Geriatric assessment in hematology: Go, Slow go or No go!

BHS course
23/4/2022
Dr Jan Lemmens
GZA Hospitals, Antwerp

Importance

Hematological condition	Median age (y)
MDS	75
AML	70
MM	70
NHL	67
CLL	72

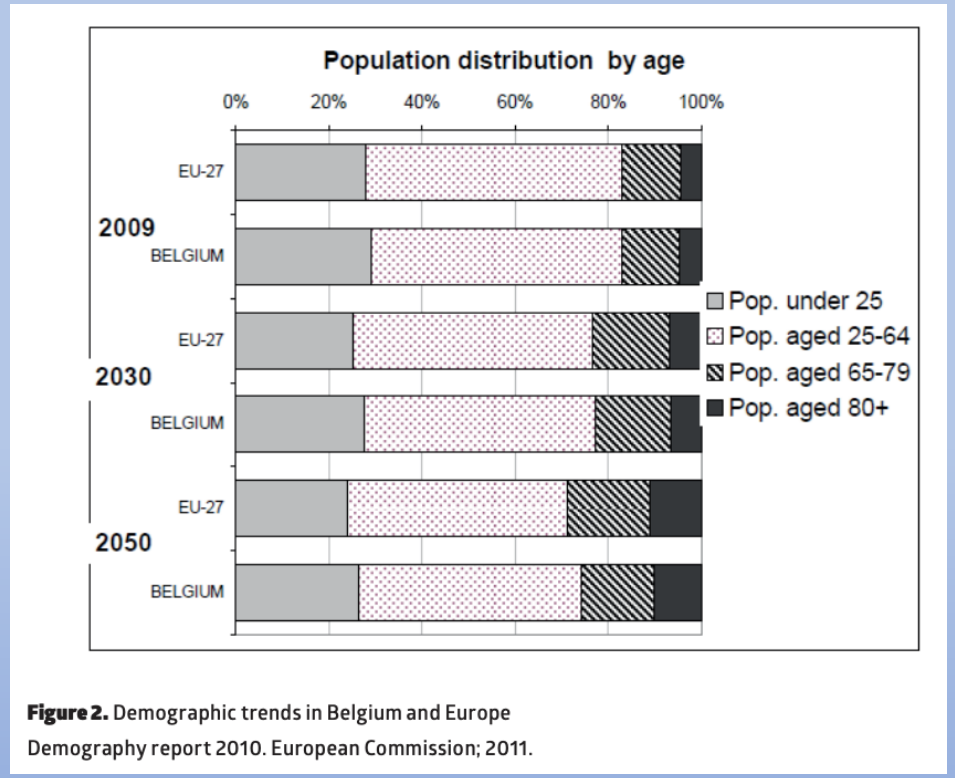
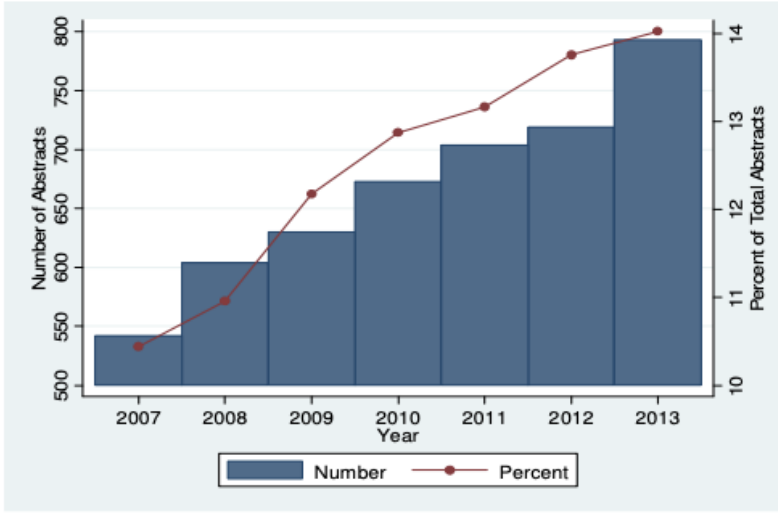


Figure 2. Demographic trends in Belgium and Europe
Demography report 2010. European Commission; 2011.

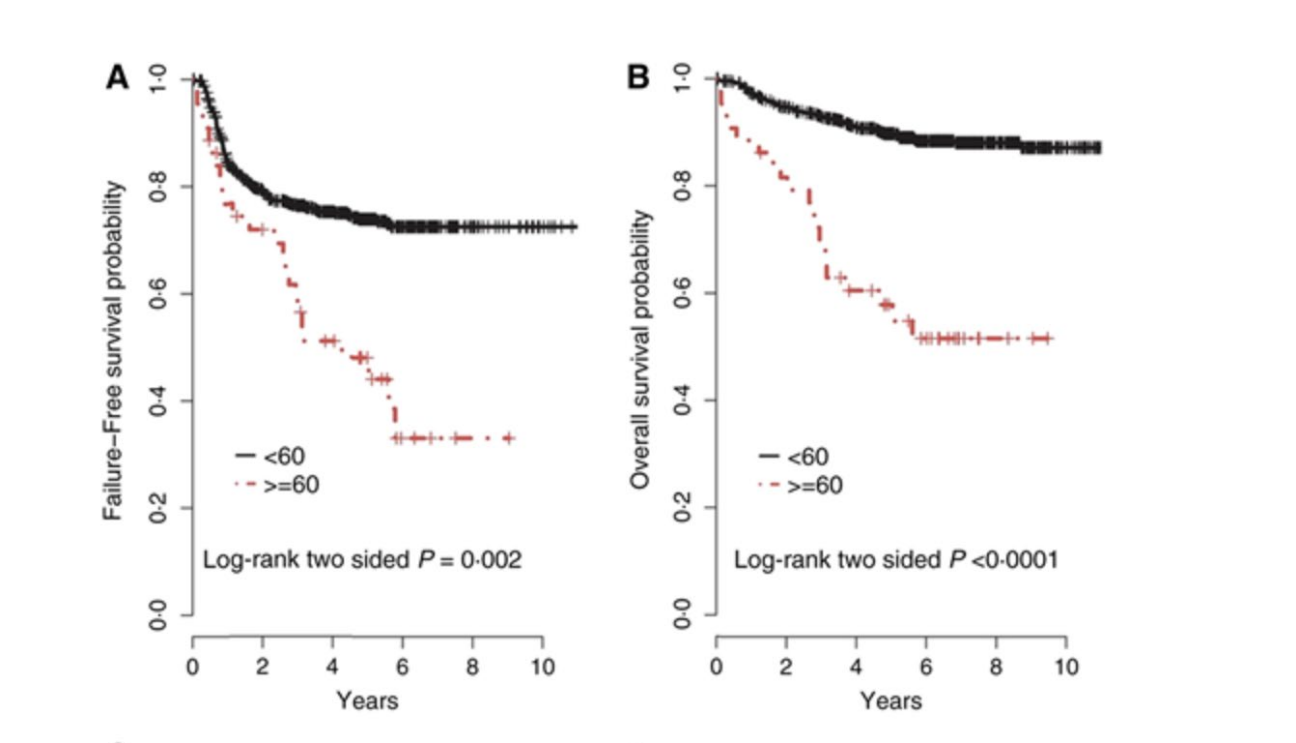


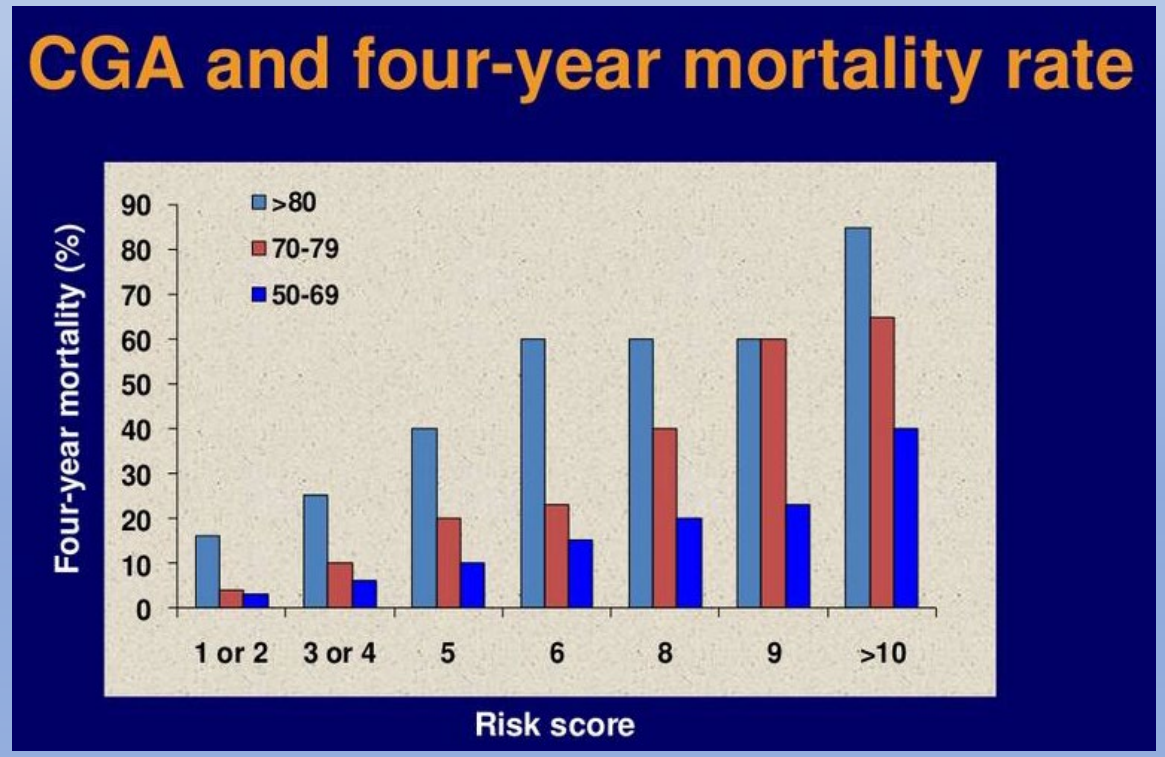
Life expectancy (in years)

Age	80	85	90	95
men				
healthy	10,8	7,9	5,8	4,3
frail	3,3	2,2	1,5	1,0
women				
healthy	13,0	9,6	6,8	4,8
frail	4,6	2,9	1,8	1,7

Walter LC JAMA 2001;285:2750-6

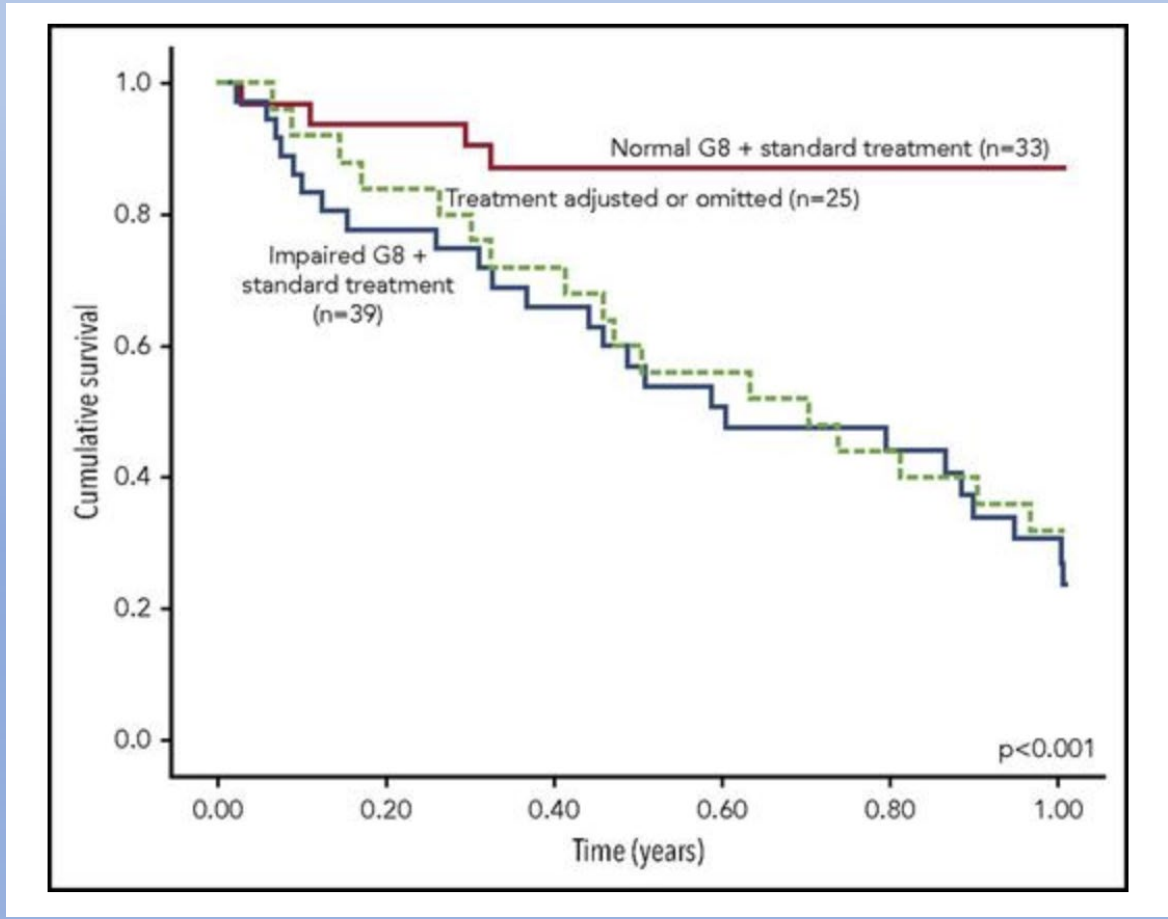
Does age matter? Yes, but…





Evens:. *Br J Haematol*. 2013

Risk factors matter, as does optimal R/!



