Side effects in older patients: differences in incidence and management

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Outline

- Complexity of managing cancer in older individuals
- Safety of specific anticancer treatments in older patients with breast cancer
  - Curative setting
  - Palliative setting
- Importance of geriatric assessments
- Conclusions

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Older adults are heterogeneous

Cancer
Comorbidities
Health behaviours
Access to healthcare
Geographical location
Social support

FIT — **FRAIL**

Life expectancy

Comorbidities

Functional status

Polypharmacy

Organ reserve

Toxicities risk

Focus on survival

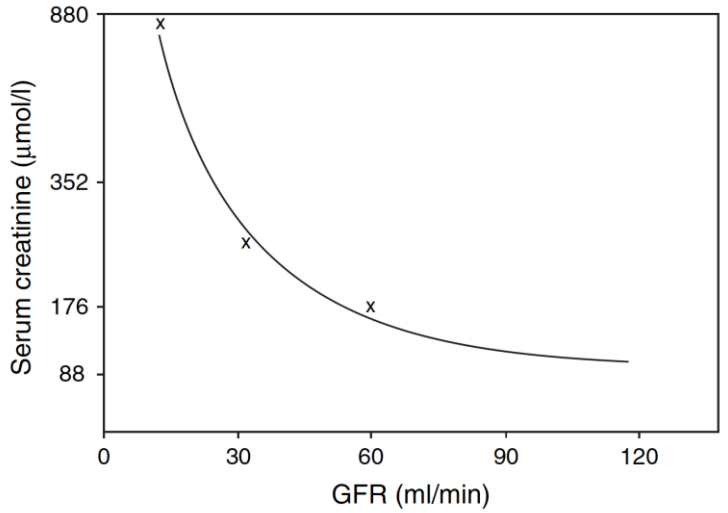
Focus on quality of life

Renal function and drug excretion

- Gradual **GFR decline** <60 mL/min/1.73m^2
- Reduced **renal mass**
- Reduced **drug clearance**
- **Hyalinisation of renal vasculature**
- **Higher peak drug levels** and more prolonged chemo exposure
- Concurrent **NSAID** use
- **Serum creatinine** not reliable ← loss of muscle mass
- Estimate **creatinine clearance** instead - Cockcroft-Gault equation
- Chemotherapy may be safely administered with **dose adjustments**

Cytotoxics
• Arsenic trioxide • Bendamustine • Bleomycin • Capecitabine • Carboplatin • Carmustine • Cisplatin • Cladribine • Clofarabine • Cyclophosphamide • Cytarabine (high dose) • Daunorubicin • Epirubicin • Eribulin • Etoposide • Fludarabine • Hydroxyurea • Ifosfamide • Irinotecan (controversial) • Ixazomib • Lenalidomide • Lomustine • Melphalan • Methotrexate • Mitomycin • Oxaliplatin • Pemetrexed • Pentostatin • Pomalidomide • Pralatrexate • Streptozocin • Topotecan • Trabectedin • Vinorelbine

Targeted agents
• Afatinib • Bosutinib • Brentuximab • **Crizotinib** • **Imatinib** • Lenvatinib • **Olaparib** • **Sorafenib** • **Sunitinib** • Talazoparib • Vandetanib



Launay-Vacher V, Chatelut E, Lichtman SM, Wildiers H, Steer C, Aapro M; International Society of Geriatric Oncology. Renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations. Ann Oncol. 2007 Aug;18(8):1314-21. doi: 10.1093/annonc/mdm011. Epub 2007 Jul 13. PMID: 17631561.

Liver function and metabolism

- **Liver size** decline
- **Hepatic blood flow** decline
  - Not warranting routine dose modifications
- Reduced **first-pass metabolism**
- Reduced **drug clearance**
- Concurrent **hepatic impairment**
  - **Malignancy**
  - **Comorbidities**
  - Concurrent **medications**
- May require dose adjustments

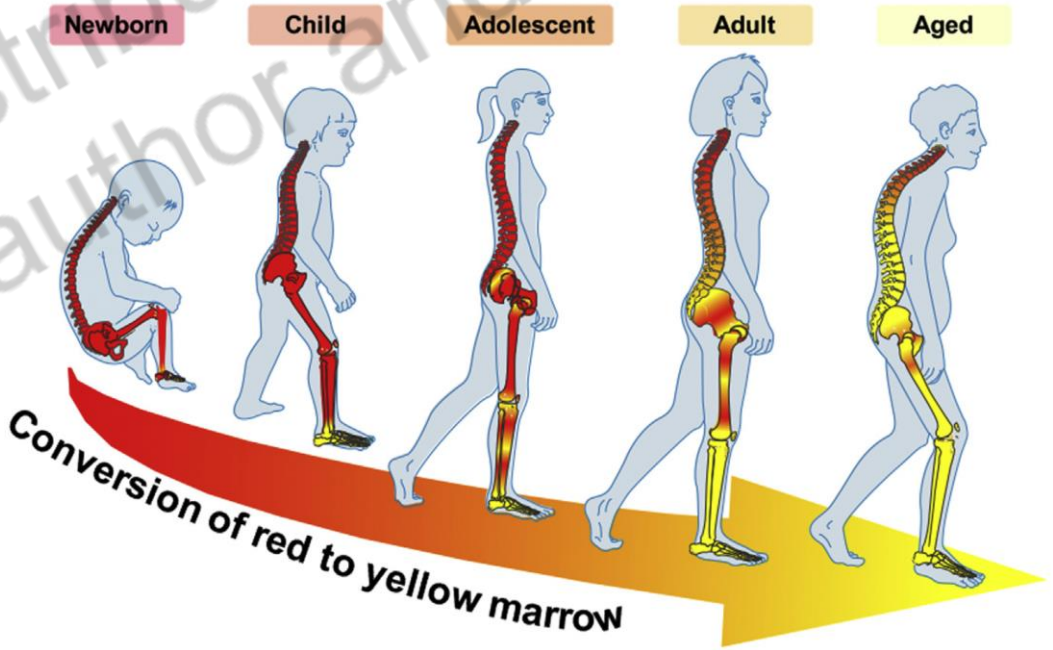
Cytotoxics

- Anthracyclines
- 5-FU
- Taxanes
- Cyclophosphamide
- Methotrexate

Egorin MJ. Cancer pharmacology in the elderly. Semin Oncol. 1993 Feb;20(1):43-9. PMID: 8475409.

Bone marrow reserve and function

- Bone marrow **stem cell reserve** decline
- Higher rates of **haematological toxicities** in older patients
- More frequent **infections**, **hospitalisations** and **mortality**
- **Neutropenia**
  - Dose reductions and G-CSF are used to avoid severe neutropenia
  - **ASCO guidelines**: G-CSF are recommended if risk of febrile neutropenia ≥20%
  - **NCCN guidelines**: G-CSF are indicated if older adults treated with curative intent
- **Anaemia**
  - Impacts **functional status**
  - Higher incidence in older individuals
  - **Erythropoietin-stimulating agents**: useful if anaemia is due to chemotherapy
    - Risk of **thrombosis** and **shorter survival**
    - Consider **treatment intent: not indicated in the curative setting**

