

# Considerações clínicas e biomarcadores para indicação de quimioterapia adjuvante em pacientes idosas

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75 anos

01



Setor de mama E + EA

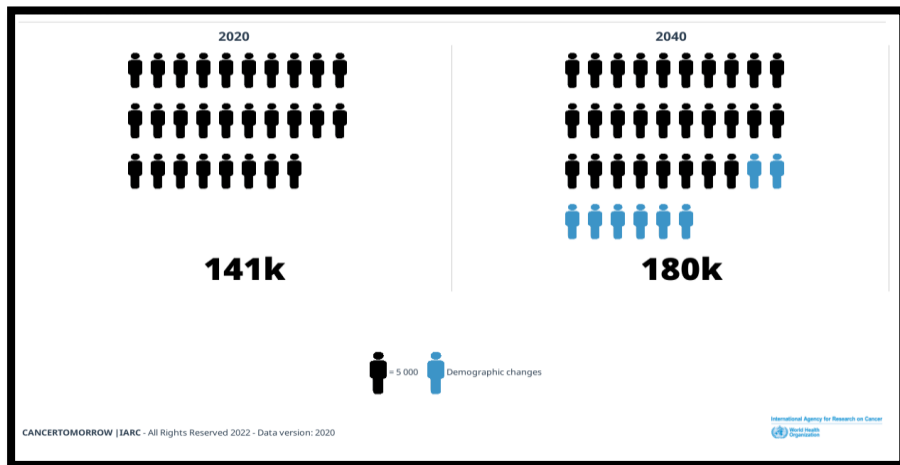
CINE G3  
pT1c pN2a (4/14)  
RE 90% RP 10% Ki67 40%  
Her2 +1/3



# QUIMIOTERAPIA ??

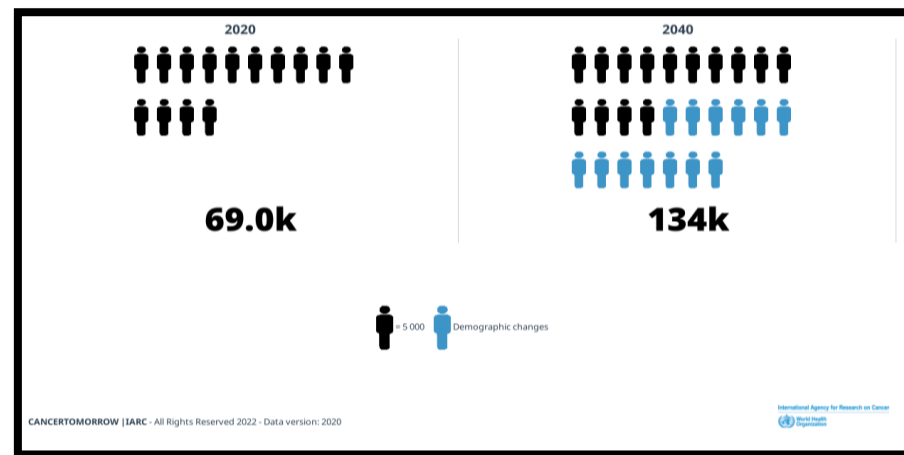
# Estimativa de novos casos de câncer de mama na América Latina 2020-2040

