



Wczesny rak piersi

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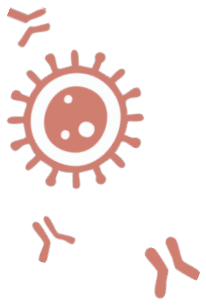




Rak HER2-dodatni

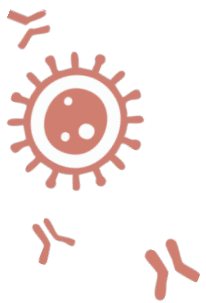
1. De-escalated neoadjuvant taxane plus trastuzumab and pertuzumab with or without carboplatin in HER2-positive early breast cancer (**neoCARHP**): A multicentre, open-label, randomised, phase 3 trial.
2. Predicting pathologic complete response (pCR) from clinicopathologic variables and HER2DX genomic test in stage II/III HER2+ breast cancer treated with taxane, trastuzumab, and pertuzumab (THP):
Secondary results from the **EA1181/CompassHER2 pCR trial**.
3. Prediction of survival after de-escalated neoadjuvant therapy in HER2+ early breast cancer: A pooled analysis of three **WSG trials**.



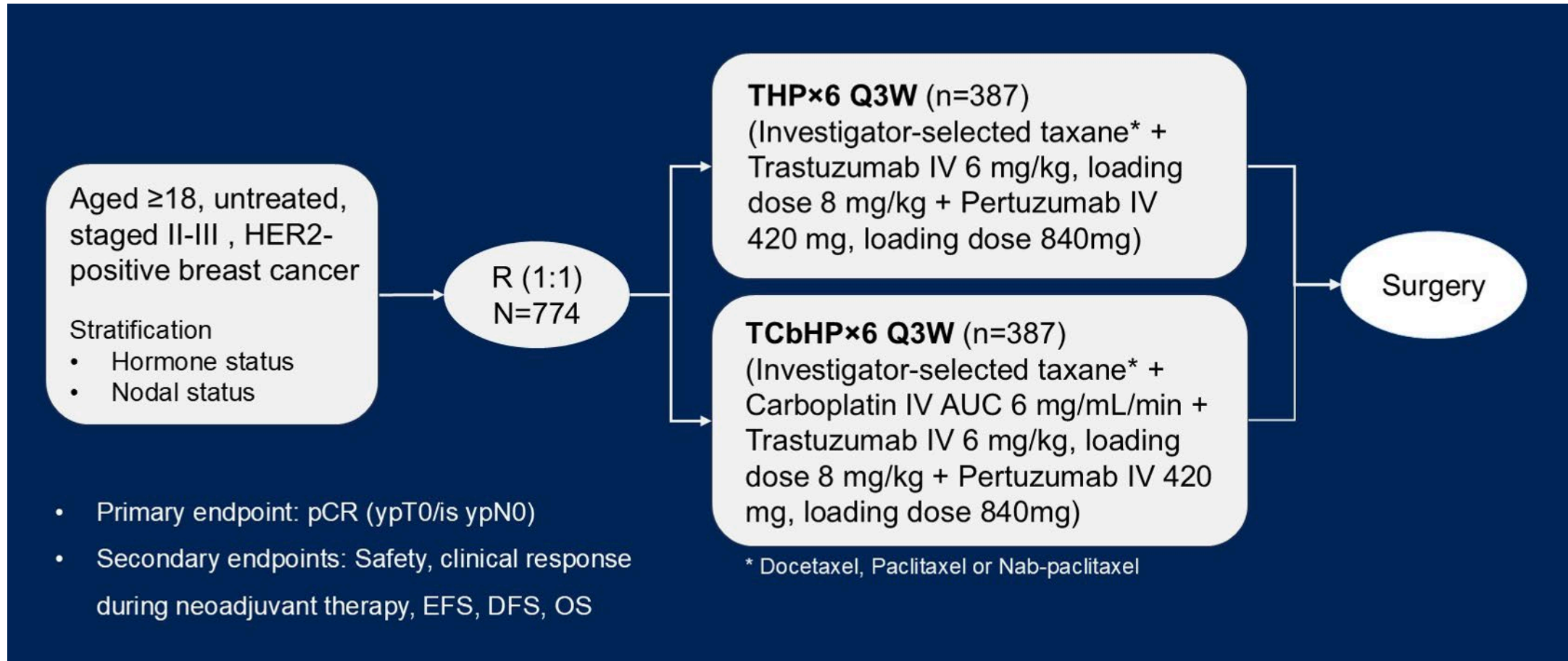


Randomizowane wieloośrodkowe badanie III fazy
oceniające skuteczność
przedoperacyjnej terapii opartej o
paklitaksel + trastuzumab + pertuzumab +/-
karboplatyna
– wyniki badania **neo CARHP**





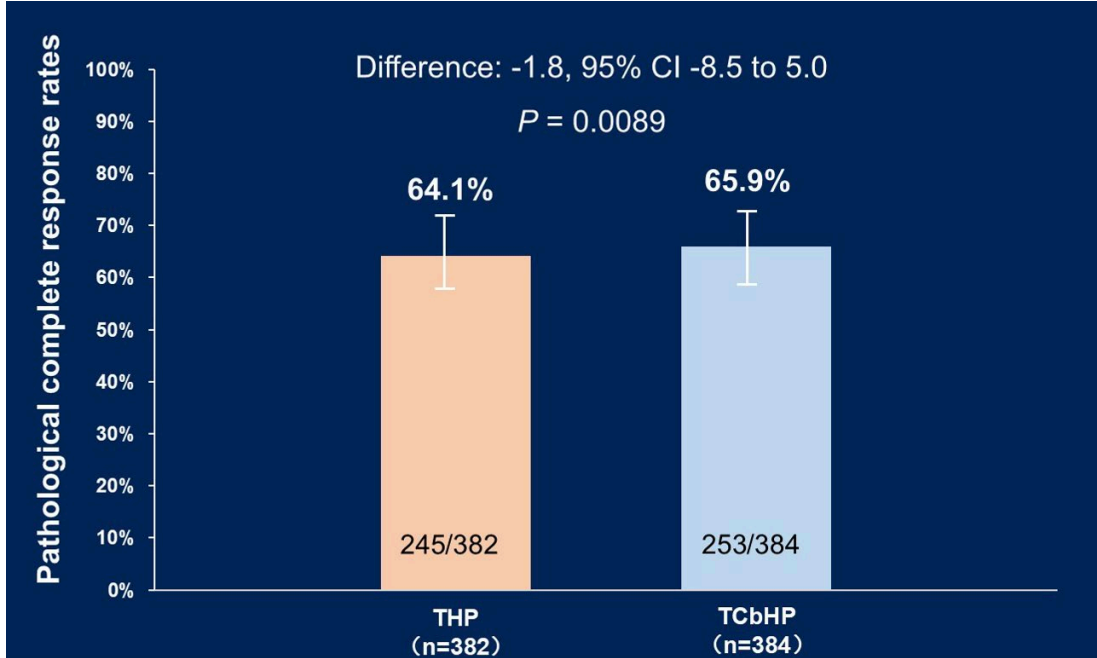
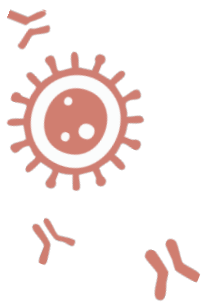
Schemat badania



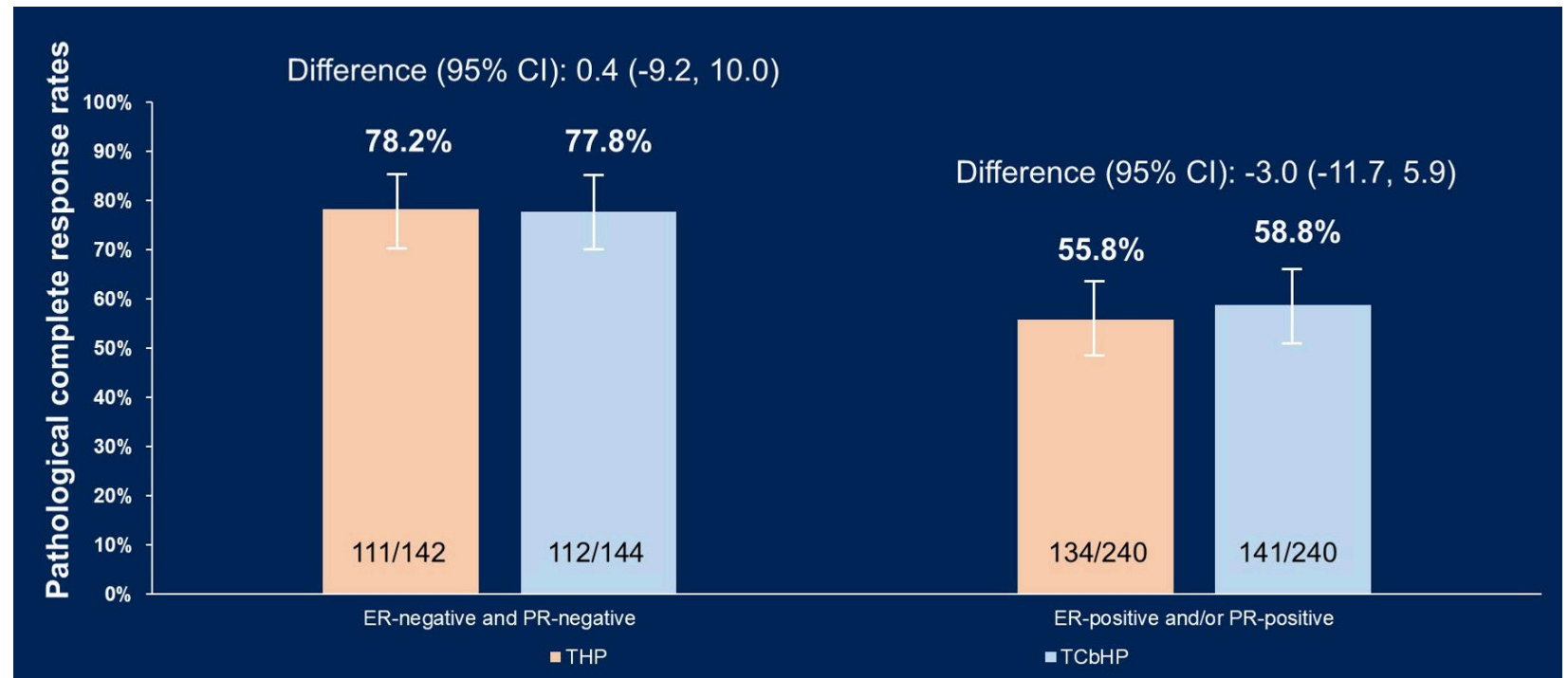
Charakterystyka pacjentów

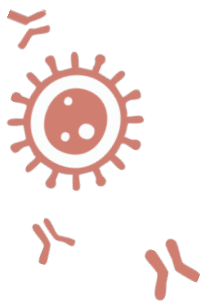
	THP (n=382)	TCbHP (n=384)		THP (n=382)	TCbHP (n=384)
Age (median [IQR], years)	52 (45-58)	51 (44-56)	Hormone receptor status, n (%)		
Menopausal status, n (%)			ER-negative and PR-negative	142 (37.2%)	144 (37.5%)
Premenopausal	191 (50.0%)	200 (52.1%)	ER-positive and/or PR-positive	240 (62.8%)	240 (62.5%)
Postmenopausal	191 (50.0%)	184 (47.9%)	HER2 status, n (%)		
T stage, n (%)			Immunohistochemistry 3+	338 (88.5%)	348 (90.6%)
T1-2	311 (81.4%)	302 (78.6%)	Immunohistochemistry 2+ and ISH-positive	44 (11.5%)	36 (9.4%)
T3-4	71 (18.6%)	82 (21.4%)	Ki67, n (%)		
Nodal status, n (%)			≤30%	163 (42.7%)	172 (44.8%)
Negative	137 (35.9%)	138 (35.9%)	>30%	219 (57.3%)	212 (55.2%)
Positive	245 (64.1%)	246 (64.1%)	Taxane therapy, n (%)		
Disease stage, n (%)			Nab-paclitaxel	170 (44.5%)	171 (44.5%)
Stage II	294 (77.0%)	275 (71.6%)	Docetaxel	137 (35.9%)	141 (36.7%)
Stage III	88 (23.0%)	109 (28.4%)	Paclitaxel	75 (19.6%)	72 (18.8%)
Histological type, n (%)					
Ductal	375 (98.2%)	376 (97.9%)			
Lobular	1 (0.3%)	2 (0.5%)			
Others	6 (1.6%)	6 (1.6%)			





Pierwszorzędowy punkt końcowy - pCR

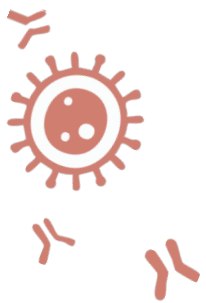




Odpowiedź w trakcie terapii neoadjuwantowej

Overall response in all breast tumours and nodes examined	THP (n=382)	TCbHP (n=384)
Complete or partial response	351 (91.9%, 95%CI: 88.7%-94.2%)	364 (94.8%, 95%CI: 92.1%-96.6%)
Non-responders (including unknown)	31 (8.1%, 95%CI: 5.8%-11.3%)	20 (5.2%, 95%CI: 3.4%-7.9%)





Tolerancja

AE term	THP (n=382) n (%)			TCbHP (n=384) n (%)		
	Grade 3	Grade 4	Total	Grade 3	Grade 4	Total
Neutropenia	14 (3.7%)	12 (3.1%)	26 (6.8%)	35 (9.1%)	28 (7.3%)	63 (16.4%)
Febrile neutropenia	5 (1.3%)	0	5 (1.3%)	10 (2.6%)	0	10 (2.6%)
Leucopenia	14 (3.7%)	7 (1.8%)	21 (5.5%)	45 (11.7%)	12 (3.1%)	57 (14.8%)
Thrombocytopenia	1 (0.3%)	0	1 (0.3%)	10 (2.6%)	6 (1.6%)	16 (4.2%)
Anaemia	8 (2.1%)	0	8 (2.1%)	24 (6.3%)	1 (0.3%)	25 (6.6%)





Podsumowanie

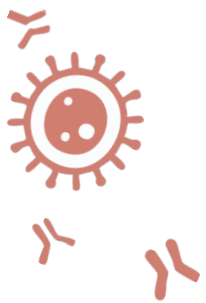
- Schemat THP był nie gorszy niż TCbHP pod względem częstości **pCR**
- Tolerancja leczenia THP była lepsza niż TCbHP
- Schemat bez karboplatyny jest możliwą opcją postępowania u wybranych chorych na HER2+ raka piersi w II i III stopniu zaawansowania





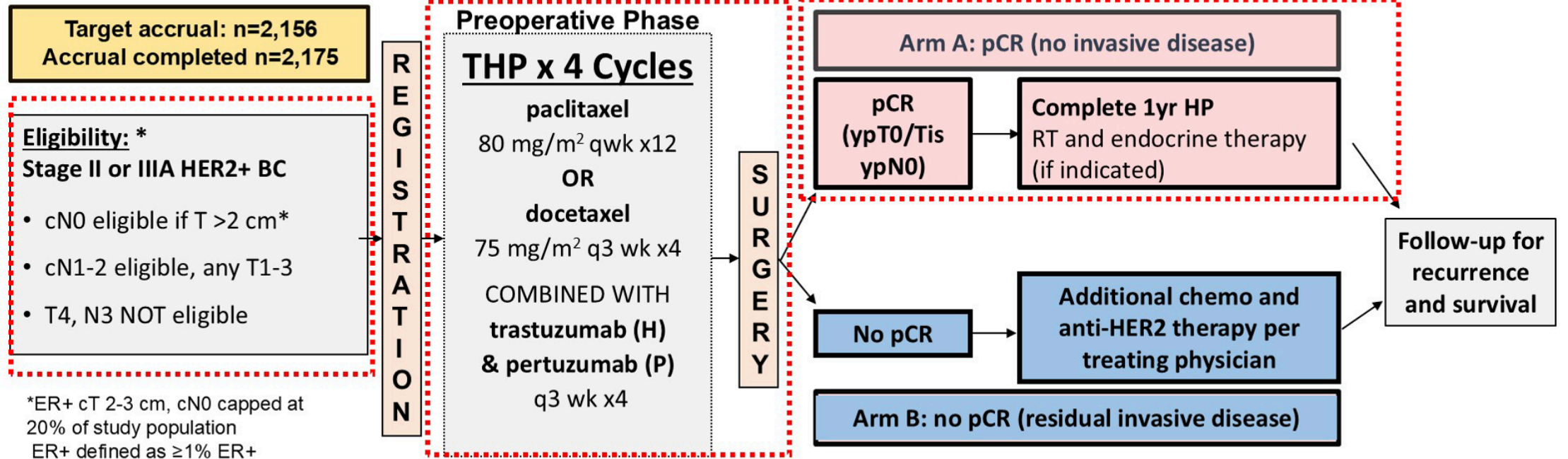
Ocena pCR na podstawie czynników kliniczno-
patologicznych oraz wyniku testu HER2DX u chorych
na raka HER2-dodatniego w II i III stopniu
zaawansowania leczonych taksanami +
trastuzumabem + pertuzumabem
– wyniki badania **CompassHER2 pCR**





