



Tomás Reinert

- Oncologista Clínico do Hospital do Câncer Mãe de Deus

31 MAIO
A 2 JUN
2018

XIX CONGRESSO SUL-BRASILEIRO
DE GINECOLOGIA E OBSTETRÍCIA
IV JORNADA SUL-BRASILEIRA
DE MASTOLOGIA



Quando indicar tratamento neoadjuvante?

Tomás Reinert

Oncologista Clínico - Hospital do Câncer Mãe de Deus

Doutorando em Ciências Médicas – UFRGS

Diretor Científico – Centro de Pesquisa da Serra Gaúcha



Quando indicar tratamento neoadjuvante?

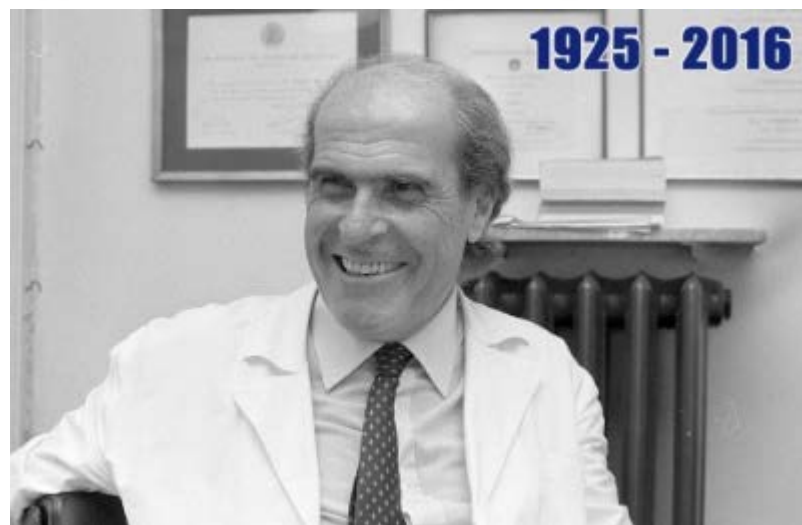
- Racional e objetivos da neoadjuvância
- Ensaios clínicos históricos
- Desafios relacionados a anatomia e biologia
- Resposta patológica completa como biomarcador
- Tumores HER-2 positivos
- Tumores triplo-negativos
- Tumores luminais
- Take-home messages

Multimodal treatment for locally advanced breast cancer. Result of chemotherapy-radiotherapy versus chemotherapy-surgery.

De Lena M, Varini M, Zucali R, Rovini D, Viganotti G, Valagussa P, Veronesi U, Bonadonna G.

Abstract

In a prospective randomized study, the efficacy of two combined modality approaches (chemotherapy plus radiotherapy or chemotherapy plus mastectomy) was tested in a total of 132 women with locally advanced breast cancer. Chemotherapy consisted of Adriamycin plus vincristine (AV) administered for three cycles before either local-regional modality and subsequently for seven additional cycles. Although a higher proportion of women achieved complete remission after mastectomy (100%) compared to women given radiotherapy (60%), the total response rate at the end of combined modality was identical (75%). There was no significant difference between the two treatment groups in terms of patterns of treatment failure, median duration of response, and total survival. Treatment was not influenced by menopausal or estrogen receptor status. Two patients of the surgical group showed Adriamycin-induced cardiomyopathy after cumulative doses less than 500 mg/m². The results of present study failed to indicate that surgery per se improved the overall results including local control, over radiotherapy in a combined modality setting.



RAPID PUBLICATION

Effect of Preoperative Chemotherapy on Local-Regional Disease in Women With Operable Breast Cancer: Findings From National Surgical Adjuvant Breast and Bowel Project B-18

By Bernard Fisher, Ann Brown, Eleftherios Mamounas, Samuel Wieand, Andre Robidoux, Richard G. Margoese, Anatolio B. Cruz, Jr, Edwin R. Fisher, D. Lawrence Wickerham, Norman Wolmark, Arthur DeCillis, James L. Hoehn, Alan W. Lees, and Nikolay V. Dimitrov

