Zhrnutie sekcie karcinóm prsníka

MUDr. Bela Mriňáková, PhD., MPH

I. Onkologická klinika LFUK a OÚSA

Onkologický ústav sv. Alžbety

Vyhlásenie o konflikte záujmov autora

□ Nemám potenciálny konflikt záujmov

✓ Deklarujem nasledujúci konflikt záujmov

Forma finančného prepojenia	Spoločnosť
Participácia na klinických štúdiách/firemnom grante	Novartis
Nepeňažné plnenie (v zmysle zákona)	Novartis, Roche
Prednášajúci	Angelini Pharma, Novartis, Roche, Sandoz
Akcionár	
Konzultant/odborný poradca	GOMED, EMS Biomedical
Ostatné príjmy (špecifikovať)	

Podľa UEMS (upravené v zmysle slovenskej legislatívy)

Prezentáciu podporila agentúra

We Make Media Slovakia s.r.o.

Včasný karcinóm prsníka na ASCO© 2020

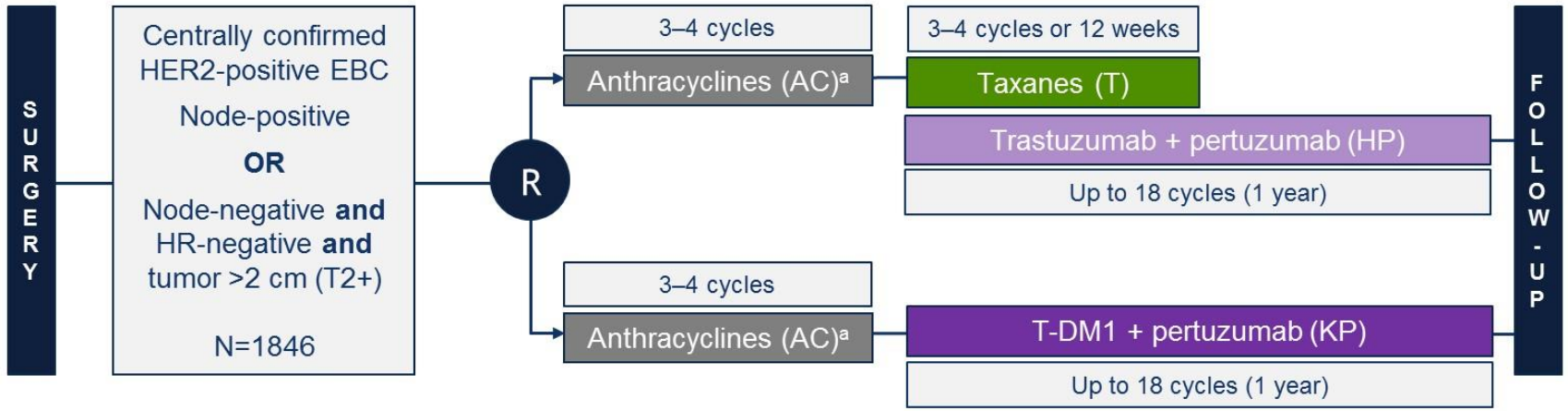
HER2 pozitívny karcinóm prsníka

Abstrakt č.: 500

Primary analysis of KAITLIN: A phase III study of trastuzumab emtansine (T-DM1) + pertuzumab versus trastuzumab + pertuzumab + taxane, after anthracyclines as adjuvant therapy for high-risk HER2-positive early breast cancer (EBC).

Nadia Harbeck, Seock-Ah Im, Carlos H. Barrios, Herve R. Bonnefoi, Julie Gralow, Masakazu Toi, Paul Ellis, Luca Gianni, Sandra M. Swain, Young-Hyuck Im, Michelino De Laurentiis, Zbigniew Nowecki, Jigna Shah, Thomas Boulet, Haiying Liu, Harrison Macharia, Peter Trask, Chunyan Song, Eric P. Winer, and Ian E. Krop
Journal of Clinical Oncology 2020 38:15_suppl, 500-500

KAITLIN Study Design



Stratification factors:

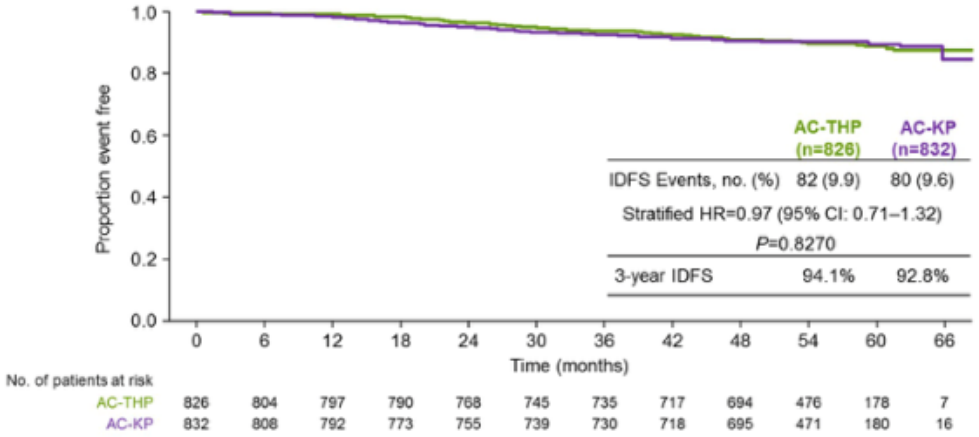
- Region: United States/Canada, Western Europe/Australia/New Zealand, Asia, or rest of the world
- Nodal status: 0, 1–3, or ≥4 positive nodes
- Centrally assessed hormone receptor status: positive (ER-positive and/or PgR-positive) or negative (ER-negative and PgR-negative)
- Type of anthracycline: doxorubicin or epirubicin

[a]Anthracyclines (AC) = investigator's choice of FEC, AC, or EC [5-fluorouracil (F), epirubicin (E), cyclophosphamide (C), doxorubicin (A)].

Nadia Harbeck, et al. ASCO©2020. Abstract 500

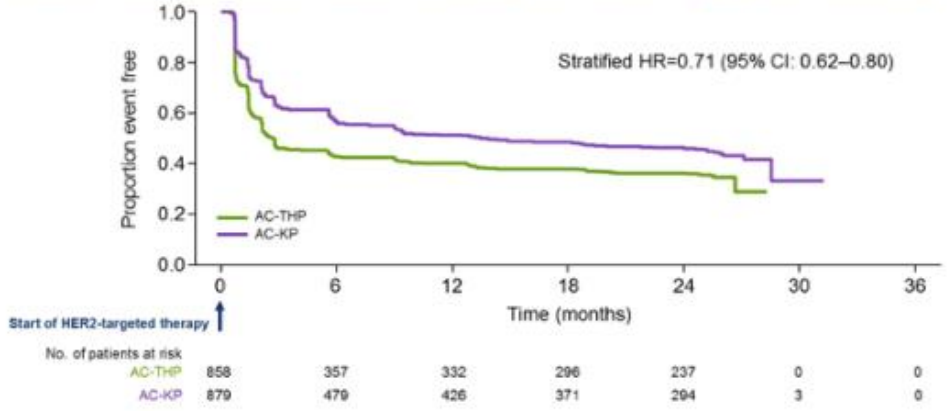
Primary Endpoint: IDFS, Node-Positive Disease

- AC-KP did not reduce the risk of an IDFS event compared with AC-THP in the node-positive population



Patient-Reported Outcomes: Deterioration in Global Health Status/QoL

- From the start of HER2-targeted therapy, a lower risk of deterioration was observed in the AC-KP arm, with differences between the treatment arms during taxane treatment
- A similar pattern was observed for Physical Functioning, Role Functioning, Cognitive Functioning



Nedosiahol sa primárny cieľ
IDFS bez štatisticky signifikantného rozdielu

Zníženie rizika zhoršenia QOL v experimentálnom ramene

Adjuvantná liečba trastuzumab + pertuzumab + chemoterapia zostáva štandardom liečby

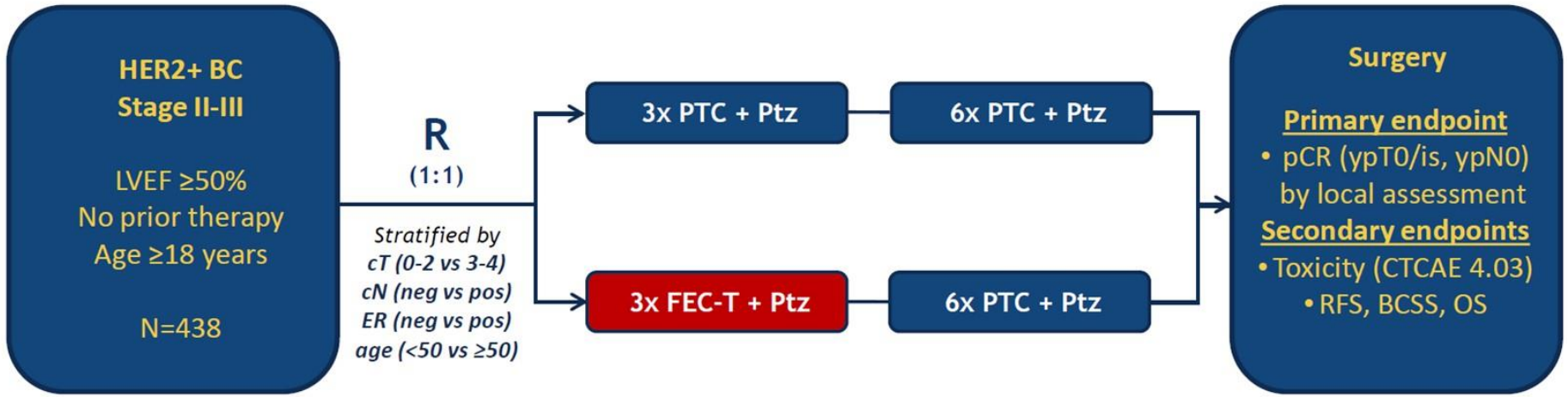
Nadia Harbeck, et al. ASCO©2020. Abstract 500

Abstrakt č.: 501

Three-year follow-up of neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2-blockade for HER2-positive breast cancer (TRAIN-2): A randomized phase III trial.

Anna van der Voort, Mette S. van Ramshorst, Erik D. van Werkhoven, Ingrid A. Mandjes, Inge Kemper, Annelie J. Vulink, Irma M. Oving, Aafke H. Honkoop, Lidwine W. Tick, Agnes J. van de Wouw, Caroline M. Mandigers, Laurence J. C. van Warmerdam, Jelle Wesseling, Marie-Jeanne T.F.D Vrancken Peeters, Sabine C. Linn, Gabe S. Sonke, and on behalf of the Dutch Breast Cancer Group (BOOG)
Journal of Clinical Oncology 2020 38:15_suppl, 501-501

TRAIN-2: study design

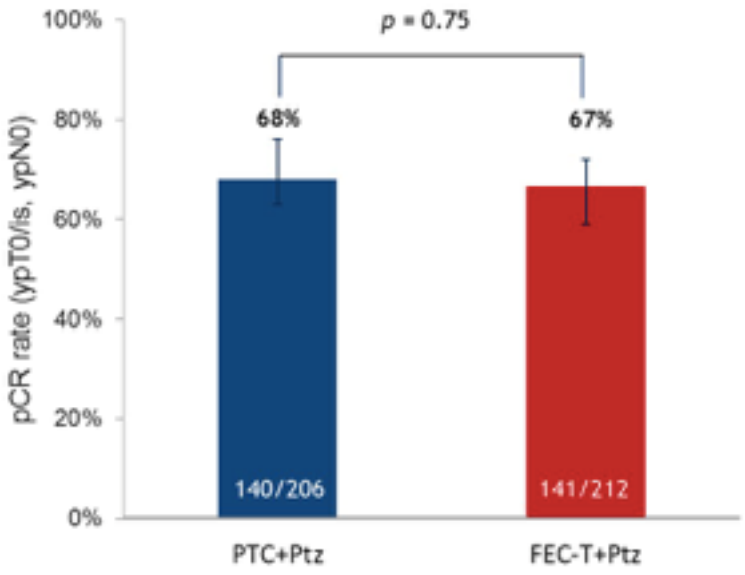


- **PTC+Ptz** cycle of 3 weeks, day 1 PTC+Ptz, day 8 only P: P = paclitaxel 80mg/m^2; T = trastuzumab 6mg/kg (loading dose 8mg/kg); C = carboplatin AUC = 6mg·min/ml; Ptz = pertuzumab, 420mg (loading dose 840mg)
- **FEC-T+Ptz** cycle of 3 weeks: F = 5-fluorouracil 500mg/m^2; E = epirubicin 90mg/m^2; C = cyclophosphamide 500mg/m^2;T = trastuzumab 6mg/kg (loading dose 8mg/kg); Ptz = pertuzumab, 420mg (loading dose 840mg)
- Adjuvant trastuzumab to complete one year of treatment and endocrine therapy for ER+ and/or PR+ tumors

van Ramshorst et al, *Lancet Oncol* 2018; van Ramshorst et al, *Eur J Cancer* 2017

ClinicalTrials.gov identifier: NCT01996267

Anna van der Voort, et al. ASCO©2020. Abstract 501



Safety: most common grade ≥3 AEs

	PTC+Ptz (n=218*) n (%)	FEC-T+Ptz (n=220#) n (%)
Hematological AEs		
Neutropenia	118 (54%)	131 (60%)
Anemia	46 (21%)	44 (20%)
Thrombocytopenia	42 (19%)	39 (18%)
Febrile neutropenia†	3 (1%)	23 (10%)
Non-hematological AEs		
Diarrhea	38 (17%)	26 (12%)
Hypokalemia†	8 (4%)	19 (9%)
Peripheral sensory neuropathy	15 (7%)	12 (5%)
Fatigue	12 (6%)	9 (4%)
Alanine aminotransferase increased	8 (4%)	11 (5%)

Vysoký podiel pCR v oboch ramenách štúdie.

Výsledok konzistentný vo všetkých podskupinách
cT (0-2 vs 3-4)
cN (negatívne vs. pozitívne)
Vek (<50 vs. >50).

Anna van der Voort, et al. ASCO©2020. Abstract 501

	PTC+Ptz (n=218) n (%)	FEC-T+Ptz (n=220*) n (%)	p-value
LVEF decrease ≥10% or LVEF <50%	49# (22%)	80 (36%)	0.0016
LVEF decrease ≥10% and LVEF <50%	7 (3%)	17 (8%)	0.044

LVEF was measured every 3 months for 1 year
* one patient was allocated to PTC+Ptz but received neoadjuvant FEC-T+PTZ
# one patient developed grade 2 LVEF decline during adjuvant treatment with anthracyclines

LVEF sa neupravilo do normy počas sledovania u cca 1/3 pacientok.

3-ročné sledovanie štúdie TRAIN-2 nepreukázalo rozdiely v EFS a OS v prospech podania antracyklínu pri HER2 pozitívnom EBC štádium II a III.

Antracyklíny zvyšujú riziko febrilnej neutropénie a kardiotoxicity.

Anna van der Voort, et al. ASCO©2020. Abstract 501

Včasný karcinóm prsníka na ASCO© 2020

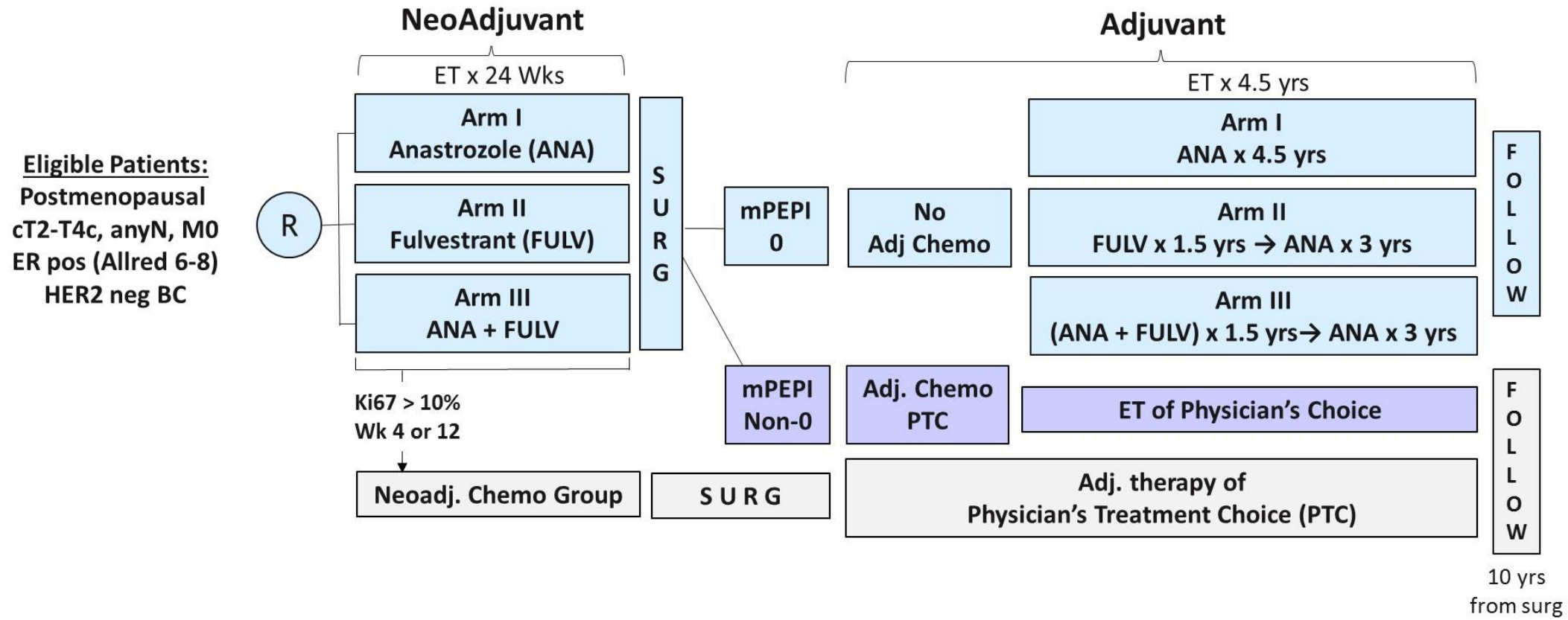
ER pozitívny karcinóm prsníka

Abstrakt č.: 504

ALTERNATE: Neoadjuvant endocrine treatment (NET) approaches for clinical stage II or III estrogen receptor-positive HER2-negative breast cancer (ER+ HER2- BC) in postmenopausal (PM) women: Alliance A011106.

