ASH Review: Geriatric Hematology

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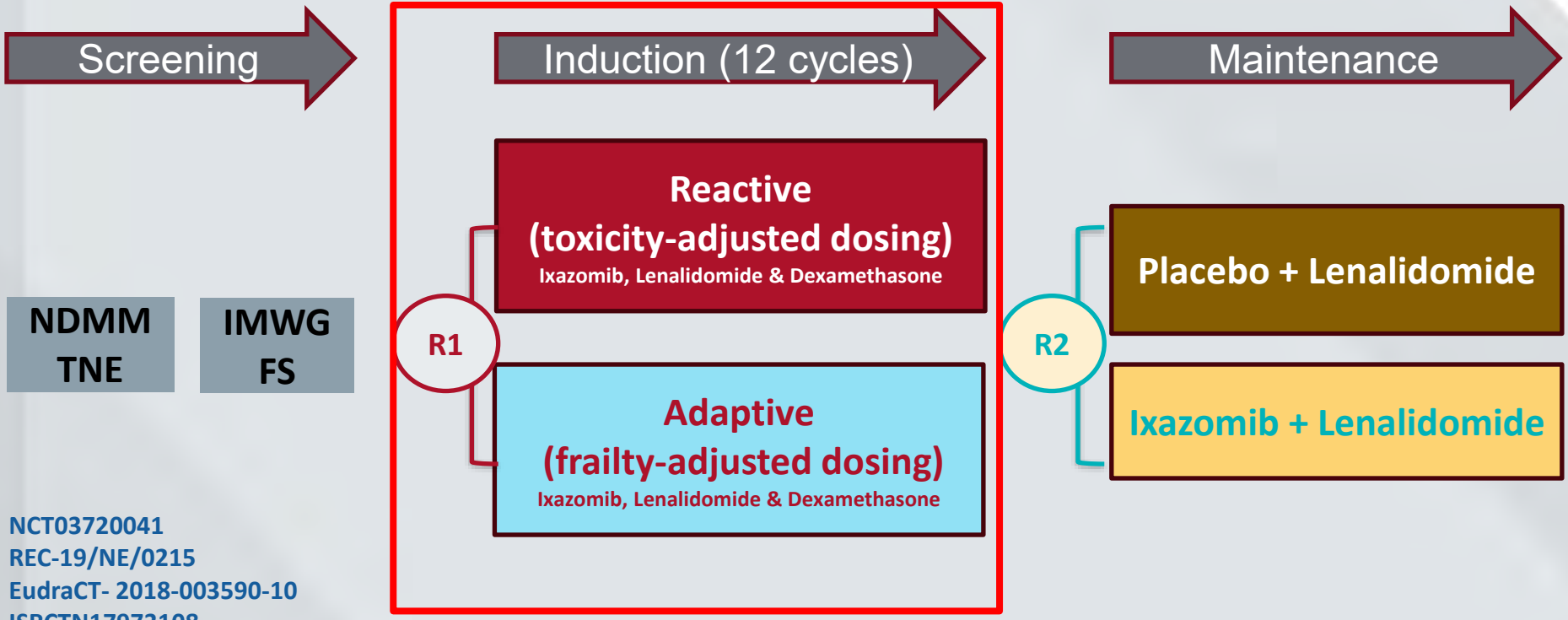
Myeloma

UK-MRA Myeloma XIV FiTNEss Trial Design

Chief Investigators: Gordon Cook, Graham Jackson



NCT03720041
REC-19/NE/0215
EudraCT- 2018-003590-10
ISRCTN17973108

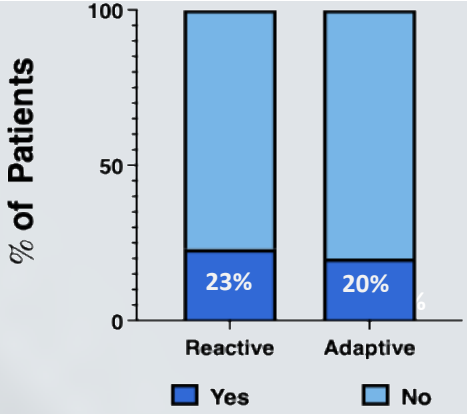
Slides courtesy of Gordon Cook

Cook *et al, Blood* (2024) 144 (Supplement 1): 673.