VOLUME 24 • NUMBER 13 • MAY 1 2006

JOURNAL OF CLINICAL ONCOLOGY

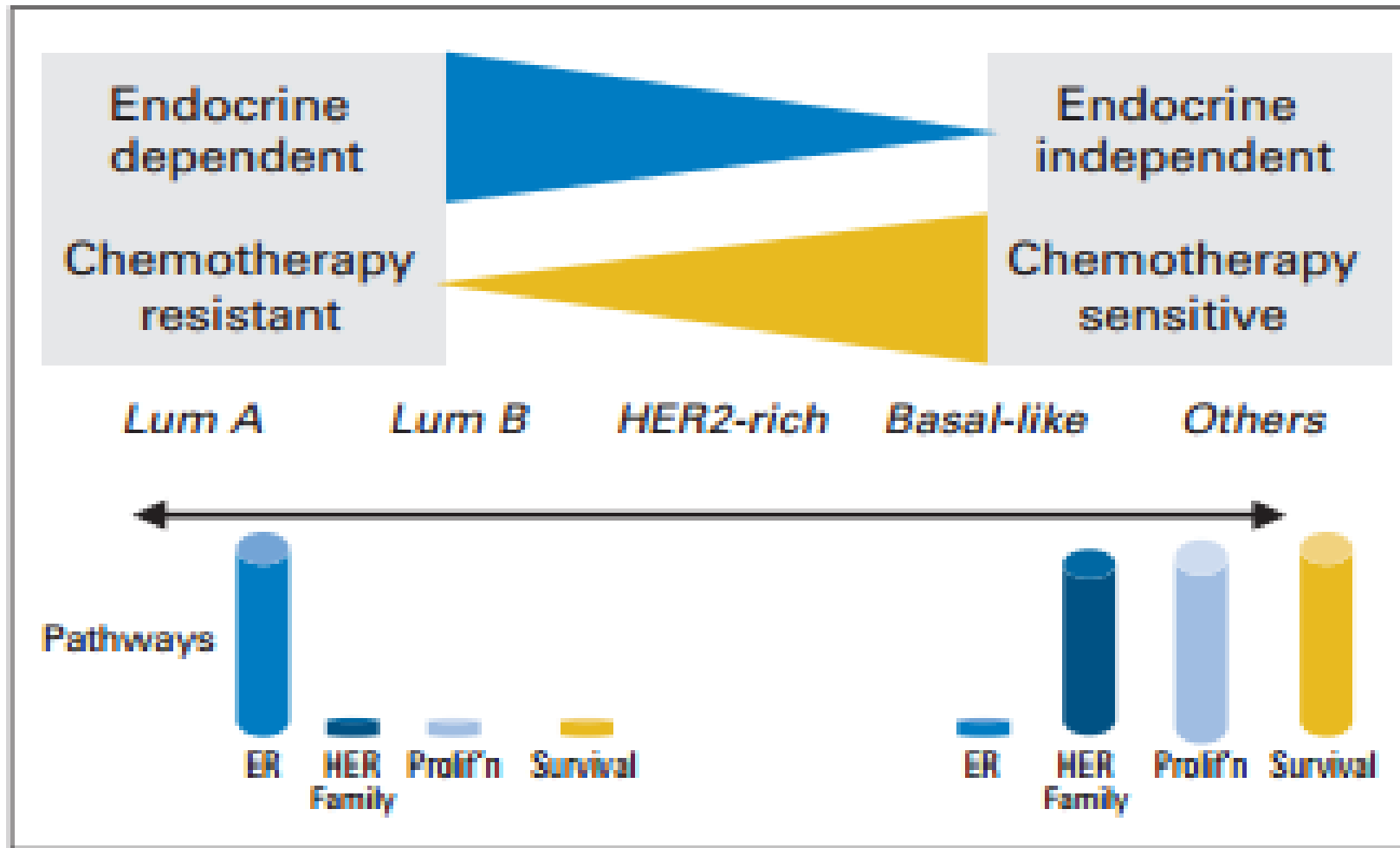
ORIGINAL REPORT

Sequential Preoperative or Postoperative Docetaxel Added to Preoperative Doxorubicin Plus Cyclophosphamide for Operable Breast Cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-27

Harry D. Bear, Stewart Anderson, Roy E. Smith, Charles E. Geyer Jr, Eleftherios P. Mamounas, Bernard Fisher, Ann M. Brown, Andre Robidoux, Richard Margoese, Morton S. Kahlenberg, Soonmyung Paik, Atilla Soran, D. Lawrence Wickerham, and Norman Wolmark

From the National Surgical Adjuvant

Heterogeneidade tumoral no câncer de mama



Racional/objetivos da terapia sistêmica neoadjuvante em câncer de mama

- Downstaging tumoral
 - Tumores inoperáveis → Tumores operáveis
 - Mastectomia → BCS
- Avaliação *in vivo* do padrão de sensibilidade ou resistência à terapia sistêmica (dentro de uma janela de curabilidade)
- Tratamento precoce da doença micrometastática
- Identificar subgrupos com diferentes prognósticos (pCR vs non-pCR)

