



HOSPITAL ISRAELITA
ALBERT EINSTEIN

instituto
Oncoguia

Terapia Neoadjuvante para tumores Her2+

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Declaração de Conflito de Interesses

De acordo com a Resolução 1595/2000 do CFM e RDC 96/08 da ANVISA

- Diretor Científico Instituto Oncoguia
 - Voluntário
- Advisory Board
 - Roche, Pfizer, AstraZeneca*
- Aulas e/ou atividades educacionais remuneradas:
 - AstraZeneca, Roche, Janssen, Pfizer, Novartis, Sanofi*

Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis

Patricia Cortazar, Lijun Zhang, Michael Untch, Keyur Mehta, Joseph P Costantino, Norman Wolmark, Hervé Bonnefoi, David Cameron,

Clinical tumour subtype

Hormone-receptor-positive, HER2-negative, grade 1/2 (n=1986)

Hormone-receptor-positive, HER2-negative, grade 3 (n=630)

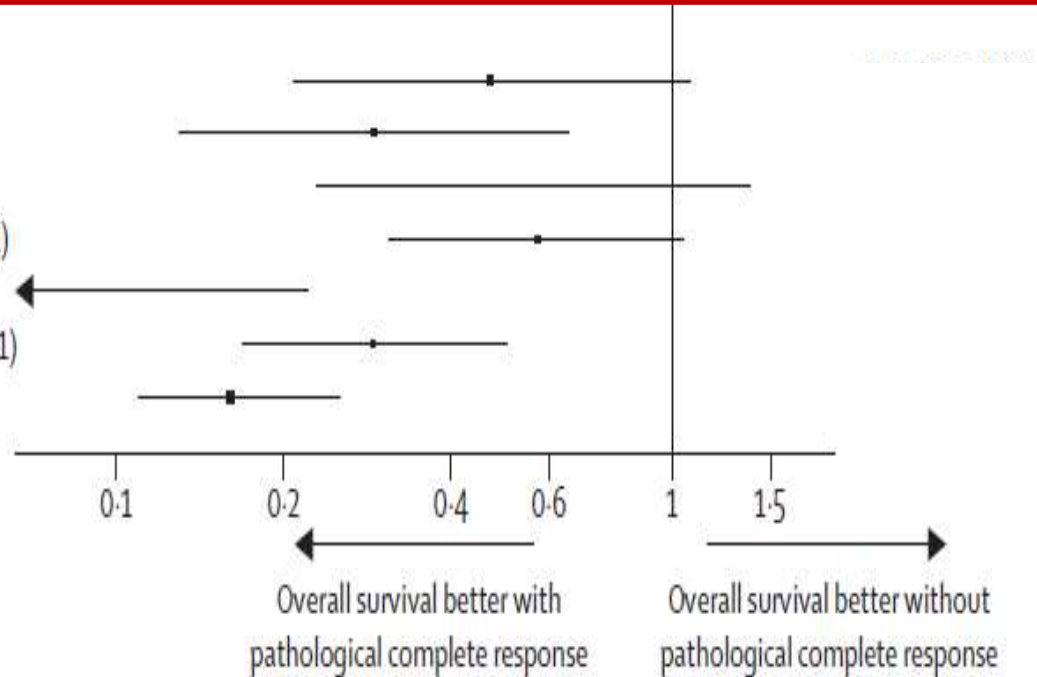
HER2-positive, hormone-receptor-positive, trastuzumab (n=385)

HER2-positive, hormone-receptor-positive, no trastuzumab (n=701)

HER2-positive, hormone-receptor-negative, trastuzumab (n=364)

HER2-positive, hormone-receptor-negative, no trastuzumab (n=471)

Triple negative (n=1157)



Duplo bloqueio Her2 melhora pCR? SLD?



Survival outcomes of the NeoALTO study: updated results of a randomized multicenter phase 3 neoadjuvant trial

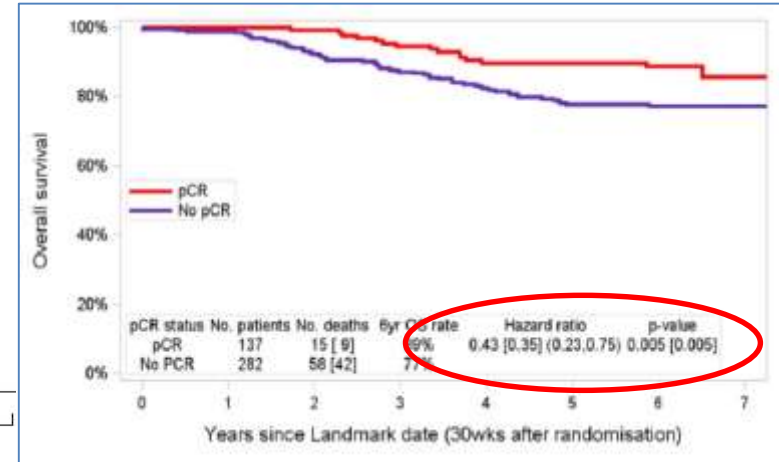
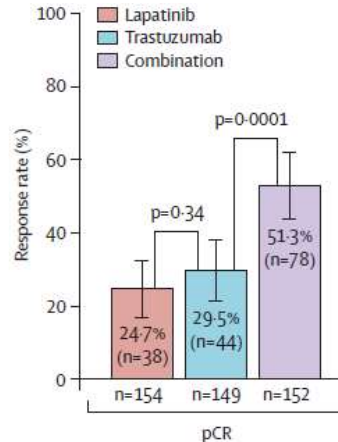
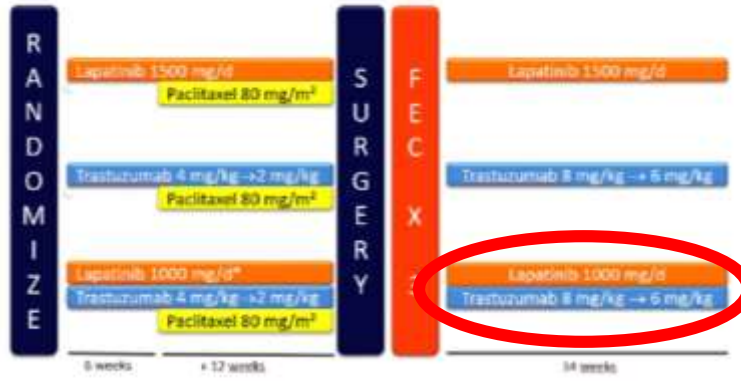
#512