Results – Early Treatment Cessation (ETC)

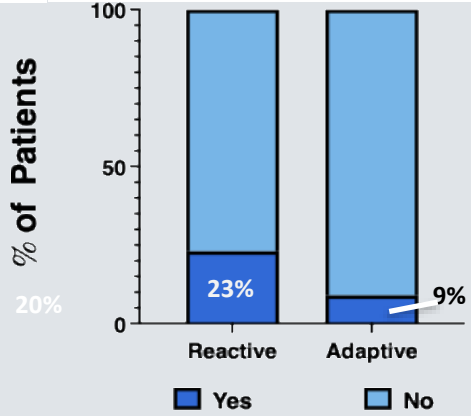
Unfit/Frail (n=535)

OR 0.83 (95% CI: 0.54, 1.25, p=0.3678)



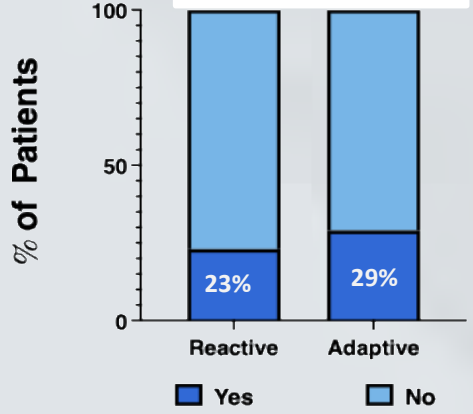
Unfit (n=240)

OR 0.34 (95% CI: 0.16, 0.72)



Frail (n=295)

OR 1.33 (95% CI: 0.79,2.25)



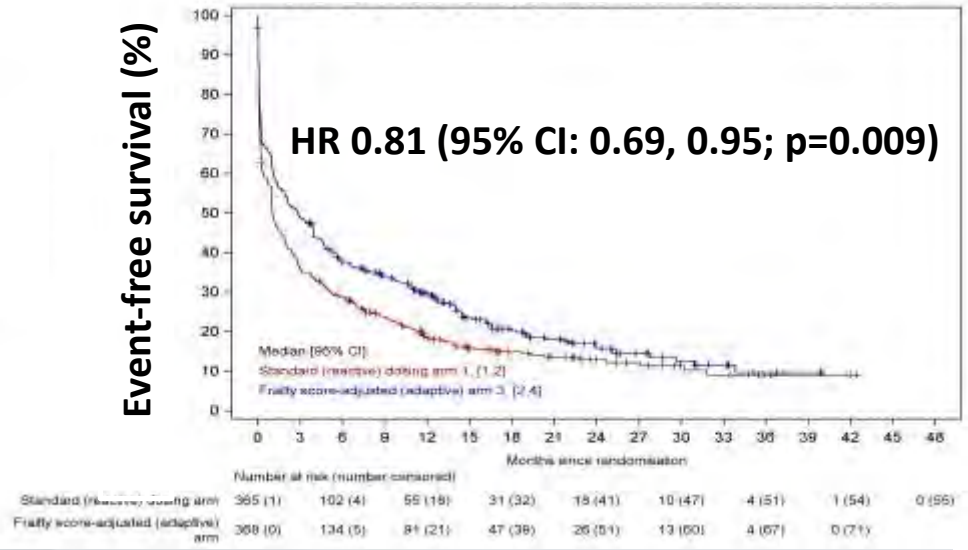
Reasons for stopping	Reactive	Adaptive
Death	26.9%	27.5%
Patient choice	28.8%	23.5%
Clinician choice	9.6%	15.7%
Toxicity	26.9%	21.6%

Slides courtesy of Gordon Cook

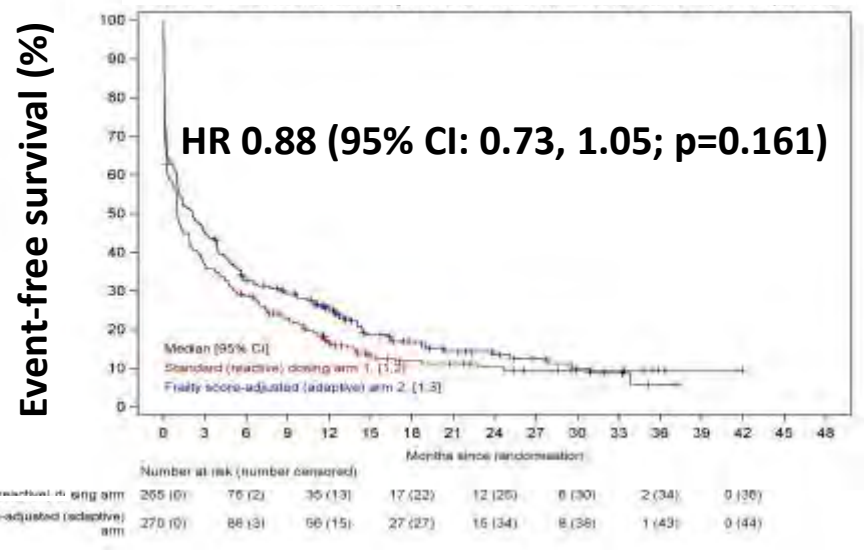
Results – Event-free survival (EFS)

EFS defined as: PD, death from any cause, withdrawal from trial treatment, non-haematological (gd≥3) & haematological (gd≥4) toxicities

EFS ITT Population



EFS Unfit/Frail Population



1-year EFS:

Reactive arm 18.8% (95% CI: 14.8%, 23.0%)