Cynthia X. Ma, Vera J. Suman, A. Marilyn Leitch, Souzan Sanati, Kiran R. Vij, Gary Walter Unzeitig, Jeremy Hoog, Mark Watson, Olwen Mary Hahn, J. Michael Guenther, Abigail Suzanne Caudle, Travis Dockter, Larissa A. Korde, Anna Weiss, Kelly Hunt, Clifford A. Hudis, Eric P. Winer, Ann H. Partridge, Lisa A. Carey, Matthew James Ellis, and Alliance
Journal of Clinical Oncology 2020 38:15_suppl, 504-504

ALTERNATE Study Design



Cynthia X. Ma, et al. ASCO©2020. Abstract 504

Breakdown of Endocrine Response Categories by Arm

	Total N=1,299	ANA N=434	FULV N=431	ANA + FULV N=434
Ki67 > 10% at Week 4 or 12	286 (22.0%)	111 (25.6%)	105 (24.3%)	70 (16.1%)
Confirmed PD during NET	13 (1.0%)	5 (1.2%)	4 (0.9%)	4 (0.9%)
Discontinued NET early	65 (5.0%)	29 (6.7%)	14 (3.2%)	22 (5.1%)
mPEPI undetermined*	22 (1.7%)	5 (1.2%)	3 (0.7%)	14 (3.2%)
mPEPI > 0	645 (49.7%)	203 (46.8%)	207 (48.0%)	235 (54.1%)
mPEPI = 0	258 (19.9%)	77 (17.7%)	94 (21.8%)	87 (20.0%)
pCR	10 (0.8%)	4 (0.9%)	4 (0.9%)	2 (0.5%)

Pokles Ki67 bez signifikantného rozdielu medzi ramenami.

Progresia počas 6 mes. neoadjuvantnej HT u menej ako 2% pacientiek.

Cynthia X. Ma, et al. ASCO©2020. Abstract 504

Primary Endpoint Result

Endocrine-Sensitive Disease Rate (ESDR) = mPEPI 0 + pCR rate

	ANA N=434	FULV N=431	ANA + FULV N=434
mPEPI = 0	77 (17.7%)	94 (21.8%)	87 (20.0%)
pCR	4 (0.9%)	4 (0.9%)	2 (0.5%)
ESDR N % (97.5% CI)	81 (18.6%) (97.5% CI: 14.6-23.2)	98 (22.7%) (97.5% CI: 18.4-27.6)	89 (20.5%) (97.5% CI: 16.3-25.2)
Fisher's Exact Test P value compared to ANA arm		p=0.15	p=0.55

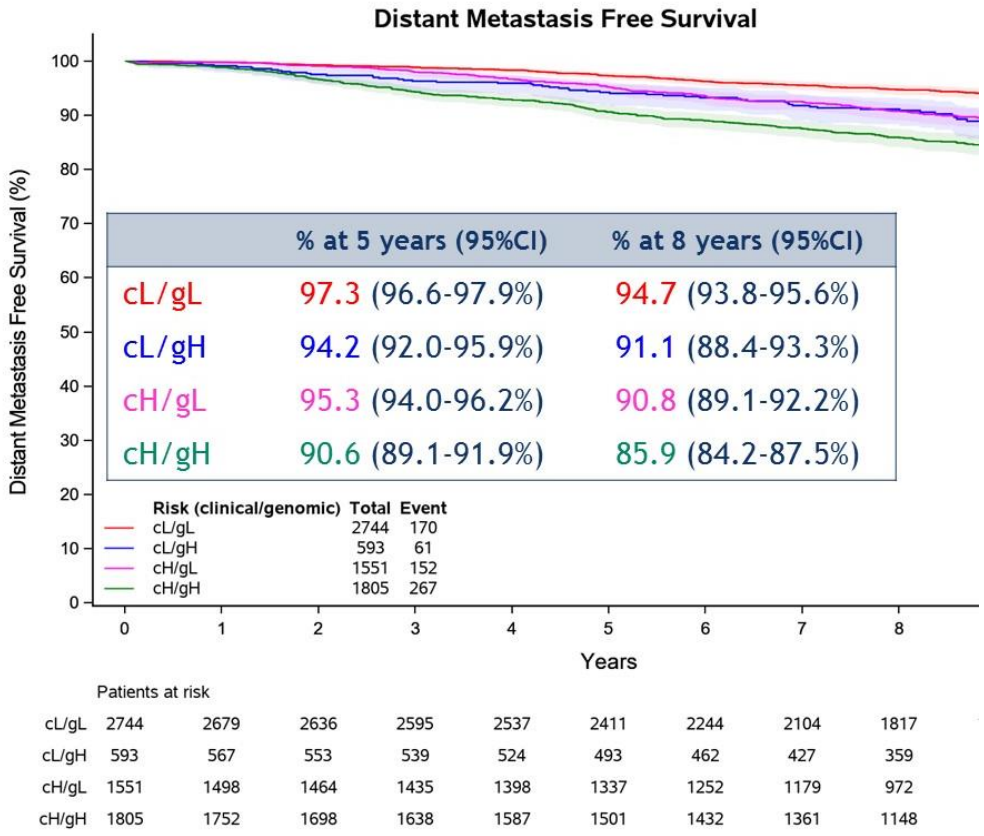
ESDR bez signifikantného rozdielu medzi jednotlivými ramenami.

Cynthia X. Ma, et al. ASCO©2020. Abstract 504

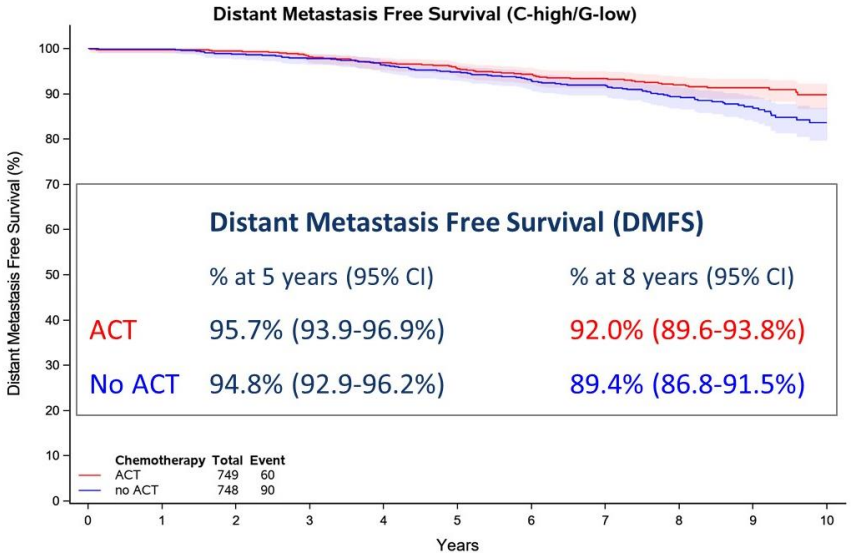
Abstrakt č.: 506

MINDACT: Long-term results of the large prospective trial testing the 70-gene signature MammaPrint as guidance for adjuvant chemotherapy in breast cancer patients.

Fatima Cardoso, Laura van 't Veer, Coralie Poncet, Josephine Lopes Cardozo, Suzette Delaloge, Jean-Yves Pierga, Peter Vuylsteke, Etienne Brain, Giuseppe Viale, Sherko Kuemmel, Isabel T. Rubio, Gabriele Zoppoli, Alastair Mark Thompson, Erika Matos, Khalil Zaman, Florentine Hilbers, Aleksandra Dudek-Perić, Bart Meulemans, Martine J. Piccart-Gebhart, and Emiel J. Rutgers
Journal of Clinical Oncology 2020 38:15_suppl, 506-506



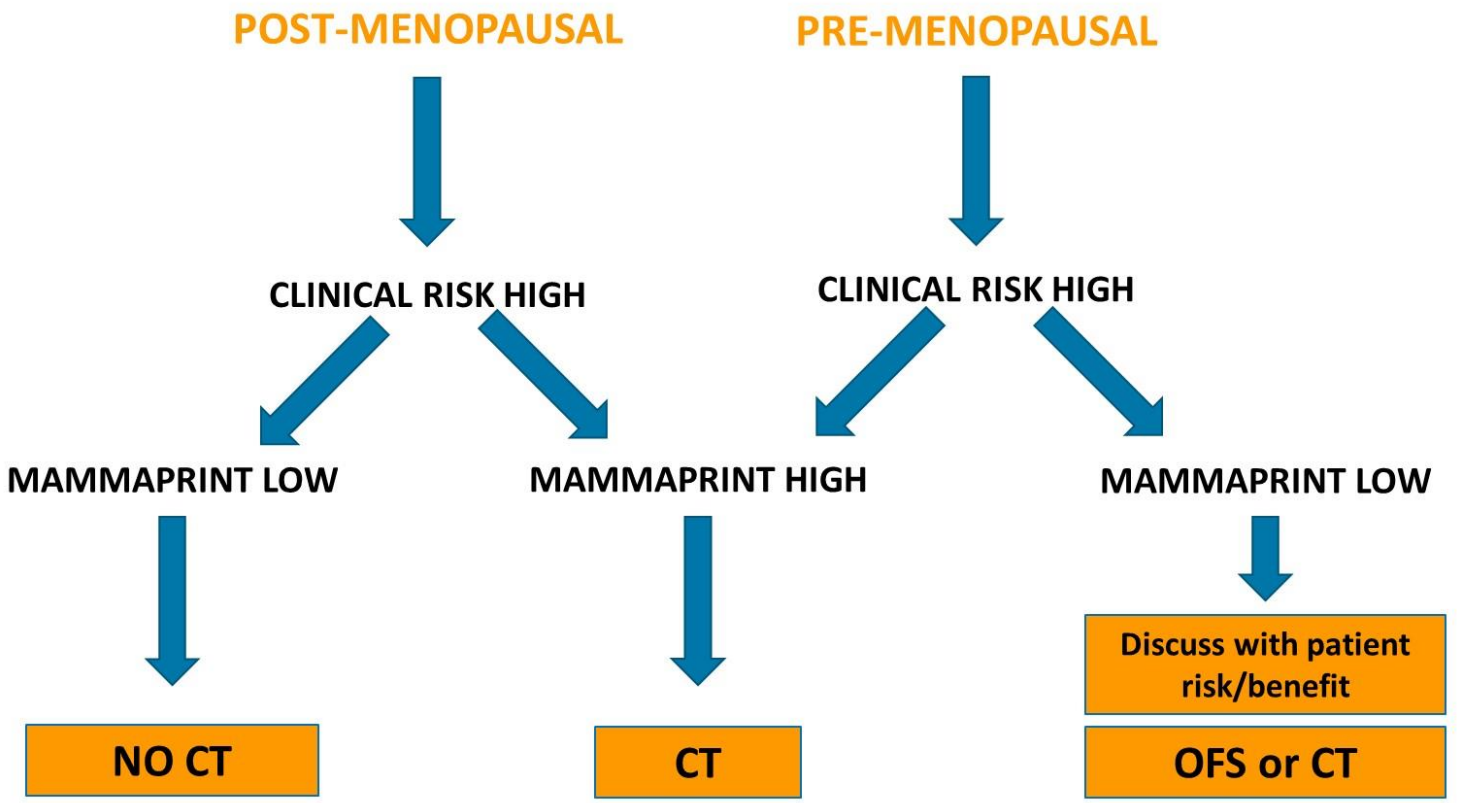
Výborná prognóza a nízke riziko recidív vo forme vzdialených metastáz vo všetkých skupinách okrem skupiny s vysokým klinickým rizikom/nízkym genomickým rizikom.



Fatima Cardoso, et al. ASCO©2020. Abstract 506

EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

Proposal for clinical implementation of MINDACT results



Vzhľadom na výsledky dlhšieho sledovania pri Mammaprint nízkorizikovej skupine individuálne zvážiť riziko/benefit CHT.

Fatima Cardoso, et al. ASCO©2020. Abstract 506

Abstrakt č.: e12544

Real-world data on adjuvant bisphosphonate use in a breast cancer center in Mexico.

Omar Peña-Curiel, Cynthia Villarreal-Garza, Héctor Díaz-Pérez, and Enrique Francisco Martinez Trevino
Journal of Clinical Oncology 2020 38:15_suppl, e12544-e12544

Abstrakt č.: 513

Validation of MAF biomarker for response prediction to adjuvant bisphosphonates in 2 clinical trials: AZURE and NSABP-B34.

Alexander H. G. Paterson, Stewart J. Anderson, Roger Gomis, Joel Jean-Mairet@inbiomotion.com, Juan-Carlos Tercero, Peter Lucas, and Eleftherios P. Mamounas
Journal of Clinical Oncology 2020 38:15_suppl, 513-513

Včasný karcinóm prsníka na ASCO© 2020

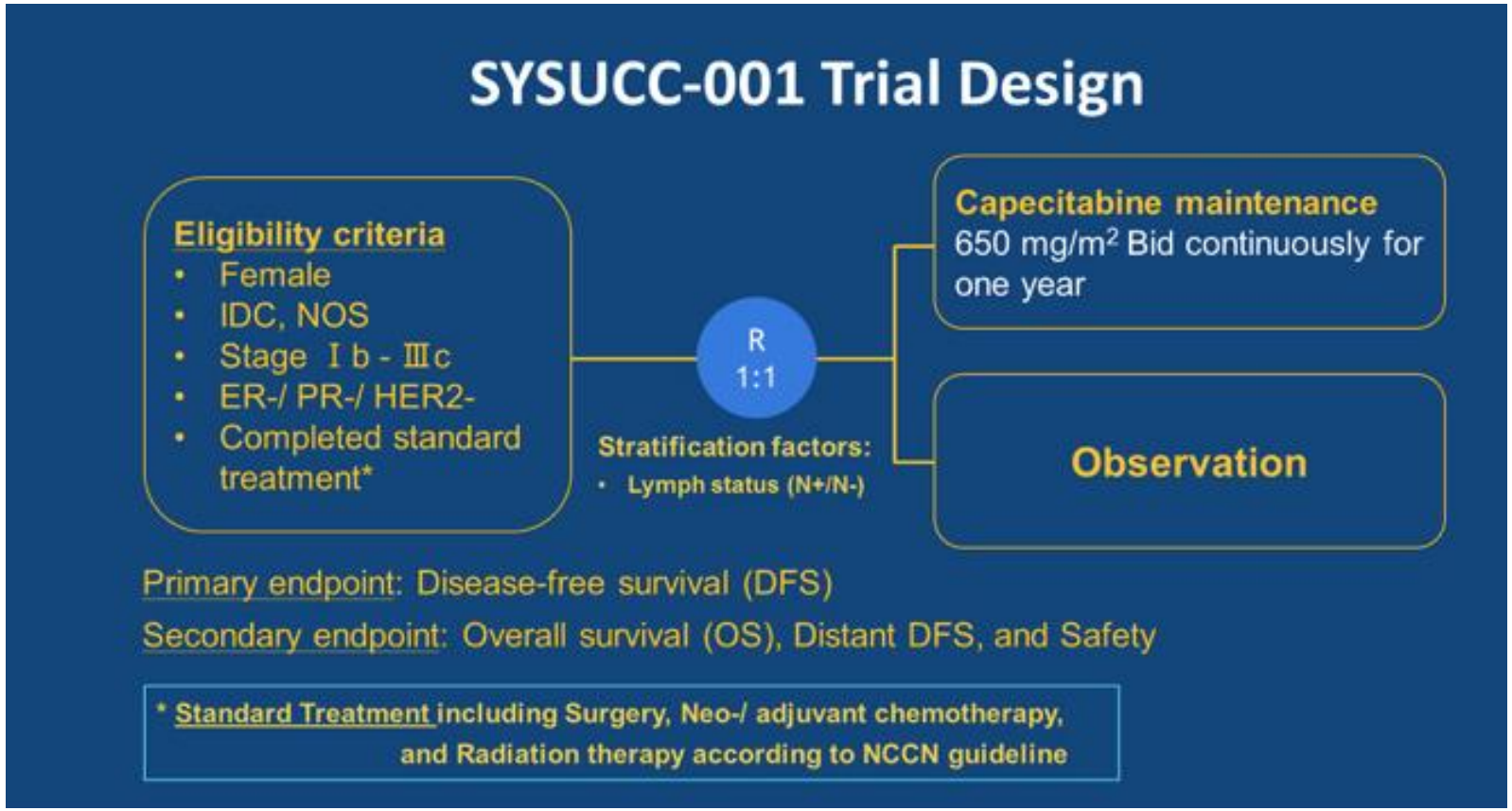
TRIPLE NEGAT karcinóm prsníka

Abstrakt č.: 507

Phase III trial of metronomic capecitabine maintenance after standard treatment in operable triple-negative breast cancer (SYSUCC-001)