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, Luca Gianni, Pinuccia Valagussa, Sandra M Swain, Tatiana Prowell, Sibylle Loibl, D Lawrence Wickerham, Jan Bogaerts, Jose Baselga, Charles Perou, Gideon Blumenthal, Jens Blohmer, Eleftherios P Mamounas, Jonas Bergh, Vladimir Semiglazov, Robert Justice, Holger Eidtmann, Soonmyung Paik, Martine Piccart, Rajeshwari Sridhara, Peter A Fasching, Leen Slaets, Shenghui Tang, Bernd Gerber, Charles E Geyer Jr, Richard Pazdur, Nina Ditsch, Priya Rastogi, Wolfgang Eiermann, Gunter von Minckwitz

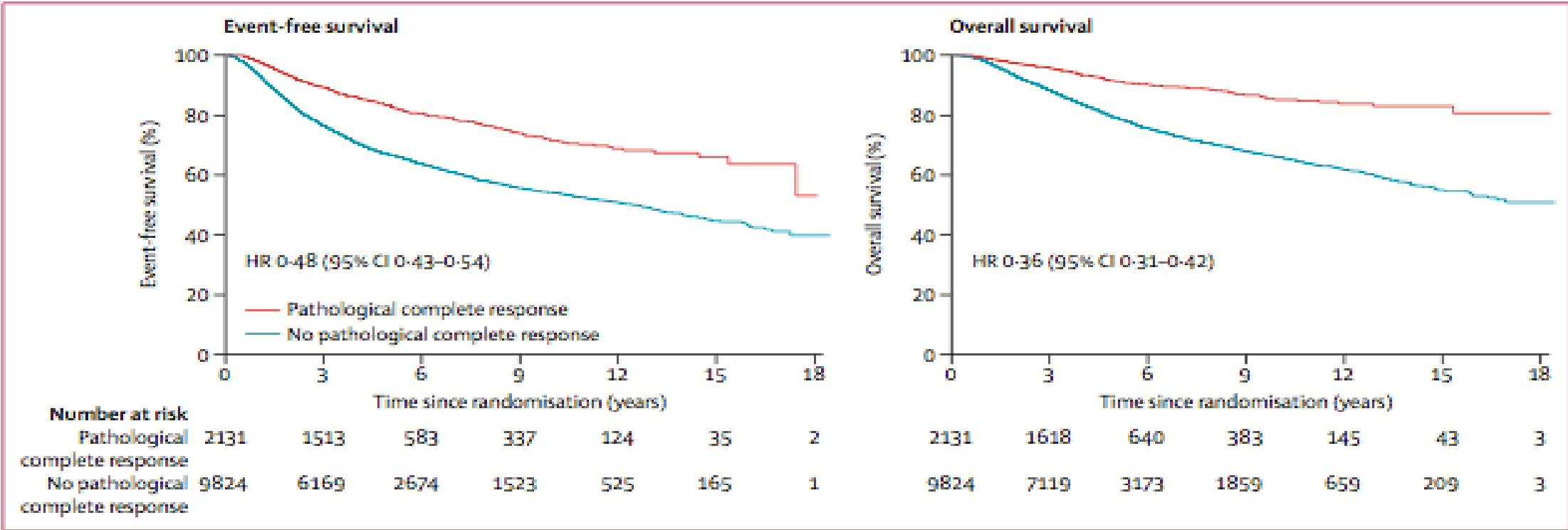


Figure 2: Associations between pathological complete response and event-free survival and overall survival