Adaptive arm 29.7% (95% CI: 25.0%, 34.5%)

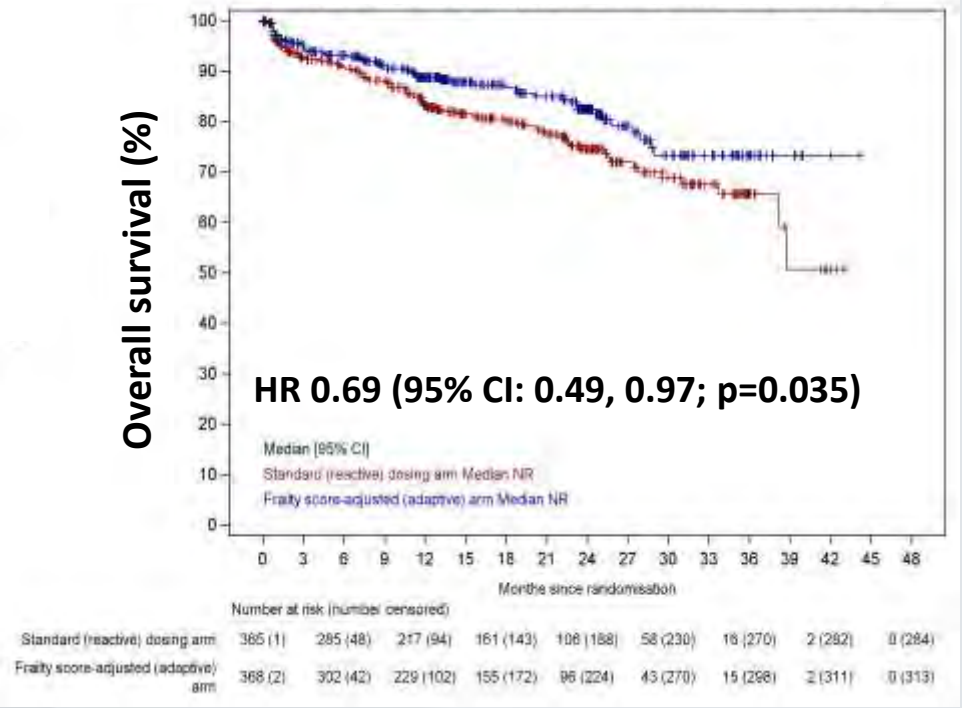
1-year EFS:

- **Reactive arm 16.9% (95% CI: 12.6%, 21.8%)**
- **Adaptive arm 25.7% (95% CI: 20.6%, 31.1%)**

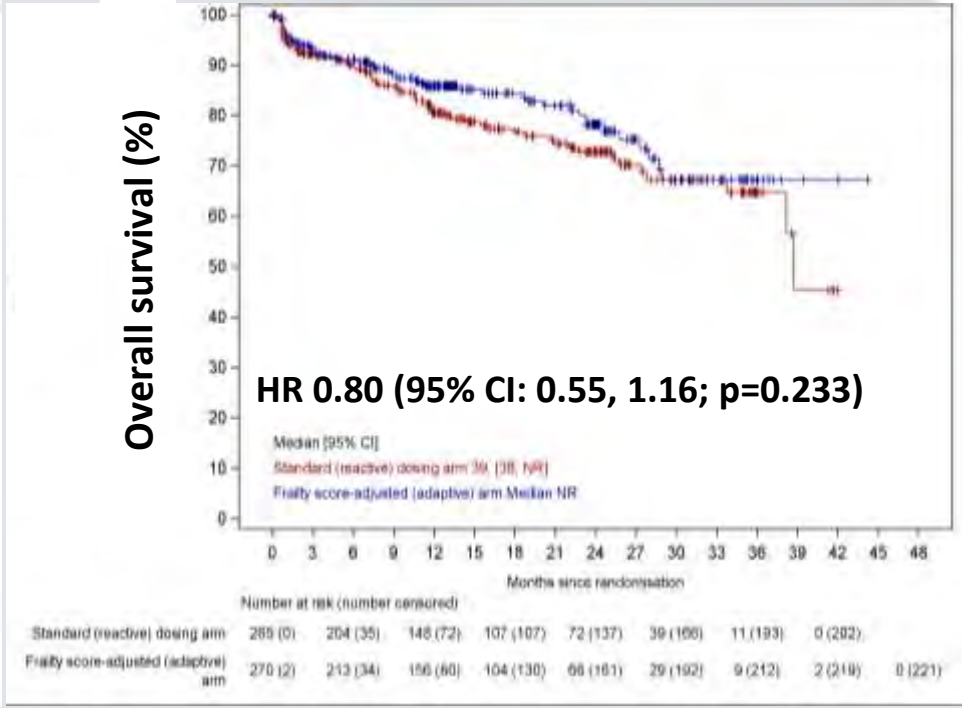
Slides courtesy of Gordon Cook

Results – Overall survival (OS)

