

# Deeskalácia lokoregionálnej liečby pri karcinóme prsníka

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# Deeskalácia

- =personalizácia liečby
- =optimalizácia (efektivita terapie vs riziko NU)
- Chirurgická
  - ME vs parciálna ME/WLE
    - Žiadna operácia ak pCR?
  - Re-excízia pri tesnom okraji
    - Stačí „no-ink on tumor“
  - ALND vs. SLNB
    - Dokončenie ALND pri pozitivite SLN vs. iba SLNB
    - Žiadna SLNB
    - TAD vs TLNB (po neoadj. CHT, klipy do LU)

# Deeskalácia

- Rádioterapeutická

- Whole-breast RT (WBRT, WBI) vs. APBI (ďalšie prednášky - Drs. P. Lukačko, D. Ščepanovič)
- Žiadna RT (na prsník, na axilu)

- Systémovej liečby

- Riziko rekurencie, genomické testy
- CHT vs no CHT

- **CAVE!**

- Deeskalácia chirurgie → eskalácia v RT
- „One-size (treatment)-fits-all“ – neplatí pri Ca prsníka

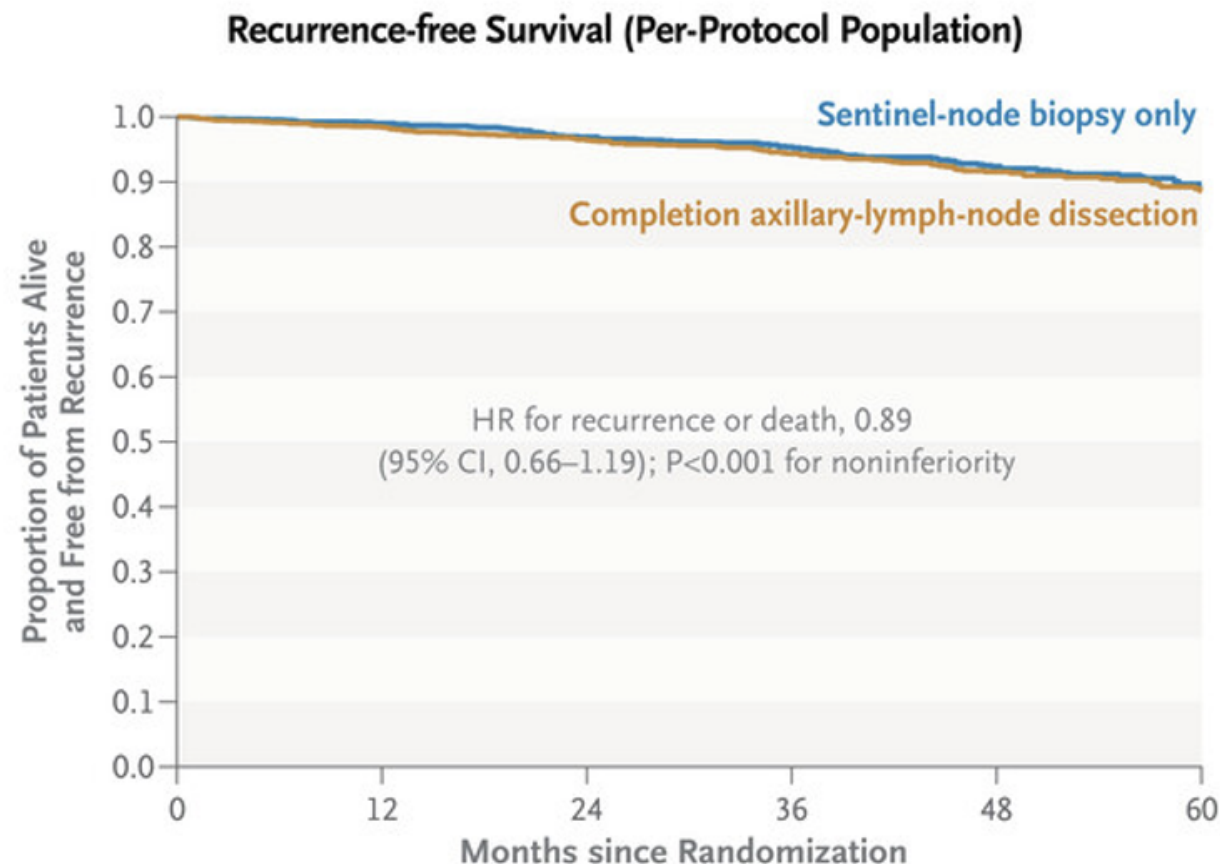
# SLNB vs ALND

- Vynechanie ALND pri pozitivite SLNB:

