Università di Brescia

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in
«Intelligenza Artificiale in Medicina e Innovazione nella Ricerca clinica e metodologica»

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A PROSPECTIVE GERIATRIC ASSESSMENT IN ELDERY PATIENTS SUBMITTED TO ALLOGENIC STEM CELL TRANSPLANTATION (ALLO-SCT): THE IDENTIFICATION OF PROGNOSTIC NON RELAPSE MORTALITY RISK FACTORS FOR CREATING AN INDIVIDUALIZED OPTIMIZAZION PLAN FOR ALLO-SCT CANDITATED.

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CICLO XL

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The Comprehensive Geriatric Assessment (CGA)

a multidisciplinary process to evaluate frail or complex older adults by assessing their medical, psychological, physical, cognitive, and social factors to develop a coordinated care plan.
The goal is to improve their health, independence, and quality of life while reducing hospitalizations and readmissions.

GCA tools

- Mini-mental state examination
- Mini-Cog
- Montreal cognitive assessment

- Chair stand
- Hand Grip
- Gait speed
- 6-min walk
- Timed up-and-go

- ADL
- IADL
- G8
- VES-13
- FIL Score
- CFS

GCA

- Geriatric depression scale
- Generalized anxiety disorder scale

- HCT-CI
- CIRS-G

- Weight loss
- BMI
- Albumin
- PCR

Materials and Methods

- In January 2020, our center started a frailty prospective assessment program
- Age ≥ 50 years at transplant
- Any disease, donor and stem cells source

GCA

30-45 min
by geriatrician

- ADL
- IADL
- G8
- VES-13
- CFS

- gait speed
- chair stand
- hand grip

- mini-cog
- MMSE

- HCT-CI
- FIL score

Allo-SCT

Overall outcome
- OS
- NRM
- CIR

Development of a **simplified risk score** based on some GCA domains

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Results: patients characteristics

135 pts
Age, median: 63 y
AML: 39%
DRI Int+High: 96%
HCT CI ≥ 3: 53%

Characteristics	N (%)
Number	135 (100)
Age at allo-SCT, years, median (range)	63 (50-75)
Male, number (%)	86 (63.7)
Diagnosis, number (%)	
AML	53 (39.3)
MDS	17(12.6)
ALL	11 (8.1)
Lymphoma	13(9.6)
MF	25 (18.5)
Other	16(11.9)
Disease risk index, number (%)	
Low	3 (2.2)
Intermediate	95 (70.4)
High	35 (25.9)
Very high	2 (1.5)
KPS, number (%)	
90-100	126 (93.4)
70-80	9 (6.6)
HCT-CI, number (%)	
0	27 (20)
1-2	37 (27.4)
≥3	71 (52.6)
FIL score, number (%)	
Fit	132 (97.8)
Unfit	3 (2.2)
Disease status, number (%)	
1st complete remission	53 (39.3)
No 1st complete remission	82 (60.7)
Donor type, number (%)	
Related	33 (24.4)
Unrelated	63 (46.7)
Haploidentical	39 (28.9)
Stem cell source, number (%)	
PBSC	124(91.9)
BM	11(8.1)
Conditioning regimen, number (%)	
MAC	85 (63)
RIC	50 (37)

