New horizon management for elderly cancer patients

(including rationale, geriatric assessment, management common cancers)

มหาวิทยาลัยมหิดล
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SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

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CANCER INCIDENCE IN OLDER ADULTS

• 2012

- 6.7M (47.5% of all cancers)
- Marked regional disparities
  - ~ 48% in less developed regions
  - Lung, CRC, prostate, stomach and BC ~ 55% global incidence, yet distinct regional patterns were observed

• 2035

- 14M (~ 60% of all cancers)
- Predicted relative increase
  - Largest in the Middle East & Northern Africa (+157%), and in China (+155%)
  - Less developed regions +144%
  - More developed regions +54%

Substantial economic & social impacts
Considerable & unique challenge to healthcare systems everywhere
Especially in those w/ limited resources & weaker health systems

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Pilleron IJC 2019

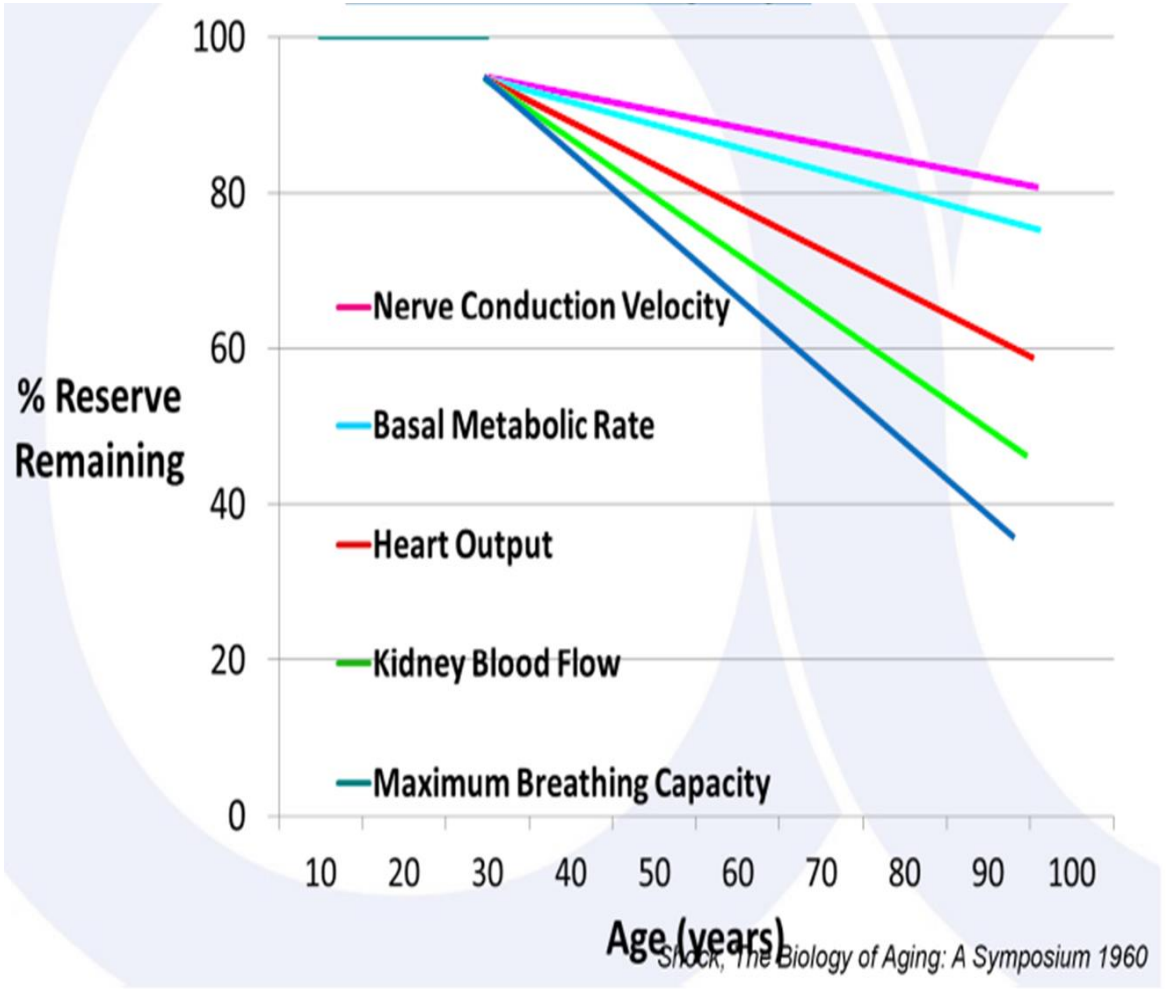
What is Different about Older adults?

- Aging is heterogeneous : Chronological Age ≠ Functional Age
- A hallmark of aging: decline in organ reserve
- May not be obvious at rest, but be apparent with a stressor

Physiology of aging

1) Mortality increases with increasing age
2) Body composition changes with increasing age
   - muscle is replaced by fat
3) Decline in capacity with increasing age (maximum pulse↓, kidney function↓)
4) Reduced capacity to deal with stress (surgery, infection), difficult to sustain homeostasis
5) Increased risk of disease and increased vulnerability when getting sick

Linear Decline Of Organ Reserve With Increasing Age



Cardiovascular function[1]

- decreased elasticity of arterial system
- loss of myocytes and atrial pacemaker cells
- increased fibrosis of cardiac fibrous skeleton

Renal function[2]

- decreased renal blood flow
- decreased glomerular filtration rate
- decreased creatinine clearance

Hepatic function[3]

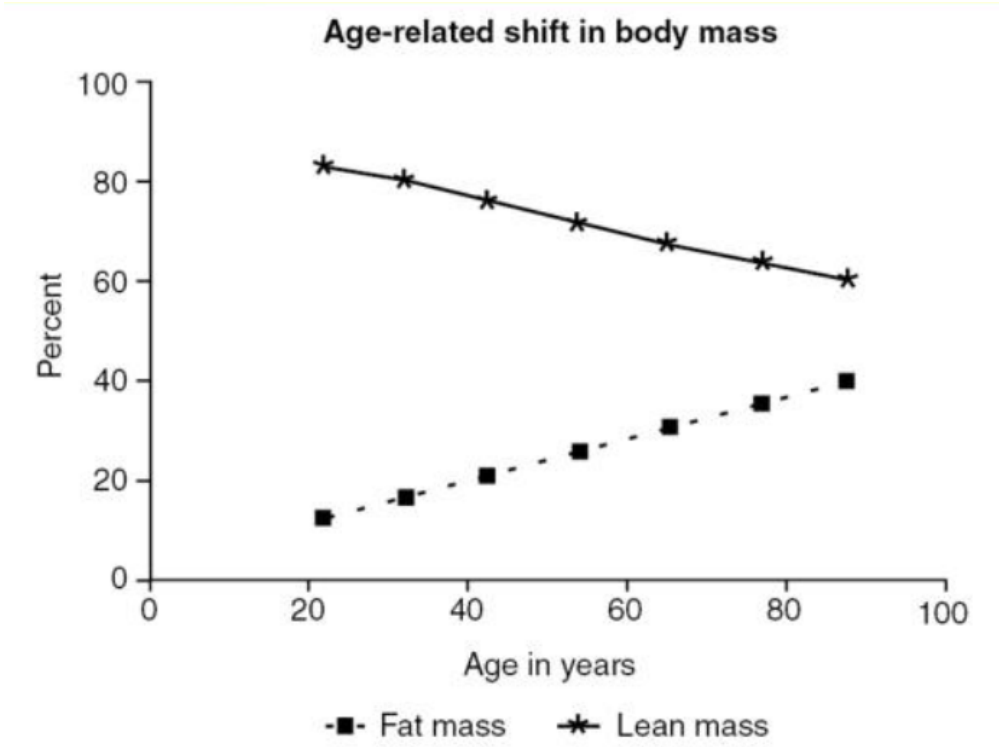
- reduced hepatic blood flow
- decline in cytochrome P450 system

Bone Marrow function[4]

- reduction of hematopoietic reserve

[1]Cheitlin MD. Am J Geriatr Cardiol 2003;12:9-13
[2]Muhlberg W, et al. Gerontology 1999,45:243-53
[3]Anantharaju A et al. Gerontology 2002;48:343-53
[4] Dees et al, Cancer Invest 2000,18:521-529

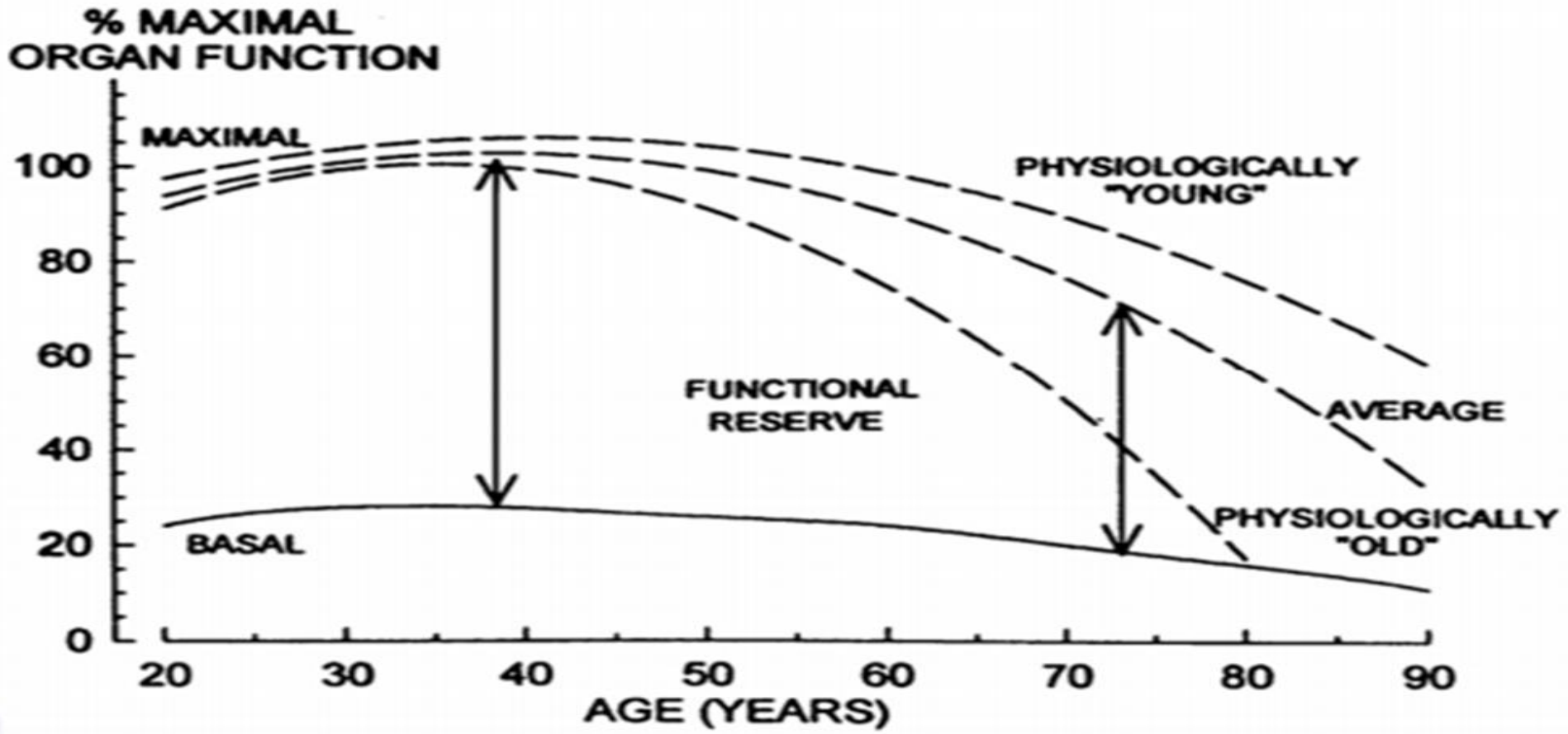
Age related changed in body composition



- Most of the fat increase occurs inside the peritoneum
- Fat significantly contribute to increased whole body inflammation, age-related declines and diseases
- Exercise increases metabolic rate and can burn fat as energy sources
- Decrease lean body mass, M strength (8% per decade after 30 Years old)

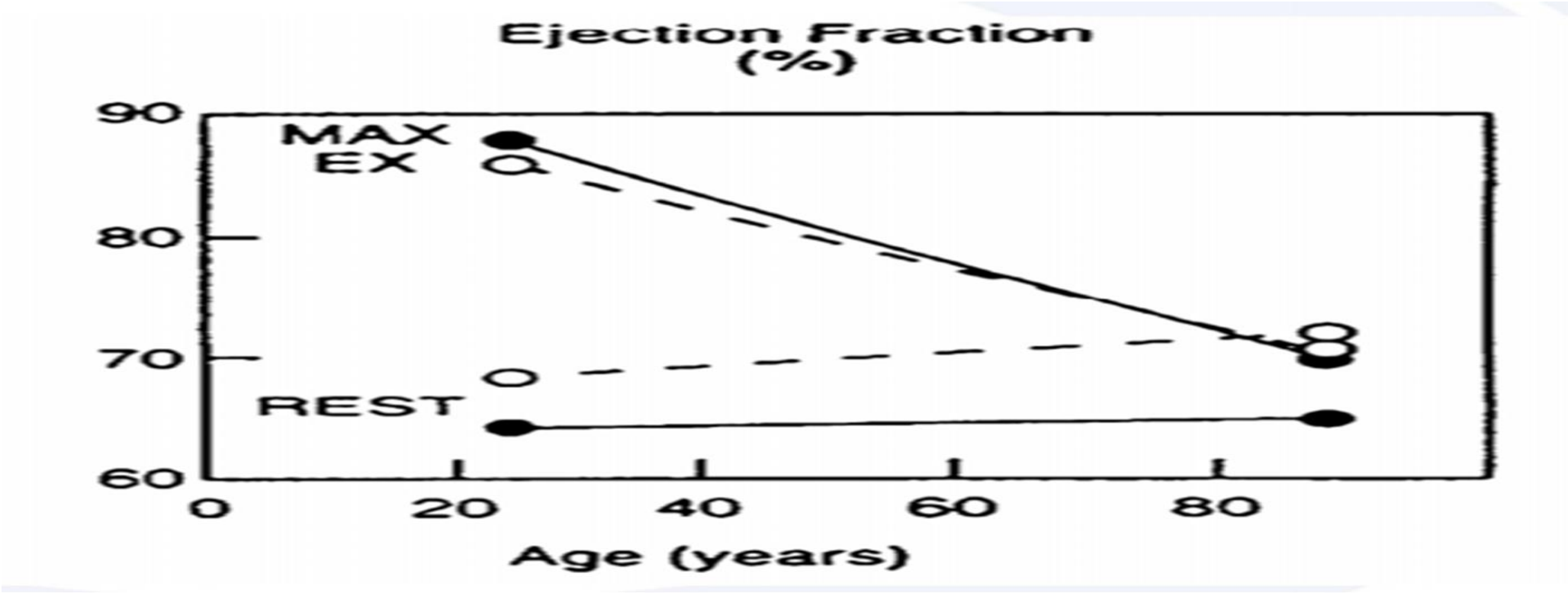
Nutrition. 2010 Feb; 26(2): 152–155.

Decrease in capacity -heterogeneity



Muravchik, Anesthesia 5th ed, 2000

Reduced ability to deal with stress



Lakatta Aging 1994

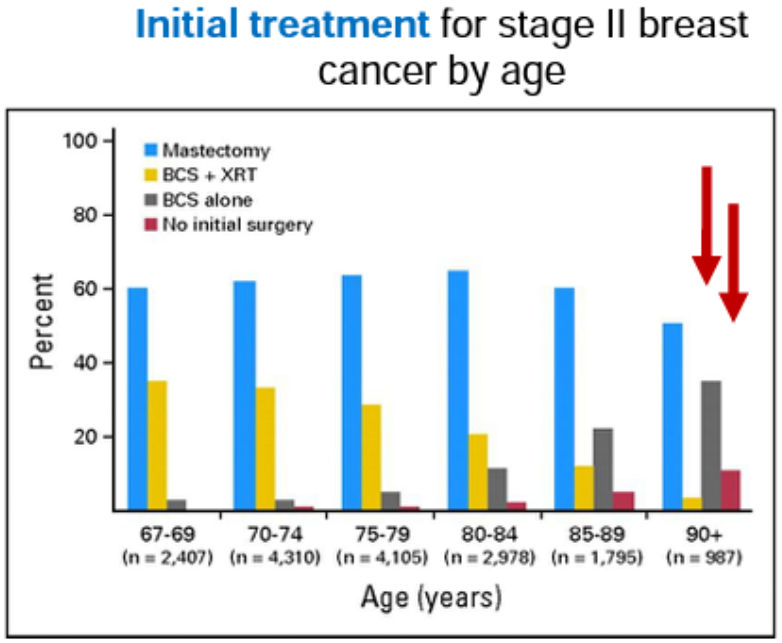
Management of the older cancer patients

- Older cancer patients may benefit from antineoplastic treatment irrespective of age
- Age is not a contraindication to antineoplastic treatment
- Guideline may be not a guideline for elderly
- Limit in evidence base data

Undertreatment vs Overtreatment

Undertreatment

- SEER data : 49,616 case of BC I-II



Schonberg JCO 2010

Overtreatment

- Patient died from non-cancer related causes, N = 14,048 FU 4.7 yr

N = 14048 new early breast cancer, ≥50y, FUP 4,7y

	Total deaths	Deaths from breast cancer	%
50–69	1334	933	70
70–74	514	293	57
75–79	696	329	47
⩾80	1681	663	39
Total	4225	2218	53

Ali Br J Cancer 2011

ROLES & SHARING OF RESPONSIBILITIES

- **Oncologist**
  - Cancer diagnosis
  - Curative versus palliative
  - Treatment
  - Follow up
- **Geriatrician**
  - Holistic view
  - Comorbidities & LE
  - Frailty, impact & reversibility
  - Recommendations
- **Together = personalized treatment plan**
  - Which treatment?
  - Which dose?
  - Which supportive cares?
  - Where?

Key messages for older cancer patients

1. Age and standard approach upfront influence treatment decision
   - Not always in the right direction: under and over treatment are frequent, but over > under
2. Geriatric problems are far more frequent than usually believed
   - 2/3 impaired G8, +50% functional dependence or risk of malnutrition, +40% significant comorbidities, 20% depression , +10% cognitive dysfunctions, polypharmacy
3. Geriatric assessment = enforceable and not opposable
   - Brings to clinicians new information > 2/3 cases
   - Modifies clinical decision in > 25% cases (function and nutrition)
4. Competing risks for mortality
   - Call for some degree of assessment of life expectancy to balance treatment decision
5. Access to innovation is unbalanced
   - Need for specific research

AGEING MAKES US UNIQUE!

Women life expectancy

Age	Top 25th% Fit	50th% Intermediate	Lowest 25th% Sick
50	40	33	24.5
70	21.3	15.7	9.5
75	17	11.9	6.8
80	13	8.6	4.6
85	9.6	5.9	2.9
90	6.8	3.9	1.8
95	4.8	2.7	1.1

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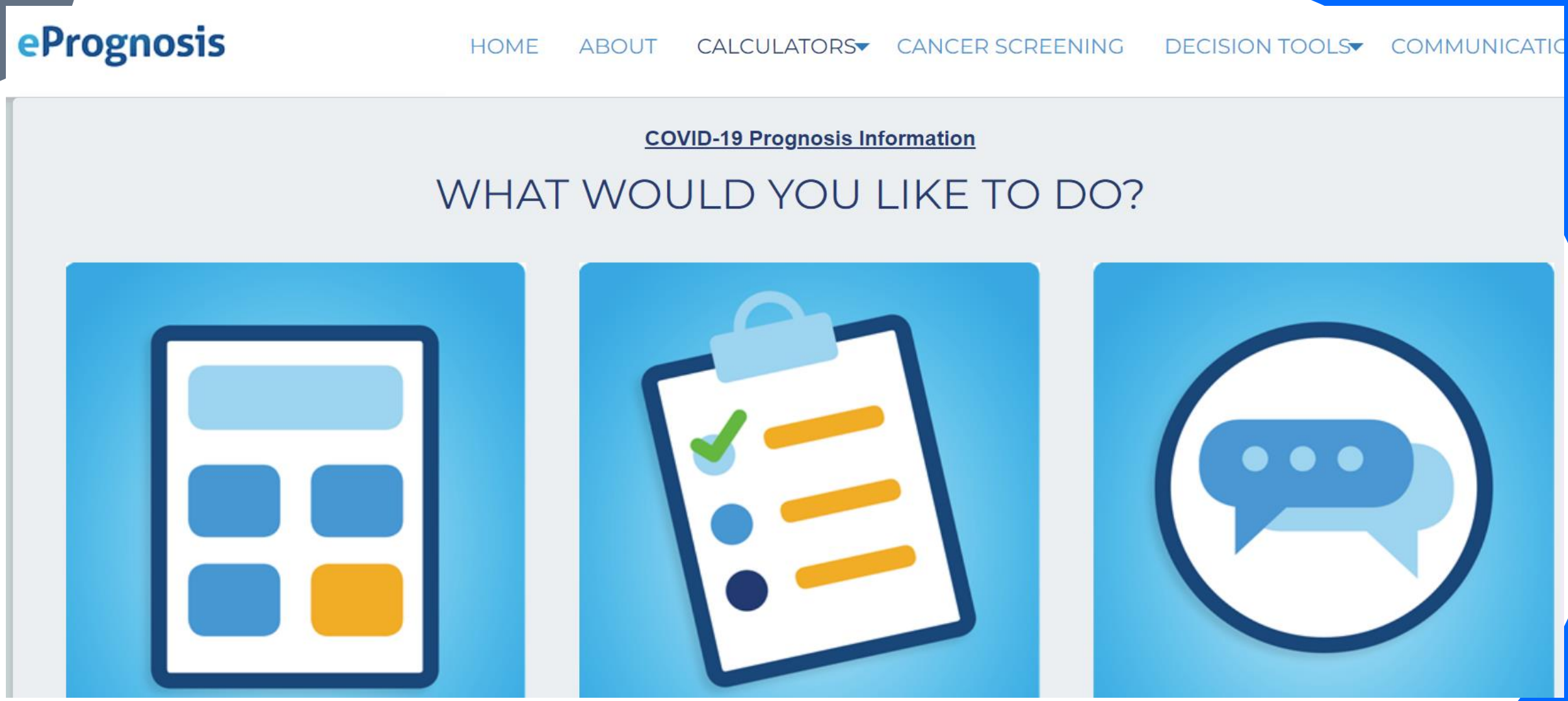
Walter JAMA 2001



https://eprognosis.ucsf.edu/

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GERIATRIC SYNDROMES

Highly prevalent in older persons

- Older adults with cancer have more geriatric syndromes than older adults without cancer (60% in cancer vs 53% in those without cancer)
- have a negative effect on function and quality of life,
- have multifactorial pathophysiology,
- often involve systems unrelated to the presenting complaint and are manifested by stereotypical clinical presentations.

Mobility impairment & falls

Osteoporosis

Cognitive impairment

Functional impairment

Malnutrition

Incontinence

Polypharmacy

When you have elderly cancer patients

- Is the patient going to die from cancer or from other causes?
  - Life expectancy
- Is the patient at risk of treatment- or cancer-related complications? Risk of AEs
- Best tools to evaluate end-organ functions?
- What does frailty stand for?
- What is a geriatric assessment and what does it bring?
- Is there any clinical research in older patients?

Approach in geriatric oncology

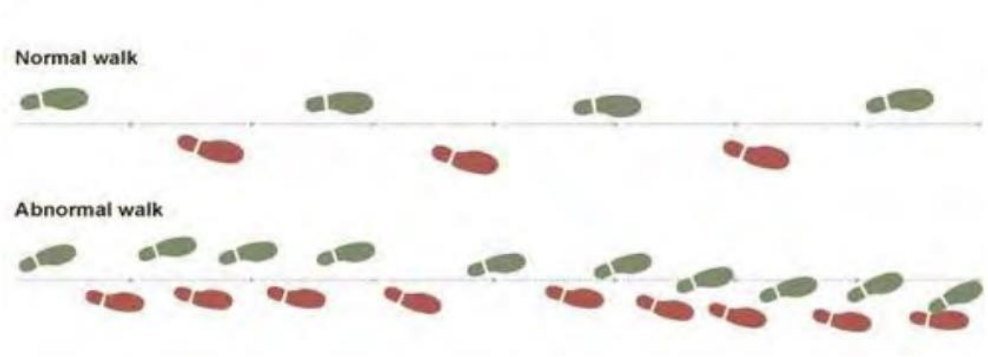
Tumour extent
TNM

General health status
Geriatric assessment
Life expectancy
Treatment toxicity

Tumour biology
Pathology
Gene expression profile

Patient preference & acceptability

Mobility impairment and falls

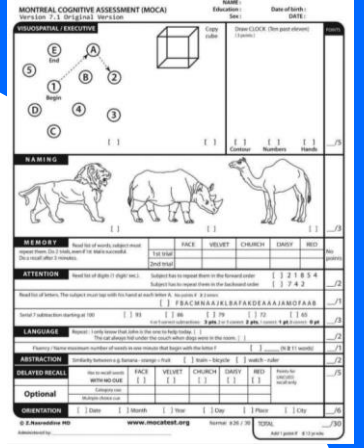


- Short step length, Loss of symmetry of movement, Difficulty initiating or maintaining gait.
- Every year, 1 in 3 adults over 65 years falls. 40% to 60% of older people, a fall results in physical damage, of which 10-15% serious damage.

Osteoporosis

- 1 in 3 women will have one or more osteoporotic fractures in their lifetime
- Risk of fracture: hip fracture impact to 25-33% mortality after 1 year, 25% permanent immobility, Only 14-21% fully recover ADL capacity.

Cognitive impairment



- Usually progressive – starts slowly, gets worse. Often ignored, or thought part of normal ageing, by family. Patients sometimes not aware.
- Dementia impact to increase x2-3 times higher mortality, Greater functional decline & more likely to need a nursing home, More likely to be diagnosed with dementia after an episode (if no previous dementia). Decrease of tolerance to chemotherapy, Decreased survival
- 24% postoperative delirium in Cancer elderly patients

J Am Coll Surg . 2010 Jun;210(6):934-41.

Functional impairment

ADL

Walking

Bathing

Dressing

Feeding

Transferring

Toileting

IADL

Housekeeping

Using a telephone

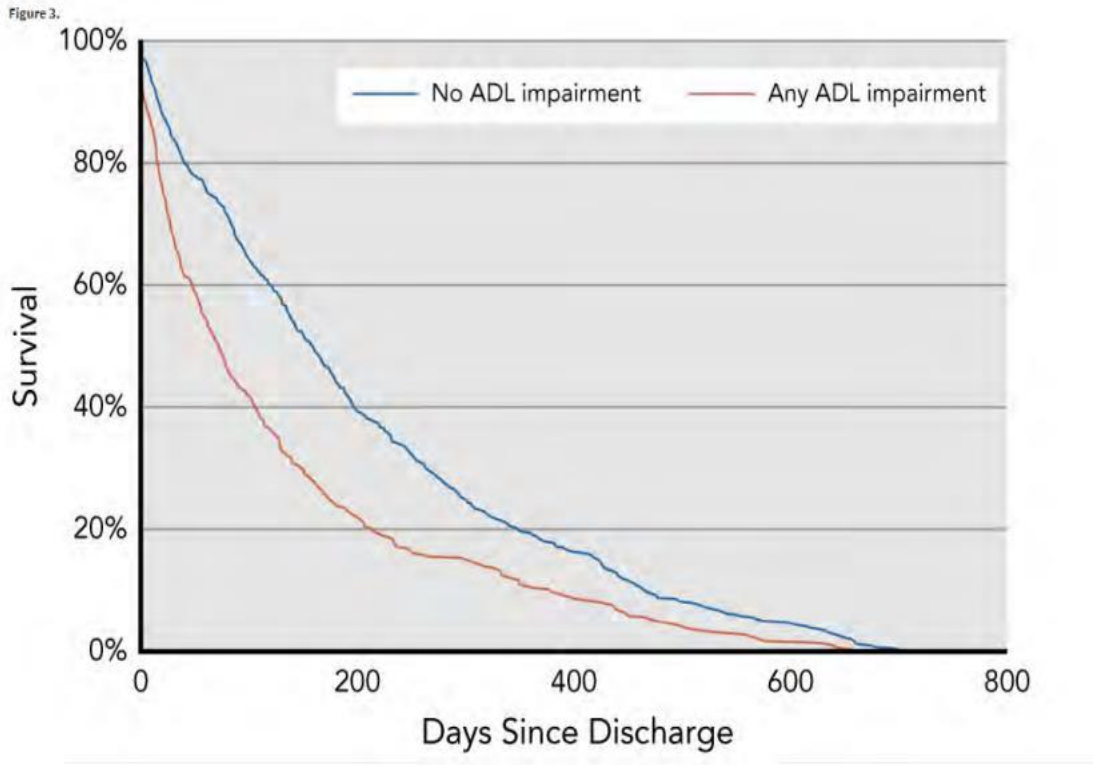
Shopping & meal preparation

Transportation

Managing money

Managing medications

Consequence of treatment



Lage et al. JNCCN 18(6):747- 754

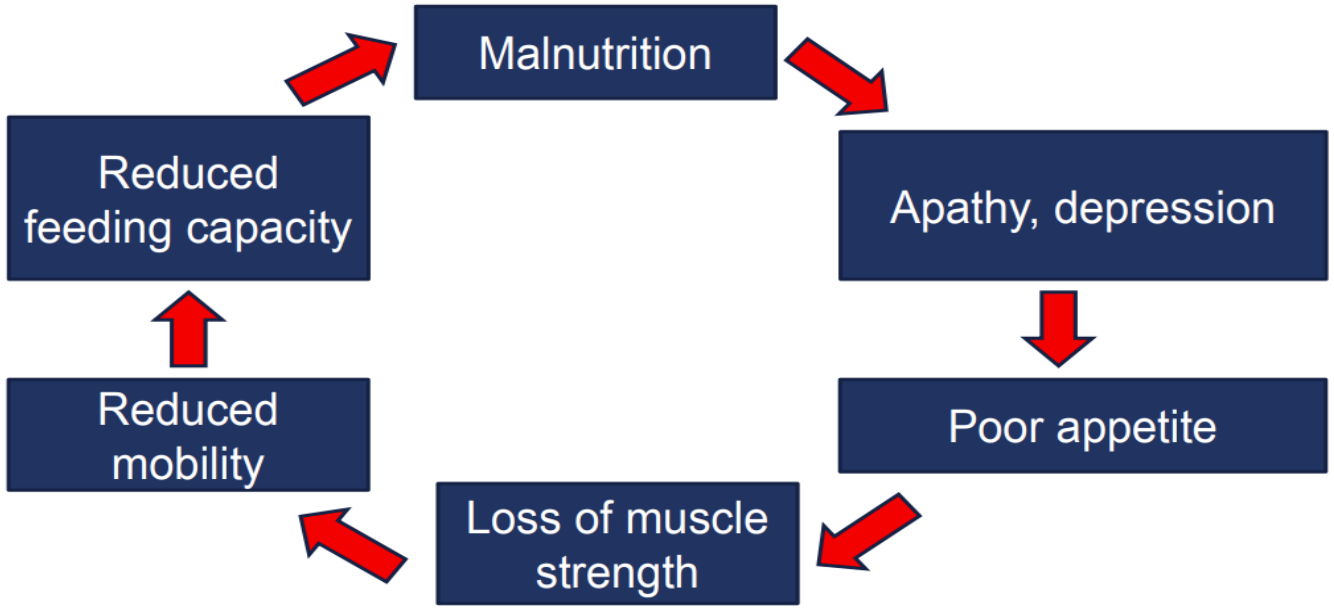
- Cancer patients: any functional impairment was associated with risk of death after discharge from hospital
- (also associated with longer hospital LOS)

ADL and IADL

- In a group of outpatients attending Hematology clinic, those who reported at least one ADL dependency (HR = 1.83; 95% CI, 1.12-3) or IADL dependency HR = 2.46; 95% CI, 1.68-3.59) had increased risk for death
- Patients with at least one IADL dependency also had higher odds of ED visits (OR = 2.76; 95% CI, 1.3-5.84) and unplanned hospitalizations (OR = 2.89; 95% CI, 1.37-6.09)

Malnutrition

- Prevalence: 2-10% of older population in the community, 30-60% of older people in hospital, 20-70% patients with cancer.



Incontinence

- Prevalence in women : 60-79 years 23%, ≥80 years 32%, Nursing homes 60-80%.
- Prevalence in men: approximately 1/3 that of women in early years, equal over 80 years.
- Results : Impact on self-esteem, Social withdrawal, Falls risk, Caregiver burden.

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Comprehensive Geriatric Assessment (CGA)

Assessment	Instrument	Administration	Prognosis
Functional status, dependence	PS, Activity of Daily Living (ADL), Instrumental ADL	Self-administered	+
Multimorbidities	Charlson Comorbidity Index (CCI), Cumulative Illness rating Scale-Geriatric (CIRS-G)	Self- or interviewer-administered, or chart-based	+
Cognition	Folstein Mini-mental State Examination (MMSE)	Interviewer-administered	+ functional status
Psychological status	Geriatric Depression Scale (GDS)	Self administered	+
Nutrition	Mini Nutritional Assessment (MNA), BMI	Interviewer-administered	+
Polypharmacy	List		?
Geriatric syndromes	Dementia, delirium, falls		+ functional status
Physical performance	Timed up and go test (TUG), Tinetti	Performance-tests	?
Economic & social support	Life conditions, relatives, care-givers		?

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Polypharmacy

- Defined as the regular use >5 drugs but may also be defined as using medications that are not clinically indicated.
- Patients age > 65, 39% use five or more drugs.
- Higher number of drugs increases the risk of interactions and adverse drug reactions.
- Necessitate a critical revision of the patient's drug list.

Polypharmacy in patients with advanced cancer and the role of medication discontinuation, Lancet Oncol. 2015 Jul;16(7):e333-41.