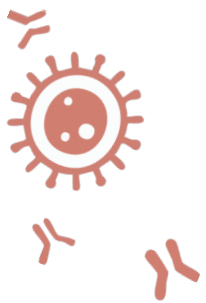
Schemat badania

Activation Feb 2020
Accrued thru Oct 2023



Primary objective: determine if 3yr RFS >92% in Arm A, separately for ER+/HER2+ and ER-/HER2+ cohorts





Charakterystyka pacjentów

Median age: 55 years
White race: 75%
ECOG PS 0: 88%
Clinical stage IIA: 58%
Clinical stage T2: 75%
Clinical stage N+: 46%

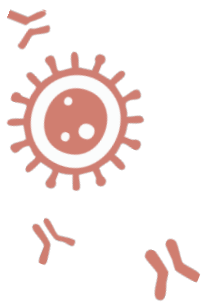
Taxane received: paclitaxel 63%

Pt characteristics similar for those with ER+/HER2+ and ER-/HER2+ disease

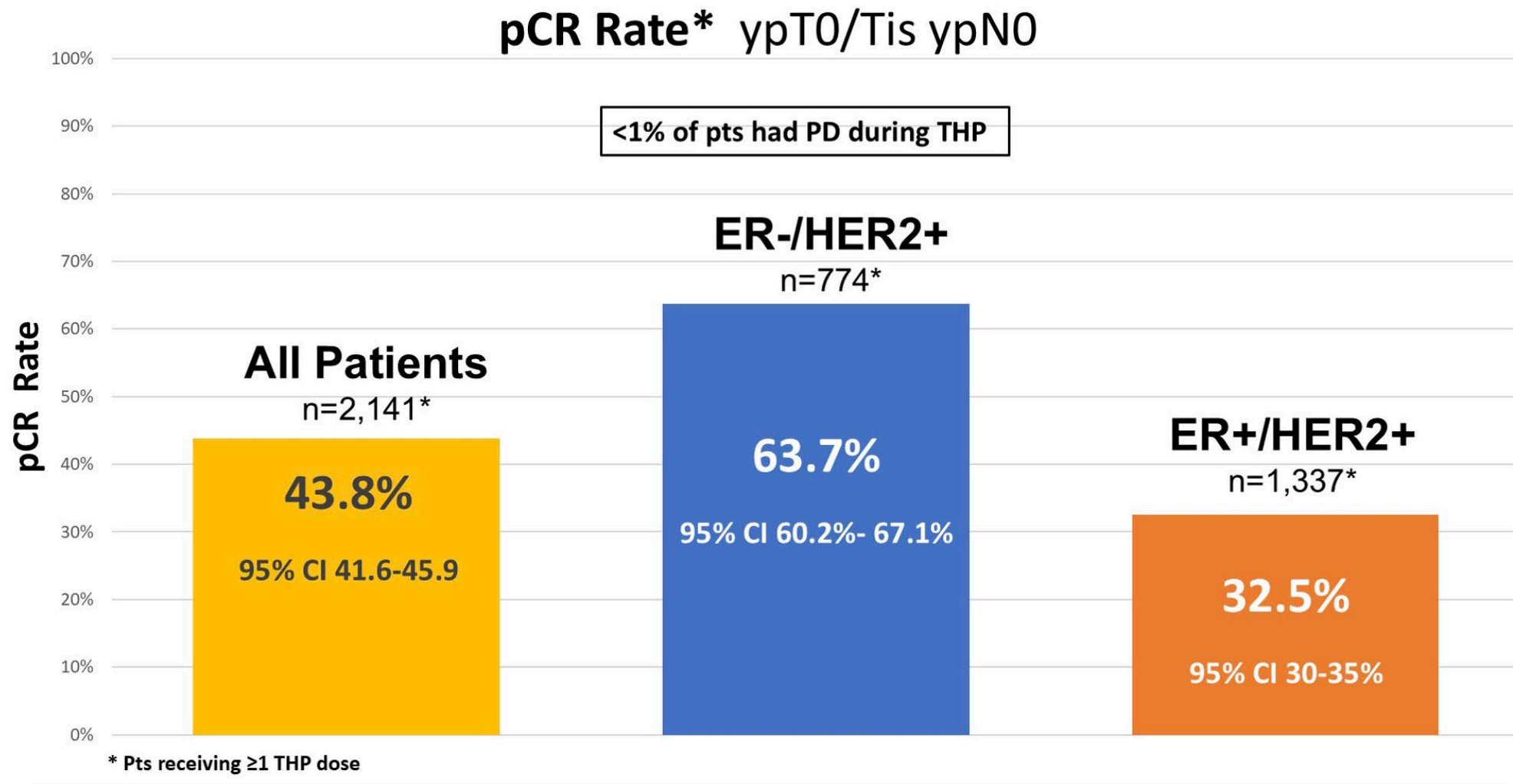
n=2175	
Age – yrs median (range)	55 (22-88)
Race	
White	75%
Black	12%
Asian	7%
Other/not reported	6%
Ethnicity	
Hispanic	12%
ECOG PS	
0	88%
1	12%
Clinical Stage	
IIA (T2N0, T1N1)	58%
IIB (T2N1, T3N0)	33%
IIIA (T3N1, T1-3 N2)	8%
Clinical T stage	
T1	11%
T2	75%
T3	14%
Clinical N Stage	
N0	55%
N1	44%
N2/N3	2%
Taxane received	n=2,141*
Paclitaxel	63%
Docetaxel	34%
Nab-paclitaxel	2%

* Pts who received ≥ 1 THP dose





Pierwszorzędowy punkt końcowy - pCR





Czynniki kliniczno-patologiczne związane z pCR

Analiza jednoczynnikowa

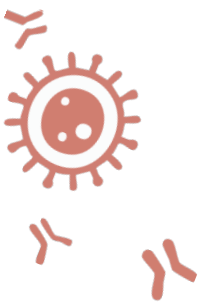
Negatively associated with pCR: age above 70 and PS > 0

Positively associated with pCR: high grade, lower ER expression, HER2 IHC 3+, and use of paclitaxel

Not associated: clinical stage (T and N)

Variable	pCR rate		
	All pts (n=2141)	ER- HER2+ (n= 774)	ER+ HER2+ (n= 1367)
Age (median, range)	55 yrs (22-88)		
< 50 years	43.6%	63.5%	34%
50-70 years	47%	67.9%	34.2%
>70 years	31.9%	48.7%	21.1%
ECOG PS			
0	44.7%	65.4%	32.9%
1	37.4%	51.6%	29.7%
Grade			
1	26.9%	60%	21.1%
2	37.2%	63%	27.9%
3	49.5%	64%	37.9%
ER (% cells staining)			
0%	63.7%	63.7%	
1-10%	62.5%	----	62.5%
11-70%	51.6%	----	51.6%
> 70%	22.5%	----	22.5%
HER2 IHC			
3+	50.3%	67.6%	39.3%
2+	11.9%	26%	8.0%
Taxane^			
paclitaxel	46.5%	68.5%	34.2%
docetaxel	39.3%	55.9%	29.7%



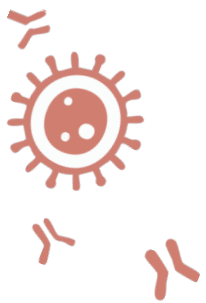


Czynniki kliniczno-patologiczne związane z pCR

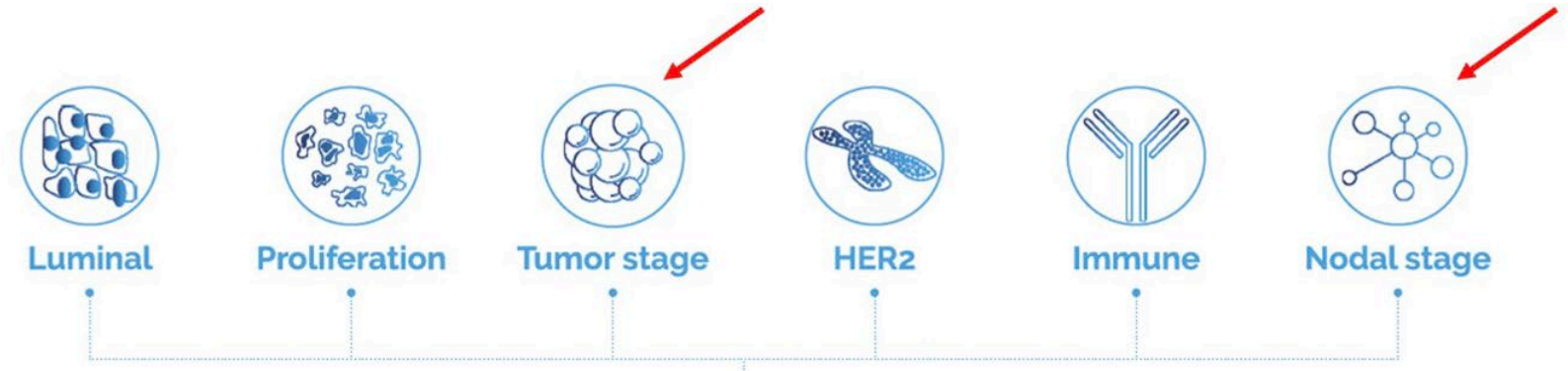
Analiza wieloczynnikowa

All patients n=2141*		
Clinical factor	OR for pCR (95% CI)	# of patients
ER status		
ER+ >70%	1.0	950
ER+ 11-70%	3.35 (2.5-4.49)	281
ER+ 1-10%	4.75 (3.2-7.06)	136
ER- 0%	5.44 (2.5-4.49)	774
HER2 IHC		
2+/ISH+	1.0	353
3+	6.25 (4.39-8.89)	1691
Taxane		
docetaxel	1.0	735
paclitaxel	1.48 (1.2-1.81)	1355





HER2Dx łączy ekspresję genów oraz czynniki kliniczne



1. HER2DX pCR likelihood score

HER2DX®

- 27 genes**
- Immune activation (14 genes)
 - Luminal differentiation (5 genes)
 - Tumor cell proliferation (4 genes)
 - HER2 amplicon (4 genes, including ERBB2)





Częstość pCR w zależności od wyniku HER2Dx pCR

	ER- (n=230)		ER+ (n=339)	
HER2Dx score	n (%) of pts	pCR rate	n (%) of pts	pCR rate
High	147 (64%)	70%	36 (11%)	58%
Low	13 (6%)	31%	214 (63%)	18%
<i>p value</i>		<i>p <0.01</i>		<i>p <0.01</i>

Wysoki wyniki HER2Dx pCR był związany z 40% wyższą częstością pCR niż niski wynik





Częstość pCR w zależności od wyniku HER2Dx pCR

	ER- (n=230)		ER+ (n=339)	
HER2Dx score	n (%) of pts	pCR rate	n (%) of pts	pCR rate
High	147 (64%)	70%	36 (11%)	58%
Medium	70 (30%)	74%	89 (26%)	61%
Low	13 (6%)	31%	214 (63%)	18%
<i>p value</i>		<i>p <0.01</i>		<i>p <0.01</i>

Częstość pCR była podobna u chorych z wynikiem wysokim i średnim

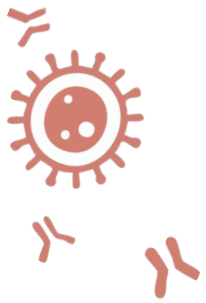




Podsumowanie

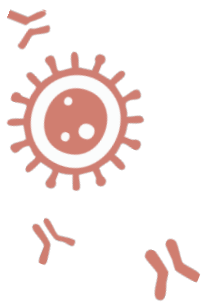
- pCR w całej populacji wynosi **44%**, **64%** w populacji HR-/HER2+, **33%** w populacji HR+/HER2+
- **Czynniki kliniczno-patologiczne** korelujące z wyższym odsetkiem pCR:
 - ER 0 lub ER+ \leq 70%
 - HER2 IHC 3+ vs IHC 2+, ISH+
 - co tygodniowy paklitaksel vs. q3wk docetaksel
- **cT, cN** nie były związane z częstością pCR
- **HER2Dx pCR** jest narzędziem pozwalającym określić prawdopodobieństwo pCR – możliwa deeskalacja terapii???





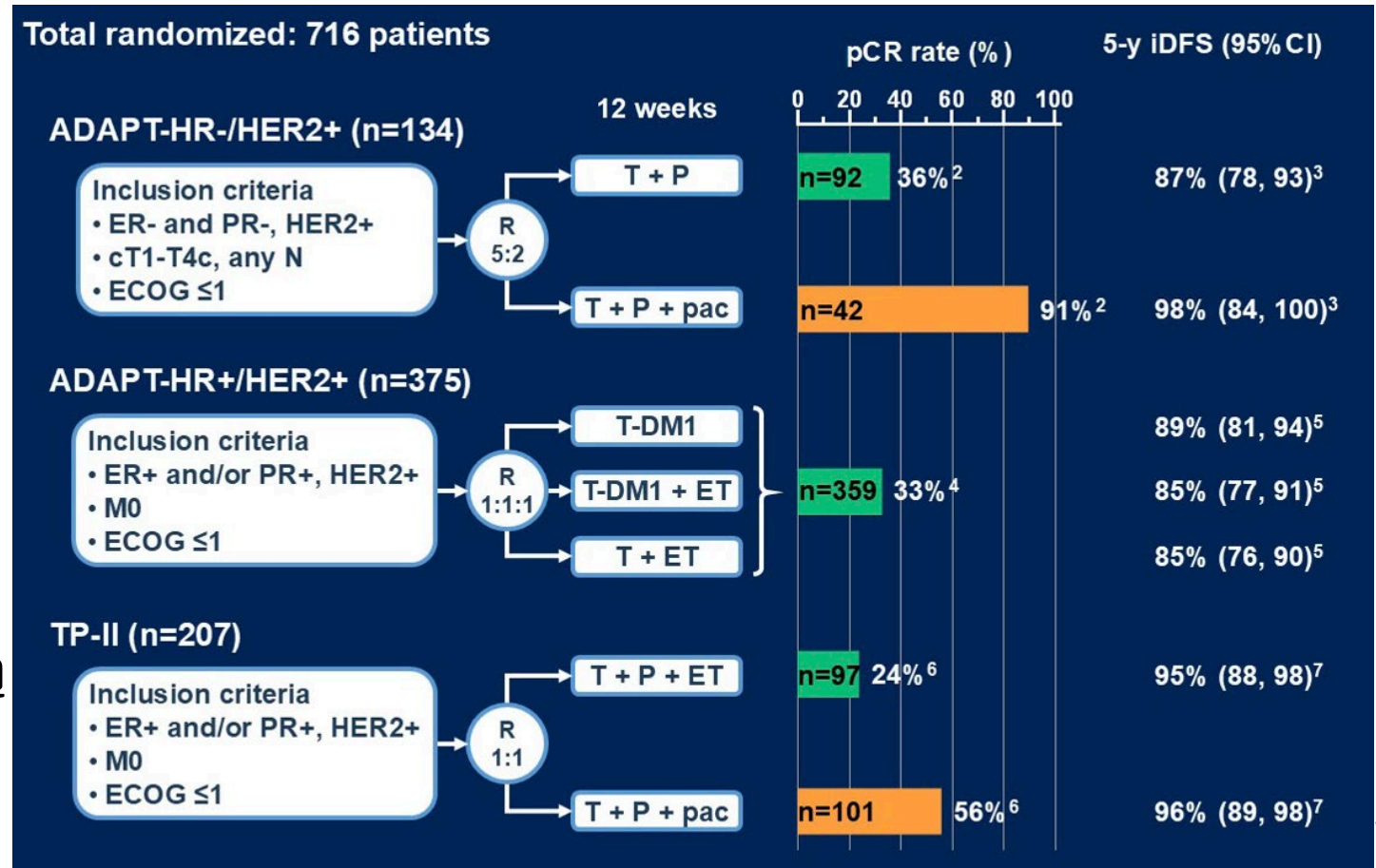
Wpływ deeskalacji terapii przedoperacyjnej na rokowanie chorych na HER2+ raka piersi – wyniki 3 badań **WSG**

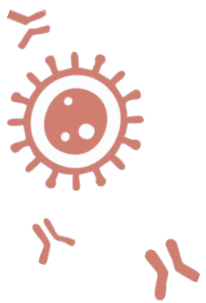




Schemat badań

- Pierwszorzędowy punkt końcowy – **pCR**
- Drugorzędowy punkt końcowy – **OS**
- W przypadku pCR – brak konieczności zastosowania chth
- U chorych z chorobą rezydualną – chth była zalecana