Jens Huober, Eileen Holmes, José Baselga, Evandro de Azambuja, Michael Untch, Debora Fumagali, Severine Sarp, Istvan Lang, Ian Smith, Frances Boyle, Binghe Xu, Christophe Lecocq, Lorena de la Pena, Christian Jackisch, Richard D Gelber, Martine Piccart, Serena Di Cosimo

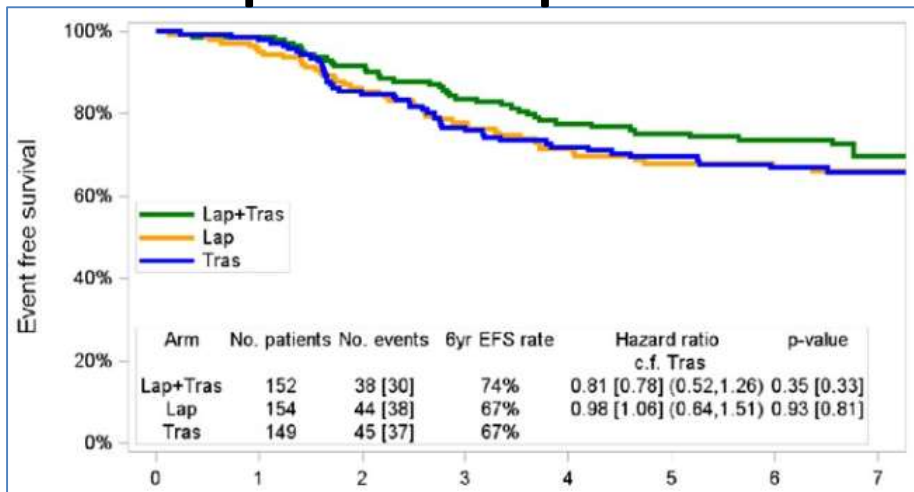


On behalf of the NeoALTO Study Team

Design of the NeoALTO trial:



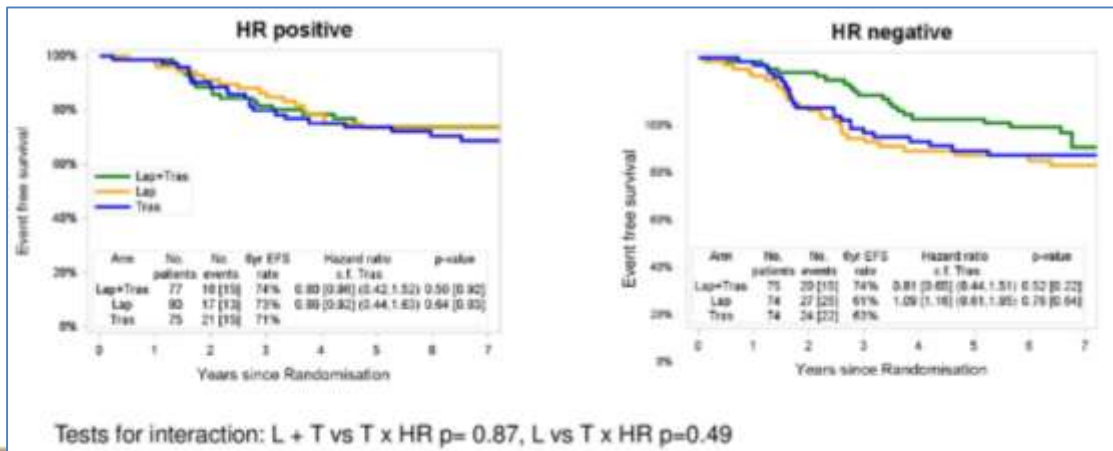
Duplo bloqueio Her2 melhora pCR? SLD?