Polypharmacy

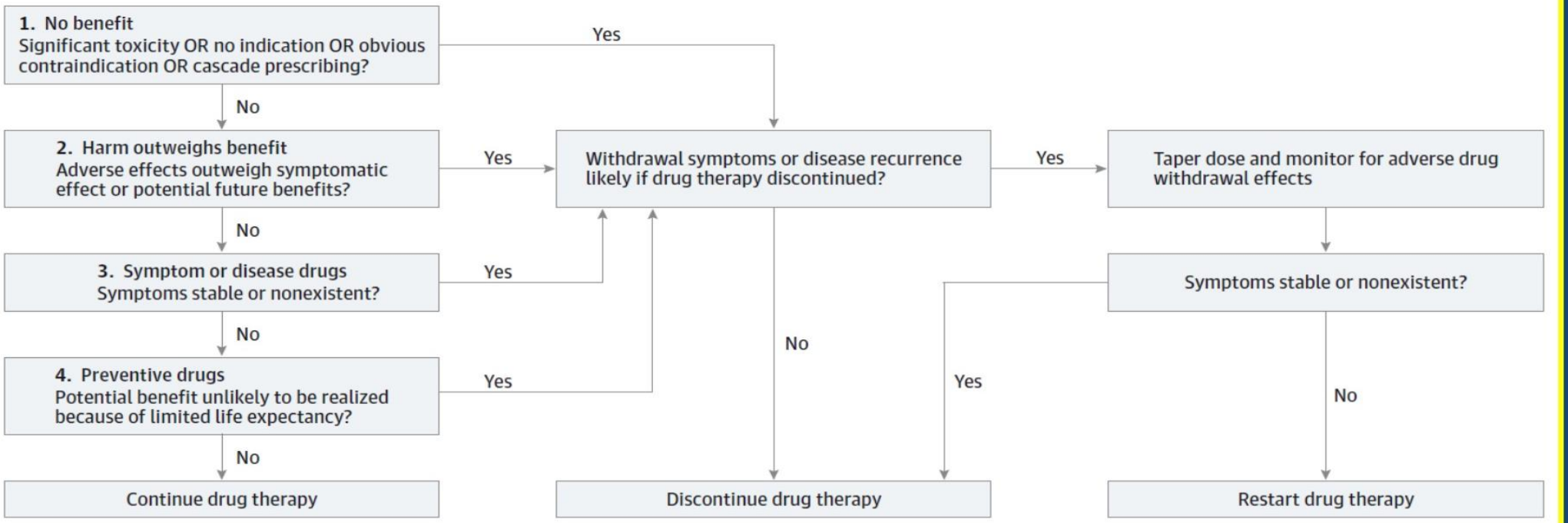
- > 21% of admissions were due to adverse drug reactions (because of medications commonly used for long-term conditions, rather than chemotherapy)
- Tool : Beers Criteria, STOPP/START
- MDT including clinical pharmacists: reduction of unnecessary medications resulting in improved patient health outcomes and improved chemotherapy tolerance.

Lavan et al, The Oncologist 2019, Kalsi et al, Br J Cancer 2015, Maher et al, Expert Opin Drug Saf. 2014

De-prescribing

De-prescribing is defined as the systematic process of identifying and discontinuing drugs in which existing or potential harms outweigh existing or potential benefits within the context of the patient's care goals, functional status, values, and preferences.

Figure. Algorithm for Deciding Order and Mode in Which Drug Use Could Be Discontinued



Scott IA, et al. JAMA Internal Medicine 2015.

Comorbidity: Key Questions

- The impact of comorbidity on overall survival, Study showed ≥ 3 comorbid conditions indicated as frail patient
- Breast cancer who had ≥ 3 of seven selected comorbid conditions had a 20-fold higher rate of mortality

William A et al. annual internal med. 15 jan 1994, Vol 12 issue 12

Charlson index

- The Charlson index is the most commonly used comorbidity assessment.
- The overall score is based on weights, which are assigned to 19 selected conditions .
- The weights, ranging from 1 to 6, are based on the condition's relative risk of 1-year mortality in a hospitalized internal medicine patient
- The 1-yr mortality rates for the different scores were: "0", 12% (181); "1-2", 26% (225); "3-4", 52% (71); and "greater than or equal to 5", 85% (82).

J Chronic Dis. 1987;40(5):373-83.

condition	weight
MI	1
CHF	1
Dementia	1
COPD	1
CNT disease	1
Ulcer disease	1
Mild liver disease	1
DM	1
DM and end organ damage	2
Moderate and severe renal disease	2
Non metas solid tumor	2
Leukemia	2
Lymphoma	2
Metastesis CA	6
AIDs	6

Geriatric Depression Scale (Short Form)

Patient's Name: _____ Date: _____

Instructions: Choose the best answer for how you felt over the past week. Note: when asking the patient to complete the form, provide the self-rated form (included on the following page).

No.	Question	Answer	Score
1.	Are you basically satisfied with your life?	YES / ***NO***	
2.	Have you dropped many of your activities and interests?	***YES*** / NO	
3.	Do you feel that your life is empty?	***YES*** / NO	
4.	Do you often get bored?	***YES*** / NO	
5.	Are you in good spirits most of the time?	YES / ***NO***	
6.	Are you afraid that something bad is going to happen to you?	***YES*** / NO	
7.	Do you feel happy most of the time?	YES / ***NO***	
8.	Do you often feel helpless?	***YES*** / NO	
9.	Do you prefer to stay at home, rather than going out and doing new things?	***YES*** / NO	
10.	Do you feel you have more problems with memory than most people?	***YES*** / NO	
11.	Do you think it is wonderful to be alive?	YES / ***NO***	
12.	Do you feel pretty worthless the way you are now?	***YES*** / NO	
13.	Do you feel full of energy?	YES / ***NO***	
14.	Do you feel that your situation is hopeless?	***YES*** / NO	
15.	Do you think that most people are better off than you are?	***YES*** / NO	
		TOTAL	

(Sheikh & Yesavage, 1986)

Scoring:

Answers indicating depression are in bold and italicized; score one point for each one selected. A score of 0 to 5 is normal. A score greater than 5 suggests depression.

Sources:

- Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol*. 1986 June;5(1/2):165-173.
- Yesavage JA. Geriatric Depression Scale. *Psychopharmacol Bull*. 1988;24(4):709-711.
- Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res*. 1982-83;17(1):37-49.

Depression and anxiety

- Common among older people

Score > 5 is abnormal and need evaluation for treatment

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		TOTAL	

(Sheikh & Yesavage, 1986)

CGA impacts to treatment

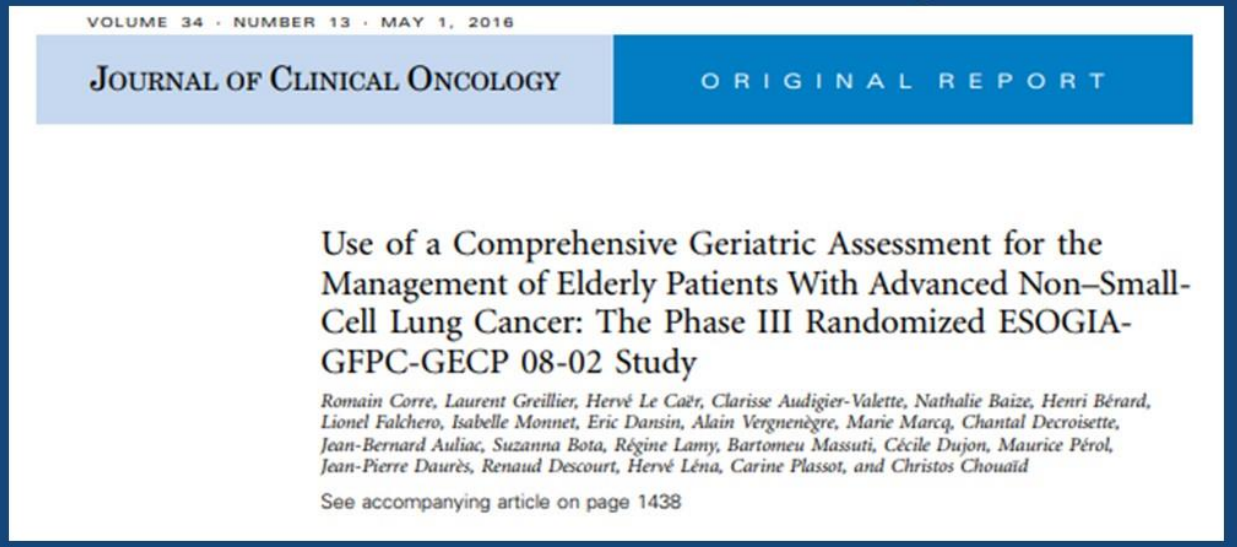
Geriatric assessment knowledge changes treatment

After geriatric evaluation a median of 28% (range 8-54%) of treatment plans changed-most to less intensive options

Presented By Heidi Klepin at TBD

GA-guided treatment allocation can decrease toxicity

Randomized trial advanced lung cancer



VOLUME 34 · NUMBER 13 · MAY 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Use of a Comprehensive Geriatric Assessment for the Management of Elderly Patients With Advanced Non–Small-Cell Lung Cancer: The Phase III Randomized ESOGIA-GFPC-GECP 08-02 Study

Romain Corre, Laurent Greillier, Hervé Le Caër, Clarisse Audigier-Valette, Nathalie Baize, Henri Bérard, Lionel Falchero, Isabelle Monnet, Eric Dansin, Alain Vergnenègre, Marie Marcq, Chantal Decroisette, Jean-Bernard Auliac, Suzanna Bota, Régine Lamy, Bartomeu Massuti, Cécile Dujon, Maurice Pérol, Jean-Pierre Daurès, Renaud Descourt, Hervé Léna, Carine Plassot, and Christos Chouaïd

See accompanying article on page 1438

Different design: GA-guided treatment intensity vs. usual care

Similar findings: Less toxicity, fewer treatment failures, no difference in survival

Key ingredient: Right treatment to the right patient?

Corre et al. JCO 2016

Gajra et. al. JCO 2016 editorial

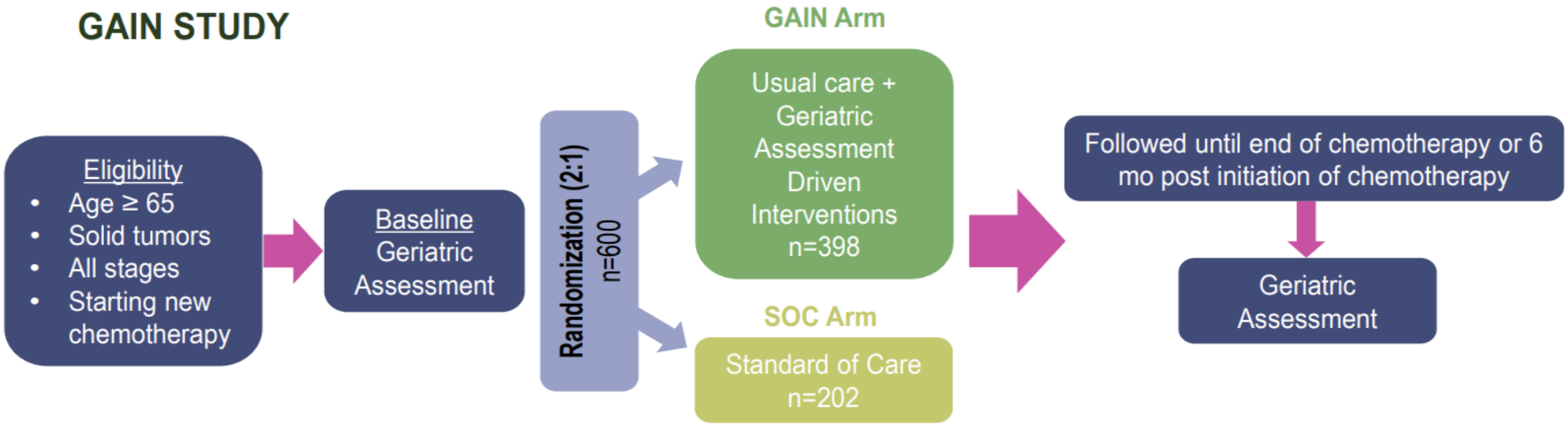
Impact of GA on treatment decision

Oncological decision before or after “some kind of” geriatric assessment

- 40% modification of initial treatment plan
- 66% w/ less intensive treatment
- Functional & nutritional status +++
- Potential interventions in > 70% patients

J Geriatr Oncol . 2018 Sep;9(5):430-440.

Geriatric Assessment-Driven Intervention (GAIN) on Chemotherapy-Related Toxic Effects in Older Adults With Cancer: A Randomized Clinical Trial



Primary endpoints:
- Incidence of grade 3-5 chemotoxicity

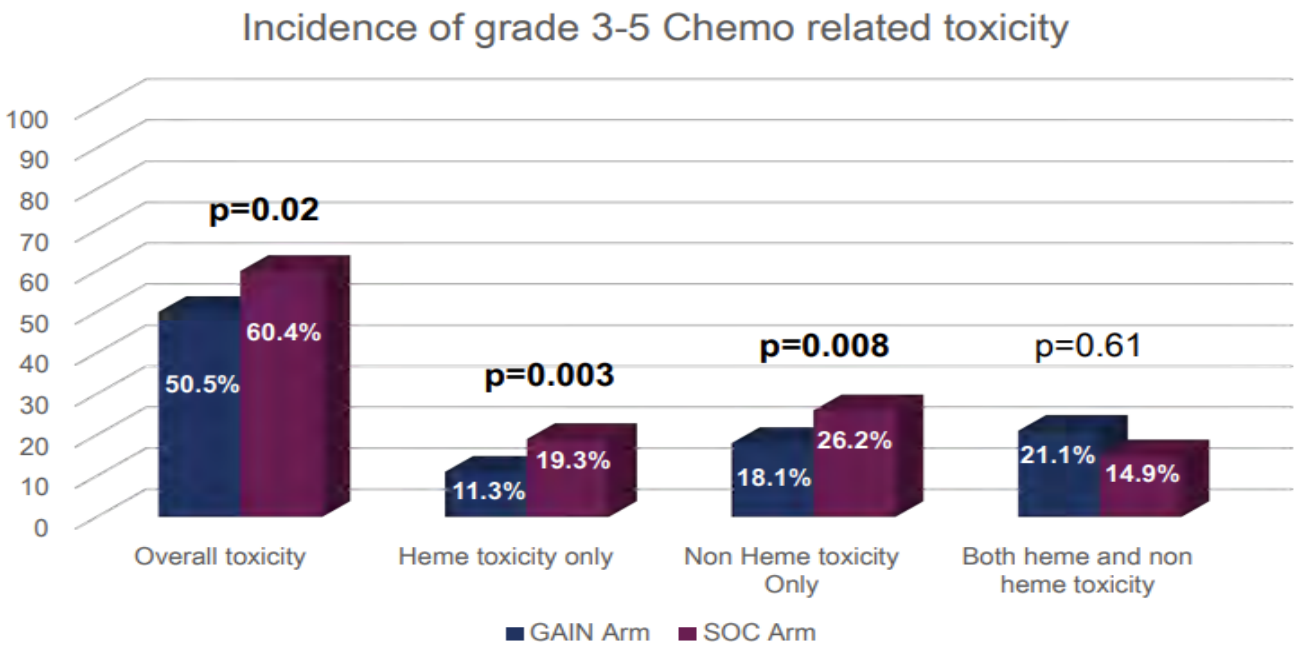
Secondary endpoints:
- Advance directive completion
- Unplanned hospitalizations
- ER visits
- Average length of stay

JAMA Oncol . 2021 Nov 1;7(11):e214158

GAIN study

GAIN significantly reduced grade 3 or higher chemotherapy-related toxic effects in older adults with cancer.

IMPACT OF GA ON CHEMOTOXICITY



Statistically significant reduction of 9.9% in chemo-related toxicity compared to the SOC Arm

Secondary endpoints

	GAIN Arm n (%)	SoC Arm n (%)	p-value
Advanced directive completion	**278 (70%)**	**119 (59%)**	**<0.01**
ER visits for chemotox	109 (27%)	62 (31%)	0.40
Hospitalizations due to grade 3+ chemotox	88 (22%)	39 (19%)	0.43
Hospitalizations due to grade 4+ chemotox	19 (22%)	14 (36%)	0.09
Average Length of stay [median (range)]	4.8 (1-23	5 (1.7-26)	0.60

Satistically significant increase in AD completion

Answers and questions: What caused the effect?

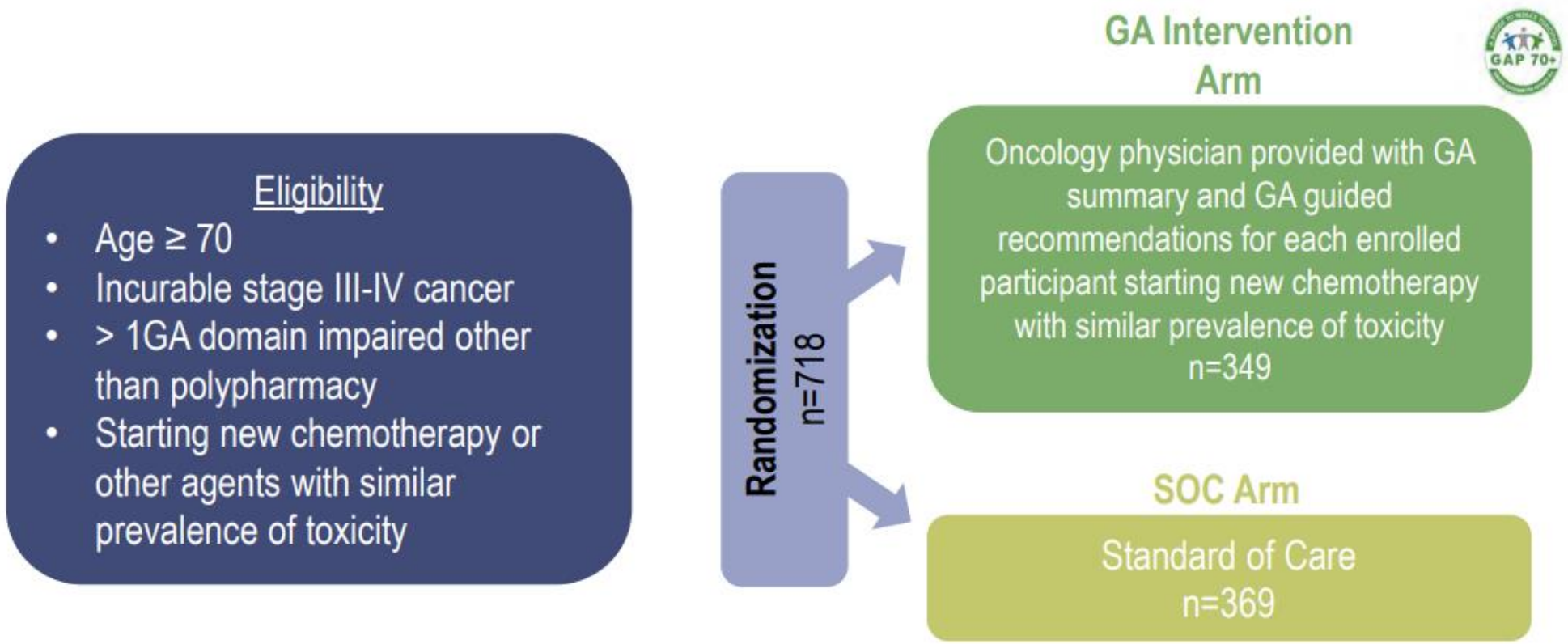
Answers:

- Effect on toxicity is consistent
- Providing GA summary alone is less effective than MDT team/navigation to decrease toxicity

Questions:

- Did the GA intervention lead to more dose reduction?
- What interventions were recommended?
- What interventions were implemented?
- Is a multi-disciplinary team necessary for the effect?
- Was there a "training" effect over time for providers?

A geriatric assessment (GA) intervention to reduce treatment toxicity in older patients with advanced cancer: A University of Rochester Cancer Center NCI community oncology research program cluster randomized clinical trial (CRCT).

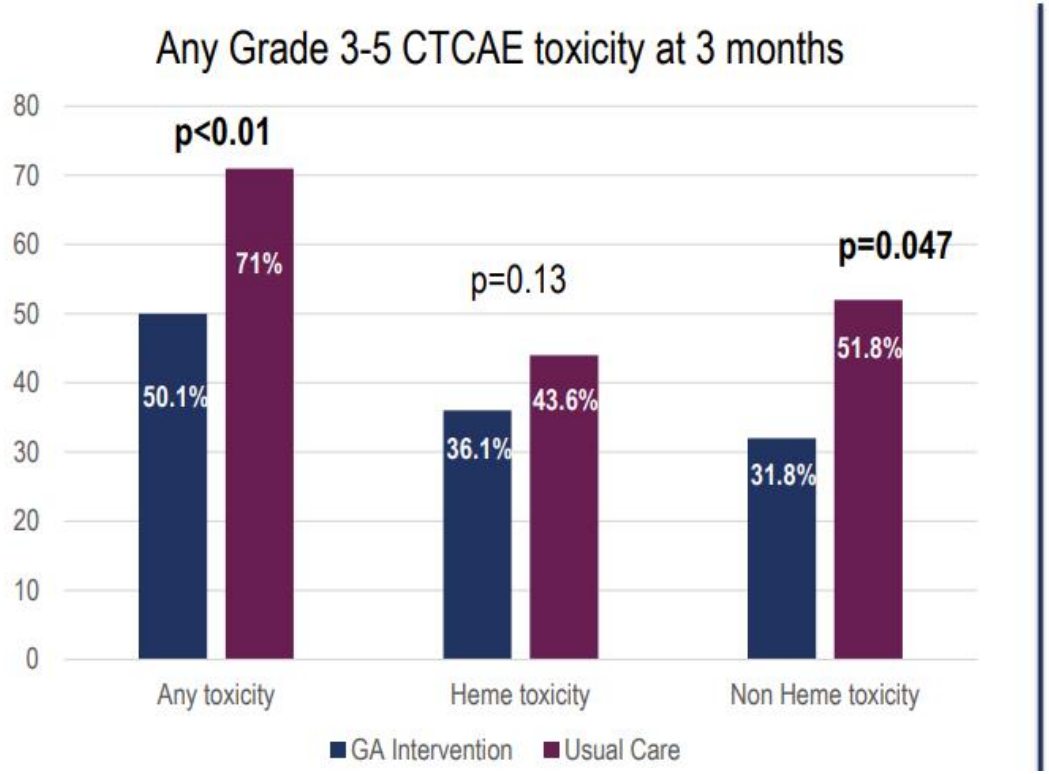


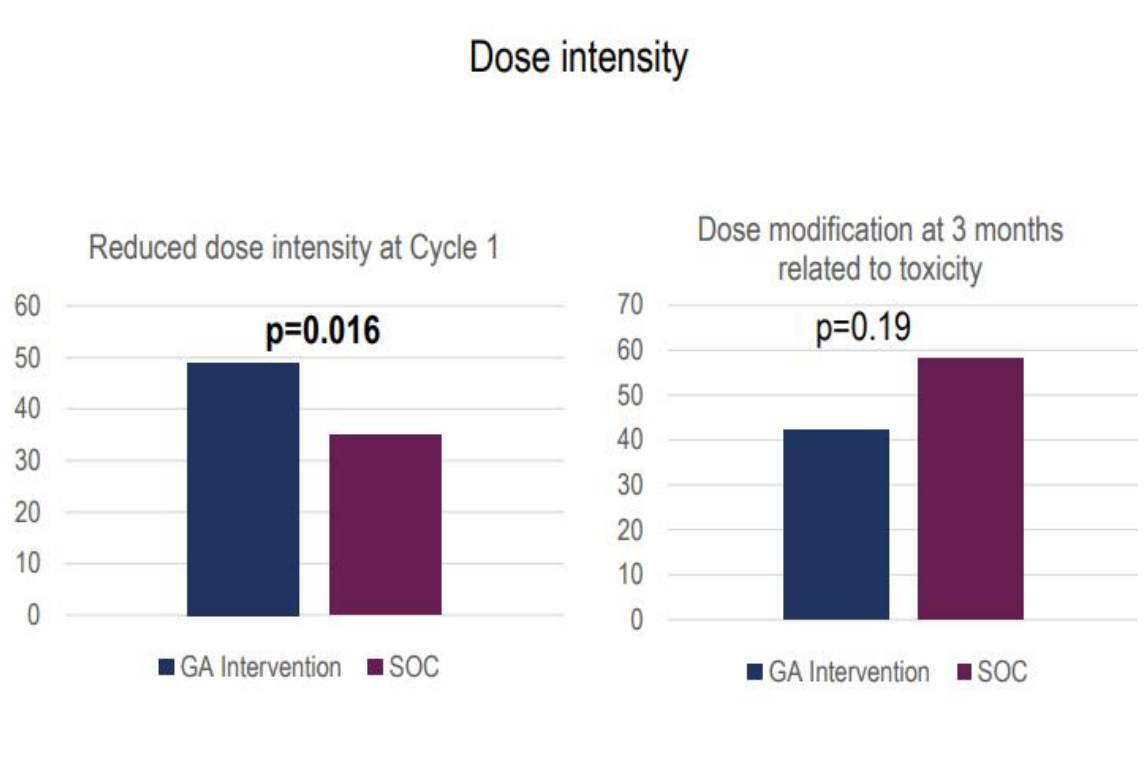
Endpoints:

- Clinician-rated grade 3-5 toxicity
- Survival at 6 months
- Treatment decisions
- Functional and physical decline
- Patient reported toxicities

CRCT results : intervention experienced a lower proportion of grade 3-5 toxicity (50%) than pts in usual care (71%).

- **RR: intervention vs usual care of grade 3-5 toxicity was 0.74 ; p=0.0002)**
- **OS was not significantly different (71% vs 74%, p=0.3).**
- **More pts in intervention received reduced intensity tx at cycle 1 (49% vs 35%, RR 0.81, p=0.01).**





Oncologist. 2020 Nov; 25(11): 909–912.

The effect of geriatric intervention in frail older patients receiving chemotherapy for colorectal cancer: a randomized trial (GERICO)

Table 1. The comprehensive geriatric assessment, results and interventions.

Domain	Assessment and screening tool				Possible interventions	Interventions implemented	
		Cut-off	Score	*n* (%)			*n* (%)
Comorbidity	CIRS-G	–	0–4	11 (15)	Optimising treatment	Referrals	23 (32)
			5–7	31 (44)	Referrals to exams/other departments		
	Review of medical records		≥8	29 (41)			
	Clinical examination						
	Patient interview						
Medication review	No. of medications/ polypharmacy	–	0–4	43 (61)	Discontinuation	Changes in medication	44 (62)
			≥5	28 (39)	Prescription		
	START/STOP criteria				Change in dosage		
Cognitive function	MMSE	≤23/30	24–30	71 (100)	Further evaluation	Cognitive evaluation	1 (1.4)
			0–23	0 (0)	Referral/medication		
Psychological function	GDS	≥ 6/ 15	0–5	67 (9)	Assessment of possible depression	Medical treatment	2 (2.8)
			≥6	4 (6)		Referrals	2 (2.8)
Nutritional status	MNA-based local nutritional screening	Weight loss ≥5%	0–5	18 (25)	Nutritional supplements	Referral: GERICO dietitian	36 (51)
			≥5	53 (75)	Referral to dietitian[a]		
Physical function	Gait speed 10 m	>1 m/s	0–1	37 (52)	Referral to the exercise programme[b]	Referral: GERICO exercise programme	28 (39)
			>1	32 (45)			
	Handgrip strength (Jamar Dynamometer)	<♀ 20 kg	below	35 (49)	Referral to the exercise training programme[b]	Referral: GERICO exercise programme	28 (39)
		<♂ 30 kg	above	36 (51)			
Functional status	Katz ADL	<6	6	62 (87)	Initiation of home care	Initiation of social support	2 (2.8)
	(In)dependence		0–5.5	9 (13)	Occupational therapy assessment	Occupational therapy	2 (2.8)
	FAQ IADL	>1	0	48 (68)	Initiation of home care	Initiation of home care	2 (2.8)
	(In)dependence		≥1	23 (32)	Transport arrangement		
Laboratory parameters	TSH, cobalamin, folate, albumin, vitamin D	Normative values	Normal	51 (72)	Treat deficiencies/control blood samples	Deficiencies treated	20 (28)
			abnormal	20 (28)			

GERICO results

	All patients n=142		
	Intervention n=71 n (%)	Control n=71 n (%)	p value
Completed planned therapy	32 (45)	20 (28)	**0.0366**
Reduced start dose	44 (62)	41 (58)	0.732
Reduction of chemotherapy during treatment	20 (28)	32 (45)	**0.037**
Treatment delay	25 (35)	24 (34)	0.860
Received initial dose in all given cycles	46 (65)	30 (42)	**0.007**
Received all planned dose	41 (58)	39 (55)	0.735

- Of 142, 58% adjuvant and 42% received first-line palliative chemotherapy.
- Interventions included medication changes (62%), nutritional therapy (51%) and physiotherapy (39%).
- More interventional patients completed scheduled chemotherapy compared with controls (45% vs. 28%, P = 0.0366).
- Severe toxicity occurred in 39% of controls and 28% of interventional patients (P = 0.156).
- QoL improved in interventional patients compared with controls with the decreased burden of illness (P = 0.048) and improved mobility (P = 0.008).

Br J Cancer . 2021 Jun;124(12):1949-1958.

Integrated Geriatric Assessment and Treatment (INTEGERATE) in older people with cancer planned for systemic anti-cancer therapy

Wee-Kheng Soo, Mac
Eastern Health and M

- **Integrated oncogeriatric care**
  - Partnership between oncologist and geriatrician
  - Comprehensive geriatric assessment and coordinated healthcare delivery
- **INTEGERATE: first RCT of integrated oncogeriatric care in older cancer patients**

≥70yo with solid cancer or DLBCL for chemo-, immuno- or targeted therapy, no treatment in prior 3 months (n=154)

Minimization factors
Age: 70-80 vs ≥80
Sex: M vs F
Cancer type:
lung vs upper GI vs lower GI vs all other
Treatment intent:
palliative vs non-palliative
ECOG PS: 0-1 vs 2

RANDOMIZE

Integrated Oncogeriatric Care n=76

Usual Care n=78

Evaluate at weeks 0, 12, 18 and 24

Outcome measures
Primary: HRQOL
Secondary: healthcare utilization, treatment delivery, function, institutionalization, mood, nutrition, health utility and survival

* measured by the ELderly Functional Index (ELFI), EORTC QLQ-C30 and QLQ-ELD14

Recruitment
August 2014 and June 2018
Three hospitals in Melbourne, Australia

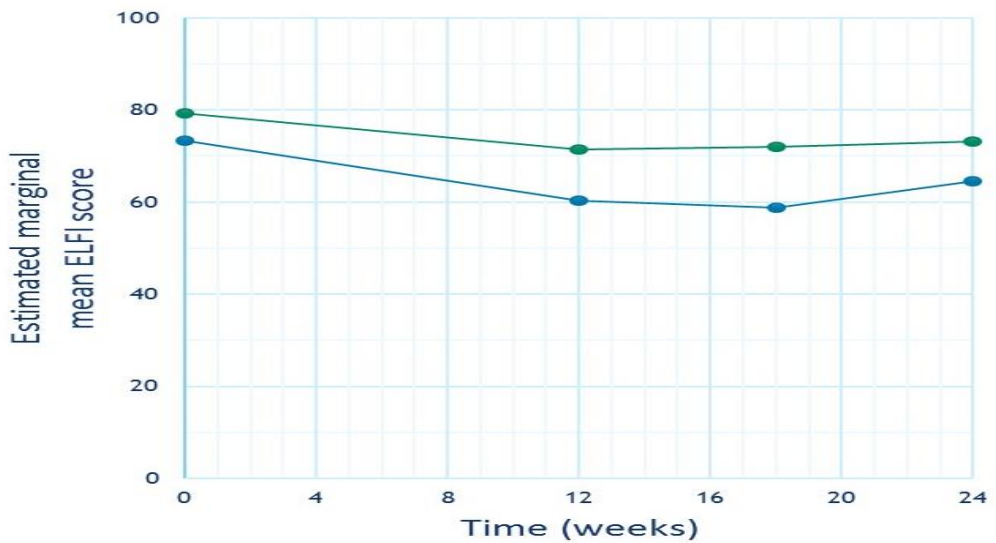
Primary Endpoint: Elderly Functional Index (ELFI)

- **12-item composite measure of self-reported functioning in cancer patients**
- **Derived from the EORTC QLQ-C30 and QLQ-ELD14 scales: *Physical, Role and Social Functioning;* and *Mobility***
- **Does not include: symptom domains, global quality of life, *Emotional* or *Cognitive Functioning***
- **Please see ASCO online abstract e19126 regarding ELFI validation**

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
9. Has your physical condition or medical treatment Interfered with your social life?	1	2	3	4
10. Have you had difficulty with steps or stairs?	1	2	3	4
11. Did you feel unsteady on your feet?	1	2	3	4
12. Did you need help with household chores such as cleaning or shopping?	1	2	3	4

Primary outcome: Health-related Quality of Life

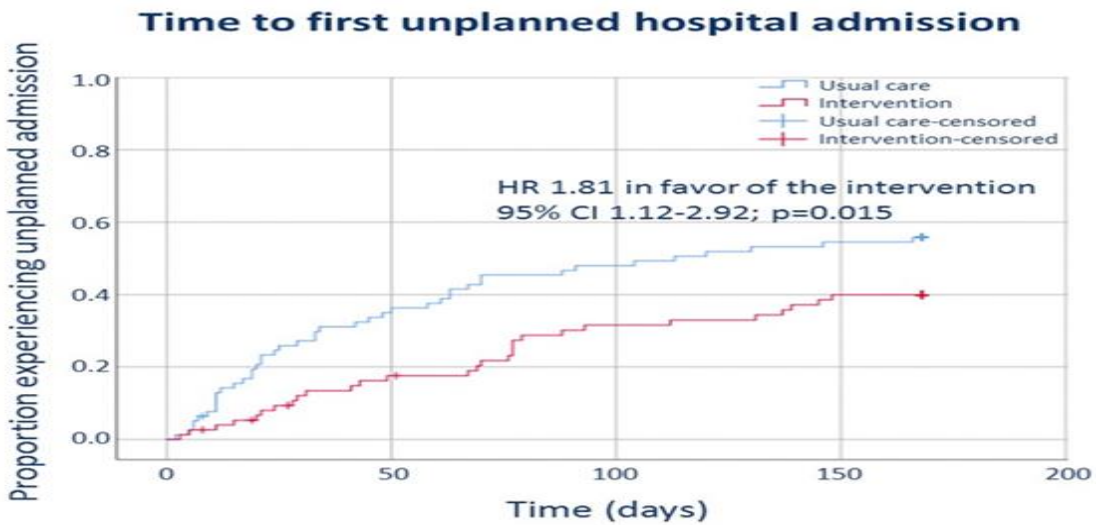
Week	ELderly Functional Index (ELFI) Estimated Marginal Mean Score			
	Intervention	Usual Care	Difference (95% CI)	*p*
12	71.4	60.3	11.1 (3.5-18.7)	0.004
18	72.0	58.7	13.4 (5.5-21.2)	0.001
24	73.1	64.6	8.5 (0.5-16.5)	0.037



Secondary outcomes: Hospitalization

- **39% less emergency presentations**
  - Incidence rate ratio (IRR)* 0.61 (95% CI 0.46-0.77, p=0.007)
  - -1.3 emergency presentations per person-year
- **41% less unplanned hospital admissions**
  - IRR* 0.59 (95% CI 0.41-0.86, p<0.001)
  - -1.2 admissions per person-year
- **24% less unplanned hospital overnight bed-days**
  - IRR* 0.76 (95% CI 0.68-0.85, p<0.001)
  - -7.0 days per person-year

* Adjusted for age, gender, ECOG-PS, cancer type and treatment intent



Conclusions

- Integrated oncogeriatric care improved quality of life, decreased unplanned hospitalization and early treatment discontinuation due to adverse events in older people with cancer receiving systemic anti-cancer therapy