< 65 anos



↑ 30%

≥ 65 anos



↑ 95%

Globocan. Cancer Tomorrow

# Quimioterapia adjuvante em idosas

## 1- Subrepresentatividade em estudos clínicos

CALGB 9344 6% da população  $\geq 65$  anos

US Oncology 9735 15% da população  $\geq 65$  anos

## 2- Efeitos adversos

Perda de funcionalidade

## 3- Magnitude do benefício de acordo com RE

## 4- Causas competitivas de mortalidade

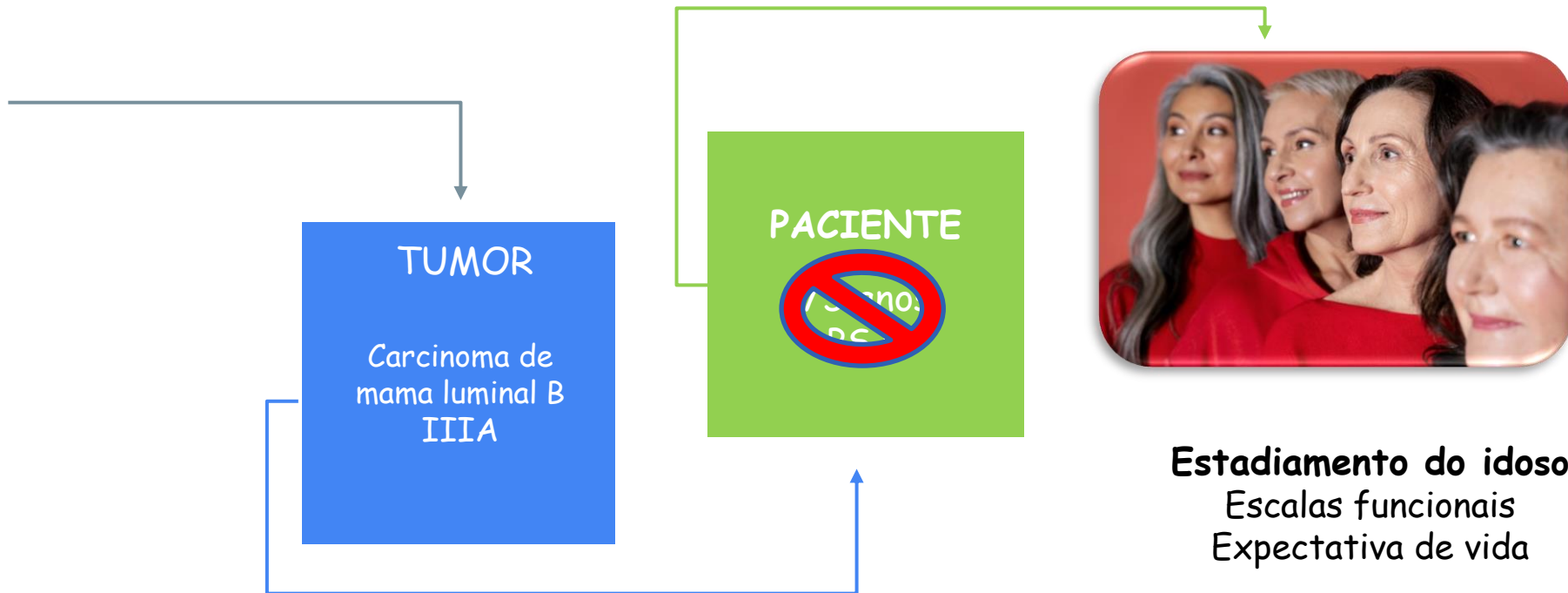


Jin J, JNCI 2023; Johnston SR, JCO 2020

# Considerações clínicas = aspectos geriátricos



# Aspectos geriátricos



# Avaliação geriátrica ampla

## Comorbidades

Charlson  
Comorbidity Index  
CIRS-G

## Nutrição

Mini-Man

## Polifarmácia

BEERs criteria

## Cognição/Humor

Mini-mental

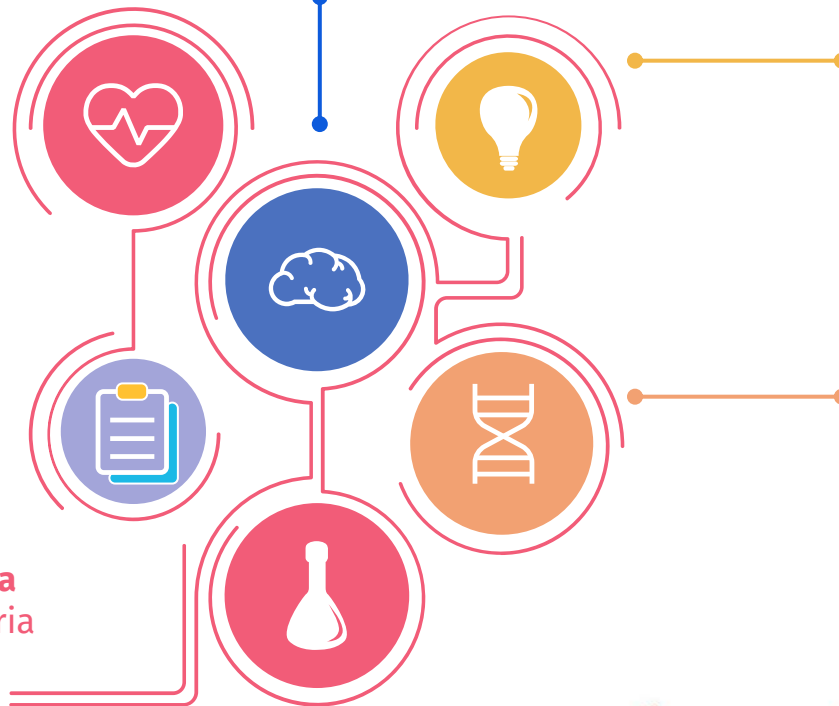
Moca

GDS

## Biopsicossocial

## Funcionalidade

ABVDs e AIVDs  
Gait speed



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**CÂNCER DE MAMA**

LACOG - GBECAM 2023





# Escore G8

Items	Escore
<b>1</b> Nos últimos três meses houve diminuição da ingesta alimentar devido à perda de apetite, problemas digestivos ou dificuldade para mastigar ou deglutir?	