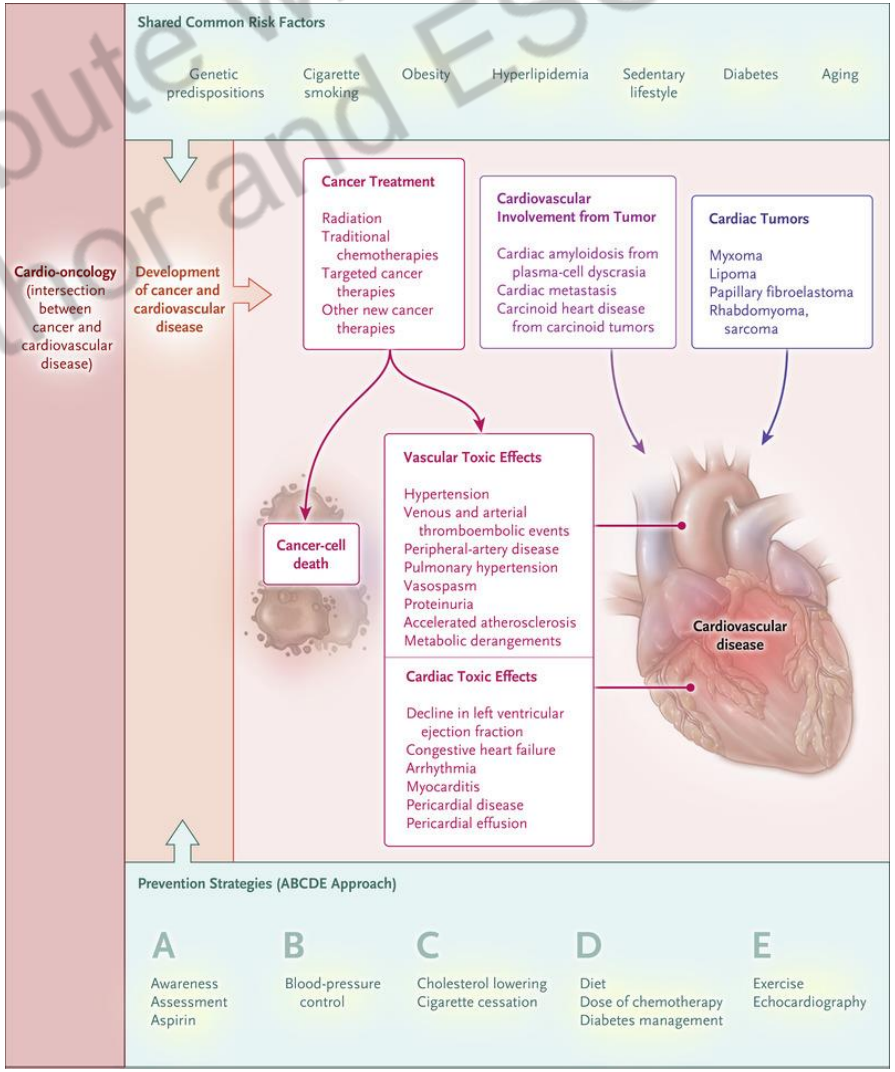


Dees, Cancer Invest, 2000; Baraldi-Junkins, Hematol Oncol Clin North Am, 2000; Anía, J Am Geriatr Soc,1997; Hoffman, Bone, 2019

Cardiac function

- Reduced **cardiac output**
- Reduced **heart rate modulation**
- **Myocardial hypertrophy**
- **Conduction abnormalities**
- Pre-existing **occult heart disease**
- Higher risk of **heart failure** due to **anthracyclines** and **trastuzumab**
- Higher risk of **coronary artery vasospasm** due to **fluoropyrimidines**
- **Radiotherapy** to the chest wall may also contribute

Sawhney R, Cancer J. 2005; Gupta, J Geriatr Oncol, 2017; Hershman, JCO, 2008; Carver, JCO, 2008



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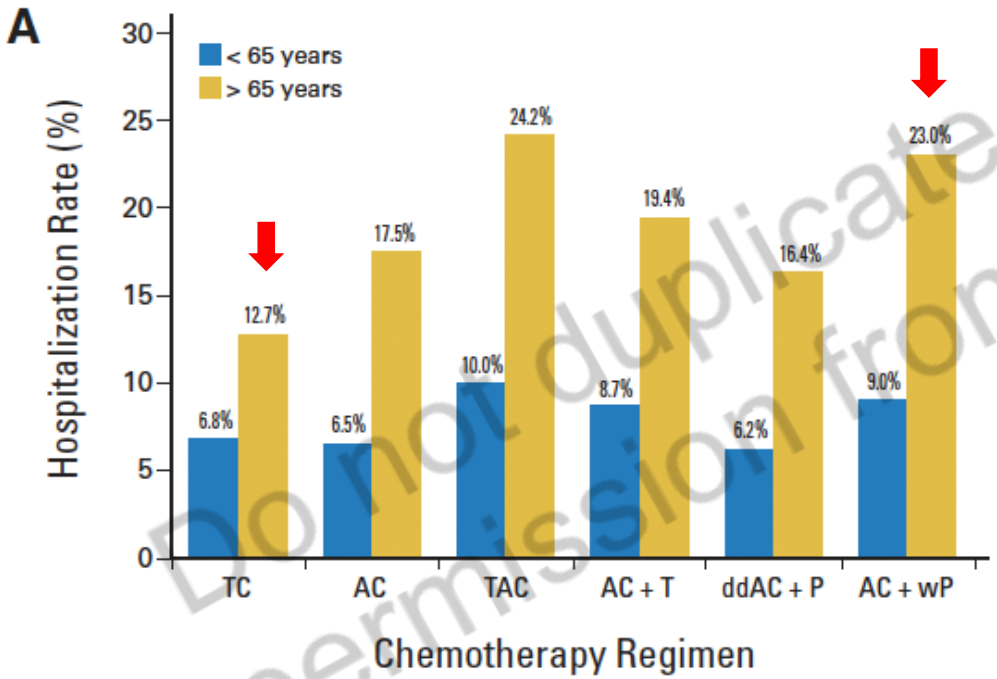
Safety of chemotherapy for older patients with EBC

SEER/Texas Cancer Registry-Medicare database analysis
2003-2007
EBC

N = 3,567



SEER database analysis
1992-2002
Stage I-III BC
Age 66-80 years
No history of CHF

N = 43,338

Table 2. Cumulative Incidence of CHF by Adjuvant Treatment Type for Patients Aged 66 to 70 Years

Time (months)	No. at Risk	Cumulative No. With Event	Probability of No Event	95% CI	
Adjuvant anthracycline					
0	2,576	0	1.000		
12	2,409	177	0.931	0.922 to 0.941	
36	1,601	341	0.861	0.847 to 0.875	
60	549	401	0.813	0.795 to 0.831	
96	166	441	0.711	0.677 to 0.747	
120	65	457	0.616	0.564 to 0.672	38%
144	18	461	0.561	0.494 to 0.638	
Adjuvant other					
0	1,652	0	1.000		
12	1,587	73	0.956	0.946 to 0.966	
36	1,183	170	0.893	0.878 to 0.909	
60	679	242	0.823	0.803 to 0.845	
96	303	298	0.732	0.702 to 0.762	
120	165	316	0.675	0.638 to 0.714	33%
144	67	321	0.640	0.595 to 0.689	
No chemotherapy					
0	10,452	0	1.000		
12	10,150	317	0.970	0.966 to 0.973	
36	7,931	866	0.914	0.909 to 0.920	
60	4,884	1,278	0.856	0.848 to 0.864	
96	2,614	1,655	0.771	0.760 to 0.782	
120	1,368	1,807	0.713	0.713 to 0.726	29%
144	446	1,876	0.654	0.636 to 0.673	

Barcenas CH, Niu J, Zhang N, Zhang Y, Buchholz TA, Elting LS, Hortobagyi GN, Smith BD, Giordano SH. Risk of hospitalization according to chemotherapy regimen in early-stage breast cancer. J Clin Oncol. 2014 Jul 1;32(19):2010-7. doi: 10.1200/JCO.2013.49.3676. Epub 2014 May 27. PMID: 24868022; PMCID: PMC4164758.
Pinder MC, Duan Z, Goodwin JS, Hortobagyi GN, Giordano SH. Congestive heart failure in older women treated with adjuvant anthracycline chemotherapy for breast cancer. J Clin Oncol. 2007 Sep 1;25(25):3808-15. doi: 10.1200/JCO.2006.10.4976. Epub 2007 Jul 30. PMID: 17664460.

Alternative chemotherapy regimens?

CALGB 49907 study
2001-2006
EBC ≥65 years
Capecitabine vs CMF or AC

N=633

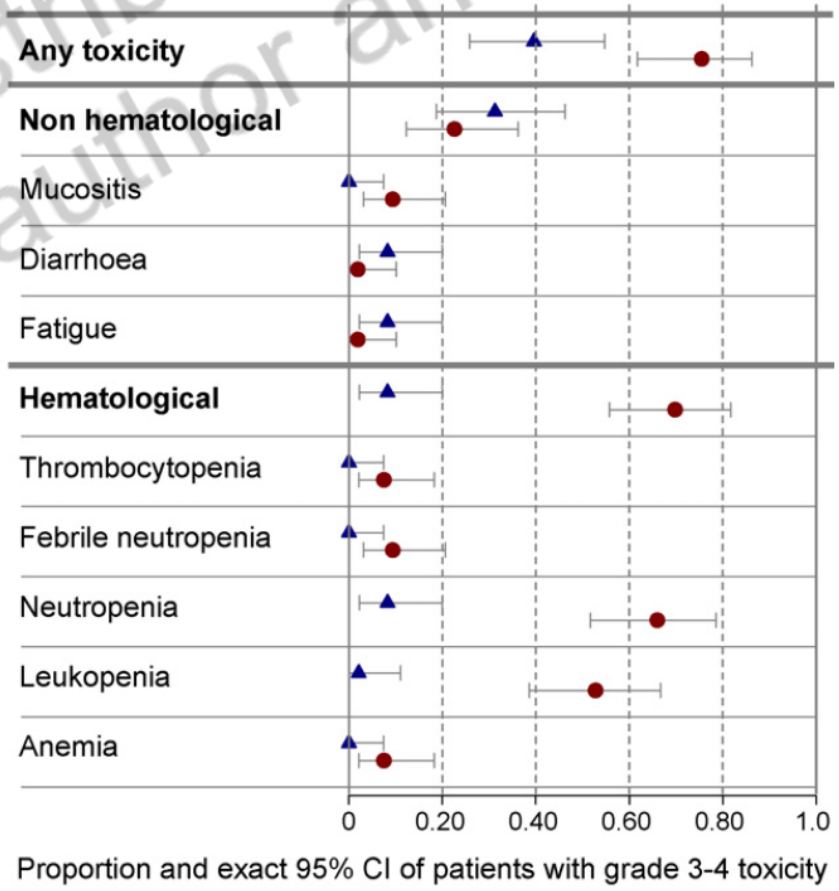
Table 4. Grade 3, 4, or 5 Adverse Events.*