- Older people (≥70 years) planned for anti-cancer therapy should receive comprehensive geriatric assessment

- INTEGERATE: randomized evidence to support wider-scale implementation of an integrated geriatric oncology model of care

2021 ASCO ANNUAL MEETING

URCC NCORP Research Base

THE EFFECTS OF GERIATRIC ASSESSMENT ON ONCOLOGIST-PATIENT COMMUNICATION REGARDING FUNCTIONAL STATUS AND PHYSICAL PERFORMANCE IN OLDER ADULTS WITH CANCER: A SECONDARY ANALYSIS OF A 541-SUBJECT NATIONWIDE URCC NCORP (NCI COMMUNITY ONCOLOGY RESEARCH PROGRAM) CLUSTER RANDOMIZED TRIAL

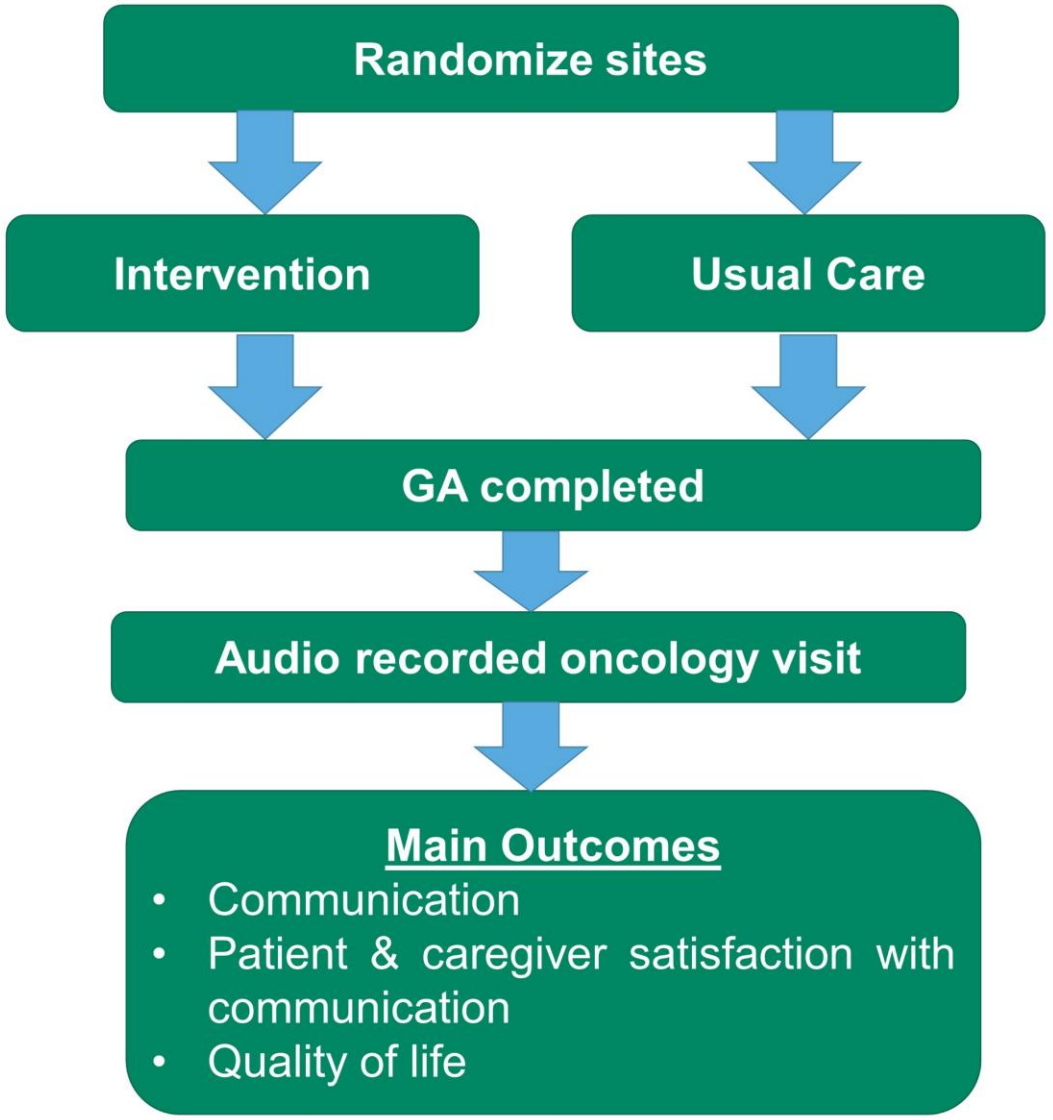
Marielle Jensen-Battaglia, Lianlian Lei, Huiwen Xu, Lee Kehoe, Amita Patil, Kah Poh Loh, Erika E. Ramsdale, Allison Magnuson, Amber Kleckner, Tanya Marya Wildes, Po-Ju Lin, Karen Michelle Mustian, Gilbert Giri, Mary I. Whitehead, James D. Bearden, Brian Leslie Burnette, Jodi Geer, Supriya Gupta Mohile, Richard Francis Dunne

June 4, 2021

COMMUNICATING ABOUT AGING COACH AND CANCER HEALTH

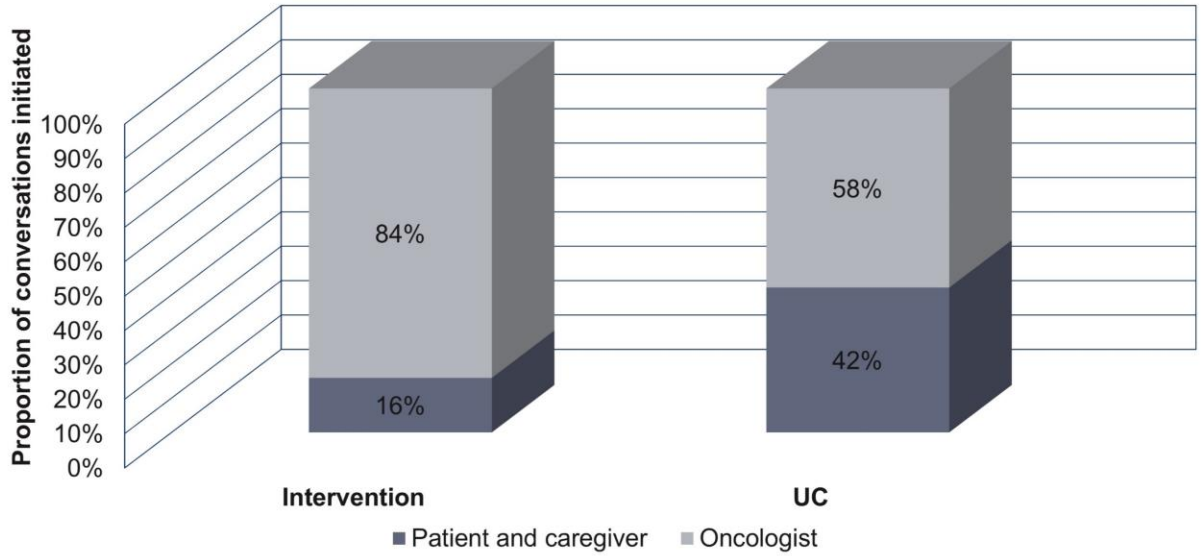
Study design

- **Multisite cluster randomized trial**
- **Inclusion criteria**
  - Age ≥70, advanced solid tumor or lymphoma, treated with palliative intent, at least 1 GA impairment (other than polypharmacy)
- **GA assessment at baseline**
  - Usual Care (UC) oncologists received an alert if patient screened for severe depression and/or cognitive impairment
  - Intervention oncologists received summary of GA impairments & associated recommendations



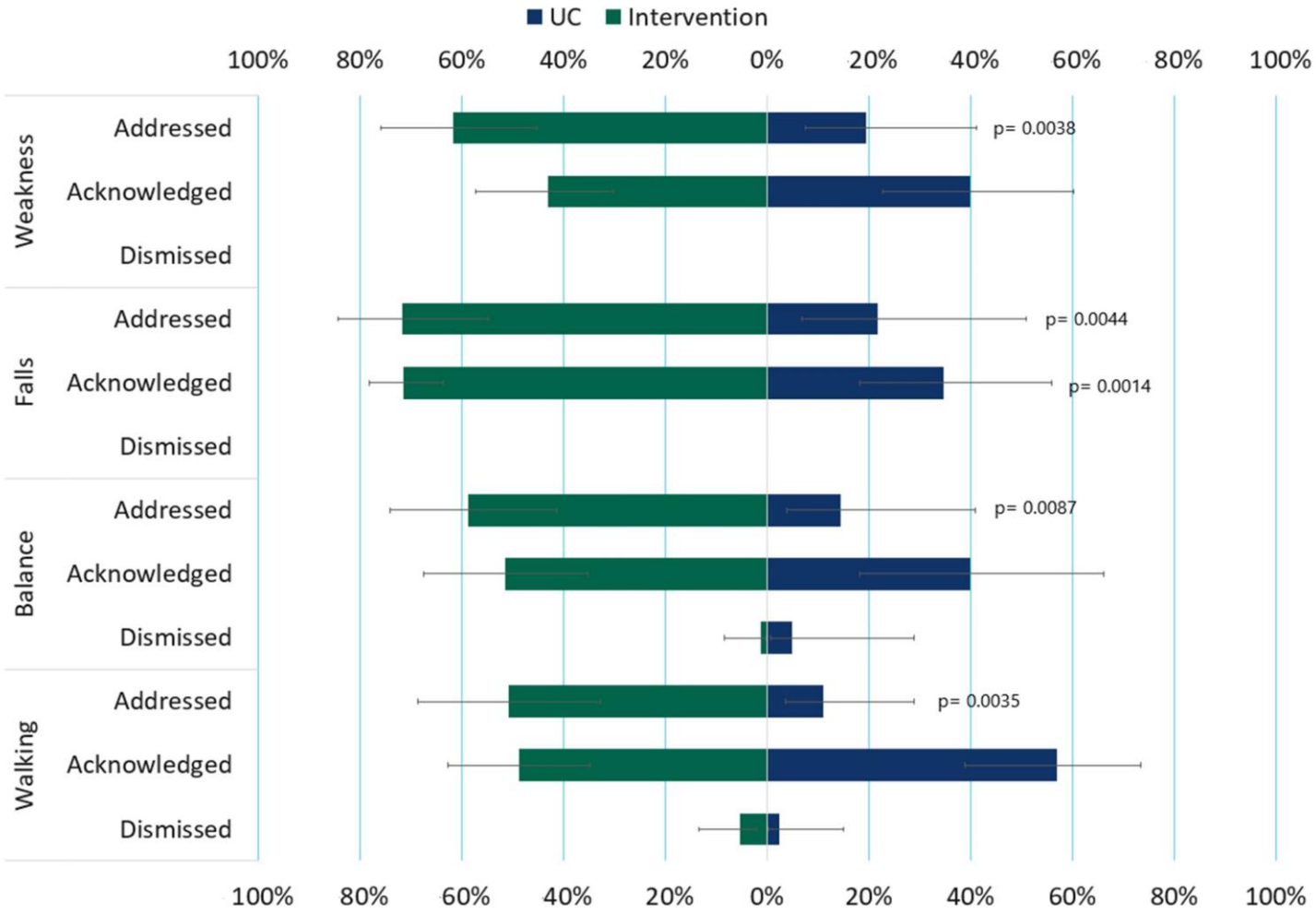
Mohile et al. JAMA Onc 2019

Results: Conversation initiation



- **Oncologists initiated significantly more conversations in the intervention than UC arm (p=0.0002)**
- **GA intervention did not reduce patient and caregiver initiation of conversations**
  - **Intervention: 15.85%** (95% CI 10.56%, 23.09%) vs. **UC: 42.10%** (95% CI 30.09%, 55.12%), **p=0.0002**
  - Unadjusted number of conversations: **Intervention (n=118)** vs. **UC (n=117)**

Results: Specific concerns & oncologist response



Overall for combined functional status and physical performance concerns:

- No significant difference in concerns acknowledged or dismissed
- More concerns addressed concerns in **Intervention: 42.58%** (95% CI 32.52, 53.29) vs. **UC: 16.52%** (95% CI (10.04, 25.99), p= 0.0003

Practice Changing Take Home Points

- **Geriatric assessment-guided intervention decreases treatment toxicity for older adults with advanced stage cancer**
- **Practice changing options (resource dependent):**
  1. Administer GA[1] and utilize published intervention recommendations[2] for adults 70 and over with advanced cancer (any practice)
  2. Administer GA and guide management with MDT (resourced practices)

GA intervention increased oncologist-initiated conversations about aging-related functional status & physical performance concerns

- Without a decrease in patient and caregiver-initiated concerns

1. Mohile et al. J Clin Oncol 2018 36: 2326-2347
2. Mohile et al. JNCCN 13: 1120-1130, 2015

Abstract 12012 (328655): Barriers and facilitators of geriatric assessment implementation in daily oncology practice: A qualitative study applying a theoretical implementation framework.

BARRIERS

Time consume

Lack of knowledge

Paternalism

Hospital culture; unwillingness to integrate change.

FACILITATORS

Knowledge

Shared approach to care

Recognition of the benefits of the GA—willingness to integrate it into the current care paradigm.

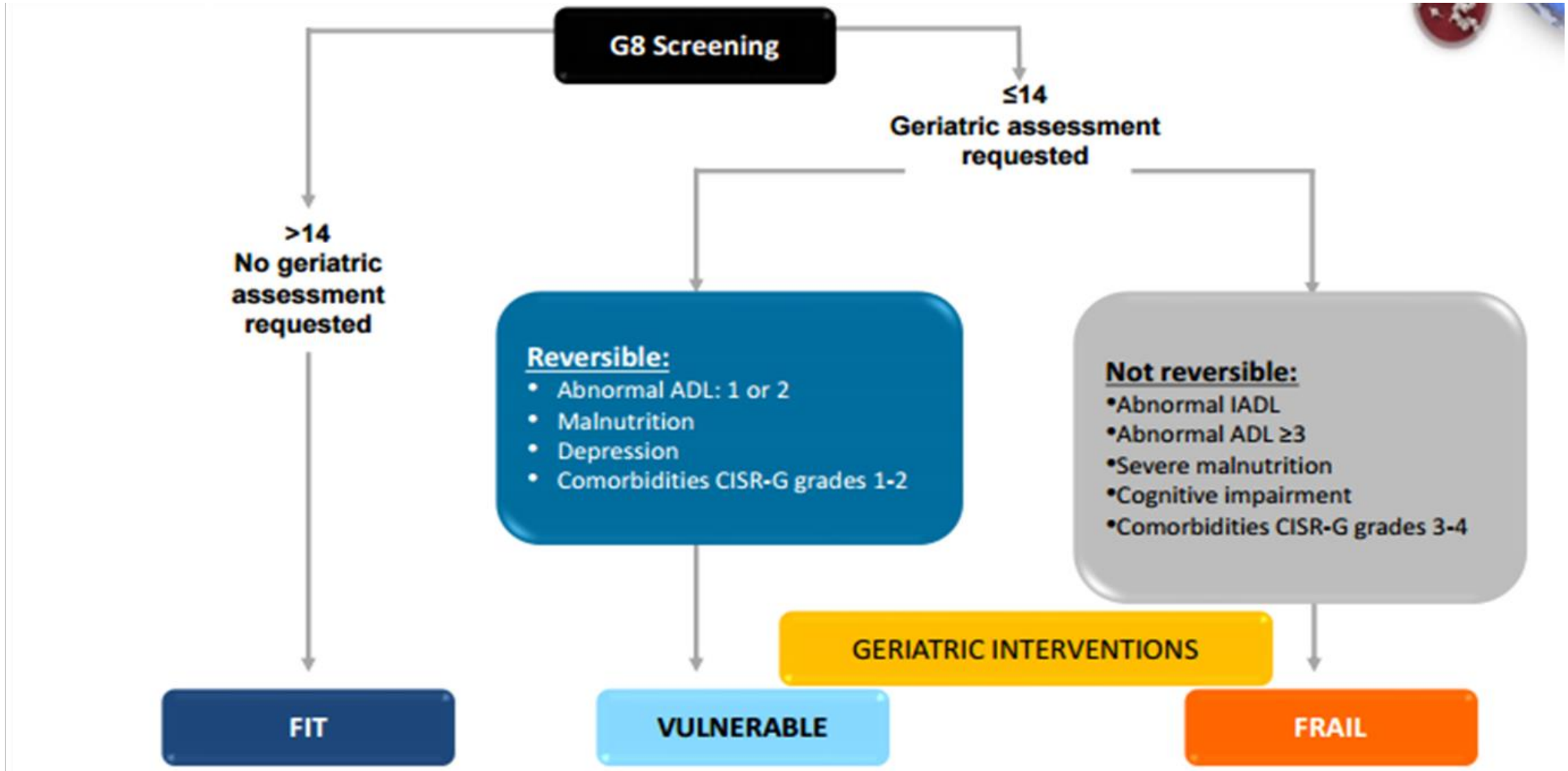
Screening tools : G8 questionnaire

- Development of a Short Geriatric Assessment Tool for Oncologists
- 8 questions that performed by nurse/ doctor
- 5 to 10 min
- Abnormal if ≤14
- Preliminary analysis : Sensitivity: 89.6% ; Specificity: 60.4%

Carine Bellera, Ann Oncol 2012;23:2066-72

G8 questionnaire

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0 : severe decrease in food intake
		1 : moderate decrease in food intake
		2 : no decrease in food intake
B	Weight loss during the last 3 months	0 : weight loss > 3 kg
		1 : does not know
		2 : weight loss between 1 and 3 kgs
		3 : no weight loss
C	Mobility	0 : bed or chair bound
		1 : able to get out of bed/chair but does not go out
		2 : goes out
E	Neuropsychological problems	0 : severe dementia or depression
		1 : mild dementia or depression
		2 : no psychological problems
F	Body Mass Index (BMI (weight in kg) / (height in m^2)	0 : BMI < 19
		1 : BMI = 19 to BMI < 21
		2 : BMI = 21 to BMI < 23
		3 : BMI = 23 and > 23
H	Takes more than 3 medications per day	0 : yes
		1 : no
P	In comparison with other people of the same age, how does the patient consider his/her health status?	0 : not as good
		0.5 : does not know
		1 : as good
		2 : better
	Age	0 : >85
		1 : 80-85
		2 : <80
	TOTAL SCORE	**0 – 17**



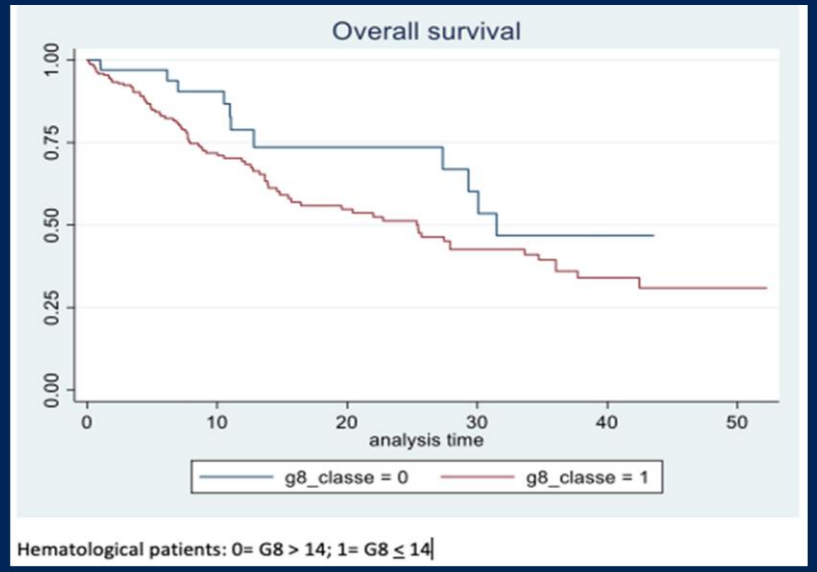
ADL, activities of daily living; IADL, instrumental activities of daily living; CISR-G, cumulative illness score rating-geriatrics.

Reprinted from Droz JP, et al. *Lancet Oncol.* 2014;15(9):e404-414.

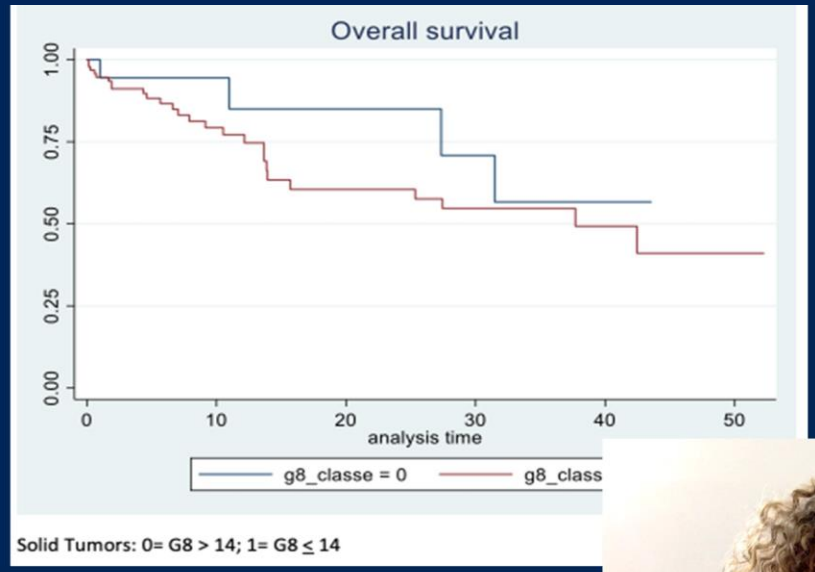
2021 ASCO ANNUAL MEETING

IMPACT OF THE G8 SCORE ON THE OUTCOME OF A COHORT OF ELDERLY PATIENTS WITH SOLID OR HEMATOLOGICAL MALIGNANCIES.

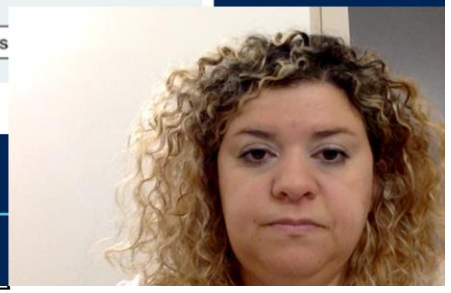
Our analysis suggest that elderly frail patients with solid tumors have a significantly increased risk of death as compared to elderly fit patients.



Hematological patients: 0= G8 > 14; 1= G8 ≤ 14



Solid Tumors: 0= G8 > 14; 1= G8 ≤ 14



Federica Biello

Key messages for older cancer patients

1. Age and standard approach upfront influence treatment decision
   - Not always in the right direction: under and over treatment are frequent, but over > under
2. Geriatric problems are far more frequent than usually believed
   - 2/3 impaired G8, +50% functional dependence or risk of malnutrition, +40% significant comorbidities, 20% depression , +10% cognitive dysfunctions, polypharmacy
3. Geriatric assessment = enforceable and not opposable
   - Brings to clinicians new information > 2/3 cases
   - Modifies clinical decision in > 25% cases (function and nutrition)
4. Competing risks for mortality
   - Call for some degree of assessment of life expectancy to balance treatment decision
5. Access to innovation is unbalanced
   - Need for specific research

HOW TO PREDICT CHEMOTOXICITY

Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer
CARG - Cancer and Aging Research Group

11 risk factors

- Age
- Cancer type
- Chemotherapy dose
- No of drugs
- Haemoglobin
- Creatinin Cl
- Hearing
- No of falls in last 6 months
- IADL
- Walking one block
- Decreased social activity because of physical/emotional health

Hurria JCO 2016

Chemotherapy Risk Assessment Scale for High-Age Patients
CRASH Score

6 risk factors (Heme and non Heme)

- Diastolic blood pressure
- LDH
- ECOG PS
- MMSE
- MNA
- IADL

Extermann Cancer 2012

CARG SCORE

https://moffitt.org/eforms/crashscoreform/

Risk factors	Points			
	0	1	2	3
Age	<72 years		≥72 years	
Cancer type	Other		GI or GU	
Chemotherapy dose	Dose reduced		Standard dose	
No. of chemotherapy drugs	Mono-chemotherapy		Polychemotherapy	
Haemoglobin	≥11 g/dL (male) ≥10 g/dL (female)			<11 g/dL (male) <10 g/dL (female)
Creatinine clearance (Jeliffe, ideal weight)	≥34 mL/min			<34 mL/min
Hearing (with hearing aid, if needed)	Excellent or good		Fair, poor or totally deaf	
No. of fall in last 6 months	None			≥1
IADL: taking medications	Without help	With some help or completely unable		
MOS: Walking 1 block	Not limited at all		Limited a little or limited a lot	
MOS: Decreased social activity because of physical/emotional health	A little of the time or None of the time	Some of the time, Most of the time, or All the time		

Total Risk Score		% risk of grade 3-5 adverse events
Low	0-3	25%
	4-5	32%
Medium	6-7	50%
	8-9	54%
High	10-11	77%
	12-19	89%

CRASH SCORE

https://www.mycarg.org/?page_id=934

Chemotherapy risk (see CRASH points table)
Haematologic risk factors
Diastolic blood pressure (>72 = 1)
IADL (<26 = 1)
LDH (>459 = 1)
Non-haematologic risk factors
ECOG PS (1-2 = 1; 3-4 = 2)
Mini Mental State Examination (<30 = 2)
Mini Nutritional Assessment (<28 = 2)
Haeme score
Non-haeme score
Combined score

CRASH score						
Heme subscore		Non-Heme subscore		Combined score		Risk category
0-1	7%	0-2	33%	0-3	50%	Low
2-3	23%	3-4	46%	4-6	58%	Intermediate-Low
4-5	54%	5-6	67%	7-9	77%	Intermediate-High
>5	100%	>6	93%	>9	79%	High

Predictive model for chemo-related grade 3-5 toxicity

CARG Cancer and Aging Research Group

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[a]

Low Risk	Intermediate Risk	High Risk
0-5 30%	6-9 52%	10-19 83%

Please circle the applicable risk factors

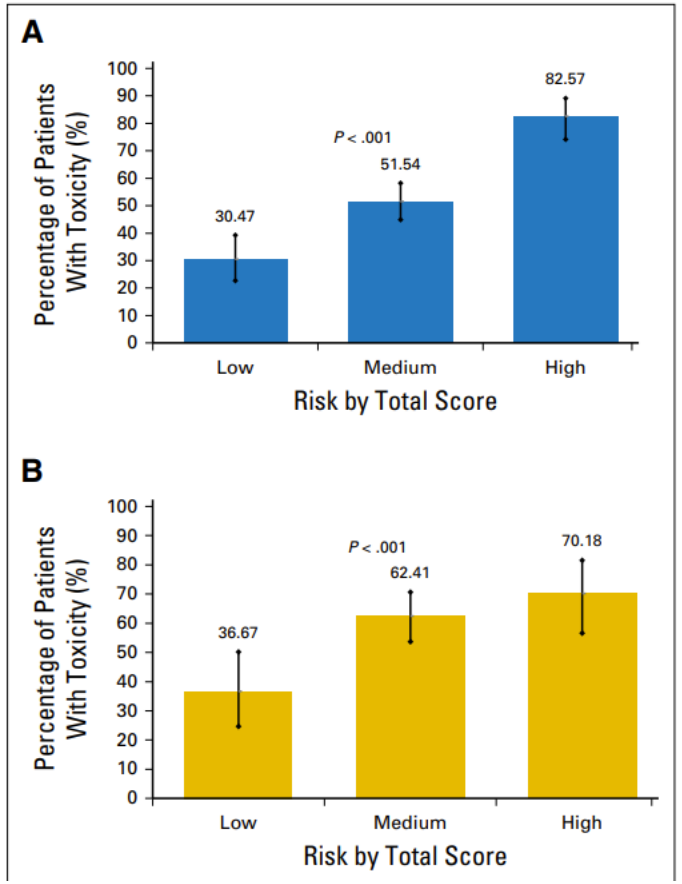
Risk Factor	Score
Age ≥ 72	2
GI or GU Cancer	2
Standard dose chemo	2
>1 chemo drug	2
Hb <110 (male) or <100 (female)	3
Creatinine Clearance <34 mL/min	3
Hearing, fair or worse	2
1 or more falls in past 6 months	3
Needs help with taking meds	1
Walking 1 block somewhat limited	2
Decreased social activity due to health	1

Total = _____

J Clin Oncol . 2016 Jul 10;34(20):2366-71.
https://www.mycarg.org/

VOLUME 34 · NUMBER 20 · JULY 10, 2016
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer



Results:

- 58% grade $\geq$ 3 toxicity , Risk increased with increasing risk score

J Clin Oncol . 2016 Jul 10;34(20):2366-71.

Key messages for older cancer patients

1. Age and standard approach upfront influence treatment decision
   - Not always in the right direction: under and over treatment are frequent, but over > under
2. Geriatric problems are far more frequent than usually believed
   - 2/3 impaired G8, +50% functional dependence or risk of malnutrition, +40% significant comorbidities, 20% depression , +10% cognitive dysfunctions, polypharmacy
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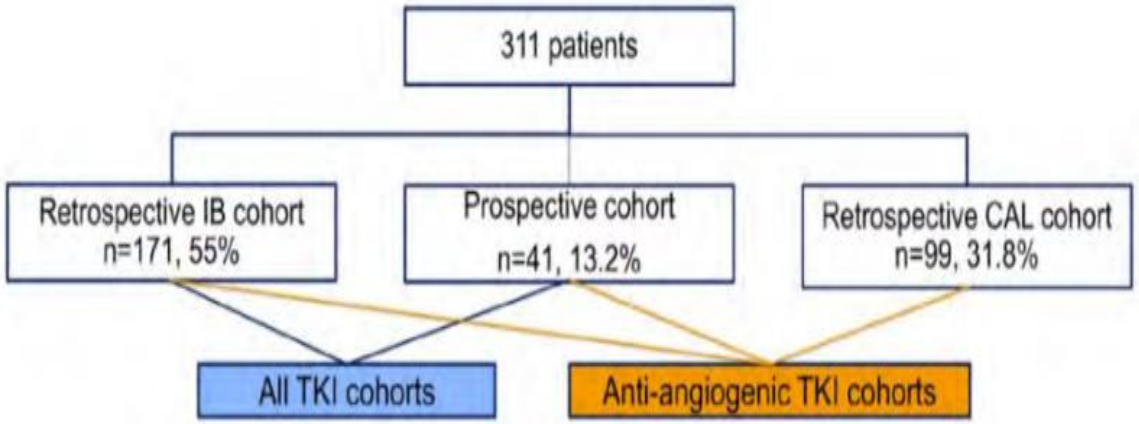
   - Call for some degree of assessment of life expectancy to balance treatment decision
5. Access to innovation is unbalanced
   - Need for specific research

TARGETED THERAPIES

- Incidence and prognostic factors of clinically meaningful toxicities of kinase inhibitors in older patients with cancer: The PreToxE study

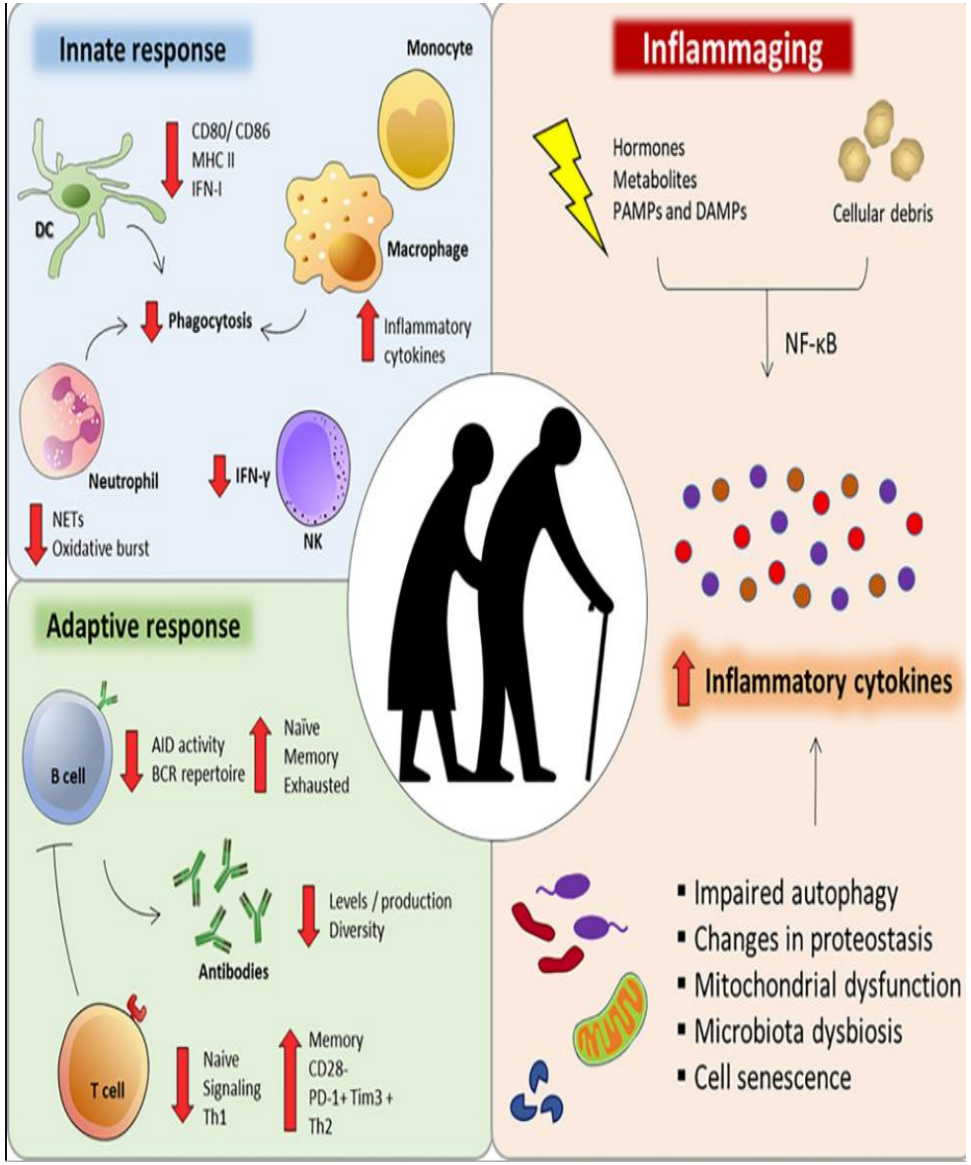
  - PreToxE study: retrospective and prospective multicentric study in patients aged 70 years old or over
  - Solid tumors: lung, breast, sarcoma



- This results indicate that despite frequent upfront dose reduction, clinically meaningful toxicities occurred in approximately 40% of older patients treated with TKIs.
- The use of at least three concomitant medications is an independent predictor of clinically meaningful toxicities.

J Geriatr Oncol . 2021 May;12(4):668-671

IMMUNOTHERAPY



- The immune aging process, called immunosenescence.
- Aging interferes in a number of innate and adaptive immune cells aspects that can impair or compromise their function and response.
- Additionally, several factors can dysregulate intracellular homeostasis during aging, intensifying the secretion of inflammatory cytokines and chemokines (inflammation).