Tumores HER2-positivo

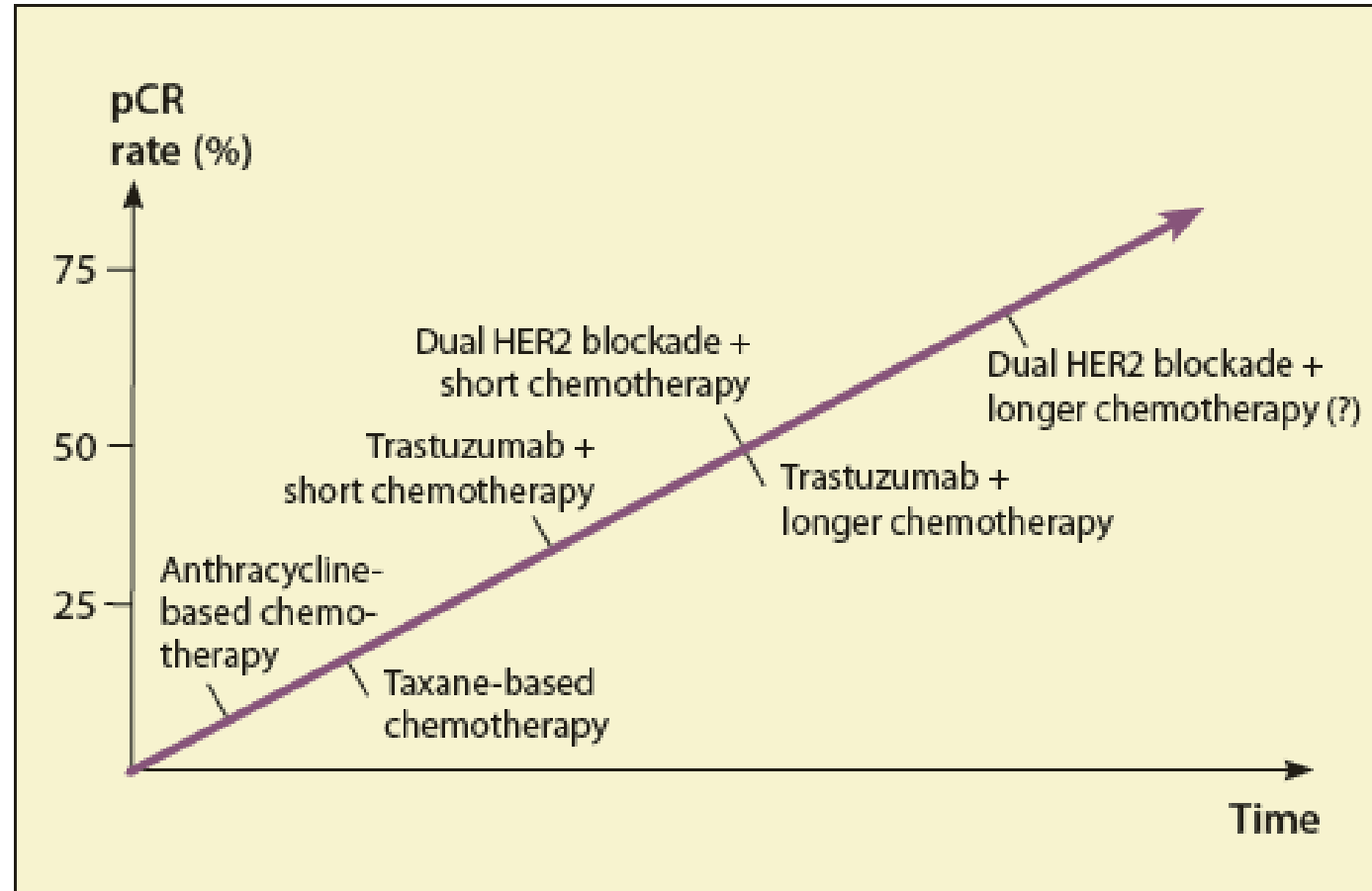
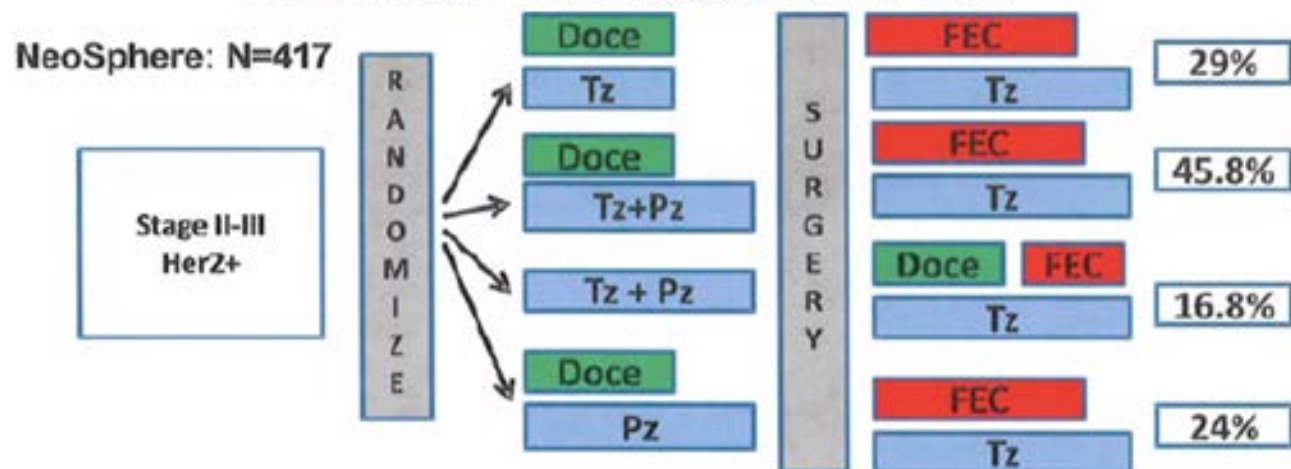