Adverse Event	CMF (N=132)	Doxorubicin plus Cyclophosphamide (N=183)	Capecitabine (N=299)
		no. of patients (%)	
Death	0	0	2 (1)†
≥1 Event	92 (70)	109 (60)	101 (34)
≥1 Hematologic adverse event	68 (52)‡	99 (54)	7 (2)
Hematologic adverse event			
Anemia	4 (3)	7 (4)	2 (1)
Requirement for transfusions	0	2 (1)	0
Leukopenia	53 (40)	79 (43)	3 (1)
Neutropenia	35 (27)	59 (32)	5 (2)
Thrombocytopenia	5 (4)	7 (4)	1 (<1)
≥1 Nonhematologic adverse event	53 (40)‡	44 (24)	98 (33)
Nonhematologic adverse event			
Fatigue	15 (11)	8 (4)	15 (5)
Mucositis	2 (2)	8 (4)	3 (1)
Nausea	9 (7)	8 (4)	6 (2)
Vomiting	8 (6)	3 (2)	6 (2)
Diarrhea	10 (8)	5 (3)	20 (7)
Hand–foot skin reaction	1 (<1)	0	47 (16)
Febrile neutropenia	11 (8)	16 (9)	2 (1)
Thrombus or embolism	5 (4)	4 (2)	3 (1)

Muss H et al, NEJM, 2009; Muss H et al, J Clin Oncol, 2019
Perrone F et al, Ann Oncol, 2014; Nuzzo F et al, Crit Rev Oncol Hematol, 2008

ELDA study
2003 – 2011
Average/high-risk EBC 65-79 years
Weekly docetaxel vs CMF

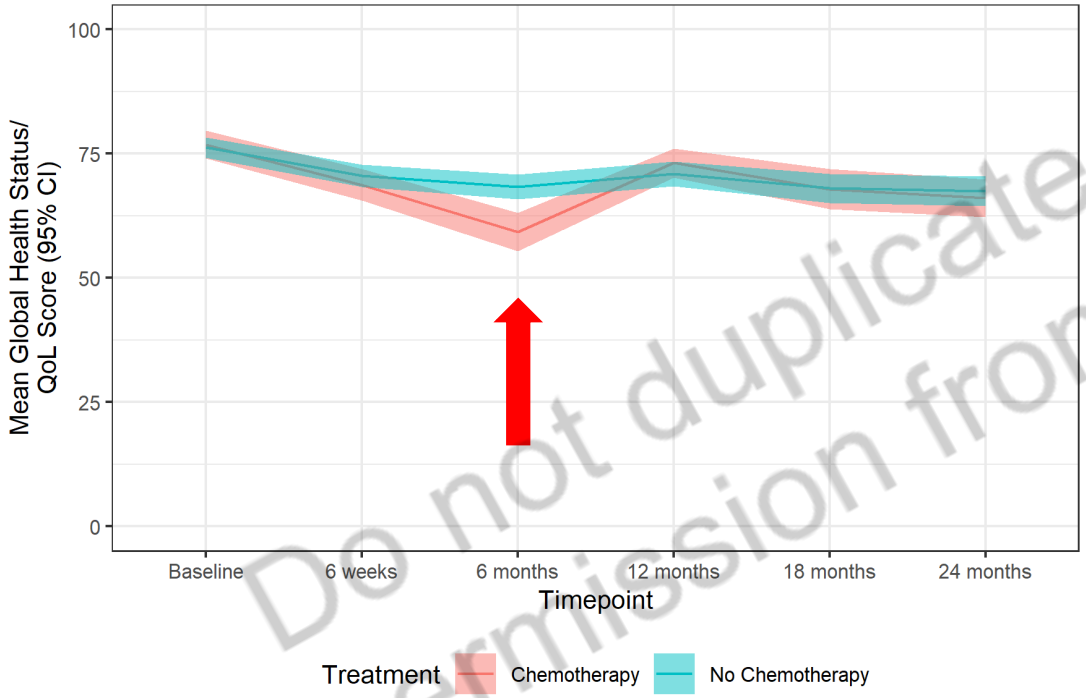
N=302



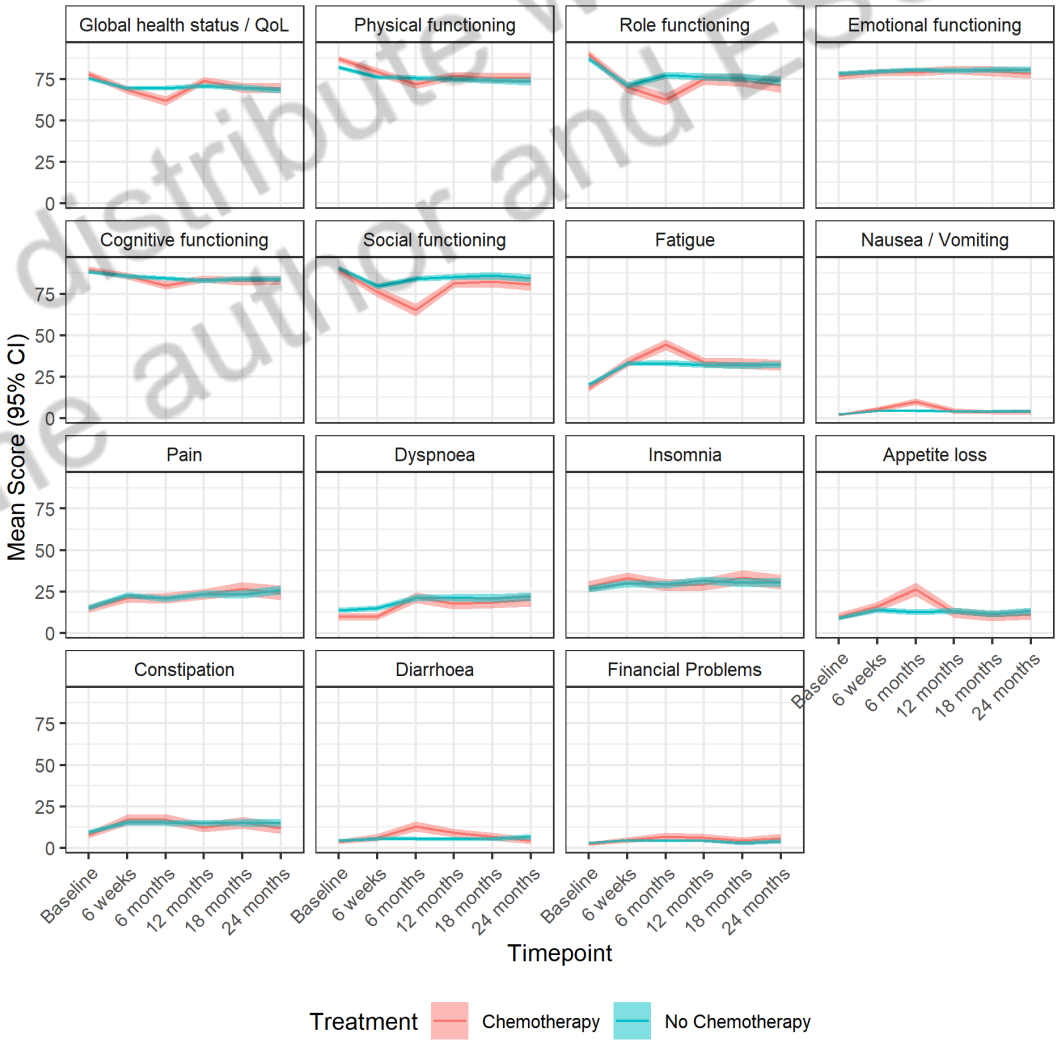
Bridging The Age Gap study: impact on QOL