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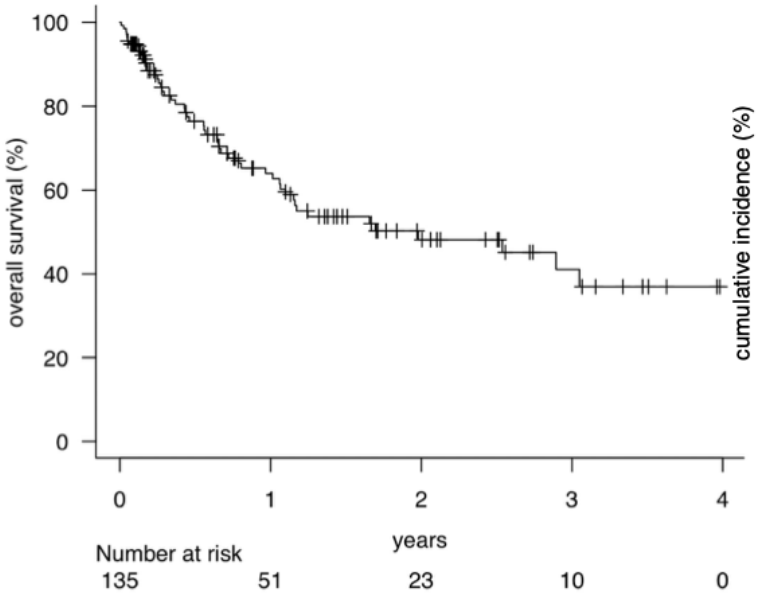
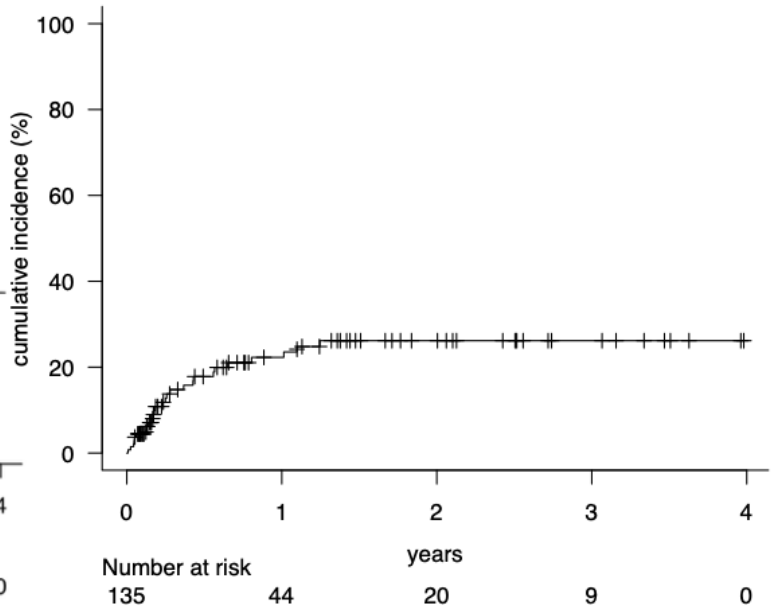
Results: outcomes