Diminuição severa da ingesta	0
Diminuição moderada da ingesta	1
Sem diminuição da ingesta	2
<b>2</b> Perda de peso nos últimos 3 meses	
>3 kg	0
paciente não sabe informar	1
1-3 kg	2
Sem perda de peso	3
<b>3</b> Mobilidade	
restrito ao leito ou à cadeira de rodas	0
deambula mas não é capaz de sair de casa	1
Normal	2
<b>4</b> Problemas neuropsicológicos	
Demência ou depressão graves	0
Demência ou depressão leves	1
Sem problemas psicológicos	2
<b>5</b> Índice de Massa Corporal(IMC) = peso em kg / (estatura em M2)	
<19	0
19≥ IMC <21	1
21≥ IMC <23	2
≥23	3
<b>6</b> Utiliza mais de três medicamentos diferentes por dia	
Sim	0
Não	1
<b>7</b> Em comparação a outras pessoas da mesma idade, como o paciente considera a sua própria saúde?	
Pior	0
Paciente não sabe informar	0.5
Igual	1
Melhor	2
<b>8</b> Idade (anos)	
>85	0
80-85	1
<80	2
<b>Total</b>	<b>/ 17</b>

Alta sensibilidade para detectar alterações na avaliação geriátrica.

Escore > 15



Escore ≤ 14



Soubeyran P et al (2014). PLoS ONE 9(12): e115060  
Camara DB; Lima JTO. JGO 2020;11(3):533-535  
Karnakis, T; Gattas-Vernaglia, I. JGO 2022; (13):381-383.