Bridging The Age Gap study
2013-2018
Operable BC ≥70 years

N = 1,520 with high-risk EBC (24.7% receiving chemotherapy)



EORTC QLQ-C30



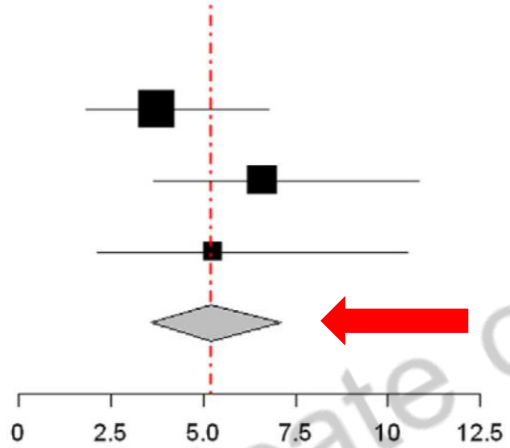
Battisti NML et al, Eur J Cancer, 2021

Anti-HER2 therapy for EBC

Pooled analysis of HERA, N9831 and NSABP B-31
N=1,084

Study	Event	N	Proportion [95% CI]
HERA	10	267	3.75 [1.81; 6.78]
N9831	14	212	6.60 [3.66; 10.83]
B-31	7	133	5.26 [2.14; 10.54]
Pooled		612	5.21 [3.59; 7.10]

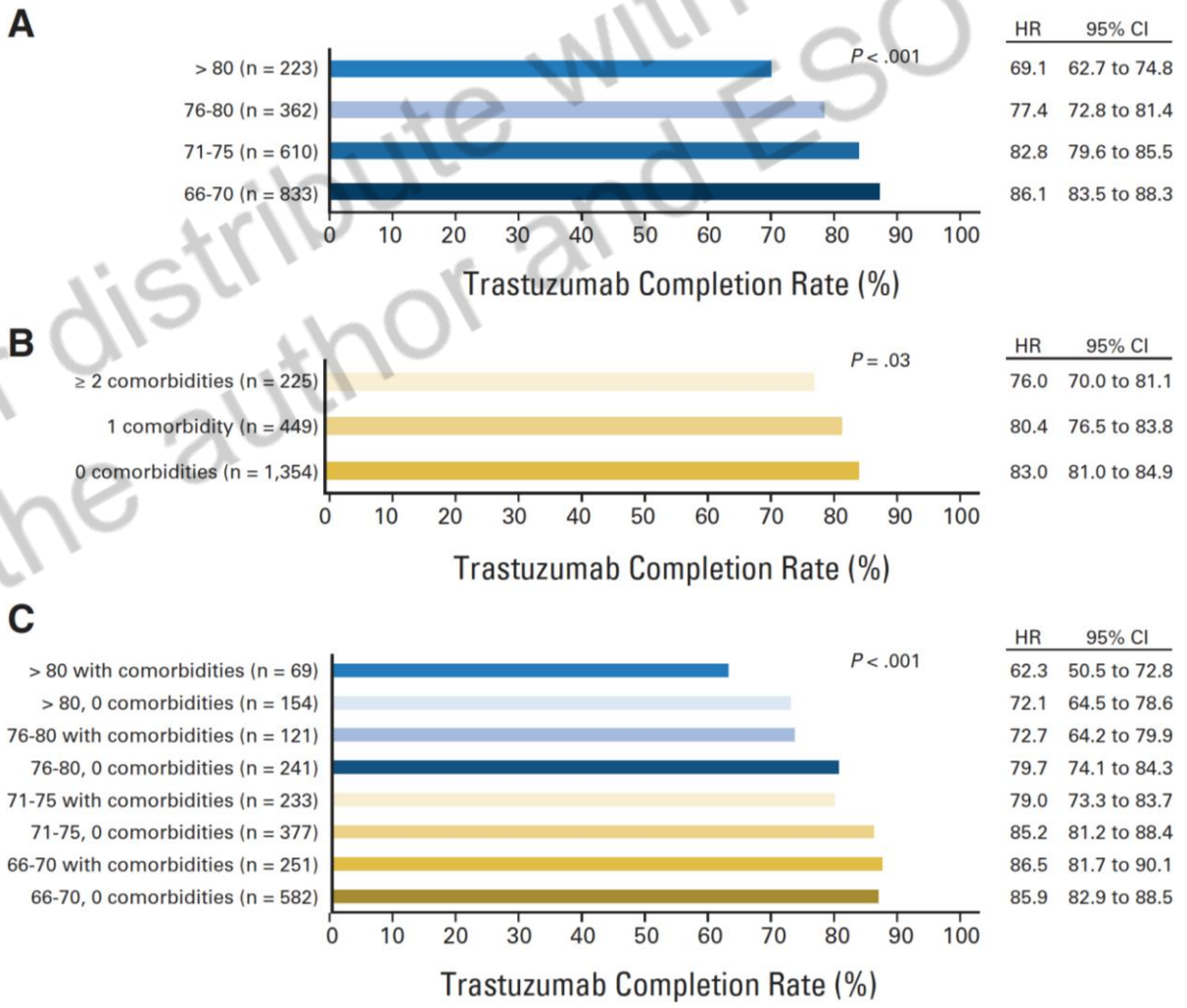
Heterogeneity: p=0.36



5% cardiac event rate

SEER database analysis
Age ≥66 years
Stage I-III BC
2005-2009
N=2,028

Overall completion rate: 81.7%

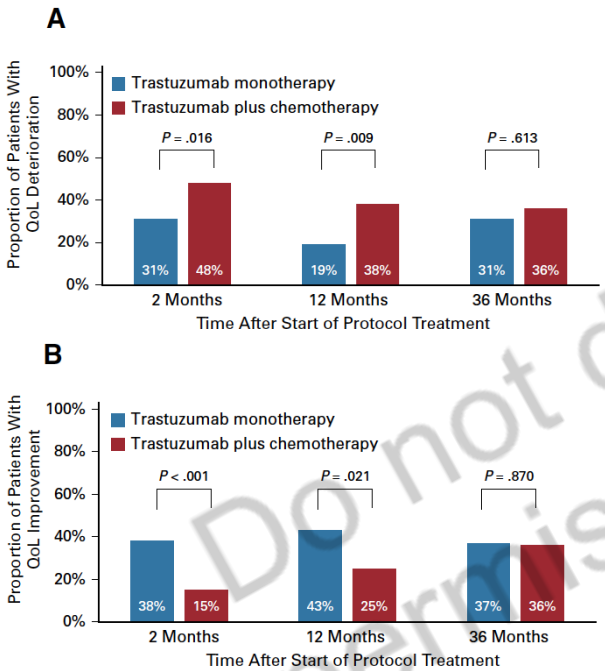


Brollo J, Curigliano G, Disalvatore D, Marrone BF, Criscitiello C, Bagnardi V, Kneubil MC, Fumagalli L, Locatelli M, Manunta S, Goldhirsch A. Adjuvant trastuzumab in elderly with HER-2 positive breast cancer: a systematic review of randomized controlled trials. Cancer Treat Rev. 2013 Feb;39(1):44-50. doi: 10.1016/j.ctrv.2012.03.009. Epub 2012 Apr 27. PMID: 22541668.
Vaz-Luis I, Keating NL, Lin NU, Lii H, Winer EP, Freedman RA. Duration and toxicity of adjuvant trastuzumab in older patients with early-stage breast cancer: a population-based study. J Clin Oncol. 2014 Mar 20;32(9):927-34. doi: 10.1200/JCO.2013.51.1261. Epub 2014 Feb 10. PMID: 24516021; PMCID: PMC3948095. Cadoo KA, Morris PG, Cowell EP, Patil S, Hudis CA, McArthur HL. Adjuvant Chemotherapy and Trastuzumab Is Safe and Effective in Older Women With Small, Node-Negative, HER2-Positive Early-Stage Breast Cancer. Clin Breast Cancer. 2016 Dec;16(6):487-493. doi: 10.1016/j.clbc.2016.07.013. Epub 2016 Aug 1. PMID: 27622751; PMCID: PMC5575753.