Conclusions

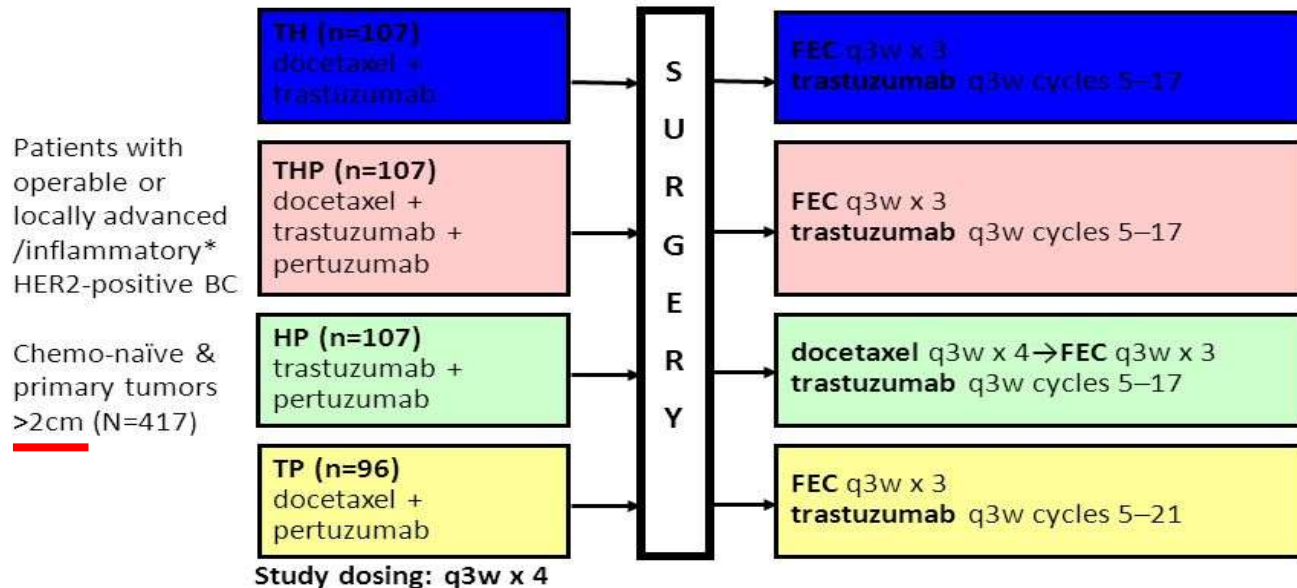
- The updated results of the NeoALTTO study confirm that pts who achieve a pCR have a better EFS and OS
- This difference was mainly observed in the hormone receptor negative group

- EFS and OS after 6 years did not differ significantly between the 3 treatment groups



Qual o embasamento para o padrão atual?

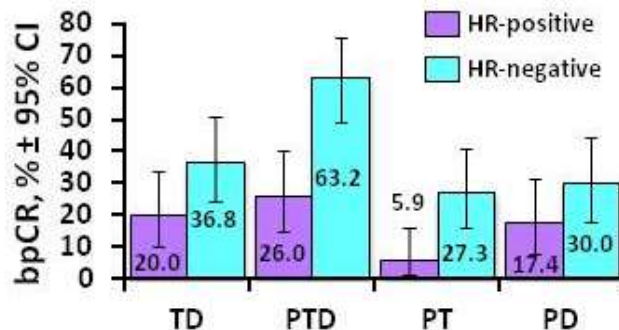
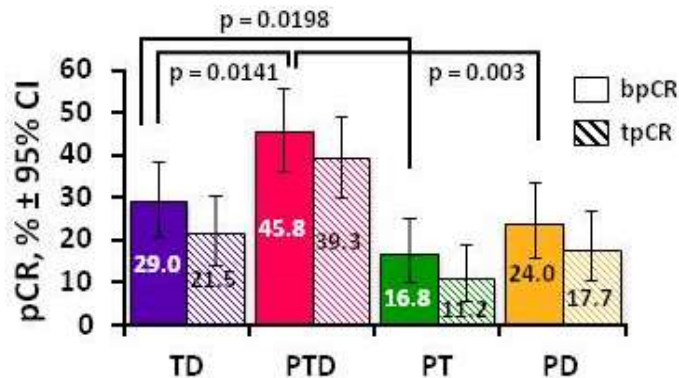
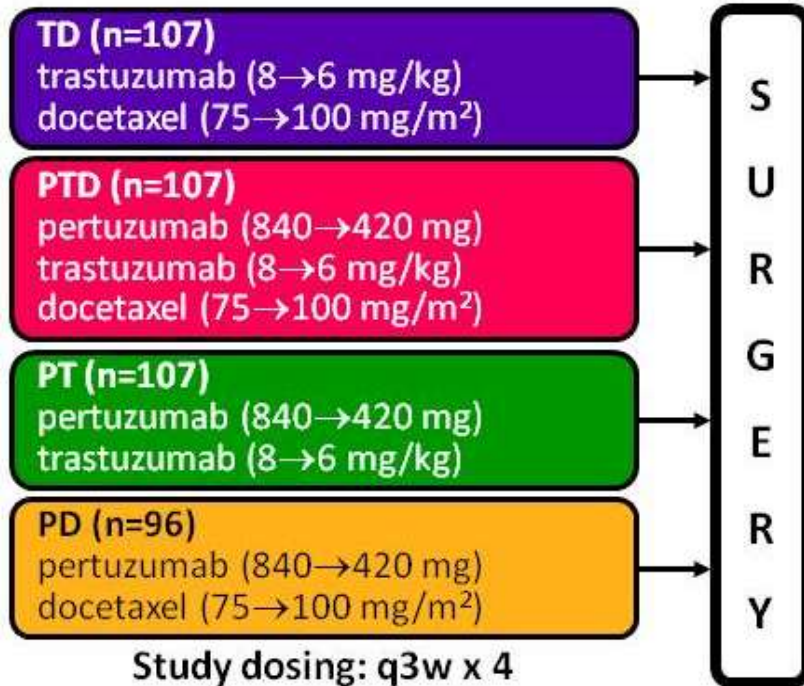
NeoSphere: study design



Qual o embasamento para o padrão atual?