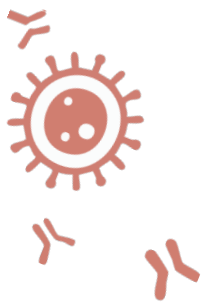




Charakterystyka chorych

	N (%)	Overall (N=713)	CTx-free/ADC NAT (N=564)	CTx NAT (N=149)
Age	≤50 years	327 (45.9)	267 (47.3)	60 (40.3)
	>50 years	386 (54.1)	297 (52.7)	89 (59.7)
Stage	Stage I	540 (76.2)	429 (76.6)	111 (74.5)
	Stage II	140 (19.8)	106 (18.9)	34 (22.8)
	Stage III	29 (4.1)	25 (4.5)	4 (2.7)
	Missing	4	4	0
cT	cT1	318 (44.6)	253 (44.9)	65 (43.6)
	cT2-3	387 (54.3)	303 (53.7)	84 (56.4)
	cT4	8 (1.1)	8 (1.4)	0 (0.0)
cN	cN0	490 (68.7)	383 (67.9)	107 (71.8)
	cN1	202 (28.3)	162 (28.7)	40 (26.9)
	cN2-3	21 (2.9)	19 (3.4)	2 (1.3)
HR status	HR-positive	578 (81.6)	471 (84.3)	107 (71.8)
	HR-negative	130 (18.4)	88 (15.7)	42 (28.2)
	Missing	5	5	0
Grade (central)	Grade 1-2	206 (28.9)	140 (24.8)	66 (44.3)
	Grade 3	502 (70.4)	419 (74.3)	83 (55.7)
	Missing	5	5	0



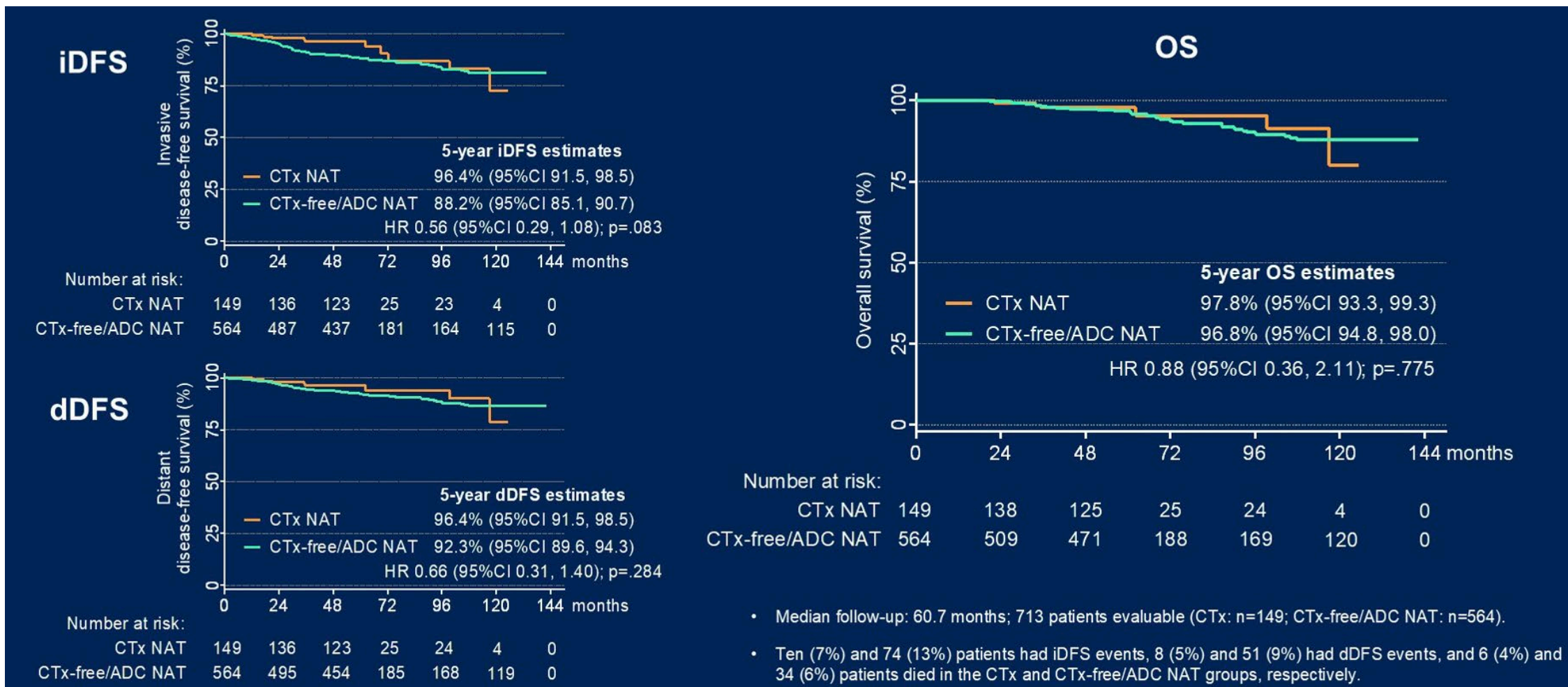


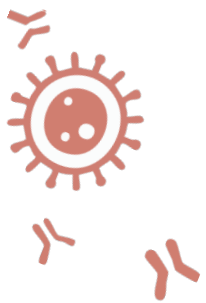
Charakterystyka chorych po operacji

N (%)		Overall (N=713)	CTx-free/ADC NAT (N=564)	CTx NAT (N=149)
pCR status	pCR	266 (38.7)	171 (31.4)	95 (66.4)
	Non-pCR	422 (61.3)	374 (68.6)	48 (33.6)
	Missing	25	19	6
Adjuvant CTx *	Adj. CTx	548 (20.0)	482 (88.4)	66 (47.1)
	No adj. CTx	137 (80.0)	63 (11.6)	74 (52.9)
	Missing	28	19	9
Adjuvant CTx after pCR	Adj. CTx	126 (47.9)	108 (63.2)	18 (19.6)
	No adj. CTx	137 (52.1)	63 (36.8)	74 (80.4)
	Missing	3	0	3

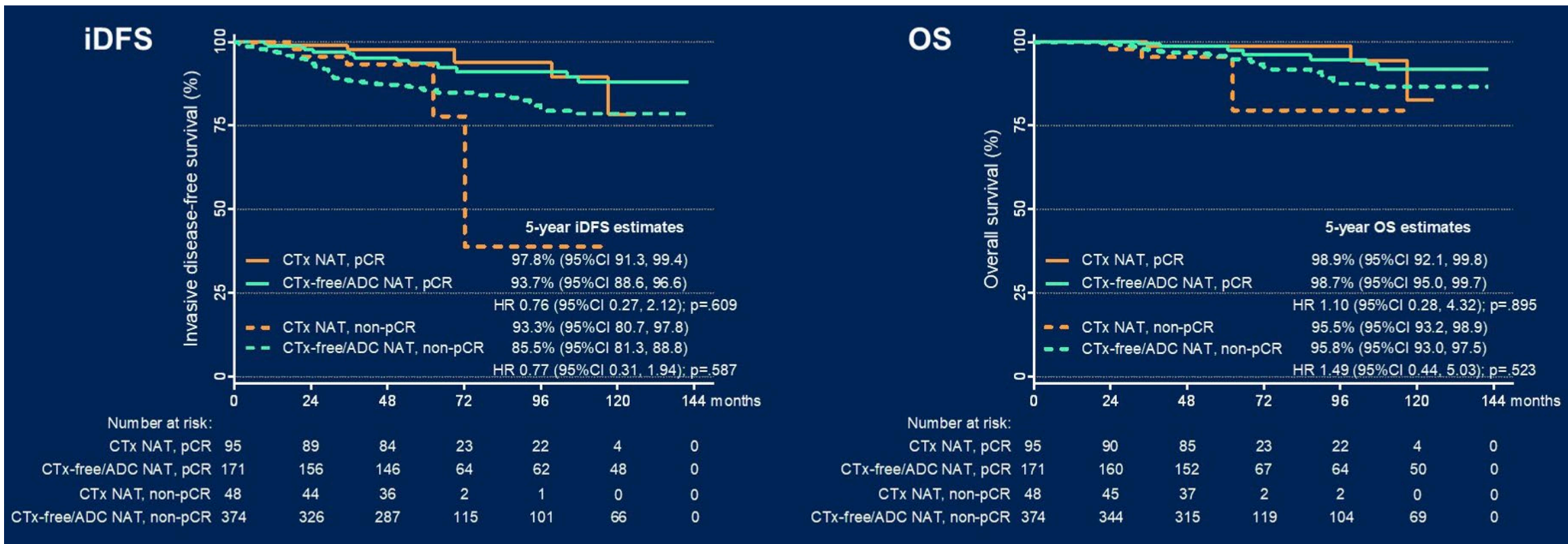


Wyniki w zależności od schematu leczenia

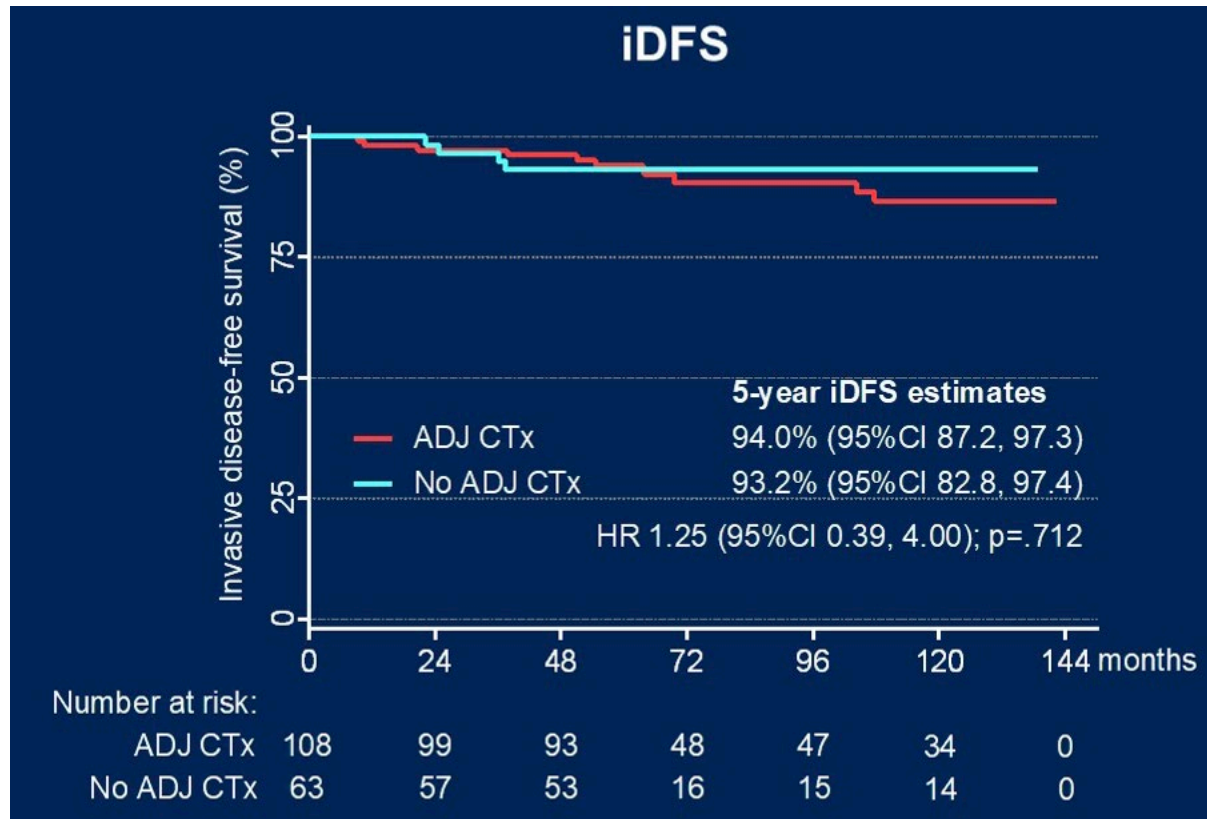


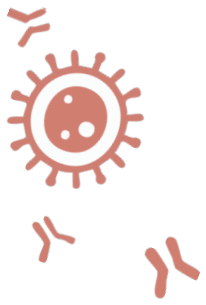


Wyniki dotyczące przeżycia w zależności od schematu leczenia – pCR vs. non pCR



iDFS w grupie pCR nie otrzymującej chth przedoperacyjnej w zależności od zastosowania chth pooperacyjnej





Podsumowanie

- Deeskalacja terapii jest możliwa i bezpieczna
- Przedoperacyjna terapia: **12 x paklitaksel + terapia anty-HER2** jest skuteczna i wiąże się z dobrymi wynikami 5-letnich przeżyć
- Zastosowanie chemioterapii uzupełniającej u chorych, u których osiągnięto pCR dzięki przedoperacyjnemu leczeniu pozbawionemu standardowej chemioterapii, nie wpływa na poprawę rokowania chorych

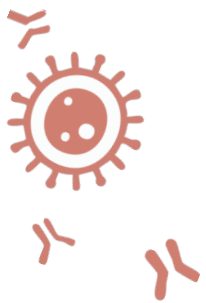




Rak potrójnie ujemny

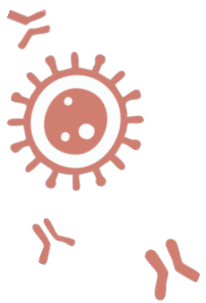
1. Prospective randomized phase II trial to assess the efficacy and safety of neo-adjuvant olaparib/carboplatin (OC) in comparison to docetaxel/epirubicin/cyclophosphamide (TAC) in patients with early triple-negative breast cancer (TNBC) with homologous recombination deficiency (HRD): Primary results from the **ABCSG 45 trial**.
2. A phase 2 study of response-guided neoadjuvant sacituzumab govitecan and pembrolizumab (SG/P) in patients with early-stage triple-negative breast cancer: Results from the **NeoSTAR trial**.



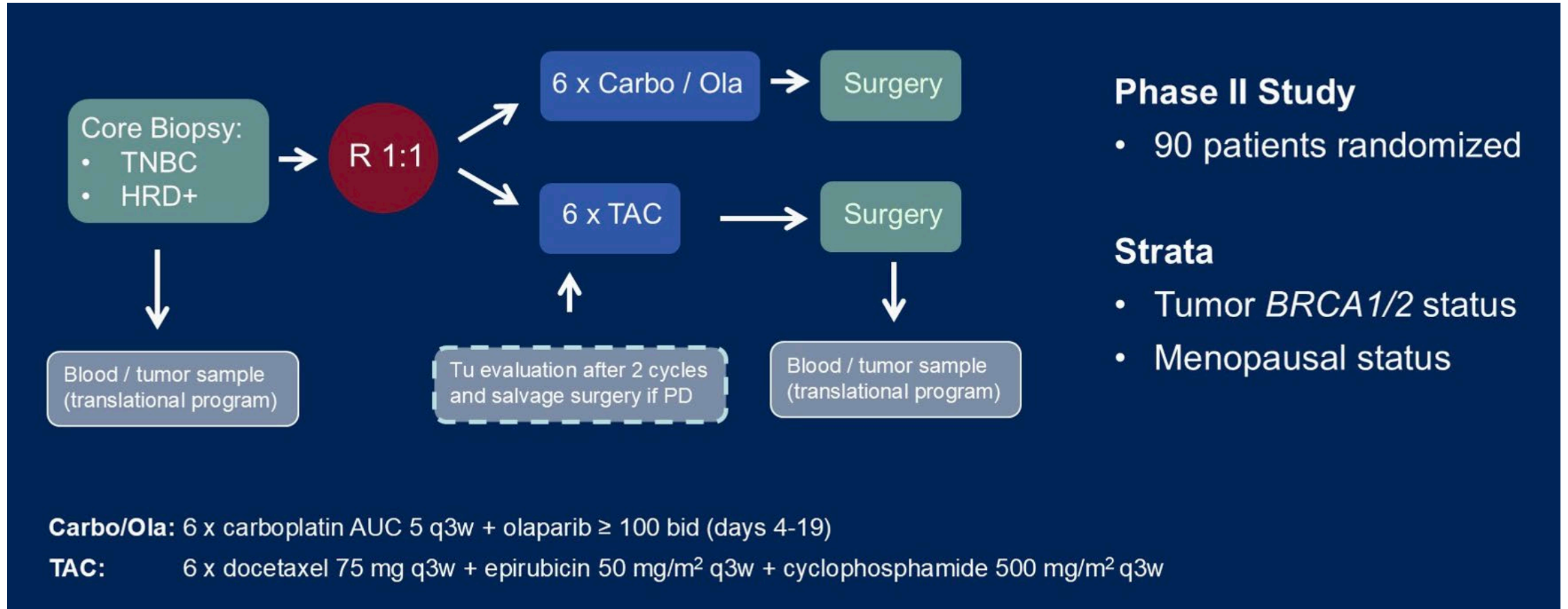


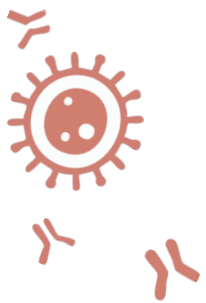
Prospektywne randomizowane badanie II fazy oceniające skuteczność olaparybu w połączeniu z karboplatyną w leczeniu przedoperacyjnym u chorych na wczesnego potrójnie ujemnego raka piersi z niedoborem homologicznej rekombinacji (HRD) -
wyniki badania **ABCSG 45**