RESPECT study: trastuzumab +/- chemotherapy

Phase III randomized non-inferiority study
Age 70-80 years
Resected HER2+ BC
N = 275

Chemo regimens: weekly paclitaxel, docetaxel x 4, AC x 4, EC x 4, CMF x 6, TC x 4, docetaxel/carboplatin x 6



Adverse Event	Trastuzumab Monotherapy AE Grade (n = 135) No. of Patients 1	2	3	4	3 or 4 %	Trastuzumab + Chemotherapy AE Grade (n = 131) No. of Patients 1	2	3	4	3 or 4 %	P
Hematologic											
Neutrophils	6	7	0	0	0.0	7	25	9	14	17.6	< .0001
Leukocytes	15	10	0	0	0.0	21	29	12	8	15.3	< .0001
Platelets	20	0	0	0	0.0	30	1	0	1	0.8	.026
Hemoglobin	37	7	0	0	0.0	46	25	8	3	8.4	< .0001
Nonhematologic											
Left ventricular systolic dysfunction: LVEF	8	3	0	0	0.0	7	2	0	0	0.0	.647
Hypertension	9	19	5	0	3.7	10	27	9	0	6.9	.043
Diarrhea	4	0	1	0	0.7	17	3	1	0	0.8	.004
Fatigue	18	7	0	1	0.7	43	19	8	1	6.9	< .0001
Anorexia	8	2	0	0	0.0	33	17	8	0	6.1	< .0001
Alopecia	3	0	NA	NA	NA	35	59	NA	NA	NA	< .0001
Oral cavity mucositis (clinical examination)	6	1	0	0	0.0	29	9	1	0	0.8	< .0001
Taste alteration (dysgeusia)	5	0	NA	NA	NA	39	8	NA	NA	NA	< .0001
Vomiting	0	1	0	0	0.0	9	4	0	0	0.0	.0037
Nausea	9	1	0	0	0.0	26	7	4	0	3.1	< .0001
Edema: limb	10	1	0	0	0.0	18	4	0	0	0.0	.026
Neuropathy: motor	1	1	2	0	1.5	2	2	1	0	0.8	.966
Neuropathy: sensory	8	1	0	0	0	30	12	4	0	3.1	< .0001

Sawaki M, Taira N, Uemura Y, Saito T, Baba S, Kobayashi K, Kawashima H, Tsuneizumi M, Sagawa N, Bando H, Takahashi M, Yamaguchi M, Takashima T, Nakayama T, Kashiwaba M, Mizuno T, Yamamoto Y, Iwata H, Kawahara T, Ohashi Y, Mukai H; RESPECT study group. Randomized Controlled Trial of Trastuzumab With or Without Chemotherapy for HER2-Positive Early Breast Cancer in Older Patients. J Clin Oncol. 2020 Nov 10;38(32):3743-3752. doi: 10.1200/JCO.20.00184. Epub 2020 Sep 16. PMID: 32936713.
Taira N, Sawaki M, Uemura Y, Saito T, Baba S, Kobayashi K, Kawashima H, Tsuneizumi M, Sagawa N, Bando H, Takahashi M, Yamaguchi M, Takashima T, Nakayama T, Kashiwaba M, Mizuno T, Yamamoto Y, Iwata H, Ohashi Y, Mukai H, Kawahara T; RESPECT Study Group. Health-Related Quality of Life With Trastuzumab Monotherapy Versus Trastuzumab Plus Standard Chemotherapy as Adjuvant Therapy in Older Patients With HER2-Positive Breast Cancer. J Clin Oncol. 2021 Aug 1;39(22):2452-2462. doi: 10.1200/JCO.20.02751. Epub 2021 Apr 9. PMID: 33835842.

Targeted agents for ER+ HER2- ABC

CDK4/6 inhibitors
Pooled analysis of 2 RCTs
N = 1,827 (≥70 years: n=456)

TABLE 3. Toxicity and Selected Adverse Events of CDK4/6 Inhibitors by Age

Variable	Age < 70 Years (n = 825)	Age ≥ 70 Years (n = 280)	Age < 75 Years (n = 980)	Age ≥ 75 Years (n = 125)
Grade 1-2	808 (97.9)	278 (99.3)	962 (98.2)	124 (99.2)
Grade 3-4	598 (72.5)	236 (84.3)	723 (73.4)	111 (88.8)
Grade 5	14 (1.7)	9 (3.2)	19 (1.9)	4 (3.2)
AE leading to dose reduction and/or interruption	577 (70.0)	222 (79.3)	697 (71.1)	102 (81.6)
AE leading to discontinuation	94 (11.4)	65 (23.2)	119 (12.1)	40 (32.0)
Serious AEs	180 (21.8)	101 (36.1)	223 (22.8)	58 (46.4)
Hepatotoxicity grades 3-4	46 (5.5)	22 (7.8)	56 (5.7)	12 (9.6)
Fatigue all grades	359 (43.5)	143 (51.1)	434 (44.3)	68 (54.4)
Fatigue grade 3	19 (2.3)	11 (3.9)	27 (2.7)	3 (2.4)
Diarrhea all grades	367 (44.4)	146 (52.1)	446 (45.5)	67 (53.6)
Diarrhea grade 3	28 (3.4)	13 (4.6)	32 (3.3)	9 (7.2)

Discontinuation due to AEs on EVE/EXE vs PBO/EXE:
<70 years: 6.3% vs 4.1%
≥70 years: 17.4% vs 0%

On-treatment deaths with AEs as primary cause on EVE/EXE vs PBO/EXE:
<70 years: 1.3% vs 1.3%
≥70 years: 7.7% vs 0%

Howie LJ et al, J Clin Oncol, 2019
Pritchard KI, Clin Breast Cancer, 2013

Everolimus
BOLERO-2 study subgroup analysis
≥70 years: N = 121

Table 5 Any Grade Treatment-Emergent Adverse Events With ≥ 10% Incidence in the EVE + EXE Groups (Regardless of Cause)

Adverse Event	Patients, %							
	Age < 70 years				Age ≥ 70 years			
	EVE + EXE		PBO + EXE		EVE + EXE		PBO + EXE	
Grade	Any	3/4	Any	3/4	Any	3/4	Any	3/4
Stomatitis	62	8	13	1	49	8	5	0
Rash	42	1	7	0	31	2	7	0
Fatigue	37	3	28	2	38	10	23	0
Diarrhea	34	3	19	1	36	2	19	0
Nausea	30	0.3	29	2	33	2	28	0
Appetite decrease	29	1	11	0.5	36	3	23	2
Weight decrease	27	1	7	0	29	3	7	0
Headache	26	0.5	15	0	11	0	12	0
Cough	25	0.3	12	0	26	3	9	0
Dysgeusia	23	0	7	0	20	0	2	0
Arthralgia	21	0.3	17	0.5	19	3	14	0
Peripheral edema	21	1	5	0.5	20	1	14	0
Dyspnea	20	4	10	2	28	8	16	0
Vomiting	18	1	13	1	17	0.8	14	0
Anemia	17	7	6	1	31	10	2	0
AST increase	16	4	7	2	7	2	0	0
Pyrexia	17	0.3	7	0.5	14	0	5	0
Pneumonitis	17	3	0	0	14	5	0	0
ALT increase	15	4	6	3	4	3	0	0
Back pain	15	0	10	2	14	0.8	14	0
Pruritus	14	0	5	0	12	0.8	5	0
Hyperglycemia	15	5	3	0.5	12	8	0	0
Epistaxis	18	0	1	0	14	0	2	0
Constipation	15	0.3	13	0.5	13	2	16	0
Insomnia	15	0.3	8	0	12	0	9	0
Hypercholesterolemia	11	0.3	1	0	7	0.8	0	0
Nasopharyngitis	12	0	10	0	6	0	2	0
Thrombocytopenia	12	2	0.5	0	15	3	0	0
GGT increase	11	6	10	8	8	7	2	2
Asthenia	12	2	3	0	20	3	12	2
Nail disorder	10	0	0.5	0	3	0	0	0
Dry mouth	10	0	6	0	14	0	14	0
Alopecia	10	0	5	0	12	0	5	0
Creatinine increase	6	1	1	0	15	0.8	0	0
Urinary tract infection	9	0.5	2	0	15	0	5	0

Anti-HER2 therapy for ABC

registHER observational study
HER2+ ABC (including 50% HR+)
2003-2006
N = 1,001 (65+: n = 209)

Table 3 Incidence of cardiac adverse events (grades ≥3) in trastuzumab-treated younger (<65 years), older (65–74 years), and elderly (≥65 years) patients