Patients with operable or locally advanced/inflammatory HER2-positive BC

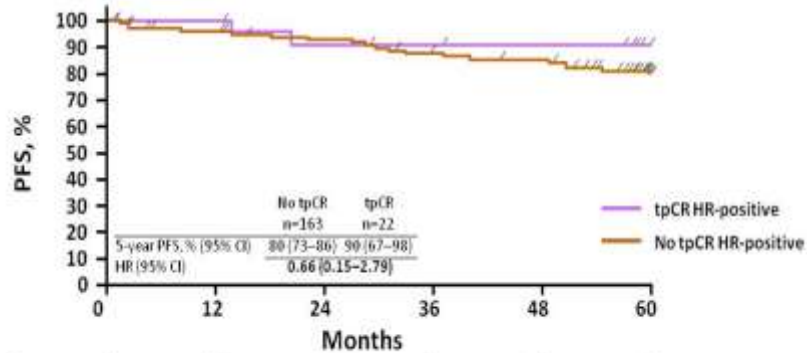
Chemo-naïve & primary tumors >2 cm (N=417)



Qual o embasamento para o padrão atual?

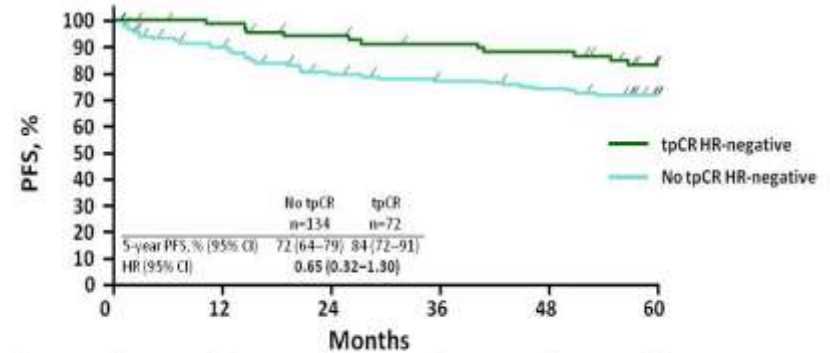
NeoSphere

PFS for tpCR and No tpCR by hormone receptor status, ITT population - HR positive tumors



	0	12	24	36	48	60
nat risk						
tpCR HR-positive	22	22	19	19	18	12
No tpCR HR-positive	175	181	153	142	137	96

PFS for tpCR and No tpCR by hormone receptor status, ITT population - HR negative tumors

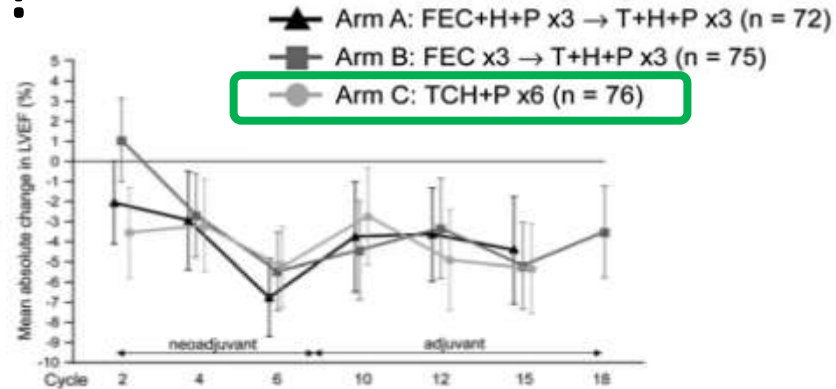


	0	12	24	36	48	60
nat risk						
tpCR HR-negative	72	69	64	60	58	43
No tpCR HR-negative	147	125	108	102	97	82

Aguardamos resultados de SLP, SG por braço de tratamento

Qual o padrão atual?

