fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

Dalle linee guida alla qualità di vita e alle cure palliative precoci e simultanee:

come la storia delle leucemie mieloidi acute sta cambiando

Roma, 2 febbraio 2024 – Starhotels Metropole

The Value of Quality of Life (QoL) Assessment in patients with Acute Myeloid Leukemia (AML)

Dr. Fabio Efficace

Head, Health Outcomes Research Unit, *Chair* GIMEMA WP Quality of Life

Gruppo Italiano Malattie EMatologiche dell'Adulto (GIMEMA)

GIMEMA Data Center, Rome, Italy

Outline of the presentation

1. How and why to measure QoL in AML research
2. QoL endpoints in AML clinical trials
3. Early palliative care in AML patients

Quality of Life vs. (symptomatic) Toxicity

Common Terminology Criteria
for Adverse Events (CTCAE)
Version 5.0
Published: November 27, 2017

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Is a "low grade" really a "low grade" from the patient's perspective

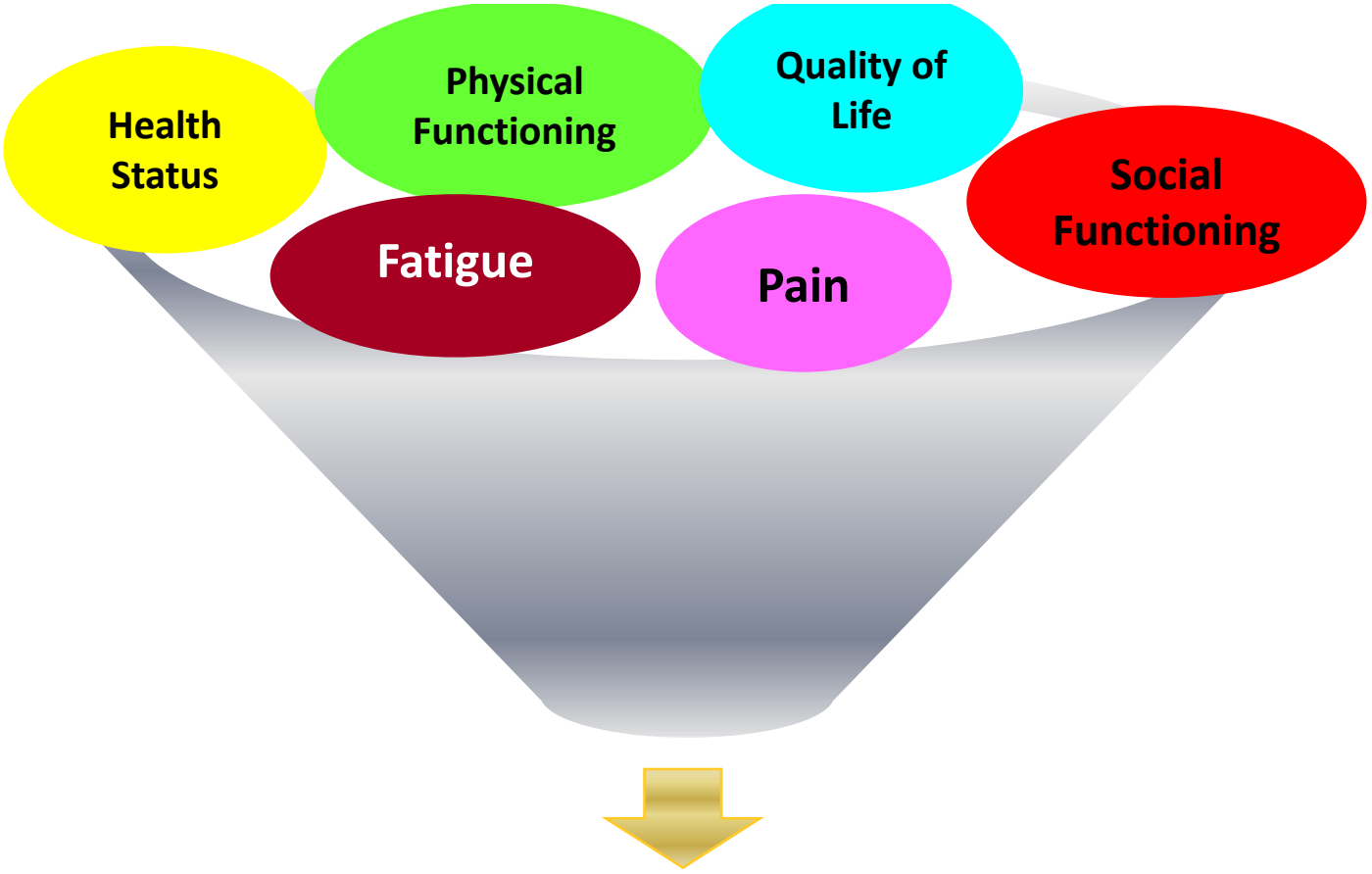
CTCAE Term	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
Abdominal Pain	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL		

CTCAE Term	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
Headache	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL		

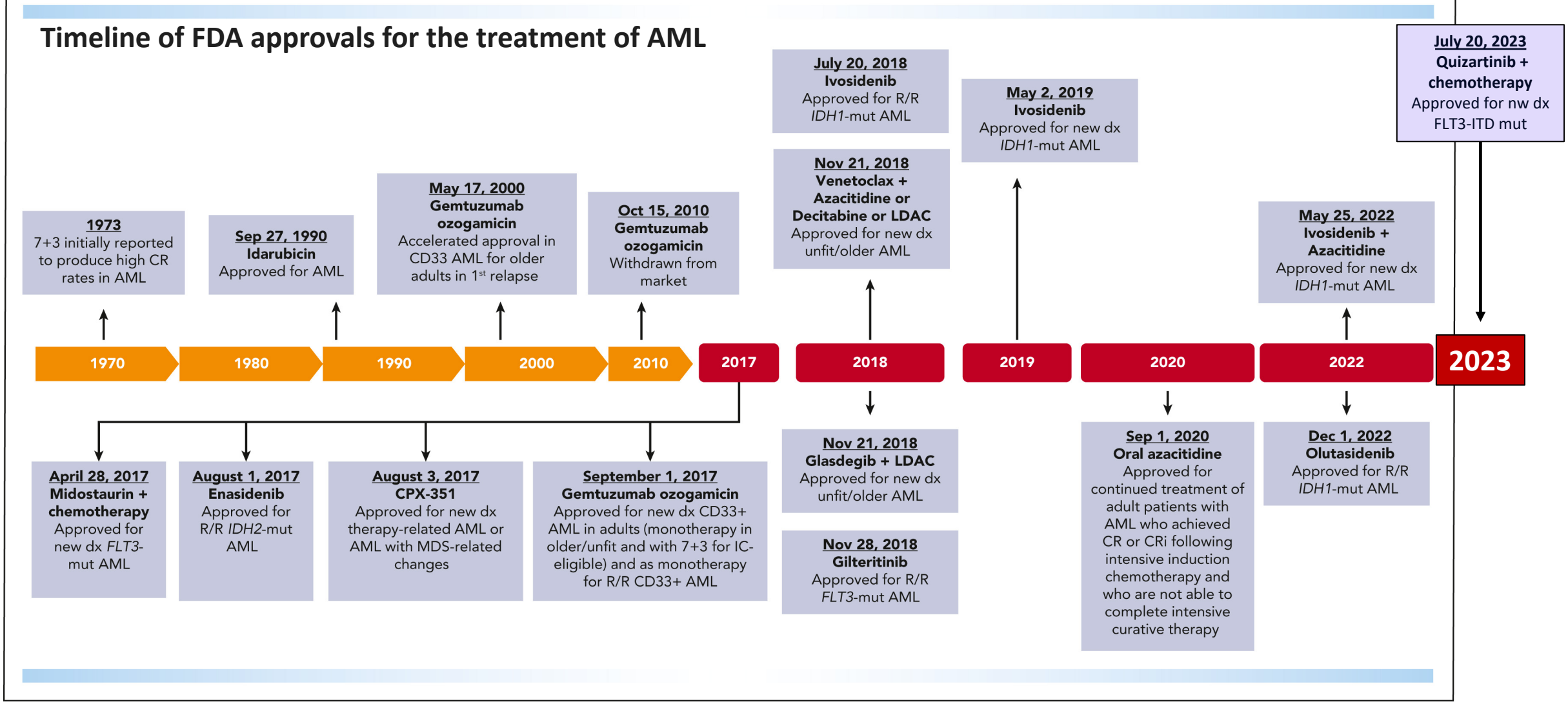
Patient-Reported Outcomes (PROs)

PRO is a measu **from the patient**
(i.e., without the interpretation of the patient's responses by a physician or anyone else)

Food and Drug Administration (FDA) definition, 2009 (http://www.fda.gov/downloads/Drugs/.../Guidances/UCM193282.pdf)



Timeline of FDA approvals for the treatment of AML



(adapted from) El Chaer F, et al., Blood. 141(23):2813-2823, 2023

Ongoing trials of drugs/regimens for AML patients ineligible to IC

Trial Mnemonic	Phase	Population	Intervention	Est. primary completion
PEVOLAM (NCT04090736)	III	de novo AML ineligible intensive	AZA + PEV vs AZA	30-06-2023
ELEVATE (NCT04150887)	I/II	de novo AML, sAML ineligible intensive	AZA + VEN + CUS	30-06-2023
(NCT03092674)	II/III	de novo AML or HR-MDS	AZA + Nivolumab vs AZA vs AZA + Midostaurin	01-08-2023
CULMINATE (NCT04023526)	III	de novo AML, sAML ineligible intensive	AZA + CUS vs AZA + PCB	15-08-2023
PEMAZA (NCT03769532)	II	MRD+ NPM1+ AML before relapse	AZA + Pembrolizumab	31-08-2023
(NCT05054543)	III	R/R AML	MEC + Uproleselan vs MEC + PCB	31-10-2023
(NCT02752035)	III	FLT3+ de novo AML ineligible intensive	GIL vs AZA + GIL vs AZA	31-12-2023
IDHENTIFY (NCT02577406)	III	R/R AML or sAML	Enasidenib vs CCR (BSC/AZA/LDAC/IDAC)	31-12-2023
APTIVATE (NCT03850574)	I/II	R/R AML, sAML, or MDS after HMA	VEN + Tuspetinib	28-02-2024
PEVENAZA (NCT04266795)	II	de novo AML, sAML ineligible intensive	AZA + VEN + PEV	18-03-2024
(NCT03897127)	III	de novo AML eligible	CPX-351 + 7 + 3 vs 7 + 3	31-03-2024
(NCT04256317)	III	de novo AML, MDS, CMML	AZA + Cedazuridine	30-04-2024
ENABLE (NCT04763928)	II	sAML ineligible intensive	DEC + VEN	30-05-2024
(NCT05356169)	II/III	de novo AML eligible intensive	7 + 3 + VEN	30-06-2024
ENHANCE-2 (NCT04778397)	III	TP53+ de novo AML	AZA + MAG vs AZA + VEN or 7 + 3	30-08-2024
(NCT03250338)	III	R/R AML	7 + 3 + Crenolanib vs 7 + 3	31-10-2024
HOVON156 (NCT04027309)	III	FLT3+ AML	GIL vs Midostaurin (induction & maintenance)	31-12-2024
REGAL (NCT04229979)	III	AML CR2/CRp2 after Salvage	Galinpepimut vs best practise (maintenance)	31-12-2024
VENAZA-5S (NCT05833438)	II	de novo AML ineligible intensive	AZA(5 days) + VEN	31-01-2025
(NCT04628026)	III	de novo AML & EB2-MDS	7 + 3 + VEN vs 7 + 3 + PCB	28-02-2025
VHA (NCT05805098)	II/III	de novo AML	Ara-C + VEN+ Homoharringtonine	01-03-2025
SAV (NCT05736965)	II	de novo AML ineligible intensive	AZA + VEN + Selinexor	30-03-2025
AARON (NCT04913922)	II	de novo & R/R AML ineligible intensive	AZA + Relatilimab+Nivolumab	31-03-2025
ENHANCE-3 (NCT05079230)	III	de novo AML ineligible intensive	AZA + VEN + MAG vs AZA + VEN + PCB	31-07-2025
(NCT03182244)	III	FLT3+ R/R AML	GIL vs Salvage	30-11-2025
ALIVE (NCT04716114)	III	FLT3+ R/R AML	SKLB vs Salvage	31-12-2025
(NCT05586074)	III	FLT3+ R/R AML	HEC73543 vs Salvage	10-02-2026
(NCT05404906)	III	AML in first remission	AZA + VEN	30-06-2028

Ara-C = Cytarabine, AZA = Azacitidine, CRR = Conventional Chemotherapy Regimens, CUS = Custatuzumab, DEC = Decitabine, EB2-MDS = Myelodysplastic Syndrome with 10–19% excess blasts, ENA = Enasidenib, GIL = Gilteritinib, IDAC = Intermediate Dose Cytarabine, IVO = Ivosidenib, LDAC = Low Dose Cytarabine, MAG = Magrolimab, MDS = Myelodysplastic Syndrome, MEC = Mitoxantrone Etoposide Cytarabine, NPM-1 = Nucleophosmine-1 protein, PCB = Placebo, PEV = Pevonedistat, R/R = Relapsed or Refractory Patients, TP53 = Tumor Protein 53, VEN = Venetoclax.