Adverse event, *n* (%)	Age (years) at MBC		
	<65 (*n* = 746)	65–74 (*n* = 134)	≥75 (*n* = 63)
Any	51 (6.8)	9 (6.7)	16 (25.4)
Angina pectoris	1 (0.13)	1 (0.75)	0 (0.0)
Atrial arrhythmia	2 (0.27)	1 (0.75)	2 (3.1)
Cardiac disorder (NOS)	8 (1.1)	2 (1.5)	4 (6.3)
Congestive heart failure	14 (1.9)	2 (1.5)	2 (3.2)
Left ventricular dysfunction	21 (2.8)	2 (1.5)	3 (4.8)
Myocardial infarction	1 (0.13)	1 (0.75)	2 (3.2)
Pericardial effusion	4 (0.53)	0 (0.0)	2 (3.2)
Ventricular arrhythmia	0 (0.0)	0 (0.0)	1 (1.6)

EORTC 75111-10114 study
HER2+ ABC
≥70 years or ≥60 years & functional impairment
2013-2016

N = 80 (G8 score ≤14: n = 56)

	Trastuzumab plus pertuzumab (n=39)					Trastuzumab, pertuzumab plus metronomic cyclophosphamide (n=41)					Trastuzumab emtansine (n=29)				
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
(Continued from previous page)															
Vascular disorders															
Hypertension	1 (3%)	2 (5%)	6 (15%)	0	0	2 (5%)	2 (5%)	5 (12%)	0	0	0	2 (7%)	0	0	0
Thromboembolic event	0	1 (3%)	0	0	0	0	0	3 (7%)	1 (2%)	0	0	0	1 (3%)	0	0
Laboratory abnormalities															
Alanine aminotransferase*	6 (16%)	2 (5%)	1 (3%)	0	0	7 (18%)	0	1 (3%)	0	0	13 (50%)	0	0	0	0
Aspartate aminotransferase*	10 (27%)	2 (5%)	0	0	0	16 (40%)	1 (3%)	0	0	0	17 (65%)	2 (8%)	0	0	0
Neutropenia*	5 (13%)	1 (3%)	0	0	0	6 (15%)	3 (8%)	0	0	0	5 (19%)	1 (4%)	0	1 (4%)	0
Lymphopenia*	6 (16%)	11 (29%)	1 (3%)	0	0	4 (10%)	17 (43%)	13 (33%)	2 (5%)	0	6 (23)	7 (27%)	3 (12%)	1 (4%)	0
Anaemia*	17 (45%)	3 (8%)	0	0	0	20 (50%)	10 (25%)	1 (3%)	0	0	8 (31%)	7 (27%)	0	0	0
Thrombocytopenia*	4 (11%)	0	0	0	0	7 (18%)	0	0	0	0	9 (35%)	2 (8%)	1 (4%)	0	0

Diarrhoea: 71% on combo versus 59% on trastuzumab/pertuzumab

Kaufman PA, Brufsky AM, Mayer M, Rugo HS, Tripathy D, Yood MU, Feng S, Wang LI, Quah CS, Yardley DA. Treatment patterns and clinical outcomes in elderly patients with HER2-positive metastatic breast cancer from the registHER observational study. Breast Cancer Res Treat. 2012 Oct;135(3):875-83. doi: 10.1007/s10549-012-2209-z. Epub 2012 Aug 26. PMID: 22923238; PMCID: PMC3439611.

Wildiers H, Tryfonidis K, Dal Lago L, Vuylsteke P, Curigliano G, Waters S, Brouwers B, Altintas S, Touati N, Cardoso F, Brain E. Pertuzumab and trastuzumab with or without metronomic chemotherapy for older patients with HER2-positive metastatic breast cancer (EORTC 75111-10114): an open-label, randomised, phase 2 trial from the Elderly Task Force/Breast Cancer Group. Lancet Oncol. 2018 Mar;19(3):323-336. doi: 10.1016/S1470-2045(18)30083-4. Epub 2018 Feb 9. PMID: 29433963.

Outline

- Complexity of managing cancer in older individuals
- Safety of specific anticancer treatments in older patients with breast cancer
  - Curative setting
  - Palliative setting
- Importance of geriatric assessments
- Conclusions

Comprehensive geriatric assessment: Applying general geriatrics to oncology

Domains and tools included in CGA

Tool by domain	Time to administer (min)	Abnormal score	Tool by domain	Time to administer (min)	Abnormal score
Demographic and social status			**Mood**		
Conditions of living, marital status, educational level, financial resources, social activities, family support	10	>20	GDS (Mini-GDS, GDS-15, GDS-30)	15	<1; >5; >10
			Hospital Anxiety and Depression Scale		>7
Identification of the caregiver (Zarit Burden Interview)	15–20		Distress thermometer		
Comorbidities			**Nutrition**		
Charlson Comorbidity Index	2		BMI		<23
CIRS			Weight loss		
CIRS-G			Mini-Nutritional Assessment		<24
Physical Health Section (subscale of OARS)			Dentition		
Simplified comorbidity score					
Polypharmacy			**Fatigue**		
Beers criteria			MOB-T		
STOPP and START criteria					
Functional status			**Geriatric syndromes**		
ADL (Katz index)		<6	Dementia		
IADL (Lawton scale)		<8	Delirium		
Visual and/or hearing impairment			Incontinence		
Mobility problems			Osteoporosis or spontaneous fractures		
Timed Get Up and Go		≥14s	Neglect or abuse		
Hand grip strength		<1m/s	Failure to thrive		
Walking problems, gait assessment, gait speed			Pressure ulcer		
			Sarcopenia		
Self reported no. of falls					
Cognition					
Mini Mental State Examination	10–15	≤24			
Montreal Cognitive Assessment		<26			
Clock-drawing test		<5			
Blessed Orientation-Memory-Concentration Test		>4			
Mini-Cog		<4			

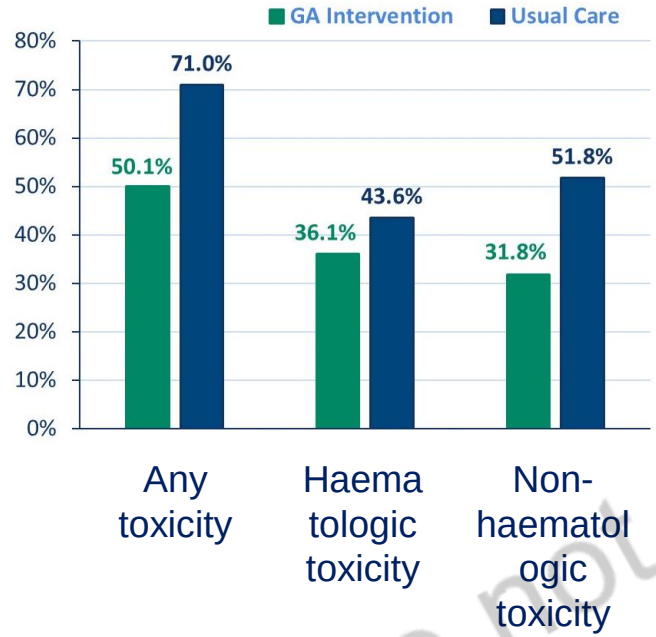
Benefits of CGA

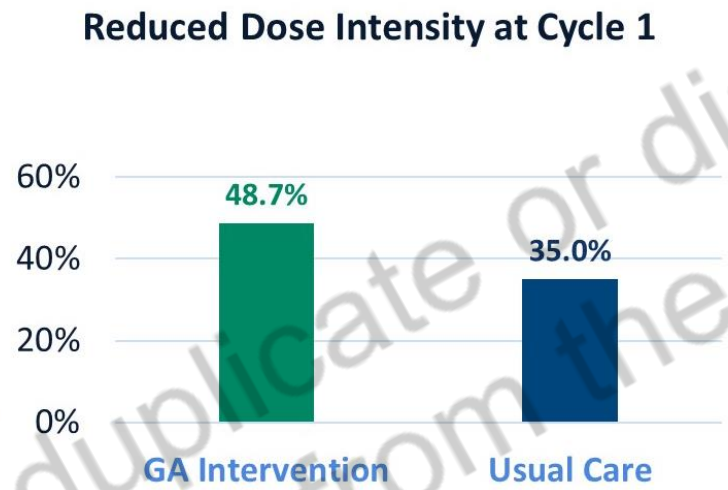
- Predicting complications and side effects from treatment
- Predicting functional decline during treatment
- Estimating survival
- Assisting in cancer treatment decisions
- Detecting problems not found by routine history and physical examination in the initial evaluation
- Identifying and treating new problems during follow-up care
- Improving mental health and well-being
- Improving pain control
- Reducing severe systemic therapy toxicity
- Reducing unplanned hospitalisations on systemic therapy
- Increasing completion of advanced directives systemic therapy
- Improving quality of life on systemic therapy

