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ORAL ABSTRACTS

903.HEALTH SERVICES AND QUALITY IMPROVEMENT -MYELOID MALIGNANCIES

Frail and Pre-Frail Older Adults with Acute Myeloid Leukemia Have Inferior Survival Due to Higher Rates of Disease-Related Deaths

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Introduction: The intensity of initial remission-inducing therapy for patients with newly diagnosed acute myeloid leukemia (AML) may be high (anthracycline and cytarabine-based), intermediate (venetoclax combinations), or low (single hypomethylating agent or targeted therapy). In older adults, it is important to consider "fitness" when selecting initial therapy. Current methods to determine "fitness" in AML include subjective measures such as physician assessment ("clinician gestalt, CG") semi-subjective measures such Eastern Cooperative Oncology Group (ECOG) or Karnofsky performance status (KPS), and those based on clinical comorbidity data like the hematopoietic cell transplantation-comorbidity index (HCT-CI). Geriatric assessments in older adults with cancer may improve therapy selection and decision-making, but whether unfit patients have better outcomes with lower intensity compared to higher intensity therapies is unknown. Freid's Frailty Phenotype (FP) combines subjective (self-reported exhaustion, weight loss >5%, activity level) and objective (4-meter walk speed and grip strength) measures to categorize patients into fit, pre-frail, and frail. We hypothesized that being frail by FP is associated with higher overall mortality (OM) and inferior overall survival (OS) and may inform decision-making for older adults. **Methods:** Eighty-fivepatients 60 years or older admitted to the Hospital of the University of Pennsylvania at the time of AML diagnosis or electively admitted for AML chemotherapy initiation were prospectively enrolled from September, 2018 to May, 2023 on an IRB approved study. FP, HCT-CI, KPS, ECOG, gait speed, and recorded CG (fit or unfit) were performed prior to initiation of disease-directed therapy. **Results:** Themedian age of the cohort was 71 (range60-91). Patients in our cohort had high-risk disease features: 64% were adverse risk by European LeukemiaNet (ELN) 2017 with 73% of patients harboring mutations associated with clonal hematopoiesis of indeterminate potential (CHIP) (Table 1). 39% of patients received IC, 52% received HMA/ven, 6% received HMA alone or targeted therapy, and 2% received best supportive care. By FP, 18% of patients were fit, 38% were pre-frail, and 45% were frail. Higher ECOG, KPS, CG, and HCT-CI were associated with frail phenotypes (Table 1). For the entire population, 60-day and 100-day OM rates were 18% and 33%, respectively. For fit, pre-frail, and frail patients 60-day OM was 7%, 13%, and 24% and 100-day OM was 13%, 22%, and 42%, respectively. Two-year OS was 65% for patients aged 60-69 years old and 15% for patients ≥70 years old (p=0.002). FP was significantly associated with OS (Figure 1; p=0.0474): 2-year OS was 57%, 42%, and 21% in fit, pre-frail, and frail patients, respectively. Of the individual components of FP, self-reported exhaustion and slower gait speed were both associated with inferior OS (p=0.0015 and p=0.0005). Neither activity level, (p=.0864), weight loss (p=0.1988), or grip strength (p= 0.7136) were associated with OS. Of the total population 19% went on to hematopoietic cell transplant (HCT) with 8% of frail patients receiving HCT compared to 27% of fit and 28% of pre-frail patients. ECOG, HCT-CI, CG, and gait speed ≤8 meters/sec were all significantly associated with OS, but KPS was not. The 6-month OS for frail patients receiving IC was 75% compared with 49.7% for those receiving HMA/Ven, although not significant due to small sample size. Cause of death was leukemia-related for 40% of fit patients, 76% of pre-frail patients, 77% of frail patients. **Conclusions:** FP was associated with a doubling of early mortality and inferior 2-year OS. Pre-frail and frail patients had increased disease-related deaths. This work supports that most geriatric assessments, including FP and clinician intuition, can be utilized to risk-stratify newly diagnosed older adults with AML. Future work is needed to evaluate whether we can integrate geriatric assessments, such as individual components of FP or gait speed, with molecular features to improve risk stratification of older adults with AML. Given frailty's association with disease-related deaths, further study is warranted to determine whether this is due to adverse disease biology or whether frail patients are undertreated.