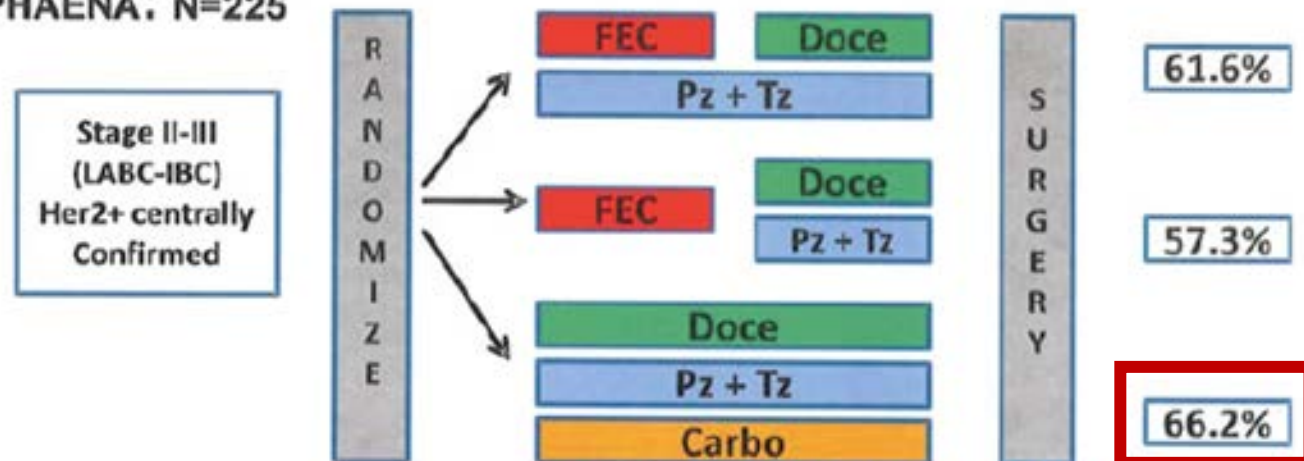
Figure 1: Incremental Improvement in Pathologic Complete Remission (pCR) Rates by Optimizing Systemic Neoadjuvant Treatment of HER2-Positive Breast Cancer.

Tumores HER2-positivo

NEOADJUVANT TRIALS ASSESSING PERTUZUMAB



TRYPHAENA: N=225



Adapted from Alvarez et. al Breast Cancer 2013

Neoadjuvant Carboplatin for TNBC

Summary of recent randomized trials

Study	Design	N	pCR	
			Control	Platinum
GeparSixto	npIDox/Pac/Bev +/- wCb (AUC1.5) X 18 wks	315	42.7%	53.2%
ALLIANCE 40603 2x2 design	wPac +/- Cb (AUC 6) +/- bev → AC X 4	433	41%	54%
GEICAM/2006-03	ECX4→D +/-Cb AUC6 X 4	94	30%	30%
ISPY2	wPac+/-Cb/veliparib → ACx4	71	26%(est)	52%(est)

Both GeparSixto and CALGB 40603 included Bev along with Cb and I spy included PARPi

Tumores triplo negativos: tratamento precoce da doença micrometastática

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Clinical Impact of Delaying Initiation of Adjuvant Chemotherapy in Patients With Breast Cancer

Debora de Melo Gagliato, Ana M. Gonzalez-Angulo, Xiudong Lei, Richard L. Theriault, Sharon H. Giordano, Vicente Valero, Gabriel N. Hortobagyi, and Mariana Chavez-MacGregor

Patients with TNBC and HER2–positive tumors treated with trastuzumab who started chemotherapy 61 days after surgery had worse survival compared with those who initiated treatment in the first 30 days after surgery.