- IBCSG 23-01 (r. 2013, 2018)
- ACOSOG Z0011 (r. 2005, 2017)
- SINODAR-ONE (r. 2022)

- Nahradenie ALND pri pozitivite SLNB rádioterapiou:

- OTOASOR (r.2013, 2017)
- AMAROS (r. 2014, 2022)
- **SENOMAC (r. 2024)**
  - cT1-3, do 2 makro-mts SLNB+, micro-mts OK, ENE+ OK



# No axillary surgery vs. SLNB

- INSEMA trial
  - Zatiaľ máme iba PRO/QoL
  - Beží v D, A
- BOOG 2013-08
  - Beží v NL
- **SOUND trial (r.2023)**
  - do 2cm, nie viacpočetné multifokálne/multicentrické
  - Medián vek 60r.
  - negat USG axily
  - Všetky pac. mali ale RT!!

## FINDINGS

Omission of SLNB was noninferior to SLNB in patients with breast cancer smaller than 2 cm and a negative ultrasound of the axillary lymph nodes



**SLNB: 5-y DDFS, 97.7%**

**No SLNB: 5-y DDFS, 98.0%**

(log-rank test,  $P = .67$ ; hazard ratio, 0.84; 90% CI, 0.45-1.54; noninferiority  $P = .02$ )

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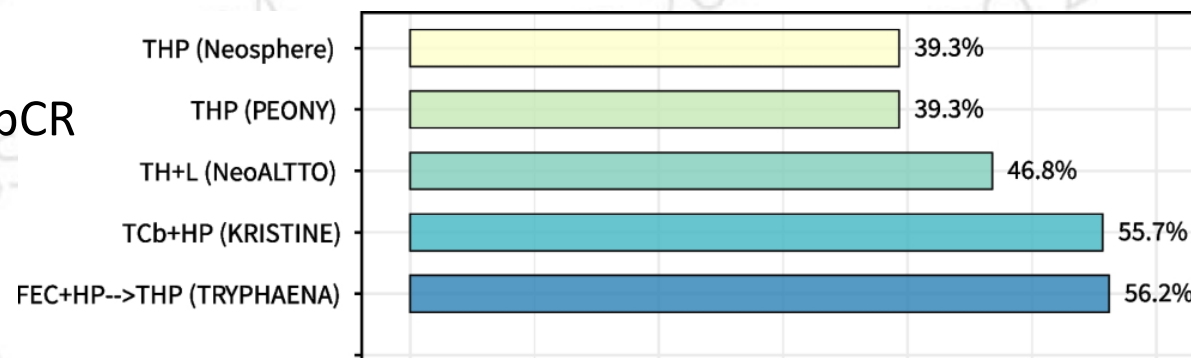
# Neoadjuvantná systémová liečba

- Výhody

- Sledovanie odpovede
- Čas naplánovať operáciu, čas na genetickú analýzu, ...
- Downstaging
- De-esklácia liečby LU – ALND vs SLNB vs TAD, RNI +/-