OS ITT Population



OS Unfit/Frail Population



Median Follow-up: 14.7 mns (7.6,24,4)

Slides courtesy of Gordon Cook

Frailty and Outcomes in Multiple Myeloma Patients Eligible for Autologous Hematopoietic Cell Transplantation

How is frailty evaluated? HCT frailty scale
Clinical frailty score (CFS): ≥3 (Frail) [vs 1-3 (Not frail)]
Instrumental activities of daily living (IADL) score: ≥1 Limitation [vs no limitation]
Timed up and go test (TUGT): Abnormal >10 seconds [vs normal]
Grip strength (GS): Abnormal [vs normal] If female less than 16 kg If male less than 26 kg
Self-rated health question (SRH-Q) Fair, poor [vs excellent , very good, good]
Fall in last 6 months: Yes [vs no]
Albumin serum level (Alb): Abnoraml (<38 g/L) [vs normal]
C-reactive protein (CRP): Abnormal (≥11 mg/L) [vs normal]

Who performs the evaluation?
Median time: 5-6 minutes
Medical doctor
Nurse coordinator
Laboratory (bloodwork)

When?
Before HCT: first consultation

Costs
Hand dynamometer
No other recurrent costs

N=296
Median age 57 (range 31-75)

	Fit	Intermediate	Frail	P-value
	23.2%	48%	18%	
Hospitalization, days	14	15	15	
Readmission	2.0%	8.6%	13.5%	0.06
1-Yr relapse	8.9%	5.6%	6.5%	0.903
1-Yr OS	98.9%	95.8%	84.3%	<0.01

Salas, *et al* *Blood* (2024) 144 (Supplement 1): 5148.

Simplified Frailty Scale

Table 1 ECOG proxy of IMWG algorithm of frailty

Category	Score
Age	
≤75 years	0
76–80 years	1
>80 years	2
Charlson Comorbidity Index	
≤1	0
>1	1
ECOG performance status	
0	0
1	1
≥2	2
Sum of scores	
Nonfrail	0–1
Frail	≥2

ECOG Eastern Cooperative Oncology Group, *IMWG* International Myeloma Working Group

Facon et al, Leukemia, 2020

Frailty and Outcomes after Bispecific T-Cell Engager Therapy for Patients with Relapsed/Refractory Multiple Myeloma

- Single institution retrospective cohort study
- Treatment: Teclistimab, talquetamab, elranatamab
- N= 112
- Age range 40 - 88
- 83 (74%) frail at the time of BsAb treatment
- Frailty measure used: Simplified (IFM) fraily score (=age, ECOG PS, Charlson comorbidity Index)

	Frail N=83	Nonfrail N=29	P-value
CRS (all grades)	62%	62%	1
ICANS (all grades)	14%	3%	0.21
Treatment-related mortality	14%	7%	0.46
Overall response rate	72%	62%	0.43
Median PFS (months)	6.5	4.6	0.45
Median OS (months)	7.5	7.3	0.16

Adegbite *et al Blood* (2024) 144 (Supplement 1): 4735.

Frailty-Based Outcomes with Bispecific Antibodies in Older Patients with Multiple Myeloma

- Retrospective cohort study, single-institution
- Treatment: Teclistimab, talquetamab or investigational
- N= 99
- Age range 65-89 years
- 71% frail at the time of BsAb treatment
- Frailty measure used: Simplified (IFM) frailty score (=age, ECOG PS, Charlson comorbidity Index)

	Frail N=70	Nonfrail N=29	P-value
All-grade CRS	59%	66%	NS
Grade 3-4 CRS	3%	7%	NS
ICANS	9%	3%	NS
Early mortality (90 days)	23%	10%	P=0.17
Overall response rate	52%	62%	NS
1-Yr PFS	36%	48%	P=0.26
1-Yr OS	57%	61%	P=0.30

Abdallah, *et al*, *Blood* (2024) 144 (Supplement 1): 4695.

Outcomes of Frailty Subgroups Treated with Teclistamab in the Real-World: An International Myeloma Foundation Study Database Analysis

- Retrospective analysis, 7 institutions
- Treatment: Teclistimab
- N= 81
- Age: Median 76 yrs (range 70-91)
- 73% frail at the time of BsAb treatment
- Frailty measure used: Simplified (IFM) frailty score (=age, ECOG PS, Charlson comorbidity Index)

	Frail N=59	Nonfrail N=22	P-value
All-grade CRS	47%	55%	
Grade 2 CRS	29%	8%	0.23
ICANS	14%	9%	0.72
Infection	59%	45%	0.32
Overall response rate	66%	50%	0.61
1-Yr PFS	42.4%	47.6%	
1-Yr OS	61.5%	64.9%	

