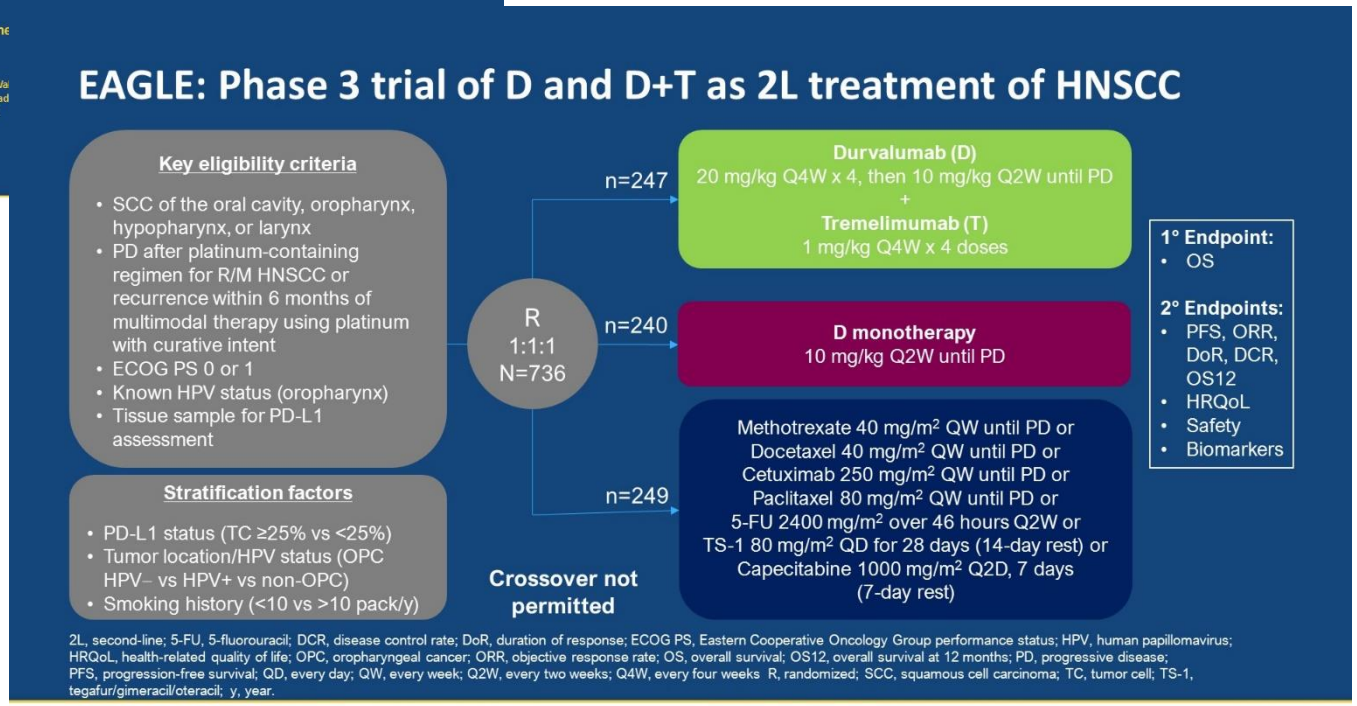
Prezentované na ASCO© 2020, Guigay, J., Abstract No. 6507

Nádorová mutačná nálož (TMB) – ako prediktor prežívania Abstrakt 6511 – EAGLE štúdia fázy III, Durvalumab +– Tremelimumab verzus CHT v liečbe R/M SCCHN po zlyhaní na platine

Plasma-based Tumor Mutational Burden as Predictor of Survival in Phase 3 EAGLE Study: Durvalumab ± Tremelimumab Versus Chemotherapy in Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma After Platinum Failure