Schemat badania





Punkty końcowe

- **Pierwszorzędowy punkt końcowy:**

RCB

- **Drugorzędowy punkt końcowy:**

pCR

bezpieczeństwo i tolerancja

QoL

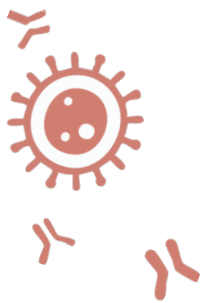




Kryteria badania

- **Kryteria włączenia:**
 - wczesny potrójnie ujemny rak piersi
 - HRD+
 - $\geq T1c$, każdy N
- **Kryteria wyłączenia:**
 - miejscowo zaawansowany lub nieoperacyjny rak piersi
 - przeciwwskazania do któregośkolwiek z leków





Charakterystyka pacjentów

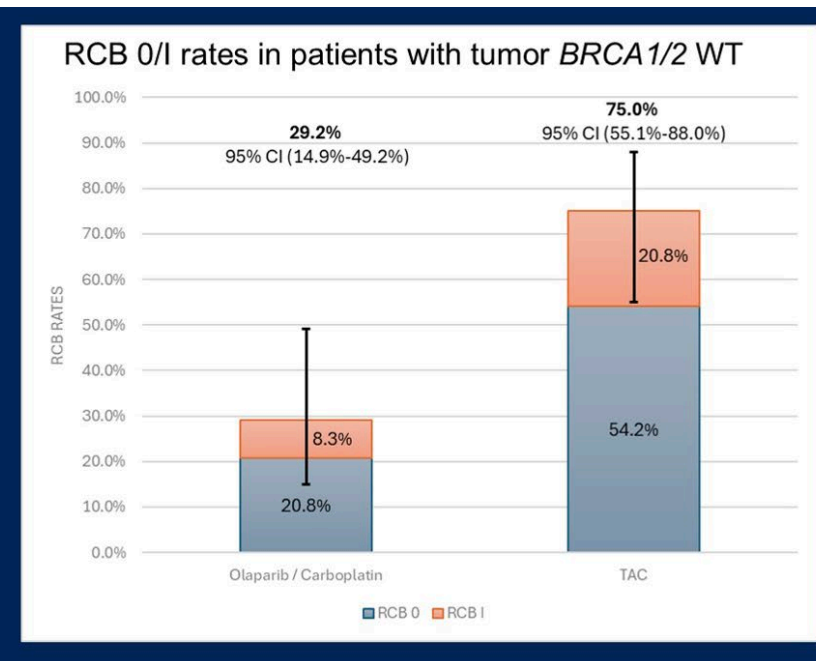
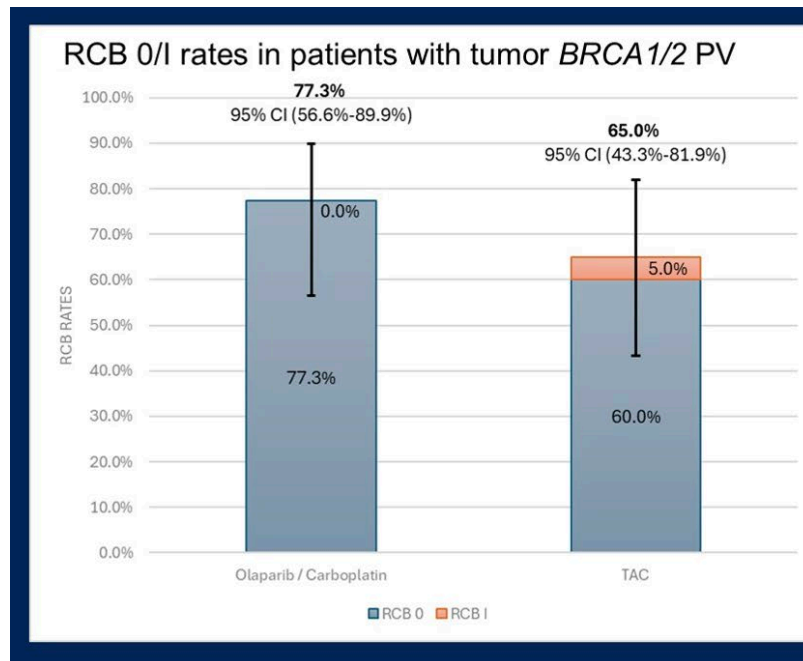
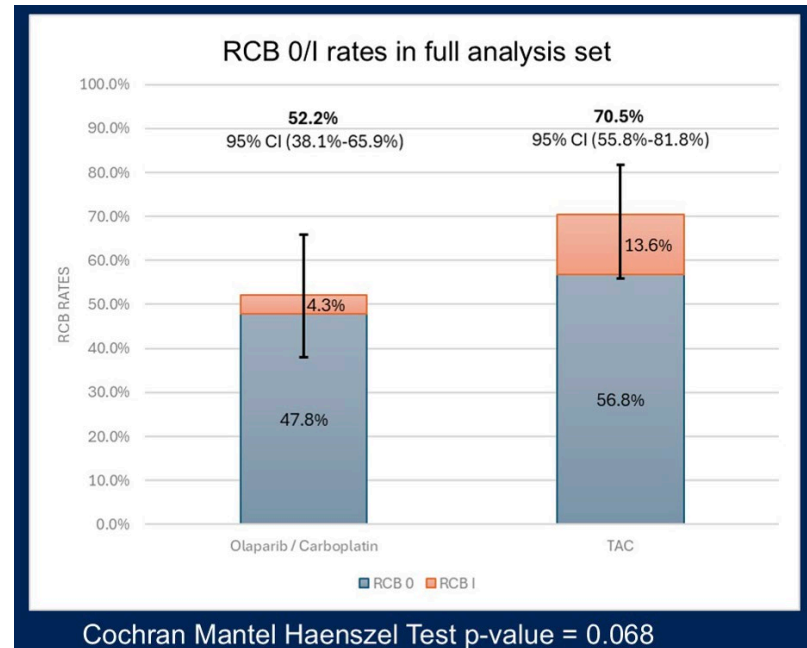
	Carbo/Ola (n=46)	TAC (n=44)	Total (n=90)
Age, mean (SD)	50.2 (12.7)	51.6 (12.5)	50.9 (12.5)
Menopausal status			
pre- and peri-menopausal	23 (50.0%)	23 (52.3%)	46 (51.1%)
postmenopausal	23 (50.0%)	21 (47.7%)	44 (48.9%)
Tumor BRCA1/2 PV status			
negative	24 (52.2%)	24 (54.5%)	48 (53.3%)
positive	22 (47.8%)	20 (45.5%)	42 (46.7%)
Genomic Instability Status			
positive	42 (91.3%)	41 (93.2%)	83 (92.2%)
negative	1 (2.2%)	2 (4.5%)	3 (3.3%)
missing	3 (6.5%)	1 (2.3%)	4 (4.4%)
Genomic Instability Score			
mean (SD)	59.6 (11.7)	62.0 (12.1)	60.8 (11.9)
Germline BRCA1/2 PV*			
negative	17 (37.0%)	19 (43.2%)	36 (40.0%)
positive	16 (34.8%)	16 (36.4%)	32 (35.6%)
missing	13 (28.3%)	9 (20.5%)	22 (24.4%)

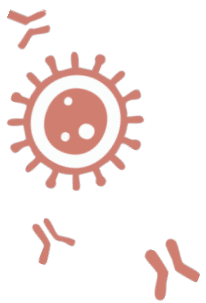
	Carbo/Ola (n=46)	TAC (n=44)	Total (n=90)
T-stage			
T1	21 (45.7%)	15 (34.1%)	36 (40.0%)
T2	22 (47.8%)	28 (63.6%)	50 (55.6%)
T3	1 (2.2%)	0	1 (1.1%)
T4	2 (4.3%)	1 (2.3%)	3 (3.3%)
N-stage			
N0	28 (60.9%)	26 (59.1%)	54 (60.0%)
N1	14 (30.4%)	16 (36.4%)	30 (33.3%)
N2	2 (4.3%)	1 (2.3%)	3 (3.3%)
N3	1 (2.2%)	1 (2.3%)	2 (2.2%)
NX	1 (2.2%)	0	1 (1.1%)
Grading			
G2	2 (4.3%)	3 (6.8%)	5 (5.6%)
G3	44 (95.7%)	41 (93.2%)	85 (94.4%)
KI67 [%]			
mean (SD)	72.0 (17.4)	72.3 (18.2)	72.1 (17.6)



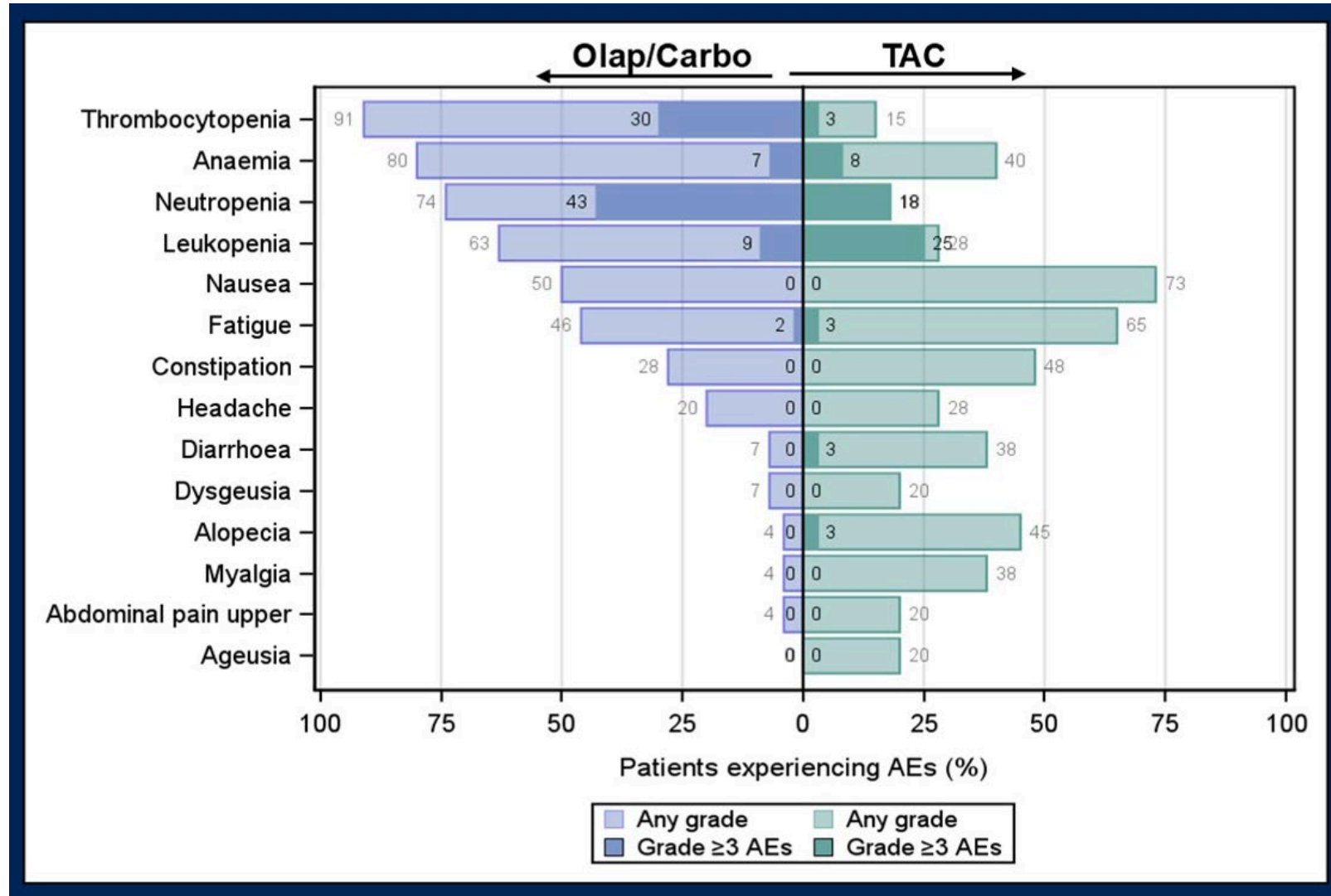


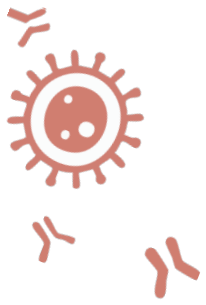
Pierwszorzędowy punkt końcowy RCB 0/I





Bezpieczeństwo

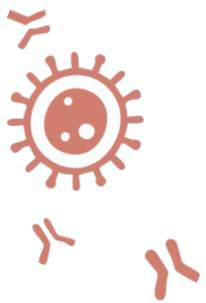




Podsumowanie

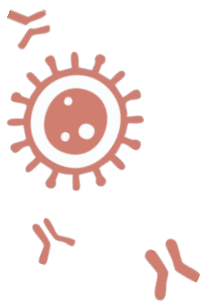
- Somatyczne warianty patogenne *BRCA1/2* są obecne u ok. 50% chorych HRD+
- U > **77%** chorych z wariantami patogennymi *BRCA1/2*, które otrzymały 6 cykli olaparybu i karboplatyny osiągnięto pCR





Badanie II fazy oceniające skuteczność
sacituzambu gowiteku w połączeniu z
pembrolizumabem u chorych na wczesnego
potrójnie ujemnego raka piersi – wyniki **badania**
NeoSTAR





Schemat badania

Primary Objective:

- pCR with neoadjuvant SG/P

Secondary Objectives:

- Need for additional NACT
- Radiographic response (RR)
- Safety and tolerability (adverse events [AEs] per CTCAE v5.0)
- 2-year event-free survival (EFS)