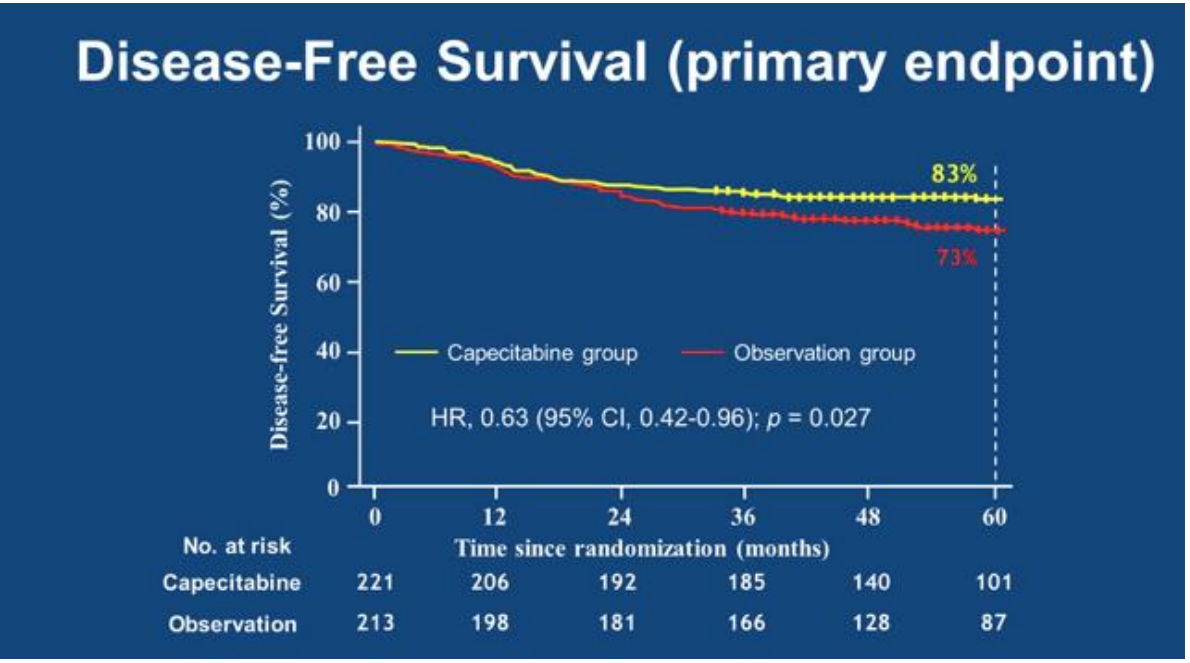
XI Wang, Shu-Sen Wang, Heng Huang, Li Cai, Rou-Jun Peng, Li Zhao, Ying Lin, Jian Zeng, Le-Hong Zhang, Yong-Li Ke, Xian-Ming Wang, Xin-Mei Liu, Qian-Jun Chen, An-Qin Zhang, Dan-Mei Pang, Fei Xu, Jia Jia Huang, Yanxia Shi, Jun Tang, and Zhongyu Yuan

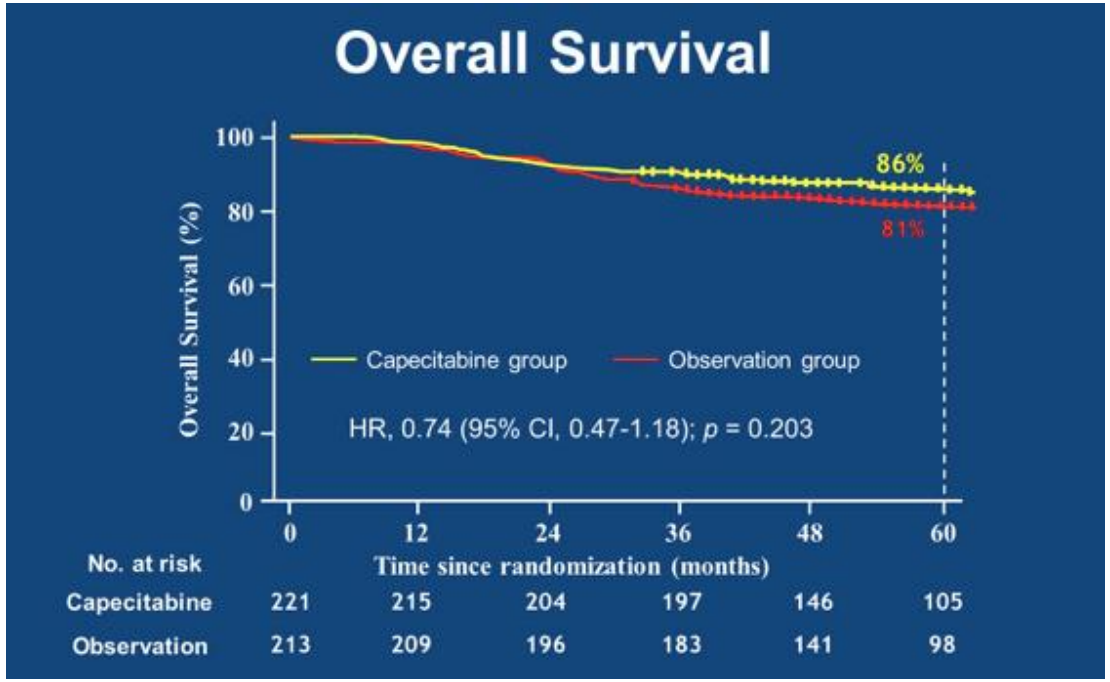
Journal of Clinical Oncology 2020 38:15_suppl, 507-507



443 pacientok
Medián sledovania 36mes
Št. Ib-IIIc
91.4 % zvládlo rok liečby.
Z toho 152 v plnej dávke
Intenzita dávky 84,7 %.

XI Wang, et al. ASCO©2020. Abstract 507





Signifikantné zlepšenie 5-ročného bez relapsového prežívania 83 % vs. 71 %.

Dobre tolerovaná liečba, bez neočakávaných závažných nežiadúcich účinkov.

XI Wang, et al. ASCO©2020. Abstract 507

Metastatický karcinóm prsníka na ASCO© 2020

Metastatický karcinóm prsníka

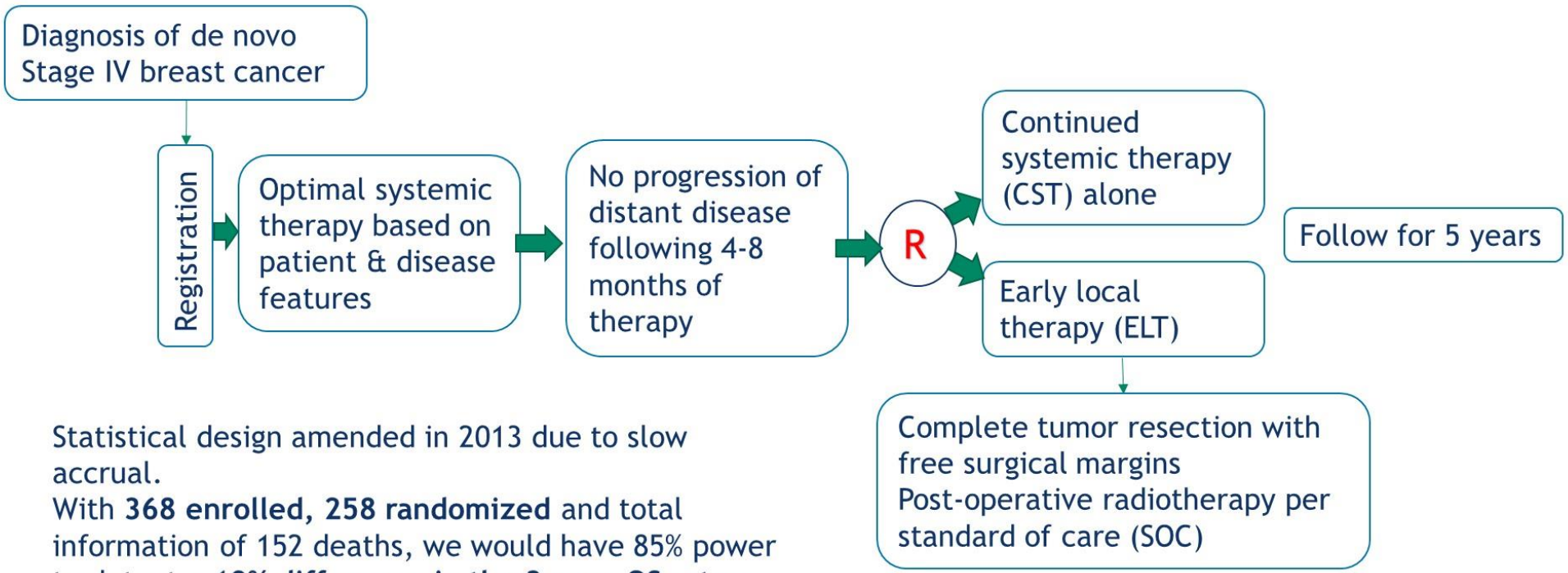
Abstrakt č.: LBA2

A randomized phase III trial of systemic therapy plus early local therapy versus systemic therapy alone in women with de novo stage IV breast cancer: A trial of the ECOG-ACRIN Research Group (E2108).

Seema Ahsan Khan, Fengmin Zhao, Lawrence J. Solin, Lori J. Goldstein, David Cella, Mark Basik, Mehra Golshan, Thomas B. Julian, Barbara A. Pockaj, Christine A Lee, Wajeeha Razaq, Joseph A. Sparano, Gildy V Babiera, Irene Ang Dy, Sarika Jain, Paula Silverman, Carla Fisher, Amye Juliet Tevaarwerk, Lynne I. Wagner, and George W. Sledge
Journal of Clinical Oncology 2020 38:18_suppl, LBA2-LBA2

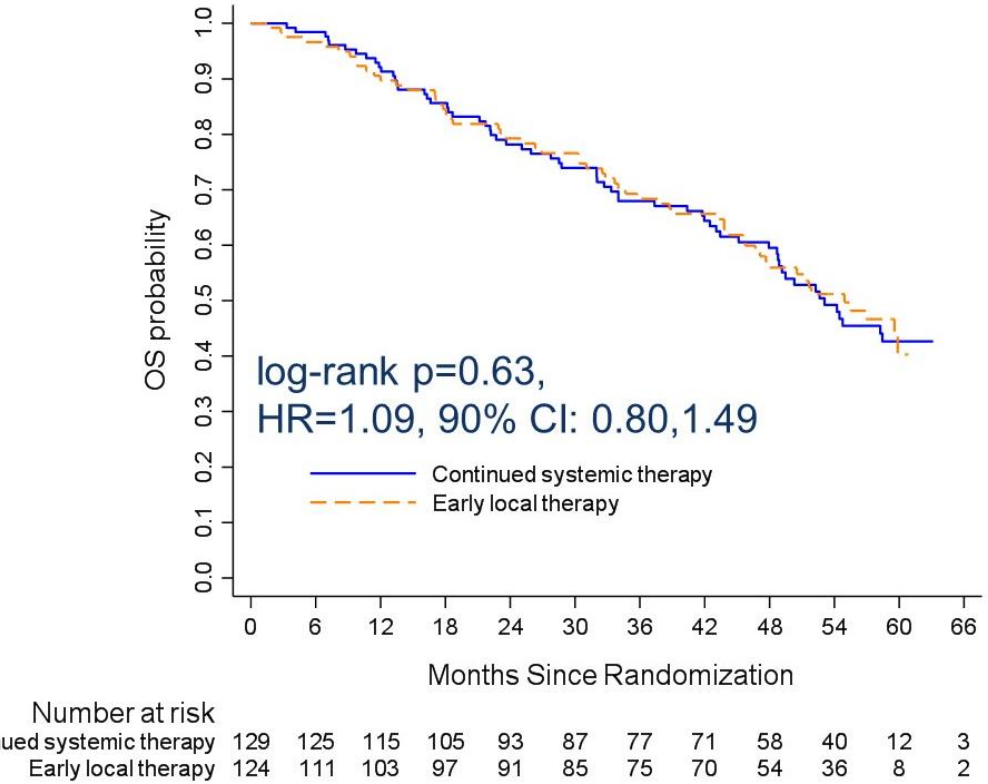
Design of E2108

Opened in 2011, last patient enrolled in 2015.



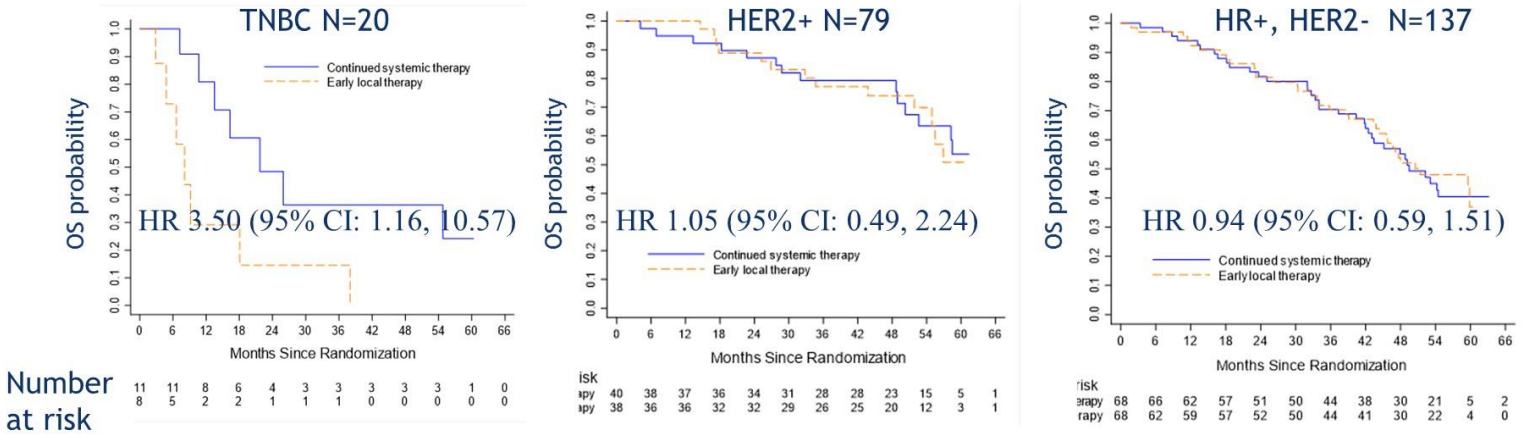
Statistical design amended in 2013 due to slow accrual.
With **368 enrolled, 258 randomized** and total information of 152 deaths, we would have 85% power to detect a **19% difference in the 3-year OS rates**

Seema Ahsan Khan, et al. ASCO©2020. Abstract LBA2



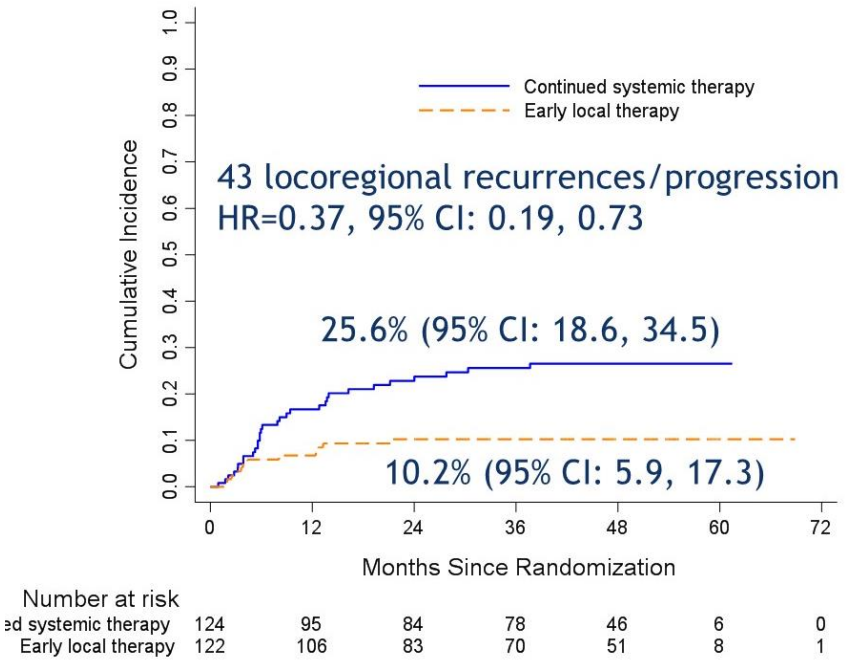
Medián prežívania 53 mesiacov (0-91). Bez signifikantného rozdielu OS a PFS.

Results: overall survival by tumor subtype



- For 20 women with TNBC, survival was worse in the early local therapy arm.

Seema Ahsan Khan, et al. ASCO©2020. Abstract LBA2



Lokoregionálna progresia/recidíva:

1. **Progresia v regionálnych LU**
2. **Progresia v oblasti hrudnej steny, resp. invazívna progresia v prsníku**

2,5- násobné zvýšenie rizika lokálnej progresie. Lokoregionálna liečba neviedla k zlepšeniu HRQoL.

LOKÁLNA LIEČBA BY NEMALA BYŤ INDIKOVANÁ S CIEĽOM ZLEPŠENIA OS V IV. ŠTÁDIU OCHORENIA.

V PRÍPADE SYSTÉMOVO KONTROLOVANÉHO OCHORENIA S PROGRESIOU V MIESTE PRIMÁRNEHO NÁDORU JE LOKÁLNA LIEČBA NA ZVÁŽENIE.

Seema Ahsan Khan, et al. ASCO©2020. Abstract LBA2

Abstrakt č.: 1008

Randomized trial of a collaborative palliative and oncology care intervention to improve communication about end-of-life care in patients with metastatic breast cancer.