TNBC → HR 1.54 (95% CI 1.09-2.18)

HER2+ → HR 3.09 (95% CI 1.49-6.39)

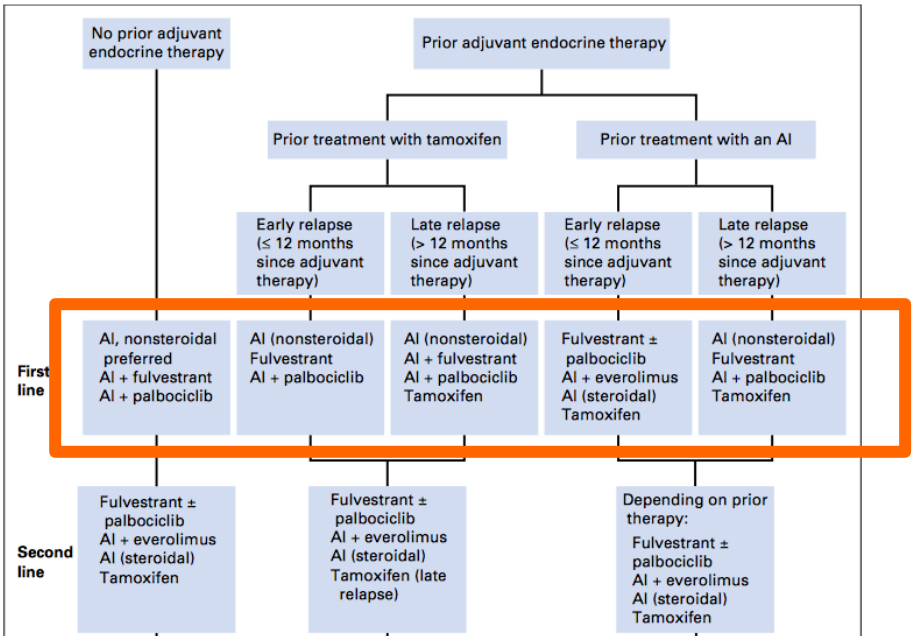
Tumores luminais: menor benefício com quimioterapia

VOLUME 34 • NUMBER 25 • SEPTEMBER 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Endocrine Therapy for Hormone Receptor–Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 25, 2016

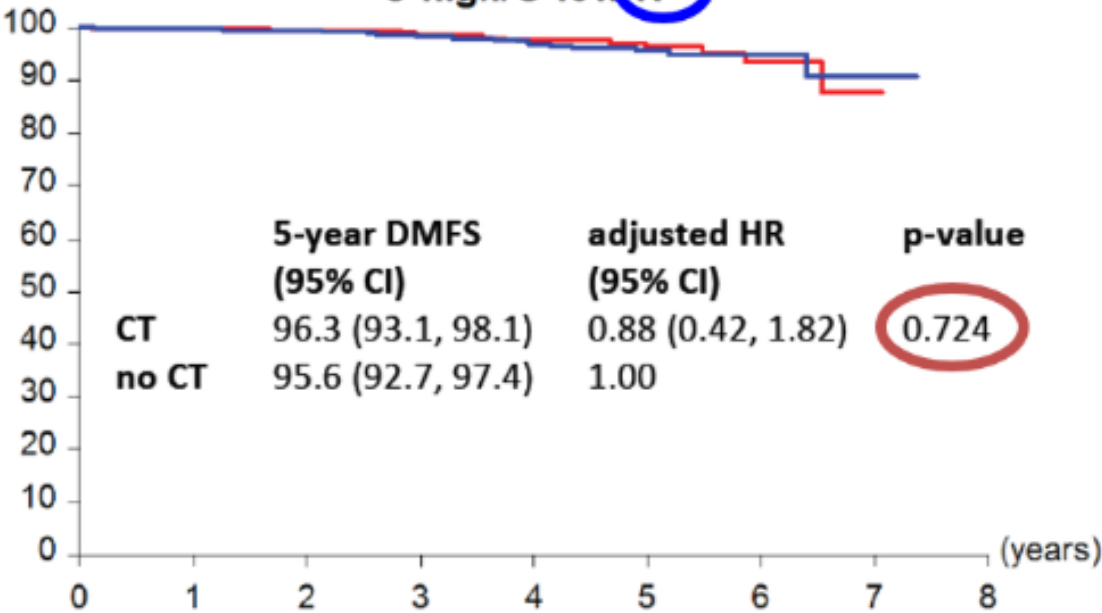
VOL. 375 NO. 8

70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer

F. Cardoso, L.J. van't Veer, J. Bogaerts, L. Slaets, G. Viale, S. Delaloge, J.-Y. Pierga, E. Brain, S. Causeret, M. DeLorenzi, A.M. Glas, V. Goulinopoulos, T. Goulioti, S. Knox, E. Matos, B. Meulemans, P.A. Neijenhuis, U. Nitz, R. Passalacqua, P. Ravdin, I.T. Rubio, M. Saghatelyan, T.J. Smilde, C. Sotiriou, L. Stork, C. Strahle, G. Thomas, A.M. Thompson, J.M. van der Hoeven, P. Vuylsteke, R. Bernards, K. Tryfonidis, E. Rutgers, and M. Piccart, for the MINDACT Investigators*