Lymphoma

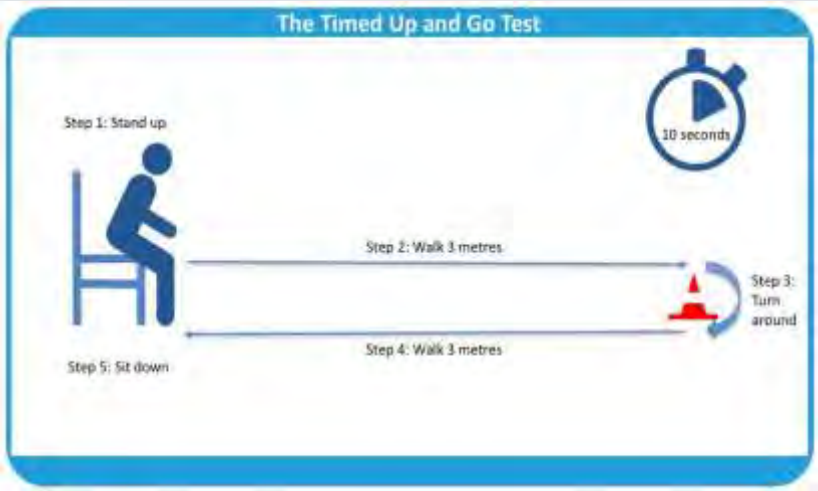
Frailty's Impact on CAR T-Cell Therapy Outcomes in Patients with Lymphoproliferative Disorders: Insights from a Spanish Multicenter Pilot Study Conducted on Behalf of the Geth-CT

- N=36
- Frailty measure: HCT frailty scale
- median age 61 (range 28-76)

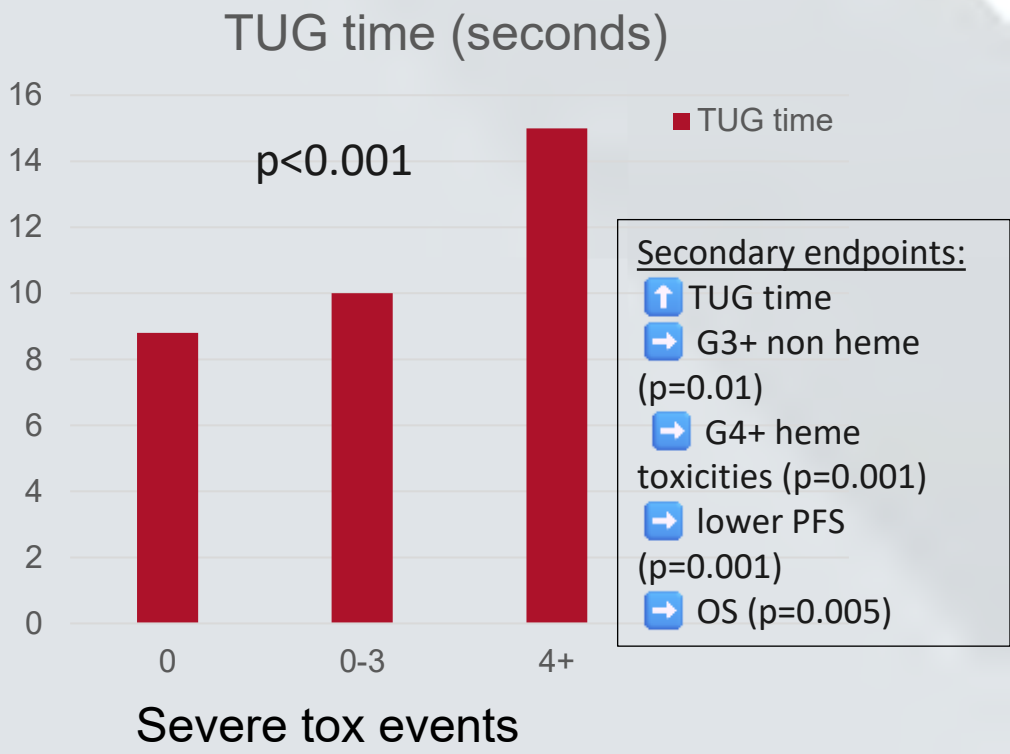
	Fit N=7	Intermediate N=22	Frail N=7	P-value
N=36	19%	62%	19%	
Grade 2-4 CRS	50%	33%	50%	0.874
Grades 2-4 ICANS	20%	33%	67%	**0.065**
ICU admission	24%	26.7%	50%	P=0.354
Relapse	12.5%	26.7%	50.0%	**0.026**
Death	12.5%	13.2%	50.0%	**0.050**

Salas *et al, Blood* (2024) 144 (Supplement 1): 3757.