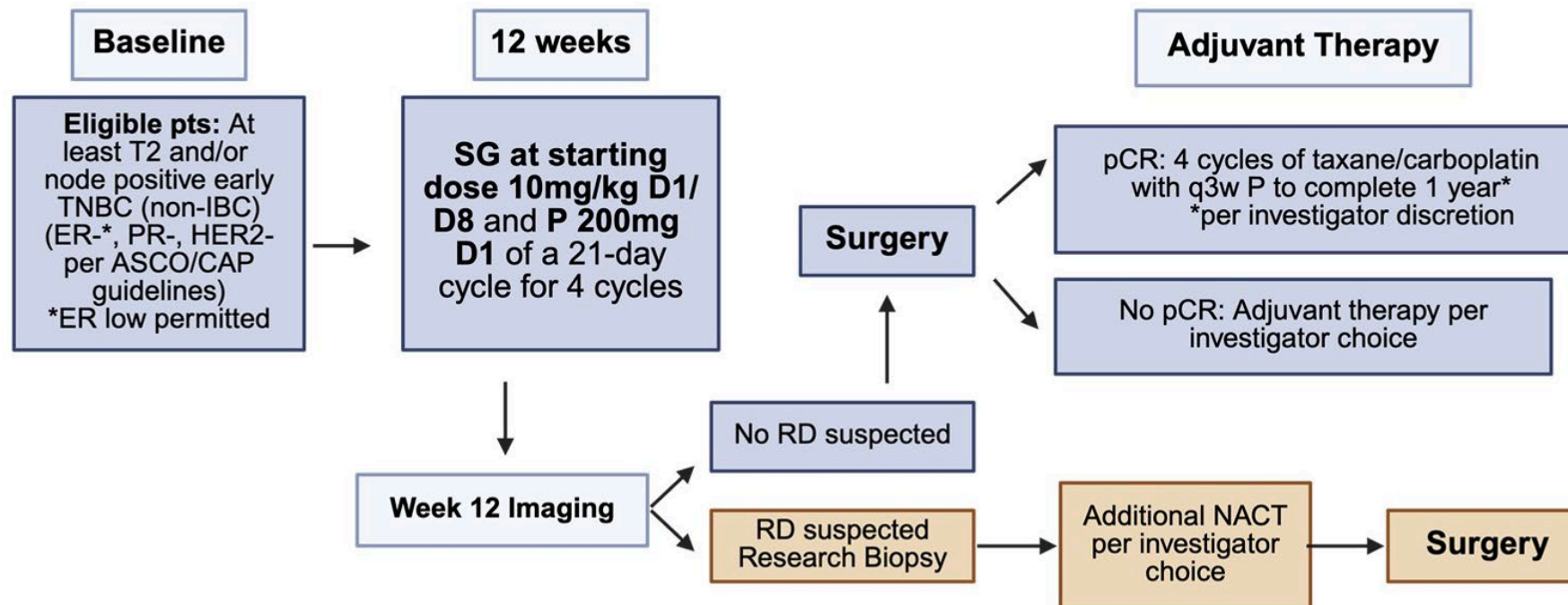
RD: Residual disease

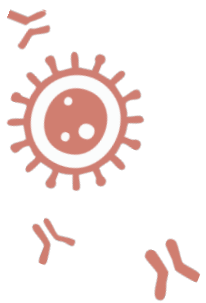
NACT: Neoadjuvant chemotherapy

SG: Sacituzumab govitecan

P: Pembrolizumab

IBC: Inflammatory breast cancer

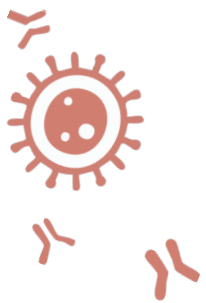




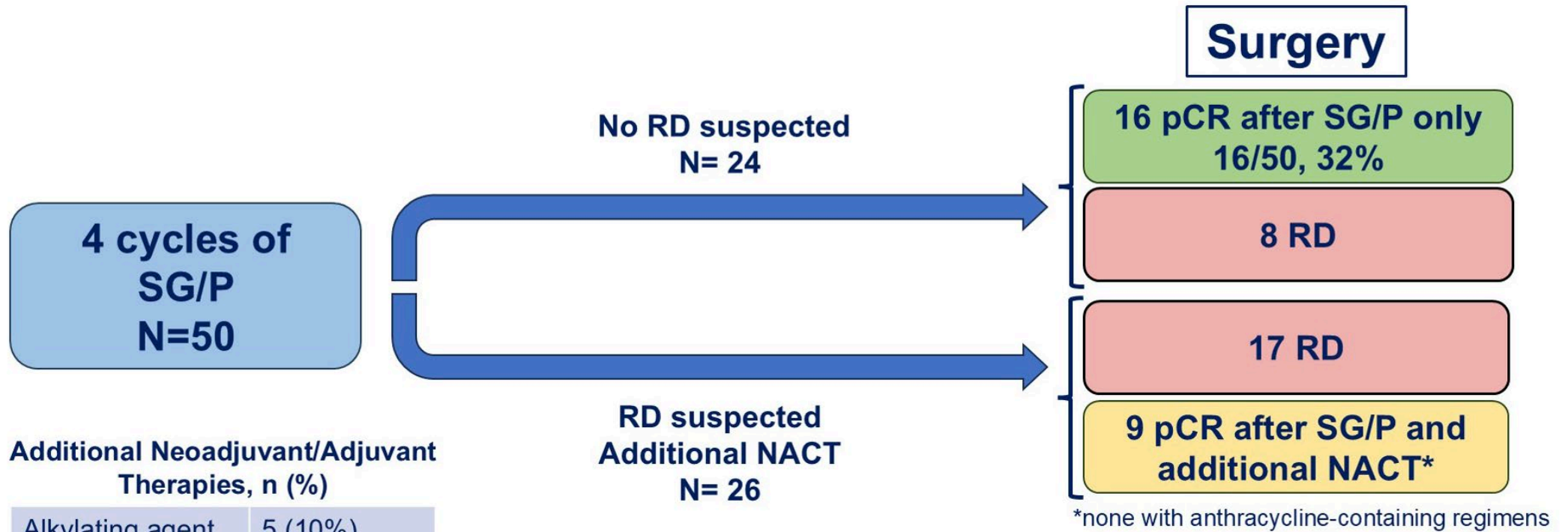
Charakterystyka pacjentów

Category		
Age at diagnosis (years)	Median (range)	57 (23-77)
Disease stage, <i>n</i> (%)	II	48 (96)
	III	2 (4)
T stage, <i>n</i> (%)	T0	1 (2)
	T1	4 (8)
	T2	42 (84)
	T3	3 (6)
Lymph node status, <i>n</i> (%)	Node negative	32 (64)
	Node positive	18 (36)
Germline BRCA mutation, <i>n</i> (%)	Pathogenic	5 (10)
	Variant of uncertain significance (VUS)	2 (4)
	None	40 (80)
	Unknown	3 (6)
ER status at initial biopsy	ER negative	42 (84)
	ER low (1-10%)	8 (16)





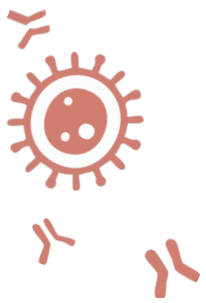
Wyniki - pCR



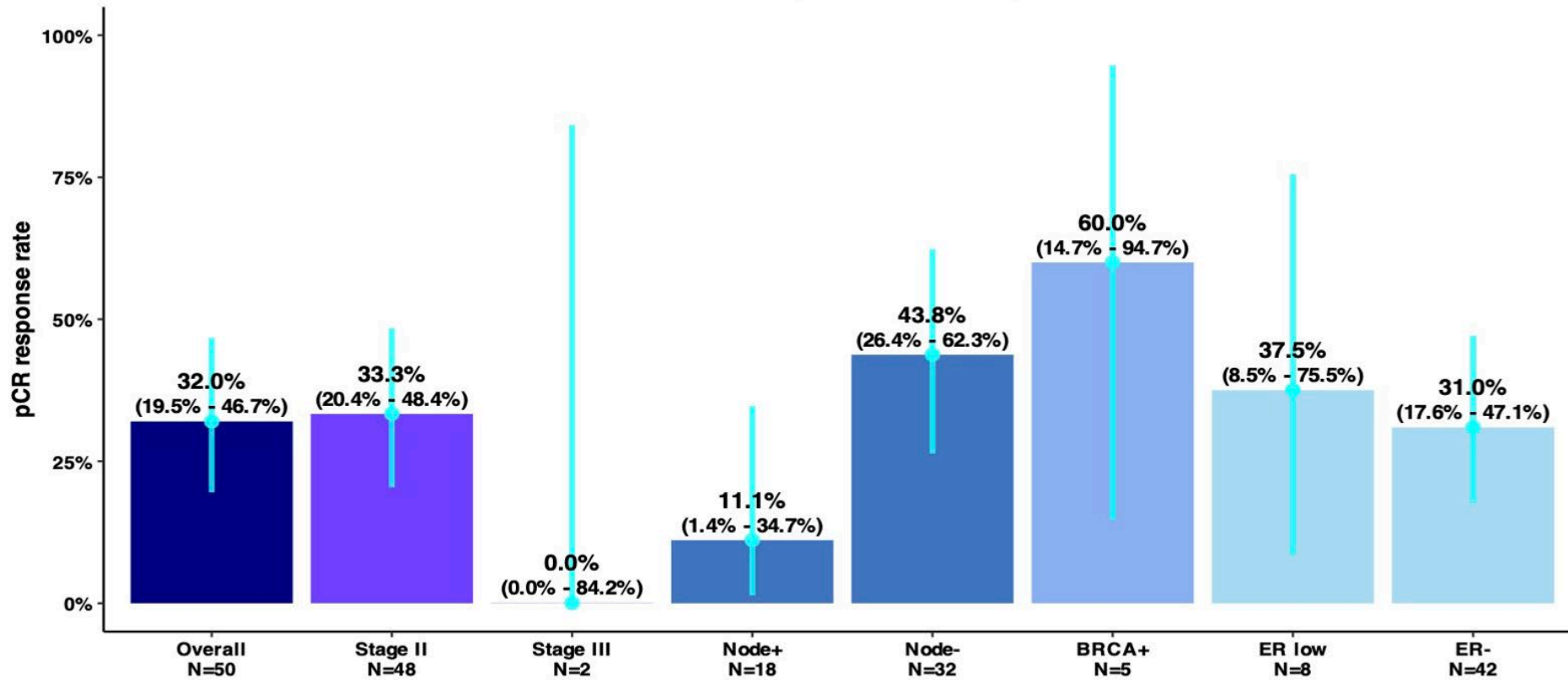
Additional Neoadjuvant/Adjuvant Therapies, n (%)

Alkylating agent	5 (10%)
Anthracycline	5 (10%)
Capecitabine	11 (22%)
Olaparib	1 (2%)
Platinum	49 (98%)
Taxane	49 (98%)
CMF	1 (2)





Wyniki – analiza podgrup



- **18-month Event-Free Survival (EFS)*: 90.6%, 95% CI(89.2% - 100.0%)**
- Radiographic response rate (RRR): 66% (95% CI 50-78%): 30% CR, 36% PR

*24-month EFS not yet evaluable



Bezpieczeństwo

Completion and Dose Reductions	<i>n</i> (%)
Trial regimen	
Completed	44 (88)
Stopped for toxicity	5 (10)
Stopped for progression	1 (2)
Dose reduction	4 (8)
Dose holds	12 (24)
Use of growth factor	13 (26)

IO (pembrolizumab) Toxicities Grade 2 or higher

Toxicity	Grade 2	Grade 3	Grade 4	Total	%
Hypothyroid	8	0	0	8	16.0%
Colitis	1	2	1	4	8.0%
ALT elevation	0	1	0	1	2.0%
Dermatitis	0	1	0	1	2.0%
Hyperglycemia	0	1	0	1	2.0%
Psoriasis	1	0	0	1	2.0%

SG Toxicities Grade 2 or higher

Toxicity	Grade 2	Grade 3	Grade 4	Total	%
Alopecia	24	0	0	24	48.0%
Neutropenia	13	5	1	19	38.0%
Nausea	14	2	0	16	32.0%
Diarrhea	8	2	0	10	20.0%
Fatigue	7	1	0	8	16.0%
Anemia	5	1	0	6	12.0%
Leukopenia	4	0	0	4	8.0%

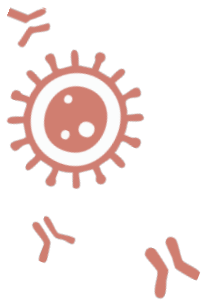




Podsumowanie

- Ograniczenia badania:
 - u **10/32** chorych z podejrzeniem choroby rezydualnej nie wykonano biopsji
 - **6/10** chorych bez podejrzenia choroby rezydualnej otrzymało chemioterapię neoadjuwantową
- U **25 (50%)** chorych uzyskano pCR z zastosowaniem SG/P lub SG/P + neoadjuwantowa chemioterapia bez antracyklin

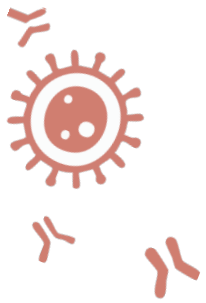




Rak hormonozależny

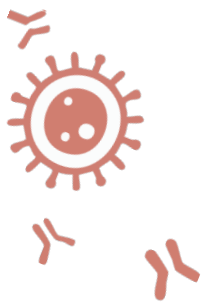
1. 15-year outcomes for women with premenopausal hormone receptor-positive early breast cancer (BC) in the **SOFT and TEXT** trials assessing benefits from adjuvant exemestane (E) + ovarian function suppression (OFS) or tamoxifen (T)+OFS.
2. Efficacy and safety of elinzanetant for vasomotor symptoms associated with adjuvant endocrine therapy: Phase 3 **OASIS 4 trial**.
3. Efficacy and safety of ribociclib (RIB) + nonsteroidal aromatase inhibitor (NSAI) in **NATALEE**: Analysis across menopausal status and age.
4. **The TRADE study**: A phase 2 trial to assess the tolerability of abemaciclib dose escalation in early-stage HR+/HER2- breast cancer.





Rokowanie chorych przed menopauzą z rozpoznaniem wczesnego HR+/HER2- raka piersi leczonych eksemestanem w połączeniu z analogiem GnRH vs. tamoksyfen w połączeniu z analogiem GnRH – 15-letnie wyniki badań **SOFT/TEXT**





Schemat badań SOFT i TEXT

Enrolled: Nov 2003 – Apr 2011
Premenopausal ER and/or PR $\geq 10\%$

- Premenopausal HR+
- Planned OFS
- No planned chemo (40%)
OR planned chemo (60%)

R
A
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TEXT TAMOXIFEN AND EXEMESTANE TRIAL (N=2672)

Tamoxifen+OFS x 5y
Exemestane+OFS x 5y

SOFT

SUPPRESSION OF OVARIAN FUNCTION TRIAL (N=3066)

Tamoxifen x 5y
Tamoxifen+OFS x 5y
Exemestane+OFS x 5y

- Premenopausal HR+
- No chemo (47%)
OR
- Remain premenopausal
 ≤ 8 mos after chemo (53%)

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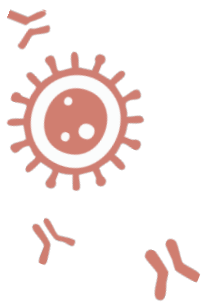
Joint Analysis
(N=4690)

Tamoxifen+OFS x 5y
Exemestane+OFS x 5y

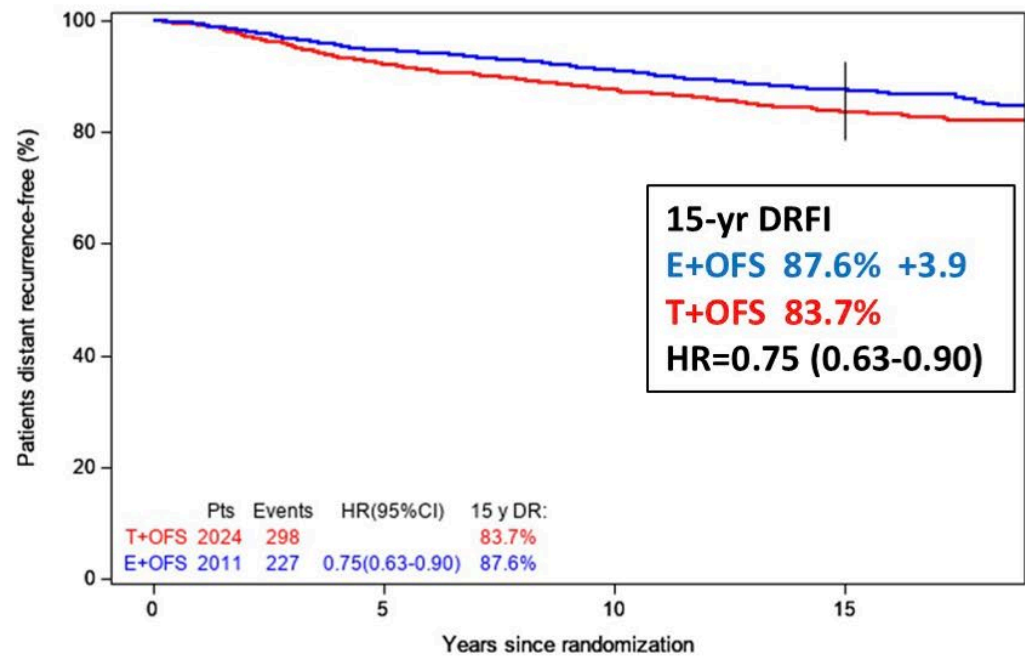
Median follow-up 16 years (max 21 years)

OFS=ovarian function suppression

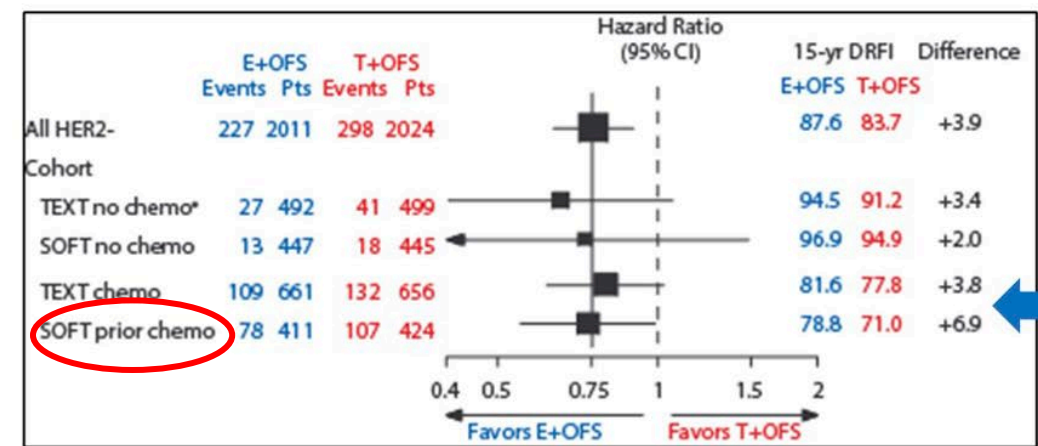


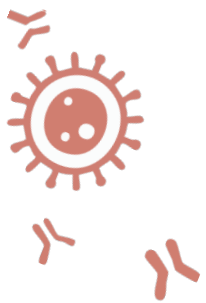


DRFI – SOFT i TEXT

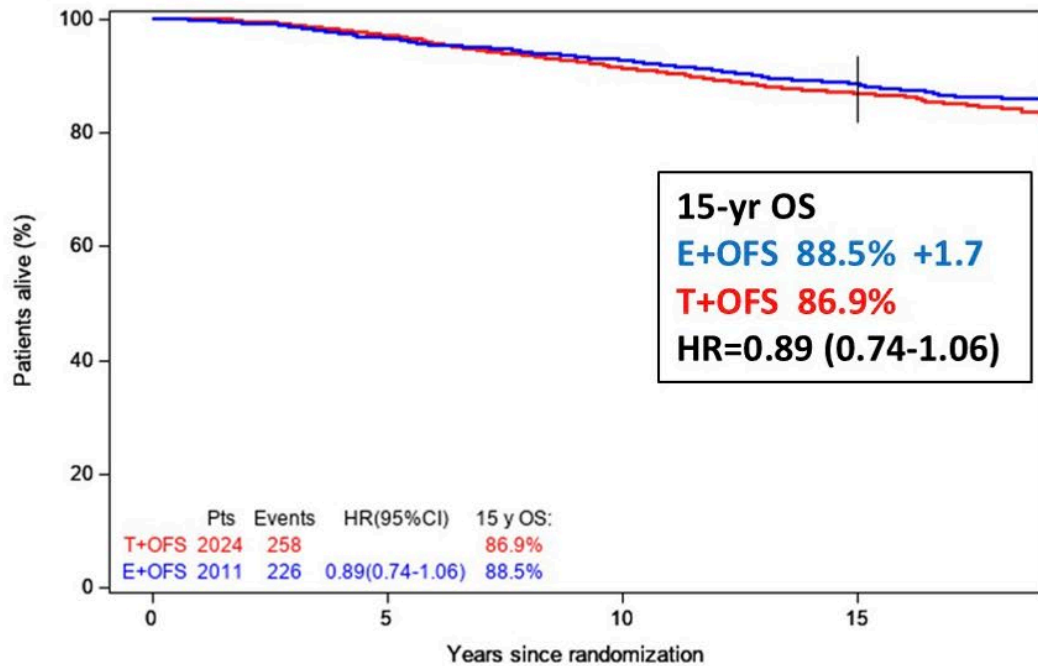


	At risk (censored)	5	10	15
T+OFS	2024	1715(158)	1438(354)	807(931)
E+OFS	2011	1740(170)	1461(387)	838(961)