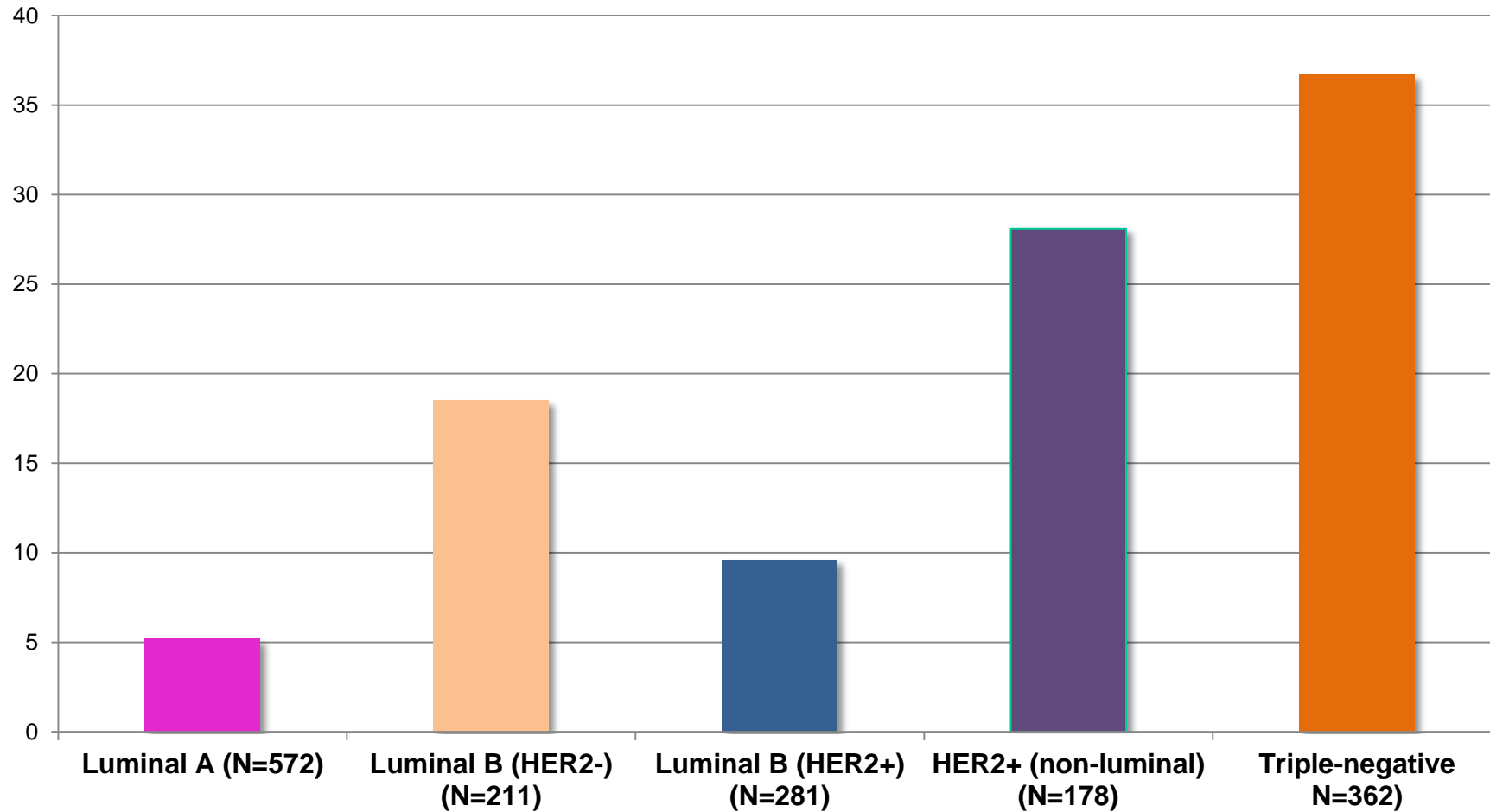
Distant Metastasis Free Survival

C-high/G-low N+



CT
no CT

Tumores luminais: menores taxas de pCR com quimioterapia neoadjuvante



Curr. Treat. Options in Oncol. (2018) 19:23
DOI 10.1007/s11864-018-0538-9

Breast Cancer (ML Telli, Section Editor)