Front. Immunol., 27 October 2020

Efficacy of immune checkpoint inhibitors in older adults with advanced stage cancers: A meta-analysis

- In 19 trials comparing ICI monotherapy VS non-ICI
  - No significant in treatment-age interaction (age ≥ 65 years: N = 6064, HR 0.73; age < 65 years: N = 7250, HR 0.79; P-interaction = 0.27).
  - Similar at older age cut-offs of 70 years (age ≥ 70 years: N = 433, HR = 0.93; age < 70 years: N = 169, HR = 0.95; P-interaction = 0.91)
  - Age 75 years (age ≥ 75 years: N = 139, HR = 0.75; age < 75 years: N = 1133, HR = 0.61; P-interaction = 0.72) for trials of ICI combination therapy.

J Geriatr Oncol . 2020 Apr;11(3):508-514,
J Geriatr Oncol . 2021 Jun;12(5):813-819,

IMMUNOTHERAPY – TOXICITY

- Pooled Analysis of Pembrolizumab

	Pembrolizumab		Chemotherapy	
Patient with ≥ 1AE	**Age ≥ 75 y n=149**	**Age < 75 y n= 1323**	**Age ≥ 75 y n=105**	**Age < 75 y n= 969**
Treatment duration, median (range) mo	5.6 (0.03-34.8)	4.3 (0.03-37.5)	3.5 (0.03-29.5)	3.5 (0.03-37)
Treatment related AE	68%	65%	94%	87%
Grade 3-4	23%	16%	59%	37%
Led to death (grade 5)	1%	1%	2%	2%
Led to discontinuation	11%	7%	15%	10%
Immune-mediated Aes and infusion reactions	25%	25%	7%	6%
Grade 3-4	9%	7%	0	1
Led to death (grade 5)	0	<1%	0	<1%

Lung Cancer . 2019 Sep;135:188-195

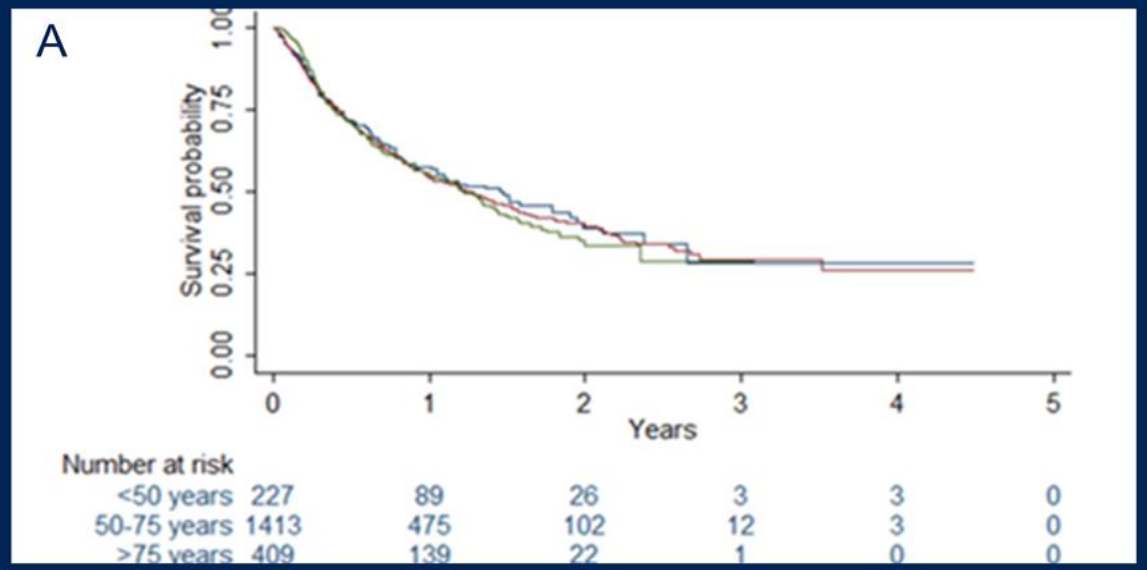
2021 ASCO ANNUAL MEETING

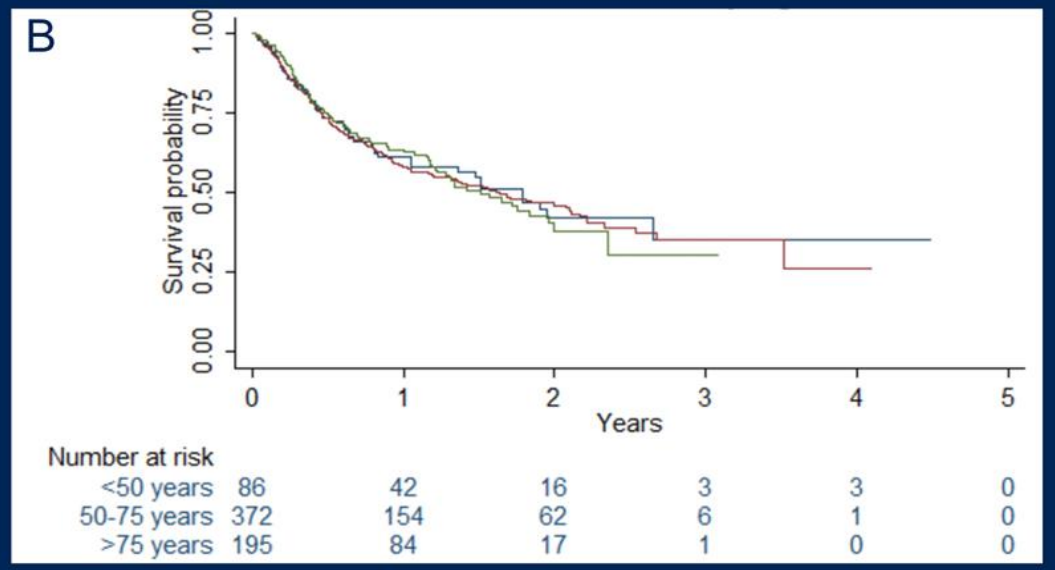
REAL-WORLD OUTCOMES IN OLDER ADULTS TREATED WITH IMMUNOTHERAPY: A UNITED KINGDOM MULTI-CENTRE SERIES OF 2049 PATIENTS

Dr Anna Olsson-Brown

- Across the total cohort patients aged >75 had no increased risk of any irAE (35%(a) v 33%(b) v 41%(c),p=0.074).
- There was an increase in irAEs in older patients treated with MT (36%(a) v 26(b) v 25%(c), p=0.011) However there was no difference in the >75s with regard parameters of severity
- In the overall cohort younger patients were more likely to develop irAEs and be admitted.

There was no difference in median overall survival across age groups in the cohort as a whole (p=0.822) or for the individual tumour groups when treated with single agent ICI.

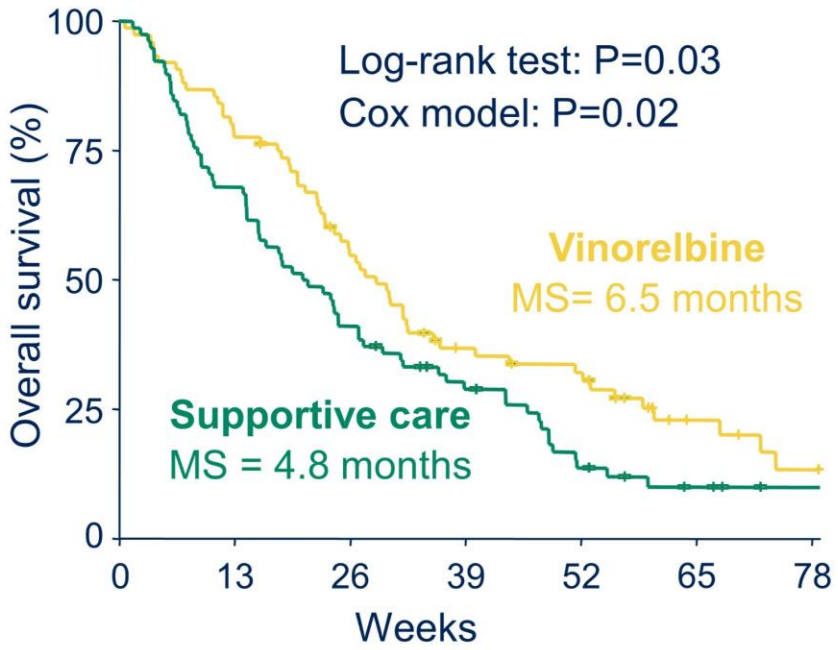




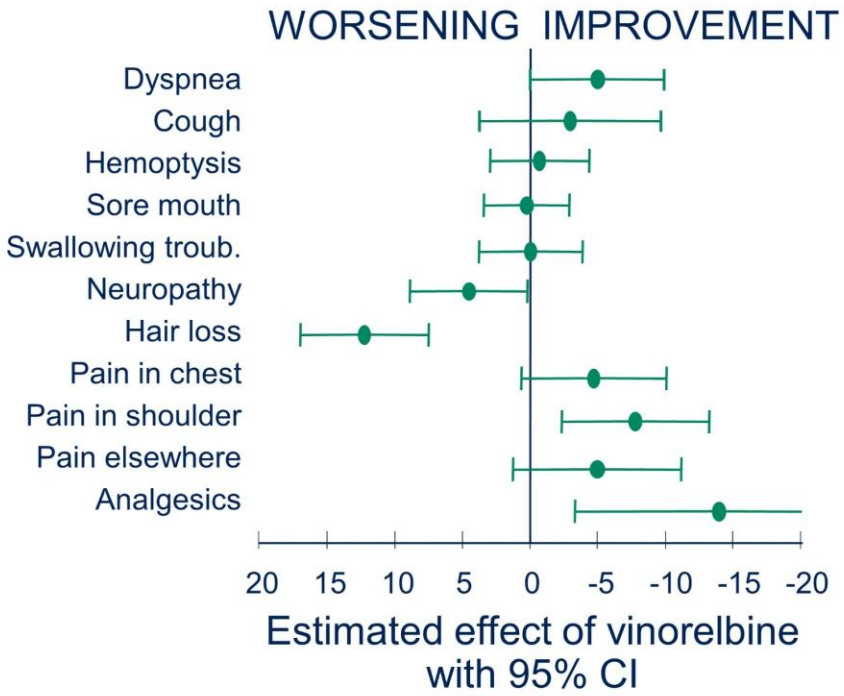
Lung cancer

The ELVIS study

Overall survival



EORTC LC-13: QoL analysis



Gridelli C, *et al.*, J Natl Cancer Inst 1999;91:66–72, .

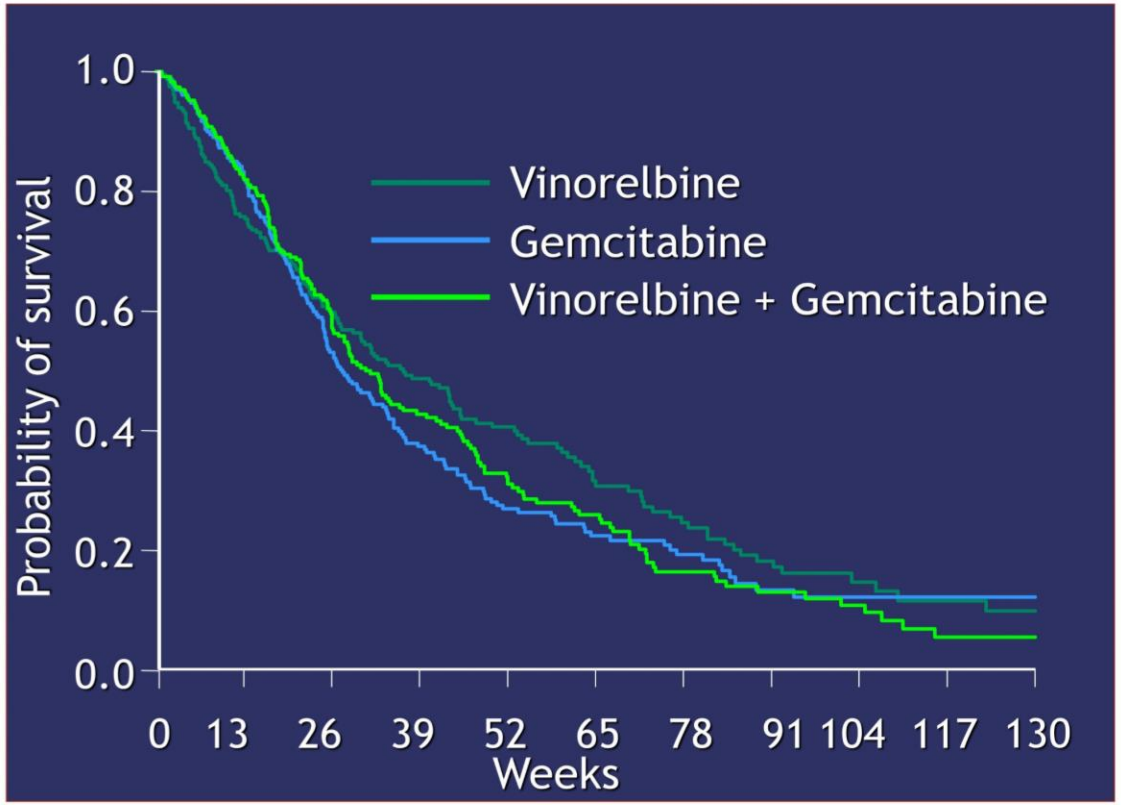
MILES study : 707 patients

R

Vinorelbine
30 mg/m²D1-D8, Q3wks

Gemcitabine
1200 mg/m² D1-D8, Q3wks

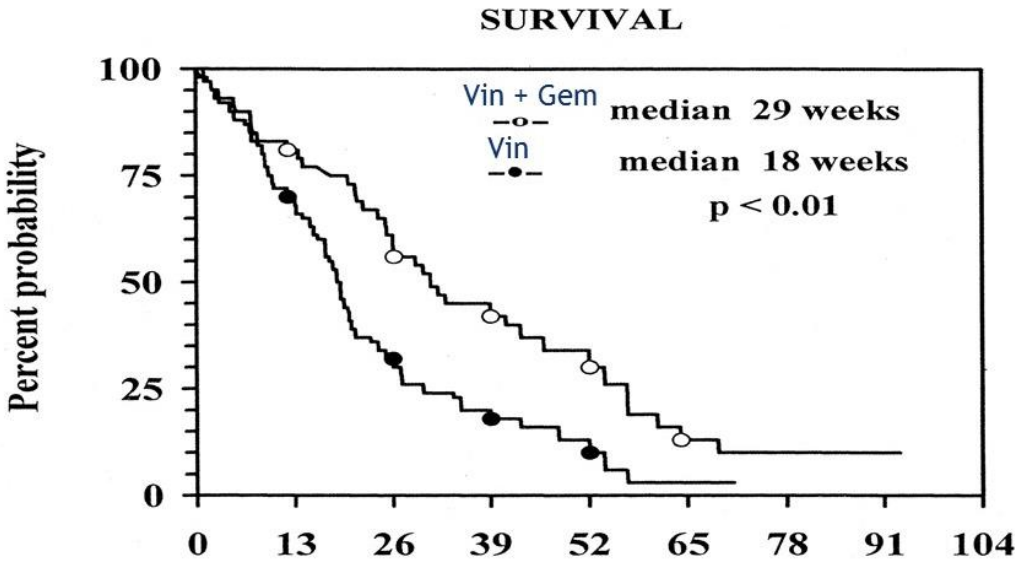
Gemcitabine+Vinorelbine
Vin: 25 mg/m² D1-D8
Gem: 1000 mg/m² D1-D8
Q3 wks



Gridelli C et al. J Natl Cancer Inst, 2003

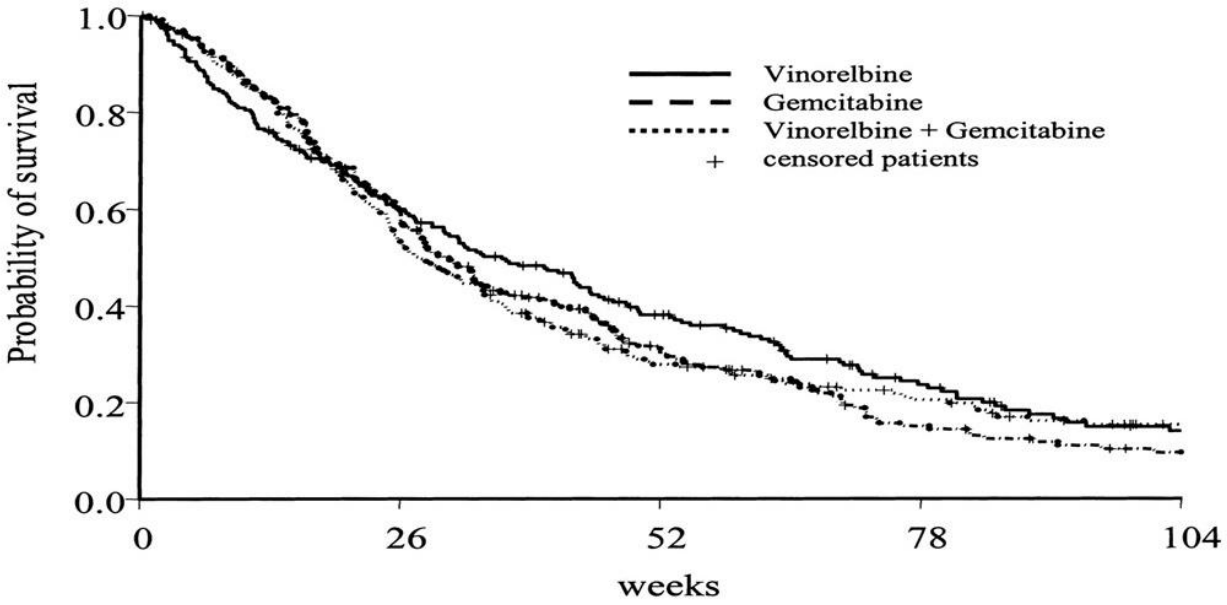
Is single agent the standard?
Gemcitabine-Vinorelbine vs Single agent

N=120



Frasci G. JCO 2000;18:2529-2536

N=700



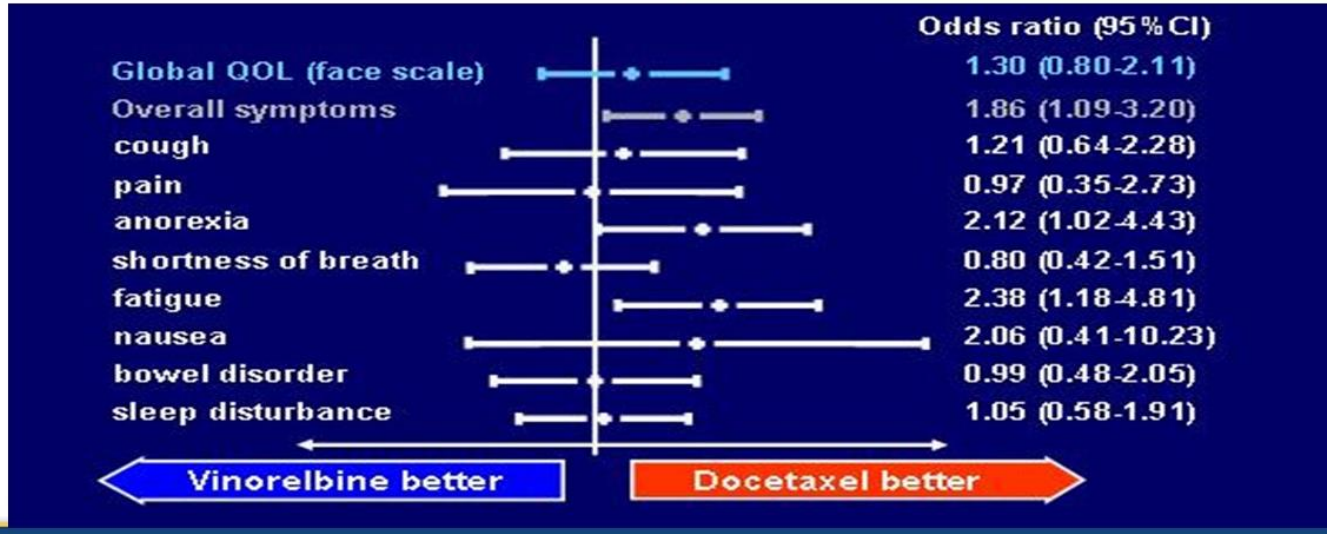
Gridelli C. JNCI 2003;95:362-372

Is vinorelbine the only standard? Vinorelbine vs docetaxel

	Docetaxel	Vinorelbine	P value
ORR (%)	22.7	9.9	0.019
PFS (mo.)	5.5	3.1	<0.001
OS (mo.)	14.3	9.9	0.138
1-Y OS	59%	37%	NS

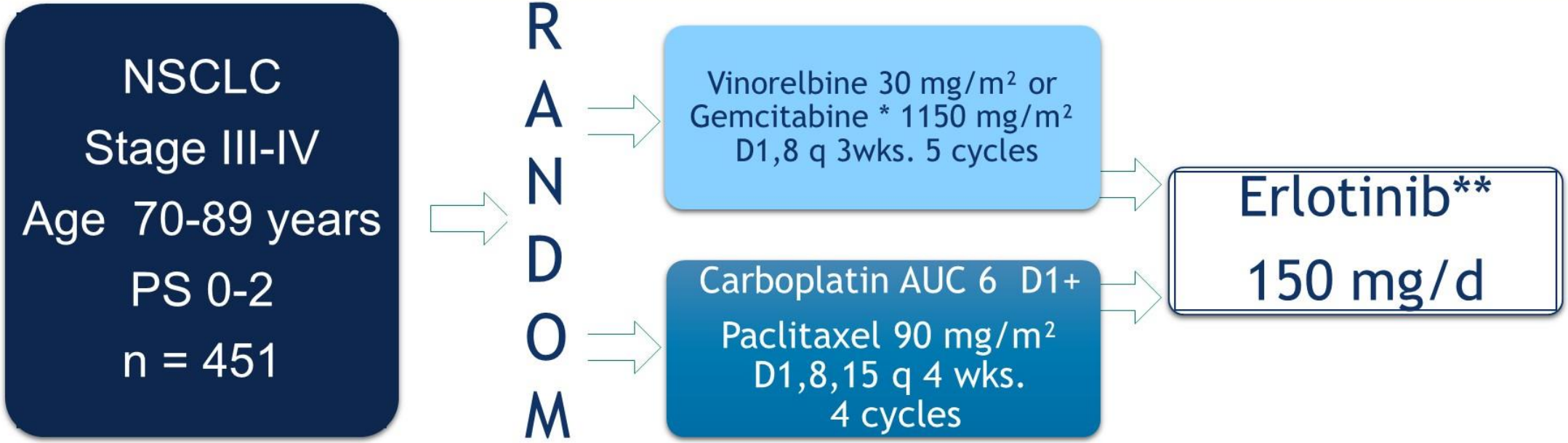
Median age 76 (70-86)

Kudoh et al, J Clin Oncol 2006;24 : 3657-63



Doublet Carboplatin

The IFCT-0501 Study: Design



Stratification: center, PS 0-1 vs. 2, age ≤80 vs. >80, stage III vs. IV

*Choice of the treatment facility at the beginning of the study
** In case of PD or excessive toxicity

E. Quoix et al. Lancet 2011;378:1079-88

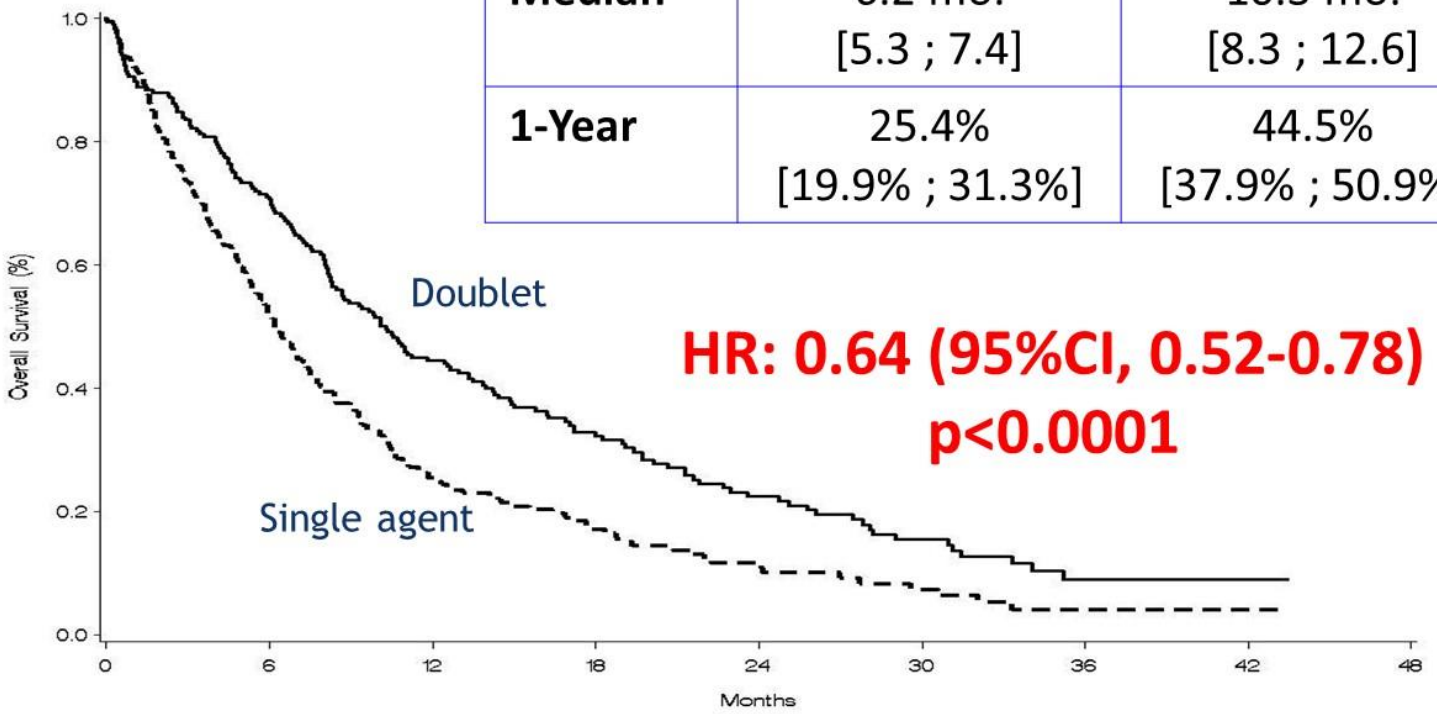
Presented By Elisabeth Quoix at 2019 ASCO Annual Meeting

Overall survival (ITT)

Characteristics	All Patients (N=451)
Male	333 (73.8)
Median age	77.1
PS 0-1	327 (72.7)
Histology: ADC	229 (50.8)
Never smoker	94 (20.9)

No difference between both groups

OS	Single arm (n=226)	Doublet arm (n=225)
Median	6.2 mo. [5.3 ; 7.4]	10.3 mo. [8.3 ; 12.6]
1-Year	25.4% [19.9% ; 31.3%]	44.5% [37.9% ; 50.9%]



HR: 0.64 (95%CI, 0.52-0.78)
p<0.0001

E. Quoix et al. Lancet 2011;378:1079-88

IFCT 05-01: Grade 3-5 Toxicities

Grade 3-4 hematologic	Single agent N = 225	Doublet N= 223	p
Neutropenia	28 (12,4%)	108 (48.4%)	$< 10^{-4}$
Febrile Neutropenia	6 (2,7%)	21 (9.4%)	0.002
Anemia	10 (4,4%)	16 (7.7%)	0.041
Thrombocytop-enia	2 (0.9%)	13(6.3%)	0.001

Grade 3-4 non hematologic	Single agent (N=225)	Doublet (N=223)
Asthenia	13 (5.8)	23 (10.3)
Anorexia	2 (0.9)	9 (4.0)
Diarrhea	2 (0.9)	6 (2.7)
Nausea/Vomiting	2 (0.9)	6 (2.7)
Pulmonary disorder	5 (2.2)	3 (1.3)
Sensitive neuropathy	1 (0.4)	7 (3.1)

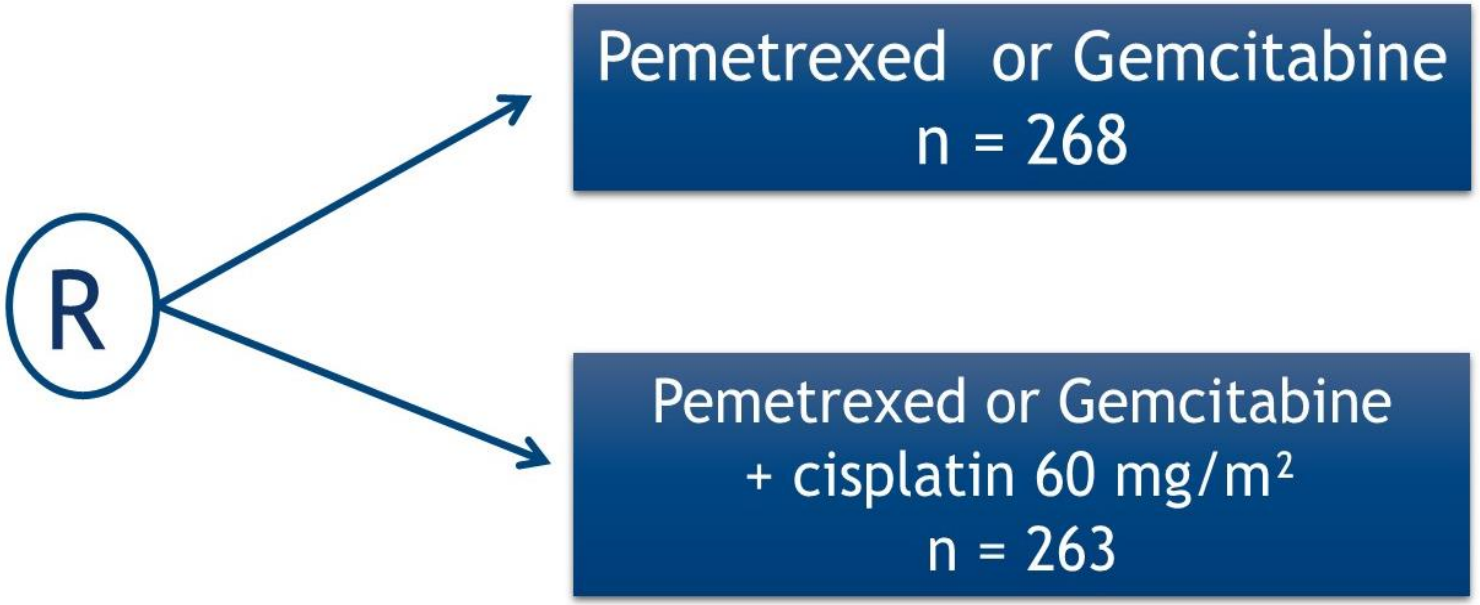
Toxic deaths : 3 (1.3 %) in the single arm, 10 (4.4 %) in the doublet arm

E. Quoix et al. Lancet 2011;378:1079-88

Doublet Cisplatin

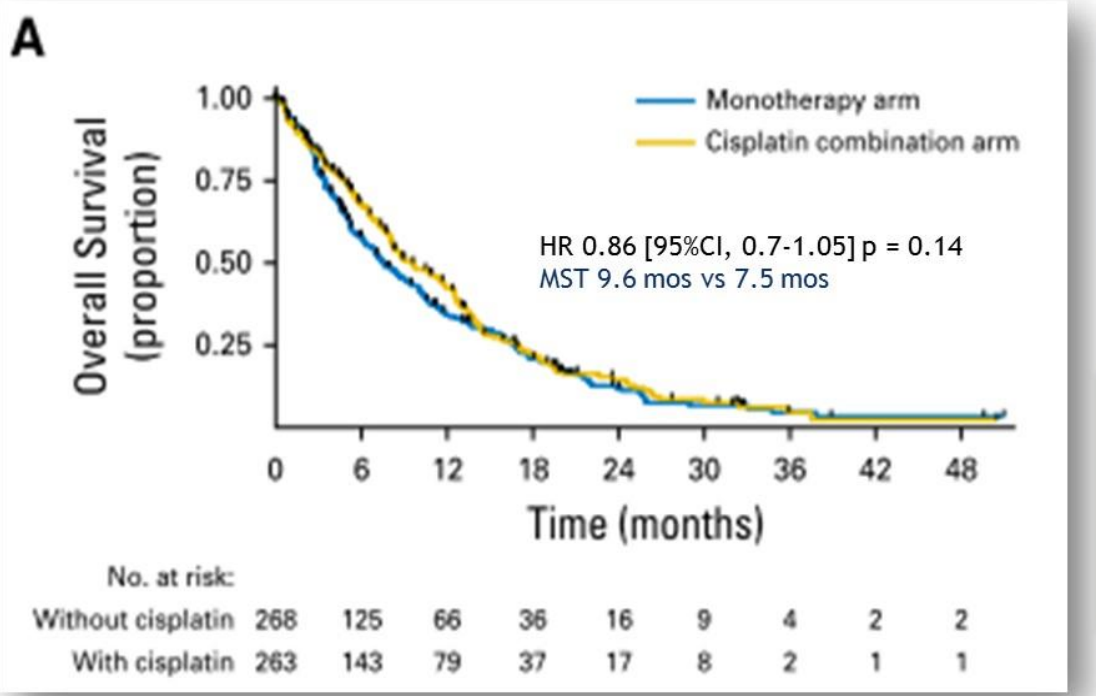
The Miles 3 and Miles 4 trials

531 pts
March 2011-August 2016
PS 0-1
>70 years, median age 75
52 pts aged 80 and over (9.8%)
70% non-squamous
79% males
Advanced NSCLC



Gridelli C J Clin Oncol 2018;36:2585-92

Miles 3-4: Outcomes



ORR : 15.5% (95%CI 11.2-20.6) in the cisplatin arm
ORR : 8.5% (95%CI 5.4-12.5) in the monotherapy arm
Significantly more frequent and more severe hematologic, and neurologic toxicity, mucositis, nausea and vomiting

No survival advantage with combined arm compared to single agent.
Cisplatin too toxic for elderly compared to carboplatin!