A Prospective Geriatric Assessment (GA) Study Predicting Toxicities in Older Adults (OA) with Non-Hodgkin Lymphoma (NHL): Timed up and Go Test (TUG) Time Emerges As a Functional Vital Sign



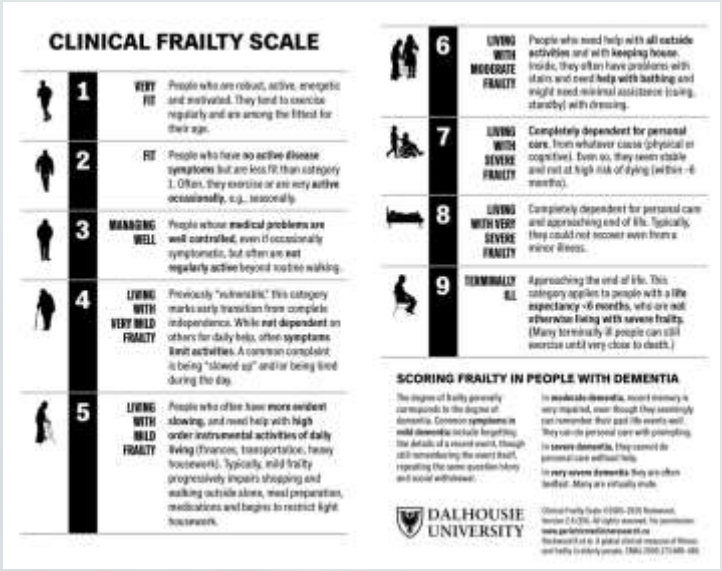
N=194
Median age 74 yrs (range 60-93 yrs)
72% DLBCL/R-CHOP
Endpoint: Severe Tox (hospitalization/<80% dose intensity/treatment discontinuation/death



Torka *et al, Blood* (2024) 144 (Supplement 1): 4474.

Myeloid Neoplasms

Impact of Frailty in a Prospective Cohort of Patients with MDS Treated with Hypomethylating Agents



MDS-specific frailty scale

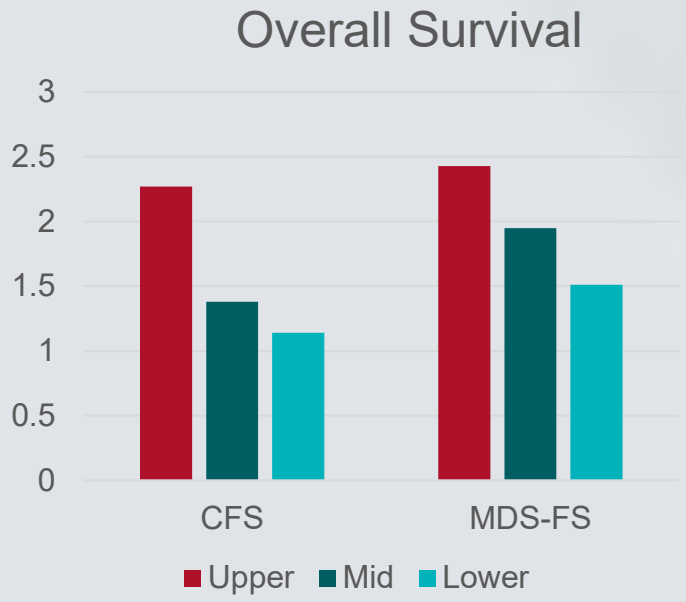
Element	Definition of deficit	Weighting
RDW	Deficit if out of hospital lab range	2
LDH	Deficit if out of hospital lab range	2
WBC	Deficit if out of hospital lab range	1
MCV	Deficit if out of hospital lab range	1
Ferritin	Deficit if out of hospital lab range	1
Reticulocyte count	Deficit if out of hospital lab range	1
ALP	Deficit if out of hospital lab range	1
ALT	Deficit if out of hospital lab range	1
Bilirubin	Deficit if >1.5 × ULN of normal hospital range	1
Creatinine clearance (ml/min)		<30:1 30–59:0.5 ≥60:0
BMI		<18.5 or ≥30:1 25–29.9:0.5 18.5–24.9:0
Any cancer history	Deficit if current or in the past	1
Plans, prepares, and serves adequate meals independently	Deficit if unable	1
Global fatigue score (0–10, 10 is the highest degree of fatigue)		≥7:1 4–6:0.5 0–3:0
4-m walk test (time to walk 4 m in seconds)		>6.67:1 4–6.67:0.5 <4:0

RDW red blood cell distribution width, *LDH* lactate dehydrogenase, *WBC* white blood cell, *MCV* mean corpuscular volume, *ALP* alkaline phosphatase, *ALT* alanine aminotransferase, *BMI* body mass index.