Diekmann B et al. J Geriatr Oncol. 2023:101631.

HOW DO WE MEASURE QoL IN THE EVOLVING TREATMENT LANDSCAPE IN AML ?

GENERIC questionnaires

EQ-5D; SF-36
PROMIS

CANCER GENERIC questionnaires

EORTC QLQ-C30
FACT-G; FACT-leu

To best capture effects of newer AML drugs

Item Libraries

- **PRO-CTCAE Library**
  https://healthcaredelivery.cancer.gov/pro-ctcae/instrument-pro.html
- **EORTC Item Library**
  https://itemlibrary.eortc.org/
- **FACIT Item Library**
  https://wizard.facit.org/
- **MDASI Symptom Library**
  http://www.mdanderson.org/symptom-research
  > Symptom Assessment Tools

Patient-Reported Outcomes version Of The Common Terminology Criteria For Adverse Events (PRO-CTCAE™)

QUICK GUIDE TO THE ITEM LIBRARY*

PRO-CTCAE Library

Oral	
Dry mouth	S
Difficulty swallowing	S
Mouth/throat sores	SI
Cracking at the corners of the mouth (cheilosis/cheilitis)	S
Voice quality changes	P
Hoarseness	S

Gastrointestinal	
Taste changes	S
Decreased appetite	SI
Nausea	FS
Vomiting	FS
Heartburn	FS
Gas	P
Bloating	FS
Hiccups	FS
Constipation	S
Diarrhea	F
Abdominal pain	FSI
Fecal incontinence	FI

Respiratory	
Shortness of breath	SI
Cough	SI
Wheezing	S

Cardio/Circulatory	
Swelling	FSI
Heart palpitations	FS

Cutaneous	
Rash	P
Skin dryness	S
Acne	S
Hair loss	A
Itching	S
Hives	P
Hand-foot syndrome	S
Nail loss	P
Nail ridging	P
Nail discoloration	P
Sensitivity to sunlight	P
Bed/pressure sores	P
Radiation skin reaction	S
Skin darkening	P
Stretch marks	P

Neurological	
Numbness & tingling	SI
Dizziness	SI

Visual/Perceptual	
Blurred vision	SI
Flashing lights	P
Visual floaters	P
Watery eyes	SI
Ringing in ears	S

Attention/Memory	
Concentration	SI
Memory	SI

Pain	
General pain	FSI
Headache	FSI
Muscle pain	FSI
Joint pain	FSI

Sleep/Wake	
Insomnia	SI
Fatigue	SI

Mood	
Anxious	FSI
Discouraged	FSI
Sad	FSI

Genitourinary	
Irregular periods/vaginal bleeding	P
Missed expected menstrual period	P
Vaginal discharge	A
Vaginal dryness	S
Painful urination	S
Urinary urgency	FI
Urinary frequency	FI
Change in usual urine color	P
Urinary incontinence	FI

Sexual	
Achieve and maintain erection	S
Ejaculation	F
Decreased libido	S
Delayed orgasm	P
Unable to have orgasm	P
Pain w/sexual intercourse	S

Miscellaneous	
Breast swelling and tenderness	S
Bruising	P
Chills	FS
Increased sweating	FS
Decreased sweating	P
Hot flashes	FS
Nosebleed	FS
Pain and swelling at injection site	P
Body odor	S

Attributes	
F: Frequency	I: Interference
S: Severity	P: Presence/Absence
A: Amount	

NIH National Cancer Institute

*Complete library of items available at: https://healthcaredelivery.cancer.gov/pro-ctcae

Version date: 3/11/2020

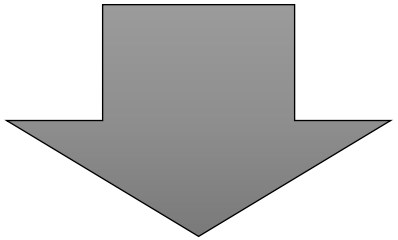
https://healthcaredelivery.cancer.gov/pro-ctcae/item-library.pdf

QoL AML Checklist

Clinical utility in

Trials investigating novel AML drugs

PROs in Regulatory decisions



Quality of Life data in the Approval of Arsenic Trioxide (ATO) by the EMA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 October 2016
EMA/CHMP/623089/2016
Committee for Medicinal Products f

Assessment repor

Trisenox

International non-propr

3.2. Favourable effects

Results from pivotal study APL0406 support the use of ATRA-ATO in first line APL. With respect to the primary endpoint, the 2-year EFS rates observed (97% with ATRA-ATO and 86% with ATRA+chemotherapy (p=0.02 for superiority) are considered adequate to demonstrate the superiority of ATRA-ATO to ATRA+chemotherapy. These results are considered of high clinical relevance; especially taking into account that the majority of relapses in APL are usually recorded within 2 years from the achievement of response (i.e., 75% and 65% of relapses occurred within 2 year from the end of treatment in the AIDA-0493 and AIDA-2000 studies, respectively). EFS results observed in the per-protocol analysis at different median follow-up (50-month EFS rate was 96% with ATRA-ATO vs 81% with ATRA+chemotherapy, p=0.0034) and in the extended cohort (the 2-year EFS rate was 98% in the ATRA+ATO group and 87% in the ATRA+chemotherapy group, p <0.0001) were all consistent with the primary analysis and supported its robustness.

The results in the secondary endpoints also supported the significant benefit obtained with ATRA+ATO vs. ATRA+chemotherapy: a statistically significant and clinically relevant 8% advantage in the 2-year OS rate with a consistent positive trend in terms of 2-year DFS rate was observed and was confirmed in the longer follow-up analysis and in the extension cohort. Consistently, also the CIR analysis demonstrated a clinical advantage with ATRA-ATO compared to ATRA+chemotherapy, both in the original and in the extended cohort of study APL0406. A non-statistically significant trend in favour of ATRA-ATO was also observed in terms of haematological CR (HCR 100% vs. 95%, p=0.12 in the original cohort; 100% vs. 97%, p=0.12 in the extended cohort).

With respect to QoL, a significant improvement in patients who received ATRA-ATO compared to the AIDA regimen was observed. However, this advantage was lost after consolidation.

GIMEMA QoL data APL0406

Lo Coco F, et al, N Engl J Med. 2013 Jul 11;369(2):111-21.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 11, 2013 VOL. 369 NO. 2

Retinoic Acid and Arsenic Trioxide for Acute Promyelocytic Leukemia

F. Lo-Coco, G. Avvisati, M. Vignetti, C. Thiede, S.M. Orlando, S. Iacobelli, F. Ferrara, P. Fazi, L. Cicconi, G. Specchia, S. Sica, M. Divona, A. Levis, W. Fiedler, E. Cerqui, M. Breccia, G. Fioritoni, H.R. Salih, M. L. Melillo, A.M. Carella, C.H. Brandts, E. Morra, M. von Lilienfeld-Toal, B. Hertenstein, M. Wattad, M. M. Hänel, N. Schmitz, H. Link, M.G. Kropp, A. Rambaldi, G. La Nasa, M. Luppi, F. Ciceri, O. Finizio, F. Fabbiano, K. Döhner, M. Sauer, A. Ganser, S. Amadori, F. Mandelli, H. Döhner, G. Ehninger, R.F. and U. Platzbecker for Gruppo Italiano Malattie Ematologiche dell'Adulto, the German–Austrian Acute Myeloid Leukemia Study Group, and Study Alliance Leukemia

GIMEMA APL 0406

(**Primary** endpoint)

GIMEMA APL 0406

(**Secondary** endpoint)

Fabio Efficace, Franco Mandelli, Francesco Cottone, and Marco Vignetti, Gruppo Italiano Malattie Ematologiche dell'Adulto; Giuseppe Avvisati, Università Campus Biomedico; Massimo Breccia, Università "La Sapienza,"; Simona Sica, Università Cattolica Sacro Cuore; Sergio Amadori and Francesco Lo-Coco, Università Tor Vergata; Francesco Lo-Coco, Fondazione Santa Lucia, Roma; Felicetto Ferrara, Ospedale Cardarelli; Olimpia Finizio, Ospedale Cardarelli, Napoli; Eros Di Bona, Ospedale San Bortolo, Vicenza; Giorgina Specchia, Università di Bari, Bari; Alessandro Levis, Ospedale SS Antonio e Biagio, Alessandria; Maria Grazia Kropp, Azienda Ospedaliera Pugliese Ciaccio, Catanzaro; Giuseppe Fioritoni, Ospedale Civile, Pescara; Elisa Cerqui, Spedali Civili, Brescia, Italy; Richard F. Schlenk, University of Ulm, Ulm; and Uwe Platzbecker, Universitatsklinikum Carl Gustav Carus, Dresden, Germany.

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Terms in blue are defined in the glossary, found at the end of this article and online at www.jco.org

Efficace F, et al, J Clin Oncol. 2014 Oct 20;32(30):3406-12.

VOLUME 32 · NUMBER 30 · OCTOBER 20 2014

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Phase III Trial of Retinoic Acid and Arsenic Trioxide Versus Retinoic Acid and Chemotherapy in Patients With Acute Promyelocytic Leukemia: Health-Related Quality-of-Life Outcomes

Fabio Efficace, Franco Mandelli, Giuseppe Avvisati, Francesco Cottone, Felicetto Ferrara, Eros Di Bona, Giorgina Specchia, Massimo Breccia, Alessandro Levis, Simona Sica, Olimpia Finizio, Maria Grazia Kropp, Giuseppe Fioritoni, Elisa Cerqui, Marco Vignetti, Sergio Amadori, Richard F. Schlenk, Uwe Platzbecker, and Francesco Lo-Coco

A B S T R A C T

Purpose
A randomized clinical trial compared efficacy and toxicity of standard all-*trans*-retinoic acid (ATRA) plus chemotherapy versus ATRA plus arsenic trioxide in patients with newly diagnosed, low- or intermediate-risk acute promyelocytic leukemia (APL). Here, we report health-related quality-of-life (HRQOL) results.

Patients and Methods
HRQOL was a secondary end point of this trial. The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 was used to assess HRQOL at end of induction and after consolidation therapy. All analyses were based on 156 patients who received at least one dose of treatment, with groups defined according to randomly assigned treatment. Primary analysis was performed, estimating mean HRQOL score over time and differences between treatment arms using a linear mixed model.

Results
Overall, 162 patients age 18 to 70 years were enrolled. Of these, 150 and 142 patients were evaluable for HRQOL after induction therapy and third consolidation course, respectively. Overall compliance with HRQOL forms was 80.1%. The largest difference, favoring patients treated with ATRA plus arsenic trioxide, was found for fatigue severity (mean score difference, −9.3; 95% CI, −17.8 to −0.7; $P = .034$) at end of induction therapy. This difference was also clinically relevant. HRQOL differences between treatment arms at end of consolidation showed that for several scales, differences between treatment arms were marginal.