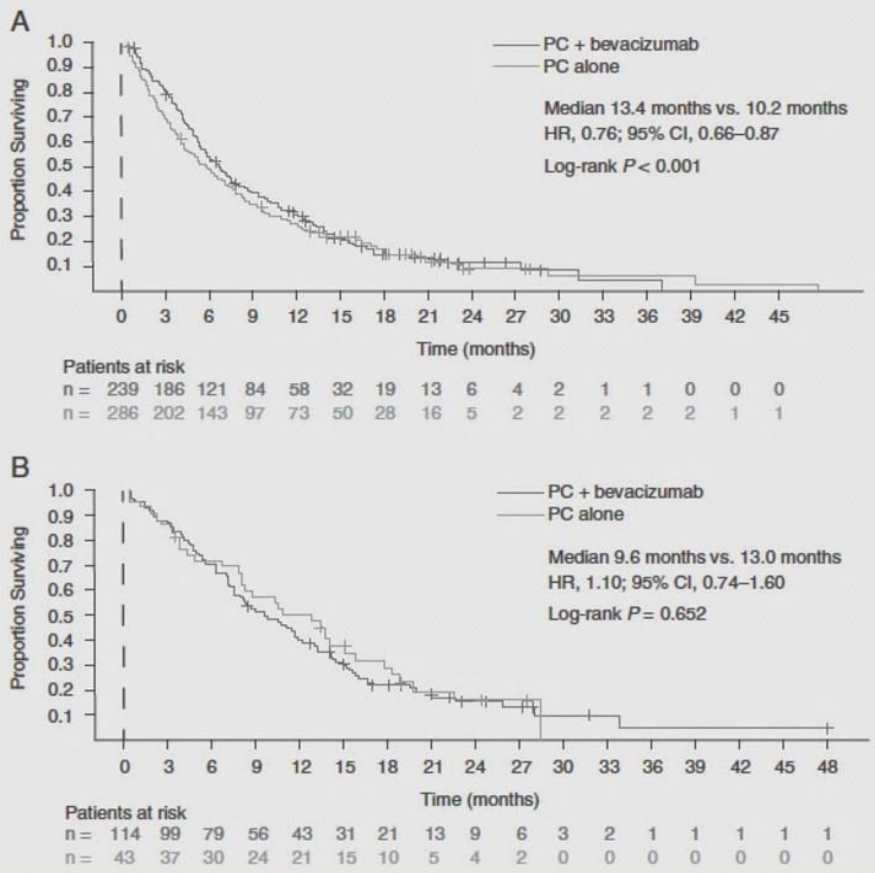
Gridelli C J Clin Oncol 2018;36:2585-92

Chemotherapy for Stage IV Non-small Cell Lung Cancer in elderly patients : Guidelines

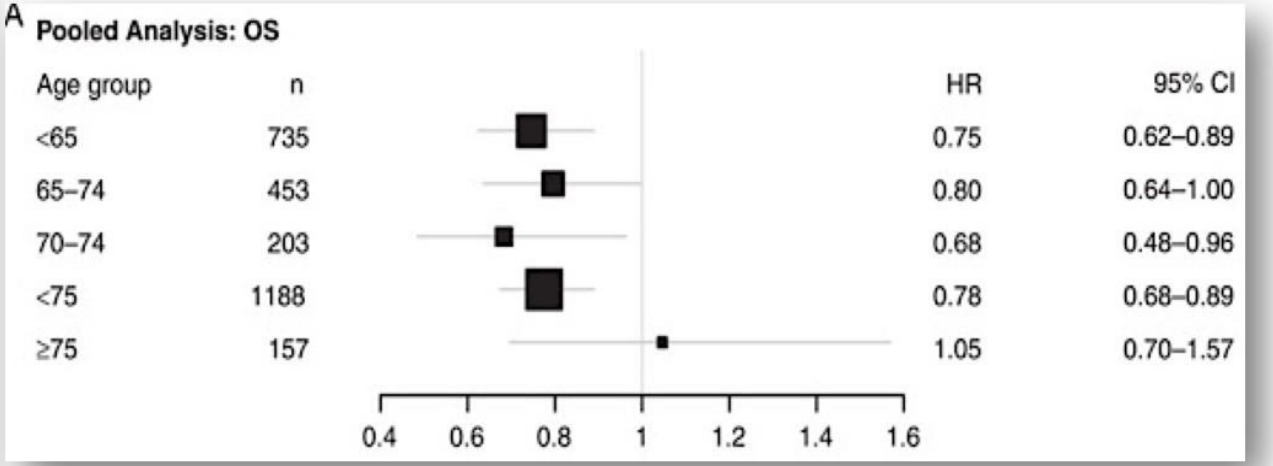
- **American College of Chest Physicians, 3rd edition**
  In elderly patients (age ≥ 70–79 years) with stage IV NSCLC who have good PS and limited co-morbidities, treatment with the two drug combination of monthly carboplatin and weekly paclitaxel is recommended (Grade 1A).
- **ASCO :** Decisions regarding chemotherapy should not be made based on age alone (evidence quality : high, strength of recommendation strong)
- **NCCN 2012** : If an older patient is deemed to be fit, it is reasonable to use the treatment options recommended for younger individuals
- **EORTC-Lung Cancer Group SIOG Recommendations in 2014:** Prospective trials support the use of carboplatin-based doublets in fit patients. For less fit patients single-agent treatment (gemcitabine, vinorelbine, taxanes) represents a valid option

M.Socinski et al. Chest 2013; 143
Masters GA JCO 2015;
Hanna N JCO 2017;35:3484-515
Ganti A, JNCCN 2012;10:230-9
Pallis AG, Ann Oncol 2014;25:1270-83

Bevacizumab in elderly patients



Pooled analysis of 2 phase III studies (E4599 /PointBreak):
A: overall survival of pts aged <75 years
B: overall survival of pts aged ≥75 years
8% grade 5 in pts ≥ 75 years treated with Bevacizumab
vs 2% for those treated with CT alone



Langer CJ Am J Clin Oncol 2016;39:441-7

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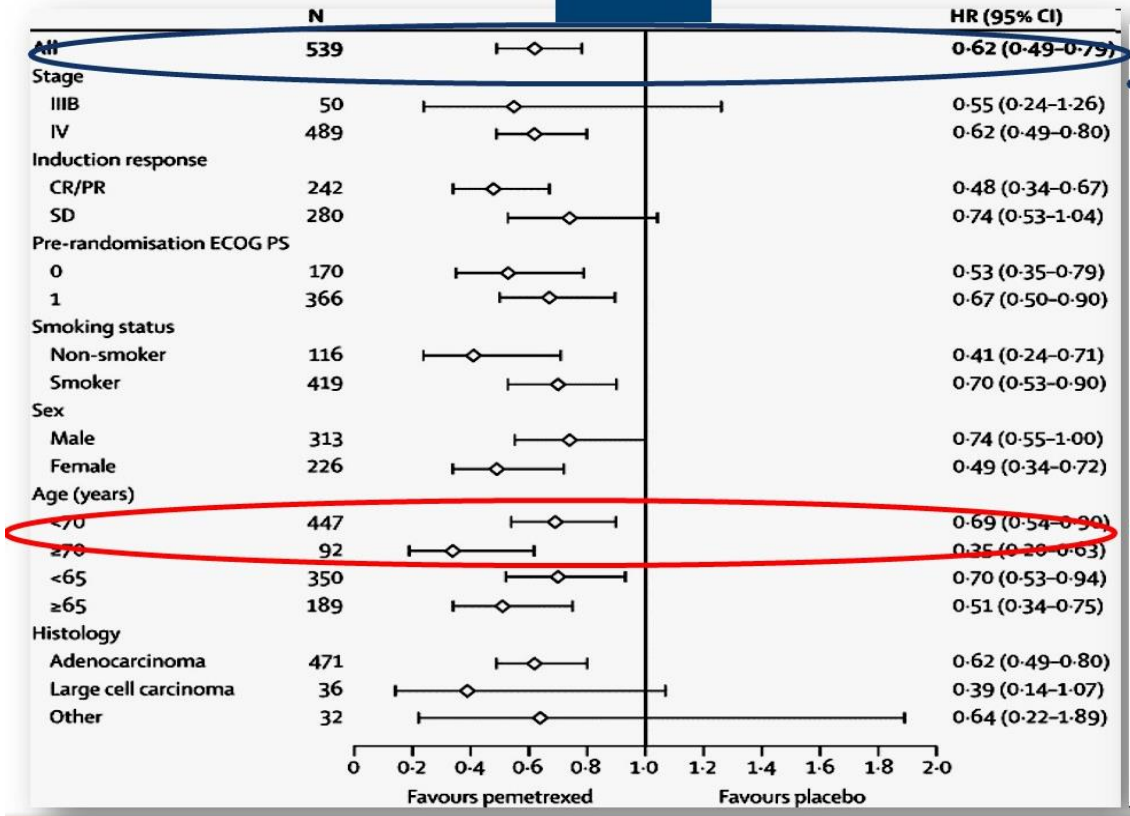
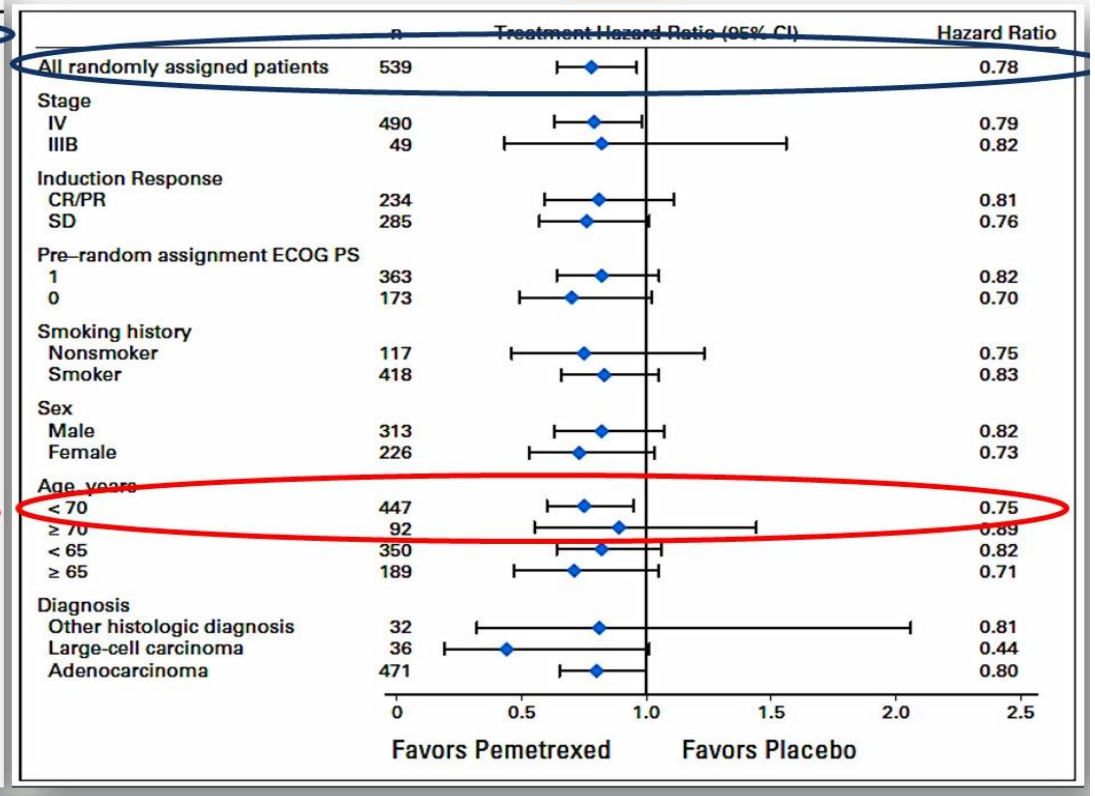
Maintenance? Subgroup analysis of the Paramount trial

OS ?

PFS



OS



Paz-Ares L JCO 2012;13:147-56 & 2013; 31 : 2895-902

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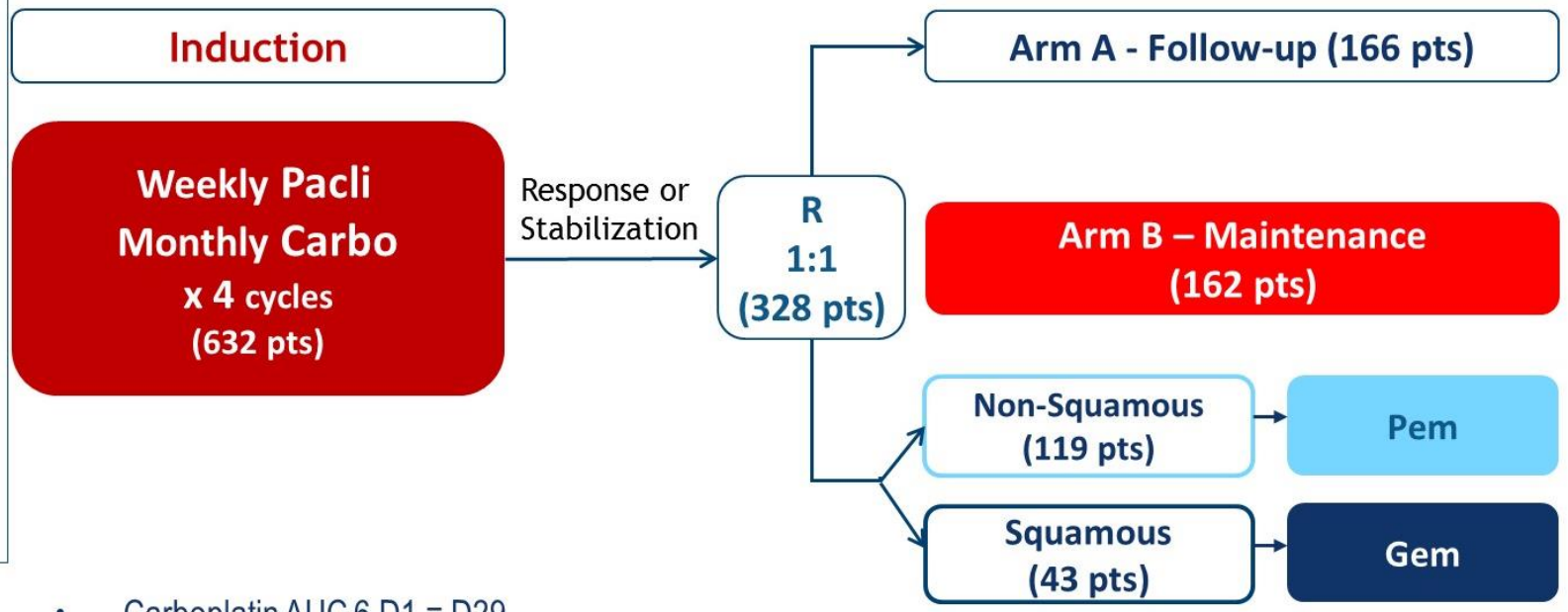
IFCT-1201 MODEL trial : phase 3 trial maintenance Gem/ Pem

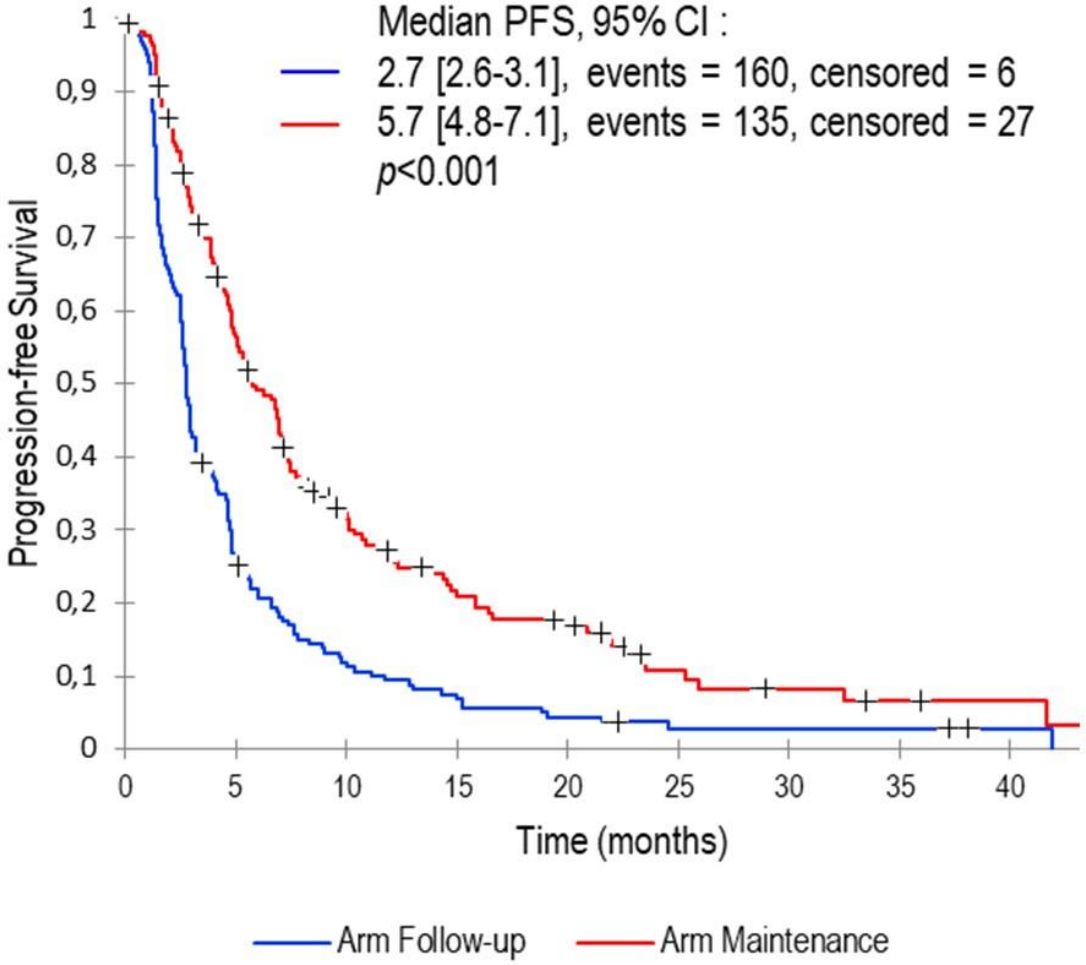
- Histological/cytological diagnosis of NSCLC
- Stage IIIB unresectable and non-irradiable or stage IV
- No EGFR/ALK mutations (or unknown)
- Measurable disease (RECIST 1.1)
- Age ≥ 70 and < 90 years
- MMS > 23
- PS 0-2

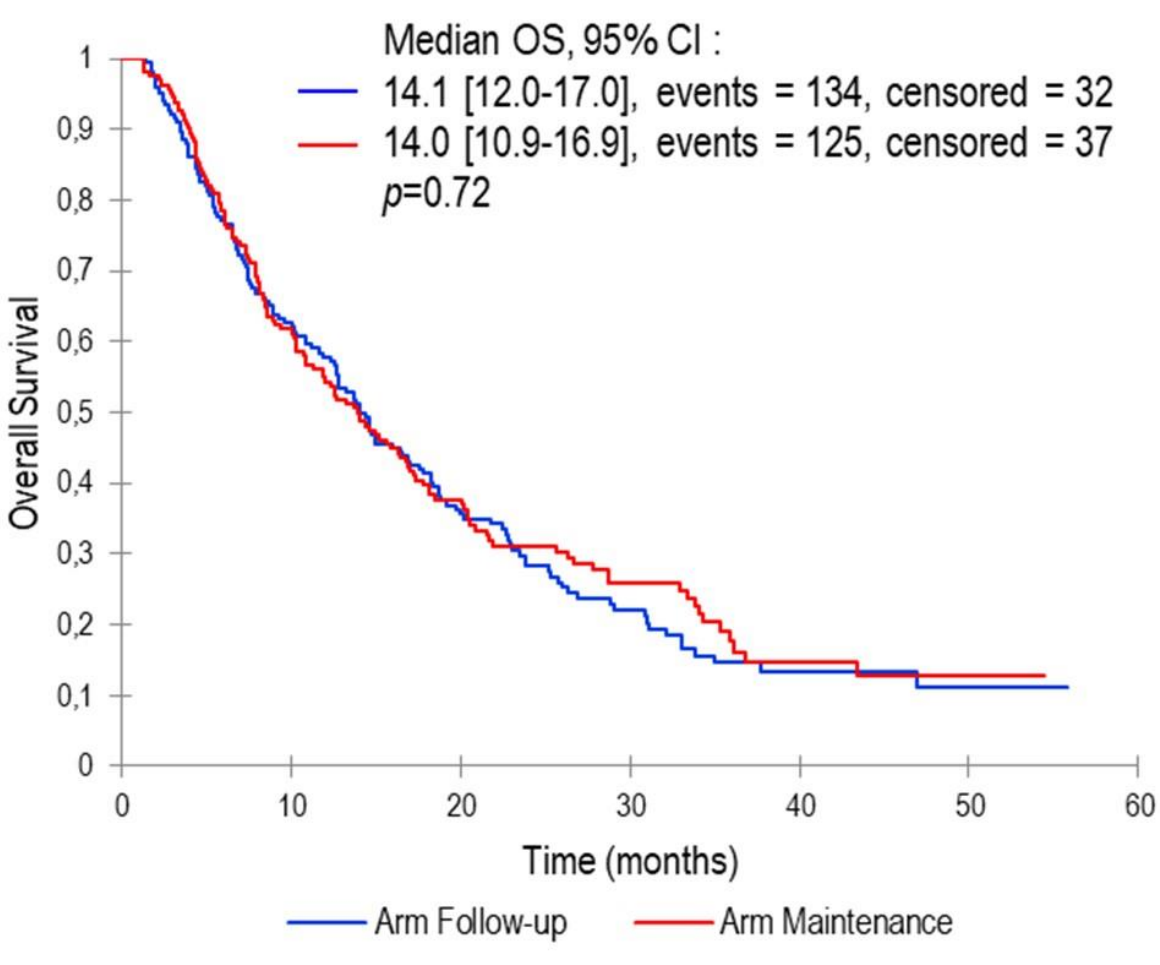


- Carboplatin AUC 6 D1 = D29
- Paclitaxel 90 mg/m², D1=D8=D15=D29
- Gemcitabine 1150 mg/m² D1=D8=D22
- Pemetrexed 500 mg/m² D1 = D22

Median age 76.4 years
≥ 80 years : 22.5%

MODEL : PFS/OS of the 328 randomised pts





Quoix E. et al. ESMO 2018 Abstract #3420

Phase II Studies with TKIs in EGFR mut Elderly Patients

Table 2. Phase II trials of gefitinib in EFGR mut (+) elderly patients

Study	Age	N	ORR	PFS (median)	OS (median)
Maemondo et al. [89]	≥75 years	31	74.2%	12.1 months	33.8 months
Inoue et al. [90]	≥75 years PS 2–4/>80 years PS 1–4/<70 years PS 3–4	30	66%	6.5 months	17.8 months
Asami et al. [91]	≥75 years	17	59%	12.9	Not reached

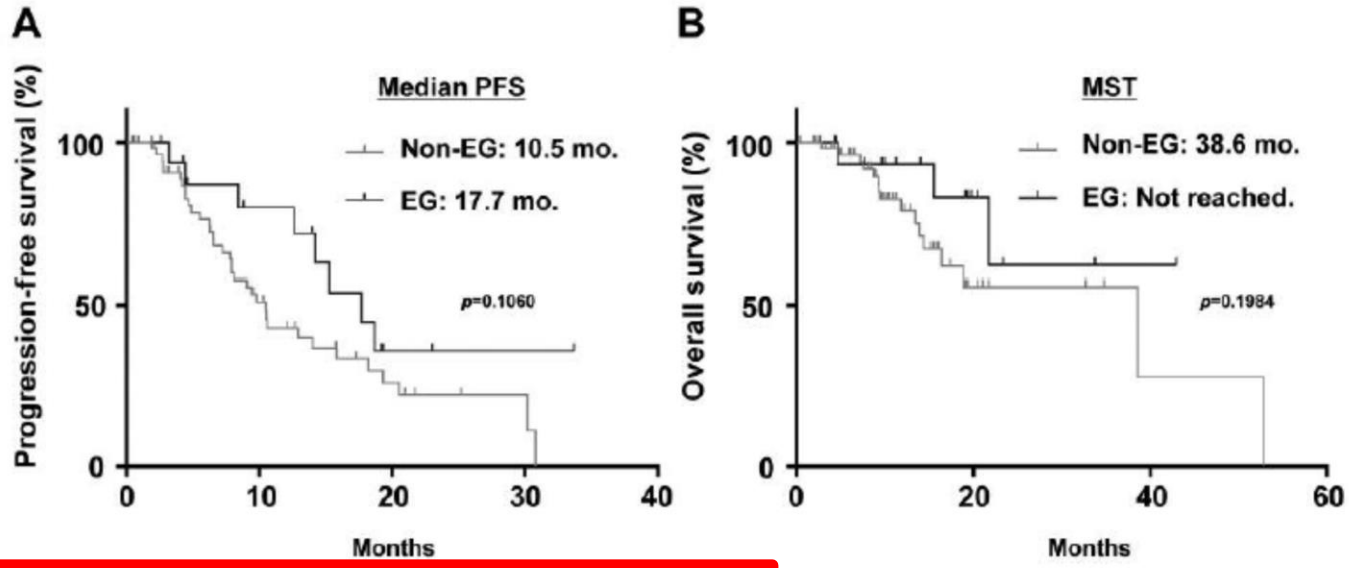
PS, performance status; PFS, progression-free survival; OS, overall survival.

Efficacy and Safety Data of Osimertinib in Elderly Patients with NSCLC Who Harbor the *EGFR* T790M Mutation After Failure of Initial EGFR-TKI Treatment

HIROMI FURUTA[1], TAKEHIRO UEMURA[1], TATSUYA YOSHIDA[1], MAKIKO KOBARA[2], TEPPEI YAMAGUCHI[1], NAOHIRO WATANABE[1], JUNICHI SHIMIZU[1], YOSHITSUGU HORIO[1], HIROAKI KURODA[3], YUKINORI SAKAO[3], YASUSHI YATABE[4] and TOYOAKI HIDA[1]

ANTICANCER RESEARCH *38*: 5231-5237 (2018)

Response	Non-EG (N=59)	EG (N=18)	*p*-Value
Partial response	30	11	
Stable disease	14	4	
Progressive disease	8	2	
Not evaluable	7	1	
Overall response rate	50.8%	61.1%	0.59

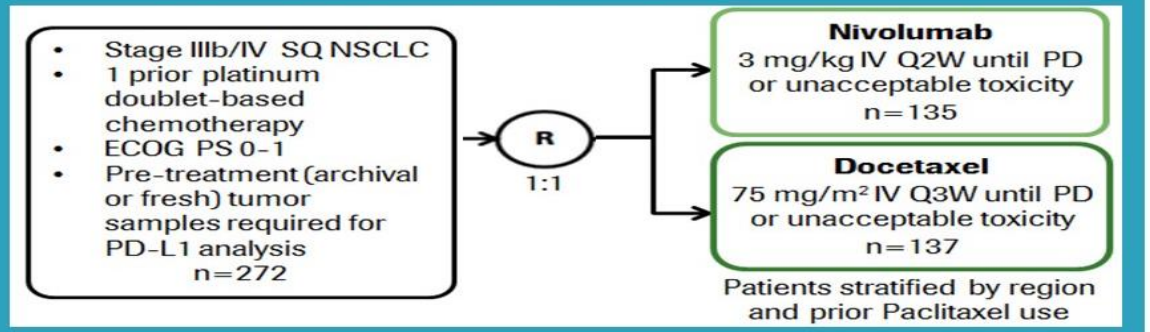


Conclusion: Osimertinib is a safe and effective treatment option for elderly patients with advanced NSCLC who harbor the EGFR mutation.

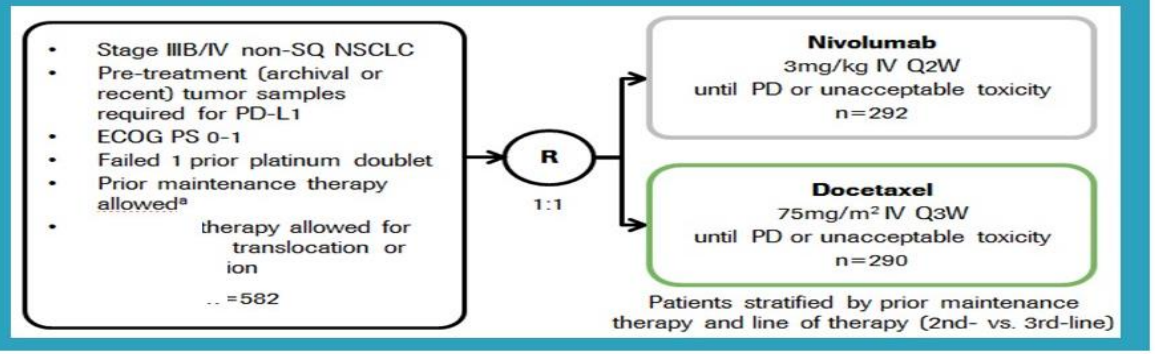
Furuta H et al. Anticancer Research, 38:5231-5237, 2018

2nd line IO vs Docetaxel

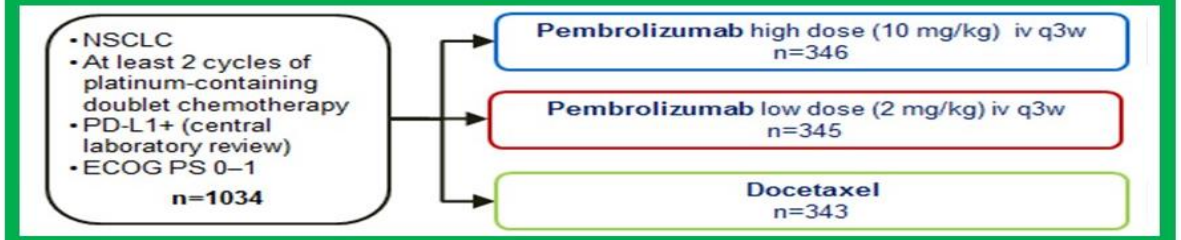
Nivolumab – CheckMate 017 (PIII)
2nd Line, squamous, PD-L1 All-Comer



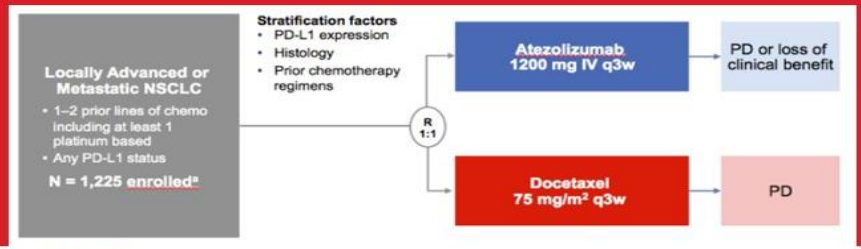
Nivolumab – CheckMate 057 (PIII)
2nd Line, non-squamous, PD-L1 All-Comer



Pembrolizumab - Keynote 010 (PII/III)
2nd+ Line, PD-L1 TPS ≥1%



Atezolizumab – OAK (PIII)
2nd+ Line, PD-L1 All-Comer

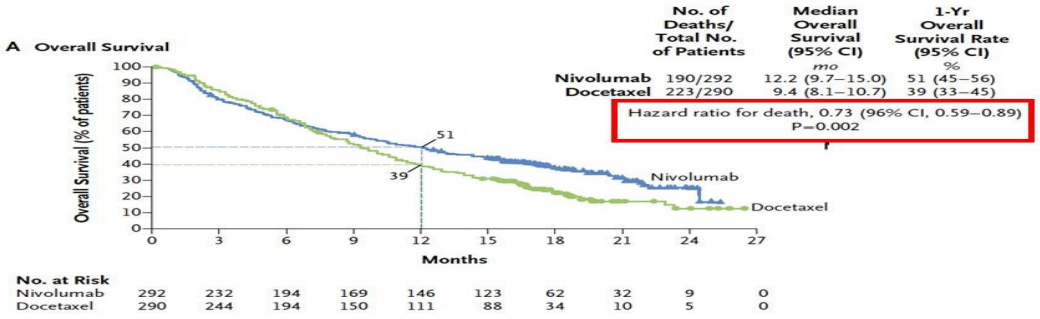


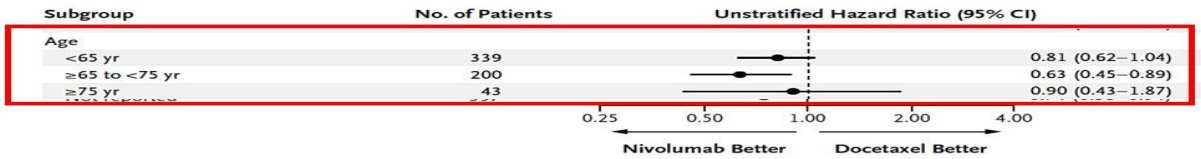
Brahmer, NEJM 2015; Borghaei NEJM 2015; Herbst, Lancet 2015; Rittmeyer, Lancet 2016

Courtesy of Laurent Greiller

CHECKMATE 057

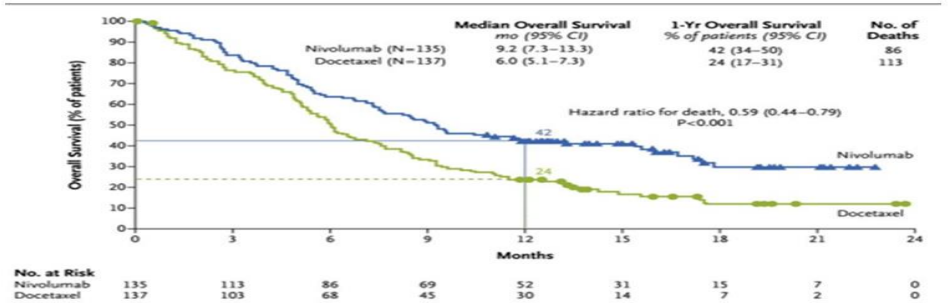
Response rate: 19% vs 12% (p = 0.02)





CHECKMATE 017

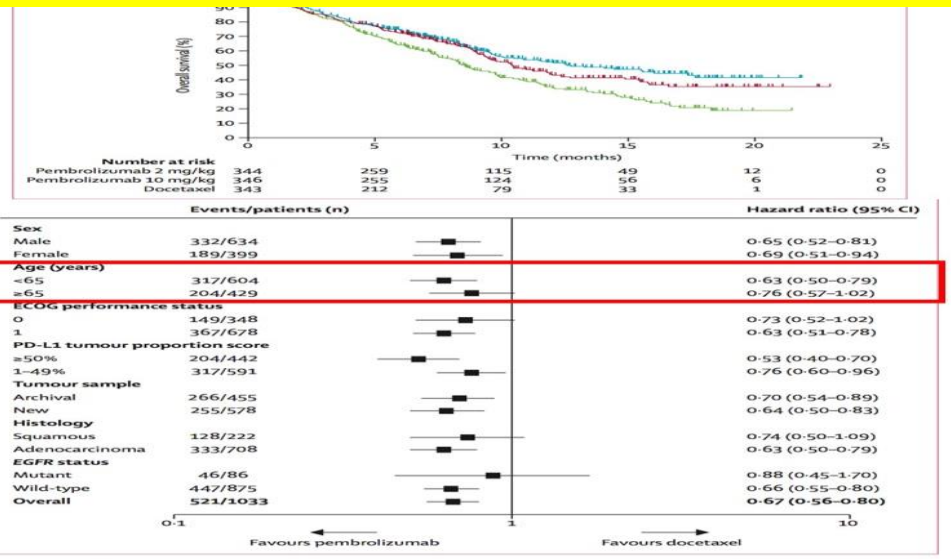
Response rate: 20% vs 9% (p = 0.008)