Hamaker et al. *Ann Hematol* 2014;93(6):1031-1040

Exclusion of older patients by diagnosis

Diagnosis	On-going clinical trials				
	Trials (n)	Trials excluding older patients (%)	Trials excluding older patients based on age (%)	Trials excluding older patients based on performance status (%)	Trials excluding older patients based on organ function (%)
Acute lymphocytic leukemia	49	**88**	**67**	8	49
Hodgkin's lymphoma	36	69	**44**	17	47
Chronic myeloid leukemia	46	72	22	11	63
Non-Hodgkin's lymphoma	122	61	16	17	51
Acute myeloid leukemia	135	78	42	19	49
Multiple myeloma	196	63	19	19	48
Myelodysplastic syndrome	64	67	17	9	56
Chronic lymphocytic leukemia	81	56	**6**	6	53
Overall	1207	**69**	**27**	**16**	**51**

Trials were considered to be excluding elderly patients based on age if they used an upper age limit of ≤75 years .

Hamaker M. et al, The Oncologist, 2014

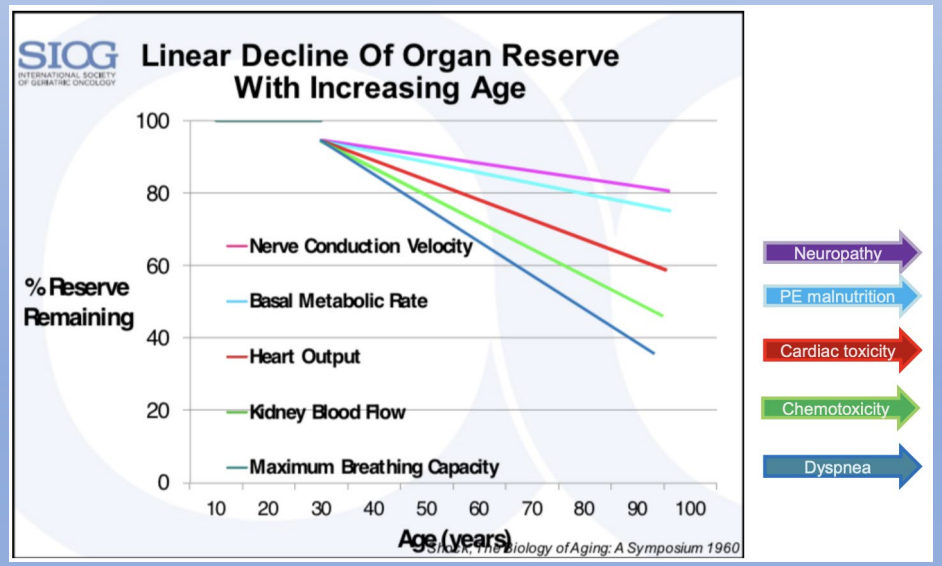
Clinical trials in elderly patients with a hematological malignancy: are we addressing the right end-points?

	Trials exclusively for elderly
Toxicity	71%
Efficacy	76%
Progression-free survival	66%
Overall survival	58%
Biological parameters	10%
Pharmacological parameters	15%
Quality of life	18%
Health care utilization	7%
Completion of treatment	3%
Functioning	2%

Hamaker M. et al, Ann Oncol, 2014

Why do elderly function worse?

- Patient factors:
  - Cardiovascular/pulmonary reserve/comorbidities
  - Nutritional status
  - Neurological tolerance
  - Bone marrow quality
  - Change in pharmacokinetics
  - Polymedication
- Disease-related factors
  - More complex cytogenetics in MDS/AML
  - DLBCL, more ABC, EBV+, C-MYC
  - …



Why do elderly function worse?

- Therapy- related factors
  - Chemo-induced febrile neutropenia: +/- 60% >80y, mortality +/-15%
  - Steroids in diabetics
  - Anthracyclines in pre-existing heart disease
  - Vinca-alkaloids and neuropathy
  - Tumor lysis syndrome and renal failure
- Socio-economic factors

Clinical judgement vs comprehensive geriatric assessment (GA)

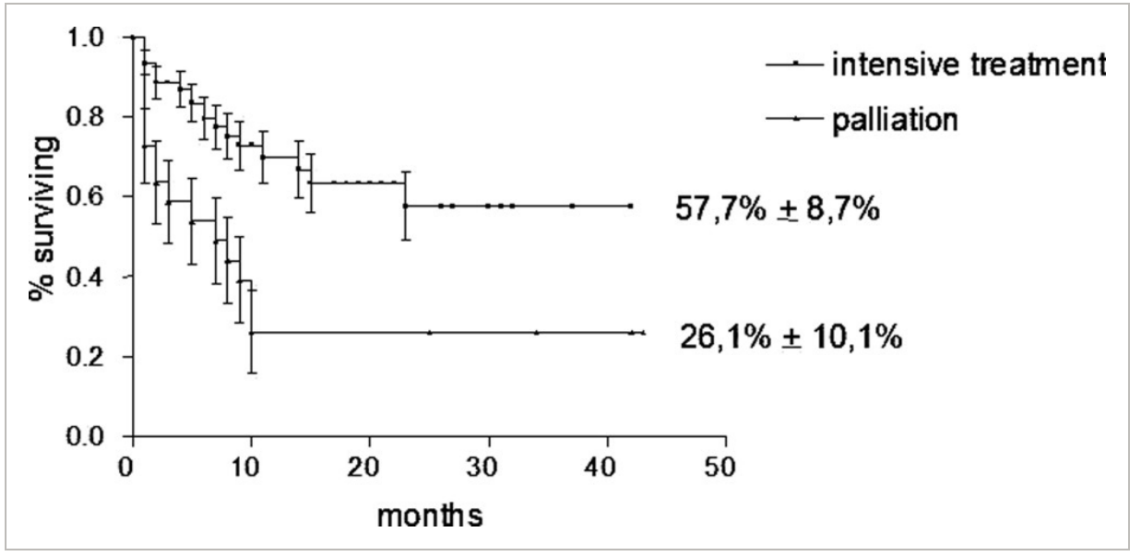


Figure 1 Open in figure viewer | PowerPoint

Actuarial overall survival curves of elderly patients with diffuse large cell lymphoma given intensive treatment or palliation according to physician's clinical evaluation are shown (log-rank analysis: *P* = .0014).

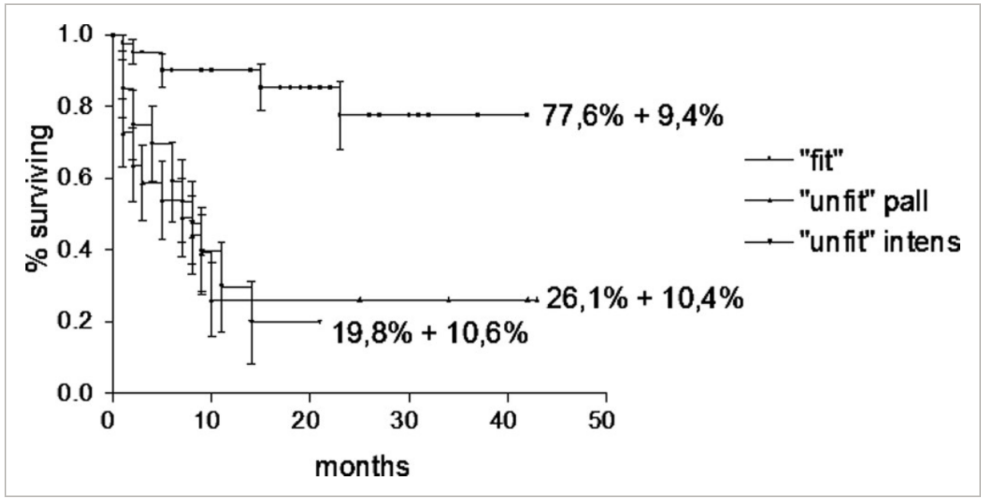
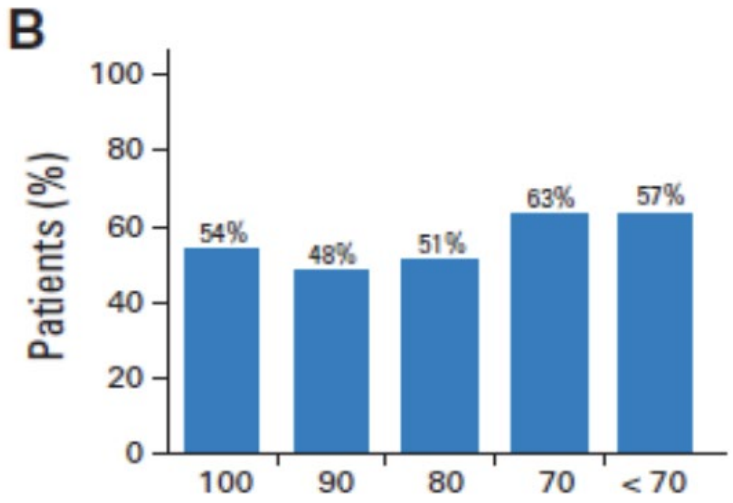


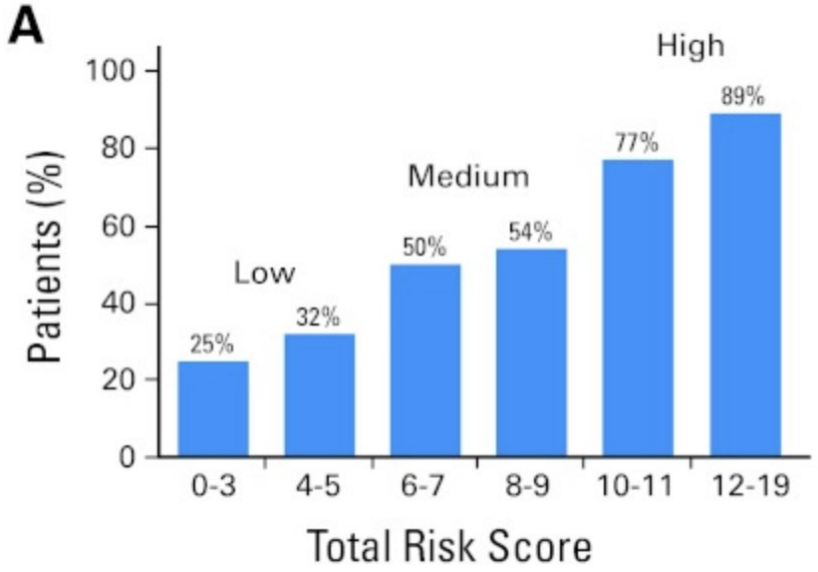
Figure 2 Open in figure viewer | PowerPoint

Actuarial overall survival curves of elderly patients with diffuse large cell lymphoma classified as fit or unfit according to comprehensive geriatric assessment are shown. Unfit patients are subdivided into 2 subgroups according to the type of treatment received (log-rank analysis: *P* < .0001). pall indicates palliation; intens, intensive treatment.