- Dosiahnutie pCR

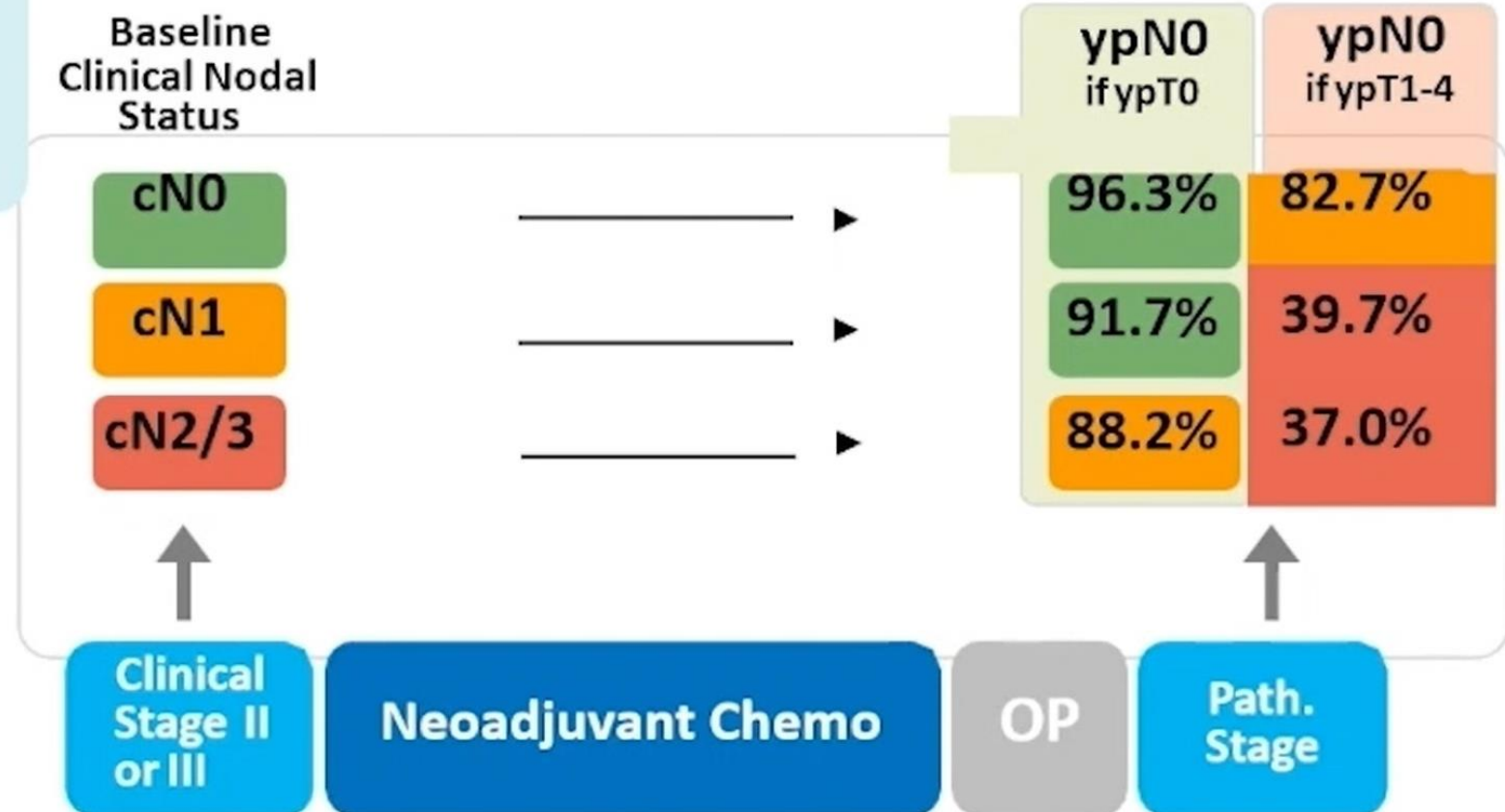
- TNBC – chemo + IO
- HER2 3+ – chemo + duálna anti-HER2 blokáda
- Odpovede – pCR – až 60%
  - Možnosť de-eskalácie liečby u pCR



# DOWNSTAGING OF AXILLA BASED ON RESPONSE TO NACT

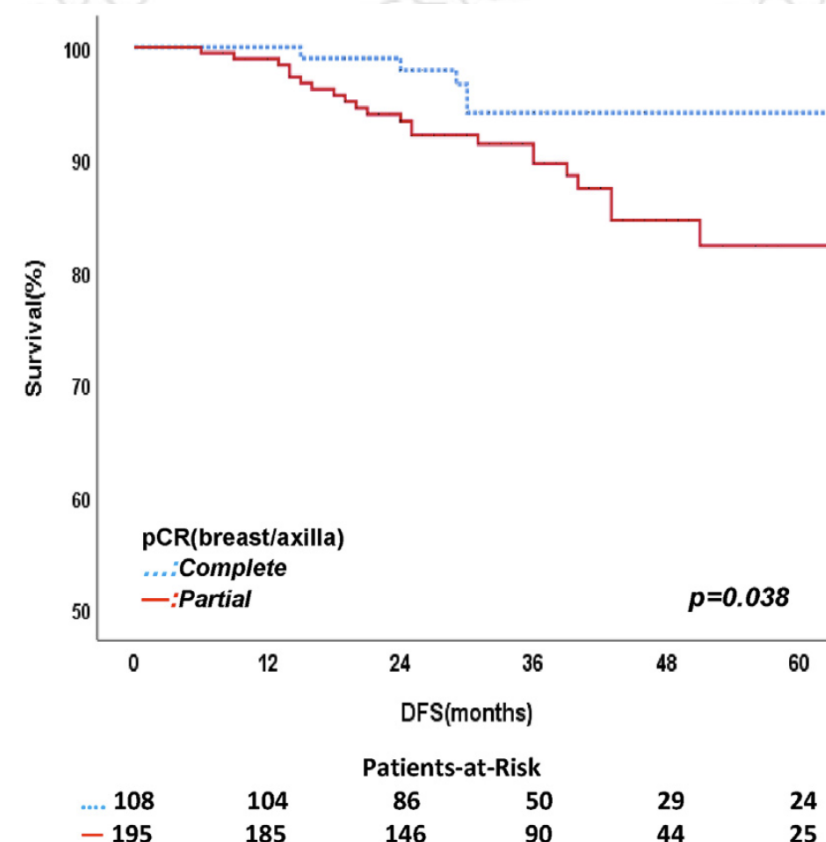
539 patients with stage II-III HER2+ or TNBC treated on CALGB 40601 or 40603