Jennifer S. Temel, Beverly Moy, Areej El-Jawahri, Vicki A. Jackson, Mihir Kamdar, Juliet Jacobsen, Charlotta Lindvall, Jennifer Adrienne Shin, Simone Rinaldi, Heather Carlson, Angela Sousa, Emily J. Gallagher, Samantha Moran, Margaret Ruddy, Maya Anand, Julia Carp, and Joseph A. Greer
Journal of Clinical Oncology 2020 38:15_suppl, 1008-1008

Metastatický karcinóm prsníka na ASCO© 2020

HER2 pozitívny karcinóm prsníka

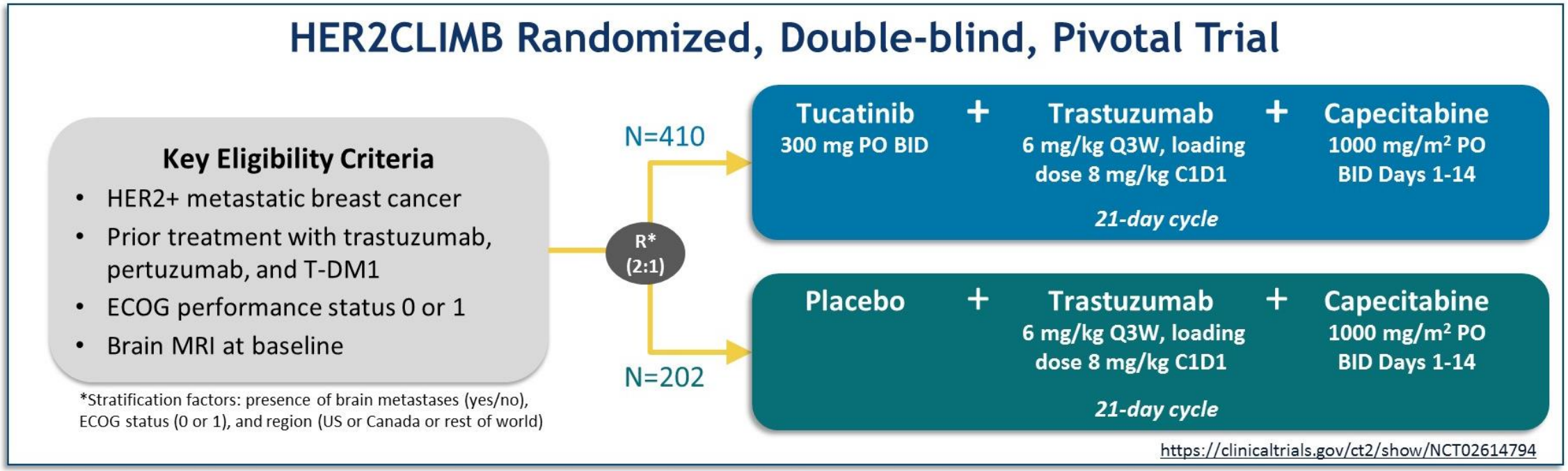
Abstrakt č.: 1005

Tucatinib versus placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ metastatic breast cancer with brain metastases (HER2CLIMB).

Nancy U. Lin, Rashmi Krishna Murthy, Carey K. Anders, Virginia F. Borges, Sara A. Hurvitz, Sherene Loi, Vandana G Abramson, Philippe L. Bedard, Mafalda Oliveira, Amelia Bruce Zelnak, Michael DiGiovanna, Thomas Bachelot, Amy Jo Chien, Ruth O'Regan, Andrew M. Wardley, Volkmar Müller, Lisa A. Carey, Suzanne M. McGoldrick, Grace An, and Eric P. Winer

Journal of Clinical Oncology 2020 38:15_suppl, 1005-1005

HER2CLIMB Randomized, Double-blind, Pivotal Trial

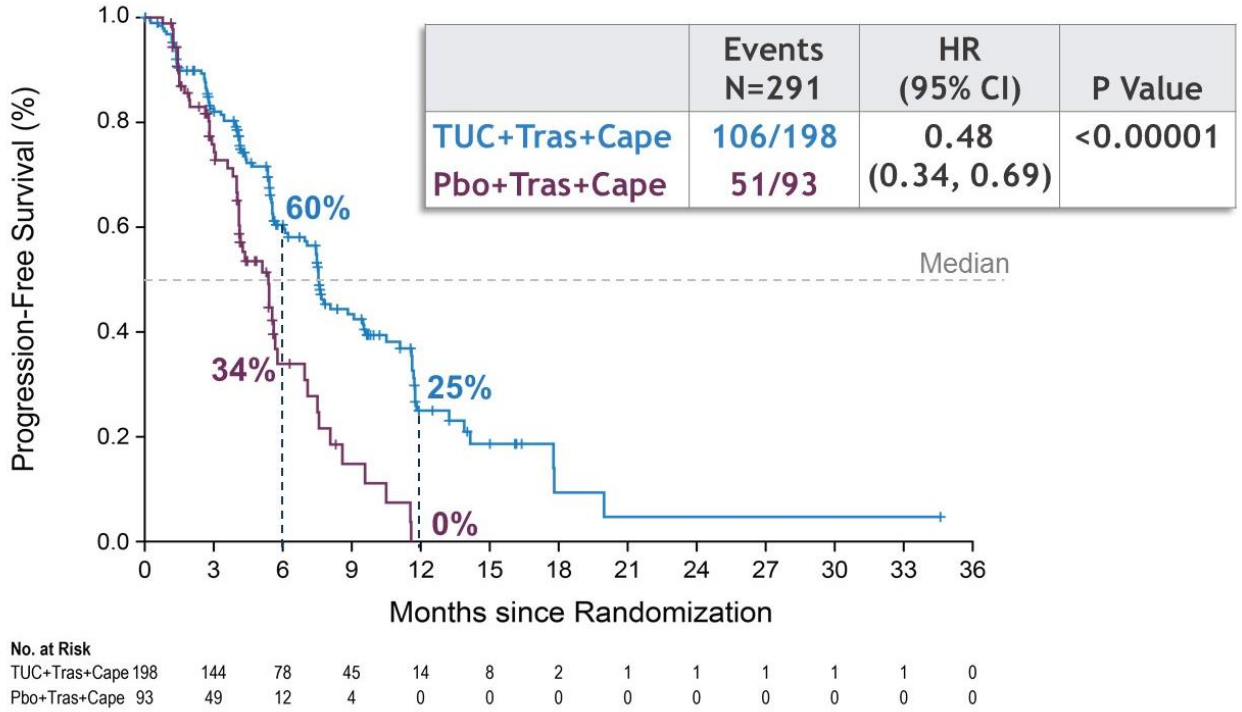


1. Bendell JC, et al. Cancer 2003;97:2972-7.
2. Brufsky AM, et al. Clin Cancer Res 2011;17:4834-43.
3. Leyland-Jones B. J Clin Oncol 2009;27:5278-86.
4. Olson EM, et al. Breast 2013;22:525-31.
5. Moulder SL, et al. Clin Cancer Res 2017;23:3529-36.
6. Pheneger T, et al. Cancer Research 2009;69:1795.

TKI: tyrosine kinase inhibitor

Nancy U. Lin, et al. ASCO©2020. Abstract 1005

ANALÝZA PFS U PACIENTOV S MOZGOVÝMI MTS



	Events N=291	HR (95% CI)	P Value
TUC+Tras+Cape	106/198	0.48 (0.34, 0.69)	<0.00001
Pbo+Tras+Cape	51/93		

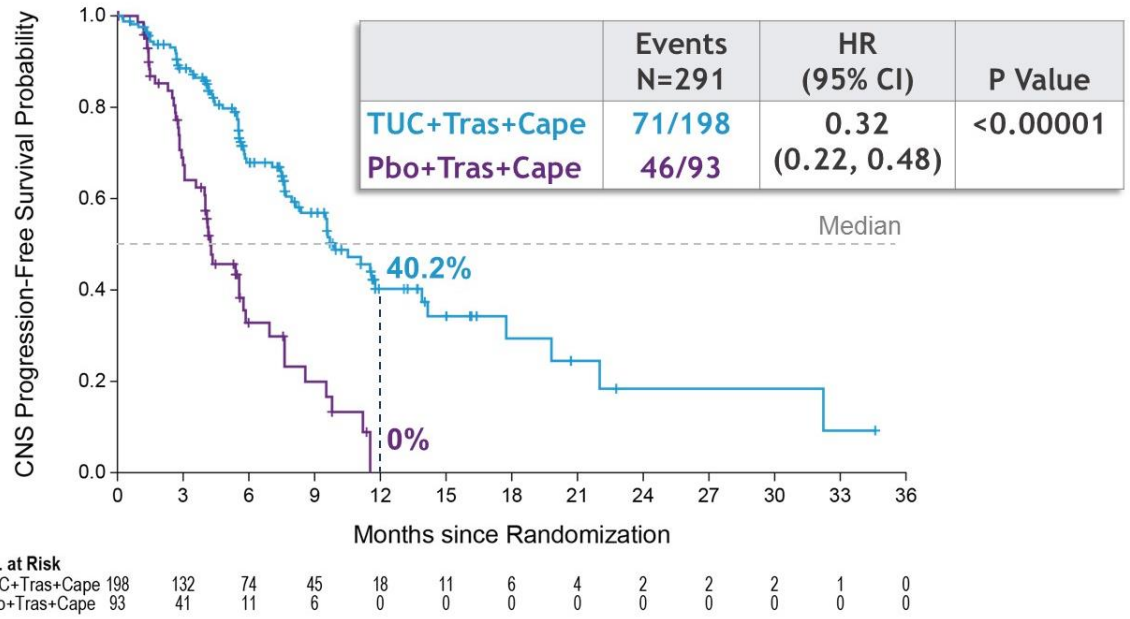
*PFS, defined as time from randomization to documented disease progression (assessed by blinded independent central review) or death from any cause. Analysis does not include patients with dural lesions only.

Ročné PFS 25 % vs. 0 % (CI 95%).
Medián PFS 7,6 vs. 5,4mes.
(CI 95 %).

RIZIKO PROGRESIE ALEBO SMRTI U PACIENTOV S MTS POSTIHNUTÍM ZNÍŽENÉ O 52 %.

Nancy U. Lin, et al. ASCO©2020. Abstract 1005

ANALÝZA CNS-PFS U PACIENTOV S MOZGOVÝMI MTS



CNS-PFS: time from randomization to disease progression in the brain or death by investigator assessment.
HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, America/Rest of World) at randomization. All P values are nominal.

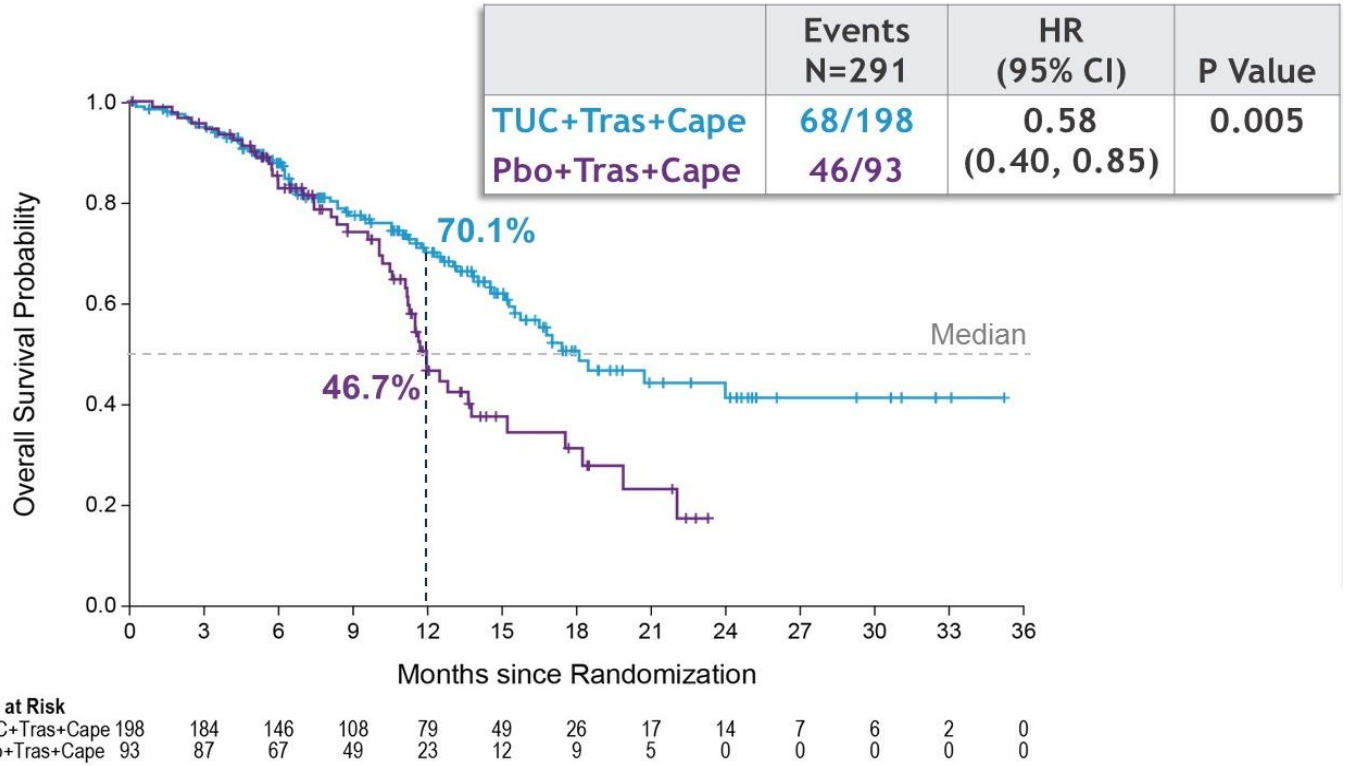
Ročné CNS-PFS 40,2 % vs. 0 %

Medián CNS-PFS 9,9 vs. 4,2 mes.

RIZIKO SMRTI U PACIENTOV S MTS POSTIHNUTÍM ZNÍŽENÉ O 42 %.

Nancy U. Lin, et al. ASCO©2020. Abstract 1005

CELKOVÉ PREŽÍVANIE U PACIENTOV S MOZGOVÝMI MTS



HR: hazard ratio computed from Cox proportional hazards model using stratification factors (ECOG performance status: 0/1, an
North America/Rest of World) at randomization. All P values are nominal.

Ročné OS 70,1 % vs. 46,7 %.
Medián OS 18,1 vs. 12,0 mes.

RIZIKO CNS PROGRESIE ALEBO SMRTI U PACIENTOV S MTS POSTIHNUTÍM ZNÍŽENÉ O 68 %.

Nancy U. Lin, et al. ASCO©2020. Abstract 1005

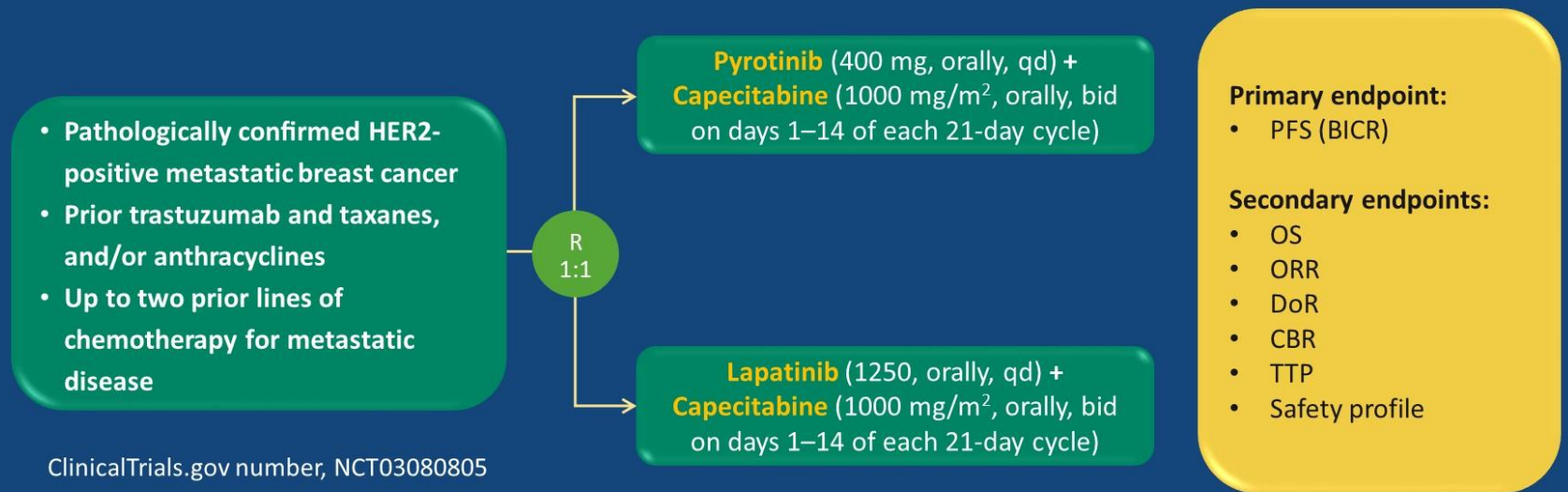
Abstrakt č.: 1003

Pyrotinib or lapatinib plus capecitabine for HER2+ metastatic breast cancer (PHOEBE): A randomized phase III trial.