Tucci et al: Cancer 2009



Ability of Karnofsky Index to predict grade 3 to 5 chemotherapy toxicity



Ability of risk score to predict for gr 3 to 5 chemotherapy toxicity

Hurria A. et al. J Clin Oncol 2011; 29(25): 3457-65

Why is GA necessary?

- Survival prediction by oncologists insufficient without validated tools
- ECOG and Karnofsky do not predict well for treatment toxicity
- Prognostic information on survival/life expectancy
- Predictive value for morbidity/QoL/TRM
- Detection of underlying conditions
- Better patient satisfaction and communication
- Highly cost –effective (reduction in R/ intensity, reduction of costs:+/- 3500 EUR)

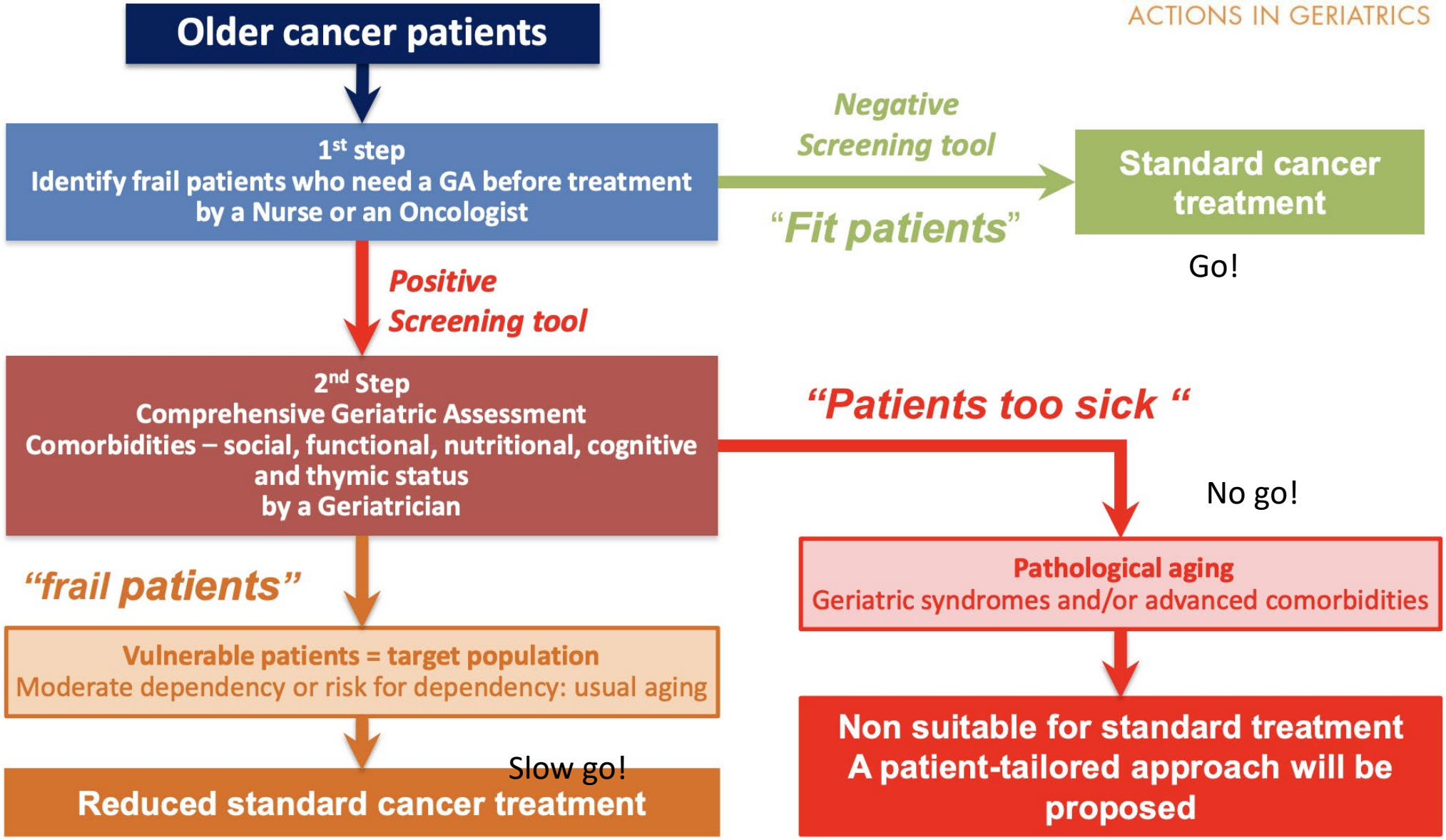
Lund: J Geriatr Oncol 2019, Hurria: JCO 2011, Mohile: JAMA Oncol 2019, Zalam: J Geriatr Oncol 2019

Geriatric assessment (GA)

- A **multidimensional** assessment to evaluate health of an older pt
- **Validated** measures of physical function, comorbidities+medication, cognitive function, psychological health, nutritional status, social support
- Gives a **score** for fitness or frailty
- **Predicts** for morbidity (health care utilization) and mortality
- Necessary in treatment **decision-making**
- Guides **supportive care**
- Helps in patient-caregiver **communication** and satisfaction

A screening strategy

EUGMS 13th
INTERNATIONAL CONGRESS OF THE EUROPEAN UNION GERIATRIC MEDICINE SOCIETY
DEVELOPING PREVENTIVE ACTIONS IN GERIATRICS



Tools

- ECOG, KPS: not specific for geriatric population
- ADL: activities of daily life (self reporting)
- IADL: instrumental ADL
- SPPB: short physical performance battery
- 5-word recall test or MMSE (mini-mental state examination)
- Comorbidity burden (CIRS, CIRS-geriatric)
- Frailty index
- Polypharmacy
- Geriatric cancer population tools i.e. G8/VES13
- Therapy-specific tools i.e. HCT-CI

ADL/KATZ scale

KATZ INDEX OF INDEPENDENCE IN ACTIVITIES OF DAILY LIVING*

Activities *POINTS (1 OR 0)*	***Independence*** *(1 POINT)* ***NO*** *supervision, direction, or personal assistance*	***Dependence*** *(0 POINT)* ***WITH*** *supervision, direction, personal assistance, or total care*
BATHING Points: _____	(1 point) Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area, or disabled extremity.	(0 points) Needs help with bathing more than one part of the body, getting in or out of bathtub or shower. Requires total bathing.
DRESSING Points: _____	(1 point) Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	(0 points) Needs help with dressing self or needs to be completely dressed.
TOILETING Points: _____	(1 point) Goes to toilet, gets on and off, arranges clothes, and cleans genital area without help.	(0 points) Needs help transferring to the toilet, cleaning self, or uses bedpan or commode.
TRANSFERRING Points: _____	(1 point) Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable.	(0 points) Needs help in moving from bed to chair or requires a complete transfer.
CONTINENCE Points: _____	(1 point) Exercises complete self-control over urination and defecation.	(0 points) Is partially or totally incontinent of bowel or bladder.
FEEDING Points: _____	(1 point) Gets food from plate into mouth without help. Preparation of food may be done by another person.	(0 points) Needs partial or total help with feeding or requires parenteral feeding.
TOTAL POINTS: _____	*6 = High (client independent)*	*0 = Low (client very dependent)*

** Slightly adapted with permission from Gerontological Society of America. Katz, S., Down, T.D., Cash, H.R., et al. (1970). Progress in the development of the index of ADL.* The Gerontologist, 10, *20-30.*

IADL

Instrumental Activities of Daily Living (IADL)

Instructions: Circle the scoring point for the statement that most closely corresponds to the patient's current functional ability for each task. The examiner should complete the scale based on information about the patient from the patient him-/herself, informants (such as the patient's family member or other caregiver), and recent records.

A. Ability to use telephone	Score
1. Operates telephone on own initiative; looks up and dials numbers, etc.	1
2. Dials a few well-known numbers	1
3. Answers telephone but does not dial	1
4. Does not use telephone at all	0

B. Shopping	
1. Takes care of all shopping needs independently	1
2. Shops independently for small purchases	0
3. Needs to be accompanied on any shopping trip	0
4. Completely unable to shop	0

C. Food preparation	
1. Plans, prepares, and serves adequate meals independently	1
2. Prepares adequate meals if supplied with ingredients	0
3. Heats and serves prepared meals, or prepares meals but does not maintain adequate diet	0
4. Needs to have meals prepared and served	0

D. Housekeeping	
1. Maintains house alone or with occasional assistance (e.g., "heavy work domestic help")	1
2. Performs light daily tasks such as dishwashing, bed making	1
3. Performs light daily tasks but cannot maintain acceptable level of cleanliness	1
4. Needs help with all home maintenance tasks	1
5. Does not participate in any housekeeping tasks	0

E. Laundry	Score
1. Does personal laundry completely	1
2. Launders small items; rinses stockings, etc.	1
3. All laundry must be done by others	0

F. Mode of transportation	
1. Travels independently on public transportation or drives own car	1
2. Arranges own travel via taxi, but does not otherwise use public transportation	1
3. Travels on public transportation when assisted or accompanied by another	1
4. Travel limited to taxi or automobile with assistance of another	0
5. Does not travel at all	0

G. Responsibility for own medications	
1. Is responsible for taking medication in correct dosages at correct time	1
2. Takes responsibility if medication is prepared in advance in separate dosages	0
3. Is not capable of dispensing own medication	0

H. Ability to handle finances	
1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank), collects and keeps track of income	1
2. Manages day-to-day purchases, but needs help with banking, major purchases, etc.	1
3. Incapable of handling money	0

(Lawton & Brody, 1969)

Scoring: The patient receives a score of 1 for each item labeled A – H if his or her competence is rated at some minimal level or higher. Add the total points circled for A – H. The total score may range from 0 – 8. A lower score indicates a higher level of dependence.

Sources:

- Cromwell DA, Eagar K, Poulos RG. The performance of instrumental activities of daily living scale in screening for cognitive impairment in elderly community residents. *J Clin Epidemiol.* 2003;56(2):131-137.
- Lawton MP. The functional assessment of elderly people. *J Am Geriatr Soc.* 1971;19(6):465-481.
- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist.* 1969;9(3):179-186.
- Polisher Research Institute. Instrumental Activities of Daily Living Scale (IADL). Available at: http://www.abramsoncenter.org/PRI/documents/IADL.pdf. Accessed February 15, 2005.

Table 3. Multivariable Models of Association of Type and Number of iADL Dependencies With Survival

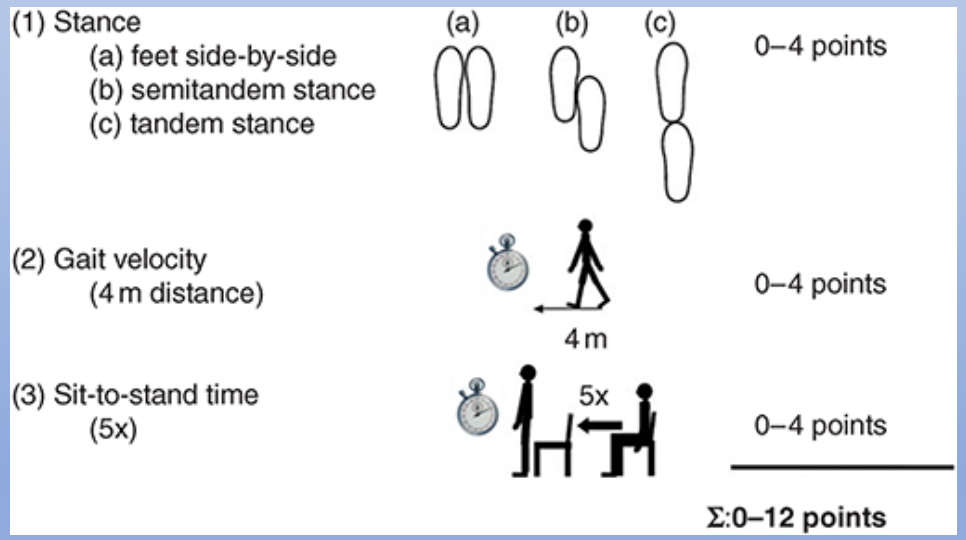
iADL Dependency[a]	Mortality, Hazard Ratio (95% CI)[b]
Type	
Shopping	2.39 (1.35-4.21)
Meals	2.42 (1.38-4.24)
Housework	2.01 (1.19-3.38)
Medications	0.99 (0.48-2.02)
Finances	1.45 (0.67-3.16)
No.	
1	1.94 (0.99-3.83)
2	2.44 (1.24-4.81)
≥3	2.98 (1.43-6.21)

Abbreviations: CI, confidence interval; iADL, instrumental activity of daily living.