1. *Wildiers H et al, J Clin Oncol, 2014*
2. *Decoster L et al, Ann Oncol, 2015*
3. *Mohile SG et al, J Clin Oncol, 2018*

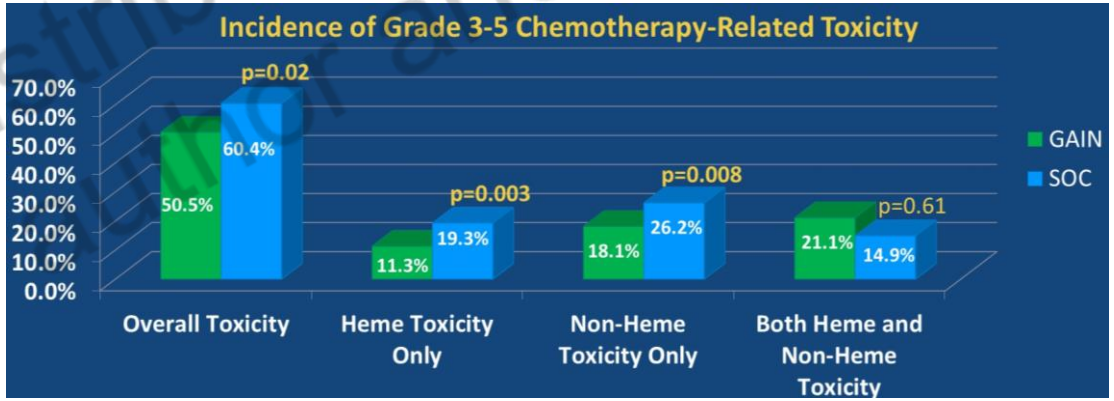
Impact on systemic anticancer therapy toxicity

GAP70 study[1]
Patients ≥70 years with incurable stage III-IV cancer starting a new systemic treatment
N = 718





GAIN study[2]
Patients ≥65 years with solid tumours (any stage) starting a new chemotherapy regimen
N = 600



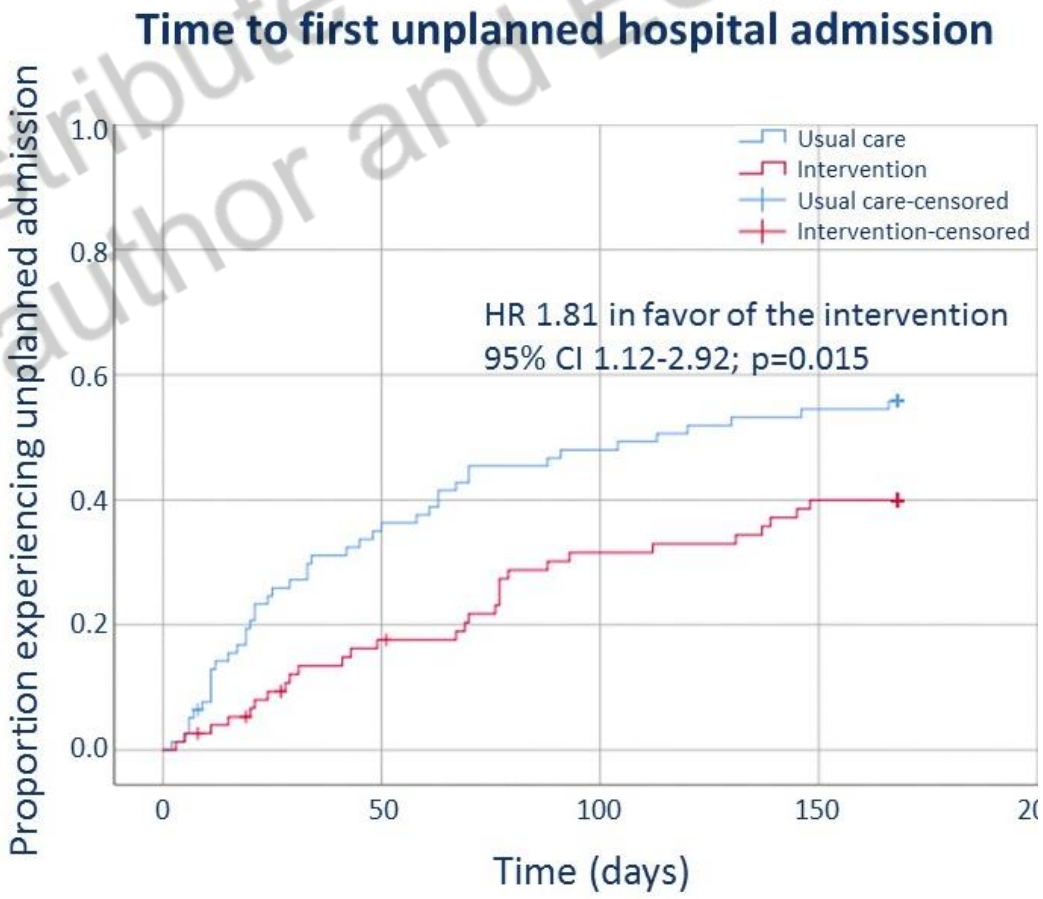
Any grade 3–5 toxicity
Adjusted risk ratio: 0.74
95% CI 0.63–0.97, p<0.01

1. *Mohile S et al. Presentation at American Society of Clinical Oncology Virtual Scientific Program, 29–31 May 2020: Abstract 12009*
2. *Li D et al. Presentation at American Society of Clinical Oncology Virtual Scientific Program, 29–31 May 2020: Abstract 12010*

Impact on hospitalizations

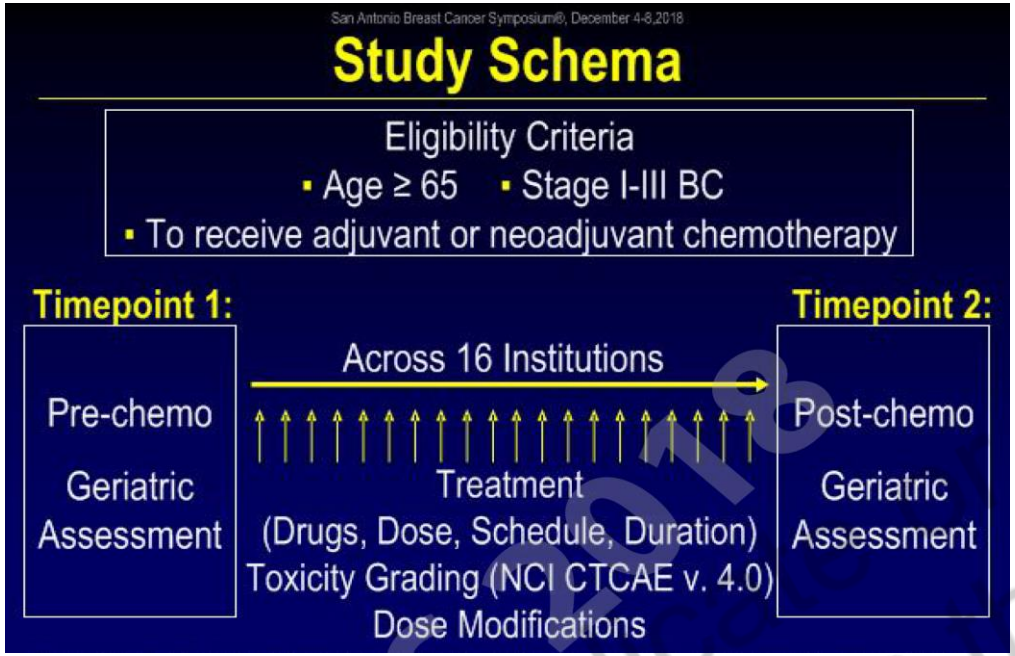
INTEGERATE study
Patients ≥70 years with solid tumours/DLBCL starting a new systemic treatment
N = 154

- **39% fewer emergency presentations**
- **41% fewer unplanned hospital admissions**
- **24% fewer unplanned hospital overnight bed-days**
- **Lower early treatment discontinuation due to adverse events: 32.9% vs 53.2%, p=0.01**
  - Driven by lower discontinuation due to toxicity
- **No difference in treatment reduction, escalation, delay**