OS



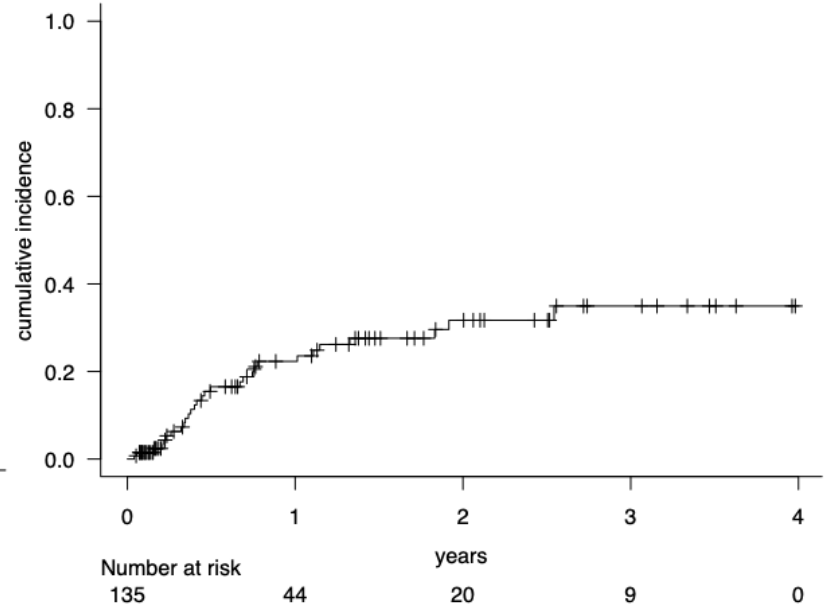
Pts	OS 1y	OS 2y	OS 4y
135	63%	48%	37%

NRM



Pts	NRM 1y	NRM 2y	NRM 4y
135	25%	26%	26%

CIR



Pts	CIR 1y	CIR 2y	CIR 4y
135	24%	32%	35%

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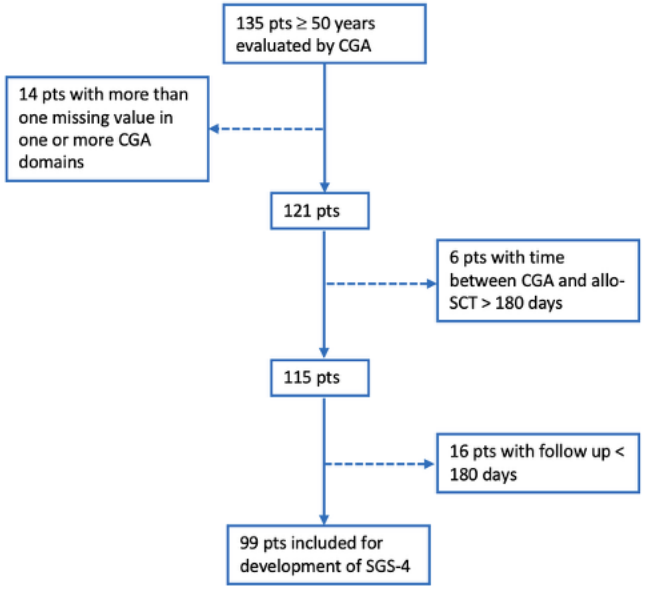
Results: outcomes according to each geriatric assessment domain

	Pts evaluated	OS 1 y	OS 2 y	P	NRM 1y	NRM 2 y	P	CIR 1 y	CIR 2 y	P
ADL										
Any limitations	4	50	-	0.5	25	-	0.95	25	-	0.73
No limitations	130	63	49		24	26		23	30	
IADL										
Any limitations	118	30	50	0.11	46	24	0.11	35	35	0.72
No limitations	15	66	30		21	46		22	21	
G8, points										
≤13	51	52	46	0.7	24	24	0.9	31	37	0.23
>13	83	67	48		24	29		17	26	
VES 13, points										
>3	14	11	11	**0.04**	30	30	0.93	58	58	**0.01**
≤3	120	67	52		23	26		18	28	
FIL score										
FIT	132	65	50	**<0.01**	24	27	0.41	21	30	**<0.01**
UNFIT	3	0	-		0	23		100	-	
CFS										
FIT	75	63	55	0.6	23	23	0.9	22	35	0.8
UNFIT	12	45	-		28	-		27	-	
Gait Speed, m/s										
≤1.1	80	73	60	0.06	20	22	0.31	25	31	0.2
>1.1	49	41	27		31	34		40	40	
Chair Stand, times										
<14	90	65	50	0.5	21	22	0.37	25	32	0.83
≥14	41	54	40		27	34		24	31	
Hand Grip, Kg										
<26	37	45	30	**<0.01**	34	38	**0.05**	28	41	0.6
≥26	97	68	54		21	21		20	28	
Mini-Cog, points										
1-2	56	64	58	0.28	21	21	0.44	19	29	0.45
3	77	60	39		24	29		26	31	
MMSE, points										
≤24	13	19	19	**0.03**	52	52	0.2	29	48	0.56
>24	121	66	50		22	24		22	29	
HCT-CI, points										
0	27	88	33		17	17		18	25	
1-2	37	70	49	0.2	18	18	0.2	22	38	0.88
≥3	71	55	37		29	34		28	30	

Simplified geriatric score-4 (SGS-4)

1



2

Factor Analysis (FA)

- Mixed correlation matrix used (to handle both continuous and categorical data)
- Scree plot (elbow method)
- Two-factor model with oblimin rotation (since factors expected to correlate) and Bartlett's method (for estimating factor scores)
- Variables with **factor loading ≥ 0.3** retained.

3

SGS-4 development

The factor including gait speed, hand grip, G8 score, and sex was identified as representing overall fitness.

•Continuous variables (gait speed, handgrip) were divided into quartiles and combined with categorical variables (G8 and sex).
•Each variable weighted according to its factor loading

Score = [Gait Speed] + 2 × [Handgrip Strength] + [G8] + 1.5 × [Sex].

Values	Gait speed (m/s)	Hand grip (Kg)	Sex
1	≤ 1.04	≤ 24.5	M
2	1.04 < X ≤1.17	24.5 < X ≤32.7	F
3	1.17 < X ≤1.29	32.7 < X ≤41.3	
4	1.29 < X ≤1.70	41.3 < X ≤57.6	

4

Receiver Operating Characteristic (ROC) analysis

Patients were classified as:

- **frail** (n=13; score ≤13)
- **pre-frail** (n=62; score >13 to ≤22.5)
- **fit** (n=24; score >22.5)

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Results: distribution of pts characteristics across the three risk groups of SGS-4

Patients, disease and transplant characteristics are equally balanced across the 3 groups