Binghe Xu, Min Yan, Fei Ma, Xi-Chun Hu, Ji Feng Feng, Quchang Ouyang, Zhongsheng Tong, Huiping Li, Qingyuan Zhang, Tao Sun, Xian Wang, Yongmei Yin, Ying Cheng, Wei Li, Xiaoyu Zhu, Chunxia Chen, Jianjun Zou, and The PHOEBE Group

Journal of Clinical Oncology 2020 38:15_suppl, 1003-1003

PHOEBE phase 3 trial: study design



ClinicalTrials.gov number, NCT03080805

Stratification factors:

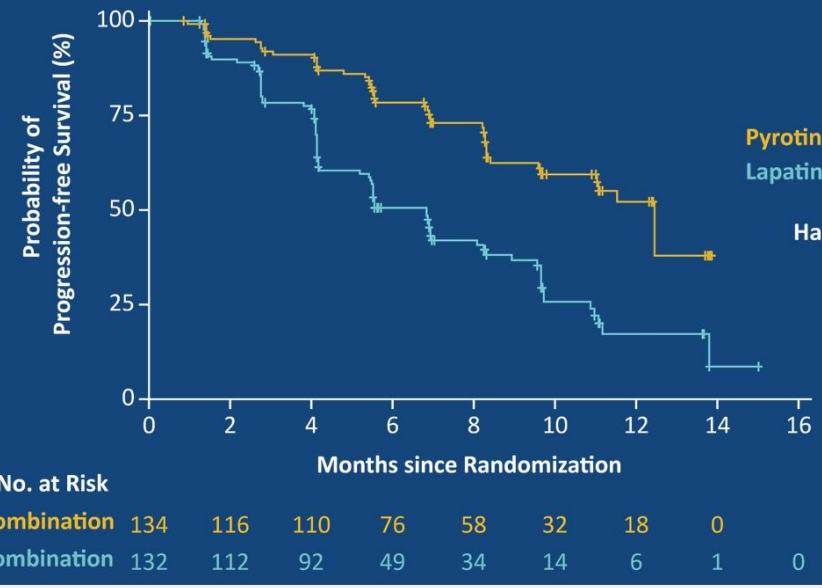
- Hormone receptor status (ER- and/or PR-positive *versus* ER- and PR-negative)
- Prior lines of chemotherapy for metastatic disease (≤1 *versus* 2)

BICR: blinded independent central review. OS: overall survival. DoR, duration of response. CBR: clinical benefit rate. TTP: time to progression.

Tumour response was assessed according to RECIST v1.1.

Binghe Xu, et al. ASCO©2020. Abstract 1003

Primary endpoint: PFS assessed by BICR



Median PFS (95% CI) months	
Pyrotinib Combination	12.5 (9.7 to NR)
Lapatinib Combination	6.8 (5.4 to 8.1)

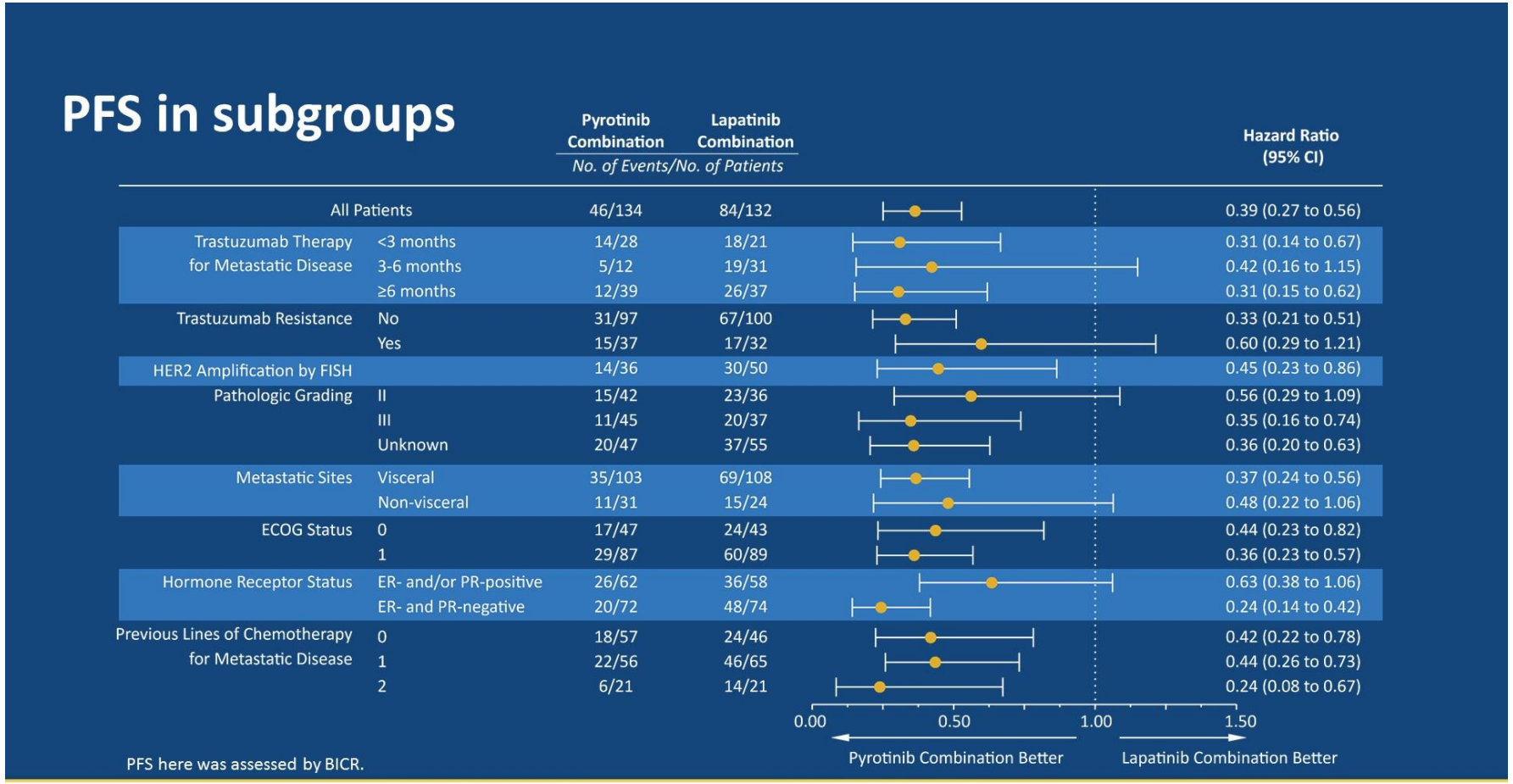
Hazard Ratio, 0.39 (95% CI 0.27 to 0.56); one-sided p<0.0001

No. at Risk								
Pyrotinib Combination	134	116	110	76	58	32	18	0
Lapatinib Combination	132	112	92	49	34	14	6	1	0

Statistically significant and clinically meaningful improvement in PFS

Comparison between groups was conducted with the log-rank test stratified by the randomization strata.

Binghe Xu, et al. ASCO©2020. Abstract 1003



Výsledok konzistentný v analýze preddefinovaných podskupín aj u pacientov rezistentných na Trastuzumab.

Binghe Xu, et al. ASCO©2020. Abstract 1003

Efficacy of HER2 TKIs and Capecitabine

	PHOEBE Phase III		NALA		HER2CLIMB	
	Capecitabine		Capecitabine		Capecitabine + Trastuzumab	
	Pyrotinib	Lapatinib	Neratinib	Lapatinib	Tucatinib	Placebo
N	267		621		480 (612)	
Median prior lines	1 (0-2)		2 (2-NA)		3 (1-14)	
Prior T+P and T-DM1	0%		35%		100%	
CNS disease	0%		16%		48%	
ORR	67%	52%	33%	27%	41%	23%
PFS	HR=0.39		HR=0.76		HR=0.54	
	12.5m	6.8m	8.8m	6.6m	7.8m	5.6m
OS	HR=0.46		HR=0.88		HR=0.58	
	Not reached		29.2m	22.8m	18.1m	12.0m
Grade 3 diarrhea	31%		24%		13%	
	Xu B et al. ASCO 2020		Saura C et al. ASCO 2019		Murthy R.K. et al. NEJM 2020	

Aleix Prat, et al. ASCO©2020. Oral Abstract Session

Current therapy landscape

1 LINE	2 LINE	3 LINE
T+P + taxane	T-DM1	Tucatinib + T + Cape

DS-8201a

Neratinib + Cape

Lapatinib + Cape or T

T+chemo

Pyrotinib + Cape

Margetuximab + chemo

Aleix Prat, et al. ASCO©2020. Oral Abstract Session

Abstrakt č.: 1038

Addition of endocrine therapy to dual anti-HER2 targeted therapy in initial treatment of HER2+/HR+ metastatic breast cancer.

Matthew Loft, Sheau Wen Lok, Richard H. De Boer, Laeeq Malik, Sally Greenberg, Belinda Yeo, Angelyn Anton, Louise M. Nott, Gary Edward Richardson, Ian M. Collins, Javier Torres, Frances Sarah Barnett, Bianca Alix Devitt, Peter Gibbs, and Lucy Gately

Journal of Clinical Oncology 2020 38:15_suppl, 1038-1038

Characteristic	With endocrine n = 78 (59%)	Without endocrine n = 54 (41%)	*p* value
Age			
Median (IQR)	56 (45 – 67)	59 (48 – 69)	0.355
Metastatic at diagnosis			
Yes	31 (39.7%)	31 (57.4%)	0.053
No	47 (60.3%)	23 (42.6%)	
Adjuvant HER2 therapy	n = 47	n = 23	
Yes	33 (70.2%)	13 (56.5%)	0.292
No	14 (29.8%)	10 (43.5%)	
ECOG			
0-1	75 (96.2%)	50 (92.6%)	0.685
>2	3 (3.8%)	3 (5.6%)	
Unknown	0 (0%)	1 (1.8%)	
Hormone receptor status			
ER+, PR+	48 (61.5%)	24 (44.4%)	0.051
ER+, PR-	28 (35.9%)	24 (44.4%)	
ER-, PR+	2 (2.6%)	6 (11.1%)	
Median progression free survival	28.8 months	17.2 months	**0.004**
Median overall survival	63.2 months	34.3 months	**0.005**

Pridanie endokrinnej liečby asociované so zlepšením:

PFS (HR 2.1, 95 % CI 1.2-3.5, *p* = 0.007)

OS (HR 2.7, 95 % CI 1.2-5.5, *p* = 0.007)

Matthew Loft, et al. ASCO©2020. Abstract 1038

Metastatický karcinóm prsníka na ASCO© 2020

ER pozitívny karcinóm prsníka

Abstrakt č.: 1006

Alpelisib (ALP) + fulvestrant (FUL) in patients (pts) with *PIK3CA*-mutated (mut) hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) advanced breast cancer (ABC) previously treated with cyclin-dependent kinase 4/6 inhibitor (CDKi) + aromatase inhibitor (AI): BYLieve study results.

Hope S. Rugo, Florence Lerebours, Eva Ciruelos, Pamela Drullinsky, Manuel Ruiz Borrego, Patrick Neven, Yeon Hee Park, Aleix Prat, Thomas Bachelot, Dejan Juric, Nicholas C. Turner, Nickolas Sophos, Juan Pablo Zarate, Christina Arce, Yu-Ming Shen, and Stephen K. L. Chia
Journal of Clinical Oncology 2020 38:15_suppl, 1006-1006

BYLieve: A Phase 2, Open-Label, 3-Cohort, Noncomparative Trial (NCT03056755)

BYLieve
Alpelisib (BYL719) In patients with PIK3CA mutant, HR+, HER2- adVanced brEast cancer

Goal: In the post-CDKi setting, assess the efficacy and safety of alpelisib + ET (fulvestrant or letrozole) in patients with *PIK3CA*-mutated HR+, HER2– ABC

Men or pre-/postmenopausal[a] women with HR+, HER2– ABC with a *PIK3CA* mutation

- Last line of prior therapy: CDKi + ET, systemic chemotherapy or ET
- ECOG PS ≤2
- Measurable disease (per RECIST v1.1) or ≥1 predominantly lytic bone lesion

Patients who received CDKi + AI as immediate prior treatment (N=112)[b]
(Cohort A)
Alpelisib 300 mg oral QD + fulvestrant 500 mg[c]

Patients who received CDKi + fulvestrant as immediate prior treatment (N=112)
(Cohort B)
Alpelisib 300 mg oral QD + letrozole 2.5 mg[d]

Patients who progressed on/after AI and received chemotherapy or ET as immediate prior treatment (N=112)
(Cohort C)
Alpelisib 300 mg oral QD + fulvestrant 500 mg[c]

Primary endpoint

- Proportion of patients alive without PD at 6 months (RECIST v1.1) in each cohort
- **Secondary endpoints include**

(assessed in each cohort)

- PFS
- PFS2
- ORR, CBR, DOR
- OS
- Safety

Treatment crossover between cohorts is not permitted

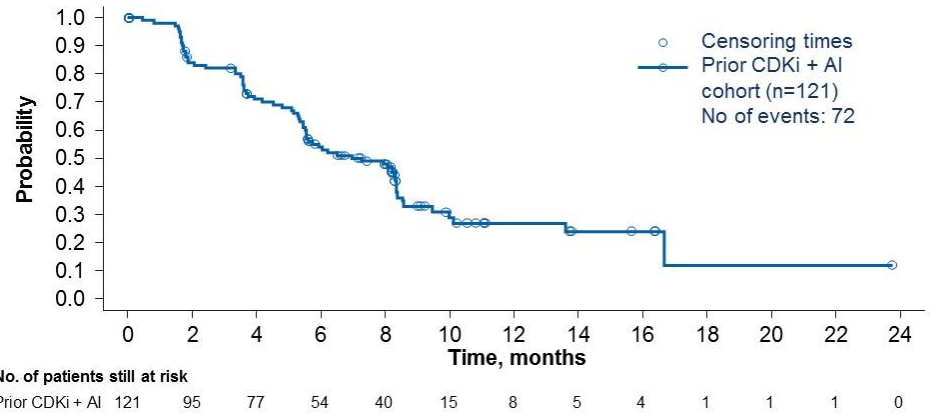
[a]Men in the letrozole cohort and premenopausal women also received goserelin 3.6 mg SC every 28 days or leuprolide 7.5 mg IM every 28 days for adequate gonadal suppression. [b]Enrollment in each cohort continued until at least 112 patients with a centrally confirmed *PIK3CA* mutation was reached. [c]IM on D1 and D15 of Cycle 1 and D1 for all other cycles thereafter. [d]Oral QD.
ABC, advanced breast cancer; AI, aromatase inhibitor; CDKi, cyclin-dependent kinase inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; CBR, clinical benefit rate; D, day; DOR, duration of response; IM, intramuscularly; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, PFS on next-line treatment; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; RECIST, Response Evaluation Criteria In Solid Tumors; SC, subcutaneously; QD, once daily.

Hope S. Rugo, et al. ASCO©2020. Abstract 1006

Efficacy: Primary Endpoint and PFS Results

BYLieve
Alpelisib (BYL719) In patients with PIK3CA mutant, HR+, HER2- adVanced brEast cancer

Endpoint	Prior CDKi + AI (Cohort A) (n=121)
Primary endpoint: Patients who were alive without disease progression at 6 mo	**50.4%** (n=61; 95% CI, 41.2-59.6)
Secondary endpoint: Median PFS	**7.3 mo** [n=72 (59.5%) with event]; 95% CI, 5.6-8.3)



The primary endpoint for the prior CDKi + AI cohort was met (lower bound of 95% CI was > 30%), with 50.4% of patients alive without disease progression at 6 months

- In SOLAR-1, 44.4% of patients in the *PIK3CA*-mutant cohort with prior CDKi treated with alpelisib plus fulvestrant were alive without disease progression at 6 months

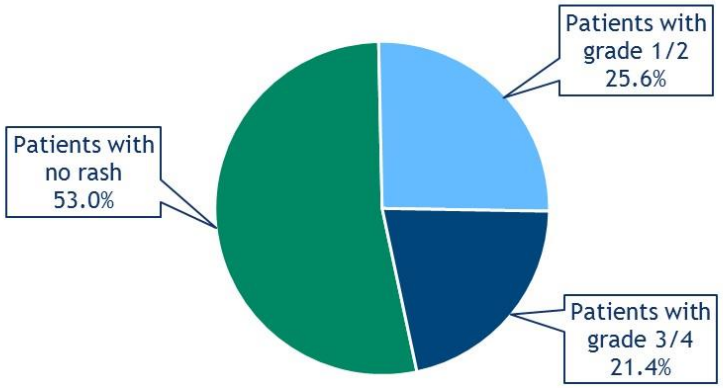
AI, aromatase inhibitor; CDKi, cyclin-dependent kinase inhibitor; CI, confidence interval; PFS, progression-free survival; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

Hope S. Rugo, et al. ASCO©2020. Abstract 1006

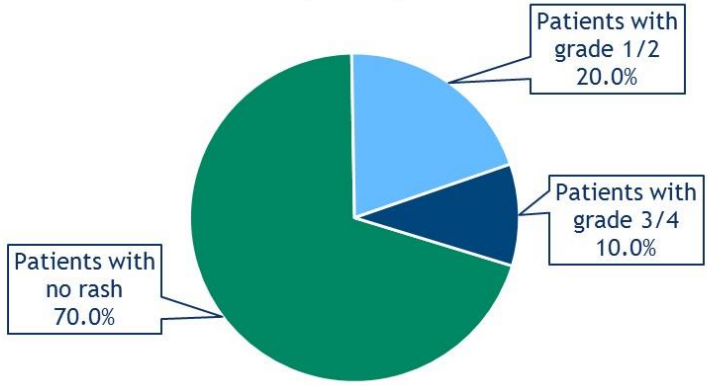
Incidence of Rash in Patients With/Without Prophylactic Antihistamines

BYLieve
Alpelisib (BYL719) In patients with PIK3CA mutant, HR+, HER2- adVanced brEast cancer

Patients who did not receive antihistamines or received antihistamines after rash (n=117)



Patients who received antihistamines before rash or had no event (n=10)