Current Status of Neoadjuvant Endocrine Therapy in Early Stage Breast Cancer

Tomás Reinert, MD^{1,2}

Rodrigo Gonçalves, MD, MSc, PhD³

Matthew J. Ellis, MB, BChir, BSc, PhD, FRCP^{4,}*

Address

¹Hospital do Câncer Mãe de Deus, Porto Alegre, Brazil

²Postgraduation Department of Medical Sciences, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil

³Setor de Mastologia, Hospital das Clínicas, Disciplina de Ginecologia, Departamento de Obstetrícia e Ginecologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

⁴Lester and Sue Smith Breast Cancer Center, Baylor College of Medicine, Houston, TX, 77030, USA

Email: mjellis@bcm.edu



Multidisciplinary Approach to Neoadjuvant Endocrine Therapy in Breast Cancer: A Comprehensive Review

Abordagem multidisciplinar em hormonioterapia neoadjuvante no câncer de mama: uma revisão

Tomás Reinert^{1,2,3} Susana Ramalho⁴ Rodrigo Gonçalves⁵ Carlos Henrique Barrios⁶
Marcia Silveira Graudenz^{7,8} José Bines⁹

Neoadjuvant Endocrine Therapy in 2016 take home messages

- Ideal candidates: postmenopausal patients with ER-enriched stage II-III breast cancer
- Als superior to tamoxifen
- Anastrozole, letrozole and exemestane are equivalent
- Optimal duration: 6 months (at least)
- Clinical response rate = 50–70%
- Downstaging to BCS = 30–50%

Impacto da neoadjuvância na taxa de esvaziamento axilar

Ann Surg Oncol
DOI 10.1245/s10434-017-6016-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY



ORIGINAL ARTICLE – BREAST ONCOLOGY

The Optimal Treatment Plan to Avoid Axillary Lymph Node Dissection in Early-Stage Breast Cancer Patients Differs by Surgical Strategy and Tumor Subtype

Melissa Pilewskie, MD¹, Emily C. Zabor, MS², Anita Mamtani, MD¹, Andrea V. Barrio, MD¹, Michelle Stempel, MPH¹, and Monica Morrow, MD¹

¹Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; ²Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY

TABLE 2 Rates of axillary lymph node dissection by tumor subtype and treatment cohort

Subtype	Upfront BCS <i>n</i> (%)	NAC <i>n</i> (%)	<i>p</i> value
ER/PR ⁺ , HER2 ⁻	85/564 (15.1)	25/73 (34.2)	<0.001
HER2 ⁺	9/68 (13.2)	9/112 (8)	0.26
ER ⁻ , PR ⁻ , HER2 ⁻	5/37 (13.5)	6/86 (7)	0.26

BCS breast-conserving surgery, *NAC* neoadjuvant chemotherapy, *ER* estrogen receptor, *PR* progesterone receptor, *HER* human epidermal growth factor

Quando indicar terapia neoadjuvante?

Estadiamento	Luminal A	Luminal B	TNBC	HER2+
I	Cirurgia primária	Cirurgia primária	Cirurgia primária (Considerar em casos de atraso no tto cirúrgico)	Cirurgia primária(Considerar em casos de atraso no tto cirúrgico)
II	Cirurgia primária (Considerar HT NEO)	Cirurgia primária (Considerar qt neo)	QT NEO (considerar carboplatina)	QT NEO + trastuzumabe (considerar duplo bloqueio)
III	HT NEO	QT NEO	QT NEO com adição de platina	QT NEO + Duplo bloqueio anti-HER2
IV	Tto sistêmico	Tto sistêmico	Tto sistêmico	Tto sistêmico

Take-home messages

Objetivos da neoadjuvância:

- Downstaging tumoral
- Avaliação in vivo do padrão de sensibilidade/resistência às terapias sistêmicas
- Biomarcador prognóstico (pCR)
- Tratamento precoce da doença micrometastática

Principais candidatos:

- Tumores estágio II-III dos subtipos triplo negativos, HER2+ e luminais B

Tumores luminais A:

- Considerar hormoniterapia neoadjuvante
- Considerar cirurgia upfront → ACOSOG Z011 e testes moleculares

**31 MAIO
A 2 JUN
2018**

XIX CONGRESSO SUL-BRASILEIRO
DE GINECOLOGIA E OBSTETRÍCIA
IV JORNADA SUL-BRASILEIRA
DE MASTOLOGIA



Obrigado pela atenção!

tomasreinert@hotmail.com