Characteristics	Total N = 99	Frail N = 13	Prefrail N = 62	Fit N = 24	p-value
Age, years (range)	63.0 (56.0, 66.0)	64.0 (56.0, 68.0)	62.0 (57.0, 66.0)	63.0 (56.0, 65.0)	>0.9
Diagnosis, n (%)					
AL	41 (41.4)	10 (76.9)	23 (37.1)	8 (33.3)	
MDS	11 (11.1)	2 (15.4)	6 (9.7)	3 (12.5)	
Lymphoma	14 (14.1)	0 (0)	11 (17.7)	3 (12.5)	0.10
MPN	1 (1.0)	0 (0)	0 (0)	1 (4.2)	
MM	5 (5.1)	0 (0)	5 (8.1)	0 (0)	
Other	27 (27.3)	1 (7.7)	17 (27.4)	9 (37.5)	
DRI, n (%)					
low	2 (2.0)	0 (0)	1 (1.6)	1 (4.2)	
intermediate	70 (70.7)	7 (53.8)	50 (80.7)	13 (54.2)	
high	24 (24.3)	6 (46.2)	10 (16.1)	8 (33.2)	0.08
very high	2 (2.0)	0 (0)	1 (1.6)	1 (4.2)	
missing	1 (1)	0	0	1 (4.2)	
KPS, n (%)					
90-100	92 (92.9)	11 (84.6)	57 (91.9)	24 (100)	0.6
70-80	7 (7.1)	2 (15.4)	5 (8.1)	0 (0)	
HCT-CI, n (%)					
0	21 (21.2)	1 (7.7)	12 (19.4)	8 (33.3)	
1-2	28 (28.3)	3 (23.1)	16 (25.8)	9 (37.5)	0.13
≥3	50 (50.5)	9 (69.2)	34 (54.8)	7 (29.2)	
Disease status, n (%)					
1st CR	33 (33.3)	6 (46)	20 (32.2)	7 (29.2)	0.6
2nd or subsequent CR	66 (66.6)	7 (54)	42 (67.8)	17 (70.8)	
Line of Therapy, n (%)					
1	48 (49.5)	8 (61.5)	28 (45.2)	12 (52.0)	0.5
≥2	50 (50.5)	5 (38.5)	34 (54.8)	11 (48.0)	
Missing	1 (1.0)	0	0	1	
Stem cell source, n (%)					
PBSC	91(92.0)	12 (92.3)	56 (90.3)	23 (95.8)	0.9
BM	8 (8.0)	1 (7.7)	6 (9.7)	1 (4.2)	
Conditioning regimen, n (%)					
MAC	40 (40.4)	4 (30.7)	25 (40.3)	11(45.8)	0.7
RIC	59 (59.6)	9(69.3)	37 (59.7)	13(54.2)	
TCI score, n	2.5	2.8	2.7	3.0	0.4
Donor age, years (range)	37 (28-50)	40 (28-45)	36 (28-47))	38 (28-55)	0.9
Donor, n (%)					
Related	23 (23.2)	3(23.1)	13 (21.0)	7 (29.2)	
Unrelated	44 (44.5)	6 (46.1)	27 (43.5)	11 (45.8)	0.9
Haploidentical	32 (32.3)	4 (30.8)	22 (35.5)	6 (25.0)	
Time to allo-SCT, months (range)	11.3 (6.5-31.9)	6.3 (5.7-10.2)	12.4 (7.1-29.0)	19.5 (6.7-54.9)	0.08
aGVHD	48 (48.5)	4 (30.8)	29 (46.8)	15 (62.5)	0.166
cGVHD	16 (16.2)	0 (0.0)	10 (16.1)	6 (25.0)	0.12