[a] Adjusted for age, sex, comorbidity, cancer aggressiveness, prior treatment, current/new treatment intensity, and ADL dependency.

[b] Cox proportional hazards model.

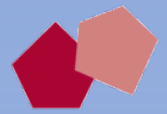
SPPB (short physical performance battery)



Balance	
Side-by-side stand > 10 seconds	1 point
Semi-tandem stand > 10 seconds	1 point
Tandem stand	
≥10 seconds	2 points
3.00–9.99 seconds	1 point
≤2.99 seconds	0 points
4 m gait speed	
Unable to walk	0 points
>8.70 seconds	1 point
6.21–8.70 seconds	2 points
4.82–6.20 seconds	3 points
<4.82 seconds	4 points
Chair stands	
Unable to perform maneuver or >60 seconds to complete	0 points
≥16.70 seconds	1 point
13.70–16.69 seconds	2 points
11.20–13.69 seconds	3 points
<11.2 seconds	4 points

Mini-Mental State Examination (MMSE)

Max. Score	Score	
		Orientation
5	_____	What is the (year) (season) (day of the week) (month) (date)?
5	_____	Where are we: (state) (county) (town) (hospital) (floor)?
		Registration
3	_____	Name 3 unrelated objects, allow 1 second to say each. Then ask the patient to repeat all 3. Give 1 point for each correct answer. Repeat them until he learns all 3. Count trials and record. Trials: _____
		Attention and Calculation
5	_____	Ask patient to count backwards from 100 by sevens. 1 point for each correct answer. Stop after 5 answers.
		Recall
3	_____	Ask patient to recall the 3 objects previously stated. Give 1 point for each correct answer.
		Language
9	_____	• Show patient a wristwatch; ask patient what it is. Repeat for a pencil (2 points). • Ask patient to repeat the following: "No ifs, ands, or buts" (1 point). • Ask patient to "take a piece of paper in your right hand, fold it in half, and put it on the floor" (3 points). • Ask patient to read and obey the following sentence which you have written on a piece of paper: "Close your eyes" (1 point). • Ask patient to write a sentence (1 point). • Ask patient to copy a design (1 point).



Total Score _____

Suggested guideline for determining the severity of cognitive impairment:

Mild: MMSE ≥ 21
Moderate: MMSE 10-20
Severe: MMSE ≤ 9

*Expected decline in MMSE scores in untreated mild to moderate Alzheimer's patient is 2 to 4 points per year.**

Table 1 – Dimensions used for the development of the GAH scale.

Dimension	Measurement	Range of score	Cut-off point (1 point)
No. of drugs	Medication count of drugs of current use.	Continuous	≥5[17]
Gait speed	Double determination of gait speed at usual pace over a 4 meter course[19,20]	Continuous	<0.8 m/s[21]
Mood	Single item from the CES-D[22]: *In the last week, did you feel depressed?*	Never, rarely, or occasionally (no more than 2 days); frequently, most of the time or all time (3–7 days)	Frequently, most of the time or all time (3–7 days)
Activities of daily living	• Item no. 4 of the VES-13 Instrument[24]: *Do you have any difficulty in …?* • Do you need any help in your daily living? • Do you have a caregiver?	Yes/no	Needs help in at least one area
Subjective health status	Single item from the VES-13 Instrument[24]: *Compared to other people your age, would you say your health is…?*	Poor, fair, good, very good, or excellent	Poor and fair
Nutrition	Four items from the MNA-SF[30]: *BMI, weight loss during the last 3 months, food intake decline over the past 3 months, and psychological stress or acute disease.*	0–10	≤8
Mental status	SPMSQ[31]	Right/wrong	≥3 errors
Comorbidities	Prognostic Index for 4-year Mortality in Older Adults[35]	0, for absence; 1 point for DM or BMI < 25 kg/m^2; 2 points for cancer, lung disease, heart failure, or smoking habit.	≥3

Abbreviations: BMI, body mass index; CES-D, Centre for Epidemiological Studies Depression Scale; DM, diabetes mellitus; MNA-SF, Mini-Nutritional Assessment questionnaire; SPMSQ, Short Portable Mental Status Questionnaire; VES-13, 13-item Vulnerable Elders Survey.

Prevalence of abnormal CGA in pts with hematological diseases

Screening tool	All pts (n=389)	80+ (n=60)
ADL (activity of daily life)	11%	20%
IADL (instrumental ADL)	25%	36%
GDS (geriatric depression scale)	28%	62%
MNA (mini nutritional assessment)	44%	64%
MMSE (mini mental state assessment)	35%	50%
CIRS gr 3-4 (comorbidities)	21%	42%
Toxic death	12%	22%

Selected trials highlighting prevalence of geriatric impairments among older patients with hematologic malignancies

Disease type/setting	No. patients	ADLs, %	IADLs, %	Physical performance, %	Cognitive, %	Mood, %	Comorbidity burden, %	Nutritional status, %
Chronic lymphocytic leukemia[8]	75	n/a	19	63	49	n/a	36	n/a
Multiple myeloma[10]	869	14	18	n/a	n/a	n/a	17	n/a
Acute myeloid leukemia[20]	54	48	41	54	32	39	46	n/a
Acute myeloid leukemia/myelodysplastic syndrome[7]	195	34	n/a	55	9	14	n/a	n/a
Myelodysplastic syndrome[14]	98	29	34	31	11	32	23	27
Myelodysplastic syndrome[19]	455	n/a	45	35*	n/a	n/a	58	n/a
Non-Hodgkin lymphoma[11]	84	12	n/a	n/a	n/a	n/a	50	n/a
Non-Hodgkin lymphoma[22]	143	18	21	n/a	n/a	n/a	56	n/a
Non-Hodgkin lymphoma[23]	70	n/a	n/a	n/a	28	41	n/a	36
Bone marrow transplantation (preallogeneic transplant evaluation, mixed population, age ≥ 50 y)[12]	203	7	40	33	n/a	56	55	58
Bone marrow transplantation (preautologous transplant evaluation, age ≥ 50 y)[24]	184	n/a	36	15	3	35	33	n/a

Tests and thresholds for impairment varied for physical performance, cognitive function, mood, comorbidity burden, and nutritional status.

n/a, not assessed or reported.

* Prevalence estimate refers to gait speed < 4.82 seconds.

Klepin H. Blood 2019,134:53-8

Table 2. Vulnerability of *clinically fit* older patients with haematological malignancies in the G8 score and Comprehensive Geriatric Assessment (CGA) (n=90)

	Score range	Cut-off score	Vulnerable %
G8 score	0-17	≤14.5	72%
CGA total score	0-8	≥2	80%
Functional status			
Activities of Daily Living (ADL)	0-6	≤5	11%
Instrumental activities of daily living (IADL)			
Men	0-5	≤4	28%
Women	0-8	≤7	49%
Risk of falls status			
Time-up and Go test (TUG)	In second	≥15	4%
Fall during the last year (Falls)	Number	≥2	13%
Fatigue status			
Mobility-tiredness scale (Mob-t)	0-6	<5	40%
Nutritional status			
Mini nutritional assessment (MNA)	0-30	≤23,5	44%
Cognitive status			
Mini mental state examination (MMSE)	0-30	<27	31%
Montreal cognitive assessment (MoCA)	0-30	<26	51%
Emotional status			
Hospital anxiety and depression scale (HADS)	0-42	≥19	16%
Geriatric depression scale four items (GDS-4)	0-4	≥2	25%
Polypharmacy			
Number of drugs (Drugs)	Number	≥5	50%
Comorbidities			
Charlson comorbidity index (CCI)	0-30	≥2	61%

Dubruille et al JGO 2015

Table 3. Selected trials highlighting predictive utility of geriatric assessment measures for older adults with hematologic malignancy

Disease type/setting	No. patients	Outcomes predicted	Measures
Chronic lymphocytic leukemia[8]	75	Overall survival	Low objective physical performance (Timed Up and Go) and cognition
Multiple myeloma[10]	869	Overall survival, nonhematologic adverse events, treatment discontinuation	Composite fitness score (ADLs, IADLs, comorbidity, age)
Acute myeloid leukemia[9]	74	Overall survival	Low objective physical function (Short Physical Performance Battery) and cognition
Acute myeloid leukemia/myelodysplastic syndrome[7]	195	Overall survival	ADLs and fatigue in nonintensively treated patients
Myelodysplastic syndrome[14]	98	Overall survival and treatment duration.	IADLs and comorbidity associated with overall survival. IADLs, cognition, and low objective physical function (Timed Up and Go) associated with treatment duration.
Myelodysplastic syndrome[19]	455	Overall survival	Clinical frailty score and comorbidity
Non-Hodgkin lymphoma[22]	143	Overall survival	IADLs and comorbidity
Non-Hodgkin lymphoma[32]	173	Overall survival	Composite fitness score (ADLs, IADLs, comorbidity, age)
Non-Hodgkin lymphoma[33]	99	Overall survival, response rates, progression-free survival	IADLs, composite score (albumin, comorbidity, age)
Non-Hodgkin lymphoma[23]	70	Overall survival, early discontinuation of chemotherapy	Nutritional status associated with both outcomes
Hodgkin lymphoma[33]	48	Progression-free survival	Loss of IADLs
Bone marrow transplantation (mixed population)[12]	203	Overall survival	IADLs, gait speed, comorbidity, mental health
Bone marrow transplantation (mixed population)[24]	184	Overall survival	IADLs, physical subscale of Functional Assessment of Cancer Therapy Bone Marrow Transplant
Bone marrow transplantation (mixed population, allogeneic transplantation)[21]	106	Overall survival	Low objective physical performance (Timed Up and Go), fatigue
Bone marrow transplantation (multiple myeloma)[29]	100	Hospital readmission, hospital length of stay	Decreased grip strength, anxiety/depression, falls, and weight loss associated with readmission. Objective (Short Physical Performance Battery) and self-reported physical function associated with length of stay.
Mixed population (myelodysplastic syndrome, leukemia, multiple myeloma, lymphoma)[34]	314	Overall survival, unplanned hospitalization	Slower gait speed associated with increase mortality and unplanned hospitalizations Lower grip strength associated with shorter survival

Klepin H. Blood 2019,134:53-8

Some examples

- Non Hodgkin’s lymphoma
- Myeloma
- AML
- Stem cell transplantation

Non Hodgkin's lymphoma

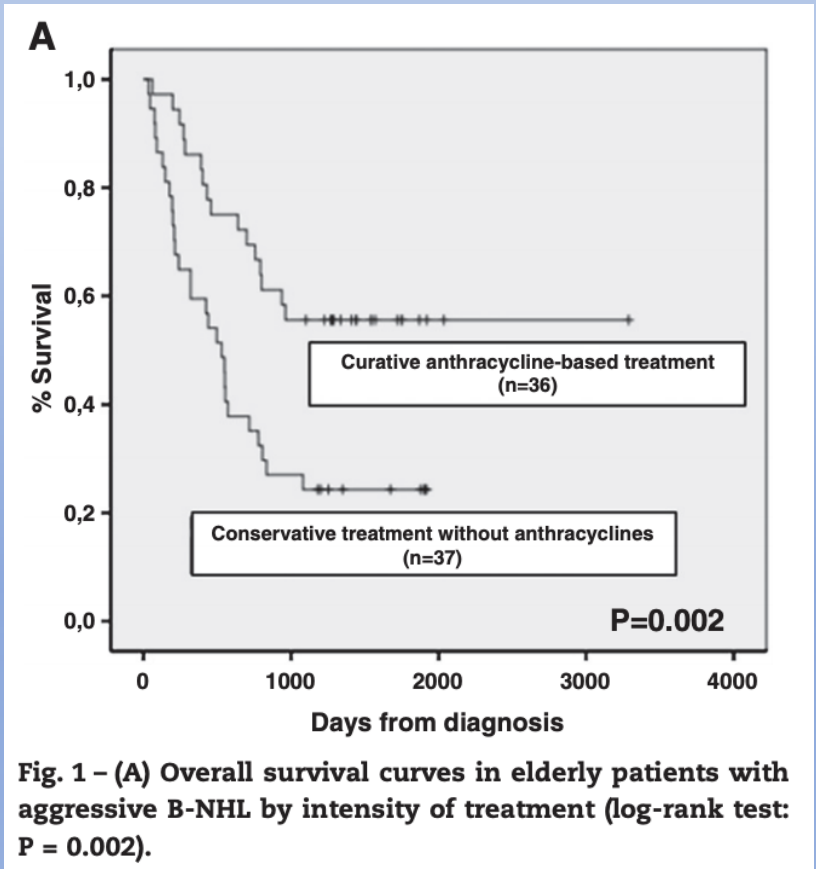


Fig. 1 – (A) Overall survival curves in elderly patients with aggressive B-NHL by intensity of treatment (log-rank test: P = 0.002).