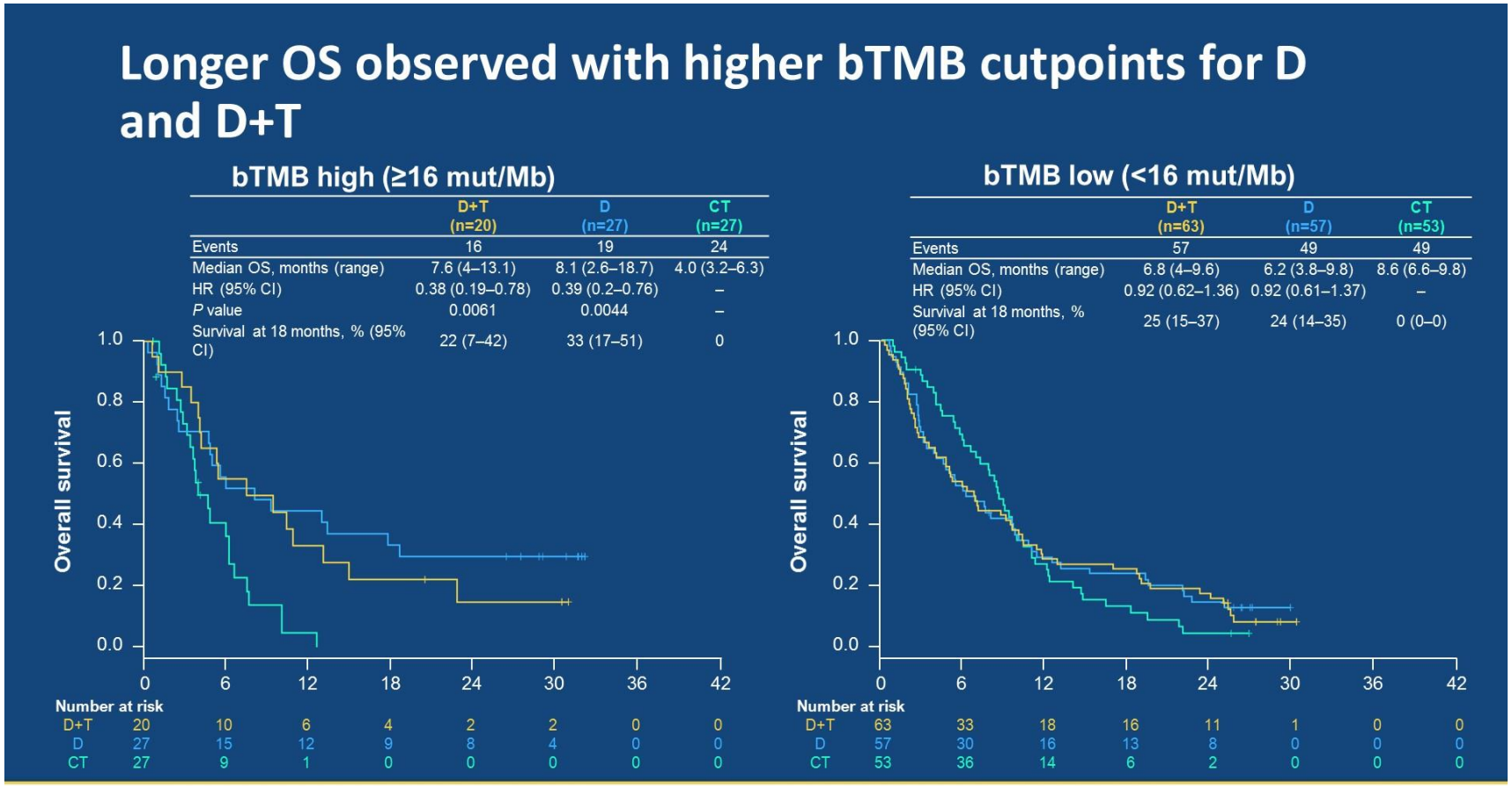
Li W,[1] Wildsmith S,[2] Ye J,[1] Si H,[1] Morsli N,[2] He P,[1] Shetty J,[1] Yovine
Zhang Q,[1] Xie M,[3] Mesia R,[4] Haddad R,[5] Licitra L,[6] Ferris RL[7]

[1]AstraZeneca, Gaithersburg, MD, USA; [2]AstraZeneca, Cambridge, UK; [3]AstraZeneca, Wa
[5]Department of Medical Oncology, Dana Farber Cancer Institute, Boston, MA, USA; [6]Head
Milan, Italy; [7]UPMC Hillman Cancer Center, University of Pittsburgh, Pittsburgh, PA, USA



Prezentované na ASCO© 2020, Ricard Mesia, Abstract No. 6511

Nádorová mutačná nálož (TMB) – ako prediktor prežívania Abstrakt 6511 – EAGLE štúdia fázy III, Durvalumab+– Tremelimumab verzus CHT v liečbe R/M SCCHN po zlyhaní na platine