- NACT highly effective in downstaging the axilla
- De-escalation of axillary surgery can be considered if good response to NACT
- Consider SLN or TAD in cN+ with ypT0/is



# Post-neoadjuvatne

- De-eskalácia chirurgie axily
  - ALLIANCE A110202, ADARNAT, TAXIS (štúdie bežia)
    - SLNB+RT vs ALND+RT u ypN+
  - AXSANA, ATNEC (beží)
    - SLNB vs TAD vs ALND u ycN0
  - EUBREAST-01, ASIC, ASLAN (štúdie bežia)
    - Ak pCR v prsníku:
      - cN0 -> 100% čisté LU – bez axil. chirurgie
      - cN1 -> 89% čisté LU -> SLNB
  - **NEOSENTI-TURK MF-18-02 (r. 2021)**
    - cN1->SLNB (pri ypT0 a/alebo ypN0) + RNI (bez ALND)



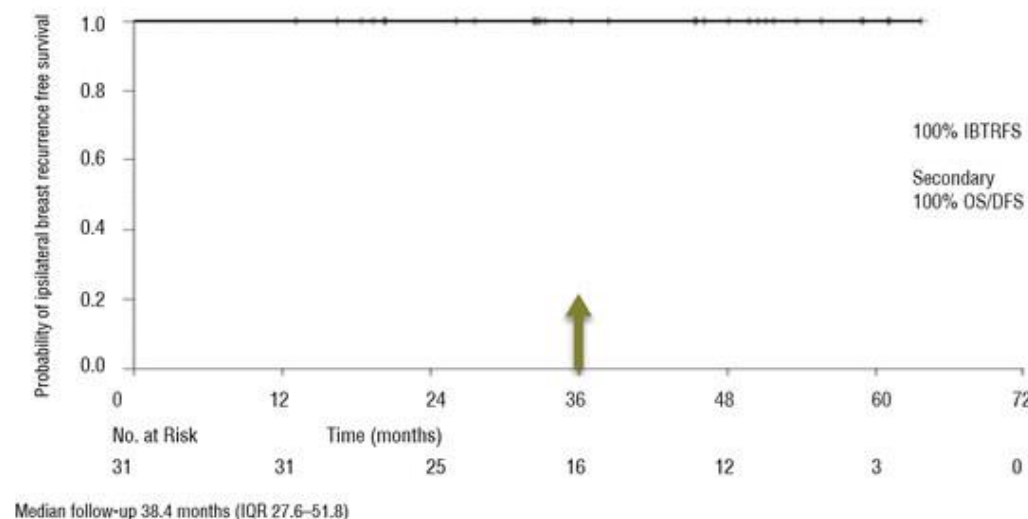


# Post-neoadjuvatne

- De-eskalácia chirurgie prsníka
  - OPTIMIST – beží
    - VACB s pCR, na MRI < 1.0cm,
  - **MD Anderson (r.2022)**
    - pCR (TNBC, HER2 3+) na základe VACB, USG/MRI < 2cm
    - Bez operácie prsníka, iba RT+boost všetky pac.
    - 3-r. follow-up – žiadne IBTR



**RESULTS: Primary objective IBTR-free survival among patients who did not undergo breast surgery 3-year planned analysis**