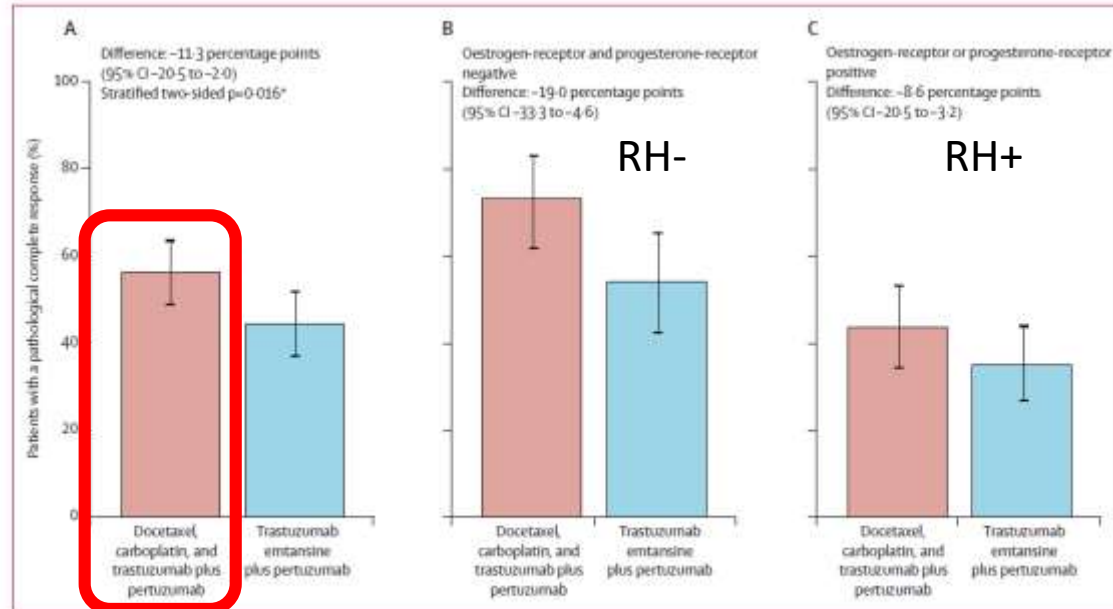
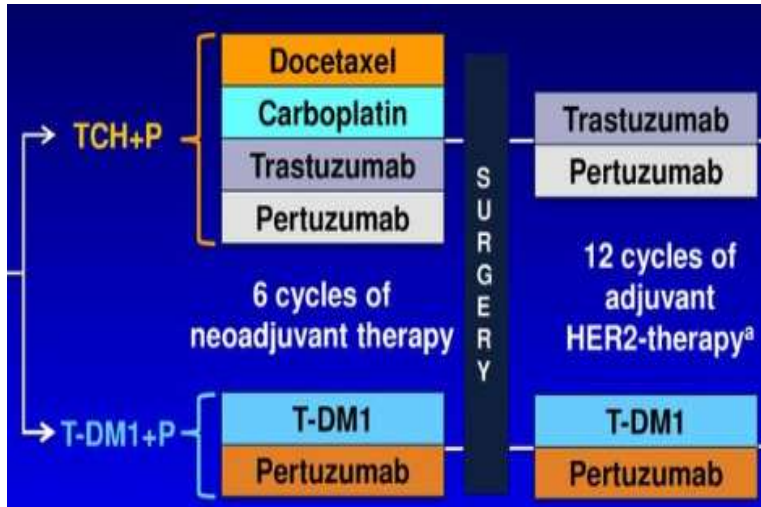
Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and **anthracycline-free chemotherapy regimens** in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA)



Braço de tratamento	N	pCR
Docetaxel + Carboplatina + Trastuzumabe + Pertuzumabe	77	63
5FU + Epirrubicina + Ciclofosfamida Seguido de Docetaxel + Carboplatina + Trastuzumabe	75	54

Qual o padrão atual?

Neoadjuvant trastuzumab, pertuzumab, and chemotherapy versus trastuzumab emtansine plus pertuzumab in patients with HER2-positive breast cancer (KRISTINE): a randomised, open-label, multicentre, phase 3 trial



Qual o padrão atual?

Pertuzumab, trastuzumab, and standard anthracycline- and taxane-based chemotherapy for the neoadjuvant treatment of patients with HER2-positive localized breast cancer (BERENICE): a phase II, open-label, multicenter, multinational cardiac safety study

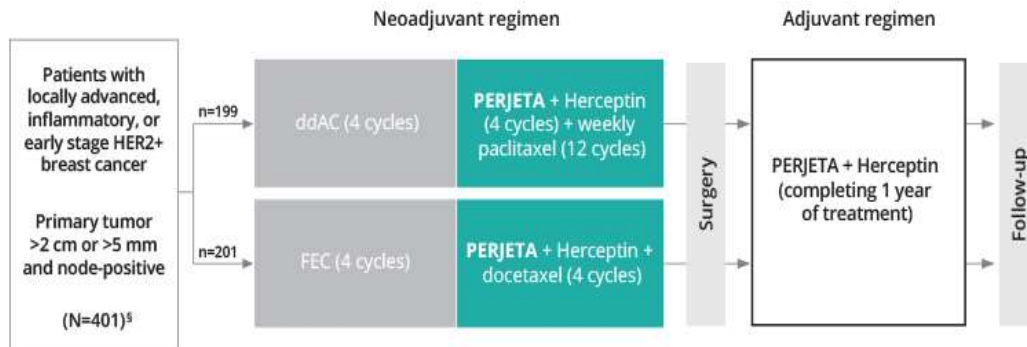
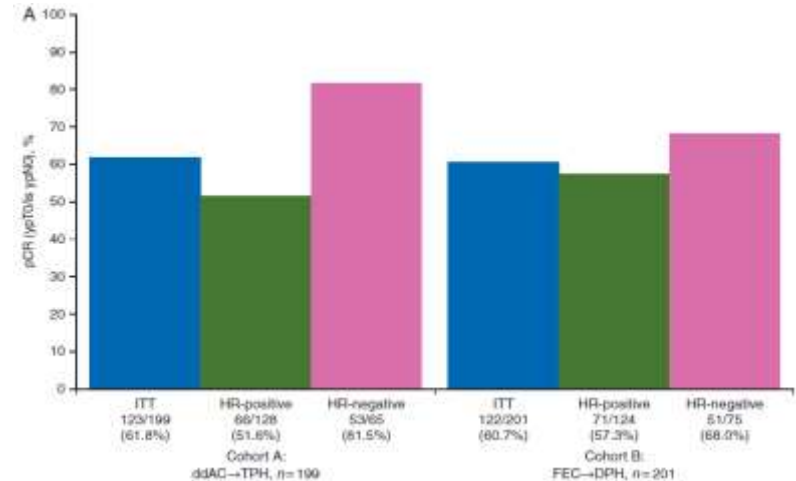