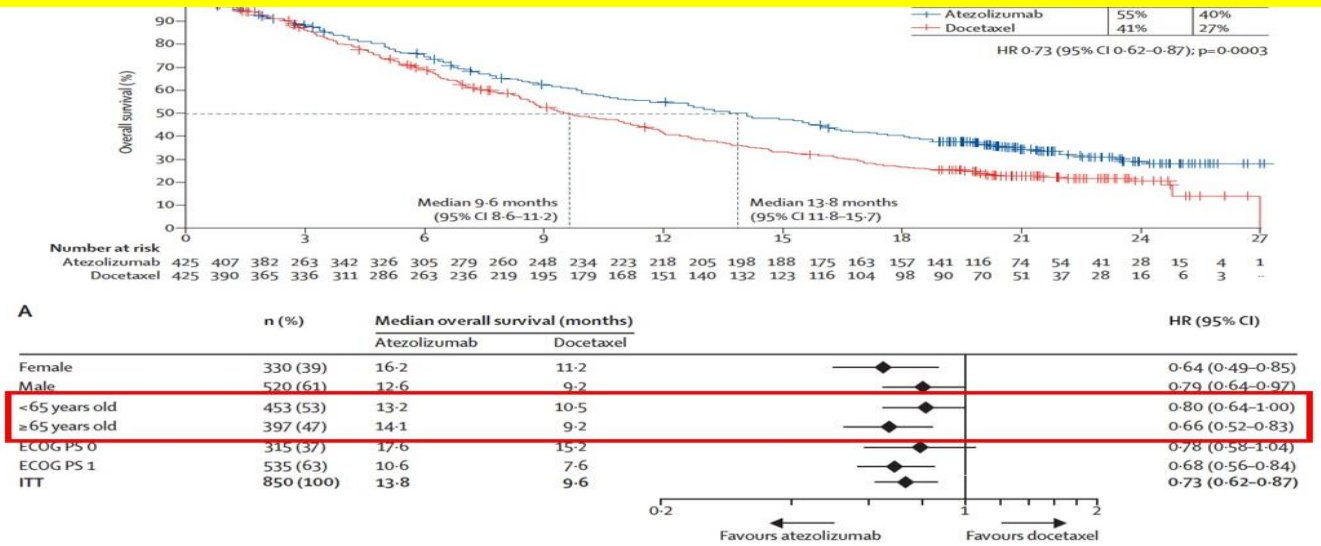


Median age 63 (39-85) 29 pts aged ≥75 years (11%)
Again, no survival benefit for the subgroup of pts aged ≥ 75 years

Brahmer J, NEJM 2015;373:123-35

Benefit same as young adults, but less data in Age > 75





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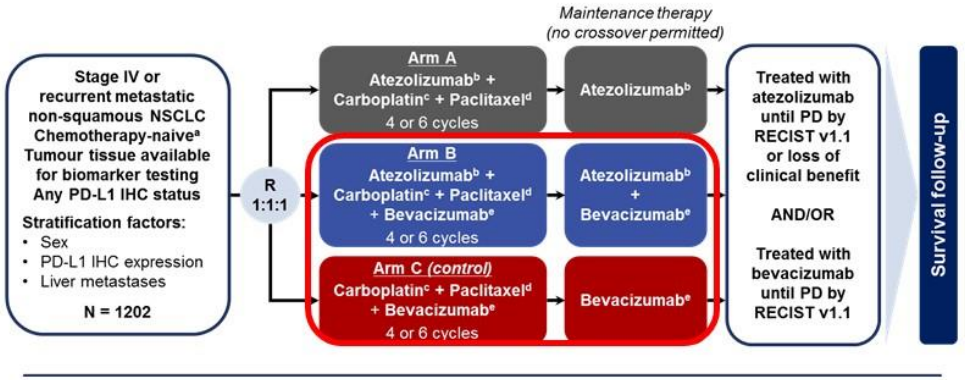
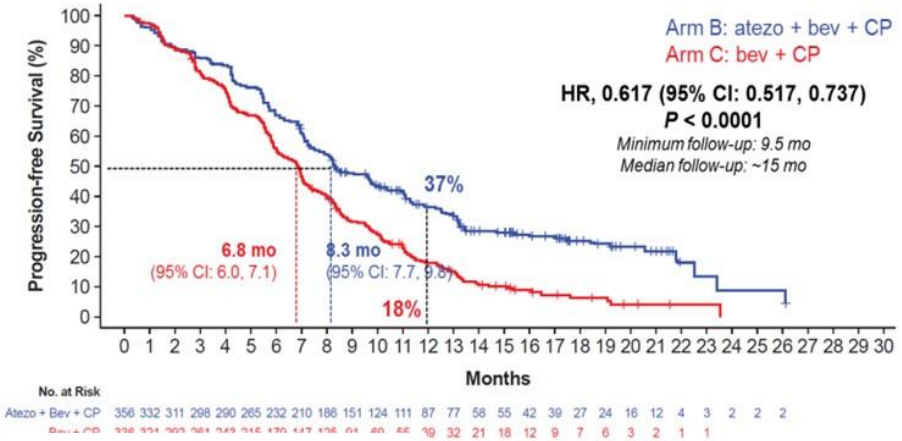
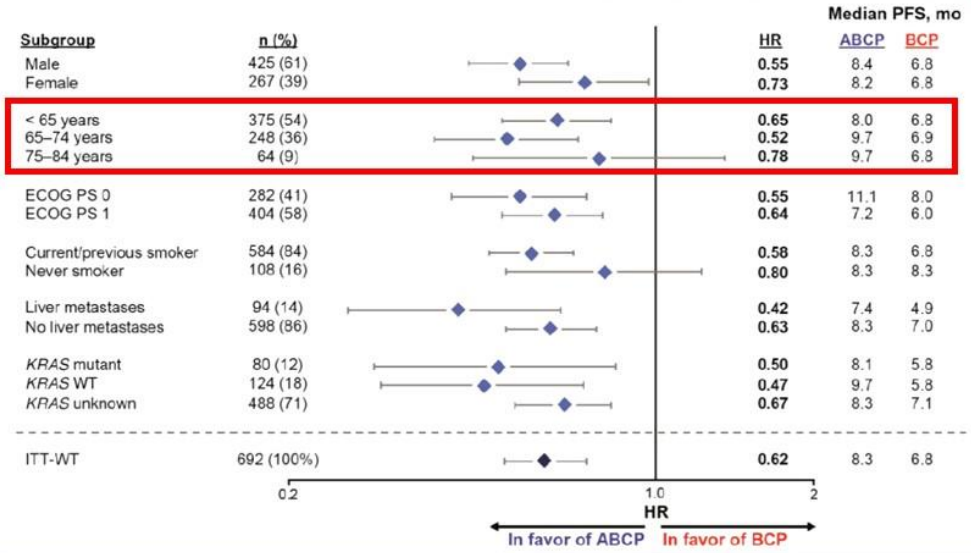
First line : IMPOWER 150 Trial







Socinski, NEJM 2018;378:2288-2301

Apparently, no difference in immunotoxicity with age

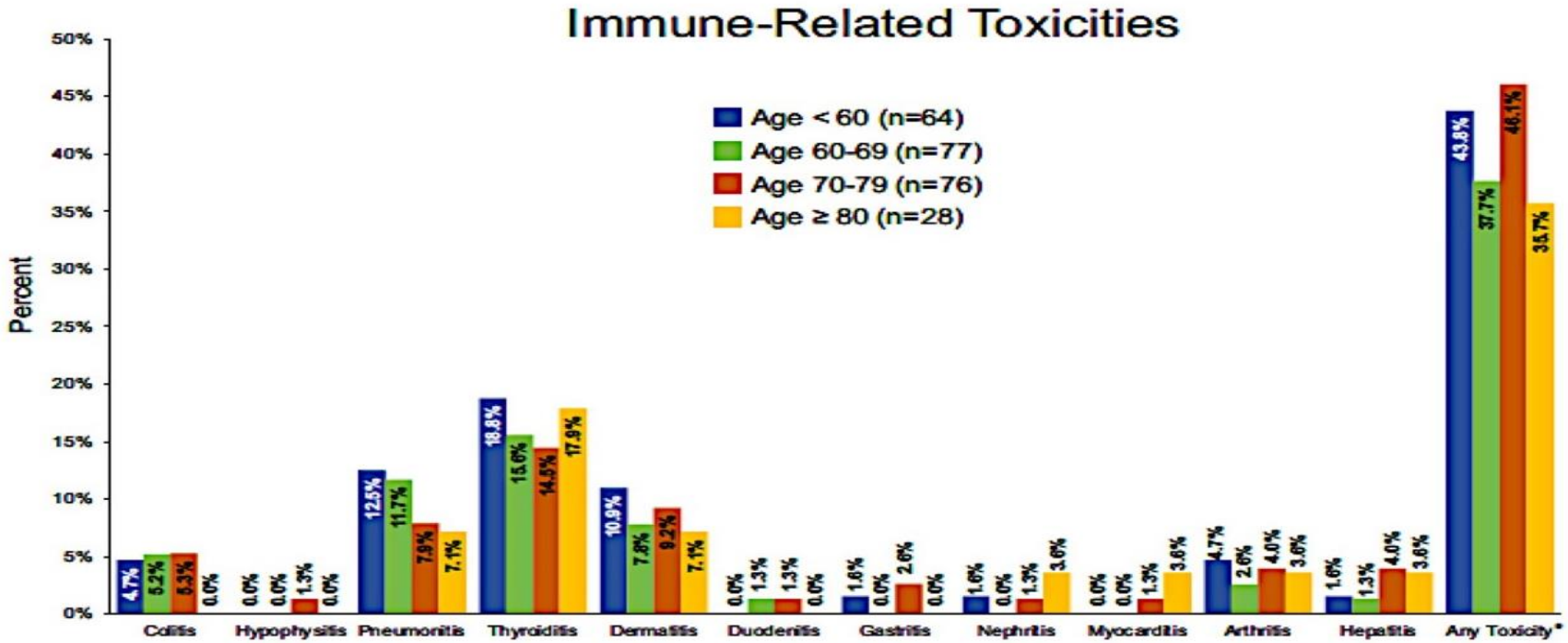
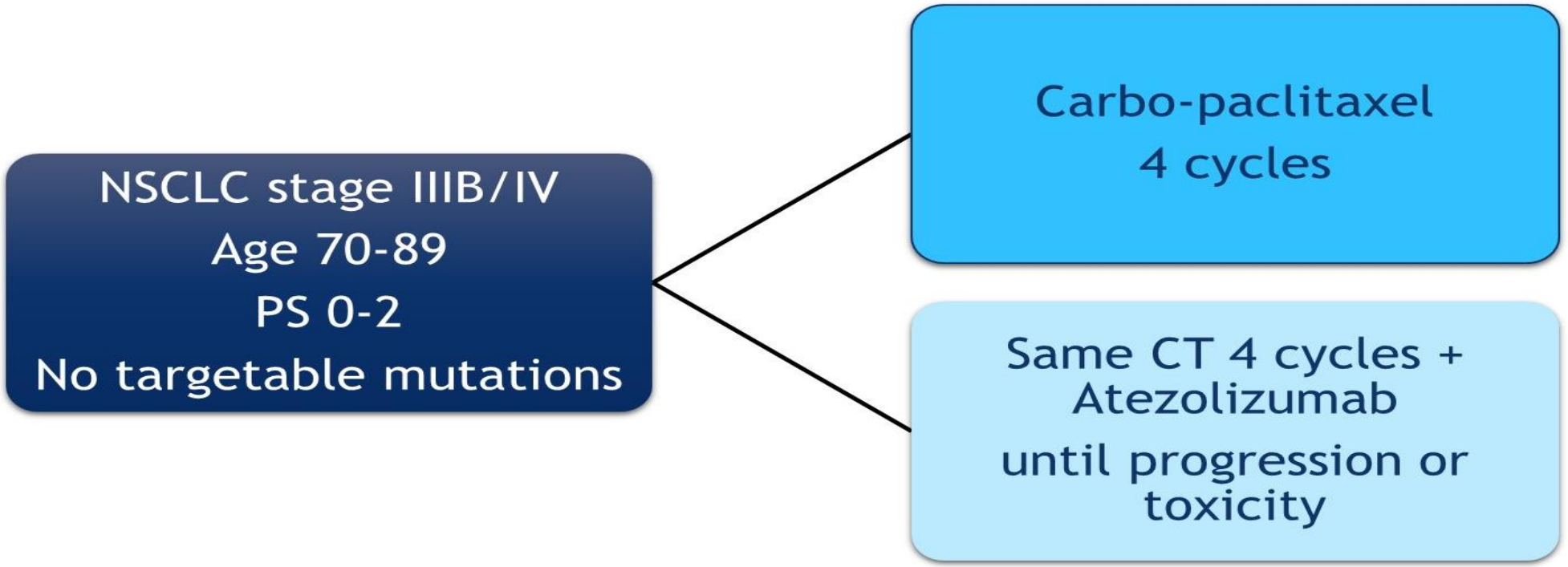


Figure 3. Immunotherapy toxicity rates. *Includes treatment-related adrenal insufficiency, allergic response, autoimmune hemolytic anemia, bullous pemphigoid, carpal tunnel syndrome, celiac disease, sclerosing cholangitis, costochondritis, diabetes, labyrinthitis, neuritis, pancreatitis, pleuritis, polymyalgia rheumatica-like syndrome, and psoriatic arthritis.

Next Phase III Study Devoted to Elderly Patients with metastatic NSCLC

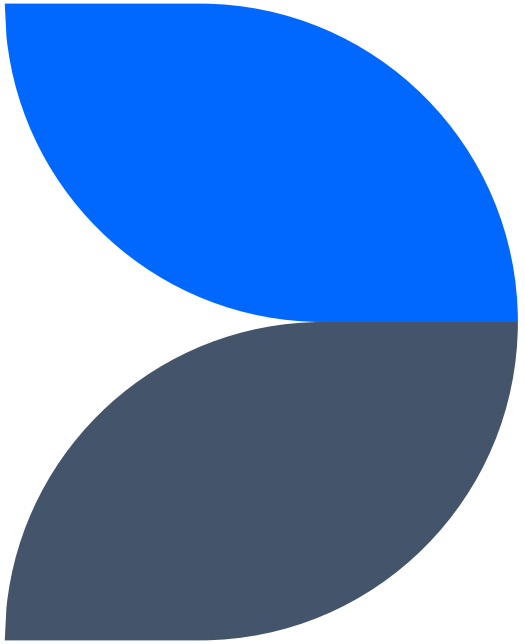


Stratification on centre, histology (squamous versus non squamous), age 70-79 vs 80-89, PD-L1 expression <1% vs >=1%

NSCLC in Elderly patients

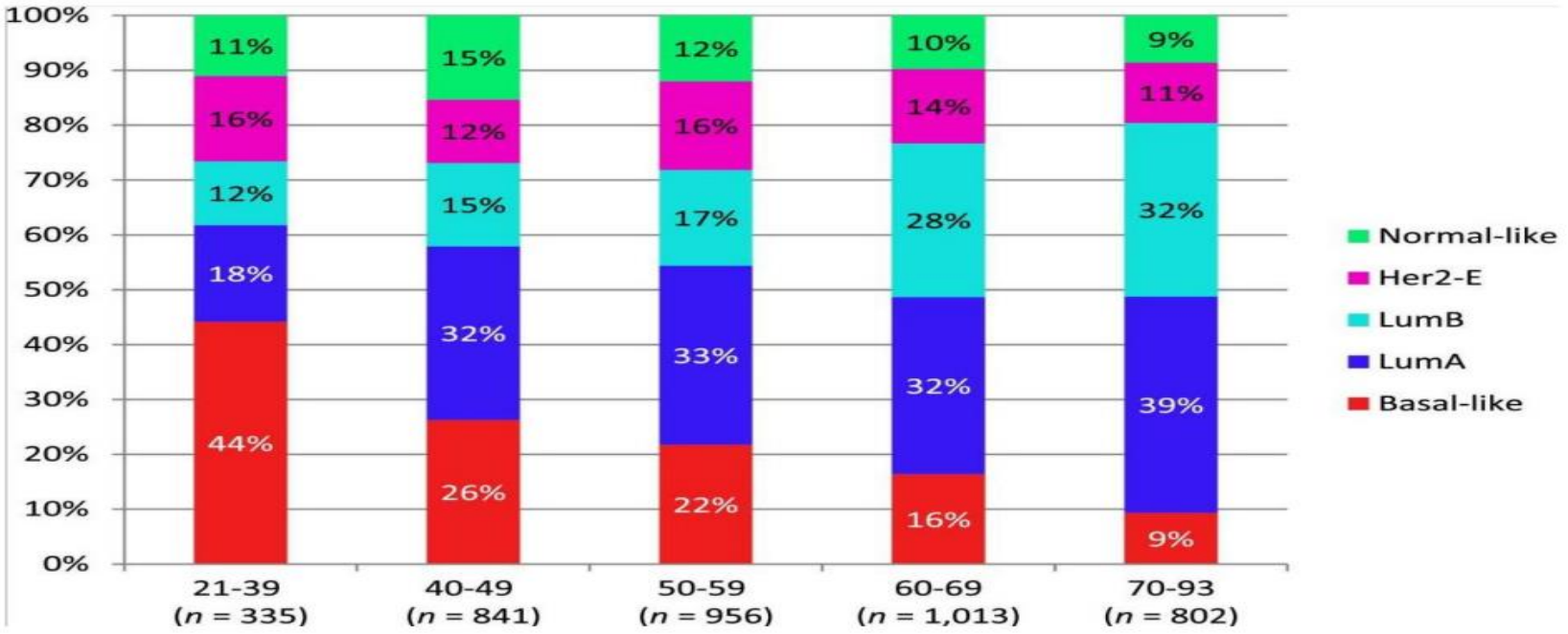
- Chemotherapy :
  - fit patient use carbo-doublet, (Carbo q 4 wk + wkly Paclitaxel preferred)
  - Single agent in less fir patients
- Maintenance therapy results in increase of PFS but not OS
- Bevacizumab : probably no benefit after 75 years
- *EGFR* mutations : higher rate in elderly patients.
  Lower *ALK* rearrangement rate in elderly men compared to elderly women?
  TKIs to be used as in younger patients whatever the PS, with similar results (beware of AE: diarrhea +++)
- Immunotherapy : No benefit in older elderly ?Need for dedicated studies
  cf. IFCT trial Carboplatin+paclitaxel +/-Atezolizumab in patients aged 70-89 years

Breast cancer



Breast cancer

BC biology according to age



de Kruijf Mol Oncol 2014, Jenskins Oncologist 2014

Endocrine therapy Compliance is the issue

Hot flushes
Thrombosis & embolism
Uterus cancer
Gynecological tractus
Vaginal discharge
Cataract

Tamoxifen

?

Neurocognition
Sexuality

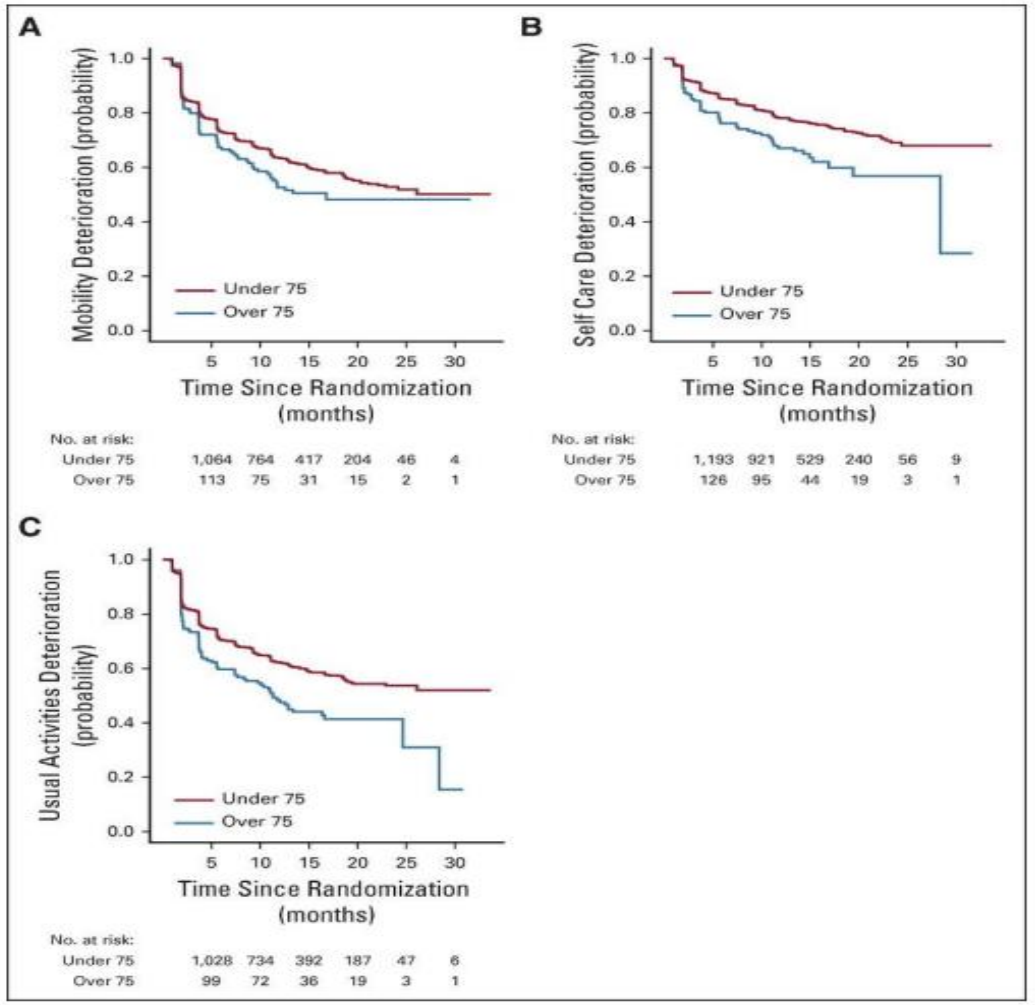
Arthralgias & myalgias
Osteoporosis
Fractures
Dryness
Cardiovascular
Lipid profile

Aromatase inhibitor

CDK4-6 inhibitors

Outcomes of Older Women With Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor-Negative Metastatic Breast Cancer Treated With a CDK4/6 Inhibitor and an Aromatase Inhibitor: An FDA Pooled Analysis

1. CDK4/6 inhibitor + AI as 1st line treatment of HR+ MBC in older women → **similar efficacy** benefit as seen in younger women
2. Incidence and severity of Grade 1-4 AEs similar between age groups, **but** **greater SAEs and discontinuations occurred in patients ≥75 (89% vs 73%)**
3. EQ-D5 → **decline in HRQoL** regardless of treatment
4. Need for inclusion of greater numbers of patients ≥70 in **clinical trials**



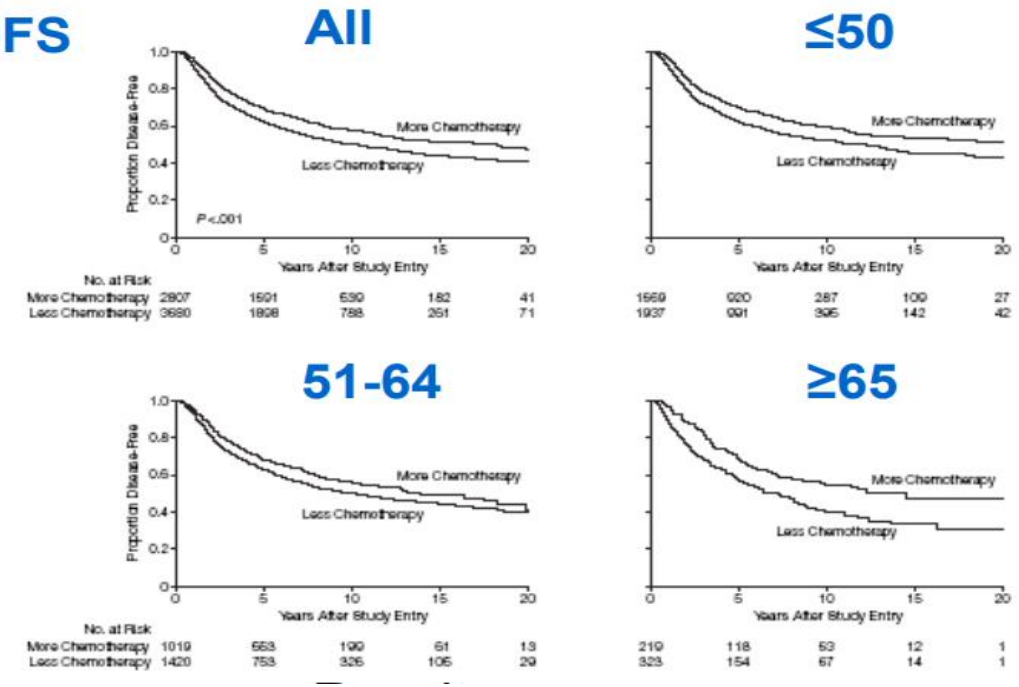
lin Oncol . 2019 Dec 20;37(36):3475-3483

Adjuvant chemotherapy among breast cancer

- To compare the benefits and toxic effects of adjuvant chemotherapy among breast cancer patients in age groups of 50 years or younger, 51 to 64 years, and 65 years or older.
- There was no association between age and disease-free survival. Overall survival was significantly (P<.001) worse for patients aged 65 or older because of death from causes other than breast cancer.

JAMA. 2005 Mar 2;293(9):1073-81

DFS



OS

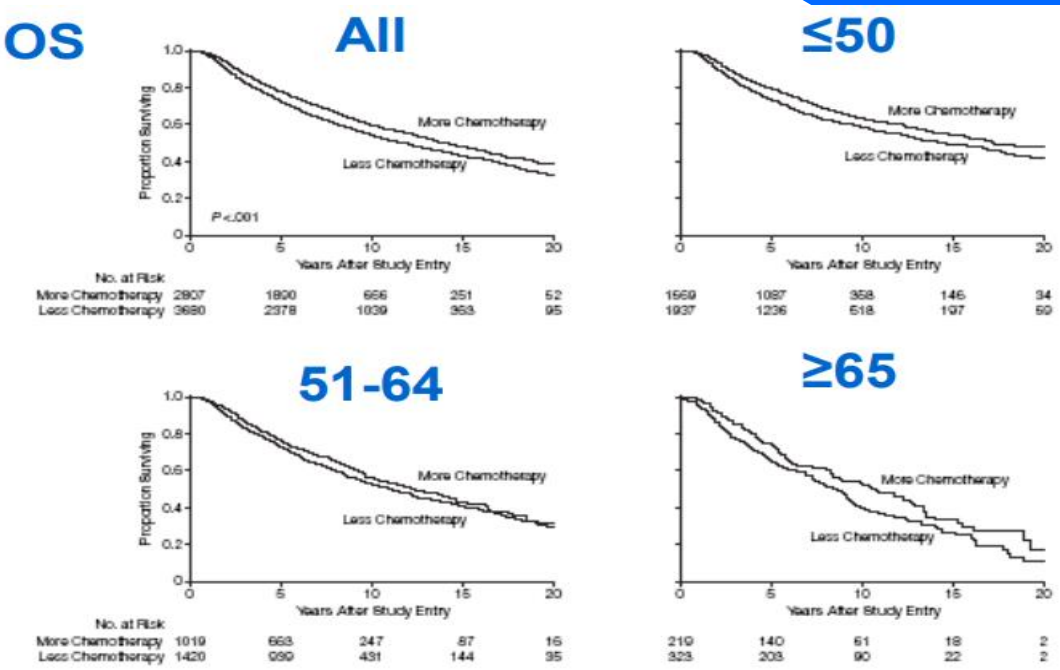


Table 3. Incidence and Causes of Treatment-Related Death

	Age, y			
	≤50 (n = 3506)	51-64 (n = 2439)	≥65 (n = 542)	Total (n = 6487)
Death due to treatment, No. (%) [95% CI]	8 (0.2) [0.1-0.5]	17 (0.7) [0.4-1.1]	8 (1.5) [0.6-2.9]	33 (0.5) [0.4-0.7]
Specific cause of death, No.				
Cardiac toxicity	4	2	1	7
Thromboembolism	1	3	2	6
AML/MDS	0	4	1	5
Infection	2	2	1	5
Other/unknown	1	6	3	10

Abbreviations: AML, acute myelogenous leukemia; CI, confidence interval; MDS; myelodysplastic syndrome.

JAMA. 2005 Mar 2;293(9):1073-81

CARG-BC score

CARG-BC Risk Score

Risk factors for Gr. 3-5 Toxicity	OR (95% CI)	Score
CARG Score: Medium Risk High Risk	2.47 (1.35-4.51) 2.26 (0.70-7.35)	3
Anthracycline	1.37 (0.65-2.85)	1
Stage II/III	1.79 (1.00-3.23)	2
Duration of tx > 3 months	2.98 (1.46-6.09)	4
Abnormal liver function	2.21 (0.90-5.47)	3
Limited in walking a mile	2.22 (1.21-4.05)	3
Lack of someone to provide advice	2.34 (0.99-5.58)	3

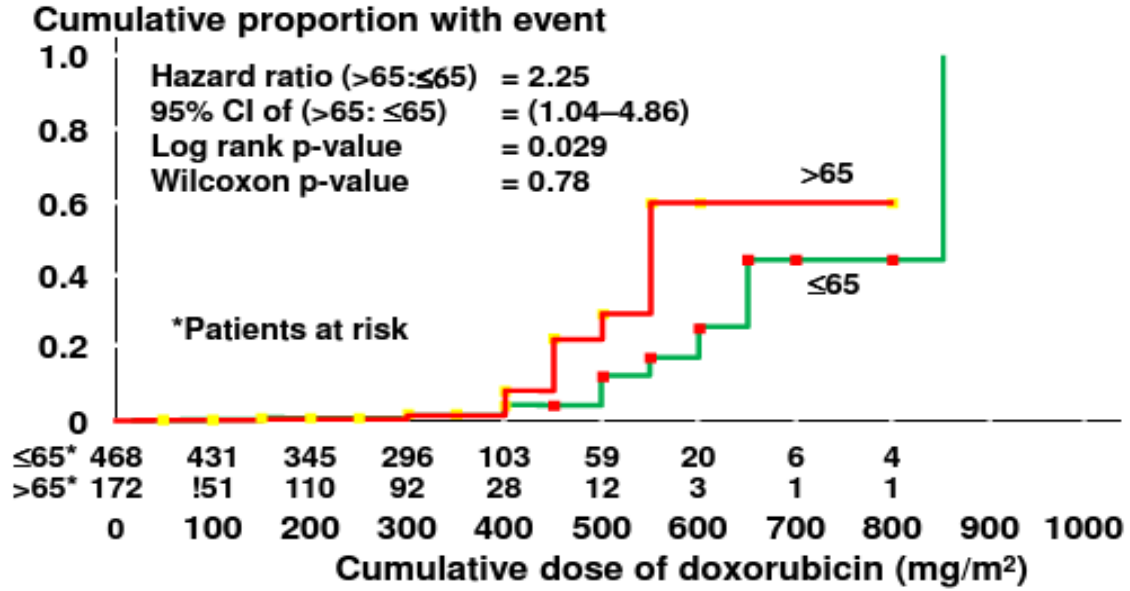
low risk = 0 to 5 points, intermediate risk = 6 to 11 points, and high risk = at least 12 points.

- Among all patients, grade 3 to 5 toxicity occurred in 22%, 51%, and 81% of patients in low-, intermediate-, and high-risk groups, according to CARG-BC score.
- validation cohort, prediction of grade 3 to 5 toxicity was better with the CARG-BC score vs the generalized CARG toxicity tool (AUCs = 0.69 vs 0.56, P = .004) vs physician-rated Karnofsky performance status (AUC = 0.50, P < .001).

J Clin Oncol. 2021 Feb 20;39(6):608-618

Doxorubicine, CHF and age

- 630 patients (3 phase III) with 32 CHF
  - 26% >550 mg/m²
  - >50%: reduction of LVEF <30% w/CT
- HR_{age} 2.25 (1.04–4.86) vs 3.28 (1.4–7.65) if >400 mg/m²



Swain. Cancer 2003

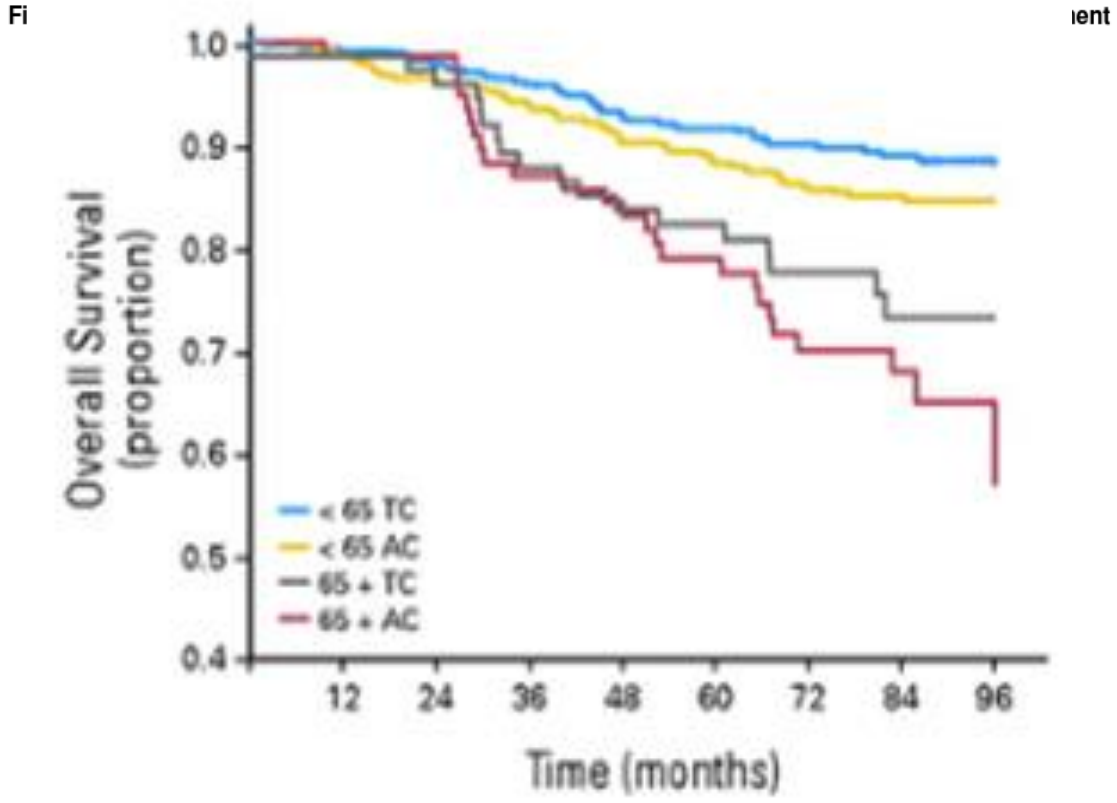
SEER 1992-2002: 43,338 women 66-80 years, no CHF history
- stage I to III BC, chemotherapy vs no
- AC: younger, fewer comorbidities, advanced (p=.001)
- $CHF_{10\ years}$ (%)

AC	Other chemo	No chemo
N = 4,712	N = 3,921	N = 34,705
38.4	32.5	29

- Women aged 66 to 70 years who received adjuvant anthracyclines had significantly higher rates of CHF.