# Post-neoadjuvatne

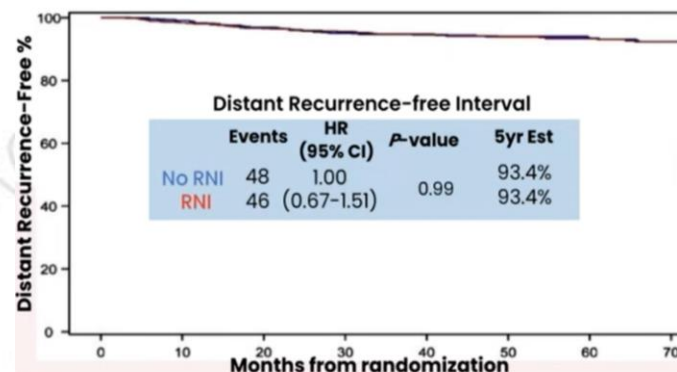
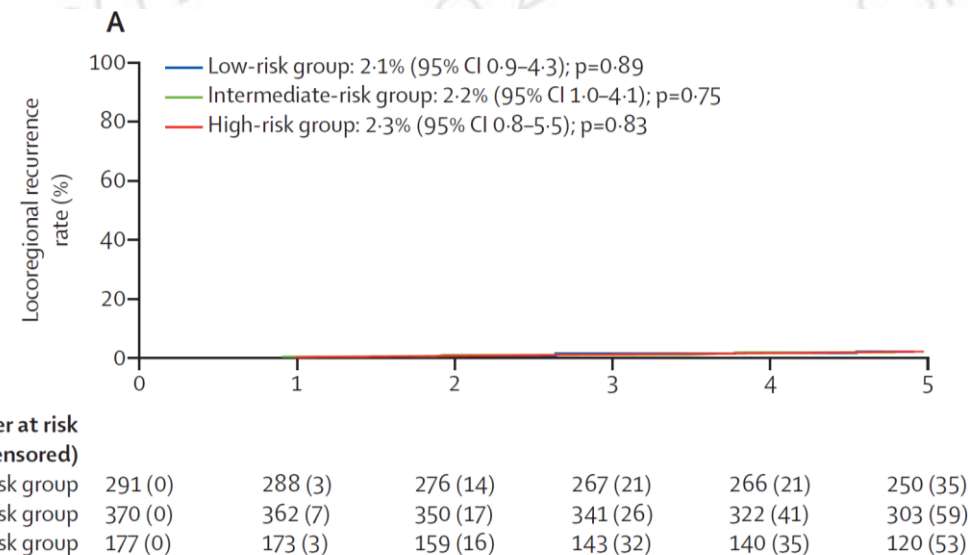
- De-eskalácia RT axily

- RAPCHEM (r. 2022)**

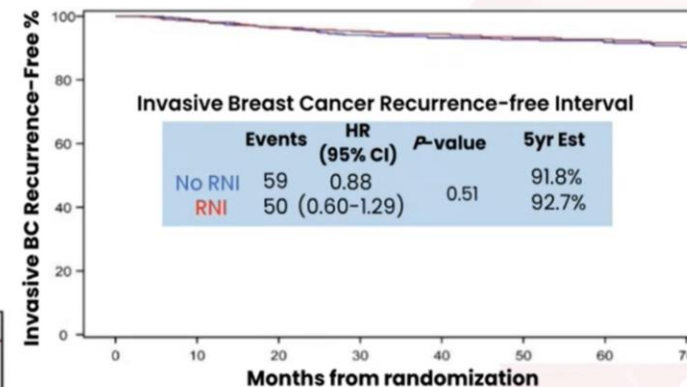
- cT1-2N1
    - ypN0 pri ALND – iba WBR, bez RNI
    - 5-r. LRR 1%

- NSABP B-51 (r. 2023)**

- cT1-T3, pN1 (biopsia)
    - pN1 -> ypN0 pri SLNB (min. 2LU)
    - Žiaden benefit RNI