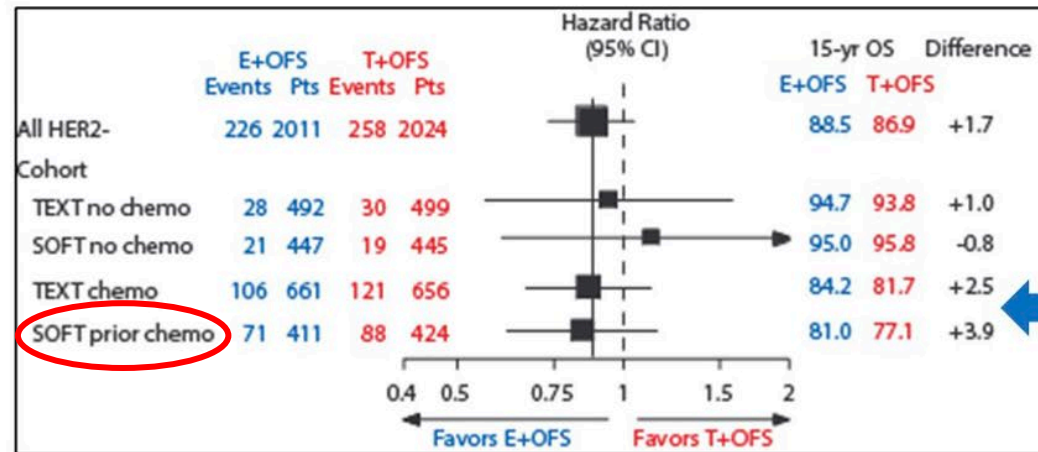


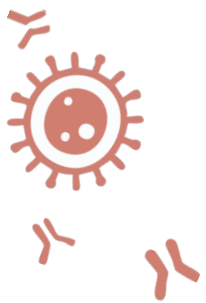
OS – SOFT i TEXT



At risk (censored)

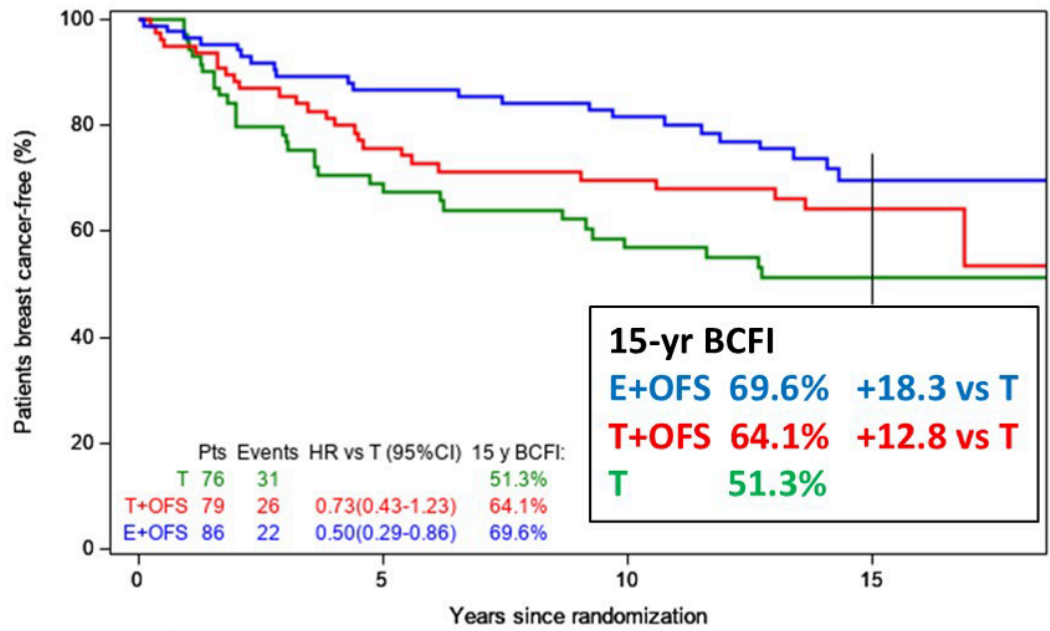
T+OFS	2024	1860(107)	1620(241)	987(803)
E+OFS	2011	1848(95)	1633(242)	987(820)





SOFT – chore < 35 r.ž.

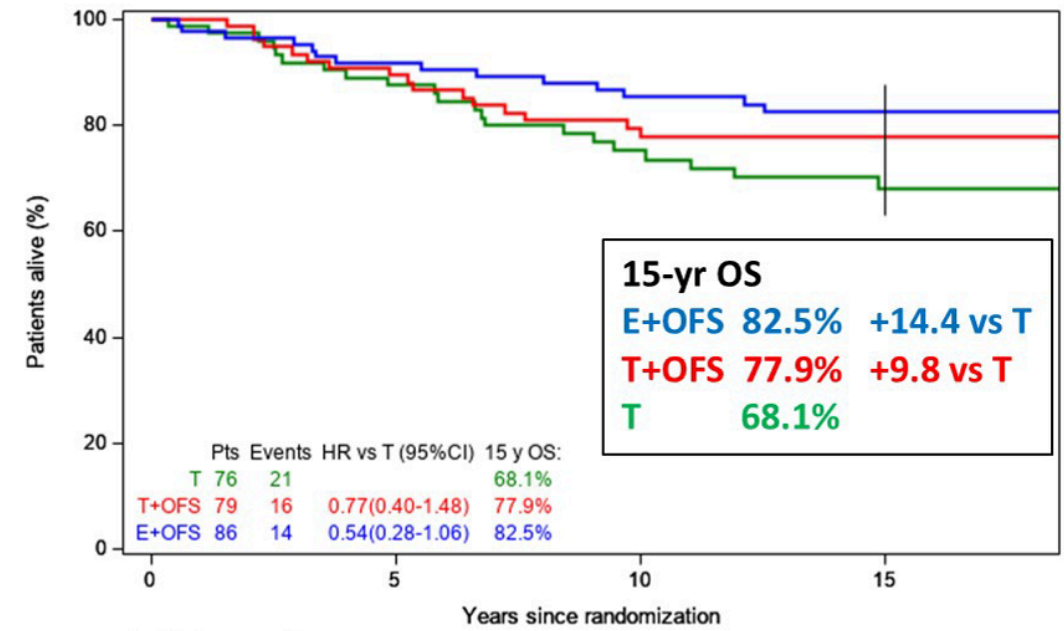
Breast Cancer-Free Interval



At risk (censored)

	0	5	10	15
T	76	43(12)	32(16)	17(28)
T+OFS	79	53(8)	44(13)	20(34)
E+OFS	86	70(5)	57(14)	27(37)

Overall Survival

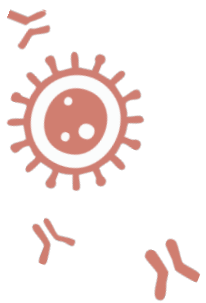


At risk (censored)

	0	5	10	15
T	76	60(7)	47(12)	30(25)
T+OFS	79	66(5)	53(11)	25(38)
E+OFS	86	75(4)	63(11)	37(35)

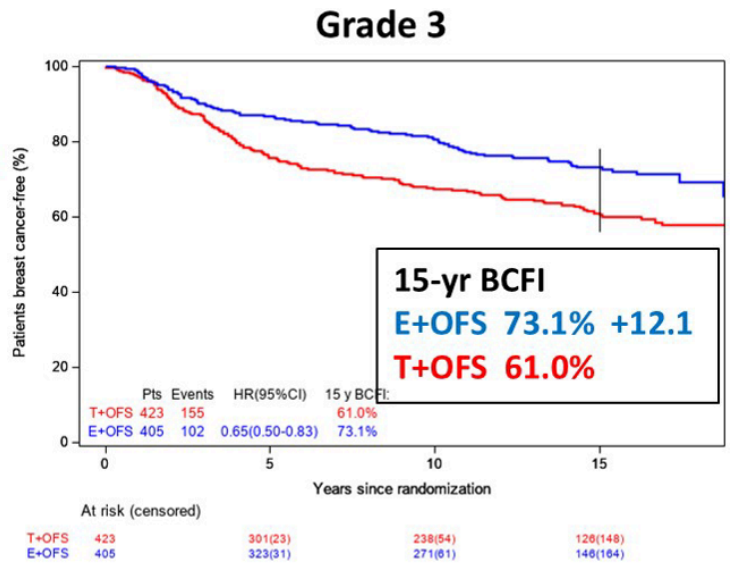
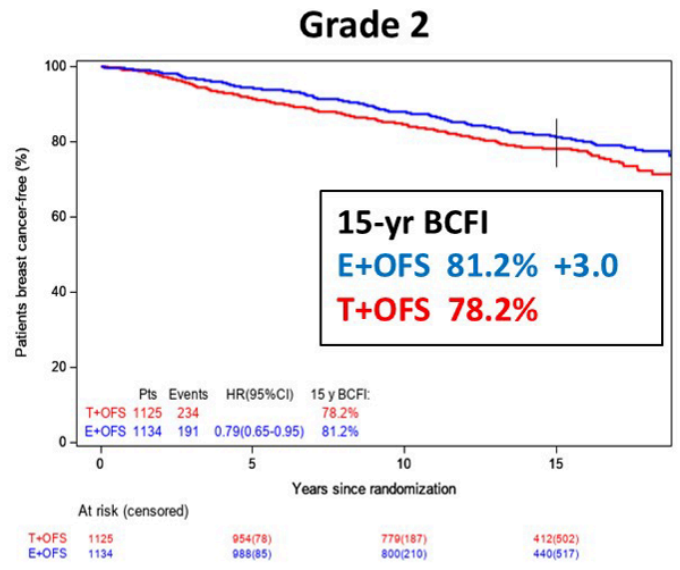
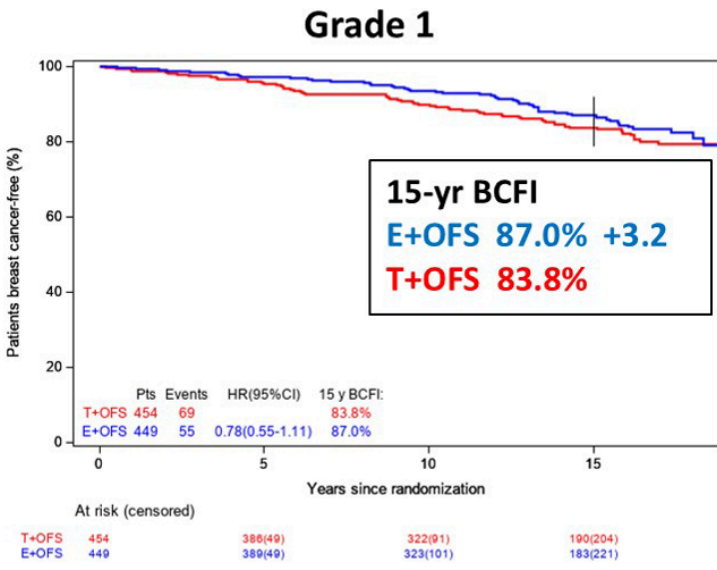
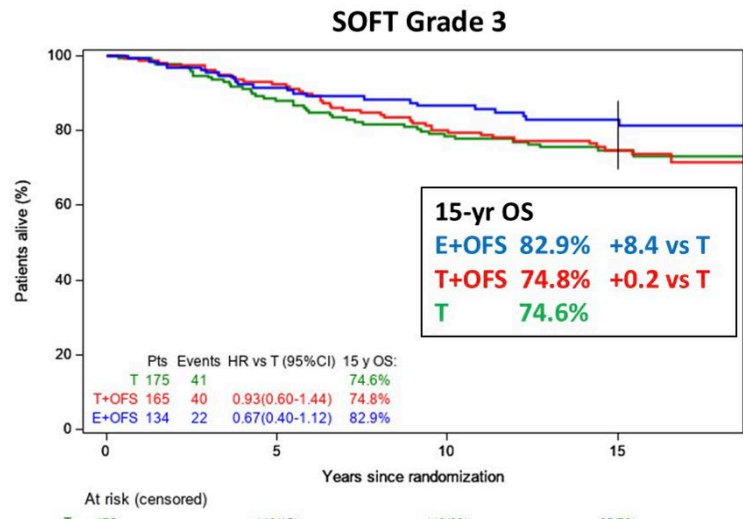
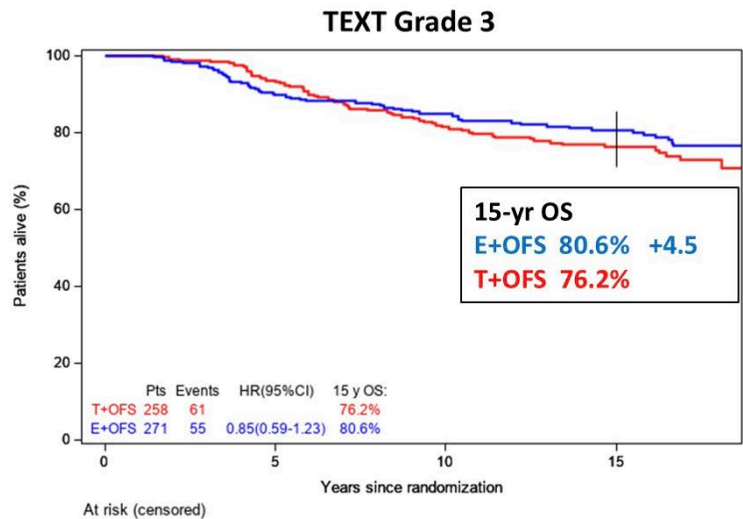
93% in subgroup had prior chemotherapy





OS

BCFI





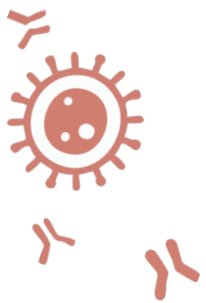
Podsumowanie

- Dołączenie analogu GnRH u chorych przed menopauzą wydłuża BCFI w 15-letniej obserwacji

E+GnRH 78,6% > T + GnRH 75,7% > T 72,1%

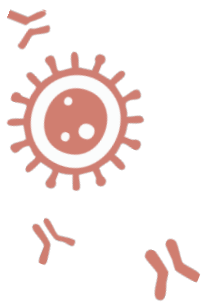
- W grupie E + GnRH obserwowano zmniejszenie ryzyka nawrotu o 25% vs. T + GnRH
- E + GnRH vs. T + GnRH - największe wydłużenie DRFI i OS obserwowano u chorych < **35 r.ż.** oraz z nowotworami **G3**





Badanie III fazy oceniające skuteczność i bezpieczeństwo elinzanetantu w terapii objawów naczynioruchowych u chorych stosujących leczenie hormonalne – wyniki badania **OASIS 4**