Conclusion
Overall, current HRQOL findings further support the use of ATRA plus arsenic trioxide as preferred first-line treatment in patients with low- or intermediate-risk APL.

Clinical decision-making for patients with AML has become highly challenging

For example…

- Patients eligible for intensive chemotherapy **(IC) (3+7)** have poor survival unless allogeneic hematopoietic cell transplantation (allo-HSCT) is performed (Döhner H, et al., N Engl J Med, 373:1136–52, 2015).

- However, **IC may not be well tolerated by older patients with AML** limiting its value as a **bridging approach** to **allo-HSCT**. Approximately 32% of older AML patients starting with **IC** reach transplant with continuous CR (Von dem Borne, PA, et al., Leuk Res. 46:45–50, 2016)

Can we replace IC (3+7) with a less aggressive approach before allo-HSCT ?

10-day decitabine versus 3 + 7 chemotherapy followed by allografting in older patients with acute myeloid leukaemia: an open-label, randomised, controlled, phase 3 trial

Michael Lübbert, Pierre W Wijermans*, Michal Kicinski, Sylvain Chantepie, Walter J F M Van der Velden, Richard Noppeney, Laimonas Griškevičius, Andreas Neubauer, Martina Crysandt, Radovan Vrhovac, Mario Luppi, Stephan Fuhrmann, Ernesta Audisio, Anna Candoni, Olivier Legrand, Robin Foà, Gianluca Gaidano, Danielle van Lammeren-Venema, Eduardus F M Posthuma, Mels Hoogendoorn, Anne Giraut, Marian Stevens-Kroef, Joop H Jansen, Aniek O de Graaf, Fabio Efficace, Emanuele Ammatuna, Jean-Pierre Vilque, Ralph Wäsch, Heiko Becker, Nicole Blijlevens, Ulrich Dührsen, Frédéric Baron, Stefan Suciu, Sergio Amadori, Adriano Venditti, Gerwin Huls on behalf of the EORTC Leukemia Group, GIMEMA, and German MDS Study Group†*

AML 21 RCT:
Decitabine (DEC) vs IC (3+7)

-No difference in OS
-Similar transplantation rates

Lubbert M, et al., Lancet Haematol. 2023 Nov;10(11):e879-e889.

Is Quality of Life different between patients treated with DEC vs IC

AML 21 RCT: QoL Secondary Endpoint

10-Day Decitabine Versus Intensive Chemotherapy Followed By Transplantation in Fit AML Patients Aged ≥60 Years: Health-Related Quality of Life Outcomes of the Randomized Phase III Trial AML21 of the EORTC Leukemia Group, GIMEMA, CELG, and GMDS-SG

Efficace F, Huls GA, Kicinski M, et al. Blood 2022; 140 (suppl 1): 1281–83 (abstr).

RESULTS (n=549)

Baseline QoL Assessment

Overall HRQoL compliance: 549/606, **91%**

DEC= 279/303**, 92%**

IC (3+7)=270/303, **89%**

Baseline QoL

	NO	YES
	100% N=57	100% N=549
Age, years, %		
60-64	35	24
65-69	35	42
≥70	30	34
ECOG performance status, %		
0	35	53
1	56	39
2	9	8
ELN 2017 risk group, %	96 [100]	90 [100]
Favorable	16	21
Intermediate	47	47
Adverse	36	32

Efficace F, Huls GA, Kicinski M, et al. Blood 2022; 140 (suppl 1): 1281–83 (abstr).

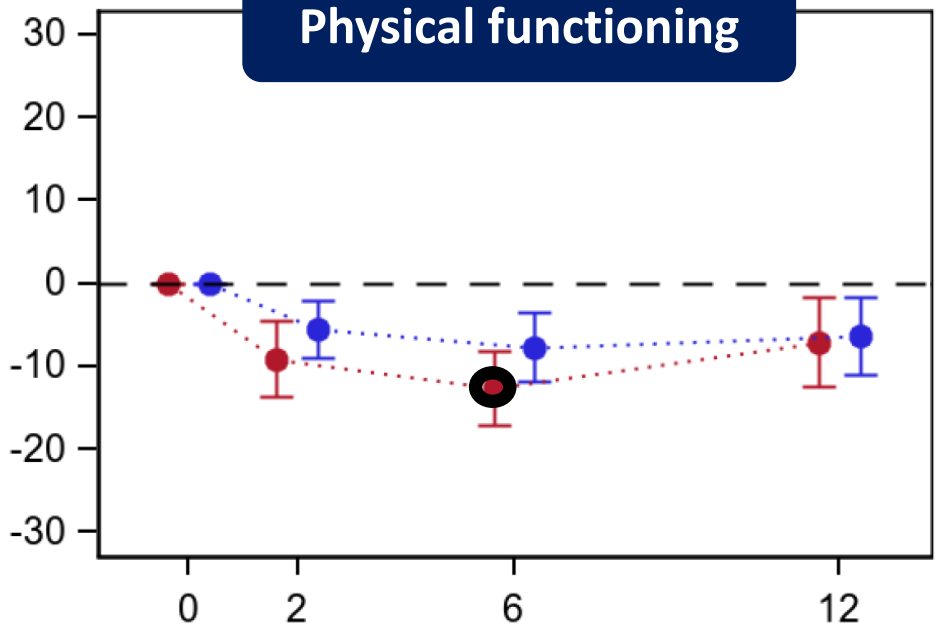
DEC

IC (3+7)

Quality of Life over time at 2, 6 and 12 months

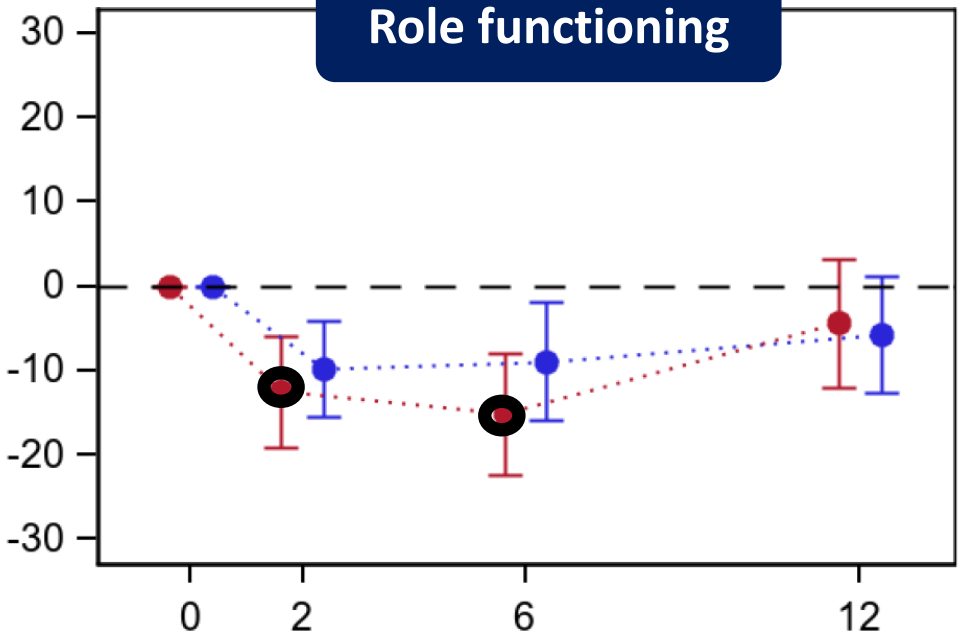
Negative differences indicate reduction in functional aspects

Physical functioning



Timing of Assessments	Decitabine, estimate (95% CI)	3+7, estimate (95% CI)
2 months	-5.57 (-8.97,-2.17)	-9.16 (-13.67,-4.64)
6 months	-7.77 (-11.92,-3.62)	-12.69 (-17.21,-8.18)
12 months	-6.33 (-11.03,-1.64)	-7.10 (-12.41,-1.78)

Role functioning

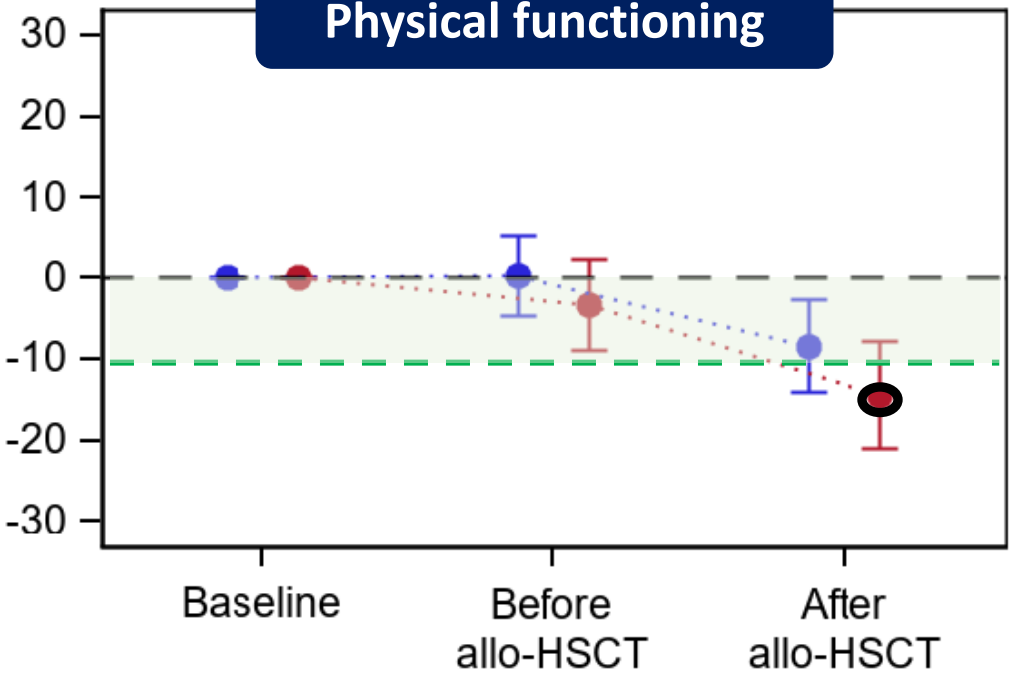


Timing of Assessments	Decitabine, estimate (95% CI)	3+7, estimate (95% CI)
2 months	-9.75 (-15.42,-4.08)	-12.49 (-19.12,-5.87)
6 months	-9.00 (-16.01,-1.99)	-15.20 (-22.47,-7.92)
12 months	-5.78 (-12.76,1.21)	-4.42 (-12.07,3.23)

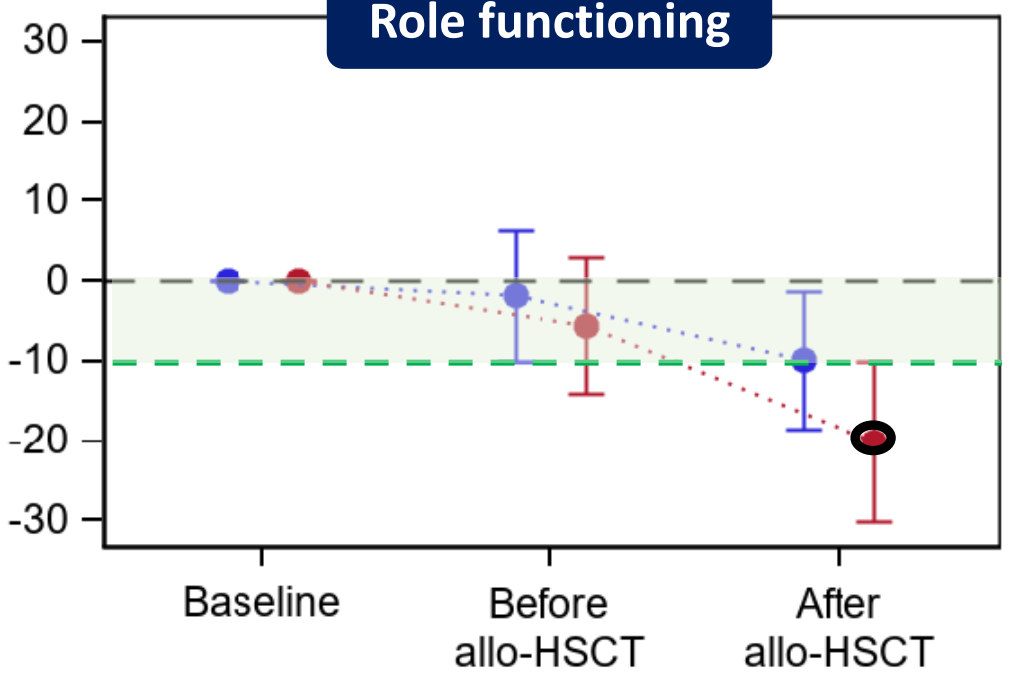
Quality of Life pre and post allo-HSCT

Negative differences indicate reduction in functional aspects

Physical functioning



Role functioning



DEC

IC (3+7)