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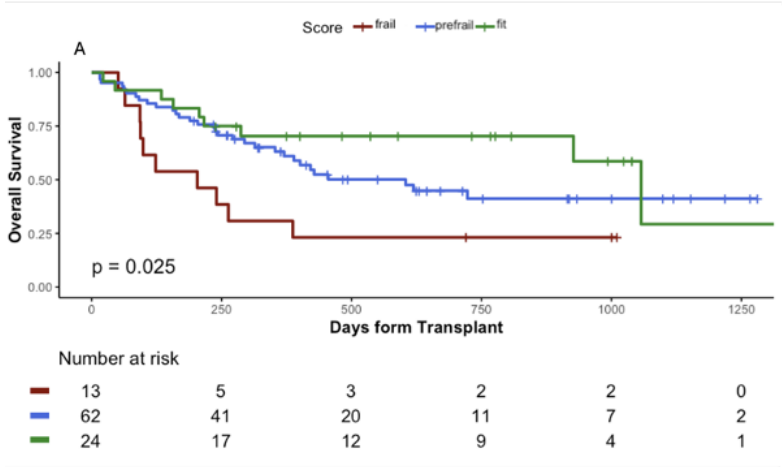
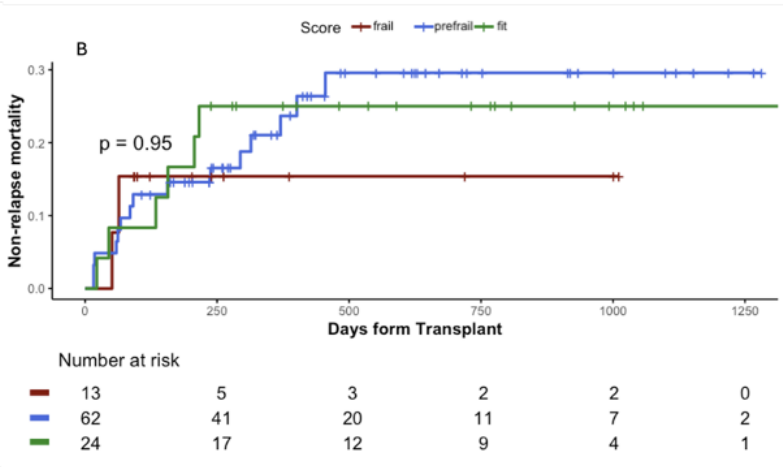
Results: outcomes according to SGS-4

OS



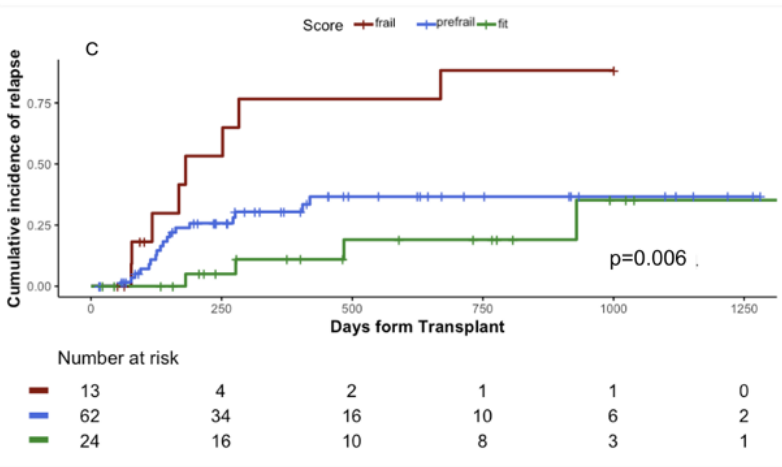
	Frail	Prefrail	Fit	*p*
OS 1y	30%	63%	70%	<0.03

NRM



	Frail	Prefrail	Fit	*p*
NRM 1y	16%	21%	25%	0.95

CIR



	Frail	Prefrail	Fit	*p*
CIR 1y	69%	30%	11%	<0.01

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Discussion

- The **GCA** remains limited in the clinical practice

Hand grip, MMSE, VES-13 and **FIL score** correlated with outcome

HCT-CI failed to correlate with OS or NRM, suggesting comorbidity alone is insufficient for risk assessment.

- Developed a **Simplified Geriatric Score-4 (SGS-4)** combining: **gait speed, handgrip, G8 score, and sex.**

The **SGS-4** effectively stratified patients into **fit**, **prefrail**, and **frail** groups with distinct outcomes:
•2-year **OS:** 70.3% (fit) vs. 24.5% (frail), $p = 0.025$
•2-year **CIR:** 19% (fit) vs. 80.4% (frail), $p < 0.01$

NRM was *not* influenced by fitness, likely due to advances in **conditioning regimens** and **supportive care**.

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Discussion

- Baseline clinical characteristic (diagnosis, number of prior treatment lines, conditioning intensity, donor type, GVHD) are evenly distributed across the three fitness groups and thus did not influence relapse risk.

→This supports the hypothesis that our score captures an underlying physiological reserve, not reflected by the standard risk stratification.

- Emerging preclinical and clinical evidence supports this link between fitness and relapse risk. Factors such as malnutrition, gut microbiota disruption, and heightened systemic inflammation—all common in frail populations—may favor disease recurrence.