Table 2. Cardiac safety during the neoadjuvant period in the safety population

	Cohort A: ddAC → TPH n = 199	Cohort B: FEC → DPH n = 198
NYHA classification, events		
Class III	3 (1.5%)	0
Class IV	1 (0.5%)	0
LVEF declines during the neoadjuvant period ^{a,b}		
Patients with at least one LVEF decline	13 (6.5%; 95% CI 3.5% to 10.9%)	4 (2.0%; 95% CI 0.6% to 5.1%)



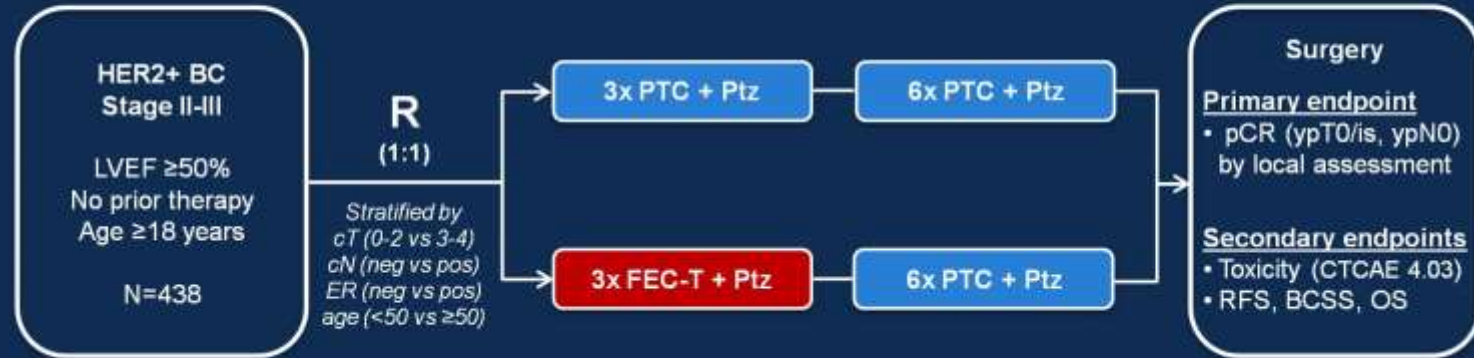
Swain, Ann Oncol 2018

Efeito do RH sobre neoadjuvância com duplo bloqueio

Estudo	Tratamento	pCR em RH+	pCR em RH-
NeoALTTO	Lapatinibe/Trastuzumabe	42%	61%
CALGB 40601	Lapatinibe/Trastuzumabe	42%	77%
NSABP B41	Lapatinibe/Trastuzumabe	56%	73%
NeoSphere	Pertuzumabe/Trastuzumabe	26%	63%
TRYPHAENA	Pertuzumabe/Trastuzumabe	46/50%	65-84%
KRISTINE	Pertuzumabe/Trastuzumabe	44%	73%
TRAIN2	Pertuzumabe/Trastuzumabe	51/55%	84-89%
BERENICE	Pertuzumabe/Trastuzumabe	51/57%	81/68%

Podemos eliminar a antraciclina como na adjuvância?

TRAIN-2 study design



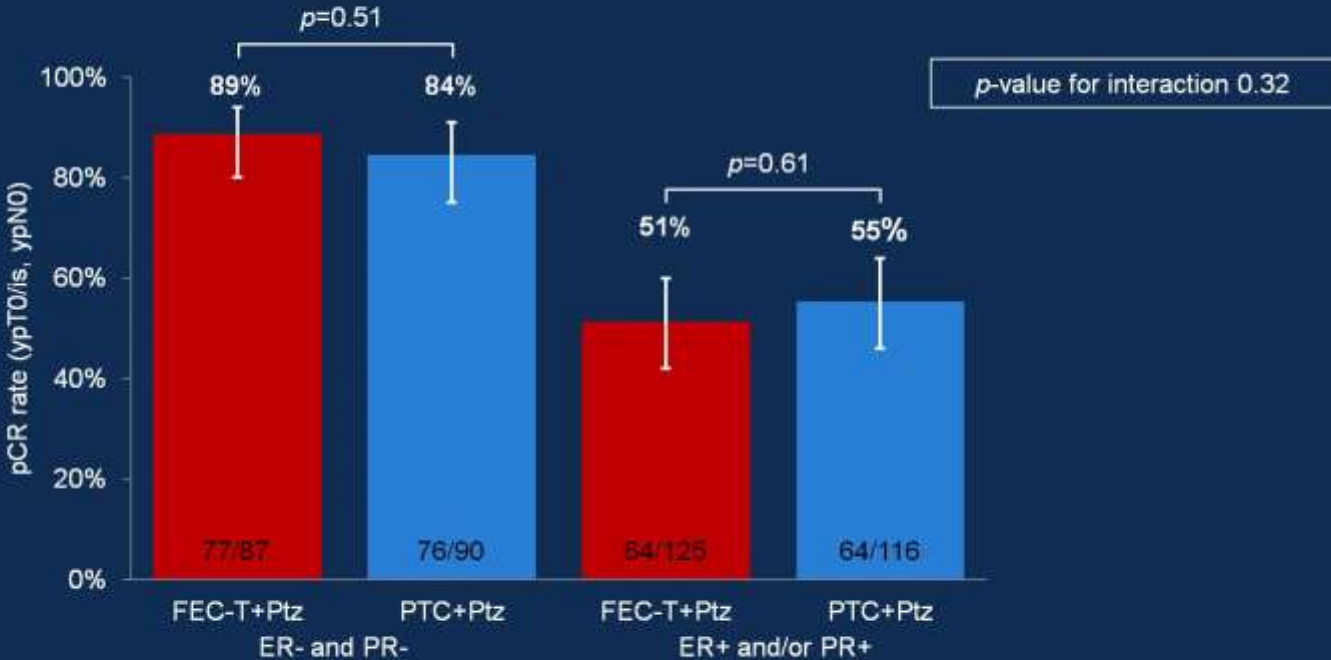
Adjuvant trastuzumab to complete one year of treatment and endocrine therapy for ER+ and/or PR+ tumors