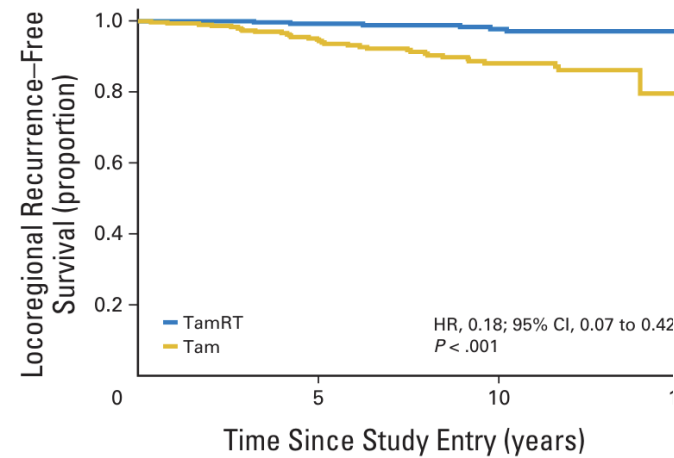


## NSABP B-51

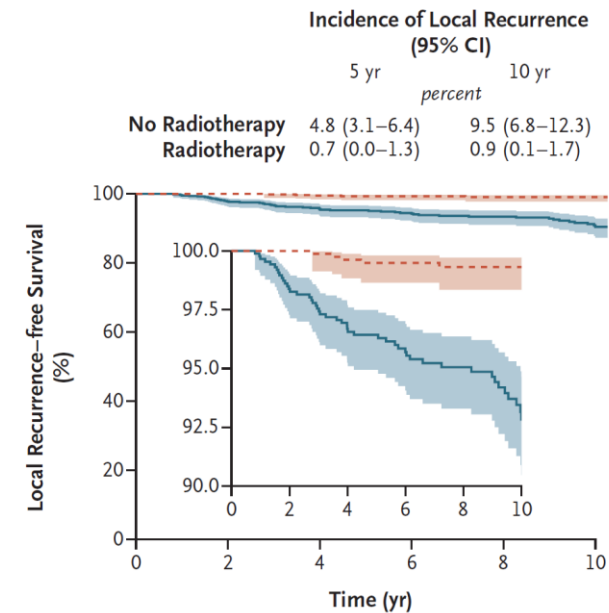


# Vynechanie RT prsníka (po parc. oper.)

- *NSABP B21 trial (r. 2002)*
  - *RT vs RT+TMX vs TMX sólo u pT1N0*
  - *LRR 9,3 vs 2,8 vs 16,5%, rovnaké OS*
- *CALGB 9343 (r. 2004, 2013)*
  - Nad 70r
  - pT1N0, ER+,
  - LRR 2 vs 9%, rovnaké OS
- *PRIME-II (r. 2015, **2023**)*
  - Nad 65r
  - pT1-2<sub>(3cm)</sub> N0, R0, HR+
  - Lokálne rekurencie z 0,9% na 9,5%
  - Rovnaké DDFS, OS



No. at risk			
TamRT	317	261	162
Tam	319	243	144



No. at Risk						
No radiotherapy	668	628	569	463	369	209
Radiotherapy	658	625	585	478	383	207

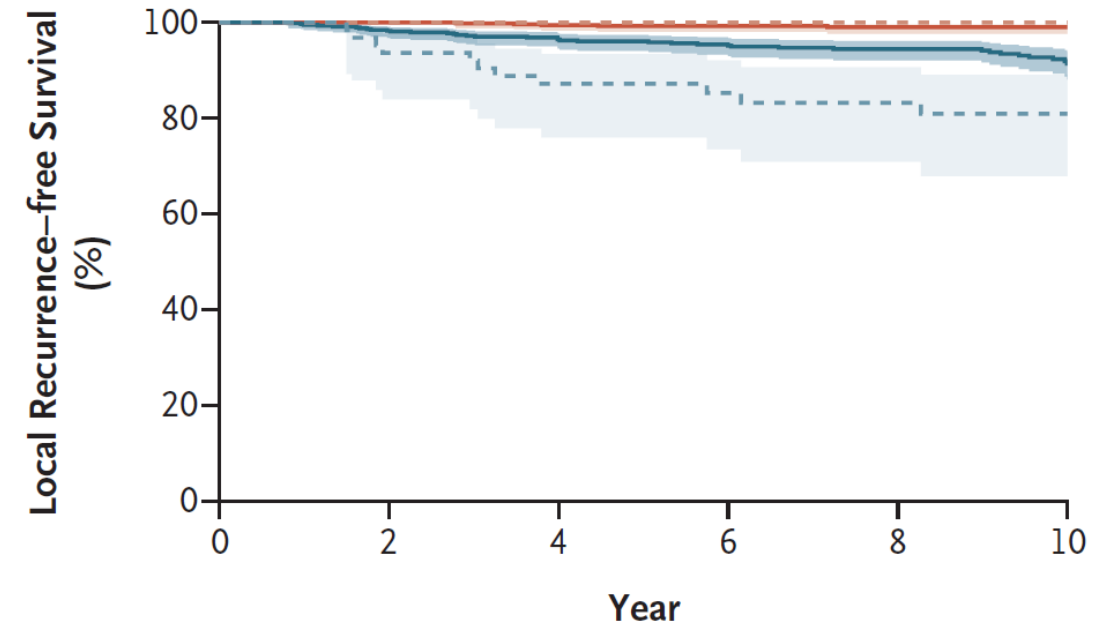
# Vynechanie RT prsníka (po parc. oper.)

- PRIME-II (r. 2015, 2023)
  - ER low – 19 % LRR !
  - ER high (nad 50%) – 8,6%
  - Nie u: ER < 50%
  - LVSI+
  - Gr 3
  - zlá adherencia ku HT

— ER-high, radiotherapy — ER-high, no radiotherapy  
 - - ER-low, radiotherapy - - ER-low, no radiotherapy

Incidence of Local Recurrence  
(95% CI)

	5 yr percent	10 yr
ER-high, Radiotherapy	0.7 (0.0–1.5)	1.0 (0.1–1.9)
ER-high, No Radiotherapy	3.9 (2.3–5.6)	8.6 (5.7–11.4)
ER-low, Radiotherapy	0.0	0.0
ER-low, No Radiotherapy	12.7 (4.3–21.2)	19.1 (8.2–29.9)