Wan et al Leukemia 2020 34:3434-3438

Impact of Frailty in a Prospective Cohort of Patients with MDS Treated with Hypomethylating Agents

- N=513
- Median age 72.7 (66-81)
- Treatment: Azacitidine and Decitabine
- Frailty measures used:
  - Clinical Frailty Scale
  - MDS-specific frailty scale



Lower MDS FS-15 scores predictive of completing≥4 cycles of HMA

Allogeneic Stem Cell Transplant

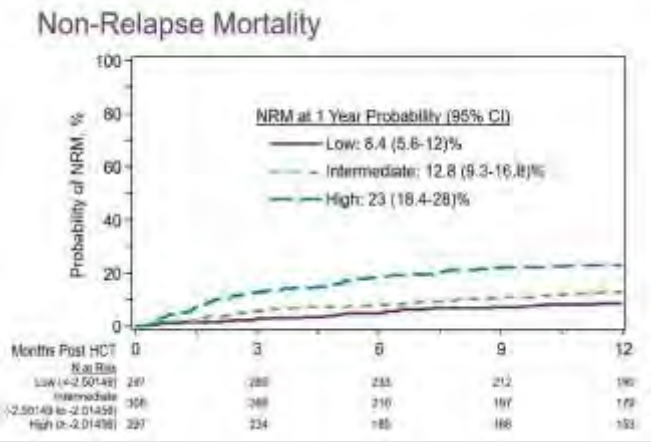
The Composite Health Risk Assessment Model (CHARM) Predicts Risks of Toxicities, Functional and Cognitive Decline Among Survivors of Allogeneic Hematopoietic Cell Transplantation (allo-HCT): A Prospective BMT-CTN Study 1704

- Development and validation of the CHARM model: *(Artz et al ASH 2023)*
  - Comorbidities
  - C-reactive protein
  - Albumin
  - Weight loss

Table: Covariates selected by multivariate analysis influencing NRM within 1 year

Variable (continuous)	Subdistribution Hazard Ratio **	95% CI	p-value
HCT-CI	1.166	1.092 - 1.245	<0.0001
LOG (CRP)*, mg/L	1.142	1.020 – 1.278	0.0188
Albumin, g/dL	0.491	0.347 – 0.693	<0.0001
% Weight Loss, squared***	1.002	1.000 – 1.002	0.0023

*natural log. **values > 1.0 indicate a positive association with risk of NRM. ***weight gain or no weight loss is scored as a 0;
CHARM formula = 0.15310*(HCT-CI)+0.13247*(LOG(CRP))
0.71227*(ALBUMIN)+0.00119*(% Weight Loss)^2



The Composite Health Risk Assessment Model (CHARM) Predicts Risks of Toxicities, Functional and Cognitive Decline Among Survivors of Allogeneic Hematopoietic Cell Transplantation (allo-HCT): A Prospective BMT-CTN Study 1704

N=1105 Allo HCT candidates

Models adjusted for conditioning intensity , GVHD prophylaxis, disease-risk index, etc

Higher CHARM score

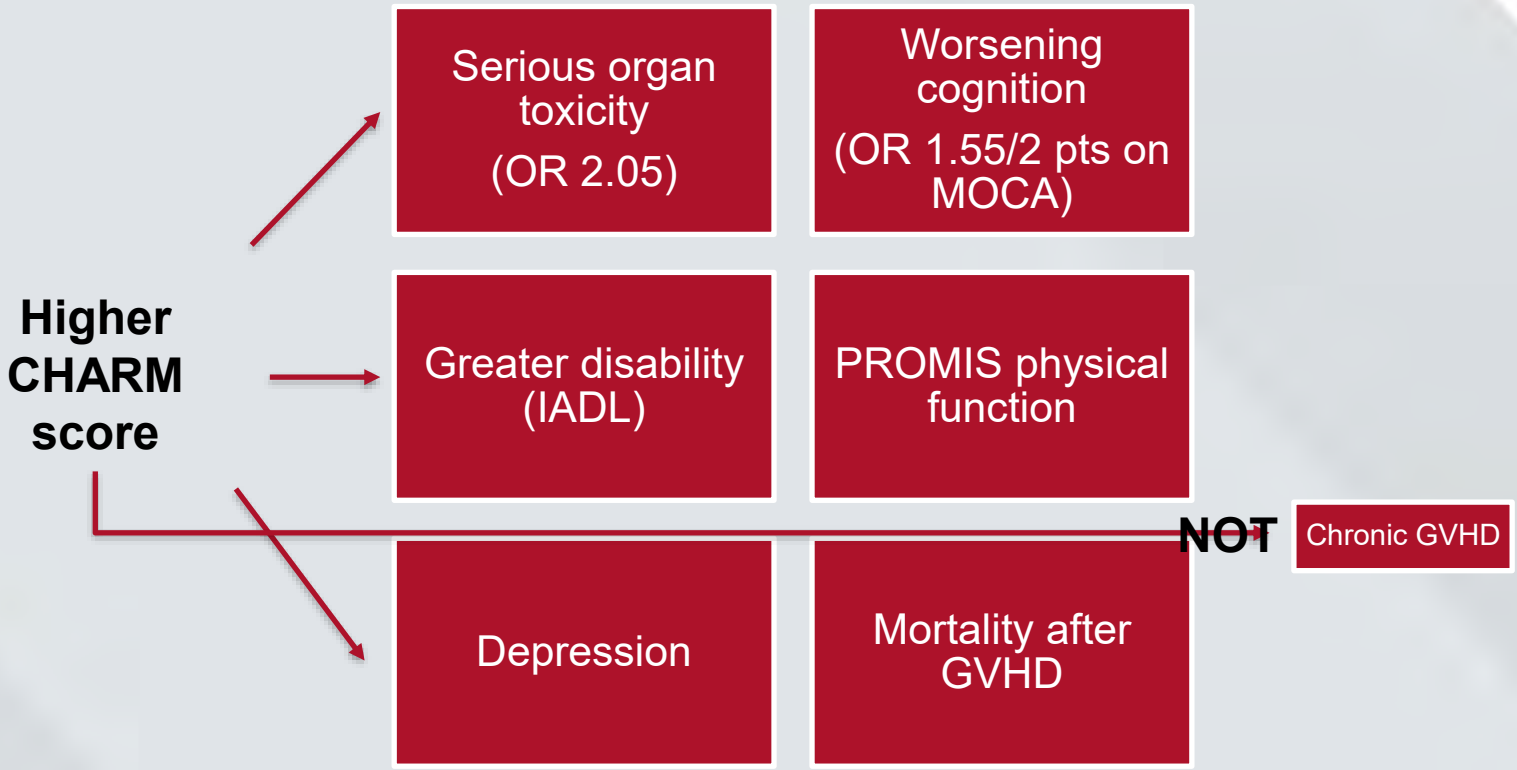
- Serious organ toxicity (OR 2.05)
- Worsening cognition (OR 1.55/2 pts on MOCA)
- Greater disability (IADL)
- PROMIS physical function
- Depression
- Mortality after GVHD