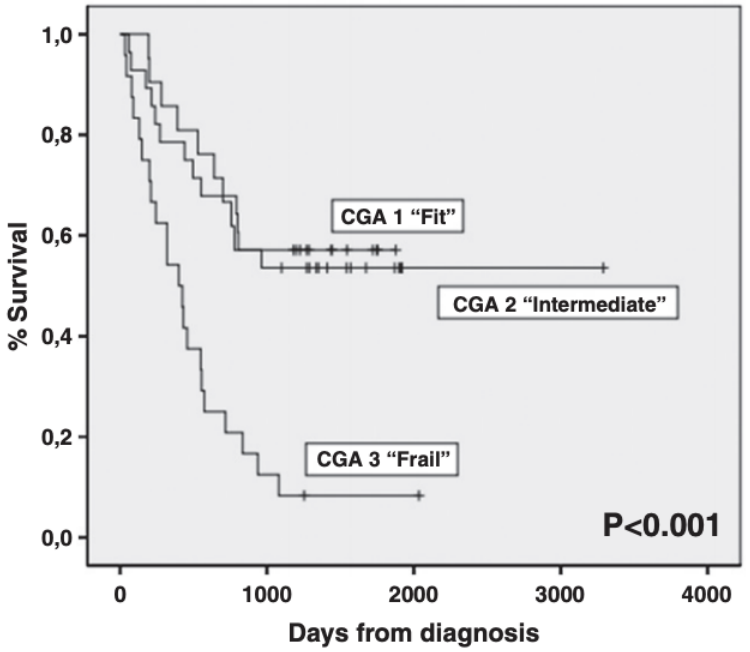


Fig. 2 – Overall survival curves in elderly patients with aggressive B-NHL according to CGA, irrespective of type of treatments ("fit" vs "intermediate" vs "frail"; log-rank test: P < 0.001).

Marchesi JGO 2013;4:242-48

Non Hodgkin's lymphoma

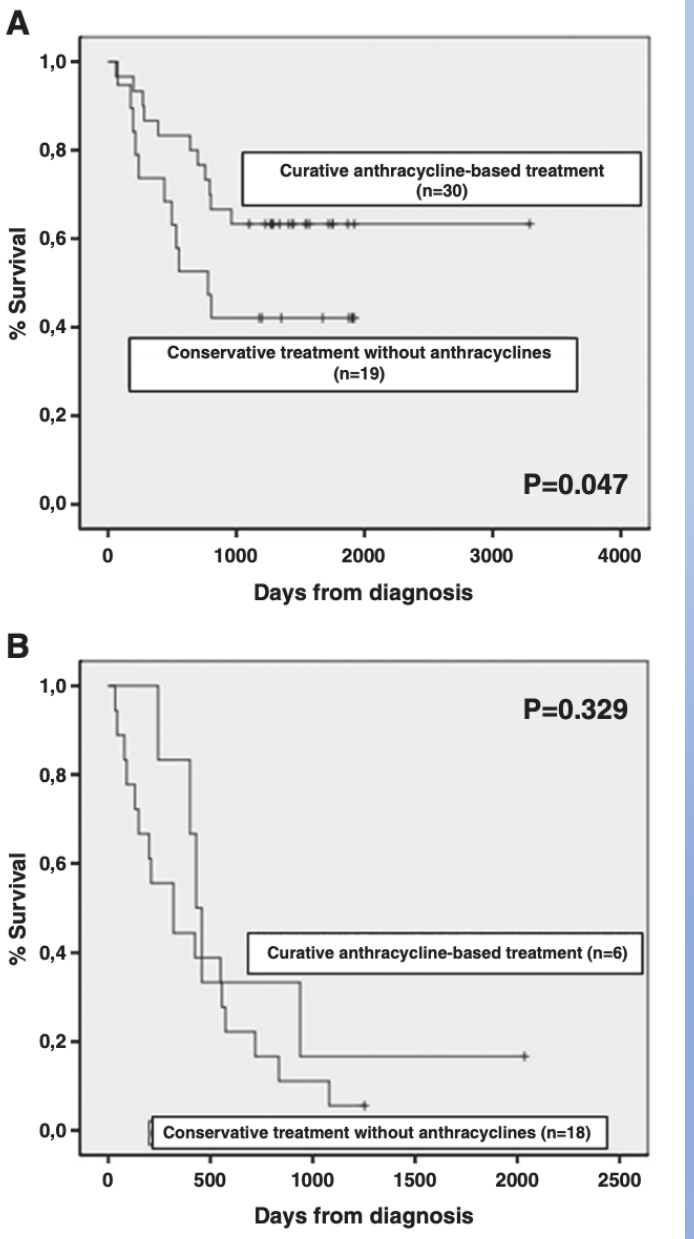


Fig. 3 – (A) Overall survival curves in elderly patients classified as "fit + intermediate" according to CGA by intensity of treatment (log-rank test: P = 0.047). (B) Overall survival curves in elderly patients classified as "frail" according to CGA by intensity of treatment (log-rank test: P = 0.329).

Marchesi JGO 2013;4:242-8.

myelomafrailtyscorecalculator.net

MYELOMA FRAILTY SCORE CALCULATOR

Developed by International Myeloma Working Group for the prognosis of elderly myeloma patients.

The score system (range 0-5), based on age, comorbidities, cognitive and physical conditions, developed by Palumbo A. et al[1], identifies 3 groups of patients:

- fit (score=0)
- intermediate-fitness (score=1)
- frail (score≥2)

The 3-year overall survival was 84% in fit patients, 76% in intermediate-fitness patients (HR 1.61, 95%CI 1.02-2.56, p=0.042) and 57% in frail patients (HR 3.57 CI 95% 2.37-5.39, p<0.001). The cumulative incidence of grade ≥3 non-hematologic adverse events at 12 months was 22.2% in fit, 26.4% in intermediate-fitness (HR 1.23, 95%CI 0.89-1.71; p 0.217) and 34.0% (HR 1.74, 95%CI 1.28-2.38; p<0.001) in frail patients. The cumulative incidence of treatment discontinuation at 12 months was 16.5% in fit, 20.8% in intermediate-fitness (HR 1.41, 95%CI 1.00-2.01, p=0.052) and 31.2% (HR 2.21, 95%CI 1.57-3.09; p<0.001) in frail patients.

This frailty score predicts mortality and the risk of toxicity in elderly myeloma patients. The International Myeloma Working group proposes this score for the measurement of frailty in the treatment decision-making process and in designing future clinical trials.

[1]Palumbo A, Bringhen S, Mateos MV, et al. Geriatric assessment predicts survival and toxicities in elderly myeloma patients: an International Myeloma Working Group report. Blood. 2015 Mar 26;125(13):2068-7

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Click here to calculator

IMWG frailty index predicts for:
-toxicity
-treatment discontinuation
-mortality
-adds to clinical judgement for unfit 70-75y in selecting for auto HSTP (Belotti)

Open Access Publication
Haematologica the hematology journal
Official Journal of the European Hematology Association

Haematologica. 2016 Sep; 101(9): 1110–1119.
doi: 10.3324/haematol.2016.148189
PMCID: PMC5060028
PMID: 27479825

Geriatric assessment in multiple myeloma patients: validation of the International Myeloma Working Group (IMWG) score and comparison with other common comorbidity scores

Monika Engelhardt,[1] Sandra Maria Dold,[1] Gabriele Ihorst,[2] Alexander Zober,[1] Mandy Möller,[1] Heike Reinhardt,[1] Stefanie Hieke,[3] Martin Schumacher,[3] and Ralph Wäsch[1]

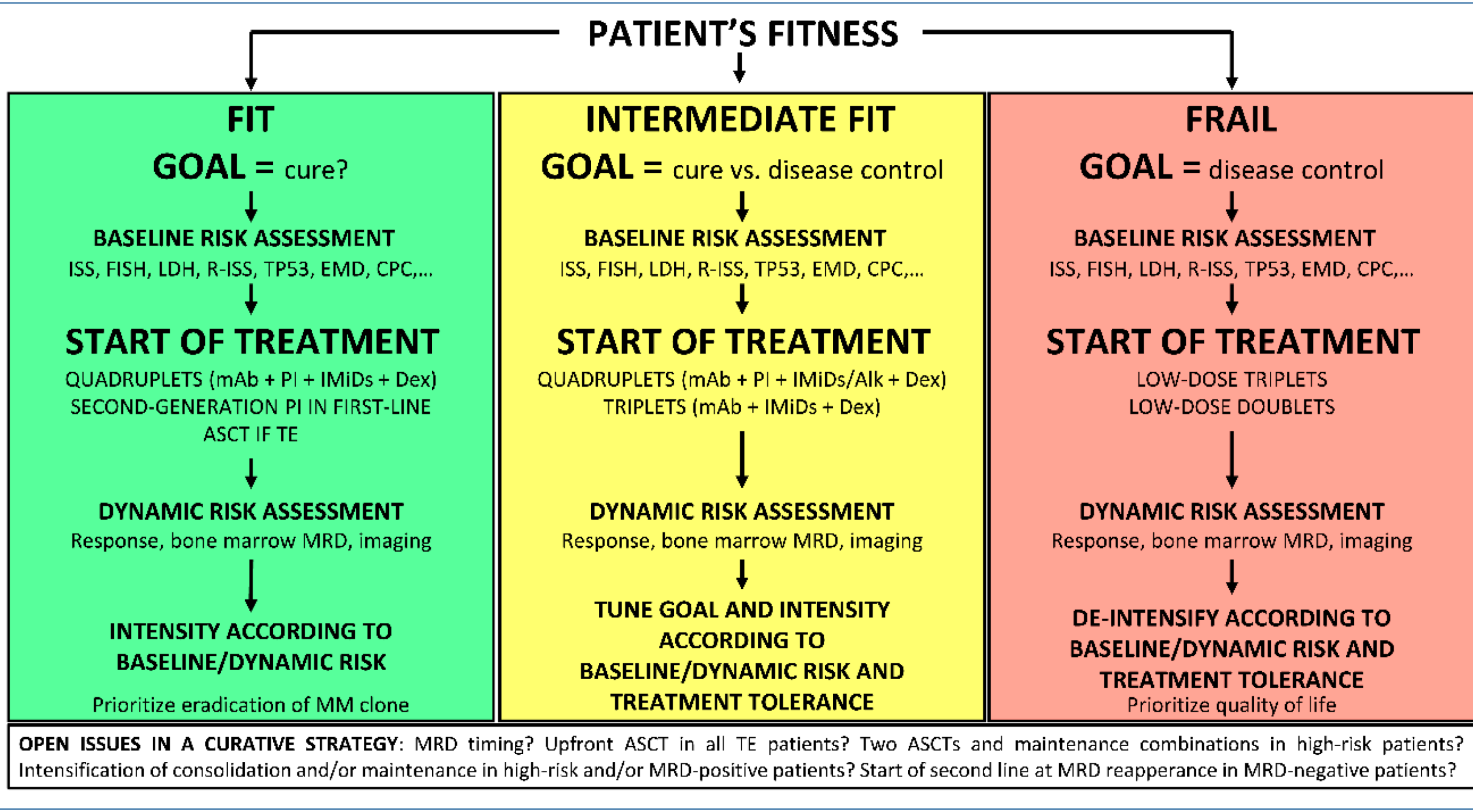
731. CLINICAL AUTOLOGOUS TRANSPLANTATION: RESULTS: POSTER I | NOVEMBER 29, 2018

The IMWG Frailty Score and Age Can be More Effective Than Clinical Judgement in the Selection of Elderly Patients with Newly Diagnosed Multiple Myeloma Who Can Benefit from an Intensive Treatment Approach with High Dose Melphalan and Autologous Stem Cell Transplantation