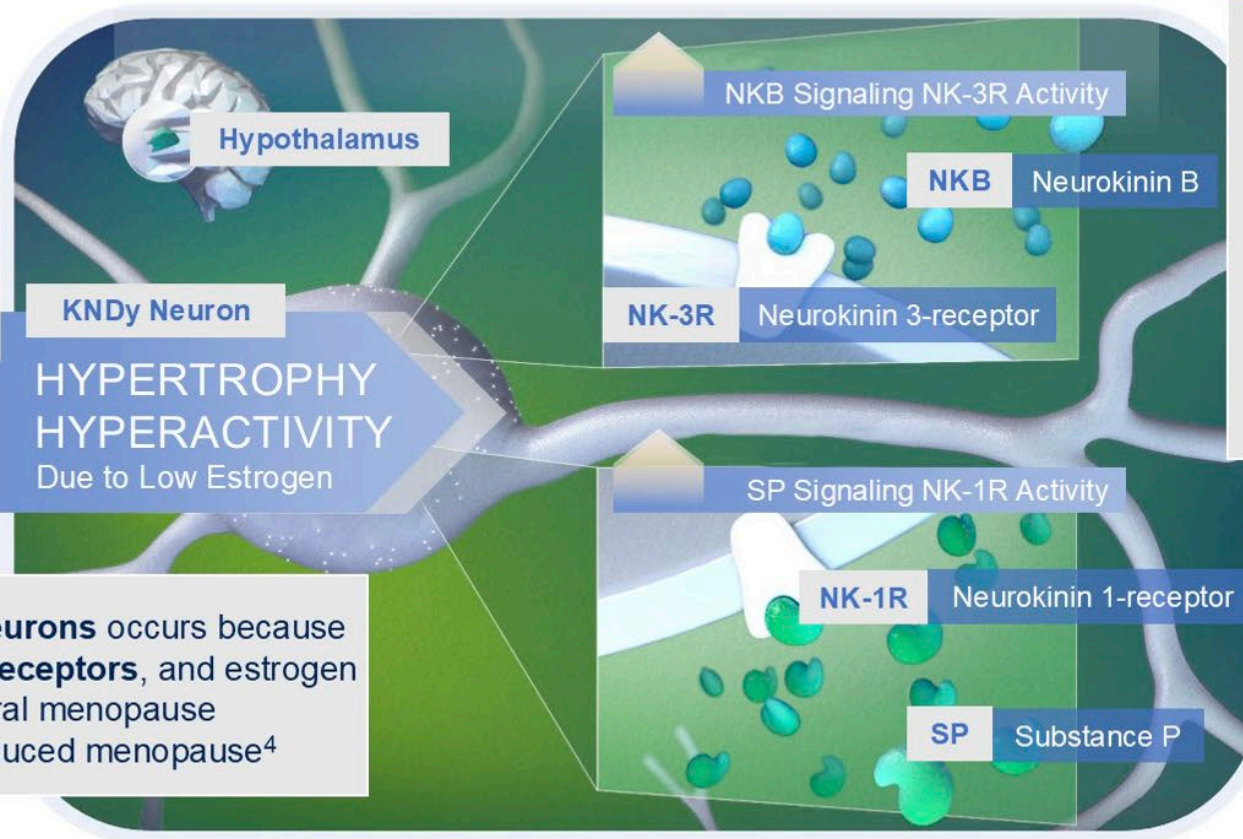




Patomechanizm VMS

1

Specific neurons called **KNDy neurons**, located in the **hypothalamus**, are thought to play a **key role in thermoregulation and sleep**¹⁻³



2

VMS are thought to be caused by hyperactivity of KNDy neurons, in which several neuropeptides and receptors are upregulated, including **NK-1 and NK-3 receptors**. This hyperactivity leads to dysregulation of the thermoregulatory center resulting in VMS.⁴⁻¹¹ NK-1 receptors may have a role in peripheral vasodilatation and primary insomnia.¹²

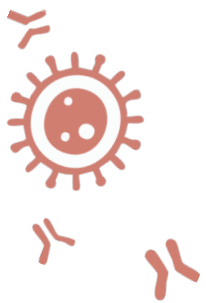
3

Hyperactivity of **KNDy neurons** occurs because they **express estrogen receptors**, and estrogen levels decline in the natural menopause transition or as part of induced menopause⁴

4

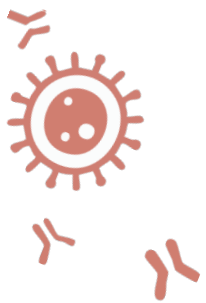
Targeted **dual antagonism of NK-1 and NK-3 receptors decreases the frequency and severity of VMS and sleep disturbances**¹²





Schemat badania



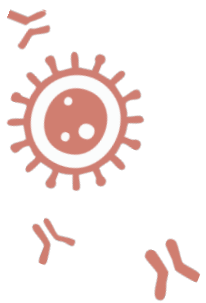


Kryteria kwalifikacji

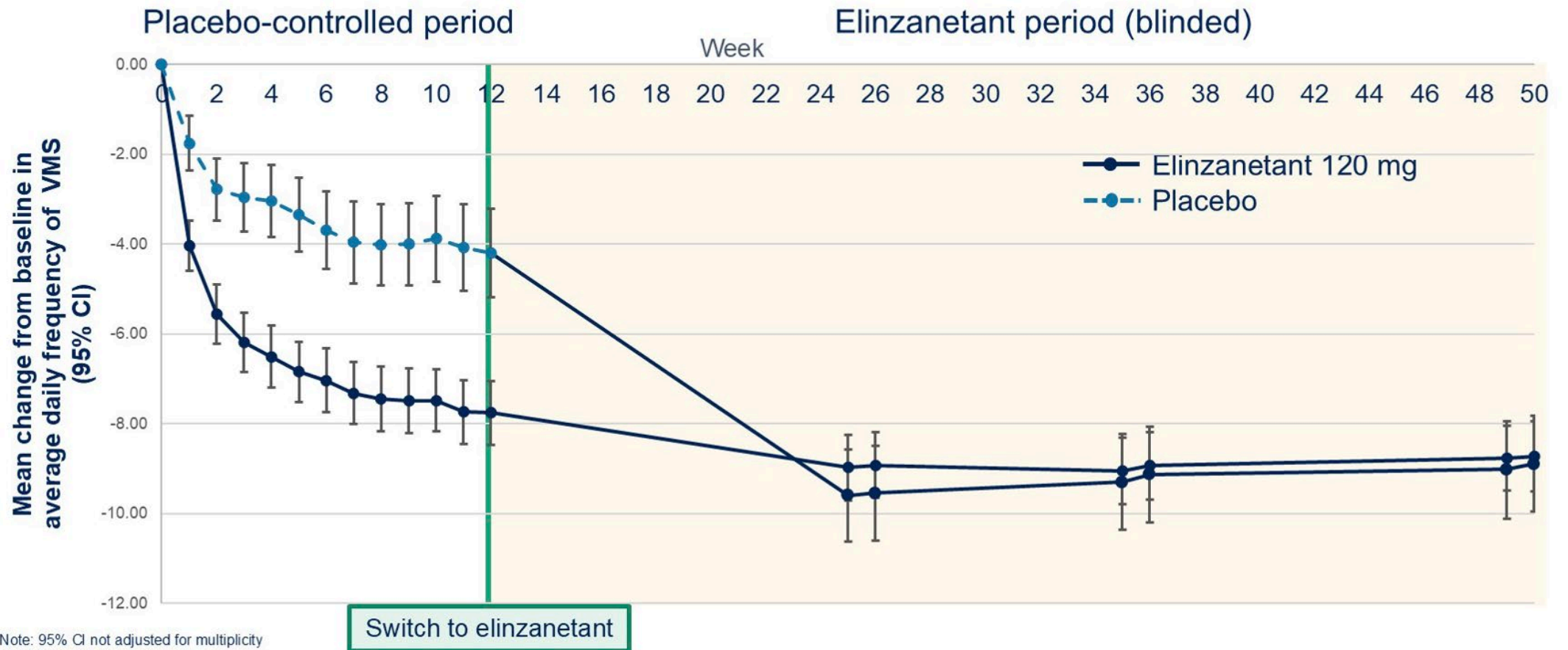
- Wiek – 18-70
- HR+ rak piersi lub wysokie ryzyko zachorowania na raka piersi
- Objawy VMS związane z terapia hormonalną: tamoksyfen, IA +/- GnRH
- Codzienny dzienniczek wybuchów gorąca przez 11 dni w ciągu 2 tygodni przed włączeniem do badania - **≥35** umiarkowanych lub ciężkich wybuchów gorąca w ciągu tygodnia, z uwzględnieniem epizodów nocnych

ŁAGODNE	UMIARKOWANE	CIĘŻKIE
Uczucie ciepła bez pocenia się	Uczucie ciepła z poceniem się	Uczucie ciepła z poceniem się oraz upośledzeniem aktywności



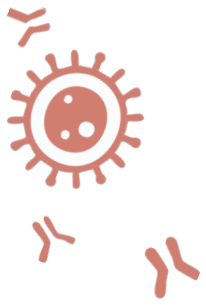


Zmiany w częstości występowania objawów VMS



Note: 95% CI not adjusted for multiplicity
VMS, vasomotor symptoms.





Podsumowanie

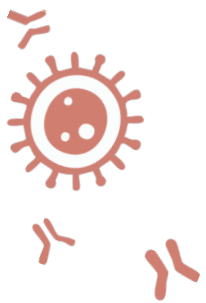
- Elinzanetant zmniejsza częstość oraz nasilenie VMS
- Efekt był obserwowany po tygodniu stosowania
- Leczenie było dobrze tolerowane
- Ograniczenia badania:
 - 1 osoba z wysokim ryzykiem zachorowania na raka
 - nie określono wpływu terapii na rokowanie
 - wykluczono chore z rozsiałym rakiem piersi



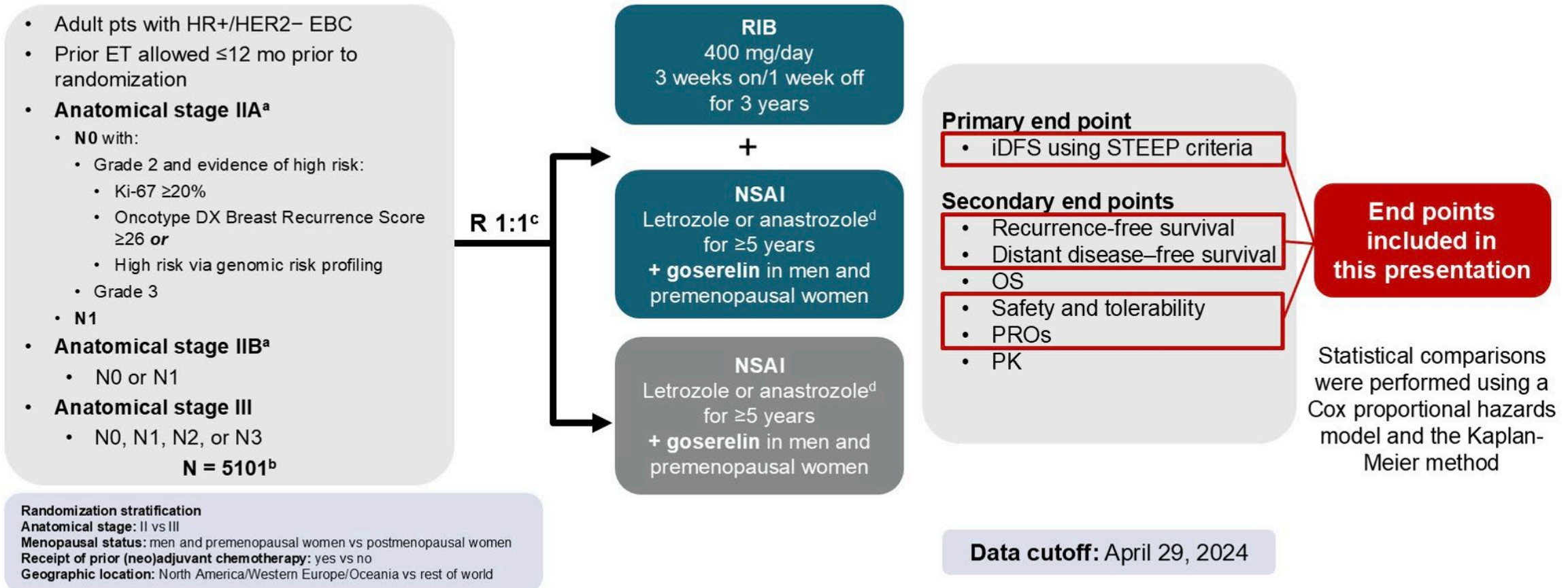


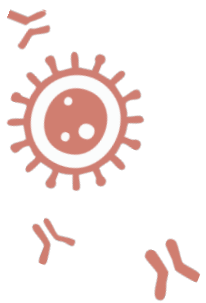
Skuteczność i bezpieczeństwo rybocyklibu w
połączeniu z IA w zależności od wieku oraz
statusu menopauzalnego
– wyniki badania NATALEE





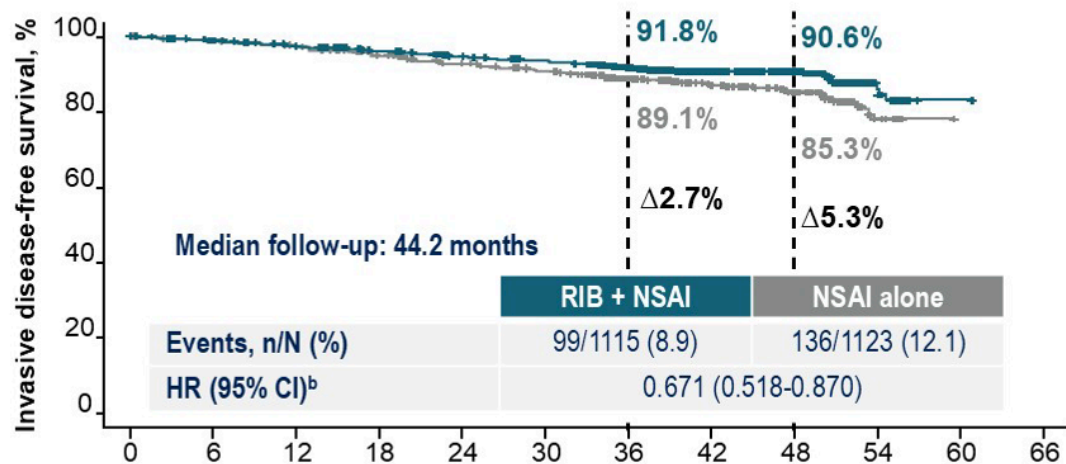
Schemat badania





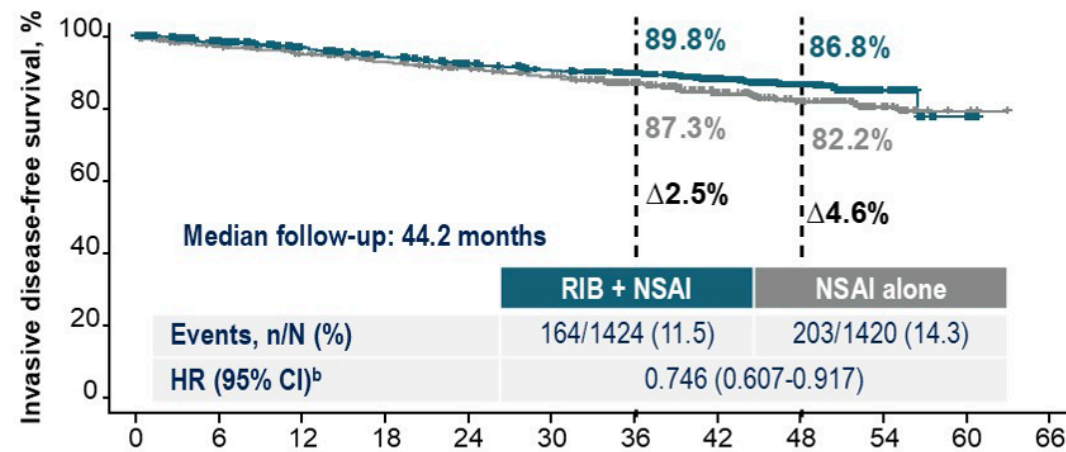
iDFS w zależności od statusu menopauzalnego

iDFS in Premenopausal Pts



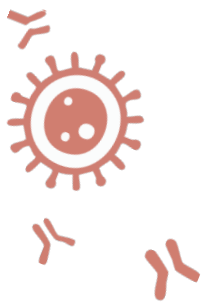
No. at risk	Time, months											
	0	6	12	18	24	30	36	42	48	54	60	66
RIB + NSAI	1115	1038	1013	987	958	939	810	646	375	59	2	0
NSAI alone	1123	994	974	932	894	864	736	592	350	52	0	0

iDFS in Postmenopausal Pts



No. at risk	Time, months											
	0	6	12	18	24	30	36	42	48	54	60	66
RIB + NSAI	1424	1305	1254	1212	1167	1133	1027	830	535	96	6	0
NSAI alone	1420	1237	1187	1143	1105	1064	944	768	495	96	6	0

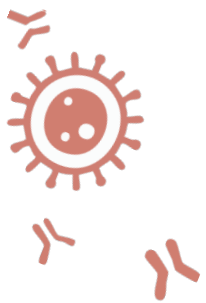




Wyniki u chorych przed menopauzą

n = 2238	All		<40 years		≥40 years	
	RIB + NSAI n = 1115	NSAI alone n = 1123	RIB + NSAI n = 237	NSAI alone n = 276	RIB + NSAI n = 878	NSAI alone n = 847
iDFS						
Events, n	99	136	27	37	72	99
4-y rate, %	90.6%	85.3%	88.6%	82.3%	91.2%	86.2%
4-y ΔiDFS, %	Δ5.3%		Δ6.3%		Δ5.0%	
HR ^b (95% CI)	0.671 (0.518-0.870)		0.690 (0.419-1.137)		0.662 (0.488-0.897)	
DDFS						
Events, n	88	124	24	35	64	89
4-y rate, %	91.6%	86.6%	90.0%	83.0%	92.0%	87.6%
4-y ΔDDFS, %	Δ5.0%		Δ7.0%		Δ4.4%	
HR ^b (95% CI)	0.655 (0.498-0.861)		0.647 (0.383-1.091)		0.659 (0.478-0.908)	
RFS						
Events, n	85	122	25	33	60	89
4-y rate, %	92.0%	86.6%	89.5%	84.0%	92.7%	87.4%
4-y ΔRFS, %	Δ5.4%		Δ5.5%		Δ5.3%	
HR ^b (95% CI)	0.641 (0.486-0.845)		0.723 (0.429-1.220)		0.610 (0.439-0.846)	
DRFS						
Events, n	77	113	23	33	54	80
4-y rate, %	92.7%	87.6%	90.4%	83.9%	93.3%	88.6%
4-y ΔDRFS, %	Δ5.1%		Δ6.5%		Δ4.7%	
HR ^b (95% CI)	0.627 (0.469-0.837)		0.659 (0.386-1.126)		0.615 (0.435-0.869)	