Clinically meaningful difference

Patient-reported outcomes from the phase 3 ADMIRAL trial in patients with *FLT3*-mutated relapsed/refractory AML

Ellen K. Ritchie[a], David Cella[b], Francesco Fabbiano[c], Arnaud Pigneux[d], Yoshinobu Kanda[e], Cristina Ivanescu[f], Bhavik J. Pandya[g] and Manasee V. Shah[g]*

[a]Department of Medicine, Weill Cornell Medicine, New York City, NY, USA; [b]Department of Medical Social Sciences, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA; [c]Department of Hematology, Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy; [d]Department of Hematology and Cell Therapy, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [e]Division of Hematology, Jichi Medical University, Tochigi, Japan; [f]Patient Centered Solutions, IQVIA, Amsterdam, Netherlands; [g]Medical Affairs, Astellas Pharma, Inc., Northbrook, IL, USA

ABSTRACT

Patient-reported outcomes (PROs) can inform treatment selection and assess treatment value in acute myeloid leukemia (AML). We evaluated PROs from the ADMIRAL trial (NCT02421939) in patients with *FLT3*-mutated relapsed/refractory (R/R) AML. PRO instruments consisted of Brief Fatigue Inventory (BFI), Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu), Functional Assessment of Chronic Illness Therapy-Dyspnea Short Form (FACIT-Dys SF), EuroQoL 5-Dimension 5-Level (EQ-5D-5L), and leukemia treatment-specific symptom questionnaires. Clinically significant effects on fatigue were observed with gilteritinib during the first two treatment cycles. Shorter survival was associated with clinically significant worsening of BFI, FACT-Leu, FACIT-Dys SF, and EQ-5D-5L measures. Transplantation and transfusion independence in gilteritinib-arm patients were also associated with maintenance or improvement in PROs. Health-related quality of life remained stable in the gilteritinib arm. Hospitalization had a small but significant effect on patient-reported fatigue. Gilteritinib was associated with a favorable effect on fatigue and other PROs in patients with *FLT3*-mutated R/R AML.

ARTICLE HISTORY

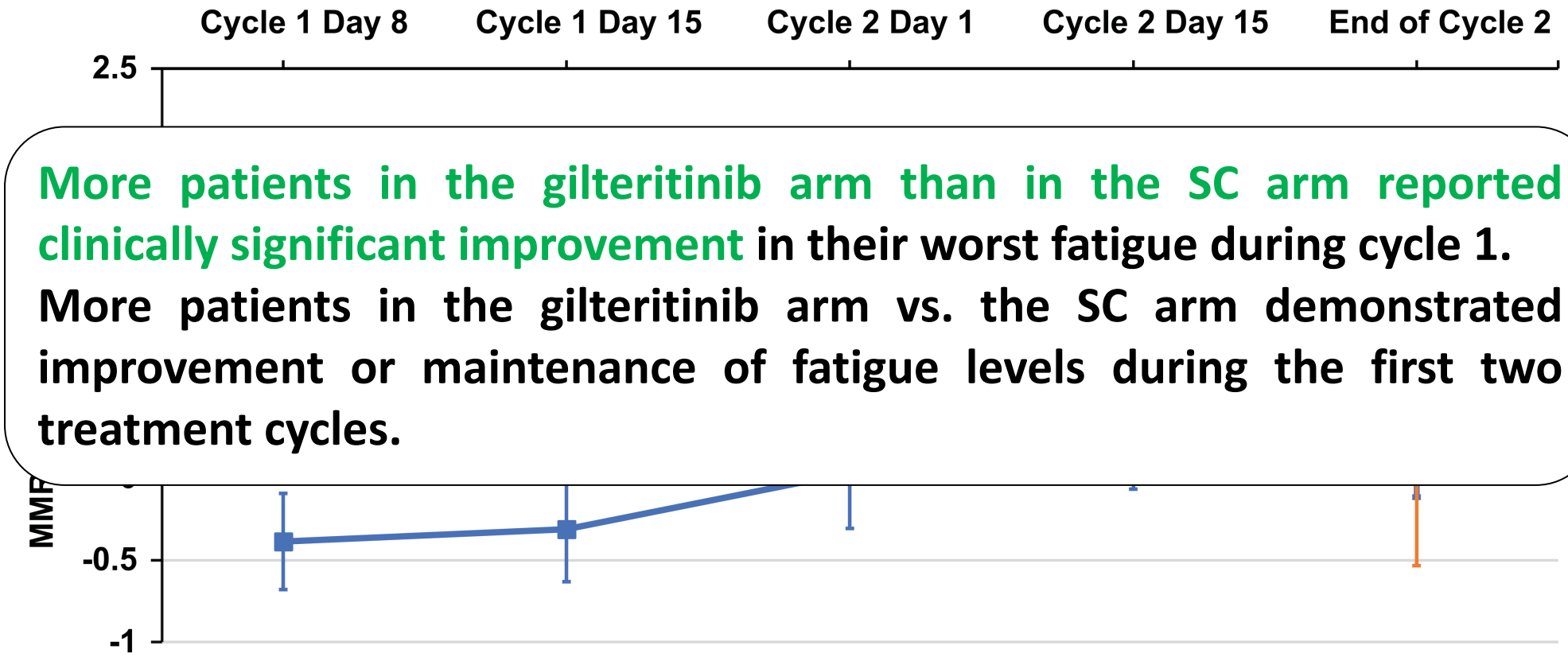
Received 1 September 2022
Revised 14 February 2023
Accepted 25 February 2023

KEYWORDS

Acute myeloid leukemia; FLT3 inhibitor; fatigue; health-related quality of life

Mean longitudinal change in Fatigue in patients with FLT3^{mut+} R/R AML. MMRM estimated change from baseline in BFI total score

A. BFI Total Score[a,b]



More patients in the gilteritinib arm than in the SC arm reported clinically significant improvement in their worst fatigue during cycle 1.

More patients in the gilteritinib arm vs. the SC arm demonstrated improvement or maintenance of fatigue levels during the first two treatment cycles.

[a]Data were missing for 41 patients in the gilteritinib arm and 109 patients in the SC arm at cycle 2 day 1. [b]Error bars represent 95% CI.

Ritchie EK et al. Leuk Lymphoma. 2023;64(5):938-950.

The NEW ENGLAND JOURNAL of MEDICINE

2022

ORIGINAL ARTICLE

Ivosidenib and Azacitidine in *IDH1*-Mutated Acute Myeloid Leukemia

Pau Montesinos, M.D., Ph.D., Christian Recher, M.D., Ph.D., Susana Vives, M.D., Ewa Zarzycka, M.D., Jianxiang Wang, M.D., Giambattista Bertani, M.D., Michael Heuser, M.D., Rodrigo T. Calado, M.D., Ph.D., Andre C. Schuh, M.D., Su-Peng Yeh, M.D., Scott R. Daigle, M.S., Jianan Hui, Ph.D., Shuchi S. Pandya, M.D., Diego A. Gianolio, Ph.D., Stephane de Botton, M.D., Ph.D., and Hartmut Döhner, M.D.

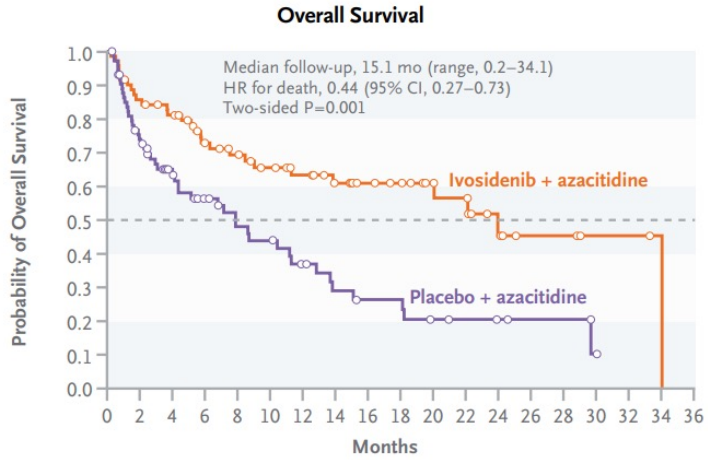
ABSTRACT

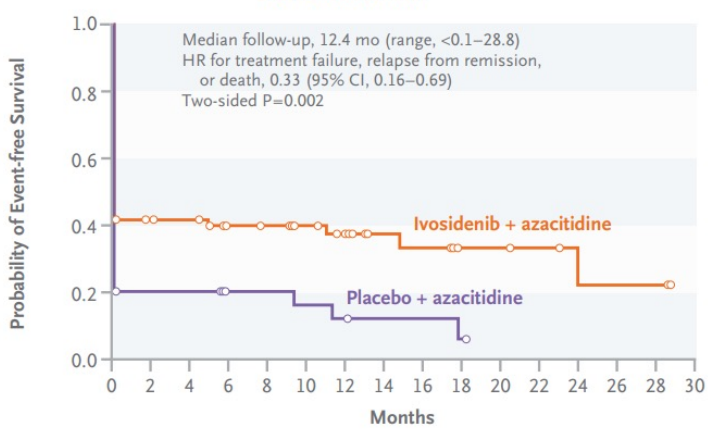
METHODS

In this phase 3 trial, we randomly assigned patients with newly diagnosed *IDH1*-mutated acute myeloid leukemia who were ineligible for intensive induction chemotherapy to receive oral ivosidenib (500 mg once daily) and subcutaneous or intravenous azacitidine (75 mg per square meter of body-surface area for 7 days in 28-day cycles) or to receive matched placebo and azacitidine. The primary end point was event-free survival, defined as the time from randomization until treatment failure (i.e., the patient did not have complete remission by week 24), relapse from remission, or death from any cause, whichever occurred first.

RESULTS

The intention-to-treat population included 146 patients: 72 in the ivosidenib-and-azacitidine group and 74 in the placebo-and-azacitidine group. At a median follow-up of 12.4 months, event-free survival was significantly longer in the ivosidenib-and-azacitidine group than in the placebo-and-azacitidine group (hazard ratio for treatment failure, relapse from remission, or death, 0.33; 95% confidence interval [CI], 0.16 to 0.69; P=0.002). The estimated probability that a patient would remain event-free at 12 months was 37% in the ivosidenib-and-azacitidine group and 12% in the placebo-and-azacitidine group. The median overall survival was 24.0 months with ivosidenib and azacitidine and 7.9 months with placebo and azacitidine (hazard ratio for death, 0.44; 95% CI, 0.27 to 0.73; P=0.001). Common adverse events of grade 3 or higher included febrile neutropenia (28% with ivosidenib and azacitidine and 34% with placebo and azacitidine) and neutropenia (27% and 16%, respectively); the incidence of bleeding events of any grade was 41% and 29%, respectively. The incidence of infection of any grade was 28% with ivosidenib and azacitidine and 49% with placebo and azacitidine. Differentiation syndrome of any grade occurred in 14% of the patients receiving ivosidenib and azacitidine and 8% of those receiving placebo and azacitidine.