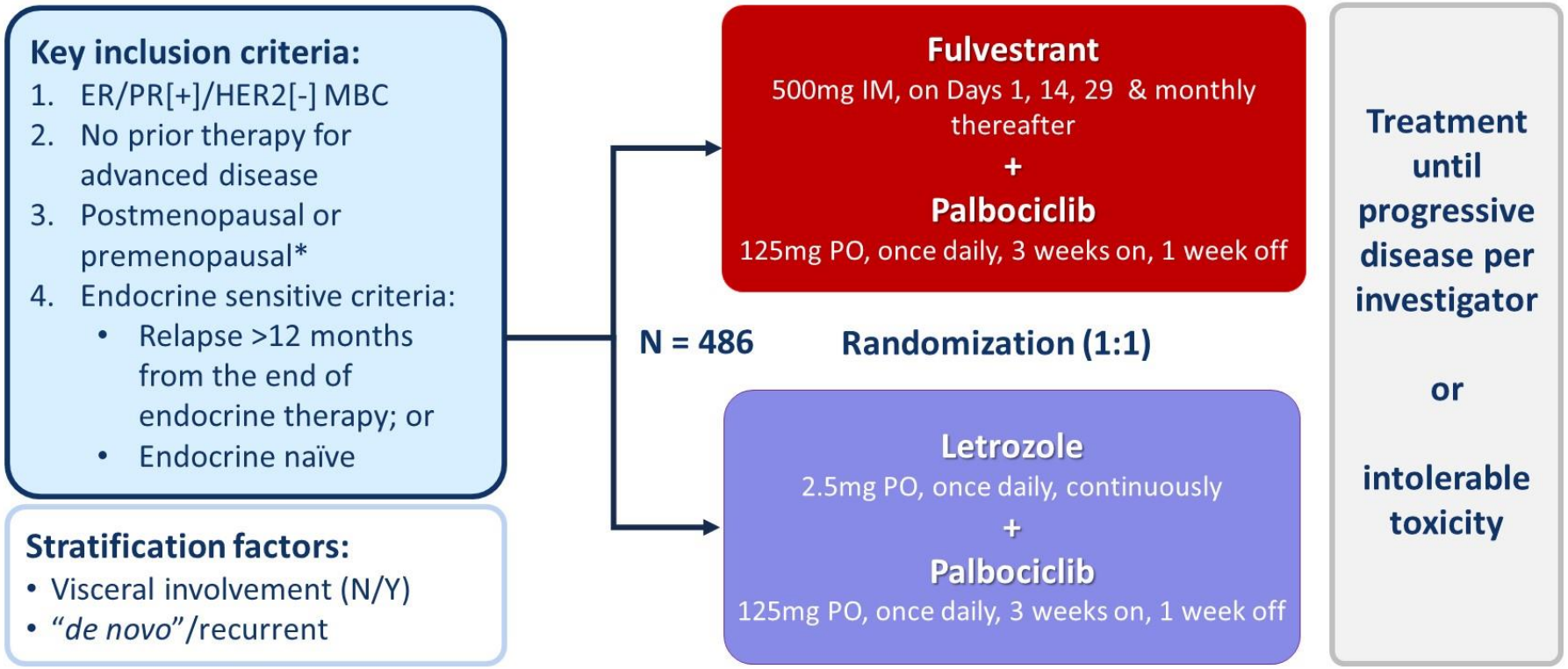
Hope S. Rugo, et al. ASCO©2020. Abstract 1006

Abstrakt č.: 1007

PARSIFAL: A randomized, multicenter, open-label, phase II trial to evaluate palbociclib in combination with fulvestrant or letrozole in endocrine-sensitive patients with estrogen receptor (ER)[+]/HER2[-] metastatic breast cancer.

Antonio Llombart-Cussac, José Manuel Pérez-García, Meritxell Bellet, Florence Dalenc, Miguel J. Gil Gil, Manuel Ruiz Borrego, Joaquín Gavilá, Miguel Sampayo-Cordero, Elena Aguirre, Peter Schmid, Frederik Marmé, Serena Di Cosimo, Joseph Gligorov, Andreas Schneeweiss, Joan Albanell, Pilar Zamora, Duncan Wheatley, Eduardo Martínez-De Dueñas, Kepa Amillano, and Javier Cortes
Journal of Clinical Oncology 2020 38:15_suppl, 1007-1007

PARSIFAL: Study Design

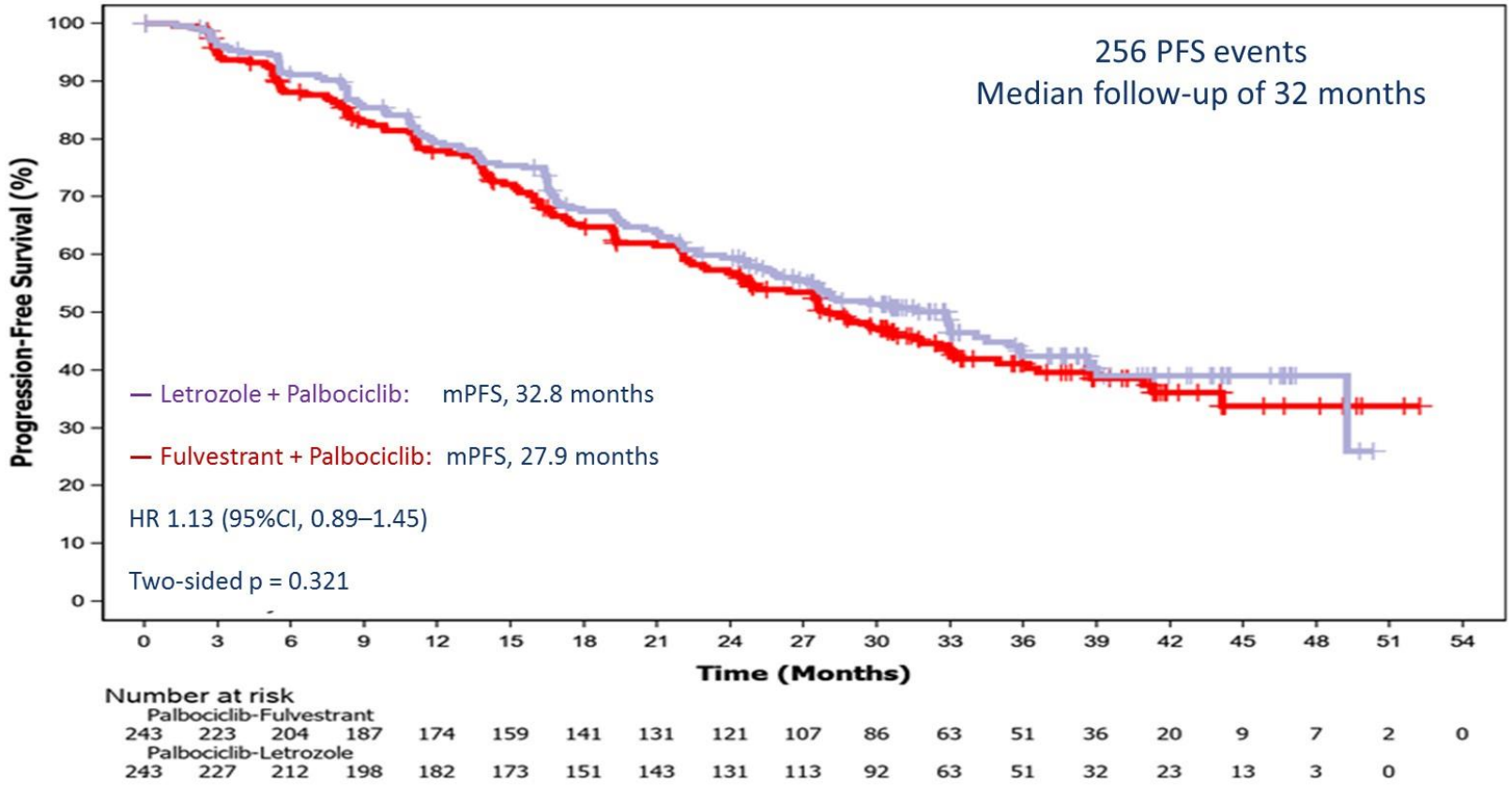


*If pre-menopausal, an ovarian suppression method was required.

ER: Estrogen receptor; HER2: Human Epidermal Growth Factor Receptor 2; IM: Intramuscular; MBC: Metastatic breast cancer; PO: Oral administration; PR: Progesterone receptor.

Antonio Llombart-Cussac, et al. ASCO©2020. Abstract 1007

Primary Objective PFS (ITT Population)

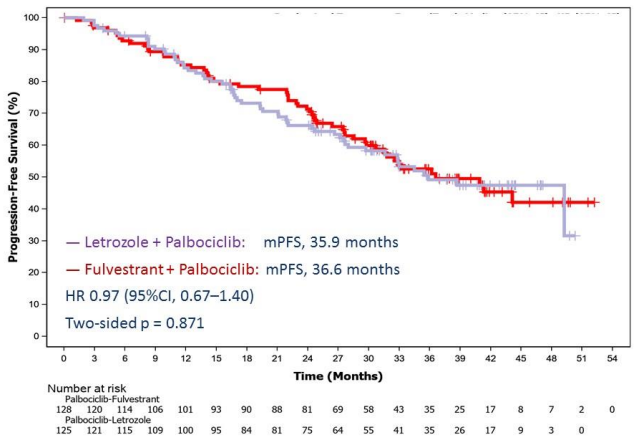


CI: Confidence interval; HR: Hazard ratio; ITT: Intention to treat; mPFS: Median progression-free survival; PFS: Progression-free survival.

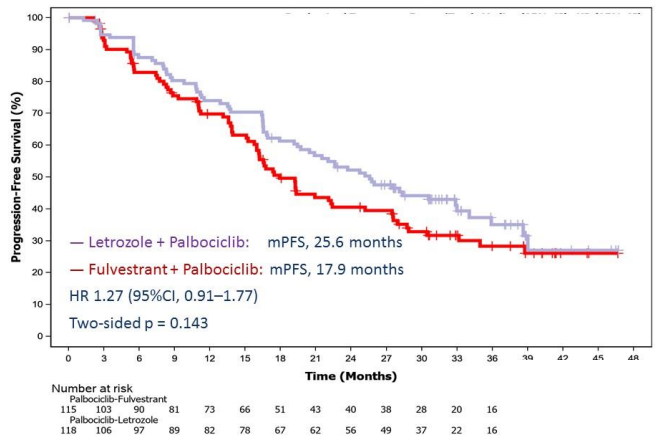
Antonio Llombart-Cussac, et al. ASCO©2020. Abstract 1007

PFS by Visceral Disease (ITT Population)

Non-visceral disease



Visceral disease

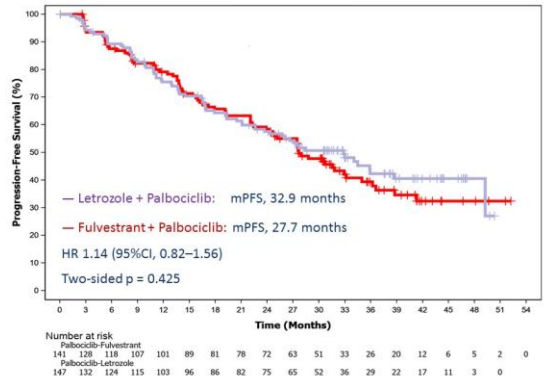


Interaction p-value = 0.275

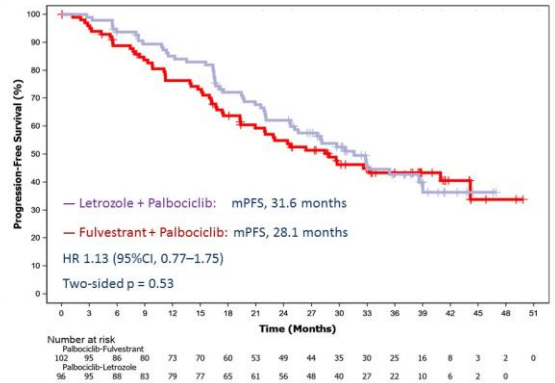
CI: Confidence interval; HR: Hazard ratio; ITT: Intention to treat; mPFS, Median progression-free survival; PFS, Progression-free survival.

PFS by Disease Presentation (ITT Population)

Recurrent



De novo



Interaction p-value = 0.979

CI, Confidence interval; HR: Hazard ratio; ITT, Intention to treat; mPFS, Median progression-free survival; PFS, Progression-free survival.

Antonio Llombart-Cussac, et al. ASCO©2020. Abstract 1007

Abstrakt č.: 1054

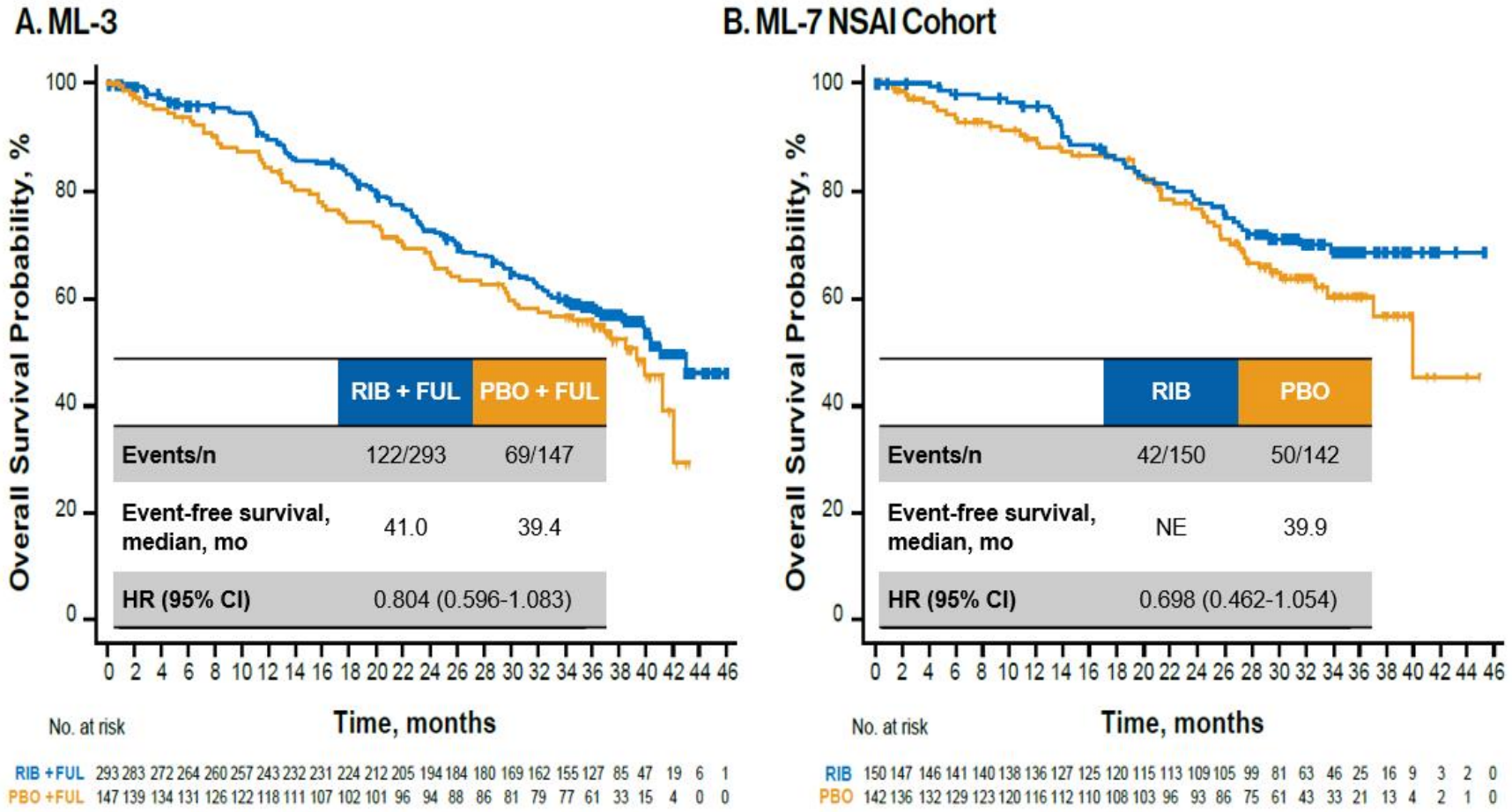
Overall survival (OS) in patients (pts) with advanced breast cancer (ABC) with visceral metastases (mets), including those with liver mets, treated with ribociclib (RIB) plus endocrine therapy (ET) in the MONALEESA (ML) -3 and -7 trials.