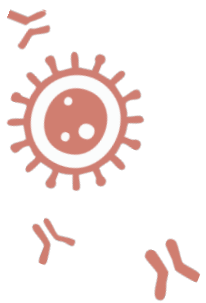




Wyniki u chorych po menopauzie

n = 2844	All		<60 years		≥60 years	
	RIB + NSAI n = 1424	NSAI alone n = 1420	RIB + NSAI n = 703	NSAI alone n = 735	RIB + NSAI n = 721	NSAI alone n = 685
iDFS						
Events, n	164	203	82	91	82	112
4-y rate, %	86.8%	82.2%	86.7%	84.0%	86.8%	80.4%
4-y Δ iDFS, %	$\Delta 4.6\%$		$\Delta 2.7\%$		$\Delta 6.4\%$	
HR ^b (95% CI)	0.746 (0.607-0.917)		0.835 (0.619-1.128)		0.673 (0.506-0.896)	
DDFS						
Events, n	152	186	76	83	76	103
4-y rate, %	87.7%	83.6%	87.6%	85.4%	87.8%	81.9%
4-y Δ DDFS, %	$\Delta 4.1\%$		$\Delta 2.2\%$		$\Delta 5.9\%$	
HR ^b (95% CI)	0.759 (0.612-0.941)		0.854 (0.625-1.168)		0.681 (0.506-0.916)	
RFS						
Events, n	139	175	72	82	67	93
4-y rate, %	88.8%	84.5%	88.3%	85.5%	89.3%	83.5%
4-y Δ RFS, %	$\Delta 4.3\%$		$\Delta 2.8\%$		$\Delta 5.8\%$	
HR ^b (95% CI)	0.735 (0.588-0.919)		0.811 (0.590-1.114)		0.668 (0.487-0.915)	
DRFS						
Events, n	133	162	68	75	65	87
4-y rate, %	89.2%	85.6%	88.8%	86.7%	89.6%	84.6%
4-y Δ DRFS, %	$\Delta 3.6\%$		$\Delta 2.1\%$		$\Delta 5.0\%$	
HR ^b (95% CI)	0.763 (0.606-0.960)		0.842 (0.606-1.172)		0.693 (0.502-0.956)	





Bezpieczeństwo

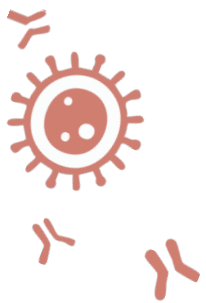
Safety set, n (%)	Premenopausal pts (n = 2178)			Postmenopausal pts (n = 2771)		
	All RIB = 1108	<40 years RIB = 237	≥40 years RIB = 871	All RIB = 1409	<60 years RIB = 697	≥60 years RIB = 712
AESI, any grade						
Neutropenia	739 (66.7)	169 (71.3)	570 (65.4)	845 (60.0)	416 (59.7)	429 (60.3)
Liver-related AEs	270 (24.4)	51 (21.5)	219 (25.1)	403 (28.6)	177 (25.4)	226 (31.7)
QT prolongation	67 (6.0)	15 (6.3)	52 (6.0)	68 (4.8)	27 (3.9)	41 (5.8)
RIB discontinuation due to AE^b	179 (16.1)	25 (10.5)	154 (17.5)	326 (22.9)	125 (17.8)	201 (27.9)
Without dose reduction ^c	135 (75.4)	13 (52.0)	122 (79.2)	220 (67.5)	85 (68.0)	135 (67.2)
ALT elevation	69 (6.2)	8 (3.4)	61 (7.0)	113 (8.0)	44 (6.3)	69 (9.7)
AST elevation	25 (2.3)	2 (0.8)	23 (2.6)	47 (3.3)	21 (3.0)	26 (3.7)
RIB dose reduction due to AE	248 (22.4)	64 (27.0)	184 (21.1)	332 (23.6)	169 (24.2)	163 (22.9)
Neutropenia ^d	178 (16.1)	47 (19.8)	131 (15.0)	177 (12.6)	103 (14.8)	74 (10.4)
ALT elevation	13 (1.2)	3 (1.3)	10 (1.1)	35 (2.5)	16 (2.3)	19 (2.7)

AE, adverse event; AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FSH, follicle-stimulating hormone; pt, patient; RIB, ribociclib.

^a Postmenopausal status was defined as 1 of the following: bilateral oophorectomy; age ≥60 years; age <60 years with ≥12 months of amenorrhea (not due to chemotherapy, tamoxifen, toremifene, or ovarian suppression) and FSH and plasma estradiol in the postmenopausal range per local laboratories; or, if on tamoxifen or toremifene and age <60 years, FSH and plasma estradiol in the postmenopausal range. All women who do not meet the criteria for postmenopausal status are considered premenopausal. ^b Percentage calculated based on pts in the full analysis set. ^c Percentage calculated out of total pts who discontinued RIB due to AEs. ^d Grouped term that combines neutropenia and neutrophil count decreased.

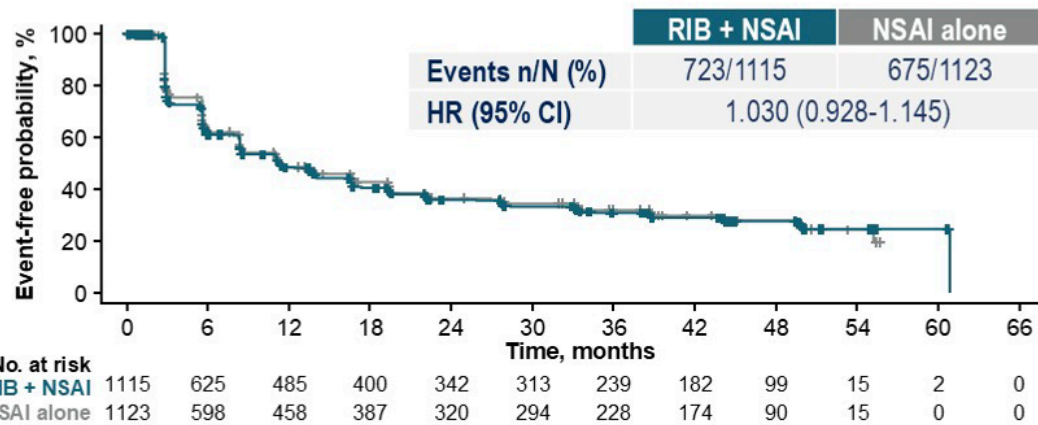
Data on file. NATALEE CLEE011O12301C (TRIO033). Clinical study protocol. V4.0. Novartis Pharmaceuticals Corp; August 27, 2020.



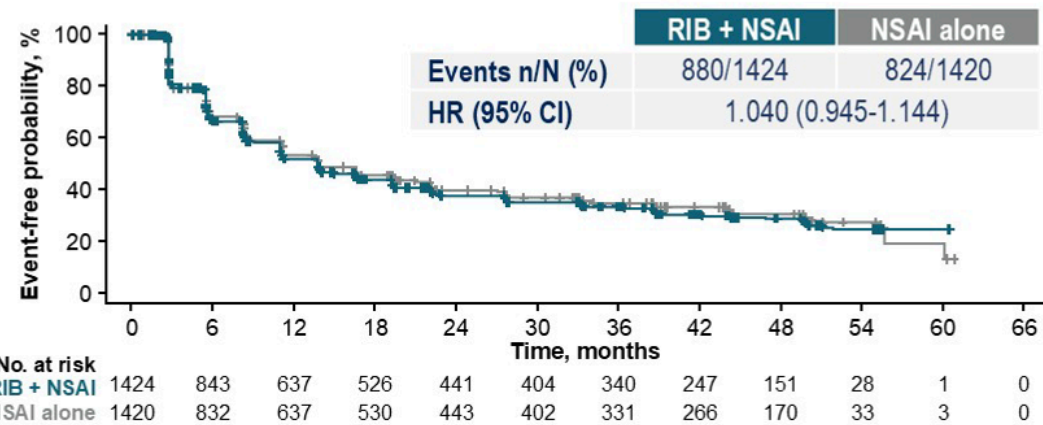


Ocena jakości życia

TTD of GHS in Premenopausal Pts



TTD of GHS in Postmenopausal Pts



TTD of GHS by Menopausal Status and Age

	Premenopausal pts (N = 2238)						Postmenopausal pts (N = 2844)					
	All		<40 years		≥40 years		All		<60 years		≥60 years	
	RIB	NSAI	RIB	NSAI	RIB	NSAI	RIB	NSAI	RIB	NSAI	RIB	NSAI
Events/n	723/1115	675/1123	159/237	154/276	564/878	521/847	880/1424	824/1420	426/703	422/735	454/721	402/685
HR (95% CI)	1.030 (0.928-1.145)		1.085 (0.867-1.356)		1.018 (0.903-1.147)		1.040 (0.945-1.144)		0.996 (0.870-1.141)		1.082 (0.945-1.238)	

EORTC, European Organisation for Research and Treatment of Cancer; FSH, follicle-stimulating hormone; GHS, global health status; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; QoL, quality of life; RIB, ribociclib; TTD, time to first deterioration.
^a Postmenopausal status was defined as 1 of the following: bilateral oophorectomy; age ≥60 years; age <60 years with ≥12 months of amenorrhea (not due to chemotherapy, tamoxifen, toremifene, or ovarian suppression) and FSH and plasma estradiol in the postmenopausal range per local laboratories; or, if on tamoxifen or toremifene and age <60 years, FSH and plasma estradiol in the postmenopausal range. All women who do not meet the criteria for postmenopausal status are considered premenopausal. ^b TTD is defined as the time from baseline to the first occurrence of a ≥10-point decrease in the EORTC QLQ-C30 score.
 Data on file. NATALEE CLEE011O12301C (TRIO033). Clinical study protocol. V4.0. Novartis Pharmaceuticals Corp; August 27, 2020.





Podsumowanie

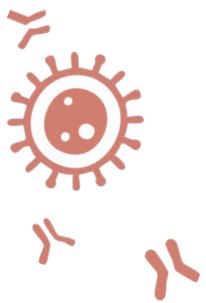
- Dołączenie rybocyklibu do IA u chorych na raka piersi w II i III stopniu zaawansowania poprawia rokowanie niezależnie od wieku i statusu menopauzalnego
- Tolerancja leczenia była dobra
- Zakończenie leczenia z powodu działań niepożądanych obserwowano rzadziej w grupie chorych przed menopauzą





Ocena tolerancji eskalacji dawki abemacyklibu u chorych na wczesnego HR+/HER2- raka piersi – wyniki badania **TRADE**

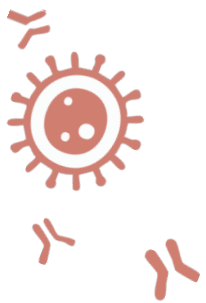




Schemat badania

Patient disposition in monarchE		
Outcome in monarchE	By 12 weeks	Overall at 2 years
Discontinued abemaciclib for any reason	10%	30.6%
<ul style="list-style-type: none">Discontinued for adverse events	7%	18.5%
Required abemaciclib dose reduction	27%	43.4%

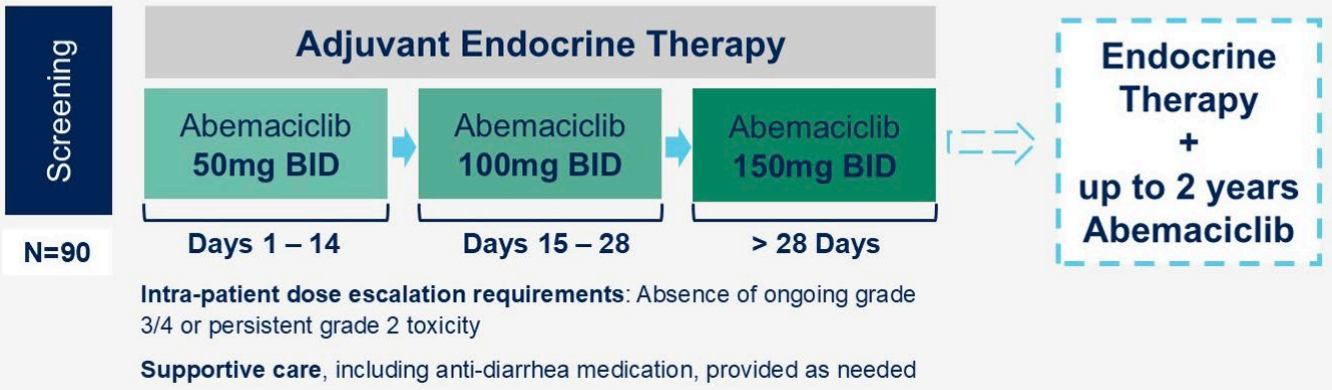


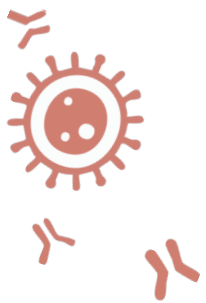


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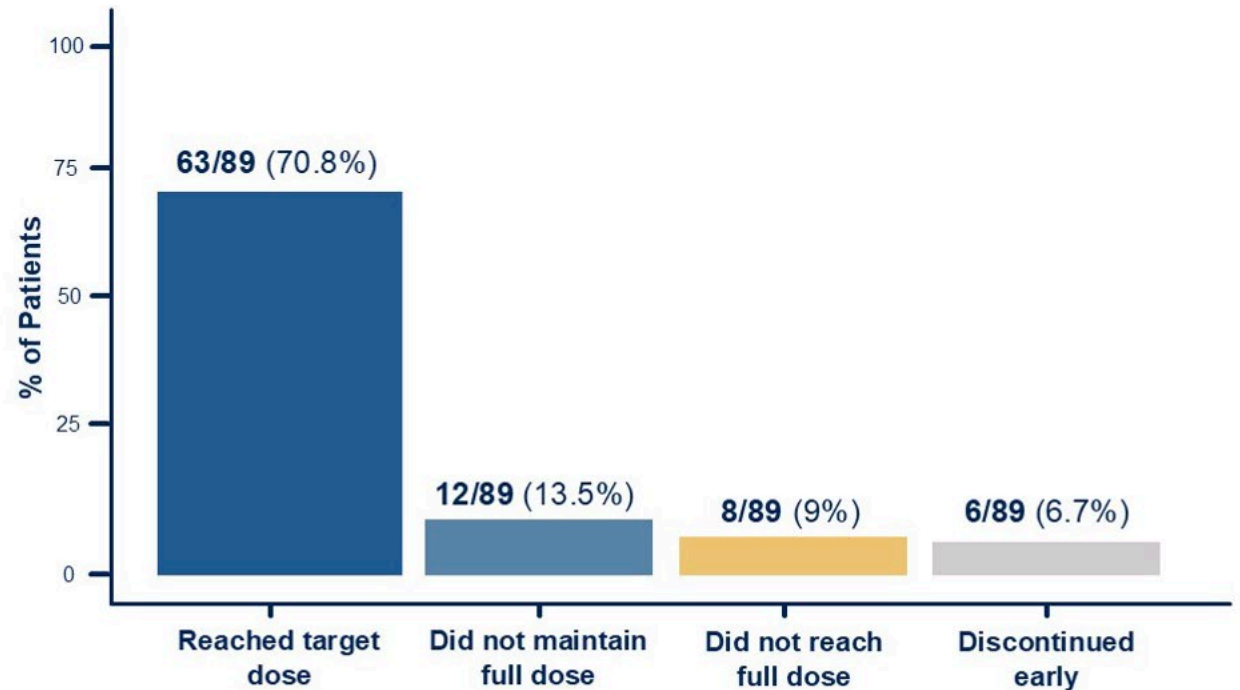
- HR-positive, HER2-negative, early breast cancer
- Adjuvant abemaciclib is indicated based on patient risk/stage

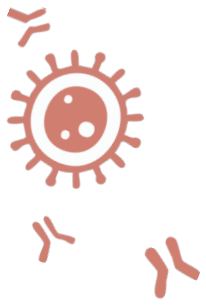




Wyniki

- **70,8%** chorych otrzymywało dawkę 150mg 2 x dziennie w 12. tygodniu badania vs **60%** w badaniu monarchE
- Rzadko obserwowano wczesne zakończenia leczenia – **93,3%** otrzymywało terapię po 12 tygodniach od rozpoczęcia

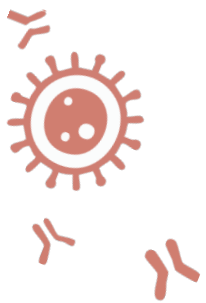




Podsumowanie

- Strategia eskalacji dawki pozwoliła większości chorym na osiągnięcie dawki docelowej oraz zmniejszyła ryzyko przedwczesnemu zakończeniu leczenia
- 93,3% chorych kontynuowało leczenie > 12 tygodni





Dziękuję za uwagę!!!