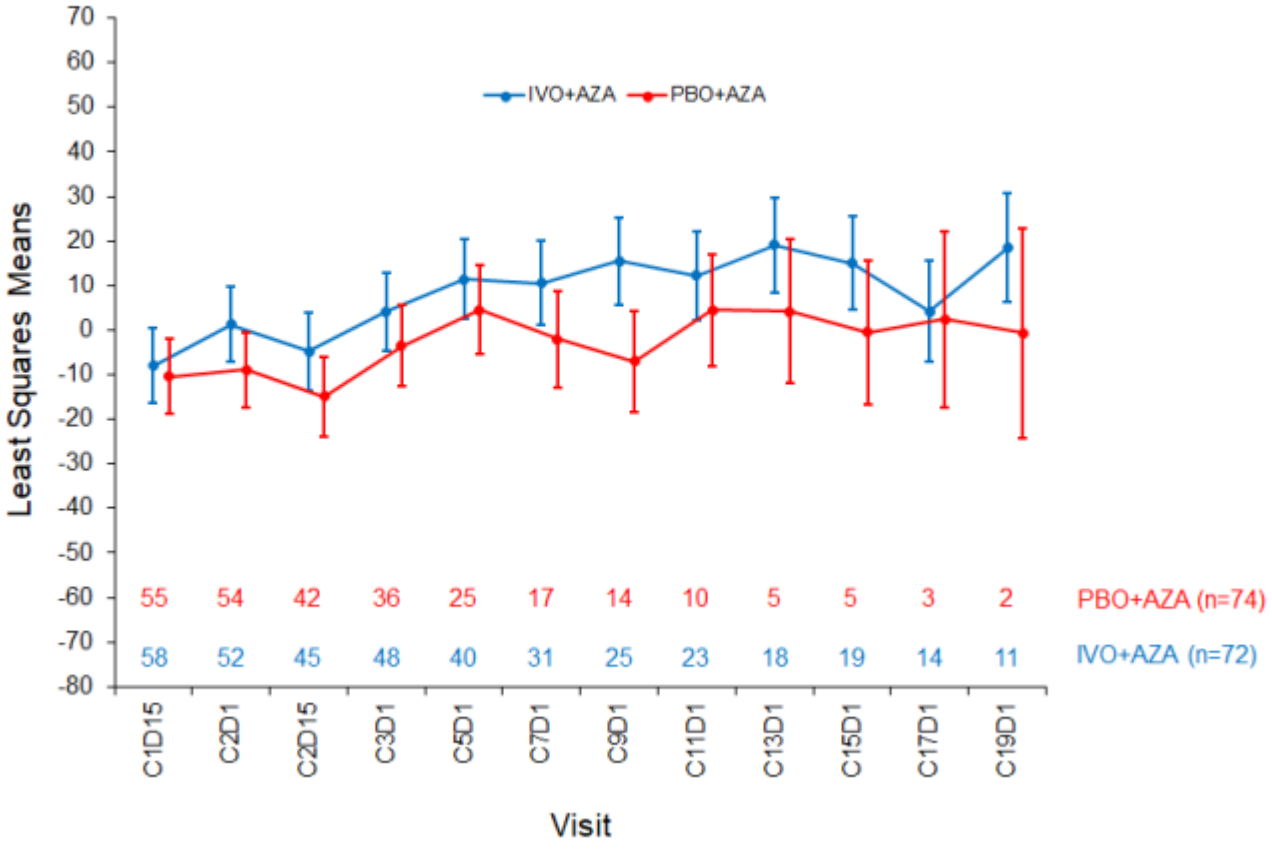


CONCLUSIONS

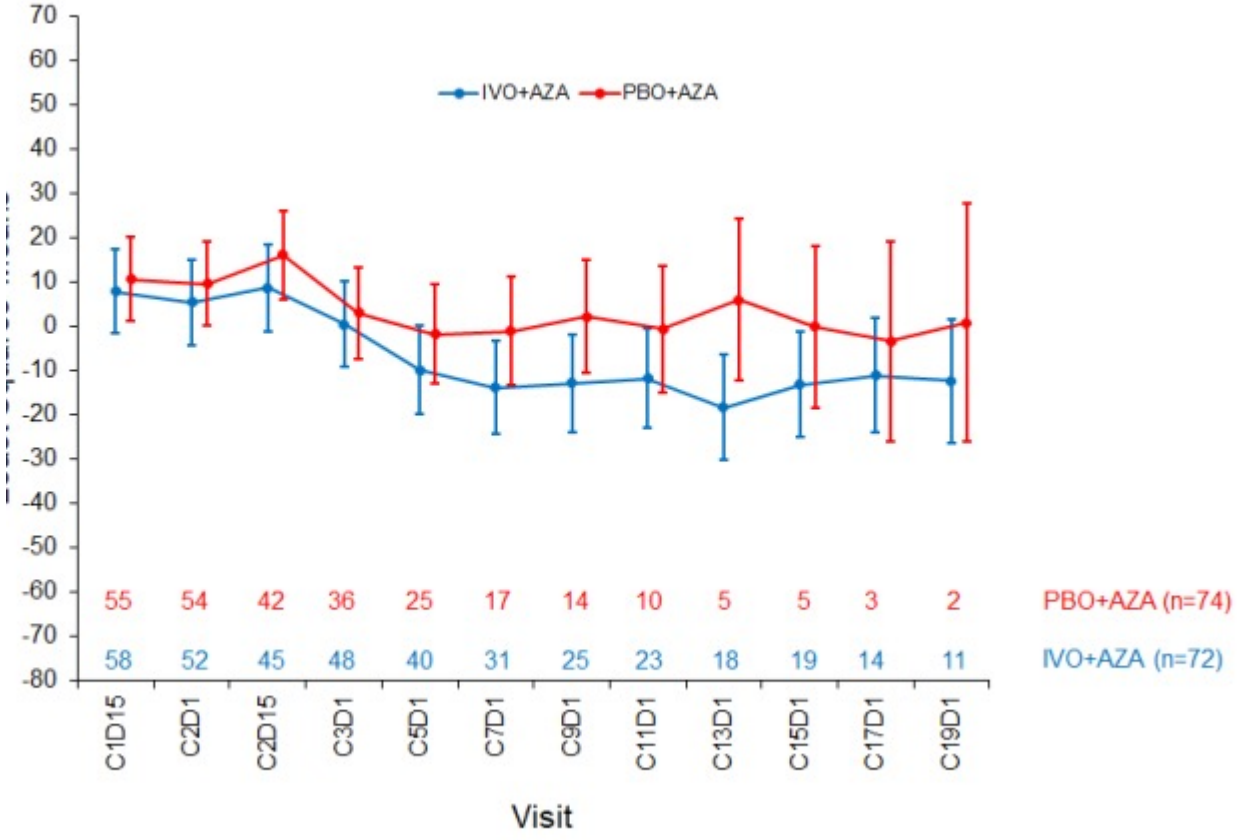
Ivosidenib and azacitidine showed significant clinical benefit as compared with placebo and azacitidine in this difficult-to-treat population. Febrile neutropenia and infections were less frequent in the ivosidenib-and-azacitidine group than in the placebo-and-azacitidine group, whereas neutropenia and bleeding were more frequent in the ivosidenib-and-azacitidine group. (Funded by Agios Pharmaceuticals and Servier Pharmaceuticals; AGILE ClinicalTrials.gov number, NCT03173248.)

N Engl J Med 2022;386:1519-31 DOI: 10.1056/NEJMoa2117344

EORTC QLQ-C30 Global Health Status/QoL score change from baseline



EORTC QLQ-C30 Fatigue score change from baseline



Key Message:

Patients with mIDH1 AML receiving treatment with IVO+AZA tended to report maintenance or improved HRQoL from cycle 5 through to cycle 19 compared with PBO+AZA

N Engl J Med 2022;386:1519-31.

The NEW ENGLAND JOURNAL of MEDICINE

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Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia

C.D. DiNardo, B.A. Jonas, V. Pullarkat, M.J. Thirman, J.S. Garcia, A.H. Wei, M. Konopleva, H. Döhner, A. Letai, P. Fenaux, E. Koller, V. Havelange, B. Leber, J. Esteve, J. Wang, V. Pejsa, R. Hájek, K. Porkka, Á. Illés, D. Lavie, R.M. Lemoli, K. Yamamoto, S.-S. Yoon, J.-H. Jang, S.-P. Yeh, M. Turgut, W.-J. Hong, Y. Zhou, J. Potluri, and K.W. Pratz

ABSTRACT

METHODS

We randomly assigned previously untreated patients with confirmed AML who were ineligible for standard induction therapy because of coexisting conditions, because they were 75 years of age or older, or both to azacitidine plus either venetoclax or placebo. All patients received a standard dose of azacitidine (75 mg per square meter of body-surface area subcutaneously or intravenously on days 1 through 7 every 28-day cycle); venetoclax (target dose, 400 mg) or matching placebo was administered orally, once daily, in 28-day cycles. The primary end point was overall survival.

CONCLUSIONS

In previously untreated patients who were ineligible for intensive chemotherapy, overall survival was longer and the incidence of remission was higher among patients who received azacitidine plus venetoclax than among those who received azacitidine alone. The incidence of febrile neutropenia was higher in the venetoclax–azacitidine group than in the control group. (Funded by AbbVie and Genentech; VIALE-A ClinicalTrials.gov number, NCT02993523.)

Di Nardo CD et al, N. Engl J Med. 2020;383:617–29

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CLINICAL TRIALS AND OBSERVATIONS

Venetoclax plus LDAC for newly diagnosed AML ineligible for intensive chemotherapy: a phase 3 randomized placebo-controlled trial

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KEY POINTS

- Venetoclax plus LDAC improves response rate, transfusion independence, and patient-reported outcomes vs LDAC alone in older AML patients.
- Median OS for patients receiving venetoclax plus LDAC was 8.4 months vs 4.1 months for those receiving LDAC alone.

Effective treatment options are limited for patients with acute myeloid leukemia (AML) who cannot tolerate intensive chemotherapy. Adults age ≥18 years with newly diagnosed AML ineligible for intensive chemotherapy were enrolled in this international phase 3 randomized double-blind placebo-controlled trial. Patients (N = 211) were randomized 2:1 to venetoclax (n = 143) or placebo (n = 68) in 28-day cycles, plus low-dose cytarabine (LDAC) on days 1 to 10. Primary end point was overall survival (OS); secondary end points included response rate, transfusion independence, and event-free survival. Median age was 76 years (range, 36-93 years), 38% had secondary AML, and 20% had received prior hypomethylating agent treatment. Planned primary analysis showed a 25% reduction in risk of death with venetoclax plus LDAC vs LDAC alone (hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.52-1.07; *P* = .11), although not statistically significant; median OS was 7.2 vs 4.1 months, respectively. Unplanned analysis with additional 6-month follow-up demonstrated median OS of 8.4 months for the venetoclax arm (HR, 0.70; 95% CI, 0.50-0.98; *P* = .04). Complete remission (CR) plus CR with incomplete blood count recovery rates were 48% and 13% for venetoclax plus LDAC and LDAC alone, respectively. Key grade ≥3 adverse events (venetoclax vs LDAC alone) were febrile neutropenia (32% vs 29%), neutropenia (47% vs 16%), and thrombocytopenia (45% vs 37%). Venetoclax plus LDAC demonstrates clinically meaningful improvement in remission rate and OS vs LDAC alone, with a manageable safety profile. Results confirm venetoclax plus LDAC as an important frontline treatment for AML patients unfit for intensive chemotherapy. This trial was registered at www.clinicaltrials.gov as #NCT03069352. (*Blood*. 2020; 135(24):2137-2145)