Denise A. Yardley, Arnd Nusch, Yoon Sim Yap, Gabe S. Sonke, Thomas Bachelot, Arlene Chan, Patrick Neven, Dennis J. Slamon, Paul Wheatley-Price, Agnes Lteif, Manu Sondhi, Karen Rodriguez-Lorenc, Anil Gaur, and Stephen K. L. Chia
Journal of Clinical Oncology 2020 38:15_suppl, 1054-1054

	ML-3 RIB + FUL	ML-3 PBO + FUL	ML-7 RIB + NSAI	ML-7 PBO + NSAI
Visceral metastases, n	293	147	150	142
PFS events, n (%)	182 (62.1)	117 (79.6)	82 (54.7)	103 (72.5)
PFS, median (95% CI), mo	16.6 (13.4-19.9)	10.6 (5.5-12.9)	23.9 (16.4-30.4)	10.4 (7.2-12.9)
HR (95% CI)	0.616 (0.487-0.779)		0.541 (0.404-0.725)	
Best overall response, n (%)				
Complete response	10 (3.4)	0	5 (3.3)	4 (2.8)
Partial response	111 (37.9)	36 (24.5)	74 (49.3)	48 (33.8)
Stable disease	102 (34.8)	56 (38.1)	41 (27.3)	46 (32.4)
Progressive disease	37 (12.6)	34 (23.1)	12 (8.0)	31 (21.8)
Overall response rate, n (%)	121 (41.3)	36 (24.5)	79 (52.7)	52 (36.6)
95% CI	35.7-46.9	17.5-31.4	44.7-60.7	28.7-44.5

Denise A. Yardley, et al. ASCO©2020. Abstract 1054

Pacientky s viscerálnymi metastázami



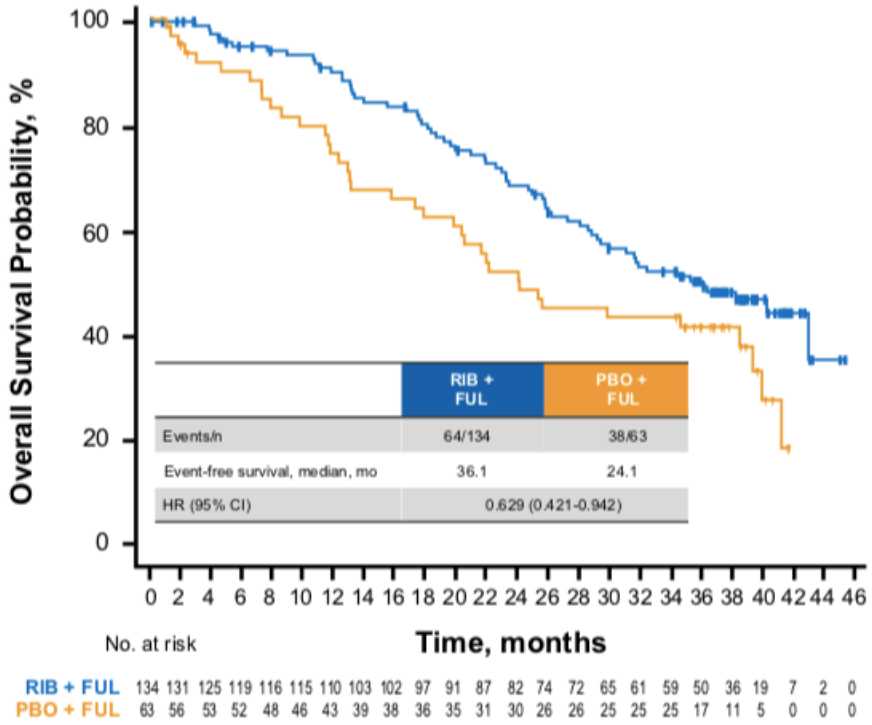
Výsledok OS konzistentný s celkovou populáciou ML3 a ML7.

Najčastejšie parciálne remisie ochorenia.

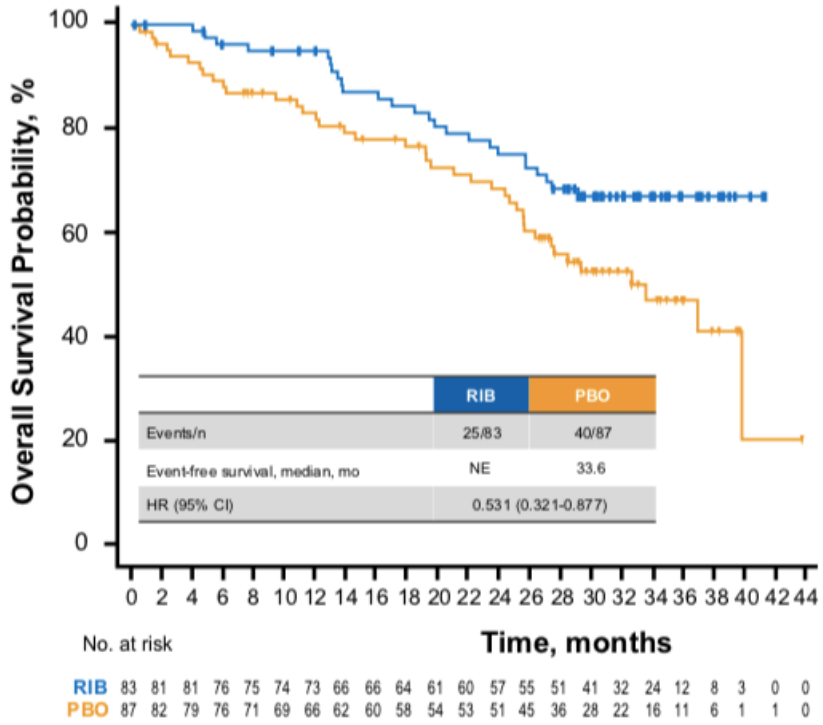
Denise A. Yardley, et al. ASCO©2020. Abstract 1054

Pacientky s pečeňovými metastázami

A. ML-3



B. ML-7 NSAI Cohort



Výsledok OS konzistentný s celkovou populáciou ML3 a ML7.

Najčastejšie parciálne remisie ochorenia.

37 % redukcia rizika úmrtia ML-3

47 % redukcia rizika úmrtia ML-7

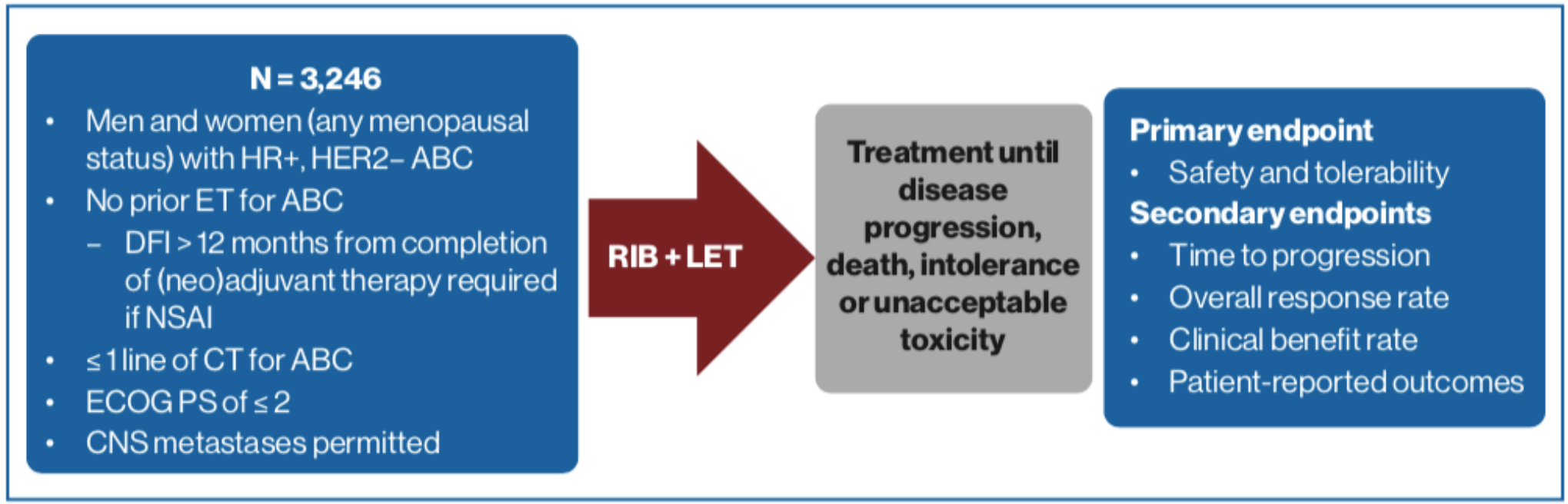
Denise A. Yardley, et al. ASCO©2020. Abstract 1054

Abstrakt č.: 1055

Updated results from the phase IIIb complement-1 study of ribociclib (RIB) plus letrozole (LET) in the treatment of HR+, HER2- advanced breast cancer (ABC).

Michelino De Laurentiis, Simona Borstnar, Mario Campone, Ellen Warner, Javier Salvador Bofill, William Jacot, Susan Faye Dent, Miguel Martin, Alistair E. Ring, Paul H. Cottu, Janice M. Lu, Eva Ciruelos, Hamdy A. Azim, Sanjoy Chatterjee, Katie Zhou, Jiwen Wu, Nii Ankrah, and Claudio Zamagni

Journal of Clinical Oncology 2020 38:15_suppl, 1055-1055



Michelino De Laurentiis, et al. ASCO©2020. Abstract 1055

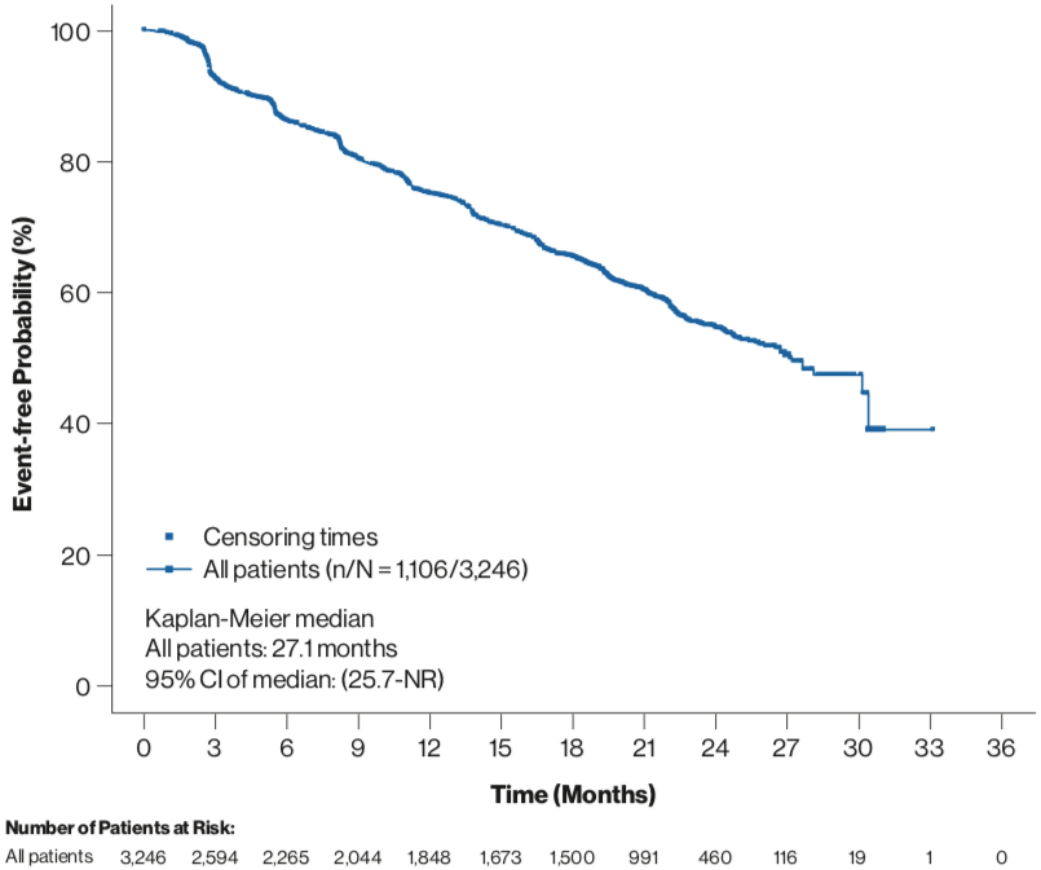
Characteristic	All Patients (N = 3,246)
Median age, years (range)	58.0 (20-92)
Age ≥ 65 years, n (%)	1,073 (33.1)
Male patients, n (%)	39 (1.2)
Premenopausal female patients, n (%)	722 (22.2)
Patient race, n (%)	
Caucasian	2,553 (78.7)
Asian	227 (7.0)
Black	29 (0.9)
Native American	18 (0.6)
Pacific Islander	1 (0.03)
Other/unknown	418 (12.9)
ECOG PS 2, n (%)	112 (3.5)
Patients with de novo advanced disease, n (%)	1,041 (32.1)
Patients with > 2 metastatic sites, n (%)	1,405 (43.3)
Patients with visceral disease, n (%)	1,992 (61.4)
Patients with CNS lesions, n (%)	51 (1.6)
Patients given chemotherapy for advanced disease, n (%)	194 (6.0)

CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status.

	All Patients (N = 3,246)	
	All Grades, n (%)	Grade ≥ 3, n (%)
Number of patients with at least 1 event	3,203 (98.7)	2,461 (75.8)
Neutropenia[a]	2,417 (74.5)	1,856 (57.2)
Nausea	1,166 (35.9)	26 (0.8)
Leukopenia[b]	887 (27.3)	345 (10.6)
Fatigue	760 (23.4)	49 (1.5)
Diarrhea	690 (21.3)	47 (1.4)
Arthralgia	677 (20.9)	14 (0.4)
Vomiting	649 (20.0)	34 (1.0)
Alopecia	638 (19.7)	—
Asthenia	632 (19.5)	34 (1.0)
Anemia	605 (18.6)	94 (2.9)
Constipation	554 (17.1)	11 (0.3)
ALT increased	526 (16.2)	249 (7.7)
Cough	493 (15.2)	4 (0.1)
Hot flush	490 (15.1)	5 (0.2)
Headache	462 (14.2)	15 (0.5)
AST increased	459 (14.1)	184 (5.7)
Back pain	437 (13.5)	29 (0.9)
Pruritus	431 (13.3)	10 (0.3)
Pyrexia	415 (12.8)	21 (0.6)
Decreased appetite	402 (12.4)	13 (0.4)
Rash	374 (11.5)	21 (0.6)

A patient with multiple severity grades for an AE was only counted under the maximum grade.
[a] Includes "neutropenia" and "neutrophil count decreased."
[b] Includes "leukopenia" and "white blood cell count decreased."
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Michelino De Laurentiis, et al. ASCO©2020. Abstract 1055



	All Patients (N = 3,246)	Patients With Measurable Disease at Baseline (n = 2,079 [64.0%])
Best overall response[a]		
CR, n (%)	99 (3.0)	56 (2.7)
PR, n (%)	851 (26.2)	851 (40.9)
Non-CR/Non-PD, n (%)[b]	952 (29.3)	—
SD, n (%)	813 (25.0)	810 (39.0)
PD, n (%)	178 (5.5)	134 (6.4)
Unknown, n (%)	353 (10.9)	228 (11.0)
ORR, n (% [95% CI])[c]	950 (29.3 [27.7-30.9])	907 (43.6 [41.5-45.8])
CBR, n (% [95% CI])[d]	2,294 (70.7 [69.1-72.2])	1,437 (69.1 [67.1-71.1])

Michelino De Laurentiis, et al. ASCO©2020. Abstract 1055

Metastatický karcinóm prsníka na ASCO© 2020

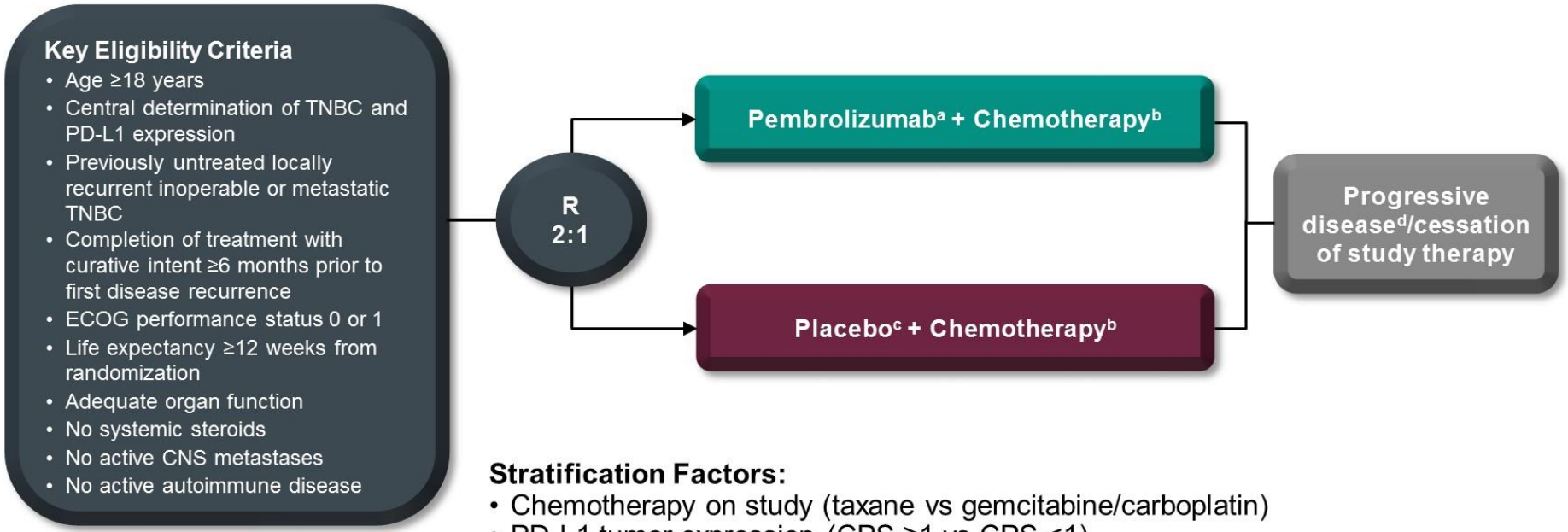
Trojito negatívny karcinóm prsníka

Abstrakt č.: 1000

KEYNOTE-355: Randomized, double-blind, phase III study of pembrolizumab + chemotherapy versus placebo + chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer.