PTC+Ptz cycle of 3 weeks, day 1 PTC+Ptz, day 8 only P; P = paclitaxel 80mg/m²; 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/m²; E = epirubicin 90mg/m²; C = cyclophosphamide 500mg/m²; T = trastuzumab 6mg/kg (loading dose 8mg/kg); Ptz = pertuzumab, 420mg (loading dose 840mg)

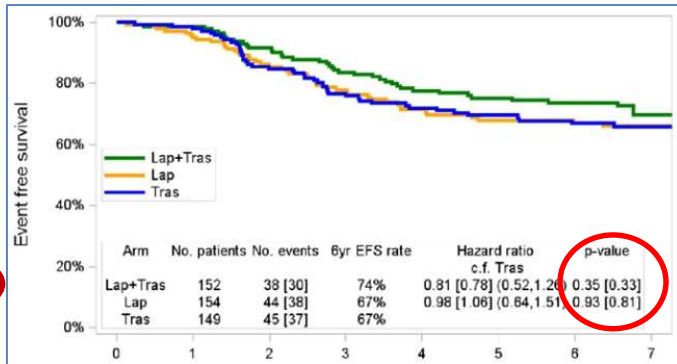
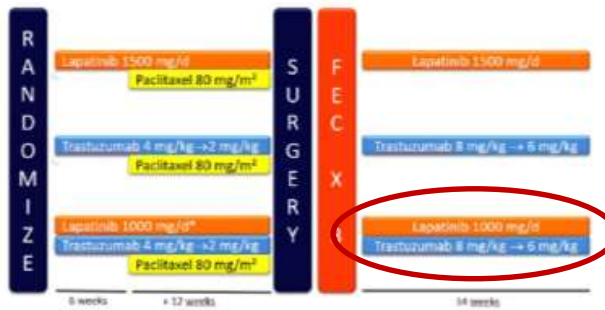
Podemos eliminar a antraciclina como na adjuvância?

pCR by hormone receptor status



Se atingir pCR, precisa continuar duplo bloqueio?

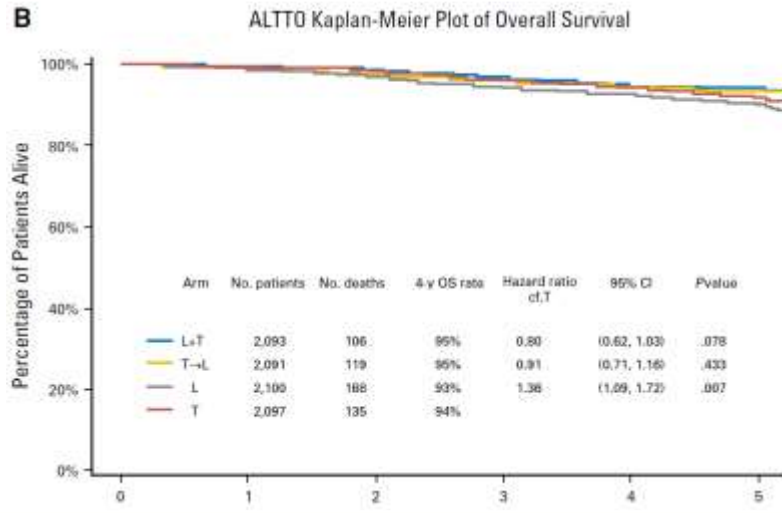
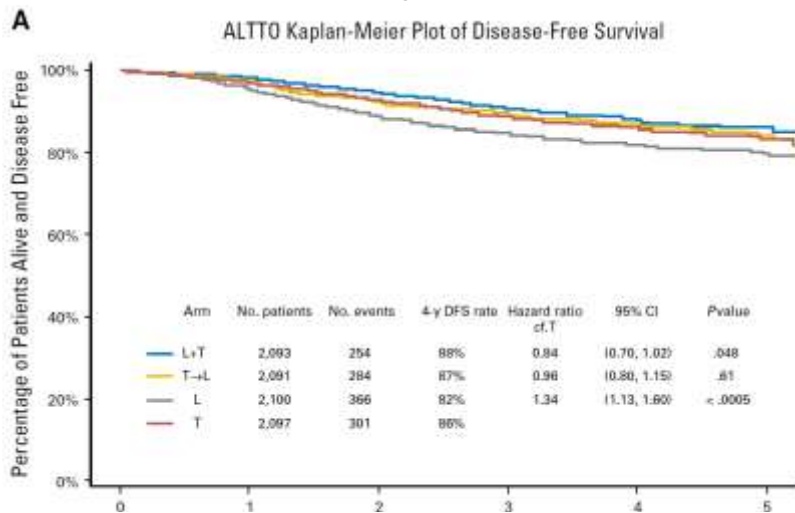
NeoALTTO