# Aspectos geriátricos



01

Funcionalidade  
Robusto, Pré-fragil,  
Frágil

Expectativa de vida  
Índice Suemoto  
Lee-Schonberg

02

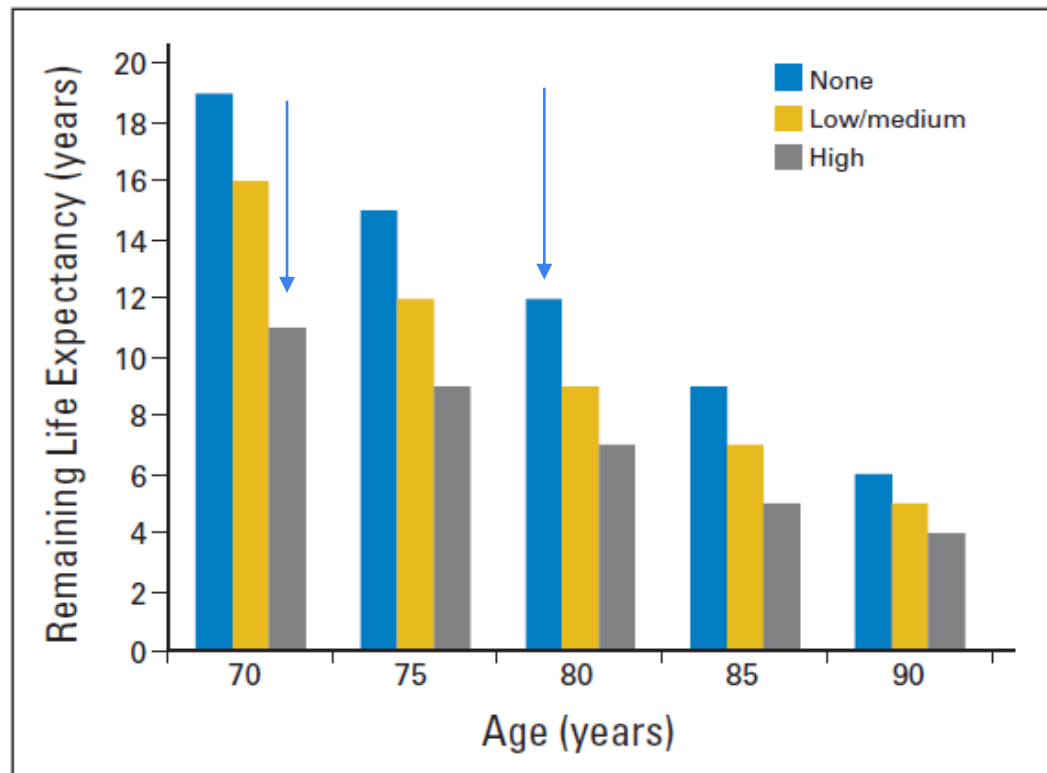


Fig 1. Estimated life expectancy by age and comorbidity level (none, low/medium, or high). Data adapted.<sup>3</sup>

JCO 2014; 19:1996

## WHAT WOULD YOU LIKE TO DO?



PROGNOSTIC  
CALCULATORS



TIME TO  
BENEFIT



CANCER  
SCREENING

# Aspectos geriátricos



01

Funcionalidade  
Idosa Robusta

Expectativa de vida  
12.6-14.3 anos (Lee)

02



## Testes de assinaturas genômicas



# Testes genômicos em paciente idosas

## 1- Subrepresentatividade em estudos randomizados

	Limite de idade	Resultados
Mindact	$\leq 70$	0.8% 70+ (56/6.693)
TAILORx	$\leq 75$	7% 70+ RS 0-10 (111/6260) 4% 70+ RS 11-25 (300/6.897)
RxPONDER	Não estabelecido	12% 70-75 RS $\leq 25$ (581/5018)

## 2. Valor prognóstico e valor preditivo



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky, W.E. Barlow, J.R. Gralow, F. Meric-Bernstam, K.S. Albain, D.F. Hayes, N.U. Lin, E.A. Perez, L.J. Goldstein, S.K.L. Chia, S. Dhesy-Thind, P. Rastogi, E. Alba, S. Delaloge, M. Martin, C.M. Kelly, M. Ruiz-Borrego, M. Gil-Gil, C.H. Arce-Salinas, E.G.C. Brain, E.-S. Lee, J.-Y. Pierga, B. Bermejo, M. Ramos-Vazquez, K.-H. Jung, J.-M. Ferrero, A.F. Schott, S. Shak, P. Sharma, D.L. Lew, J. Miao, D. Tripathy, L. Pusztai, and G.N. Hortobagyi