Wei AH et al, Blood 2020;135:2137–45

Blood Cancer Journal
ARTICLE OPEN

2022

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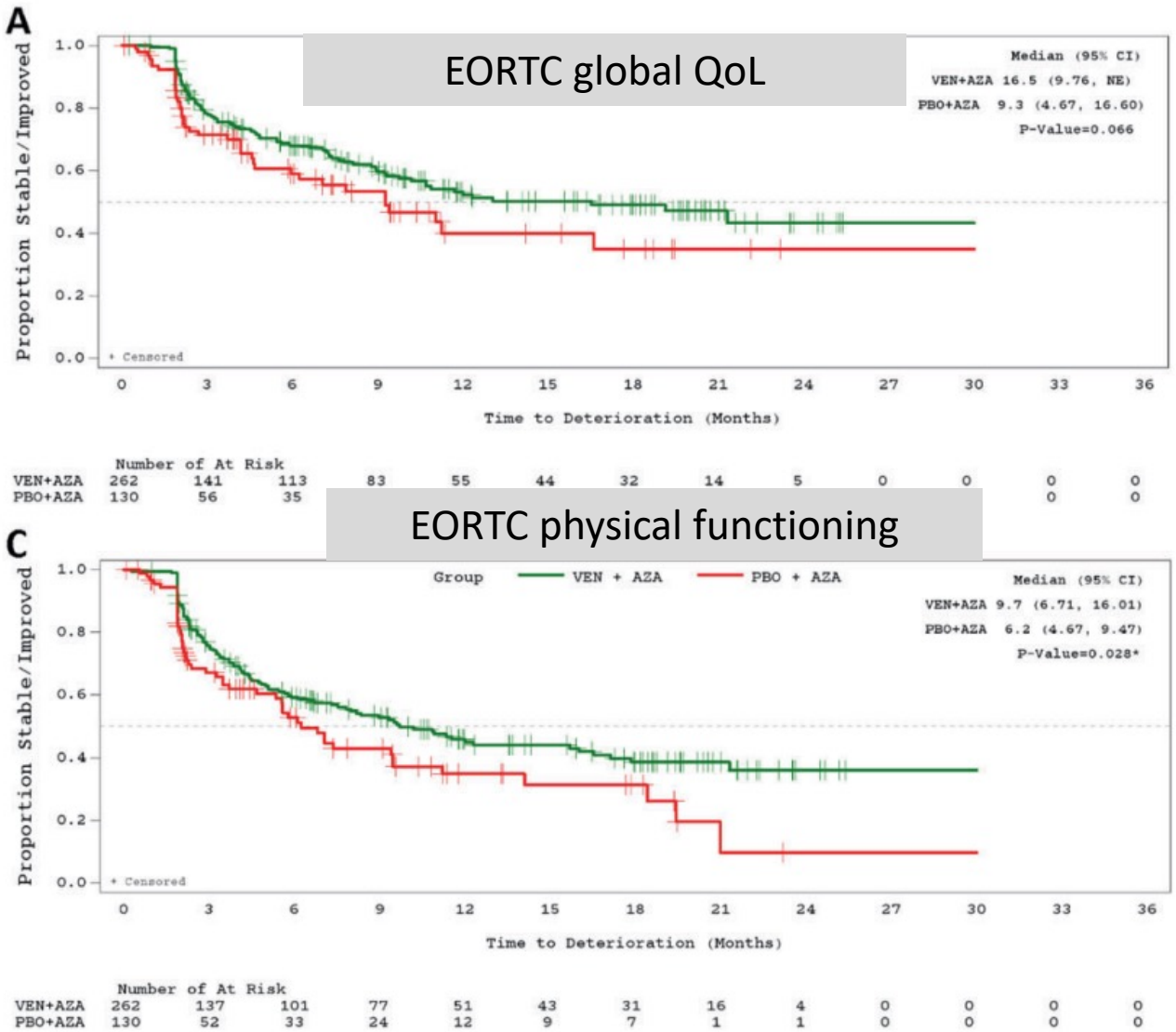
Venetoclax combinations delay the time to deterioration of HRQoL in unfit patients with acute myeloid leukemia

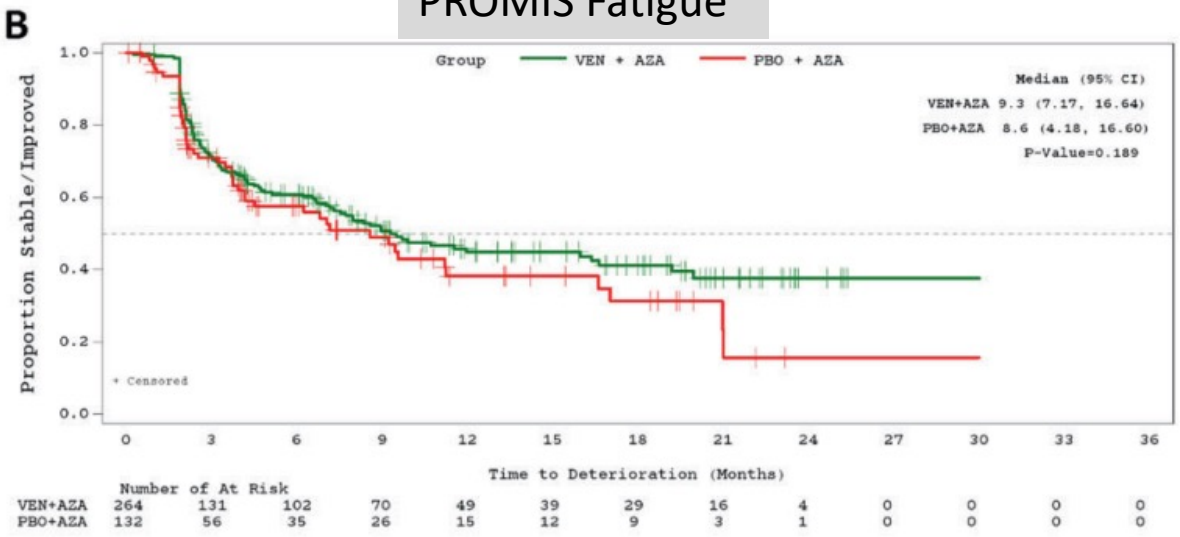
Keith W. Pratz[1✉], Panayiotis Panayiotidis[2], Christian Recher[3], Xudong Wei[4], Brian A. Jonas[5], Pau Montesinos[6], Vladimir Ivanov[7], Andre C. Schuh[8], Courtney D. DiNardo[9], Jan Novak[10], Vlatko Pejsa[11], Don Stevens[12], Su-Peng Yeh[13], Inho Kim[14], Mehmet Turgut[15], Nicola Fracchiolla[16], Kazuhito Yamamoto[17], Yishai Ofran[18], Andrew H. Wei[19], Cat N. Bui[20], Katy Benjamin[20], Rajesh Kamalakar[20], Jalaja Potluri[20], Wellington Mendes[20], Jacob Devine[21] and Walter Fiedler[22]

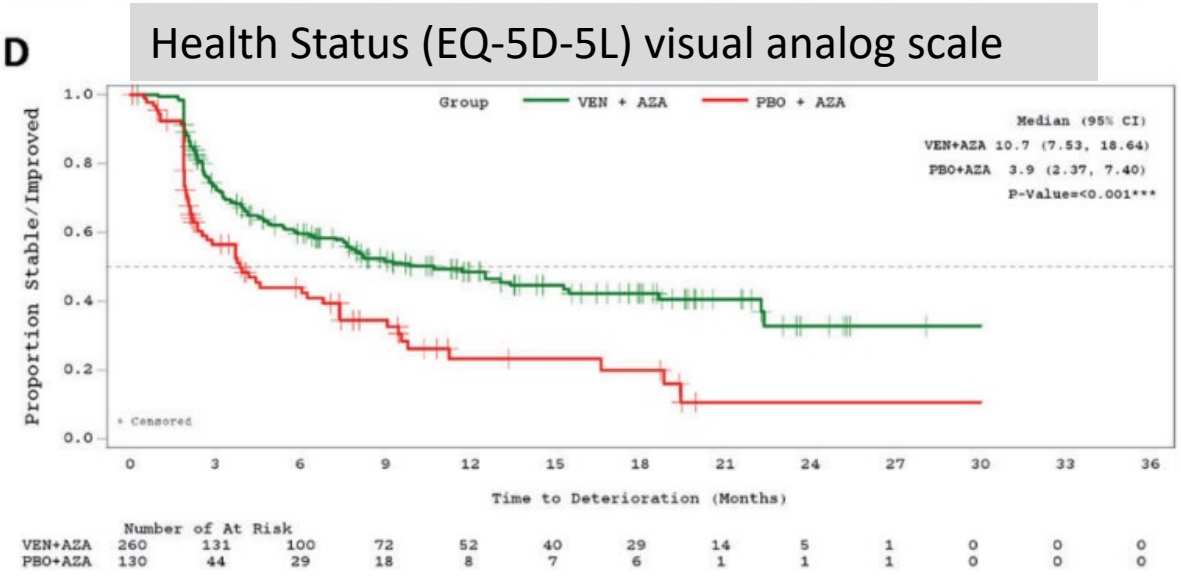
Phase 3 trials Viale-A and Viale-C evaluated health-related quality of life (HRQoL) in patients with AML unfit for intensive chemotherapy who received venetoclax (VEN) + (AZA) (Viale-A) or low-dose cytarabine (LDAC) (Viale-C) or placebo (PBO) + AZA or LDAC. Patient-reported outcomes included: EORTC QLQ-C30 global health status (GHS/QoL) and physical functioning (PF), PROMIS Cancer Fatigue Short Form 7a (Fatigue), and EQ-5D-5L health status visual analog scale (HS-VAS). Time to deterioration (TTD), defined as worsening from baseline in meaningful change thresholds (MCT) of ≥10, 5, or 7 points for GHS/QoL or PF, fatigue, and HS-VAS, respectively, was assessed; differences between groups were analyzed using Kaplan-Meier and unadjusted log-rank analyses. VEN + AZA vs PBO + AZA patients had longer TTD in GHS/QoL ($P = 0.066$) and fatigue ($P = 0.189$), and significantly longer TTD in PF ($P = 0.028$) and HS-VAS ($P < 0.001$). VEN + LDAC vs PBO + LDAC patients had significantly longer TTD in GHS/QoL ($P = 0.011$), PF ($P = 0.020$), and fatigue ($P = 0.004$), and a trend in HS-VAS ($P = 0.057$). Approximately 43%, 35%, 32%, and 18% of patients treated with VEN + AZA, AZA + PBO, VEN + LDAC, or LDAC + PBO, respectively, saw improvements >MCT in GHS/QoL. Overall, VEN may positively impact HRQoL in patients with AML ineligible for intensive chemotherapy, leading to longer preservation of functioning and overall health status.

Blood Cancer Journal (2022)12:71 ; https://doi.org/10.1038/s41408-022-00668-8

Time to deterioration of PROs for VEN+AZA vs AZA+placebo







Time to deterioration thresholds for EORTC-QLQ-C30, EQ5D-5L VAS, and PROMIS Fatigue are ≥10, 7, or 5 points, respectively
(N = VEN + AZA 262, 264, 262, and 260, and PBO + AZA 130, 132, 130, and 130 for EORTC GHS/QoL, fatigue, PF, and health status VAS, respectively).

Blood Cancer Journal (2022)12:71 ; https://doi.org/10.1038/s41408-022-00668-8

CPX-351 versus 7+3 cytarabine and daunorubicin chemotherapy in older adults with newly diagnosed high-risk or secondary acute myeloid leukaemia: 5-year results of a randomised, open-label, multicentre, phase 3 trial

Jeffrey E Lancet, Geoffrey L Uy, Laura F Newell, Tara L Lin, Ellen K Ritchie, Robert K Stuart, Stephen A Strickland, Donna Hogge, Scott R Solomon, Dale L Bixby, Jonathan E Kolitz, Gary J Schiller, Matthew J Wieduwilt, Daniel H Ryan, Stefan Faderl, Jorge E Cortes

Summary

Background Daunorubicin and cytarabine are used as standard induction chemotherapy for patients with acute myeloid leukaemia. CPX-351 is a dual-drug liposomal encapsulation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio. Primary analysis of the phase 3 trial in adults aged 60–75 years with newly diagnosed high-risk or secondary acute myeloid leukaemia provided support for approval of CPX-351 by the US Food and Drug Administration and European Medicines Agency. We describe the prospectively planned final 5-year follow-up results.