Disclosures Frey: *Sana Biotechnology:* Consultancy; *Kite Pharma:* Consultancy. **Gill:** *Kite Pharma:* Consultancy; *Carisma Therapeutics:* Current equity holder in publicly-traded company, Current holder of *stock options* in a privately-held company, Membership on an entity's Board of Directors or advisory committees, Patents & Royalties: patents, Research Funding; *Interius Biotherapeutics:* Current equity holder in private company, Current holder of *stock options* in a privately-held company, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Asher:* Research Funding; *Currus:* Membership on an entity's Board of Directors or advisory committees; *Inndura:* Membership on an entity's Board of Directors or advisory committees; *Mission Bio:* Membership on an entity's Board of Directors or advisory committees; *NKILT:* Membership on an entity's Board of Directors or advisory committees; *Vor Bio:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Lai:** *Taiho:* Consultancy; *Pfizer:* Consultancy; *Daiichi:* Consultancy; *Novartis:* Consultancy; *Genentech:* Consultancy; *BMS:* Consultancy; *Rigel:* Consultancy; *Astellas:* Consultancy, Speakers Bureau; *AbbVie:* Consultancy; *Jazz:* Consultancy, Research Funding, Speakers Bureau. **Perl:** *Daiichi-Sankyo:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Astellas:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Consultancy, Honoraria, Research Funding; *Bayer:* Research Funding; *FujiFilm:* Research Funding; *Syndax:* Research Funding; *Forma:* Consultancy; *Foghorn:* Consultancy; *Beat AML:* Other: Participation on a Data Safety Monitoring Board or Advisory Board; *BerGen Bio:* Honoraria; *Genentech:* Honoraria; *Immunogen:* Honoraria; *BMS:* Honoraria; *Aptose:* Honoraria; *Rigel:* Honoraria; *Actinium:* Honoraria. **Porter:** *National Marrow Donor Program:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Kite/Gilead:* Membership on an entity's Board of Directors or advisory committees; *Mirror Biologics:* Membership on an entity's Board of Directors or advisory committees; *Tmunity:* Patents & Royalties; *Sana Therapeutics:* Consultancy, Current equity holder in publicly-traded company; *Novartis:* Membership on an entity's Board of Directors or advisory committees, Patents & Royalties, Research Funding; *Genentech:* Current equity holder in publicly-traded company; *DeCart:* Membership on an entity's Board of Directors or advisory committees; *Capstan Bio:* Honoraria; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Bluebird Bio:* Membership on an entity's Board of Directors or advisory committees; *Angiocrine Bio:* Membership on an entity's Board of Directors or advisory committees; *Wiley and Sons Publishing:* Honoraria. **Pratz:** *Astra Zeneca:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees; *Jazz Pharamceuticals:* Membership on an entity's Board of Directors or advisory committees; *Astellas:* Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb:* Membership on an entity's Board of Directors or advisory committees; *Agios Pharmaceuticals:* Research Funding; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Consultancy, Research Funding. **Luger:** *Marker Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Consultancy; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb:* Honoraria; *Onconova:* Research Funding; *Astellas:* Honoraria.