J Clin Oncol . 2007 Sep 1;25(25):3808-15.

AC vs TC 7-Year Follow-Up of US Oncology Research Trial 9735



- 7 years follow-up, the difference in DFS between TC and AC was significant (81% TC v 75% AC; P = .033; HR, 0.74) as was OS (87% TC v 82% AC; P = .032; HR, 0.69)
- TC was superior in older patients as well as younger patients.
- Older women experienced more febrile neutropenia with TC and more anemia with AC.

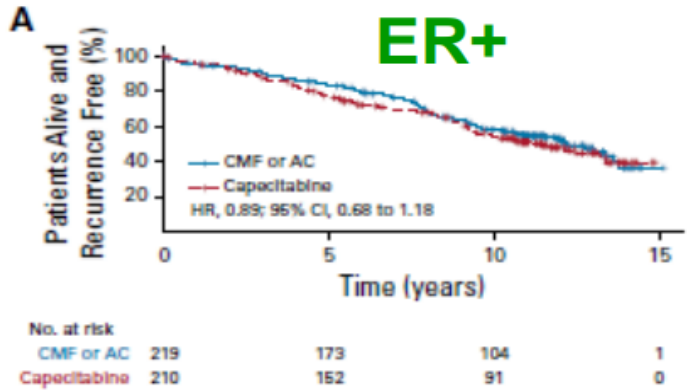
CALGB 49907 (AC or CMF vs X)

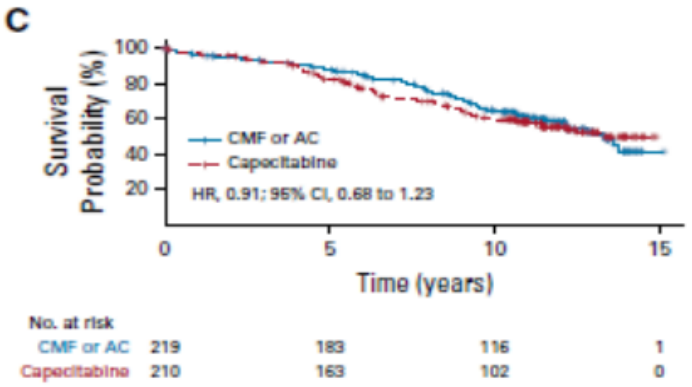
RFS 56% vs 50%
(HR 0.80; *P* = .03)
BCSS 88% vs 82%
(HR 0.62; *P* = .03)
OS 62% vs 56%
(HR 0.84; *P* = .16)

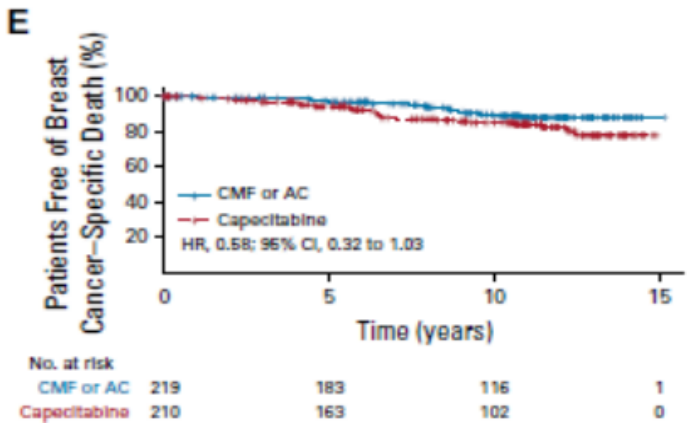
ER+ (HR 0.89; *P* = .43)
ER- (HR 0.66; *P* = .02)

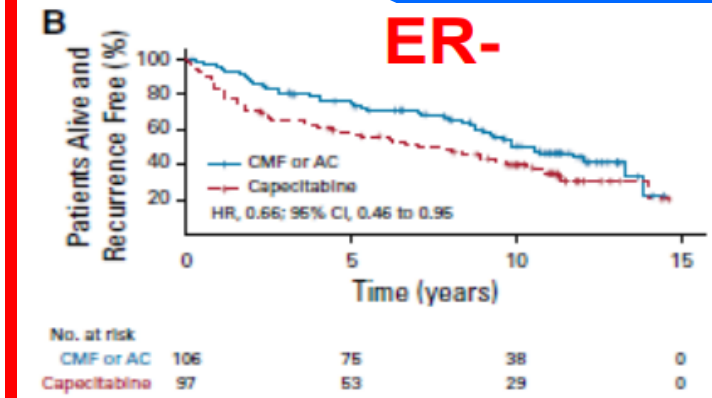
43.9% deaths
(13.1% BC vs 16.4% others vs 14.1% ?)

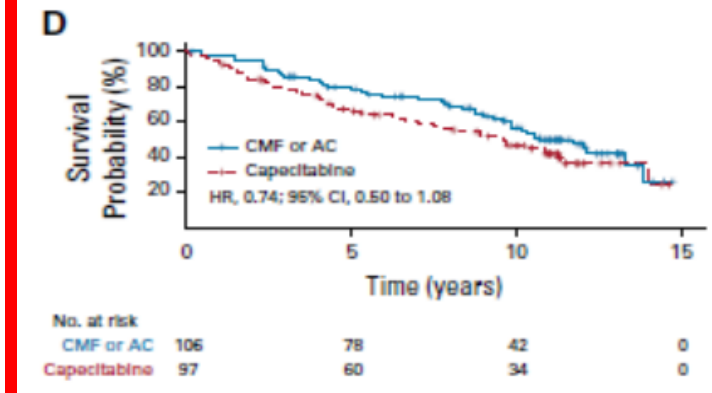
Second non BC 14.1%

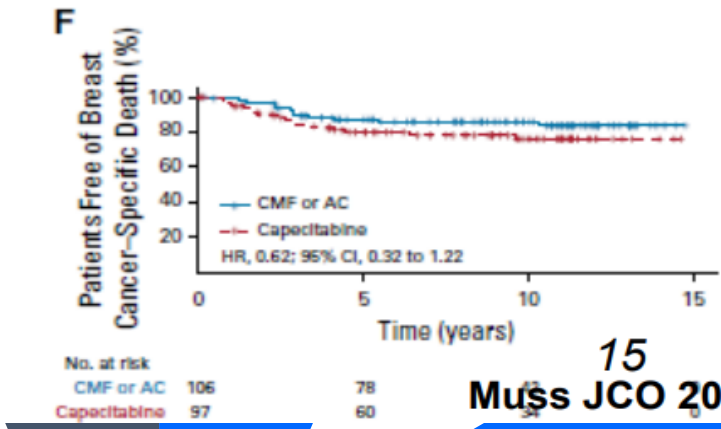






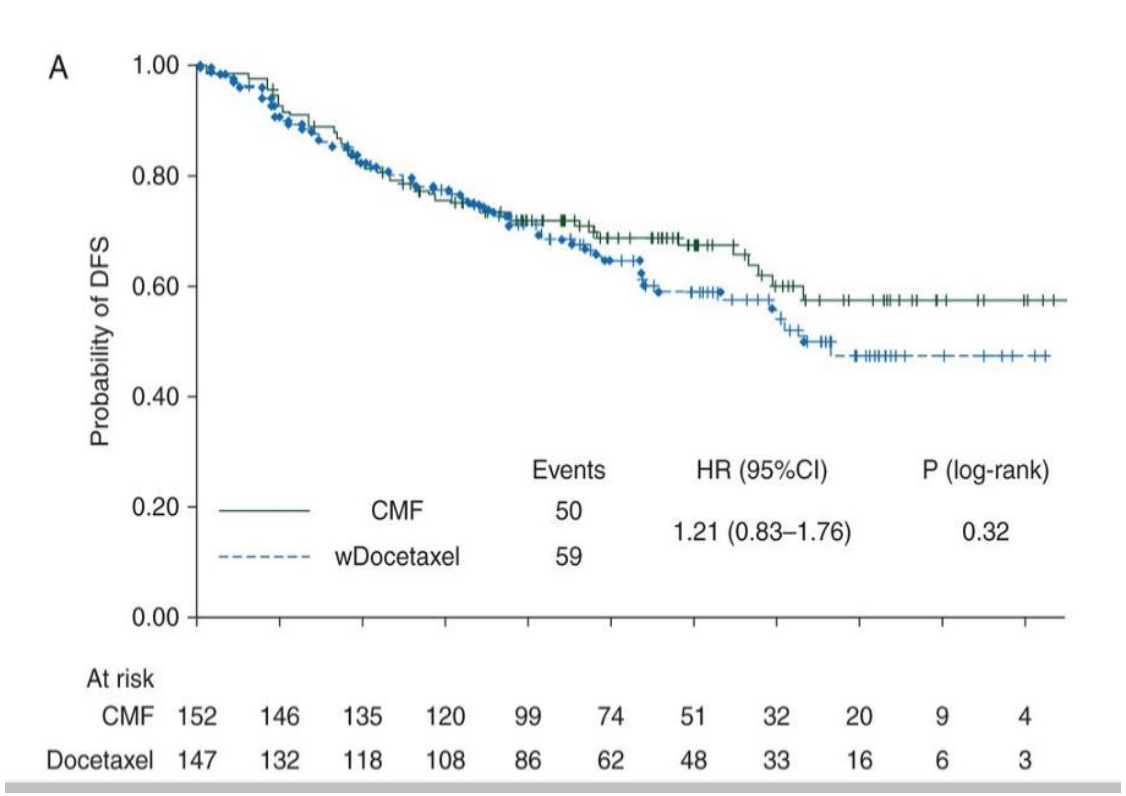


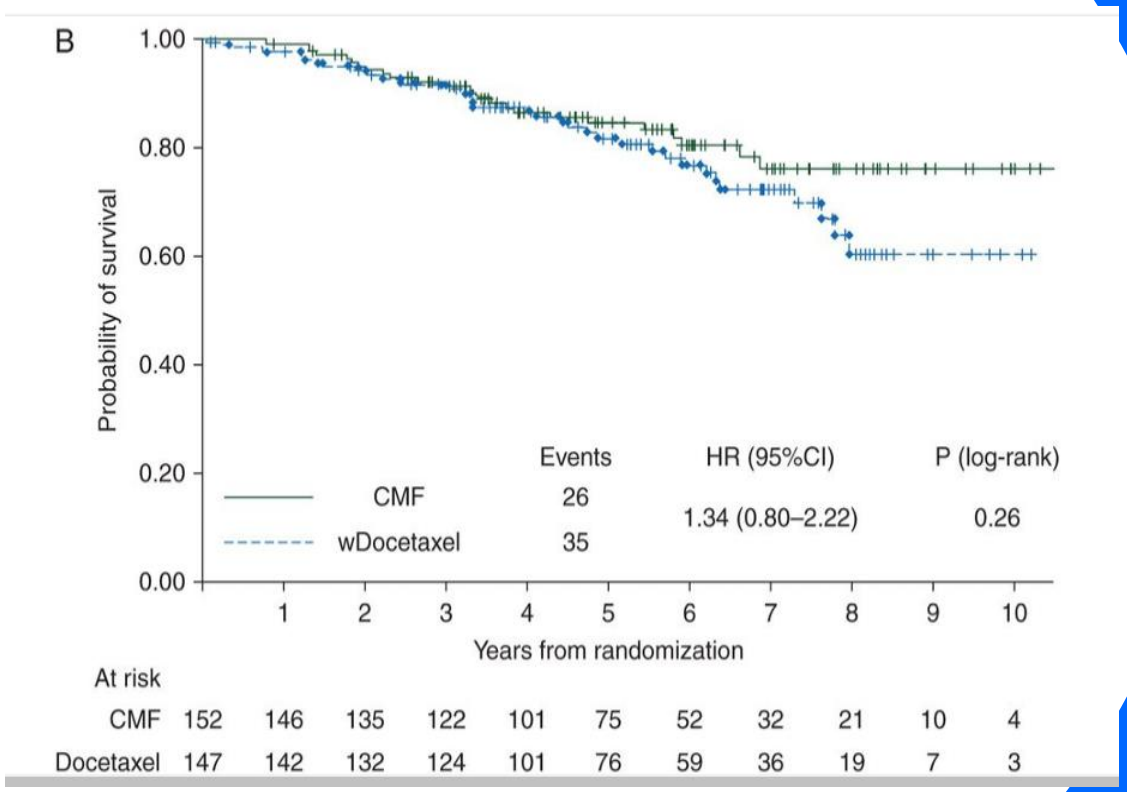




15
Muss JCO 2019

Adjuvant Weekly docetaxel versus CMF phase III ELDA trial





- Weekly docetaxel is not more effective than standard CMF as adjuvant treatment of older women with breast cancer and worsens QoL and toxicity.

Ann Oncol. 2015 Apr;26(4):675-682

The incidence of CHF from the Finnish Herceptin Study (FINHER), Herceptin Adjuvant trial (HERA), Breast Cancer International Collaborative Group trial 006 (006)

- NSABP B31
  - Age
    - 2% < 50 yo vs 5.4% > 60 yo
  - LVEF > 4 AC
    - 12% if LVEF < 55%
  - Concomitant > sequential
  - Hypertension comedications
- B31/N9831
  - 6.7% pts who had completed AC had a lower LVEF or developed cardiac symptoms preventing the initiation of TZT
  - 1/3 pts who started TZT discontinued it: 4.7% with symptomatic CHF, 14.2% with confirmed asymptomatic decline in LVEF, and the rest for noncardiac reasons

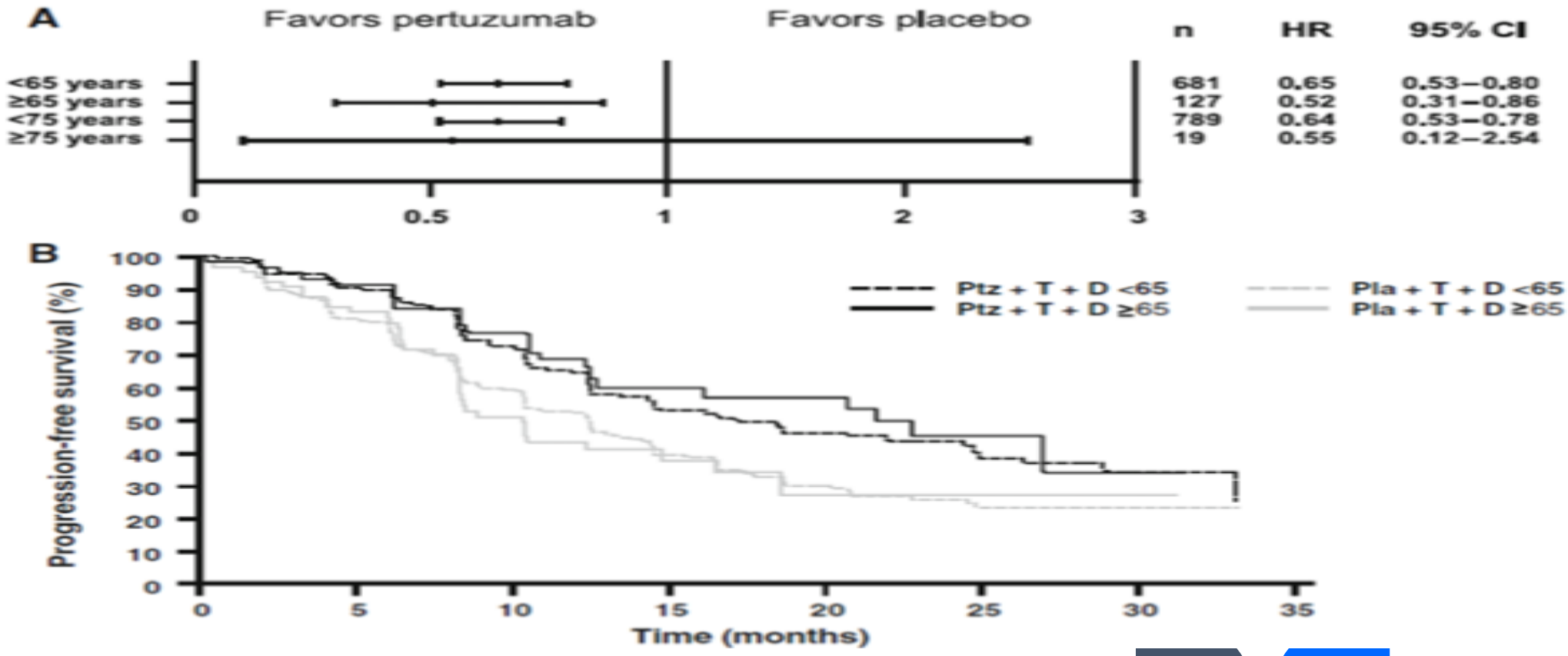
Clin Cancer Res . 2008 Jan 1;14(1):14-24

General recommendations for adjuvant chemo & trastuzumab in older BC patients

- **Focus** on ER- and HER2+ (if > 5 mm)
- **Regimen**
  - **Validated** — **4 AC, 6 CMF**
  - Options — 4 TC; paclitaxel qw x 12?; liposomal doxorubicin?
  - No! — capecitabine, docetaxel qw
  - **No data!** — Sequential regimen
- **Primary prophylaxis** of febrile neutropenia w/ G-CSF
- **No restriction on trastuzumab if chemo indicated**
  - **4 TC + trastuzumab**
  - **Paclitaxel qw x 12 + trastuzumab (Tolaney)**
  - *TCH x 6?? (but very unlikely in older patients since carboplatin AUC 6!)*
  - **Trastuzumab alone: can be considered, especially for unfit patients** (+ ET if ER+)
  - **Shorter duration for trastuzumab** (6 months?)

Cheung, Livi, Brain in Geriatric Oncology/Elsevier, Editors Extermann, Fulop, Dale, Klepin & Brain 2019
Brain J Ger Oncol 2019

CLEOPATRA : PFS benefit with pertuzumab arm (<65 years: HR: 0.65; and ≥65 years: HR: 0.52). Diarrhea, fatigue, asthenia, decreased appetite, vomiting, and dysgeusia were reported more frequently in patients 65 years of age or older



CLEOPATRA suggest that the combined use of pertuzumab, trastuzumab, and docetaxel should not be limited by patient age.

T-DM1 Kamilla study

- 373 pts ≥ 65 yrs.
- Pts ≥ 65 yrs vs younger: Median exposure was 8 cycles in each group.
- The incidence of grade ≥ 3 AEs and AE-related discontinuations were greater in older pts.

Outcome, n (%)	≥ 65 yrs (n = 373)	< 65 yrs (n = 1628)
Discontinuation due to AEs (% based on pts who discontinued)	41 (14.3)	112 (9.5)
Fatal AEs	10 (2.7)	17 (1.0)
Grade ≥ 3 AEs	160 (42.9)	540 (33.2)

Triple negative BC

- Adjuvant : A retrospective study by CALGB found that older and younger women derived similar reductions in breast cancer mortality and recurrence.
- Metastatic: ATHENA study reported that **bevacizumab plus paclitaxel** provided a median PFS of 10.4 months in patients aged ≥ 70 years, comparable with original study population (9.5 months) and in the E2100 trial (11.8 months).
- In this sub-analysis, **older patients had an increased rate of hypertension and proteinuria**

%	< 70 N = 2,018	70+ N = 233*
HBP gade ≥ 3	4.2	6.9
Proteinuria grade ≥ 3	1.5	4.0
ATE (A or V)	3.3	2.9
Stop for toxicity	15	23
ATE	1.8	2.9
CHF	0.3	0.6
HTN	1.8	2.9

*175 (7.8%) 70+, 51 (2.3%) 75+, 7 (0.3%) 80+

Ann Oncol. 2012 Aug;23 Suppl 6:vi52-5

ATHENA: CT w/o anthracyclines+ beva

%	< 70 N = 2,018	70+ N = 233*
HBP gade ≥ 3	4.2	6.9
Proteinuria grade ≥ 3	1.5	4.0
ATE (A or V)	3.3	2.9
Stop for toxicity	15	23
ATE	1.8	2.9
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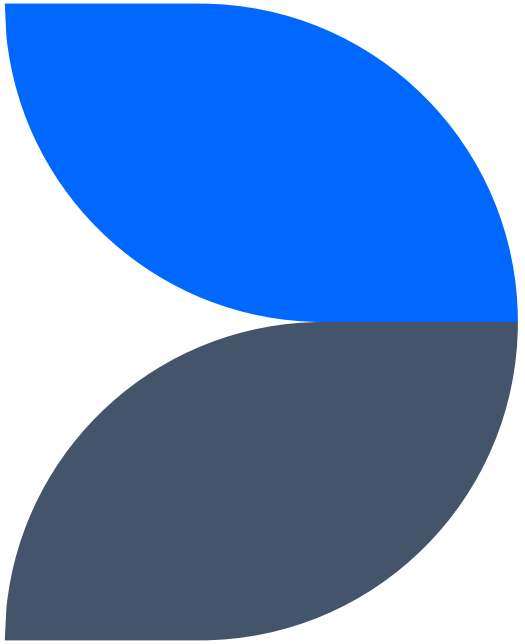
HTN	1.8	2.9

*175 (7.8%) 70+, 51 (2.3%) 75+, 7 (0.3%) 80+

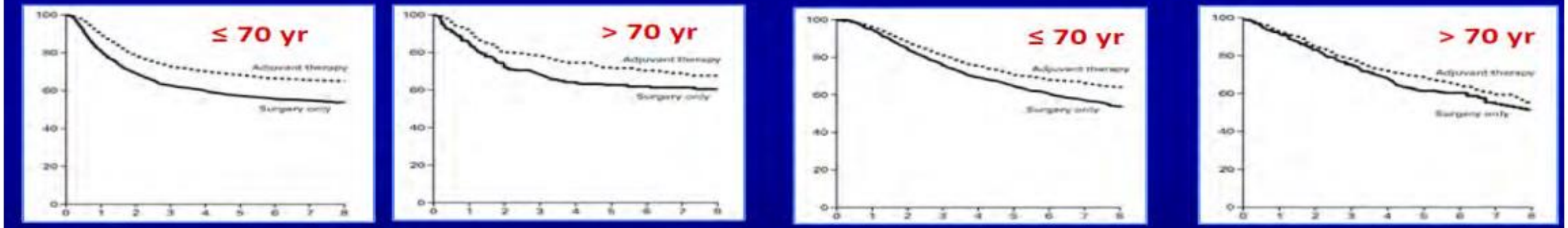
Colon cancer



Adjuvant single agent 5FU in elderly patients

7 phase III trials N = 3351 patients stade II (47%) and III (57%)
15% > 70 years
0.7% > 80 years
Fluoropyrimidines-based chemotherapy

DFS **OS**



HR for OS after 70 years: 0.76 (0.68-0.85)
No significant interaction observed between age and efficacy of treatment

Sargent D et al. NEJM 2001

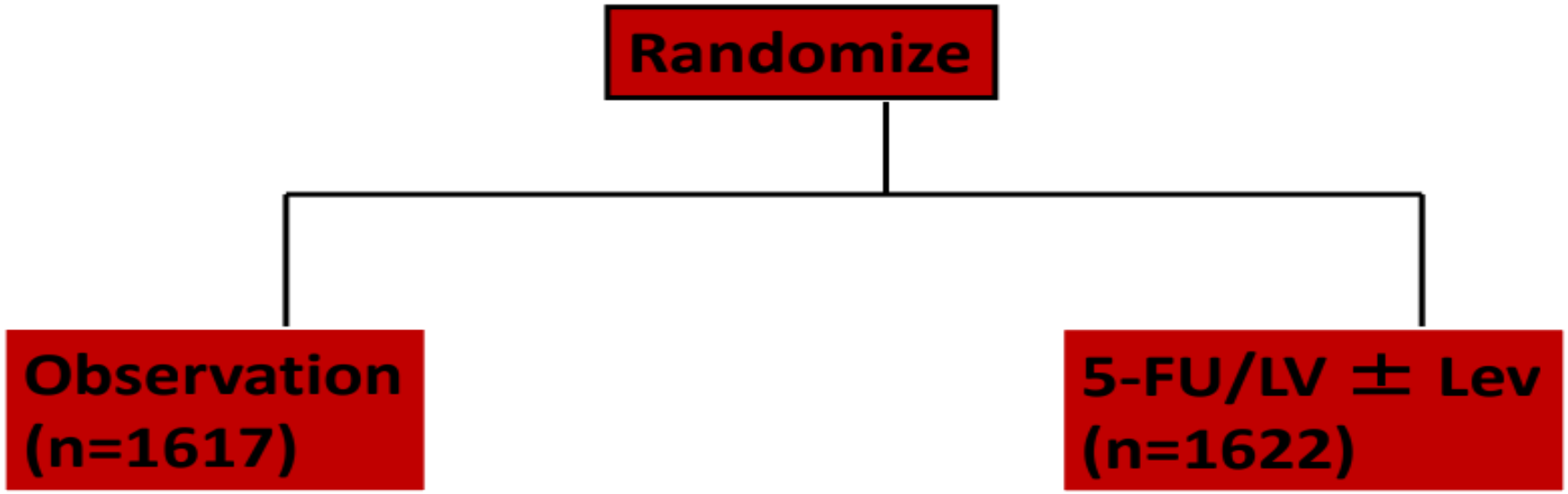
Adjuvant chemotherapy for stage II with poor prognostic features

- 20,847 pts with stage II cancer (SEER database)
- Pts 66 and older, between 1992 and 2005
- 75% had at least one poor prognostic feature
- HR (1.02 vs 1.03, non-poor vs poor) for the benefit of chemotherapy

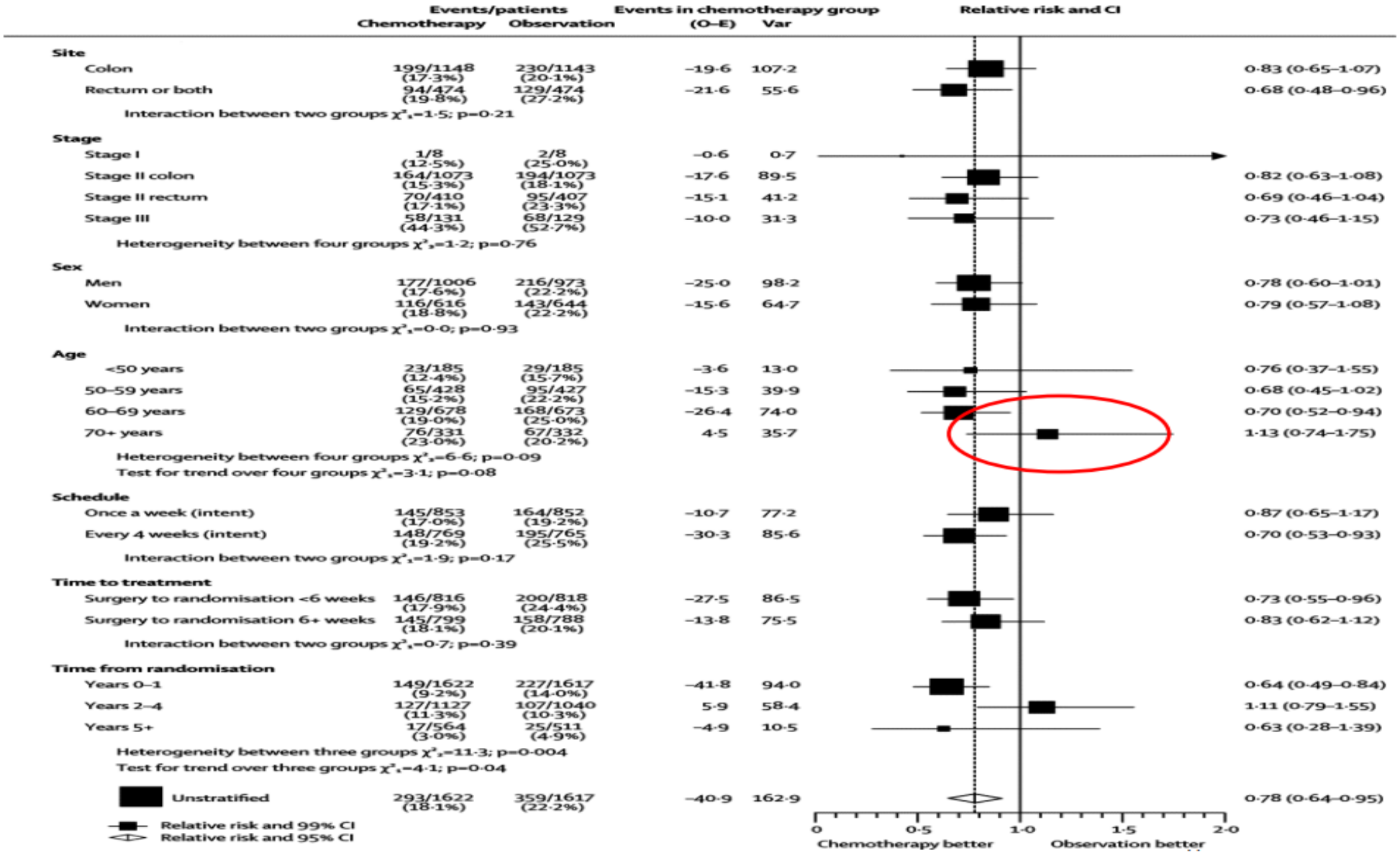
O'Connor E et al J Clin Oncol 2011;29:3381-3388

Quasar study

'Uncertain indication'
for chemotherapy
(3239 patients '94 -'03)



R Gray et al The Lancet 2007



R Gray et al The Lancet 2007

Liver metastsectomy in elderly patients

- 7764 pts evaluated for outcome of liver surgery in an international multi-centre cohort
- 12.9% 70-75 yrs, 6% 75-80 yrs, 2% over 80 yrs
- Pre-op chemo used less frequently
- Less likely to have multi-nodular and bilateral lesions ie selected population
- Higher 60-day post-op mortality and morbidity than in younger pts
- 3-yr OS: 57.1%
- Independent predictors for survival: > 3 lesions, bilobar mets, concomitant extra-hepatic disease

Adam R et al BJS 2010;97:366-367

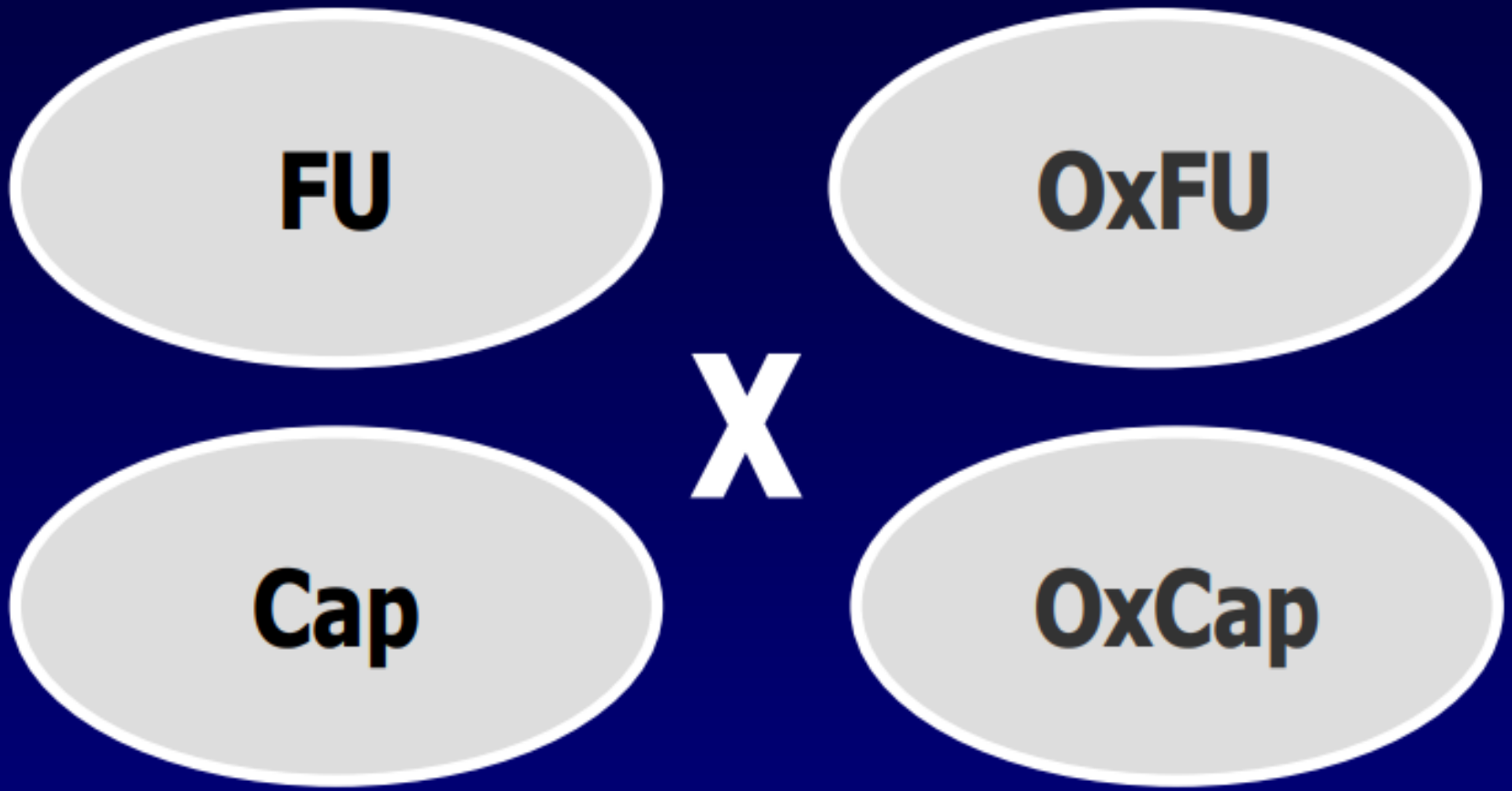
CANCER RESEARCH UK

MRC FOCUS2

Chemotherapy choices and doses in frail and elderly patients with advanced colorectal cancer

Matt Seymour, Tim Maughan, Harpreet Wasan, Alison Brewster, Steve Shepherd, Sinead O'Mahoney, Beth May, Lindsay Thompson, Angela Meade and Ruth Langley,
on behalf of
The UK NCRI Colorectal Clinical Studies Group and FOCUS2 Investigators