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Pre-Conditioning Frailty Phenotypes Influence Survival and Relapse for Older Allogeneic Transplantation Recipients

Anthony D. Sung[1], Thuy Koll[2], Shannon H. Gier[3], Alessandro Racioppi[1], Griffin White[3], Meagan Lew[1], Marcia Free[2], Priyal Agarwal[2], Lauren M. Bohannon[1], Ernaya J. Johnson[1], Bharathi Selvan[1], Daria V. Babushok[3], Noelle V. Frey[3], Saar I. Gill[3], Elizabeth O. Hexner[3], MaryEllen Martin[3], Alexander E. Perl[3], Keith W. Pratz[3], Selina M. Luger[3], Nelson J. Chao[1], Alfred L. Fisher[2], Edward A. Stadtmauer[3], David L. Porter[3], Alison W. Loren[3], Vijaya R. Bhatt[2], Phyllis A. Gimotty[4], Shannon R. McCurdy[3]

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Conclusion

➢ **Strengths:**

•Prospective design
•Real-world cohort
•Robust statistical modeling
•SGS-4 is fast and easy to use in the transplant practice

→ routine incorporation of SGS-4 into transplant decision-making may help in identifying patients who could benefit from prehabilitation

➢ **Limitations:**

•Small, heterogeneous sample
•Lack GCA data at diagnosis
•Needs external validation (planned **multicenter GITMO study**)
•Longer follow-up required

→ GITMO

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ALLO-GER Study

Multicentric Prospective Validation of the Simplified Geriatric Score (SGS-4) in Patients Aged ≥60 Years with Acute Leukemias (LA) or Myelodysplastic Syndrome (MDS) Undergoing Allogeneic Hematopoietic Stem Cell Transplantation (Allo-GER Study)

- prospective, observational, GITMO multicenter study
- Age ≥60 years at the time of transplant.
- Diagnosis of AML or ALL or MDS

At baseline, at least 30 days before Allo-SCT conditioning, each patient will undergo Geriatric evaluation using:

Gait speed test, Handgrip strength test, G8 screening tool, Sex

The SGS-4 score will be calculated as per the published model:

SGS-4 = [Gait Speed] + 2 × [Handgrip Strength] + [G8] + 1.5 × [Sex].

Patients will be categorized as frail if their score is ≤13, *pre-frail* if their score is >13 and ≤22.5, and fit if their score is >22.5.

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Primary Objective:

To prospectively validate the prognostic performance of SGS-4 in predicting 1-year OS after allo-SCT in patients aged ≥60 years with AML, ALL, or MDS

Primary endpoint

- OS at 12 months after allo-SCT

Secondary endpoints

- NRM at 100 days, 6 months and 12 months after allo-SCT
- CIR at 12 months after allo-SCT
- Feasibility of the pre alloSCT GA, defined as the proportion of enrolled patients completing gait speed, handgrip strength, and G8 screening prior to allo-SCT.
- Feasibility of a liquid biopsy Fourier transform infrared spectroscopy (FT-IR)-based approach to improve the patients' risk assessment and to predict the transplantation outcomes.

AL_GER STUDY

A Prospective, Single-Center Observational Study on the Prognostic and Dynamic Impact of the Simplified Geriatric Score (SGS-4) in Patients Aged ≥60 Years with Newly Diagnosed Acute Leukemia or Myelodysplastic Syndromes Receiving Intensive Chemotherapy

- *prospective, single-center, observational trial*
- *LAM, LLA, MDS*
- *curative-intent chemotherapy*

At diagnosis and at the completion of chemotherapy, all patients aged ≥60 years will undergo Comprehensive geriatric assessment, including:
Gait speed test, Handgrip strength test, G8 screening tool
Sex

The SGS-4 score will be calculated as per the published model:
SGS-4 = [Gait Speed] + 2 × [Handgrip Strength] + [G8] + 1.5 × [Sex].

Patients will be categorized as frail if their score is ≤13, *pre-frail* if their score is >13 and ≤22.5, and fit if their score is >22.5.

Primary Objective
To prospectively evaluate the SGS-4, assessed at diagnosis (T0), in predicting 12-month OS

Primary Endpoint
• *OS at 12 months from diagnosis.*

Secondary Endpoints
• Early mortality at 30 and 90 days from diagnosis
• PFS at 12 months from diagnosis
• Change in SGS-4 score between baseline (T0) and post-treatment reassessment (T1)
• Treatment tolerance and toxicity, including incidence of grade ≥3 treatment-related adverse events
• Treatment intensity received for each fitness category