1-3LFN  
RS  $\leq$ 25

Table 1. Baseline Characteristics of the Participants.\*

Characteristic	Endocrine-Only Group (N=2507)	Chemoendocrine Group (N=2511)	All Participants (N=5018)
Median age (range) — yr	57.2 (18.3–86.0)	57.9 (28.0–87.6)	57.5 (18.3–87.6)
Age category — no. (%)			
<40 yr	80 (3.2)	67 (2.7)	147 (2.9)
40–49 yr	547 (21.8)	530 (21.1)	1077 (21.5)
50–59 yr	838 (33.4)	837 (33.3)	1675 (33.4)
60–69 yr	761 (30.4)	777 (30.9)	1538 (30.6)
$\geq$ 70 yr	281 (11.2)	300 (12.0)	581 (11.6)
Menopausal status — no. (%)			
Premenopausal	831 (33.1)	834 (33.2)	1665 (33.2)
Postmenopausal	1676 (66.9)	1677 (66.8)	3353 (66.8)
Recurrence score — no. (%)†			
0–13	1071 (42.7)	1076 (42.9)	2147 (42.8)
14–25	1436 (57.3)	1435 (57.1)	2871 (57.2)
Axillary surgery — no. (%)			
Axillary lymph-node dissection, with or without sentinel-node mapping	1571 (62.7)	1569 (62.5)	3140 (62.6)
Sentinel-node biopsy without axillary lymph-node dissection	936 (37.3)	942 (37.5)	1878 (37.4)
Positive nodes — no. (%)			
1 node	1647 (65.7)	1628 (64.8)	3275 (65.3)
2 nodes	623 (24.8)	643 (25.6)	1266 (25.2)
3 nodes	229 (9.1)	231 (9.2)	460 (9.2)
Not reported	8 (0.3)	9 (0.4)	17 (0.3)

\* Percentages may not total 100 because of rounding.

† The recurrence score based on the 21-gene breast-cancer assay ranges from 0 to 100, with higher scores indicating a worse prognosis.

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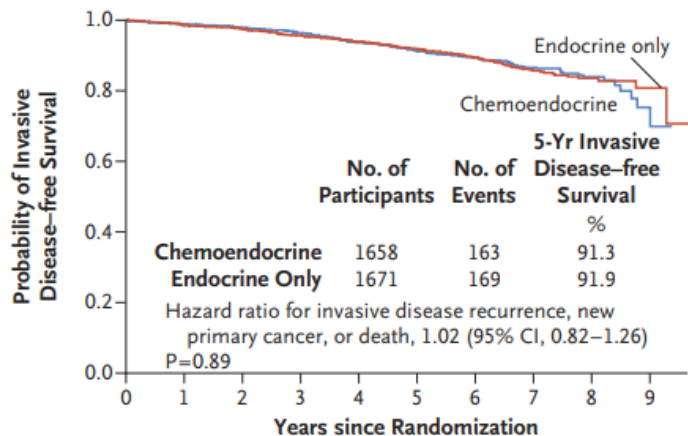
CÂNCER DE MAMA

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## 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky, W.E. Barlow, J.R. Gralow, F. Meric-Bernstam, K.S. Albain, D.F. Hayes, N.U. Lin, E.A. Perez, L.J. Goldstein, S.K.L. Chia, S. Dhesy-Thind, P. Rastogi, E. Alba, S. Delaloge, M. Martin, C.M. Kelly, M. Ruiz-Borrego, M. Gil-Gil, C.H. Arce-Salinas, E.G.C. Brain, E.-S. Lee, J.-Y. Pierga, B. Bermejo, M. Ramos-Vazquez, K.-H. Jung, J.-M. Ferrero, A.F. Schott, S. Shakh, P. Sharma, D.L. Lew, J. Miao, D. Tripathy, L. Pusztai, and G.N. Hortobagay

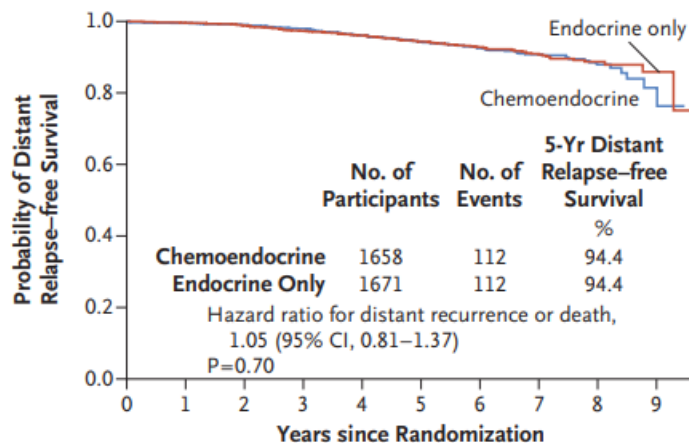
## B Invasive Disease-free Survival, Postmenopausal Participants



## No. at Risk

Chemoendo-	1658	1515	1413	1298	1145	993	659	358	129	14
crine group										
Endocrine-	1671	1568	1474	1343	1196	1030	679	364	137	21
only group										