Table 1. Patient Characteristics by Fried Frailty Phenotype

	Total N=85	Fit N=15	Pre-frail N=32	Frail N=38
Median Patient Age, years	71 (62-91)	67 (69-76)	69 (62-82)	74 (62-91)
ECOG, N (%)				
0	12 (14%)	5 (33%)	5 (16%)	2 (5%)
1-2	59 (69%)	10 (67%)	24 (75%)	25 (66%)
≥ 3	14 (17%)	0	3 (9%)	11 (29%)
KPS, N (%)				
≥ 90	17 (20%)	5 (33%)	8 (25%)	4 (11%)
< 90	68 (80%)	10 (67%)	24 (75%)	34 (89%)
HCT-CI, N (%)				
0	12 (14%)	3 (20%)	8 (25%)	1 (3%)
1-2	18 (21%)	5 (33%)	4 (12%)	9 (23%)
≥ 3	55 (65%)	7 (47%)	20 (63%)	28 (74%)
ELN 2017, N (%)				
Favorable	10 (12%)	4 (27%)	2 (6%)	4 (11%)
Intermediate	21 (25%)	7 (47%)	6 (19%)	8 (21%)
Adverse	54 (64%)	4 (27%)	24 (75%)	26 (68%)
Physician Gestalt, N (%)				
Fit	45 (53%)	12 (80%)	23 (72%)	10 (26%)
Unfit	34 (40%)	2 (13%)	7 (22%)	25 (66%)
No response	6 (7%)	1 (7%)	2 (6%)	3 (8%)
Treatment Intensity, N (%)*				
High	33 (39%)	10 (67%)	15 (47%)	8 (21%)
Intermediate	44 (52%)	5 (33%)	15 (47%)	24 (63%)
Low	5 (6%)	0	2 (6%)	3 (8%)
Best supportive care	2 (2%)	0	0	2 (5%)
Unknown	1 (1%)	0	0	1 (3%)
Allogeneic HCT, N (%)				
Yes	16 (19%)	4 (27%)	9 (28%)	3 (8%)
No	69 (81%)	11 (73%)	23 (72%)	(92%)
Laboratory Values, median				
Albumin (g/dL)	3.7	3.9	3.7	3.5
Creatinine (mg/dL)	0.91	0.83	0.95	0.93
Hemoglobin (g/dL)	8.6	8.8	8.85	8.35
Hematocrit (%)	26	25	26	25.5
WBC (THO/uL)	5.5	3.3	2.9	10.75
ANC (THO/uL)	1.18	1.24	0.915	1.25
ALC (THO/uL)	1.52	1.14	1.315	2.29
PLT (THO/uL)	51	41	45.5	58
Total bilirubin (mg/dL)	0.7	0.7	0.6	0.8
Peripheral blasts (%)	14.65	3.35	9.9	21.65
Cytogenetics, N				
Monosomal karyotype	14 (16%)	1 (7%)	4 (13%)	9 (24%)
inv(16)	4 (4%)	2 (13%)	0	2 (5%)
Trisomy 8	9 (11%)	1 (7%)	2 (6%)	6 (16%)
Deletion7q/monosomy 7	18 (21%)	2 (13%)	7 (22%)	9 (24%)
Deletion 5q/monosomy 5	16 (19%)	1 (7%)	6 (19%)	9 (24%)
t(9;22)	2 (2%)	0	0	2 (5%)
Complex karyotype	19 (22%)	1 (7%)	8 (25%)	9 (24%)
NPM1	15 (18%)	3 (20%)	6 (19%)	6 (16%)
FLT3-ITD	13 (15%)	2 (13%)	7 (22%)	4 (11%)
KIT	3 (4%)	1 (7%)	1 (3%)	0
CEBPA-single	2 (2%)	0	1 (3%)	1 (3%)
RUNX1	13 (15%)	2 (13%)	5 (16%)	6 (16%)
KRAS/NRAS	18 (21%)	4 (27%)	6 (19%)	8 (11%)
CALR	1 (1%)	0	0	1 (3%)
PTPN11	6 (75%)	1 (7%)	2 6%)	3 (8%)
CHIP mutations**	62 (73%)	9 (60%)	24 (75%)	29 (76%)
Cause of death, N (%)				
Disease	35 (73%)	2 (40%)	13 (76%)	20 (77%)
Infection	4 (8%)	2 (40%)	1 (6%)	1 (4%)
Other	5 (10%)	0	3 (18%)	2 (8%)
Unknown	4 (8%)	1 (20%)	0	3 (11%)

Abbreviations: N, number; ECOG, Eastern Cooperative Oncology Group; KPS, Karnofsky performance status; ELN, Eastern LeukemiaNet; HCT, hematopoietic cell transplant; CHIP, clonal hematopoiesis of indetermined significance
*High: 7+3 +/- targeted agent or liposomal daunorubicin/cytarabine, intermediate: hypomethylating agent + venetoclax, low: hypomethylating agent OR targeted agent
**CHIP mutations include: TP53, U2AF1, IDH1, IDH2, SF3B1, ASXL1, SRSF2, TET2, JAK2, U2AF1

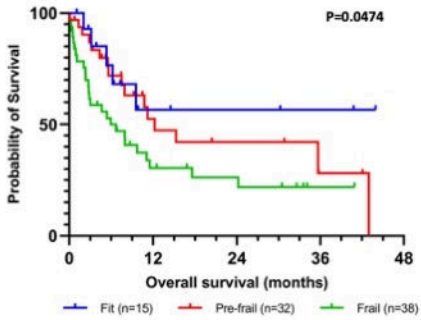

Figure 1. Overall Survival in newly diagnosed older adults with Acute Myeloid Leukemia, by Freid's Frailty Phenotype. Overall survival (OS) is significantly different by frailty phenotype, p=0.0474. 2-year OS was 57%, 42%, and 21% in fit, pre-frail, and frail patients.

Figure 1

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