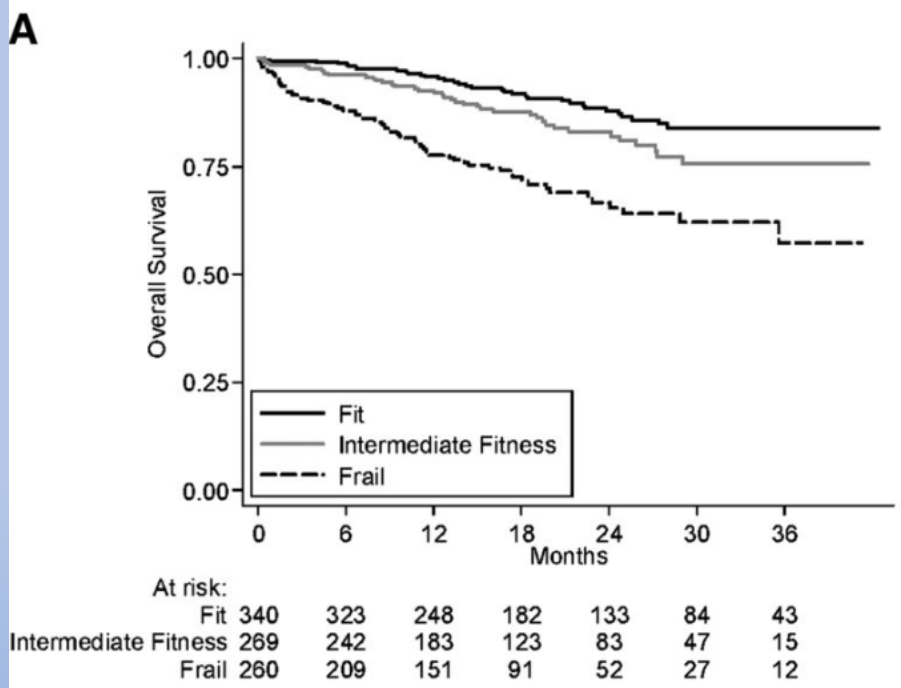
Angelo Belotti, MD, Rossella Ribolla, Valeria Cancelli, MD, Nicola Bianchetti, Claudia Crippa, MD, Samantha Ferrari, MD, Chiara Bottelli, MD, Chiara Cattaneo, MD, Vincenza Orlando, PharmD, Marco Chiarini, Luigi Grazioli, MD, Giuseppe Rossi

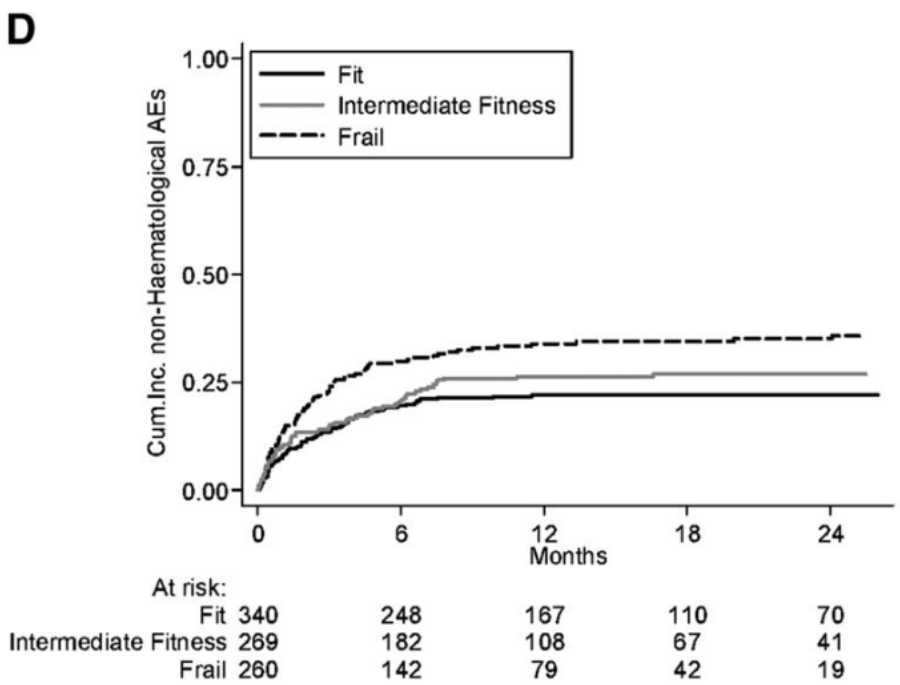
Check for updates

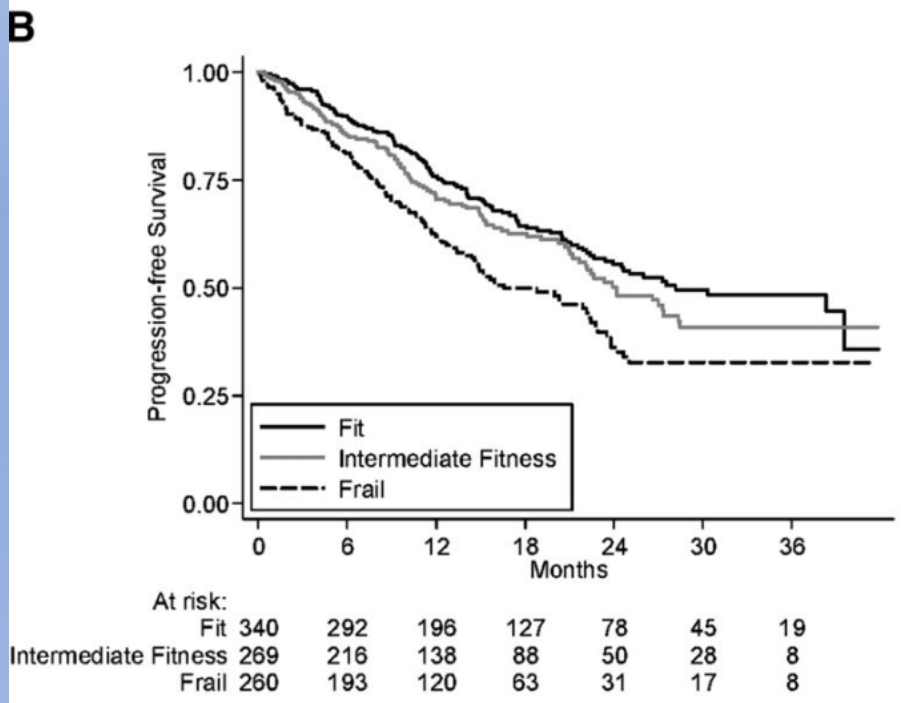
Blood (2018) 132 (Supplement 1): 2151.
https://doi.org/10.1182/blood-2018-99-113022

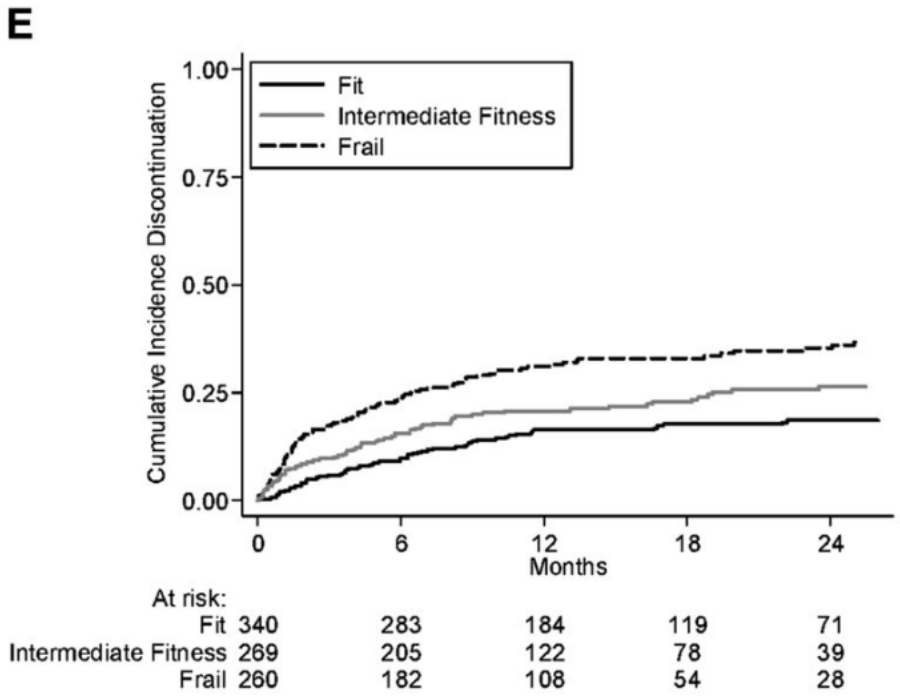

PATIENT'S FITNESS
FIT
GOAL = cure?
BASELINE RISK ASSESSMENT
ISS, FISH, LDH, R-ISS, TP53, EMD, CPC,...
START OF TREATMENT
QUADRUPLETS (mAb + PI + IMiDs + Dex)
SECOND-GENERATION PI IN FIRST-LINE
ASCT IF TE
DYNAMIC RISK ASSESSMENT
Response, bone marrow MRD, imaging
INTENSITY ACCORDING TO BASELINE/DYNAMIC RISK
Prioritize eradication of MM clone
INTERMEDIATE FIT
GOAL = cure vs. disease control
BASELINE RISK ASSESSMENT
ISS, FISH, LDH, R-ISS, TP53, EMD, CPC,...
START OF TREATMENT
QUADRUPLETS (mAb + PI + IMiDs/Alk + Dex)
TRIPLETS (mAb + IMiDs + Dex)
DYNAMIC RISK ASSESSMENT
Response, bone marrow MRD, imaging
TUNE GOAL AND INTENSITY ACCORDING TO BASELINE/DYNAMIC RISK AND TREATMENT TOLERANCE
FRAIL
GOAL = disease control
BASELINE RISK ASSESSMENT
ISS, FISH, LDH, R-ISS, TP53, EMD, CPC,...
START OF TREATMENT
LOW-DOSE TRIPLETS
LOW-DOSE DOUBLETS
DYNAMIC RISK ASSESSMENT
Response, bone marrow MRD, imaging
DE-INTENSIFY ACCORDING TO BASELINE/DYNAMIC RISK AND TREATMENT TOLERANCE
Prioritize quality of life
OPEN ISSUES IN A CURATIVE STRATEGY: MRD timing? Upfront ASCT in all TE patients? Two ASCTs and maintenance combinations in high-risk patients? Intensification of consolidation and/or maintenance in high-risk and/or MRD-positive patients? Start of second line at MRD reapperance in MRD-negative patients?