Conclusions

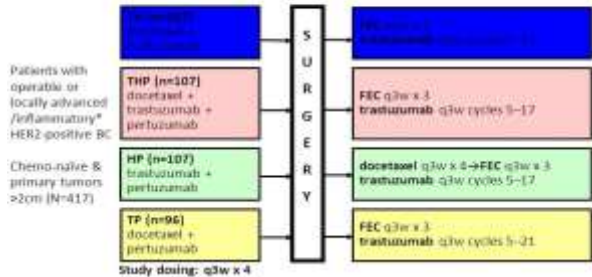
- The updated results of the NeoALTTO study confirm that pts who achieve a pCR have a better EFS and OS
- This difference was mainly observed in the hormone receptor negative group
- EFS and OS after 6 years did not differ significantly between the 3 treatment groups

... aliás, na adjuvância, estudo ALTTO...



Se atingir pCR, precisa continuar duplo bloqueio?

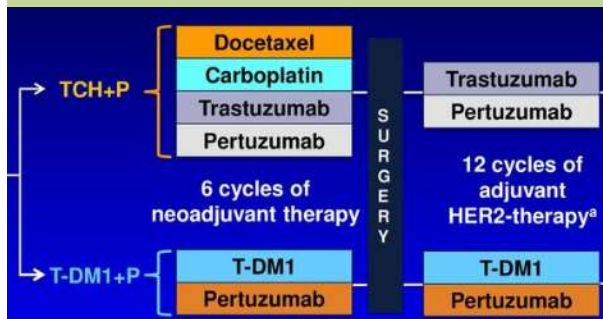
NeoSphere: study design



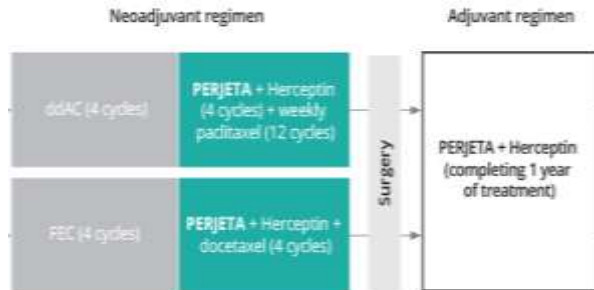
TRYPHAENA



KRISTINE



BERENICE



Não
temos
nenhum
dado

Se atingir pCR, precisa continuar duplo bloqueio?

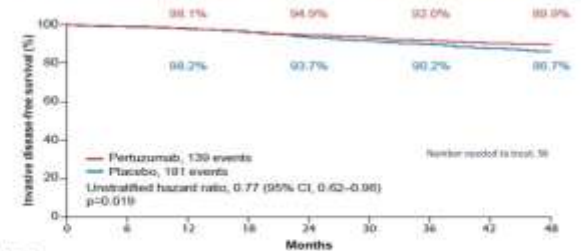
A FAVOR: seguir a regra
adjuvância = neoadjuvância

CONTRA:

iDFS subset analysis

	Δ % (H/P vs. H)	Absolute Δ
N0	96.7 v 96.2%	0.5%
N1	89.9 v 86.7%	3.2%
ER/PR+	93 v 91.6%	1.4%
ER/PR-	91 v 88.7%	2.3%

APHINITY: Node-positive Subgroup



No. of Risk	0	6	12	18	24	30	36	42	48
Pertuzumab	1503	1444	1419	1387	1356	1327	1283	912	423
Placebo	1502	1403	1439	1408	1358	1319	1264	892	405

ASCO ANNUAL MEETING '17 | BABCOFF



Cost per invasive DFS event prevented

- Pertuzumab for 1 year
 - NNT to prevent 1 iDFS event \approx 111
 - $\$86,434 \times 111 = \mathbf{\$9,594,174}$

- Neratinib for 1 year
 - NNT to prevent 1 iDFS event \approx 43
 - $\$140,196 \times 43 = \mathbf{\$6,028,428}$

Se for provável que se trate
de $pT < 2\text{cm}$

Operar primeiro e se
 $pT1pN0$: apenas TH

Se for provável que se trate
de pT<2cm

Operar primeiro e se
pT1pN0: apenas TH

Se cT1-2 cN0 MAS optar por
neoadjuvância

dar TCH

Se for provável que se trate
de pT<2cm

Operar primeiro e se
pT1pN0: apenas TH

Se localmente avançado

Neoadjuvância com
TCHP ou AC>THP

Se cT1-2 cN0 MAS optar por
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Se for provável que se trate
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Resposta à neoadjuvância

OPINIÃO PESSOAL

pCR: continuar Trastuzumab +/- HT
(Pertuzumab tem registro para continuidade, mas sem dados)

PR apenas: continuar Pert/Trast

OBRIGADO