No. at Risk

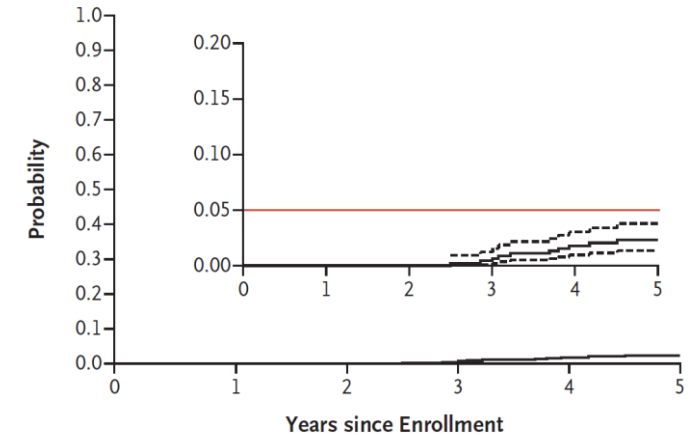
	603	574	537	439	356	193
ER-high, radiotherapy	603	574	537	439	356	193
ER-high, no radiotherapy	593	560	507	414	329	189
ER-low, radiotherapy	53	50	47	38	27	14
ER-low, no radiotherapy	65	59	53	42	38	19



# Vynechanie RT prsníka (po parc. oper.)

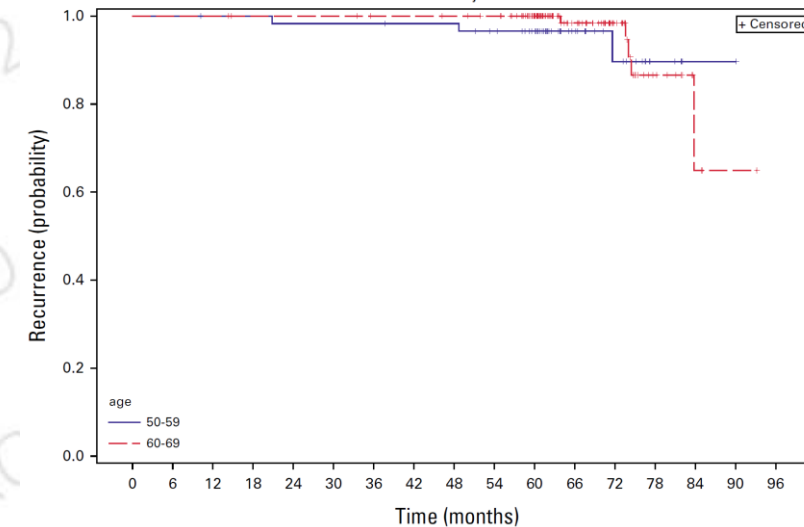
- **LUMINA (r.2023)**
  - nad 55r, ( $\tilde{x}$ =67r)
  - pT1N0, HR+, Ki 67  $\leq$  13,25% (= luminal A)
  - 5-r LR 2,3%
- **IDEA trial (r.2024)**
  - 50-69r, ( $\tilde{x}$ =62r)
  - pT1N0, HR+, Oncotype DX Breast Score  $\leq$  18
  - 5-r LR 3,5%

A Local Recurrence



No. at Risk 500 477 463 449 398 246

Freedom From Recurrence Estimates  
With No. of Subjects at Risk



age	60	60	59	59	58	58	58	57	57	54	49	22	13	5	1	1	0
50-59	60	60	59	59	58	58	58	57	57	54	49	22	13	5	1	1	0
60-69	140	140	140	138	138	138	136	136	135	133	108	58	34	13	3	1	0



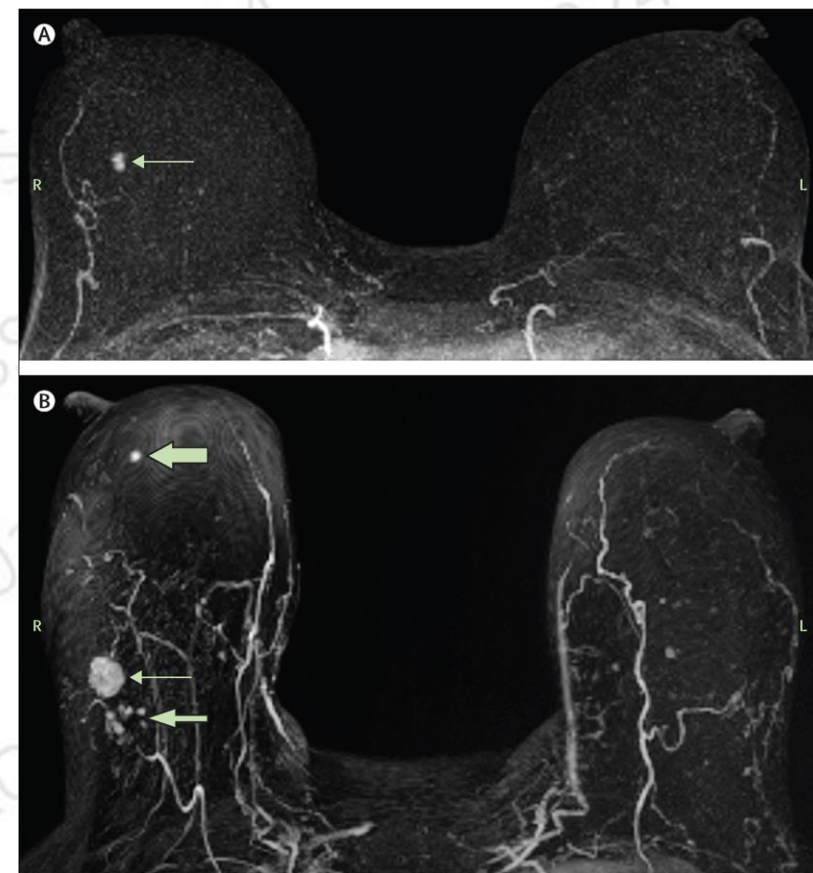
# Vynechanie RT prsníka (po parc. oper.)