Myeloma









Palumbo Blood 2015

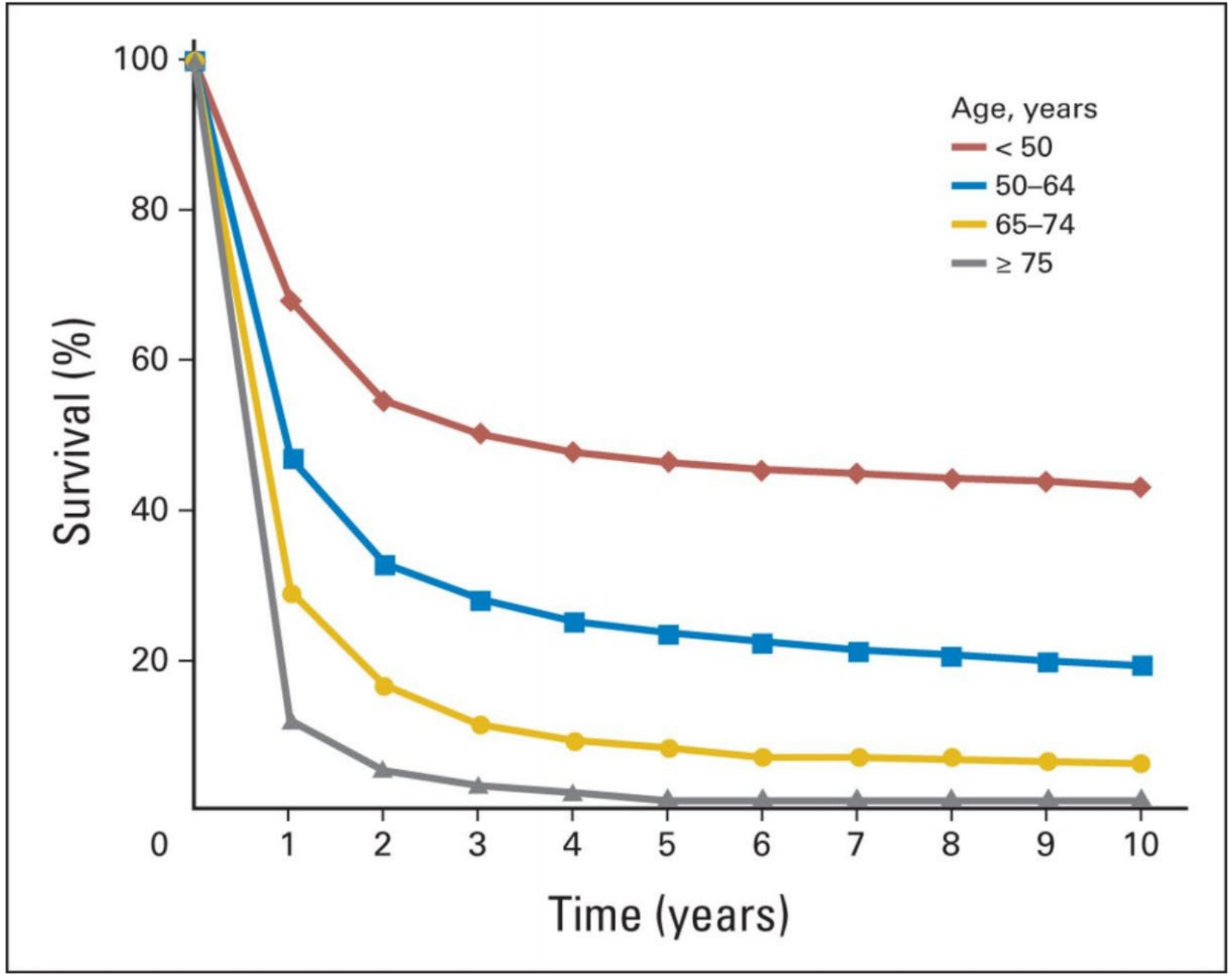
Univariate and multivariate analysis of the impact of the frailty profile of patients on OS, PFS, discontinuation rate, and incidence of grade 3 or higher toxicity

	OS		PFS		Discontinuation		Grade ≥3 hematologic toxicity		Grade ≥3 nonhematologic toxicity	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Crude										
Fit	1	—	1	—	1	—	1	—	1	—
Intermediate fitness	1.61 (1.02-2.56)	.042	1.18 (0.91-1.53)	.211	1.48 (1.05-2.10)	.026	0.97 (0.74-1.27)	.808	1.23 (0.89-1.71)	.217
Frail	3.57 (2.37-5.39)	<.001	1.68 (1.31-2.15)	<.001	2.27 (1.64-3.14)	<.001	0.83 (0.62-1.09)	.181	1.74 (1.28-2.38)	<.001
Adjusted*										
Fit	1	—	1	—	1	—	1	—	1	—
Intermediate fitness	1.37 (0.86-2.18)	.181	1.08 (0.83-1.40)	.583	1.41 (1.00-2.01)	.052	0.97 (0.74-1.28)	.831	1.13 (0.81-1.58)	.462
Frail	2.88 (1.88-4.40)	<.001	1.48 (1.15-1.92)	.003	2.21 (1.57-3.09)	<.001	0.94 (0.71-1.26)	.698	1.57 (1.12-2.19)	.008

* Adjusted for ISS, chromosome abnormalities, and therapy.

Palumbo: Blood 2015

AML



Klepin H D et al. JCO 2014;32:2541-2552

AML:
-median age 68y
-survival < with age
-poor risk cytogenetics
-more 2nd AML after MDS
-FLT3-ITD, c-KIT, TP53
-intensive R/ better than palliative R/
-35% 2y OS post RIC-allo Tx (up to 75y)
-Hematopoietic Cell Transplantation-Specific Comorbidity Index score (HCT-CI):
predicts nonrelapse mortality and OS after ASCT
-HDAC inhib, midostaurin, IDH2,
CPX-351, venetoclax/Ara-C, …
new strategies

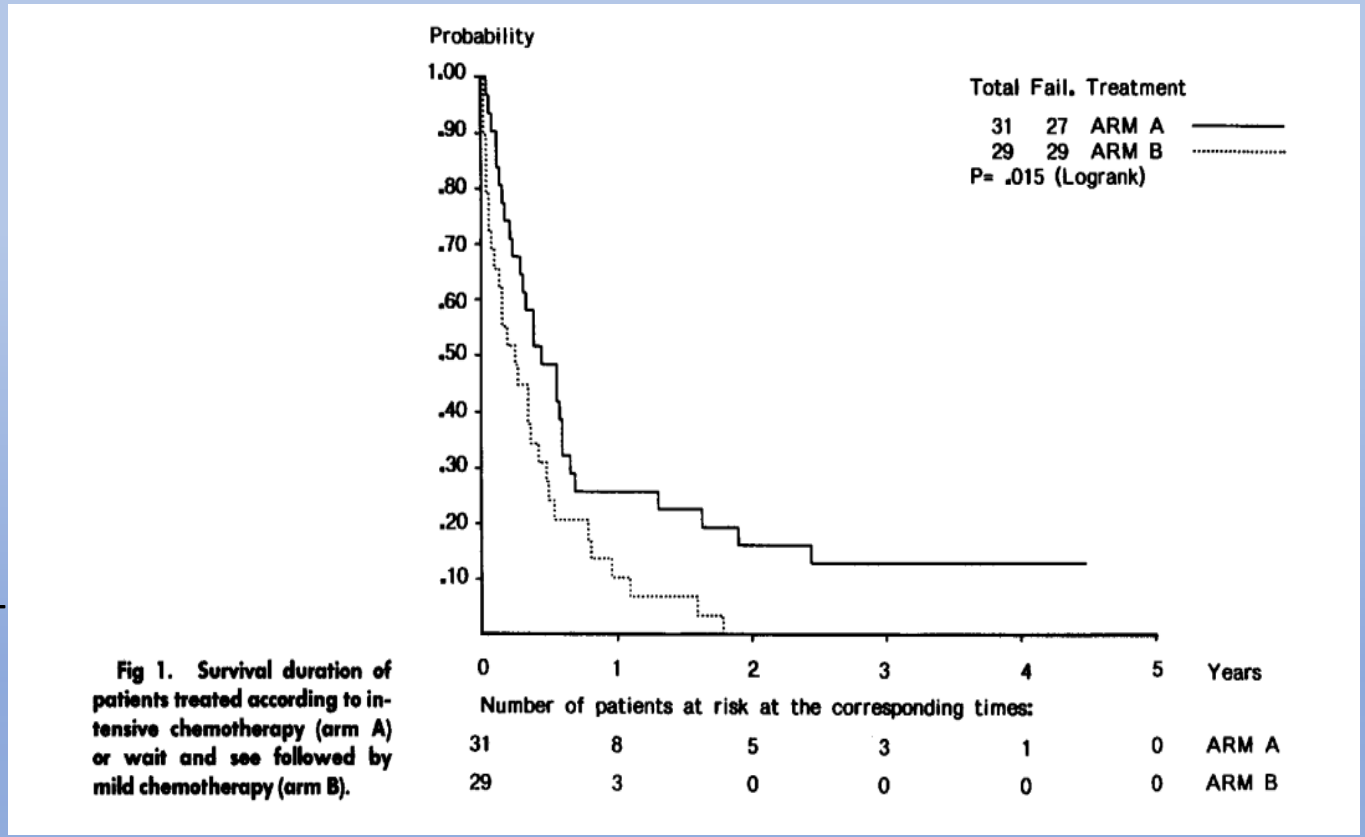
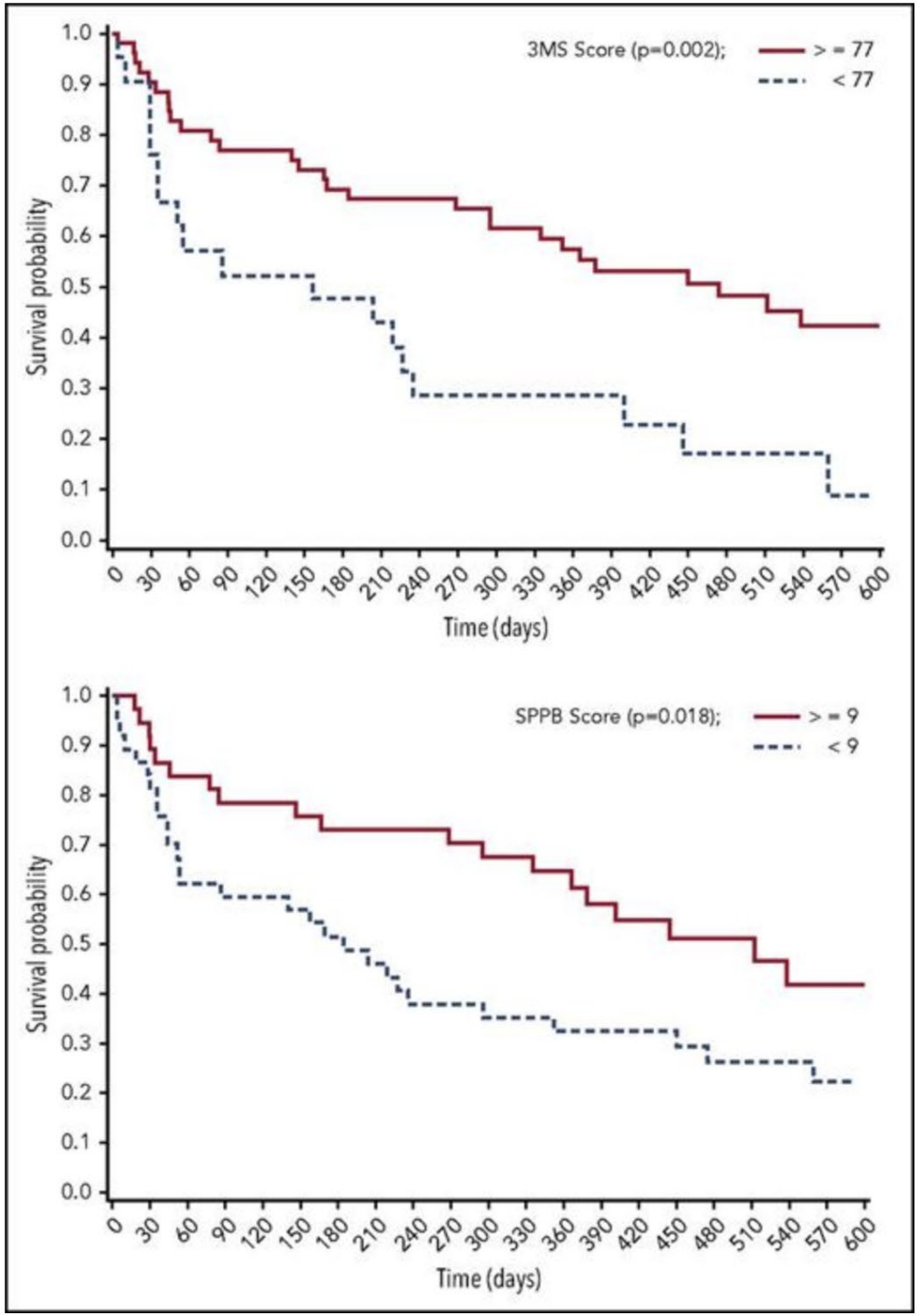


Fig 1. Survival duration of patients treated according to intensive chemotherapy (arm A) or wait and see followed by mild chemotherapy (arm B).