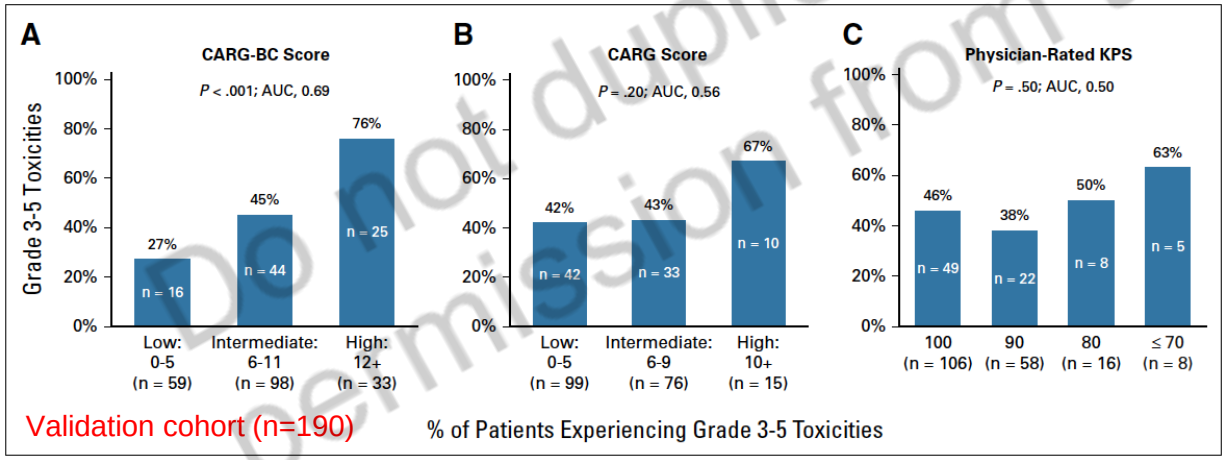


Soo W-K et al. Presentation at American Society of Clinical Oncology Virtual Scientific Program, 29–31 May 2020: Abstract 12011

Cancer and Aging Research Group BC tool



Risk factors	Points				
	0	1	2	3	4
Breast cancer stage	I		II or III		
Planned use of anthracyclines	No	Yes			
Planned treatment duration	≤3 months (12 weeks)				>3 months (12 weeks)
Haemoglobin	>13 g/dL (male) >12 g/dL (female)			≤13 g/dL (male) ≤12 g/dL (female)	
Liver function	Normal LFTs, within reference range			Abnormal LFTs, outside reference range	
How many times have you fallen in the last 6 months?	0				≥1
Does your health limit you in walking more than 1 mile?	Not limited at all			Somewhat or very limited	
How often is someone available to give you good advice about a crisis?	Most or all of the time			None, little, or some of the some	
TOTAL SCORE					
Abbreviations:	*LFTs: liver function tests*				



Validation cohort (n=190)

Total Risk Score		Risk (%)		
		Grade 3-5 adverse events	Dose reductions	Early treatment discontinuations
Low	0-5	22%	14%	13%
Intermediate	6-11	51%	25%	26%
High	≥12	81%	38%	39%

Overall cohort (n=473)

Magnuson A, Sedrak MS, Gross CP, Tew WP, Klepin HD, Wildes TM, Muss HB, Dotan E, Freedman RA, O'Connor T, Dale W, Cohen HJ, Katheria V, Arsenyan A, Levi A, Kim H, Monile S, Hurria A, Sun CL. Development and Validation of a Risk Tool for Predicting Severe Toxicity in Older Adults Receiving Chemotherapy for Early-Stage Breast Cancer. J Clin Oncol. 2021 Feb 20;39(6):608-618. doi: 10.1200/JCO.20.02063. Epub 2021 Jan 14. PMID: 33444080; PMCID: PMC8189621.

Outline

- Complexity of managing cancer in older individuals
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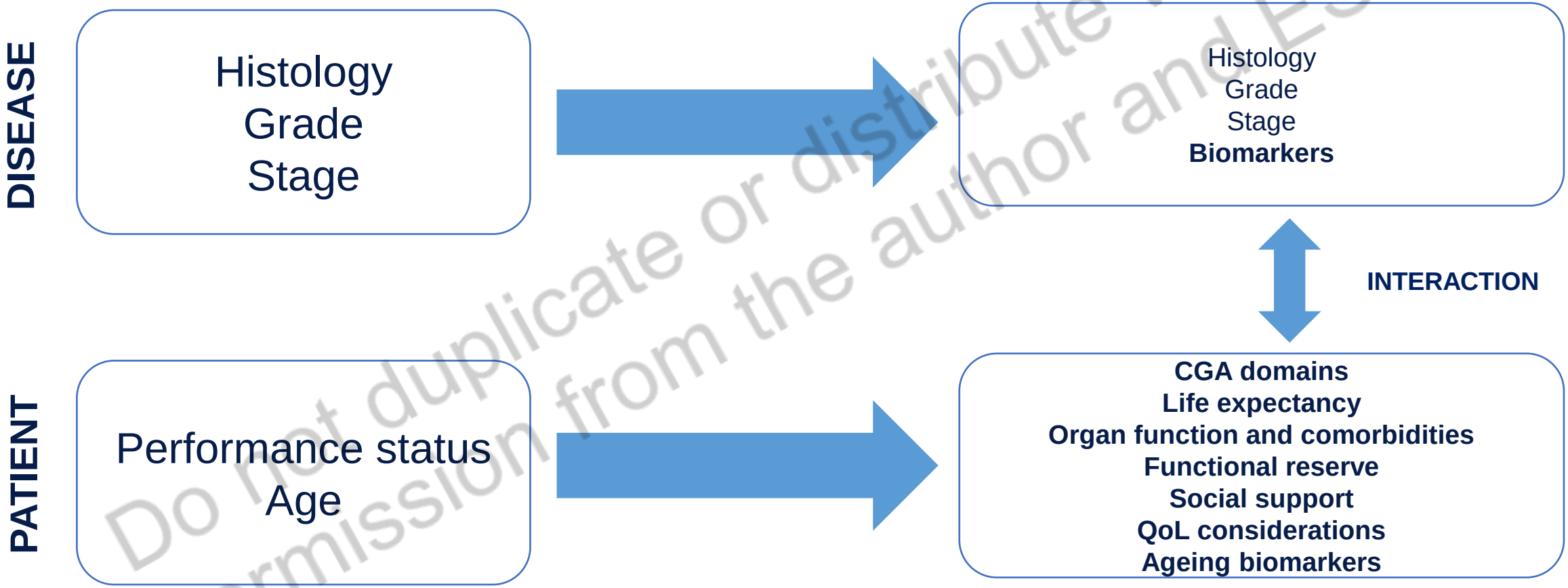
Towards a new precision oncology paradigm



Adapted from a slide courtesy of Martine Extermann

Resources

- **EUSOMA/SIOG updated recommendations**

Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG)

Laura Biganzoli, Nicolò Matteo Luca Battisti, Hans Wildiers, Amelia McCartney, Giuseppe Colloca, Ian H Kunkler, Maria-João Cardoso, Kwok-Leung Cheung, Nienke Aafke de Glas, Rubina M Trimboli, Beatriz Korc-Grodzicki, Enrique Soto-Perez-de-Celis, Antonio Ponti, Janice Tsang, Lorenza Marotti, Karen Benn, Matti S Aapro, Etienne G C Brain

- **International Society of Geriatric Oncology**
  http://www.siog.org/ *@SIOGorg* *@YoungSIOG* *@siognah*

- **Cancer and Aging Research Group**
  http://www.mycarg.org/ *@myCARG*

- **Moffitt Cancer Center Senior Adult Oncology Program Tools**
  https://moffitt.org/for-healthcare-providers/clinical-programs-and-services/senior-adult-oncology-program/senior-adult-oncology-program-tools/

- **Journal of Geriatric Oncology**
  https://www.geriatriconcology.net/ @JGeriOnc

- *#gerionc#geriheme* *#gerisurgonc* *#geriradonc*

Biganzoli L, Battisti NML, Wildiers H, McCartney A, Colloca G, Kunkler IH, Cardoso MJ, Cheung KL, de Glas NA, Trimboli RM, Korc-Grodzicki B, Soto-Perez-de-Celis E, Ponti A, Tsang J, Marotti L, Benn K, Aapro MS, Brain EGC. Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG). Lancet Oncol. 2021 Jul;22(7):e327-e340. doi: 10.1016/S1470-2045(20)30741-5. Epub 2021 May 14. PMID: 34000244.

Thank you!

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