Javier Cortes, David W. Cescon, Hope S. Rugo, Zbigniew Nowecki, Seock-Ah Im, Mastura Md Yusof, Carlos Gallardo, Oleg Lipatov, Carlos Henrique Barrios, Esther Holgado, Hiroji Iwata, Norikazu Masuda, Marco Torregroza Otero, Erhan Gokmen, Sherene Loi, Zifang Guo, Jing Zhao, Gursel Aktan, Vassiliki Karantza, and Peter Schmid
Journal of Clinical Oncology 2020 38:15_suppl, 1000-1000

KEYNOTE-355 Study Design (NCT02819518)



Stratification Factors:
- Chemotherapy on study (taxane vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥1 vs CPS <1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

[a]Pembrolizumab 200 mg intravenous (IV) every 3 weeks (Q3W)
[b]Chemotherapy dosing regimens are as follows:
Nab-paclitaxel 100 mg/m^2 IV on days 1, 8, and 15 every 28 days
Paclitaxel 90 mg/m^2 IV on days 1, 8, and 15 every 28 days
Gemcitabine 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days

[c]Normal saline
[d]Treatment may be continued until confirmation of progressive disease
CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group; PD-L1=programmed death ligand 1; R=randomized; TNBC=triple-negative breast cancer

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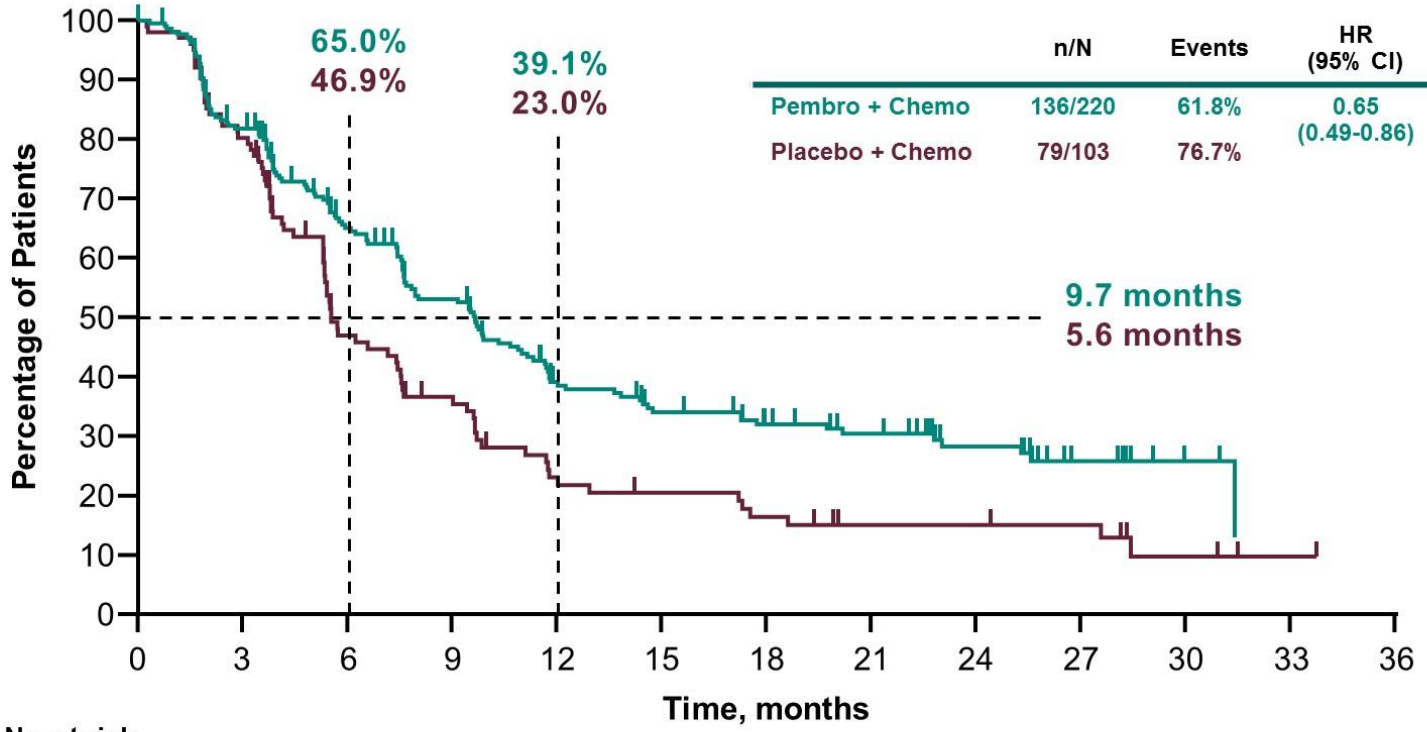
Progression-Free Survival: PD-L1 CPS ≥10



	n/N	Events	HR (95% CI)	P-value (one-sided)
Pembro + Chemo	136/220	61.8%	0.65 (0.49-0.86)	0.0012[a]
Placebo + Chemo	79/103	76.7%		

No. at risk

220	173	122	96	63	52	44	37	25	12	5	0	0
103	80	41	30	18	15	12	8	8	7	3	1	0

[a]Prespecified *P* value boundary of 0.00411 met.
Hazard ratio (CI) analyzed based on a Cox regression model with treatment as a covariate stratified by the randomization stratification factors. Data cutoff December 11, 2019.

Javier Cortes, et al. ASCO©2020. Abstract 1000

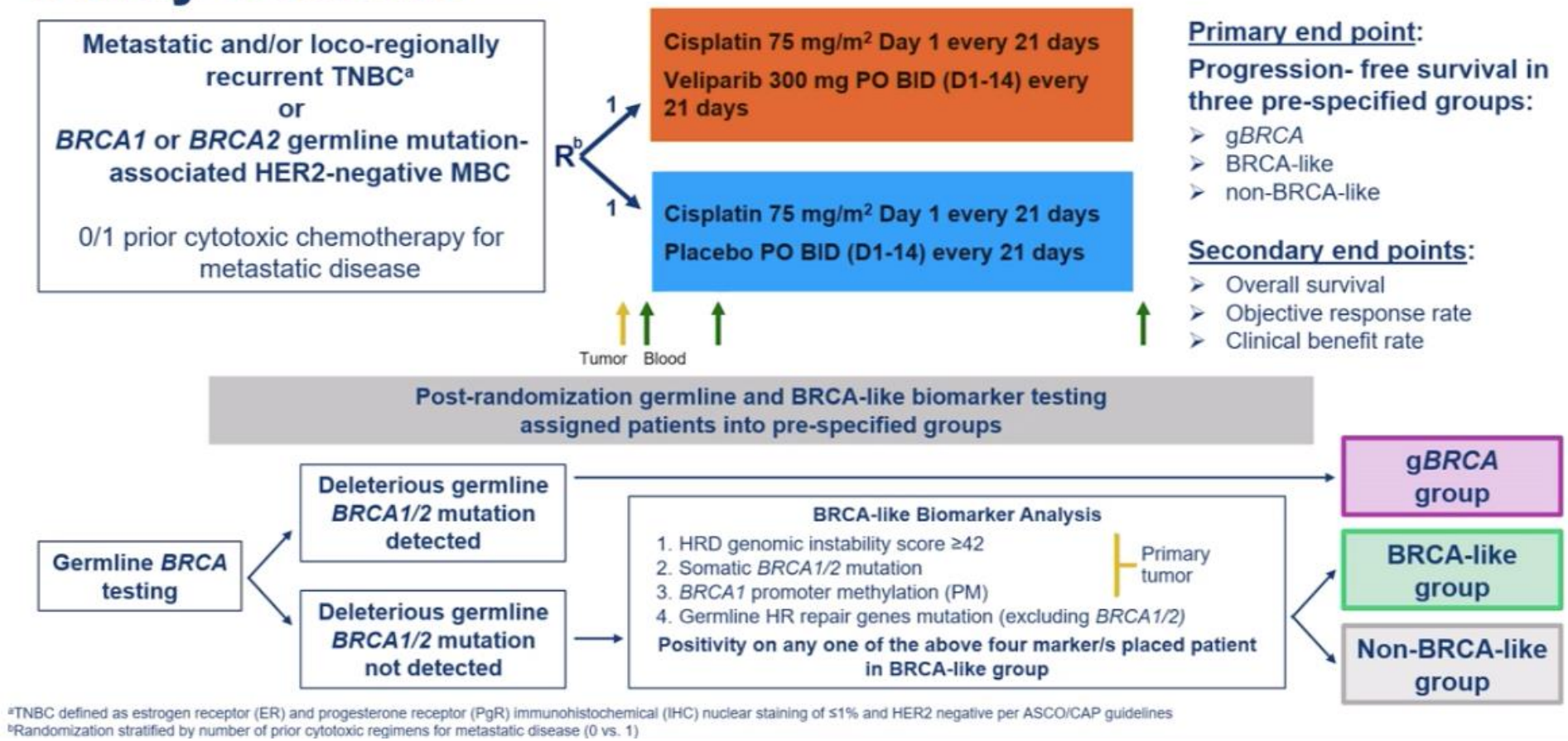
Abstrakt č.: 1001

Results of a phase II randomized trial of cisplatin +/- veliparib in metastatic triple-negative breast cancer (TNBC) and/or germline *BRCA*-associated breast cancer (SWOG S1416).

Priyanka Sharma, Eve Rodler, William E. Barlow, Julie Gralow, Shannon Leigh Huggins-Puhalla, Carey K. Anders, Lori J. Goldstein, Ursa Abigail Brown-Glaberman, Thu-Tam Huynh, Christopher Scott Szyarto, Andrew K. Godwin, Harsh B Pathak, Elizabeth M. Swisher, Marc R Radke, Kirsten M Timms, Danika L. Lew, Jieling Miao, Lajos Pusztai, Daniel F. Hayes, and Gabriel N. Hortobagyi

Journal of Clinical Oncology 2020 38:15_suppl, 1001-1001

Study schema

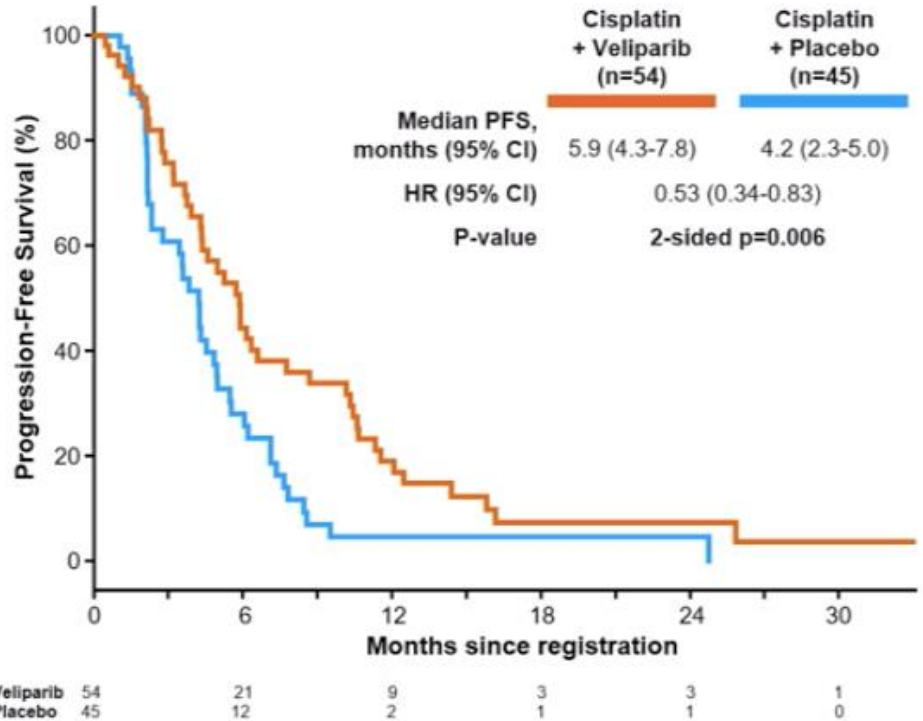


[a]TNBC defined as estrogen receptor (ER) and progesterone receptor (PgR) immunohistochemical (IHC) nuclear staining of ≤1% and HER2 negative per ASCO/CAP guidelines
[b]Randomization stratified by number of prior cytotoxic regimens for metastatic disease (0 vs. 1)

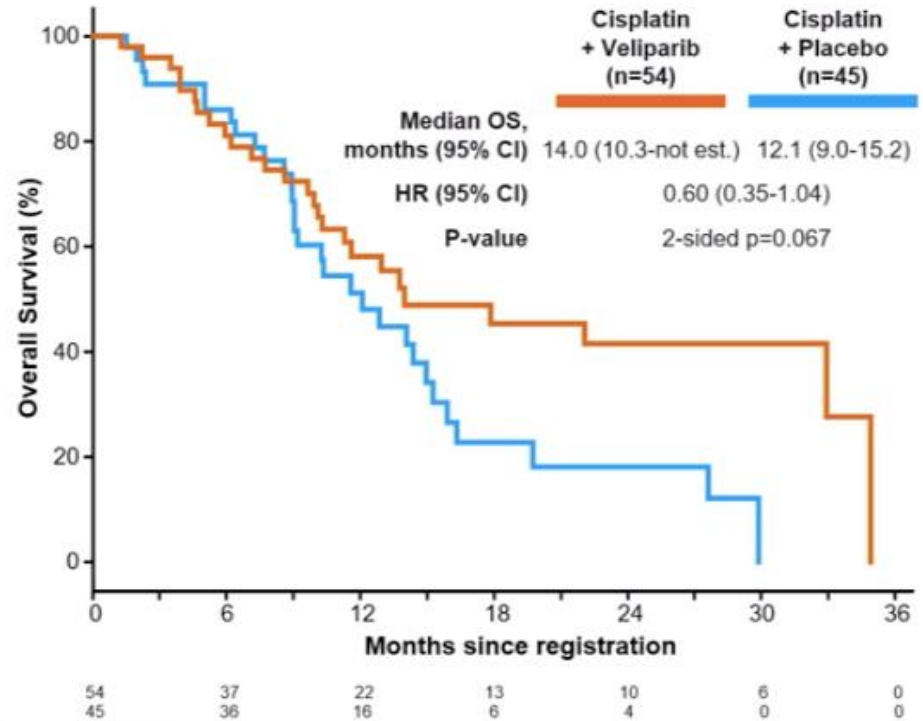
Priyanka Sharma, et al. ASCO©2020. Abstract 1001

BRCA-like group

Progression-free survival



Overall survival



ORR (n=83): 45% vs 33%

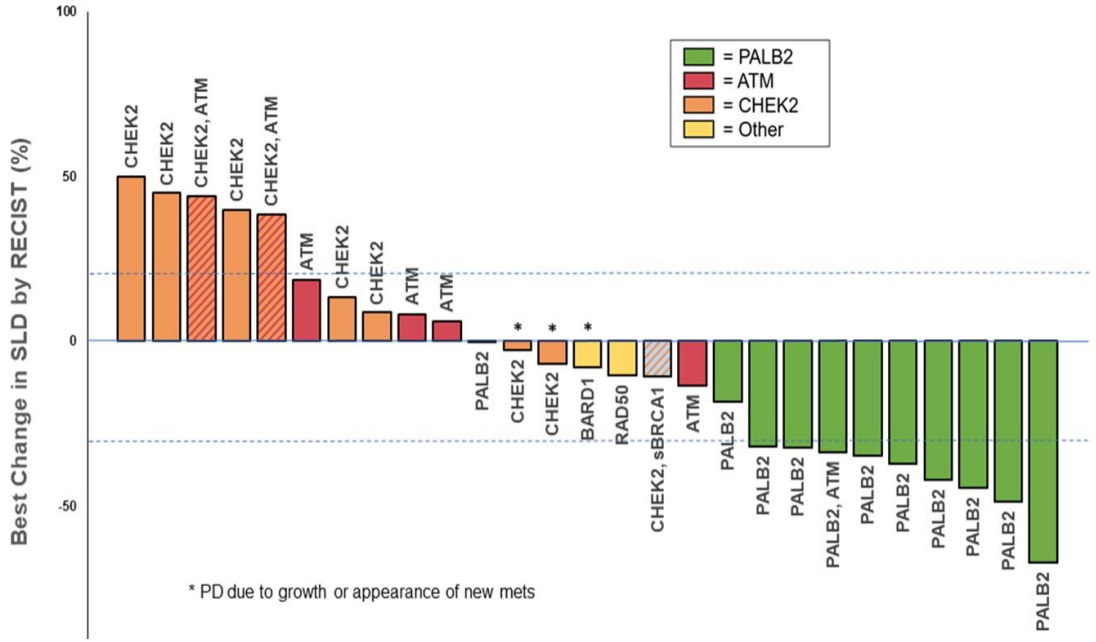
Priyanka Sharma, et al. ASCO©2020. Abstract 1001

Abstrakt č.: 1002

TBCRC 048: A phase II study of olaparib monotherapy in metastatic breast cancer patients with germline or somatic mutations in DNA damage response (DDR) pathway genes (Olaparib Expanded).

Nadine M. Tung, Mark E. Robson, Steffen Ventz, Cesar Augusto Santa-Maria, Paul Kelly Marcom, Rita Nanda, Payal D Shah, Tarah Jean Ballinger, Eddy Shih-Hsin Yang, Michelle E. Melisko, Adam Brufsky, Shaveta Vinayak, Michelle Demeo, Colby Jenkins, Susan M. Domchek, Gerburg M. Wulf, Ian E. Krop, Antonio C. Wolff, Eric P. Winer, Judy Ellen Garber, and Translational Breast Cancer Research Consortium
Journal of Clinical Oncology 2020 38:15_suppl, 1002-1002

Best Overall Responses: Cohort 1 (Germline)



Cohort 1 (Total) N=27	
Best Response	**Responses (rate, %)**
Complete Response (CR)	0 (0%)
Partial Response (PR)	9 (33%)
Stable Disease (SD)	8 (30%)
Progressive Disease (PD)	10 (37%)

ORR = 33% (9/27, 90%-CI: 19%-51%)

CBR (18 weeks) = 44% (11/25, 90%-CI: 27%-62%)

Nadine M. Tung, et al. ASCO©2020. Abstract 1002

Ďakujem pekne za pozornosť

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