Methods This randomised, open-label, multicentre, phase 3 trial was done across 39 academic and regional cancer centres in the USA and Canada. Eligible patients were aged 60–75 years and had a pathological diagnosis of acute myeloid leukaemia according to WHO 2008 criteria, no previous induction therapy for acute myeloid leukaemia, and an Eastern Cooperative Oncology Group performance status of 0–2. Patients were randomly assigned 1:1 (stratified by age and acute myeloid leukaemia subtype) to receive up to two induction cycles of CPX-351 (100 units/m² administered as a 90-min intravenous infusion on days 1, 3, and 5; on days 1 and 3 for the second induction) or standard chemotherapy (cytarabine 100 mg/m² per day continuous intravenous infusion for 7 days plus intravenous daunorubicin 60 mg/m² on days 1, 2, and 3 [7+3]; cytarabine for 5 days and daunorubicin on days 1 and 2 for the second induction [5+2]). Patients with complete remission or complete remission with incomplete neutrophil or platelet recovery could receive up to tw cycles of consolidation therapy with CPX-351 (65 units/m² 90-min infusion on days 1 and 3) or chemotherapy (5+2, same dosage as in the second induction cycle). The primary outcome was overall survival analysed in all randomly assigned patients. No additional adverse events were collected with long-term follow-up, except data for deaths. This trial is registered with ClinicalTrials.gov, NCT01696084, and is complete.

Findings Between Dec 20, 2012, and Nov 11, 2014, 309 patients with newly diagnosed high-risk or secondary acute myeloid leukaemia were enrolled and randomly assigned to receive CPX-351 (153 patients) or 7+3 (156 patients). At a median follow-up of 60·91 months (IQR 60·06–62·98) in the CPX-351 group and 59·93 months (59·73–60·50) in the 7+3 group, median overall survival was 9·33 months (95% CI 6·37–11·86) with CPX-351 and 5·95 months (4·99–7·75) with 7+3 (HR 0·70, 95% CI 0·55–0·91). 5-year overall survival was 18% (95% CI 12–25%) in the CPX-351 group and 8% (4–13%) in the 7+3 group. The most common cause of death in both groups was progressive leukaemia (70 [56%] of 124 deaths in the CPX-351 group and 74 [53%] of 140 deaths in the 7+3 group). Six (5%) of 124 deaths in the CPX-351 group and seven (5%) of 140 deaths in the 7+3 group were considered related to study treatment.

Interpretation After 5 years of follow-up, the improved overall survival with CPX-351 versus 7+3 was maintained, which supports the previous evidence that CPX-351 can contribute to long-term remission and improved overall survival in patients aged 60–75 years with newly diagnosed high-risk or secondary acute myeloid leukaemia.

Lancet Haematol 2021; 8: e481–91

See Comment page e468

H Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA (Prof J E Lancet MD); Washington University School of Medicine, St Louis, MO, USA (Prof G L Uy MD); Knight Cancer Institute, Hematology and Medical Oncology, Oregon Health & Science University, Portland, OR, USA (L F Newell MD); University of Kansas Medical Center, Kansas City, KS, USA (T L Lin MD); Weill Cornell Medical College of Cornell University, New York, NY, USA (E K Ritchie MD); Hollings Cancer Center, Medical University of South Carolina, Charleston, SC, USA (Prof R K Stuart MD); Vanderbilt-Ingram Cancer Center, Nashville, TN, USA (S A Strickland MD); Leukemia/Bone Marrow Transplant Program of British Columbia, Vancouver, BC, Canada (D Hogge MD); Leukemia Program, Northside Hospital Cancer Center Institute, Atlanta, GA, USA (S R Solomon MD); Comprehensive Cancer Center, University of Michigan, Grass Lake, MI, USA (D L Bixby MD); Monter Cancer Institute, Northwell Health System, Lake Success, NY, USA

Lancet JE et al. Lancet Haematol. 2021;8(7):e481-e491..

Quality-adjusted Time Without Symptoms of disease or Toxicity (Q-TWiST) analysis of CPX-351 versus 7 + 3 in older adults with newly diagnosed high-risk/secondary AML

Jorge E. Cortes[1*], Tara L. Lin[2], Geoffrey L. Uy[3], Robert J. Ryan[4], Stefan Faderl[5] and Jeffrey E. Lancet[6]

Abstract

Background: CPX-351 (United States: Vyxeos®; Europe: Vyxeos® Liposomal), a dual-drug liposomal encapsulation of daunorubicin and cytarabine in a synergistic 1:5 molar ratio, is approved by the US FDA and the EMA for the treatment of adults with newly diagnosed therapy-related acute myeloid leukemia or acute myeloid leukemia with myelodysplasia-related changes. In a pivotal phase 3 study that evaluated 309 patients aged 60 to 75 years with newly diagnosed high-risk/secondary acute myeloid leukemia, CPX-351 significantly improved median overall survival versus conventional 7 + 3 chemotherapy (cytarabine continuous infusion for 7 days plus daunorubicin for 3 days), with a comparable safety profile. A Quality-adjusted Time Without Symptoms of disease or Toxicity (Q-TWiST) analysis of the phase 3 study was performed to compare survival quality between patients receiving CPX-351 versus conventional 7 + 3 after 5 years of follow-up.

Methods: Patients were randomized 1:1 between December 20, 2012 and November 11, 2014 to receive induction with CPX-351 or 7 + 3. Survival time for each patient was partitioned into 3 health states: TOX (time with any grade 3 or 4 toxicity or prior to remission), TWiST (time in remission without relapse or grade 3 or 4 toxicity), and REL (time after relapse). Within each treatment arm, Q-TWiST was calculated by adding the mean time spent in each health state weighted by its respective quality-of-life, represented by health utility. The relative Q-TWiST gain, calculated as the difference in Q-TWiST between treatment arms divided by the mean survival of the 7 + 3 control arm, was determined in order to evaluate results in the context of other Q-TWiST analyses.

Results: The relative Q-TWiST gain with CPX-351 versus 7 + 3 was 53.6% in the base case scenario and 39.8% among responding patients. Across various sensitivity analyses, the relative Q-TWiST gains for CPX-351 ranged from 48.0 to 57.6%, remaining well above the standard clinically important difference threshold of 15% for oncology.

Conclusions: This post hoc analysis demonstrates that CPX-351 improved quality-adjusted survival, further supporting the clinical benefit in patients with newly diagnosed high-risk/secondary acute myeloid leukemia.

Trial registration This trial was registered on September 28, 2012 at www.clinicaltrials.gov as NCT01696084 (https://clinicaltrials.gov/ct2/show/NCT01696084) and is complete.

Keywords: Acute myeloid leukemia, Chemotherapy, Relapse, Survival, Toxicity, Quality-of-life

Cortes JE et al. Hematol Oncol. 2021;14(1):110.

Health Problems of AML survivors in real-life

SPARTA GIMEMA-EORTC 1621 Study

To compare comorbid medical conditions of long-term AML survivors with that of their peers from the general population.

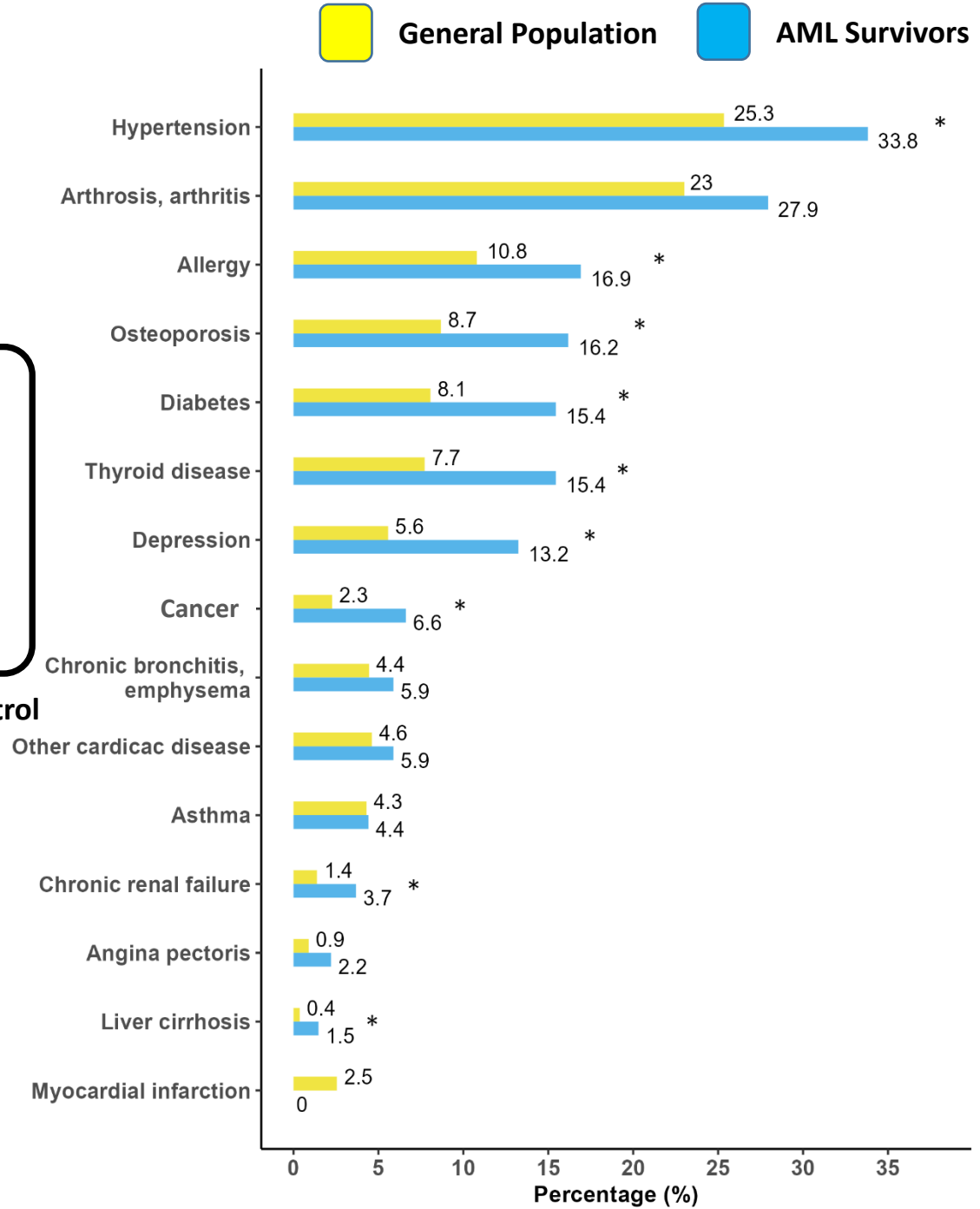
AML Survivors, Median follow-up time since diagnosis was 9.0 years

AML long-term survivors have a higher prevalence of comorbidities compared to their peers in the general population

General Population= 53,685

AML Survivors=136

Matched case-control analysis



JAMA Oncology | Original Investigation

Effectiveness of Integrated Palliative and Oncology Care for Patients With Acute Myeloid Leukemia

A Randomized Clinical Trial

Areej El-Jawahri, MD; Thomas W. LeBlanc, MD; Alison Kavanaugh, NP; Jason A. Webb, MD; Vicki A. Jackson, MD; Toby C. Campbell, MD; Nina O'Connor, MD; Selina M. Luger, MD; Ellin Gafford, MD; Jillian Gustin, MD; Bhavana Bhatnagar, DO; Alison R. Walker, MD; Amir T. Fathi, MD; Andrew M. Brunner, MD; Gabriela S. Hobbs, MD; Showly Nicholson, BS; Debra Davis, RN, BSN; Hilena Addis, BS; Dagny Vaughn, BA; Nora Horick, MS; Joseph A Greer, PhD; Jennifer S. Temel, MD

160 patients with high risk AML randomized to:

Integrated Palliative and Oncology Care Intervention (n = 86)	Usual Care (n = 74)
Patients randomized to IPC were seen by palliative care clinicians at least twice per week during their initial and subsequent hospitalizations.	Patients assigned to Uc received supportive care measures as per their oncology team. They were permitted to receive palliative care at their request or at the request of their oncologist.