Prezentované na ASCO© 2020, Ricard Mesia, Abstract No. 6511

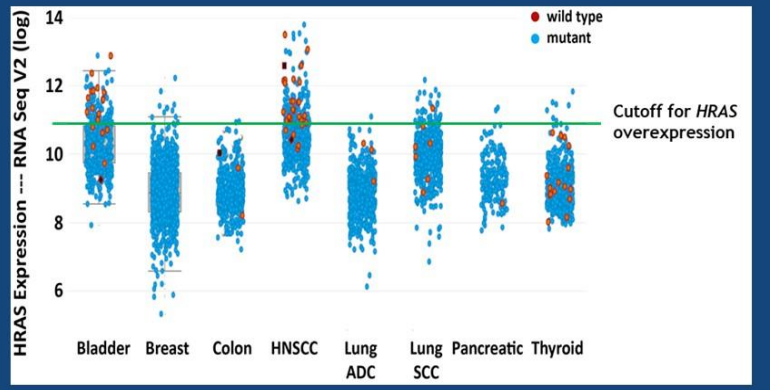
Abstrakt 6504 – aktivita Tipifarnibu v liečbe nádorov s prítomnou HRAS mutáciou (nádory hlavy a krku, slinných žliaz a uroteliálne nádory)

HRAS-dependent solid tumors may be highly sensitive to tipifarnib

- Hypothesis: *HRAS* mutations are a biomarker for tipifarnib activity
  - FTase inhibitors have activity in *HRAS*-mutant tumor cell lines and mouse models[1-3]
- Phase 2 clinical trials are investigating tipifarnib in different tumor types
  - *HRAS*-mutant solid tumors (KO-TIP-001; NCT02383927)
  - *HRAS*-mutant HNSCC (KO-TIP-007; NCT03719690)
    - *Haddad R, et al. 2020 Annual ASCO Meeting. Abstract #TPS6593*
  - *HRAS*-mutant urothelial carcinoma (IST-01; NCT02535650)
    - *Kim H, et al. 2020 Annual ASCO Meeting. Abstract #5086*

1. Lerner EC, et al. *Oncogene*. 1997;15:1283-1288.
2. Untch BR, et al. *Cancer Res*. 2018;78(16):4642-4657.
3. Chen X, et al. *Oncogene*. 2014;33(47):5442-5449.

HRAS Gene Expression in Select Cancers



Tumor	HNSCC	LSCC	UC
% mutant	6	2	5
% overexpressed	30	8	25

HNSCC, head and neck squamous cell carcinoma.
LSCC, lung squamous cell carcinoma.
UC, urothelial carcinoma

Prezentované na ASCO© 2020, Alan L.Ho, Abstract No. 6504

Abstrakt 6504 – aktivita Tipifarnibu v liečbe nádorov s prítomnou HRAS mutáciou (nádory hlavy a krku, slinných žliaz a uroteliálne nádory)

Objective response rate and duration of response in HNSCC with high *HRAS*-mutant VAF

	ORR (CR+PR)[a] % (n)	95% CI[b]	
		Lower	Upper
HNSCC pts, mITT (N=21)	42.9 (9)	21.8	66.0
HNSCC pts, response evaluable (N=17)	47.1 (8)	23.0	72.2
HNSCC pts, response evaluable, including additional patient (N=18)	50.0 (9)	26.0	74.0

	Median DoR[a] (months)	95% CI[b]	
		Lower	Upper
HNSCC with high *HRAS*-mutant VAF, including additional patient (N=18)	14.7	2.1	-

[a]Data cutoff as of September 30, 2019. Patients with *HRAS* VAF ≥20% and serum albumin ≥3.5 g/dL or *HRAS* VAF ≥35% enrolled in stages 1, 2 or in the HNSCC extension cohort. Additionally, 1 patient is included who was treated off protocol through expanded access program.
[b]2-sided 95% exact binomial confidence interval.

Prezentované na ASCO© 2020, Alan L.Ho, Abstract No. 6504

ASCO© 2020 – odporúčania pre prax?

Konkomitantná RAT + CHT s týždennou cisplatinou 40 mg/m2 je akceptovateľný štandard v pooperačnej intencii

Včasné zavedenie PD-1 je štandardom v liečbe R/M SCCHN, hlavne pri CPS ≥ 1

Vyšetrovanie HRAS mutácie/alterácie u pacientov s pokročilým refraktérnym SCCHN

Prezentované na ASCO© 2020, prof. Nabil Saba

Ďakujem za pozornosť.