Löwenberg JCO 1989

AML



Klepin Blood 2013

AML

Metric	References	Outcome	Patients	Therapy	Data source
Comorbidities					
CCI	11	ED, CR, OS	n = 133, age ≥ 70 y	Intensive	Retrospective
	12	ED, OS	n = 5480, age ≥ 65 y	Variable	Registry
	13	No effect on ED, CR	n = 2792, all ages	Variable	Registry
	14	No effect on ED, OS	n = 144, age ≥ 60 y	Intensive	Retrospective
HCTCI	15	ED, OS	n = 177, age ≥ 60 y	Intensive	Retrospective
	16	OS	n = 416, age ≥ 65 y	Intensive	Retrospective
	17	ED, OS	n = 80, age > 55 y	Intensive	Retrospective
Augmented HCTCI	18	ED, OS	n = 1100, all ages	Variable	Retrospective
Diabetes	14	ED	n = 144, age ≥ 60 y	Intensive	Retrospective
Physical function					
IADL	19	OS	n = 63, all ages	Variable	Prospective
	20	OS	n = 101, age ≥ 65 y	Variable	Retrospective
ADL	21	OS	n = 195, age ≥ 60 y, AML and MDS	Variable	Prospective
SPPB	22	OS	n = 74, age ≥ 60 y	Intensive	Prospective
Modified SPPB	23	No effect on OS	n = 97, age ≥ 60 y	Intensive	Prospective
Cognition					
Modified MMSE	22	OS	n = 74, age ≥ 60 y	Intensive	Prospective
Polypharmacy					
No. medications	24	ED, CR, OS	n = 150, age ≥ 60 y	Intensive	Retrospective

ADL, activities of daily living; CCI, Charlson Comorbidity Index; CR, complete remission; ED, early death; HCTCI, Hematopoietic Cell Transplant Comorbidity Index; IADL,

Olin R. Blood 2019, 134:63-70

Transplantation

Studies evaluating the effect of pre-alloHCT geriatric assessment on post-alloHCT outcomes in older patients

References	Patients	Geriatric measures associated with OS	Geriatric measures associated with NRM/TRM
Muffly et al[34]	n = 203, age 50-73 y	Functional status (IADL), comorbidity (HCTCI), degree of inflammation (CRP), gait speed (15 ft), mental health (SF36-MCS; multivariate analysis).	Functional status (IADL), comorbidity (HCTCI), degree of inflammation (CRP).
Huang et al[37]	n = 148, age 50-76 y	Functional status (IADL, MOS-PH)	Functional status (MOS-PH)
Deschler et al[38]	n = 106, age 60-78 y	Gait speed (TUG test), fatigue.	Comorbidity (HCTCI)

CRP, C-reactive protein; MOS-PH, Medical Outcomes Study Physical Health scale; SF36-MCS, Mental Component Summary of the Medical Outcomes Short Form-36; TRM, treatment-related mortality; TUG, Timed Up and Go.

Olin R. Blood 2019, 134:63-70

Transplantation: HCT-CI

Table 1. Definitions and Weighted Scores of the Pretransplantation Comorbidities Included in the HCT-CI and Their Prevalence Among the Allogeneic Transplantation Patients Admitted to the Intensive Care Unit

Comorbidity	Definitions	HCT-CI Weighted Score	Patients (N = 377)	
			No.	%
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmia	1	16	4
Cardiac	Coronary artery disease, congestive heart failure, myocardial infarction, or EF ≤ 50%	1	55	15
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	1	3	1
Diabetes	Requiring treatment with insulin or oral hypoglycemic but not diet alone	1	47	12
Hepatic, mild	Chronic hepatitis, bilirubin > ULN to 1.5× ULN, or AST/ALT > ULN to 2.5× ULN	1	56	15
Infection	Requiring continuation of antimicrobial treatment after day 0	1	10	3
Inflammatory bowel disease	Crohn's disease or ulcerative colitis	1	4	1
Obesity	Patients with a body mass index > 35 kg/m^2	1	41	11
Psychiatric disturbance	Depression or anxiety requiring psychiatric consult or treatment	1	40	11
Renal, moderate/severe	Serum creatinine > 2 mg/dL, on dialysis, or prior renal transplantation	2	3	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatic	2	10	3
Peptic ulcer	Requiring treatment	2	11	3
Pulmonary, moderate	DLCO and/or FEV_1 66% to 80% or dyspnea on slight activity	2	123	33
Heart valve disease	Except mitral valve prolapse	3	9	2
Hepatic, moderate/severe	Liver cirrhosis, bilirubin > 1.5× ULN, or AST/ALT > 2.5× ULN	3	16	4
Prior solid tumor	Treated at any time point in the patient's past history, excluding nonmelanoma skin cancer	3	20	5
Pulmonary, severe	DLCO and/or FEV_1 ≤ 65% or dyspnea at rest or requiring oxygen	3	179	47

Abbreviations: CTD, connective tissue disease; DLCO, diffusion capacity of carbon monoxide; EF, ejection fraction; FEV_1, forced expiratory volume in 1 second; HCT-CI, Hematopoietic Cell Transplantation–Specific Comorbidity Index; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; ULN, upper limit of normal.

Low=0, intermed= 1-2, high risk 3+

Bayraktar, JCO 2013

Transplantation

Different Prognostic Models Have Been Validated in HSCT Patients

HCT-CI

Comorbidities	HCT-CI Scores
Arrhythmia	1
Cardiovascular comorbidity	1
Inflammatory bowel disease	1
Diabetes/steroid-induced hyperglycemia	1
Cerebrovascular disease	1
Psychiatric disorder	1
Mild hepatic comorbidity	1
Obesity	1
Infection	1

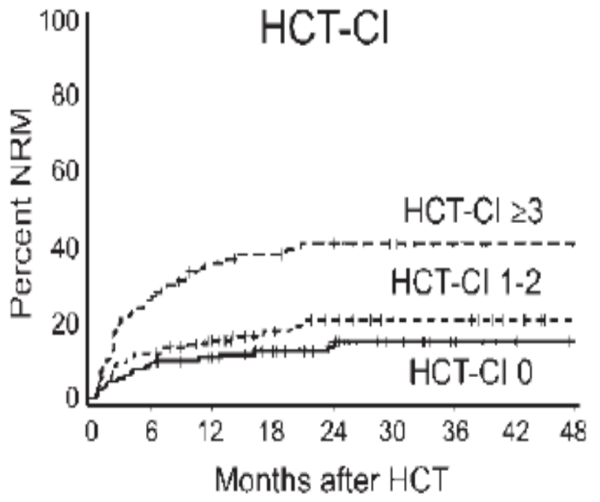
Comorbidities	HCT-CI Scores
Rheumatologic comorbidity	2
Peptic ulcer	2
Renal comorbidity	2
Moderate pulmonary comorbidity	2
Prior malignancy	3
Heart valve disease	3
Moderate/severe hepatic comorbidity	3
Severe pulmonary comorbidity	3

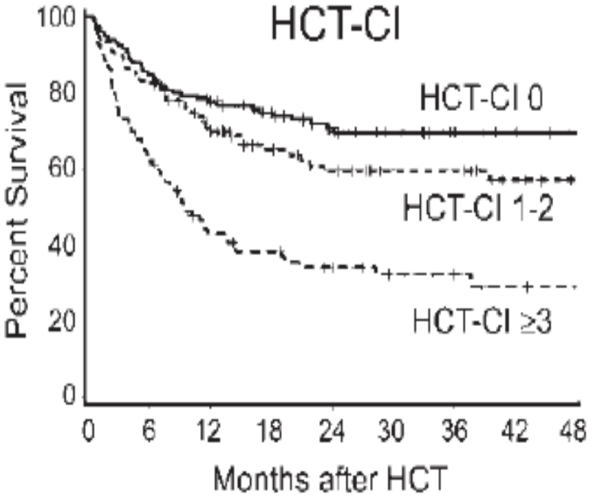
HCT-CI = hematopoietic cell transplant comorbidity index.
Sorror, 2013.

i3Health
Education on Point®

- score 0 (low risk)
- score 1 to 2 (intermediate risk)
- score ≥ 3 (high risk)

According to this, Sorror and Coll. demonstrated that the HCT-CI can stratify the patients for the risk of NRM and also for OS.





Sorror Blood 2005;106:2912-9

Solutions?

- Multidisciplinary approach
- Use easy and well validated GA tools
- Check disease characteristics and therapies
- Discuss with patient and caregivers all R/ options
  - Life expectancy, cure or disease control, therapy and toxicity, QoL,
- Intervene and optimalize at start of R/
- Intensify pt monitoring during the first cycles of therapy
- Longitudinal GA better than one
- Regular analysis and discussions about R/ outcome

Validated geriatric interventions

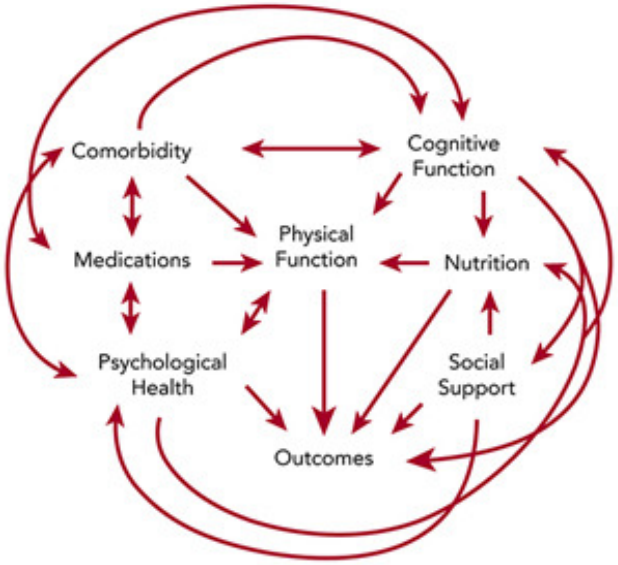
Functional status	Physiotherapy @ home Occupational therapy @ home Home nursing care Home security Assessment of risk of falling Promote physical exercise Screening and assessment of osteoporosis
Cognition	Involve the proxy caregivers Reduce potentially inappropriate medications Preventive measures of delirium Assess the ability to understand and acknowledge the treatment Identify the relatives / collaborative decisions Perform neuropsychological testing

Nutrition	Dietician advice + follow up Dietetic recommendations Oral care Nutritional support (oral, enteral) If functional impairment : occupational therapist, physiotherapy, home care, meals on wheels, caregiver involvement, vitamin D

Social support/ Caregiver burden	Transportation assistance to the hospital Home care Support groups Psychological support Spiritual assistance
Psychological status	Non pharmacological care : meditation, relaxation, acupuncture Exercise program Psychological support Medication for anxiety, depression Support programs, stress management Spiritual assistance

NCCN guidelines 2017

Geriatric assessment characterizes phenotypic heterogeneity of aging



Roles for geriatric assessment from diagnosis through survivorship

Baseline assessment:
- Predict toxicity, survival, health care utilization

Follow-up assessments:
- Monitor impact of treatment on patient-centric functional outcomes

- Guide supportive care referrals to maximize treatment tolerance and quality of life

Observe, calculate, evaluate possible therapies, discuss and decide.
This is patient-centered care!

Go-Go

Slow Go

No Go