Sorror *et al Blood* (2024) 144 (Supplement 1): 685.

The Composite Health Risk Assessment Model (CHARM) Predicts Risks of Toxicities, Functional and Cognitive Decline Among Survivors of Allogeneic Hematopoietic Cell Transplantation (allo-HCT): A Prospective BMT-CTN Study 1704

N=1105 Allo HCT candidates

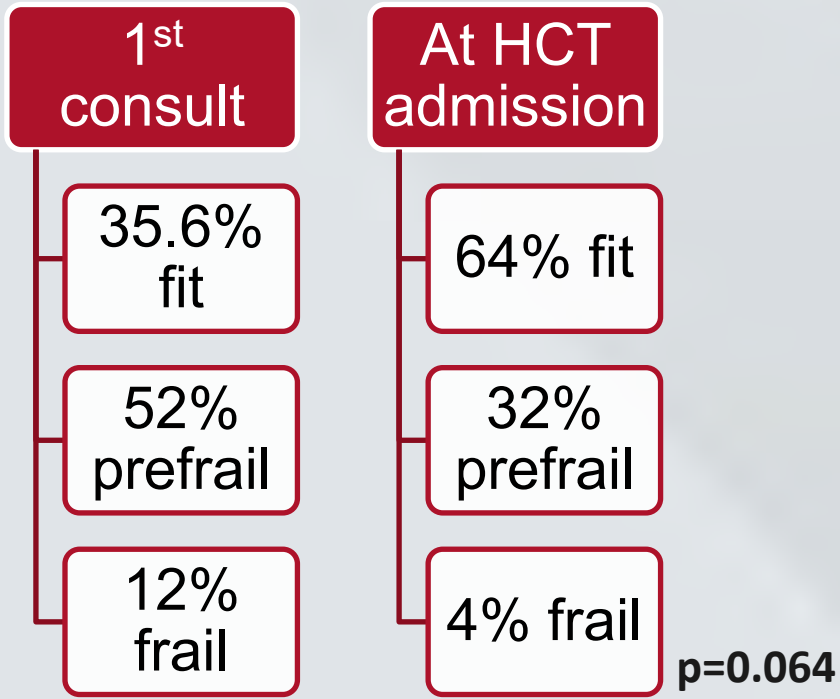
Models adjusted for conditioning intensity , GVHD prophylaxis, disease-risk index, etc



Sorror *et al Blood* (2024) 144 (Supplement 1): 685.

Transforming Frailty Care in Allo-HCT Candidates: A Prospective Assessment of a Tele-Prehabilitation Project

- Intervention: **T-PreHab**
- PM&R physician
- Tailored, home-based exercise program
- Nutritional consult + supplements
- N=25
- Adherence >80%
- Comparison: Historical controls (N=59): fitness level unchanged



Recurring themes & summary

- Many frailty measures in use
  - Some disease-specific, others adopted from geriatrics
- Considering frailty in dosing treatment for myeloma improves EFS and OS
- Frailty measures can be predictive and prognostic
  - More simplified frailty measures may miss opportunity to identify individuals at greater risk
  - More comprehensive or physical performance based measures tend to show differences in outcomes
- Frailty can be reversed with intervention (exercise)

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