- **PROSPECT (r.2024)**

- Nad 50r., ( $\bar{x}$ =63r)
- cT1N0/pN1mi, predoperačne MRI – unifokálne
- (11% pac. malo okultné tu. na MRI)
  - 63% okultných lézií > 2cm od tu.
- 5-r. IRR 1.0% + nodal R 1%

- **E4112 trial (r.2023 –SABCS)**

- Low-risk DCIS, R0
- MRI + Oncotype DX Breast DCIS Score  $\leq 39$
- 5-r. LRR 5,5% ( vs. 4,8% high-risk kt. mali RT)



**Table 5**

Ongoing trials on de-escalation/optimisation of treatment for early-stage breast cancer.

	EUROPA [87]	EXPERT	NATURAL	PRECISION	PRIMETIME [88]	IDEA	LUMINA
<b>Study type (number of patients)</b>	Phase 3 Randomised (926)	Phase 3 Randomised (1167)	Phase 3 Randomised (926)	Single arm (690)	Single arm (2400)	Single arm (202)	Single arm (500)
<b>Age (years)</b>	≥70	≥50	≥60	50–75	≥60	50–69	≥55
<b>Stage, histology, biological subtype, margins</b>	T1 N0 Any grade (≤10 mm) Grade 1–2 (11–19 mm) ER/PgR ≥10% HER2 neg Ki67 ≤ 20% Negative surgical margins (no ink)	pT1 N0 Grade 1–2 ER/PgR ≥10% negative ROR score ≤60 Negative surgical margins	pT1 N0 Grade 1–2 ER ≥ 10% HER2 negative Surgical margins ≥2 mm	pT1 N0 Grade 1–2 ER/PgR ≥10% HER2 negative Negative surgical margins	pT1 N0 Grade 1–2 Very low risk patients (based on IHC4 + C) ER/PgR positive HER2 negative Surgical margins ≥1 mm	pT1 N0 Any Recurrence Score ≤18 ER/PgR positive HER2 negative Surgical margins ≥2 mm	pT1 N0 Grade 1–2 ER ≥ 1% PgR >20% HER2 negative Surgical margins ≥1 mm
<b>Method</b>	IHC FISH for HER2 2+	PAM 50 FISH for HER2 2+	IHC FISH for HER2 2+	PAM 50 FISH for HER2 2+	IHC4+C FISH for HER2 2+	Oncotype-DX FISH for HER2 2+	IHC FISH for HER2 2+
<b>Arms</b>	RT vs ET	ET + RT vs ET	ET + RT vs ET	ET only	ET only	ET only	ET only
<b>Primary endpoint(s)</b>	5-year LR 2-year HRQoL	5-year LR	5-year LR	5-year LR	5-year LR	5-year LR	5-year LR

Abbreviations: LR, local recurrence; ET, endocrine therapy; IHC, immune histochemistry; FISH, fluorescent in situ hybridization; HRQoL, health-related quality of life; RT, radiation therapy; EIC, extensive intraductal component; IHC4 + C, immunohistochemical biomarkers plus clinical information; ER, oestrogen receptor; PgR, progesterone receptor; ROR score, risk of recurrence score.

# Záver

- Žiadna operácia ak pCR? – **áno, ak VACB, štúdie**
- Žiadna SLNB? – **áno, ak spĺňa SOUND kritéria, všetky mali RT**
- Iba SLNB po neoadj.? – **áno, ak ypT0, štúdie**
- Žiadna RNI po neoadj. – **áno, ak ypN0**
- Žiadna WBI? – **áno, vybraté pacientky s low-risk, luminal A nádormi**

Ďakujem za pozornosť