## E Distant Relapse-free Survival, Postmenopausal Participants



## No. at Risk

Chemoendo-	1658	1525	1429	1320	1175	1026	686	382	139	16
crine group										
Endocrine-	1671	1583	1492	1368	1226	1059	706	386	144	22
only group										

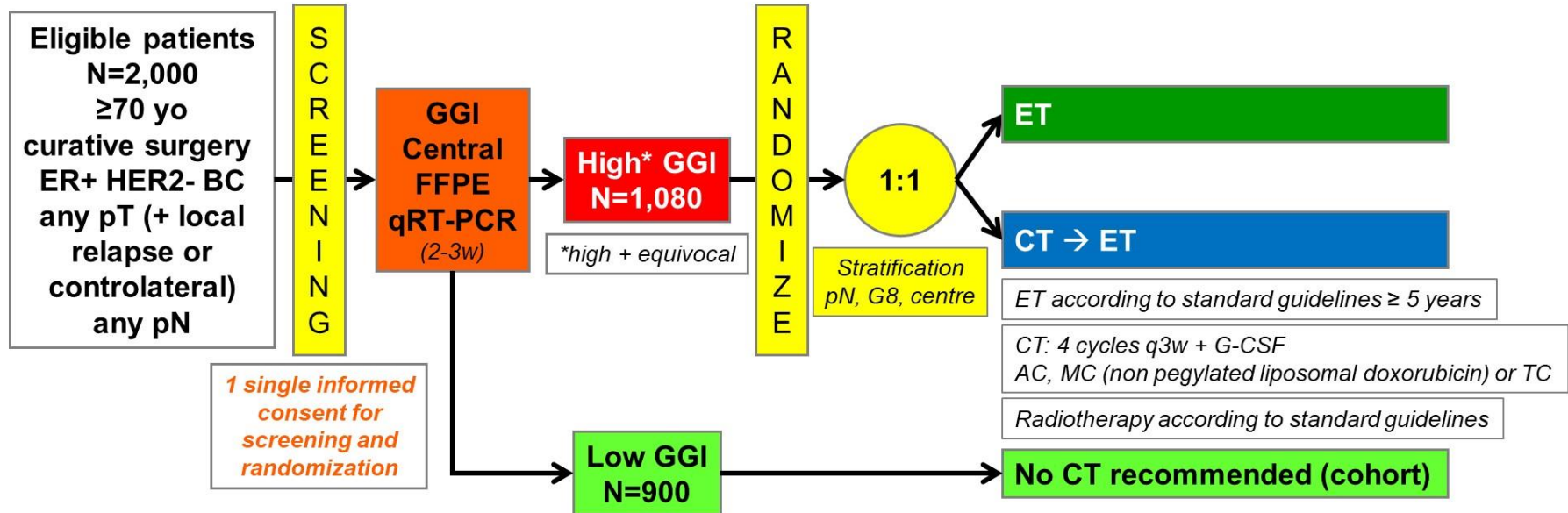
# Final results from a phase III randomized clinical trial of adjuvant endocrine therapy ± chemotherapy in women ≥ 70 years old with ER+ HER2- breast cancer and a high genomic grade index: the Unicancer ASTER 70s trial

**Etienne Brain**, Alessandro Viansone, Emmanuelle Bourbouloux, Olivier Rigal,  
Jean-Marc Ferrero, Sylvie Kirscher, Djelila Allouache, Véronique d'Hondt, Aude-Marie Savoye,  
Xavier Durando, François Duhoux, Laurence Venat-Bouvet, Emmanuel Blot, Jean-Luc Canon,  
Florence Rollot, Hervé Bonnefoi, Jérôme Lemonnier, Magali Lacroix-Triki,  
Aurélien Latouche, Franck Bonnetain, Dewi Vernerey, GERICO & UCBG/Unicancer

ASTER 70s (EudraCT 2011-004744-22/NCT01564056) was supported by the National PHRC 2011, Cephalon/Teva, Amgen, Ipsogen/Qiagen/HalioDx, L'Association d'Aide à la Recherche Cancérologique de Saint-Cloud and La Ligue Contre le Cancer