Trial Design: 2x2 Factorial



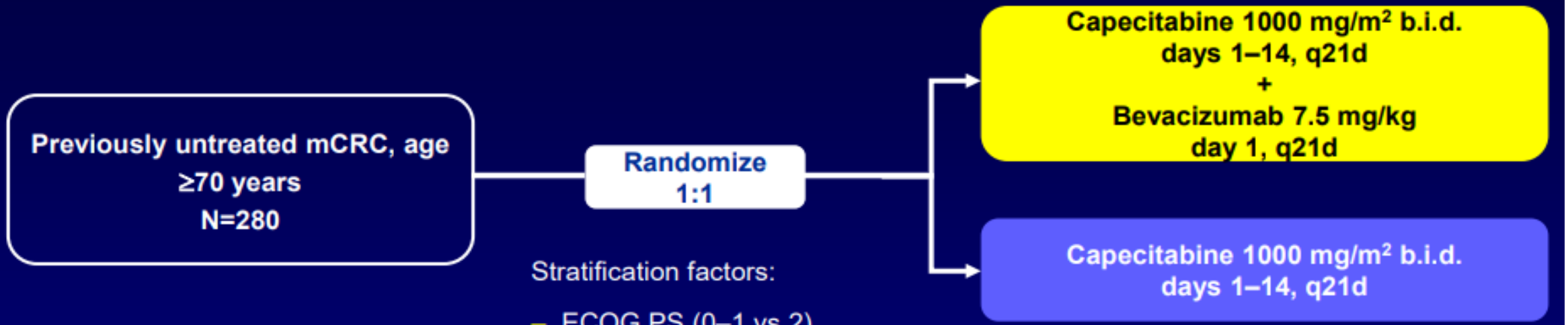
Overall Survival

Factorial Overall Survival	HR (95% CI)	p-value
no oxaliplatin vs oxaliplatin [FU + Cap] vs [OxFU + OxCap]	0.99 (0.81, 1.18)	p=0.91
FU vs capecitabine [FU = OxFU] vs [Cap + OxCap]	0.96 (0.79, 1.17)	p=0.71

115	94	81	60	38	29	15
115	102	82	62	43	30	20
115	94	78	62	44	29	23
114	100	81	67	49	28	16

Seymour et al The Lancet 2011;377:1749-1759

AVEX Trial: A prospective trial in elderly patients



- **Key inclusion criteria**
  - **ECOG PS 0–2**
  - **Prior adjuvant chemotherapy allowed if completed >6 month before inclusion**
  - **Not optimal candidates for a combination chemotherapy with irinotecan or oxaliplatin**

- **Key exclusion criteria**
  - **Prior chemotherapy for mCRC or prior adjuvant anti-VEGF treatment**
  - **Clinically significant cardiovascular disease**
  - **Current or recent use of aspirin (>325 mg/day) or other NSAID**
  - **Use of full-dose anticoagulants or thrombolytic agents**

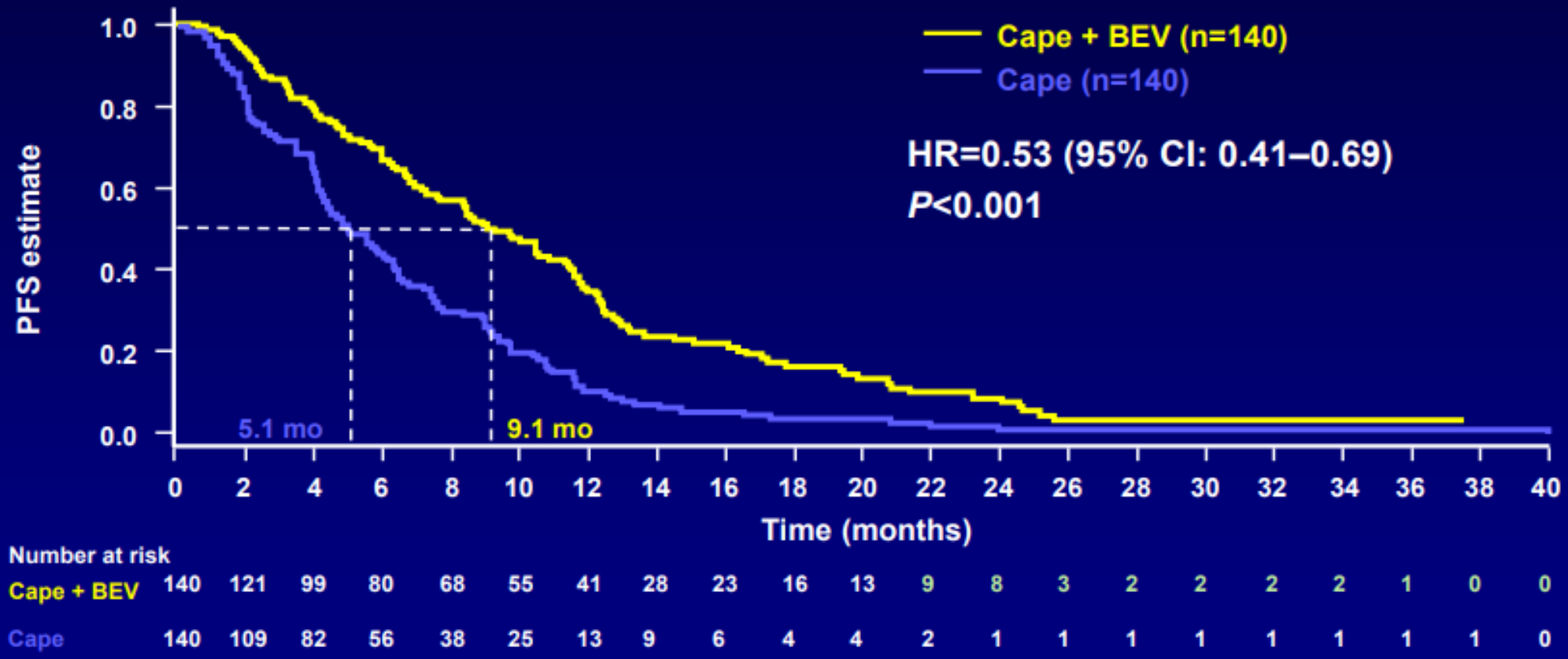
Select baseline patient characteristics

		Cape + BEV (n=140)	Cape (n=140)
Sex, %	Female	40.0	40.0
Median age, years (range)		76 (70–87)	77 (70–87)
	<75 years, %	39.3	32.9
	≥75 years, %	60.7	67.1
ECOG performance status, %	0	50.0	42.9
	1	41.4	47.9
	2	7.1	7.9
Prior adjuvant therapy, %	Yes	32.1	18.6
Site of metastatic disease, %	Liver	62.9	67.9
	Lung	35.7	40.7
	Other	35.0	22.9
	Liver only	37.1	38.6
Surgical resection, %	Yes	73.6	63.6
Location of primary disease, %	Colon only	57.9	54.3
	Rectum	31.4	25.0
	Colon and rectum	10.7	19.3

ITT population. Cape = capecitabine; ECOG PS = Eastern Cooperative Group performance status.

Cunningham D et al Lancet Oncol 2013; 14: 1077-1085.

Progression-free survival

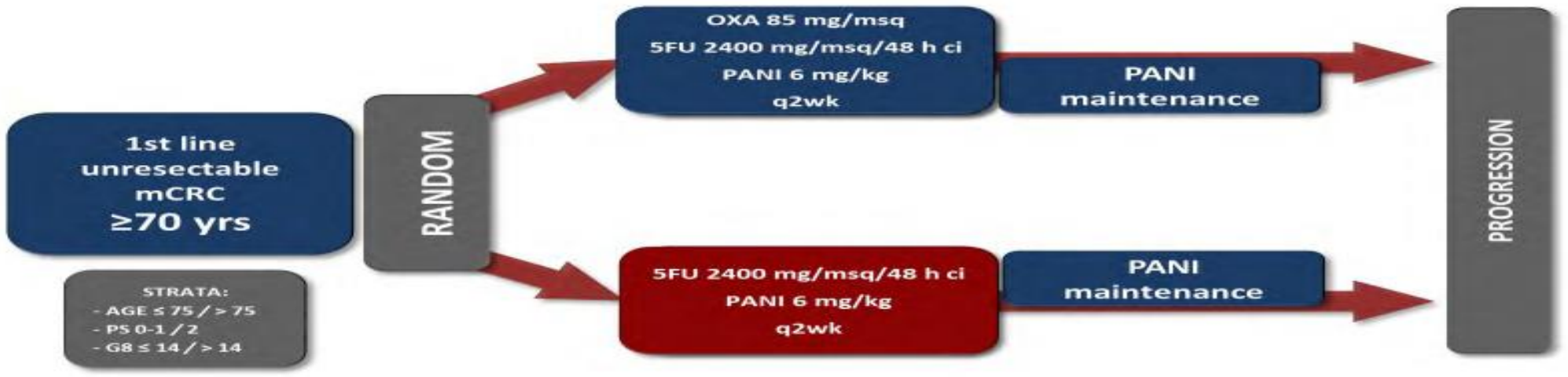


ITT population. 113 PFS events in the Cape + BEV arm; 127 PFS events in the Cape arm. CI = confidence interval; PFS = progression-free survival

Cunningham D et al Lancet Oncol 2013; 14: 1077-1085.

PANDA study: 1st-line FOLFOX plus panitu versus 5FU plus panitu in RAS-BRAF wild-type mCRC elderly patients

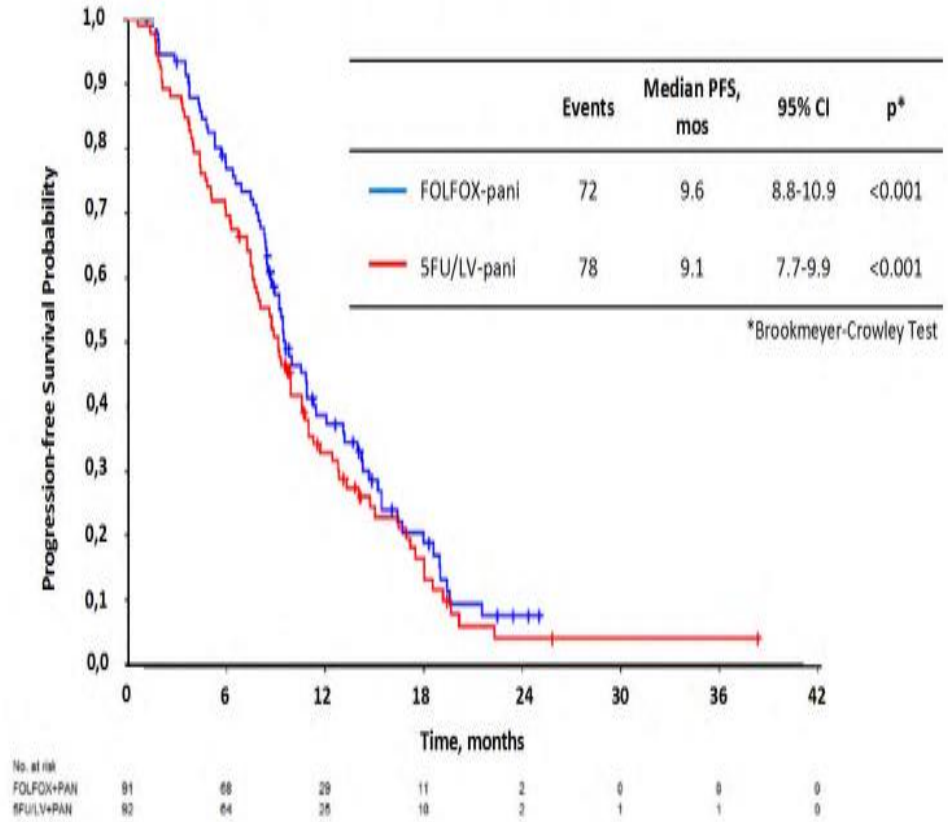
Study design



Sara Lonardi et al ASCO 2020

Primary Endpoint: Progression-free Survival

Median follow up: 20.5 mos (Data Cutoff: 04 Feb 2020)



	Events	Median PFS, mos	95% CI	p*
FOLFOX-pani	72	9.6	8.8-10.9	<0.001
5FU/LV-pani	78	9.1	7.7-9.9	<0.001

*Brookmeyer-Crowley Test

Best Response (RECIST Criteria)	ARM A FOLFOX + PANI N= 91	ARM B 5FU/LV + PANI N= 92
Complete Response	3%	5%
Partial Response	62%	52%
Stable Disease	23%	29%
Progressive Disease	3%	10%
Not Assessed	9%	4%
Overall Response Rate (CR+PR)	65% (95%CI 54-74)	57% (95%CI 46-67)
Disease Control Rate (CR+PR+SD)	88% (95%CI 79-94)	86% (95%CI 77-92)

Sara Lonardi et al ASCO 2020

TOXICITY AND EFFICACY OF 1ST LINE CETUXIMAB-BASED THERAPY IN RAS WILDTYPE (WT) OLDER PATIENTS (PTS) WITH METASTATIC COLORECTAL CANCER (MCRC): A POOLED ANALYSIS FROM 1,274 PTS IN THE ARCAD DATABASE

Demetris Papamichael MD[1], Guilherme S Lopes PhD[2], Curtis L Olswold[2], Benoist Chibaudel MD[3], John Zalcberg MD[4], Eric Van Cutsem MD[5], Alan P Venook MD[6], Timothy S Maughan FRCR[7], Volker Heinemann MD[8], Richard Kaplan MD[9], Bokemeyer Carsten MD[10], Heinz-Josef Lenz MD[11], Takayuki Yoshino MD[12], Richard A Adams FRCP[7], Axel Grothey MD[13], Aimery de Gramont MD[3], Qian Shi PhD[2]

SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

Fondation A.R.C.A.D
Aide et Recherche en CAncérologie Digestive

RAS WT pts ≥ 70 years old were more likely than pts < 70 to have ECOG PS ≥ 1, tumor in the right colon, and metastasis in lungs. Age groups (< 70 vs. ≥ 70) did not differ in sex, number of metastasis, and liver or peritoneum metastasis. (Table 1)

Pts ≥ 70 (vs < 70) had no difference in G3+ AE for neutropenia/leukopenia, diarrhea or nausea/vomiting.

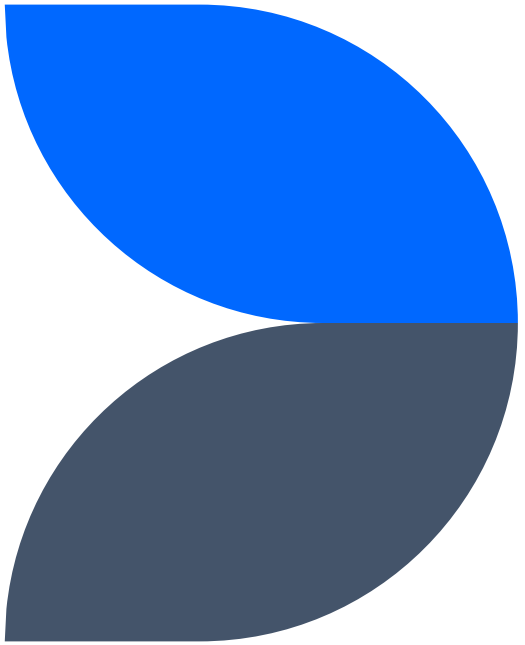
When comparing DC +/- cetuximab, no significant difference in OS was observed within each age group. PFS and RR improved by adding cetuximab in pts < 70 but not in pts ≥ 70. Interaction tests were not significant.

Pts ≥ 70 (vs < 70) receiving DC + cetuximab had similar PFS but inferior OS.

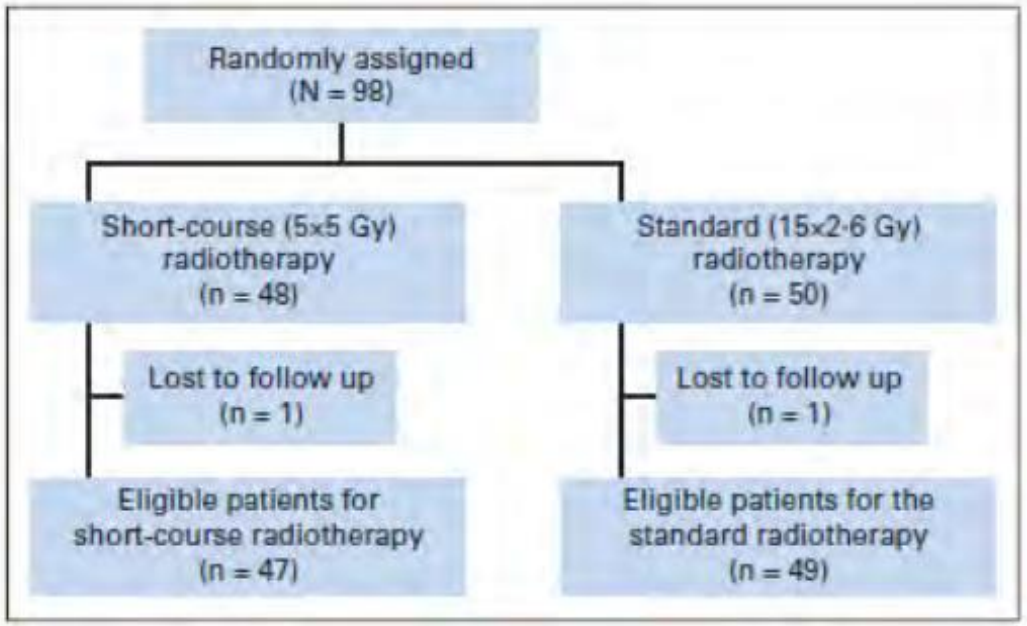
In conclusion: Pts with RAS WT mCRC ≥ 70 years old had comparable toxicity and similar efficacy to their younger counterparts when cetuximab was added to DC and adjusting for key confounders. This is the most comprehensive analysis so far on the use of cetuximab in RAS WT older pts.

Others

- GBM
- Head and Neck



GBM: Short-course radiotherapy a possible solution for frail/elderly patients affected by GBM

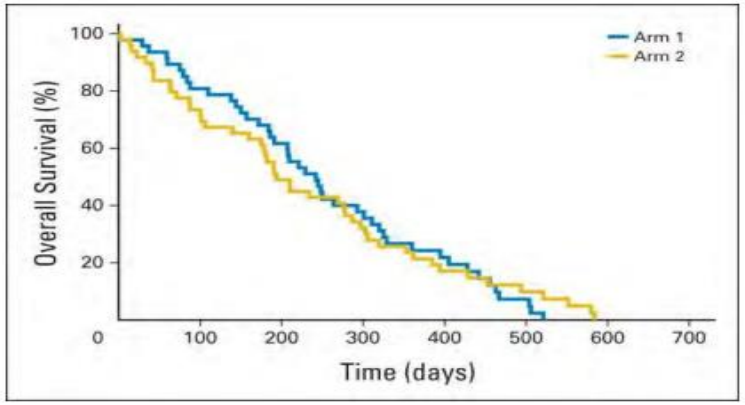


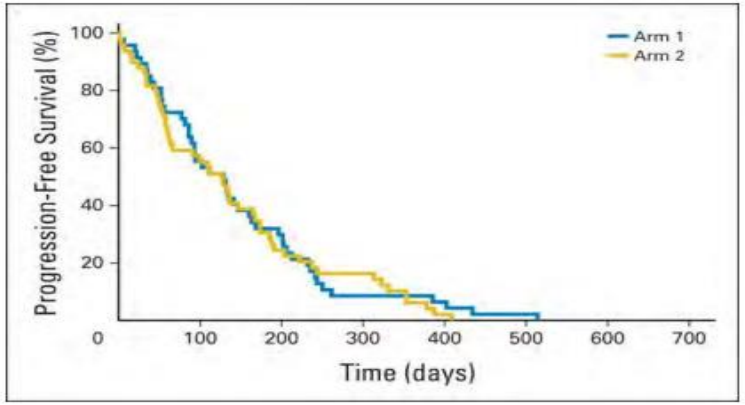
- 98 patients
  - **Frail**: age ≥50 years and KPS 50-70
  - **Elderly and frail**: age ≥65 years and KPS 50-70
  - **Elderly**: age ≥65 years and KPS 80-100
- Short-course RT (5x5 Gy) vs standard hypofractionated-RT (15x2.6 Gy)

Arm 1 received short-course radiotherapy (25 Gy in five daily fractions over 1 week), and arm 2 received commonly used radiotherapy (40 Gy in 15 daily fractions over 3 weeks).

J Clin Oncol. 2015 Dec 10;33(35):4145-50

GBM: Short-course radiotherapy a possible solution for frail/elderly patients affected by GBM





Roa et al JCO 2015

25 in # 5 Gy vs 40 in #15

PFS	4.2 months	vs	4.2 months	*p=0.716*
OS	7.9 months	vs	6.4 months	*p=0.988*

With a median follow-up time of 6.3 months, **HRQoL** between both arms at **4 weeks and 8 weeks** after treatment was not different

Short-course RT was noninferior to commonly used RT

In view of the reduced treatment time, the short 1-week RT regimen may be recommended as a treatment option for elderly and/or frail patients with newly diagnosed glioblastoma

ESMO

Reducing Temozolomide?

Short-Course Radiation plus Temozolomide in Elderly Patients with Glioblastoma

James R. Perry, M.D., Normand Laperriere, M.D., Christopher J. O'Callaghan, D.V.M., Alba A. Brandes, M.D., Johan Menten, M.D.,

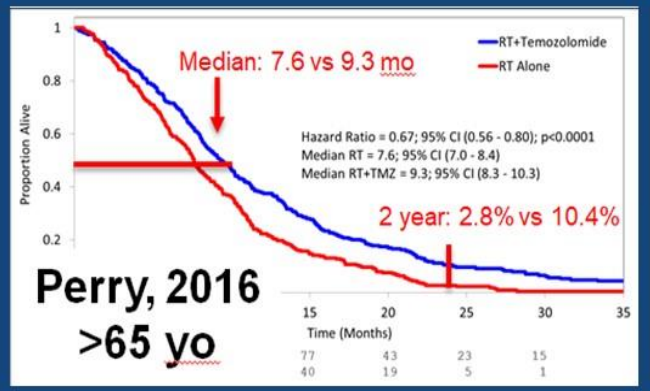
N Engl J Med 2017

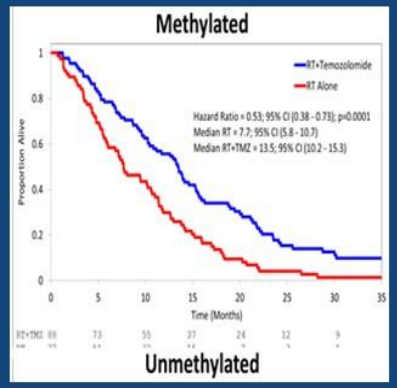
Concurrent

Radiation

No TMZ

NCIC CTG CE.6 (Perry, NEJM 2017)	Phase III, 562 pts, 65 years or older, randomized to short course RT (40 Gy/15 fx) +/- TMZ (adjuvant + concurrent)	TMZ improved MS (9.3 vs 7.6 mo) and PFS (5.3 vs 3.9 mo); for MGMT unmethylated, MS 10 vs 7.9 mo (p = 0.055)





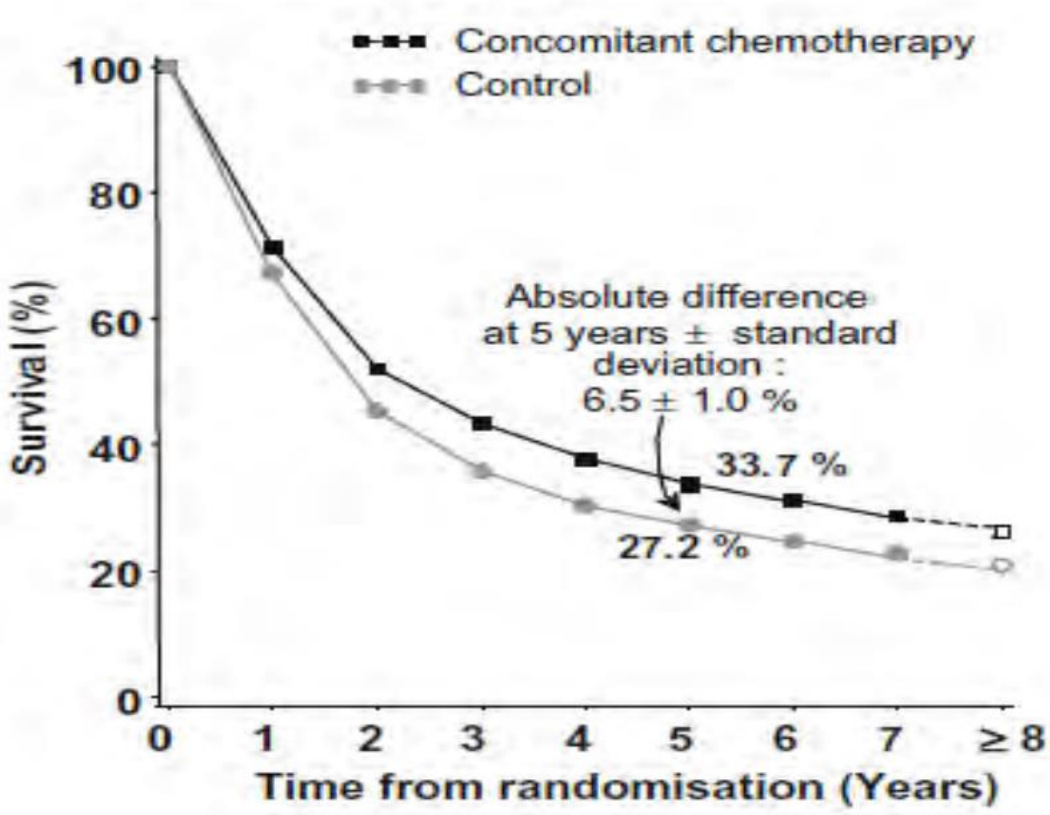
Conclusions

1. TMZ works in elderly
2. Best in MGMT methylated
3. 50% reduction in concurrent TMZ not compared to SOC

Head and Neck cancer

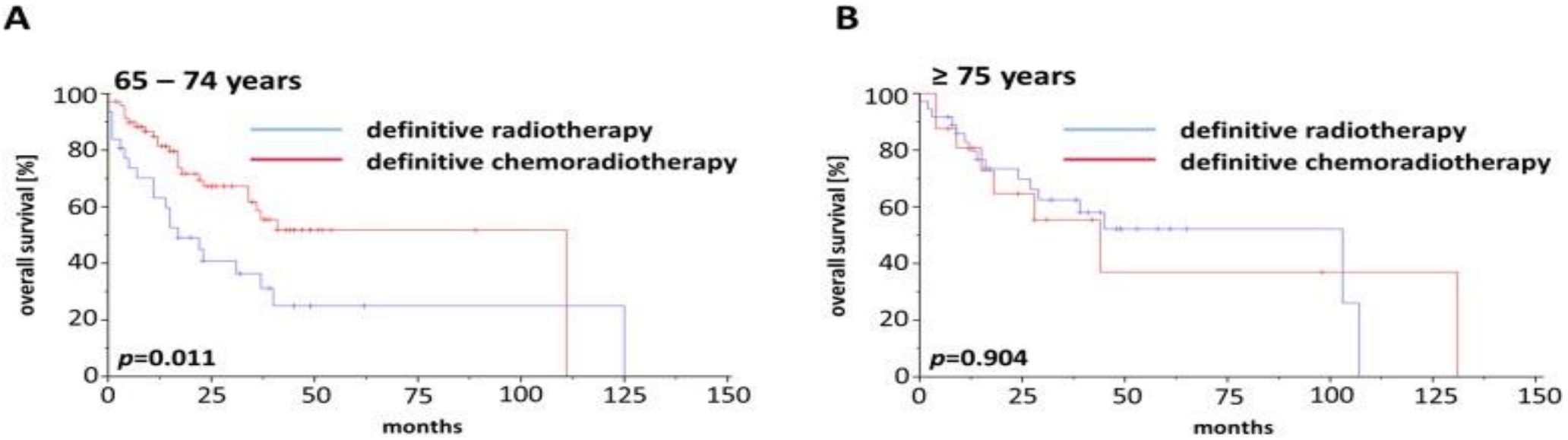
- 25% of all H&N patients are diagnosed >70 years of age, HPV-related tumors less common in elderly
- No prospective randomized data exist regarding the potential benefit of CCRT in elderly patients affected by locally advanced disease.

CCRT: SCCHN



- CRT Improves survival in locally advanced head and neck cancer
- Decreased survival benefit with age, specifically ≥71, observed on meta-analysis
- Only 6% of patients on meta-analysis were >70 years of age
- Under-represented elderly patient population on clinical trials

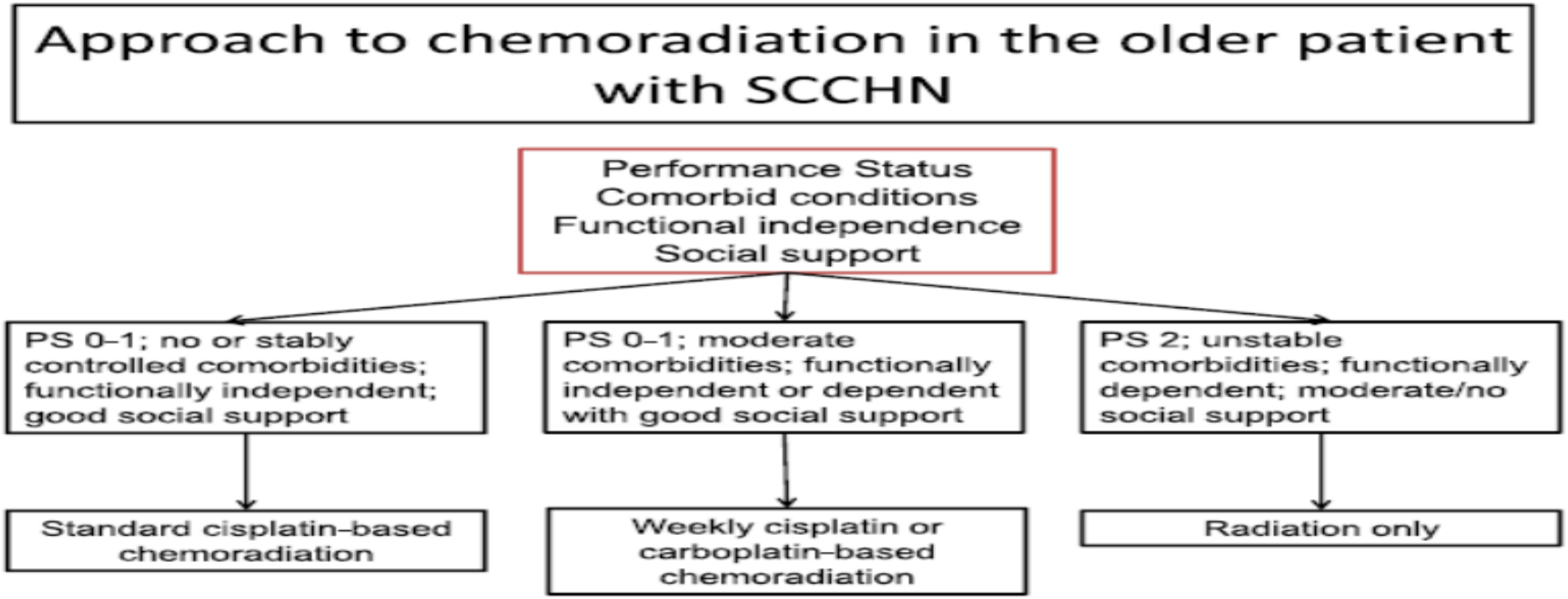
CCRT: Survival differed significantly between age groups with an OS of 40 and 22 months and a PFS of 23 and 12 months for patients aged 65–74 or ≥ 75 years, respectively ($p < 0.05$). Concomitant chemotherapy resulted in improved OS in patients aged 65–74 years compared to radiotherapy alone ($p < 0.05$) for definitive treatments, while patients ≥75 years did not benefit ($p = 0.904$).



OS of HNSCC patients treated by radiotherapy (blue line) or chemoradiotherapy (red line). a, b Elderly HNSCC patients aged 65–74 years (a) or ≥ 75 years (b) with definitive treatment.

Radiat Oncol. 2020; 15: 31.

Improved Method to Stratify Elderly Patients With Cancer at Risk for Competing Events



J Clin Oncol. 2016 Apr 10; 34(11): 1270–1277.

Case

- 78 year old male with Bright Red Blood per Rectum for the past 2 months. He has lost 3 pounds and denies any abdominal/rectal pain.
- Last colonoscopy normal 18 years ago.
- Sigmoidoscopy: friable non-obstructing rectal mass 10 cm from the anal verge.
  - Pathology: adenocarcinoma.

- Staging: MRI T3, N+.
- Metastatic workup negative.

What is Geriatric Assessment?[1]

Goals of Care: He looks forward to the next 10 years when his granddaughter is graduated from medical school. (She is currently in high school).

Basic Activities of Daily Living : Independent

Instrumental Activities of Daily living: Difficulty with taking medications

History of fall: Two times in the past year. He says he tripped.

Gait Speed: His Timed Up and Go: slightly >10 sec.

Comorbidities: Diabetes, Coronary Artery Disease, High Blood Pressure, High Cholesterol, Hypothyroidism.

Cognition: Mini-Mental Status Exam is 27/30.

Nutritional status: Three pounds weight loss in the past 3-4 months.

Emotional status: Distressed over the new diagnosis of cancer, but not depressed.

Social support: Adequate

GA interpretation and interventions

- Goal: Prolong life
- Vulnerabilities:
  - Physical – falls indicate limitations. Advice strength and balance training.
  - Cognitive? Make sure compliance is ok, written information. Caregiver history and info.
  - Nutritional? BMI? Consider advice and possibly supplement due to long treatment trajectory.
  - Comorbidities – primarily cardiovascular. Check medications and blood pressure. Interactions with planned chemotherapy?

Mohile et al, ASCO guideline JCO, 2018

Decision making for chemotherapy

Life expectancy

Comorbid conditions

Cancer and Aging Research Group (CARG) Toxicity Calculator

CRASH score

No adjuvant chemotherapy

Patient preferred not to receive adjuvant chemotherapy. In addition, for a family reason, he moved out of the US.

Six years after moving out of the US, age 84, he came back to the US complaining of abdominal distention, weight loss of 10 pounds, and more fatigued. His cat scan showed metastatic disease in the liver, and lungs.

Geriatric Assessment

Palliative Care Improves Quality of Cancer Care

Goals of Care: Not certain

Basic Activities of Daily Living : Dependent for grooming, bathing, and walking.
Instrumental Activities of Daily living: totally dependent.
History of fall: One fall, presyncopal episode.
Gait Speed: His Timed Up and Go: slightly >20 sec.
Comorbidities: Diabetes, Coronary Artery Disease, High Blood Pressure, High Cholesterol, Hypothyroidism, Atrial Fibrillation, Stroke.
Cognition: Mini-Mental Status Exam is 22/30.
Nutritional status: 10 pounds weight loss in the past 3 months.
Emotional status: Distressed over the recurrence of cancer.
Social support: Adequate

Lessons learned

We make progress

GA and intervention probably reduce toxicity of cancer treatment

GA and intervention may improve some dimensions of QoL

- Reduce unplanned Emergency Room visits
- And reduce unplanned hospitalizations

GA helps oncologists to communicate with patients

- Improves patients' satisfaction
- And facilitates implementation of Geriatric intervention on physical performance and functional status

Many cancer populations may benefit

- Including acute cancer if you have a good chance to get remissions
- And interventions should be tailored to the patients

Quality of life is a central endpoint

- But remains complex to collect and study

Thank you

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