# ASTER 70s Study Design

Adjuvant systemic treatment for ER+ HER2- BC in women over 70 according to GGI  
Hypothesis: 4-year OS with CT → ET > 4-year OS with ET only if high GGI



All patients

Lee score, G8, CCI, polypharmacy (baseline, 4 years)

Randomized patients

IADL, MMSE, QLQ C30 & ELD15, socioeconomic, willingness, blood & serum (baseline, 3 months, yearly x 4 years)



# Selected Patients Characteristics

	Randomized N=1,089			
	ET (N=548)		CT → ET (N=541)	
	N	%	N	%
Median age (min-max)	75.8 (70.01-92.4)		76.0 (70-89.9)	
PS 0	374	<b>68.6</b>	340	<b>63.0</b>
G8≤14*	210	38.8	222	41.3
Lee>8**	83	15.4	85	15.9
Adjusted CCI# >6	94	17.4	98	18.4
Prior cancer	131	<b>24.0</b>	99	<b>18.3</b>

4/10 pacientes frágeis\*

85% expectativa de vida > 10 anos

\* G8, screening tool for frailty: if  $\leq 14$ , it requires the need of a complete geriatric assessment as identifies patients at risk of frailty.

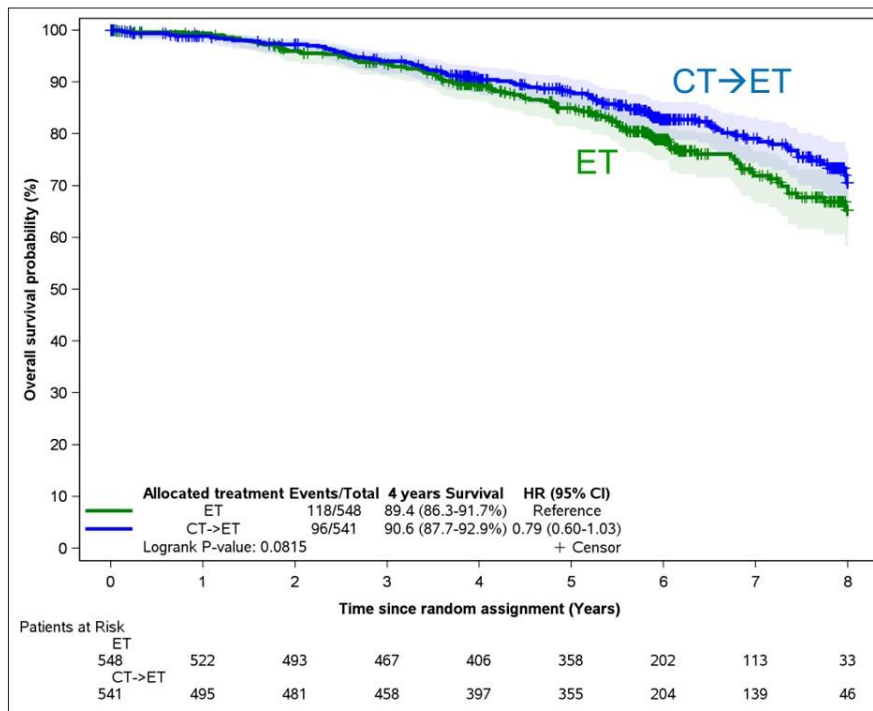
\*\* Lee, 4-year mortality score: if  $\geq 8$  in a person  $\geq 70$  yo, 4-year mortality is estimated ~ 50%

# CCI, Charlson Comorbidity Index

Randomized patients: median IADL 8 (8-8), median MMSE 28 (26-30)

# OS: ET — vs CT→ET — (intent to treat) (primary endpoint)

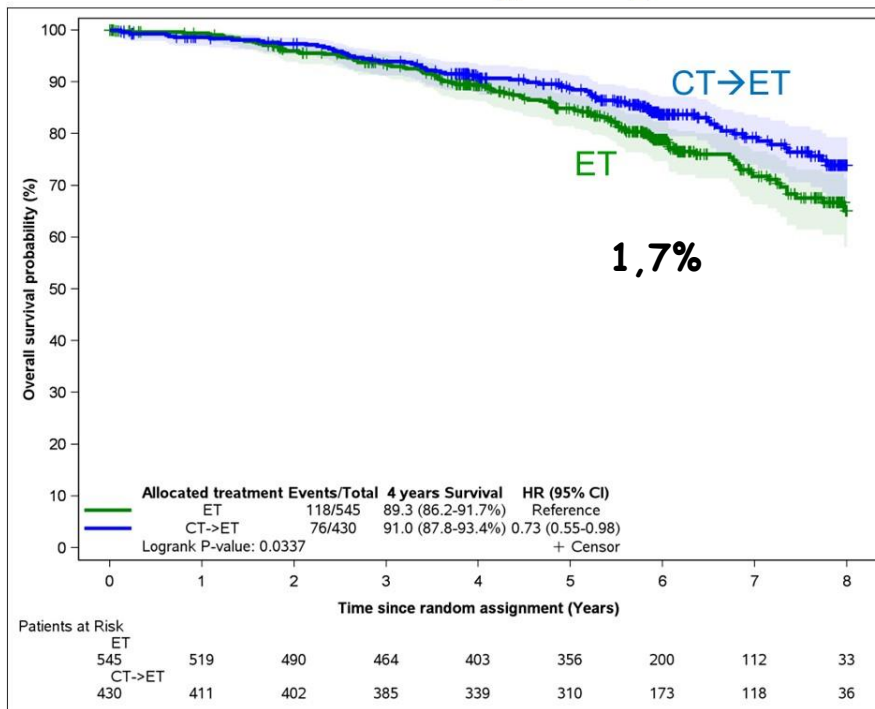
median follow-up  
5.94 years



4-year OS	89.4 (86.3-91.7)
4-year OS	90.6 (87.7-92.9)
HR	0.79 (0.60-1.03)
p	0.08

# OS: ET — vs CT→ET — (per protocol)

median follow-up  
5.94 years



4-year OS	89.3 (86.2-91.7)
4-year OS	91.0 (87.8-93.4)
HR	0.73 (0.55-0.98)
p	<b>0.03</b>



75 anos



Setor de mama E + EA  
CINE G3 pT1c pN2a  
Luminal B

Idosa Robusta  
Expectativa de vida > 10  
anos



Letrozol + Abemaciclib

15% > 65 anos



# Adjuvância na mulher idosa

Testes genômicos  
Portret tool\*



Aspectos geriátricos  
Expectativa de vida  
Outros desfechos  
Qol/funcionalidade

Quimioterapia → para a minoria\*

Inibidores de ciclina na doença de alto risco

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Laura Biganzoli, Hans Wildiers, Catherine Oakman, Lorenza Marotti, Sibylle Loibl, Ian Kunjler, Malcolm Reed, Stefano Ciatto, Adri C Voogd, Etienne Brain, Bruno Cutuli, Catherine Terret, Margot Gosney, Matti Aapro, Riccardo Audisio

Development and Validation of a Risk Tool for Predicting Severe Toxicity in Older Adults Receiving Chemotherapy for Early-Stage Breast Cancer

Allison Magnuson, DO<sup>1</sup>; Mina S. Sedrak, MD<sup>2</sup>; Cary P. Gross, MD<sup>3</sup>; William P. Tew, MD<sup>4</sup>; Heidi D. Klepin, MD<sup>5</sup>; Tanya M. Wildes, MD<sup>6</sup>; Hyman B. Muss, MD<sup>7</sup>; Etrat Dotan, MD<sup>8</sup>; Rachel A. Freedman, MD<sup>9</sup>; Tracey O'Connor, MD<sup>10</sup>; William Dale, MD<sup>11</sup>; Harvey J. Cohen, MD<sup>12</sup>; Vani Katheria, MS<sup>13</sup>; Anait Arsenyan, MS<sup>14</sup>; Abraham Levi, BS<sup>15</sup>; Heeyoung Kim, MPH<sup>16</sup>; Supriya Mohile, MD<sup>17</sup>; Arti Huria, MD<sup>18</sup>; and Can-Lan Sun, PhD<sup>19</sup>



"All oncologists are geriatric oncologists. They just don't know it yet"  
Stuart Lichtman