El-Jawahri A et al. JAMA Oncol. 2021;7(2):238-245.

IMPORTANCE Patients with acute myeloid leukemia (AML) receiving intensive chemotherapy experience substantial decline in their quality of life (QOL) and mood during their hospitalization for induction chemotherapy and often receive aggressive care at the end of life (EOL). However, the role of specialty palliative care for improving the QOL and care for this population is currently unknown.

OBJECTIVE To assess the effect of integrated palliative and oncology care (IPC) on patient-reported and EOL outcomes in patients with AML.

DESIGN, SETTING, AND PARTICIPANTS We conducted a multisite randomized clinical trial of IPC (n = 86) vs usual care (UC) (n = 74) for patients with AML undergoing intensive chemotherapy. Data were collected from January 2017 through July 2019 at 4 tertiary care academic hospitals in the United States.

INTERVENTIONS Patients assigned to IPC were seen by palliative care clinicians at least twice per week during their initial and subsequent hospitalizations.

MAIN OUTCOMES AND MEASURES Patients completed the 44-item Functional Assessment of Cancer Therapy–Leukemia scale (score range, 0-176) to assess QOL; the 14-item Hospital Anxiety and Depression Scale (HADS), with subscales assessing symptoms of anxiety and depression (score range, 0-21); and the PTSD Checklist–Civilian version to assess posttraumatic stress disorder (PTSD) symptoms (score range, 17-85) at baseline and weeks 2, 4, 12, and 24. The primary end point was QOL at week 2. We used analysis of covariance adjusting and mixed linear effect models to evaluate patient-reported outcomes. We used Fisher exact test to compare patient-reported discussion of EOL care preferences and receipt of chemotherapy in the last 30 days of life.

RESULTS Of 235 eligible patients, 160 (68.1%) were enrolled; of the 160 participants, the median (range) age was 64.4 (19.7-80.1) years, and 64 (40.0%) were women. Compared with those receiving UC, IPC participants reported better QOL (adjusted mean score, 107.59 vs 116.45; $P = .04$), and lower depression (adjusted mean score, 7.20 vs 5.68; $P = .02$), anxiety (adjusted mean score, 5.94 vs 4.53; $P = .02$), and PTSD symptoms (adjusted mean score, 31.69 vs 27.79; $P = .01$) at week 2. Intervention effects were sustained to week 24 for QOL (β, 2.35; 95% CI, 0.02-4.68; $P = .048$), depression (β, −0.42; 95% CI, −0.82 to −0.02; $P = .04$), anxiety (β, −0.38; 95% CI, −0.75 to −0.01; $P = .04$), and PTSD symptoms (β, −1.43; 95% CI, −2.34 to −0.54; $P = .002$). Among patients who died, those receiving IPC were more likely than those receiving UC to report discussing EOL care preferences (21 of 28 [75.0%] vs 12 of 30 [40.0%]; $P = .01$) and less likely to receive chemotherapy near EOL (15 of 43 [34.9%] vs 27 of 41 [65.9%]; $P = .01$).

CONCLUSIONS AND RELEVANCE In this randomized clinical trial of patients with AML, IPC led to substantial improvements in QOL, psychological distress, and EOL care. Palliative care should be considered a new standard of care for patients with AML.

End-of-life Outcomes

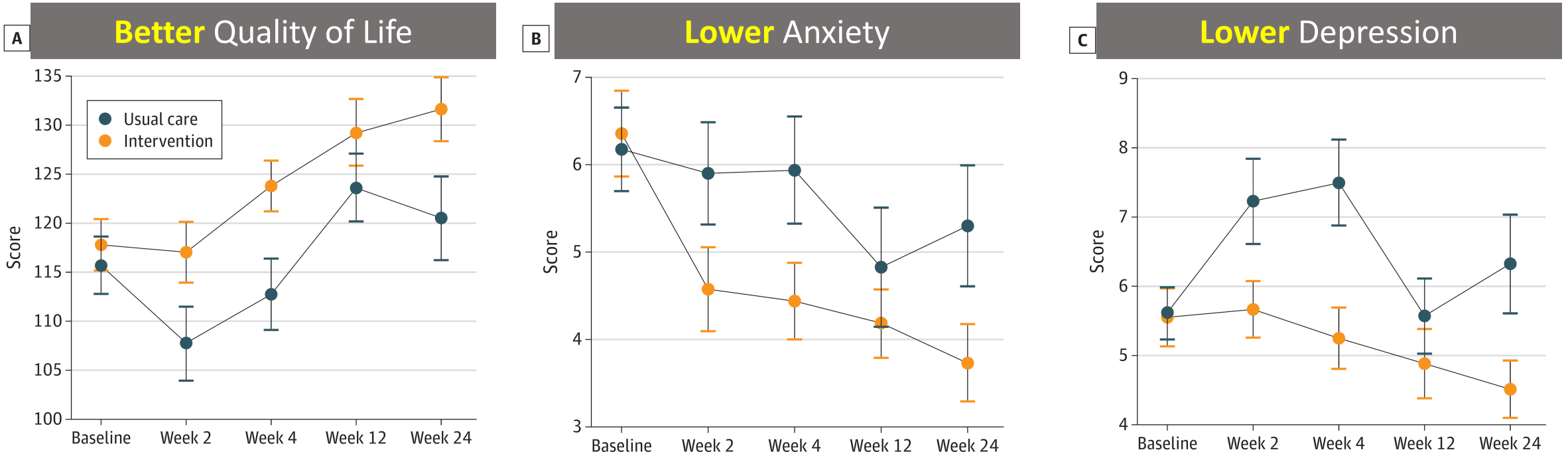
Among patients who died (n = 87; 44 of 73 in the UC group and 43 of 84 in the IPC group), those receiving IPC vs UC were:

- **more likely to report discussing their EOL care preferences with their clinicians** (21 of 28 [75.0%] vs 12 of 30 [40.0%]; *P* = .01).

- **less likely to receive chemotherapy in the last 30 days of life** (15 of 43 [34.9%] vs 27 of 41 [65.9%]; *P* = .01).

El-Jawahri A et al. JAMA Oncol. 2021;7(2):238-245.

Effect of Integrated Palliative and Oncology Care on: Quality of Life and Psychological Distress



When compared with patients assigned to usual care, patients assigned to integrated palliative and oncology care reported:
better quality of life (β, 2.35; 95%CI, 0.02-4.68; *P* = .048) **(A),**
lower anxiety (β, −0.38; 95%CI, −0.75 to −0.01;*P* = .04) **(B)**
lower depression (β, −0.42; 95%CI, −0.82 to −0.02; *P* = .04) **(C)**

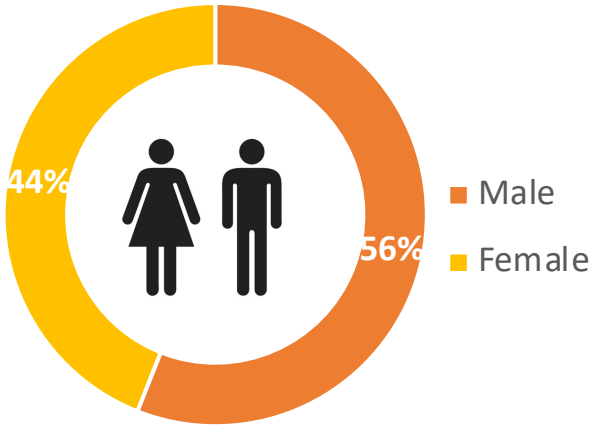
El-Jawahri A et al. JAMA Oncol. 2021;7(2):238-245.

Quality of End-of-Life Care for Patients with Blood Cancers. A GIMEMA Quality of Life WP Survey on the Italian Hematologists' Perception"

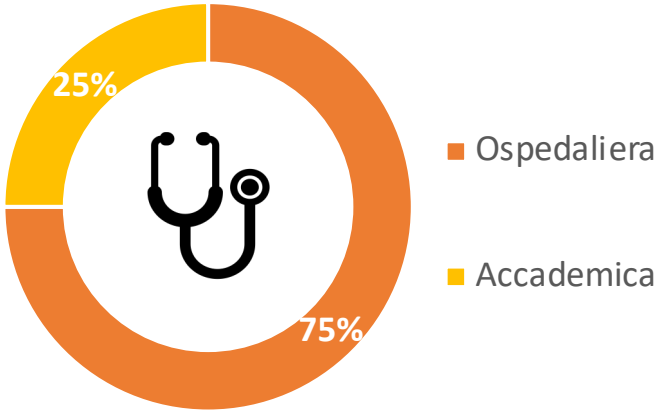
N=183 medici

AGE Mediana età : 50 anni

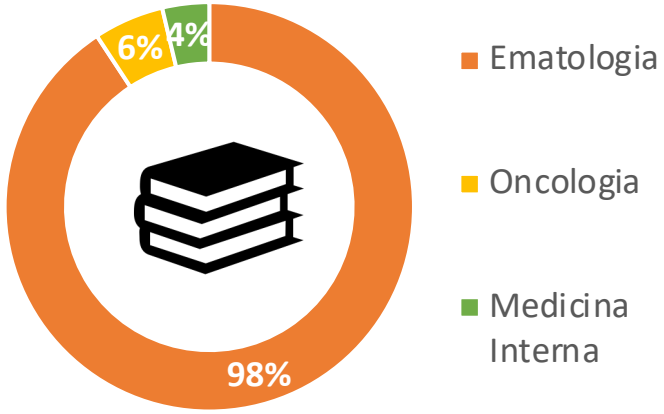
Sesso



Attività Clinica



Specializzazione



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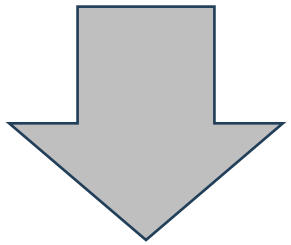
Indicatori di qualità delle cure di fine vita

INDICATORI	Accettabile	Non accettabile
Ricovero in hospice più di 7 giorni prima della morte	**150 (82%)**	32 (18%)
Nessuna chemioterapia negli ultimi 14 giorni di vita	**129 (70%)**	54 (30%)
Nessuna nuova chemioterapia negli ultimi 30 giorni di vita	**145 (80%)**	36 (20%)
Nessuna chemioterapia negli ultimi 30 giorni di vita	**119 (66%)**	62 (34%)
Nessun ricovero in ICU negli ultimi 30 giorni di vita	**154 (84%)**	30 (16%)
Non più di 1 visita in pronto soccorso negli ultimi 30 giorni di vita	**145 (80%)**	37 (20%)
Non più di 1 ospedalizzazione negli ultimi 30 giorni di vita	**147 (80%)**	36 (20%)
Non morire in un reparto per acuti	**161 (88%)**	21 (12%)
Nessuna trasfusione di globuli rossi negli ultimi 7 giorni di vita	**59 (33%)**	122 (67%)
Nessuna trasfusione di piastrine negli ultimi 7 giorni di vita	**80 (44%)**	103 (56%)
Nessuna intubazione negli ultimi 30 giorni di vita	**165 (89%)**	20 (11%)
Nessuna rianimazione cardio polmonare negli ultimi 30 giorni di vita	**159 (87%)**	24 (13%)
Nessuna attivazione di assistenza domiciliare	**20 (11%)**	162 (89%)

The Importance of the International collaboration in AML research



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PROACTIVE Project

Patient-Reported Outcomes Research in ACute Myeloid Leukemia and Myelodysplastic Syndromes: Towards a PatIent-Centered and ValuE Based Care Approach

Fabio Efficace[1], Ian Thomas[2], Rena Buckstein[3]

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[2]Centre for Trials Research, Cardiff University, Cardiff, UK
[3]Department of Medical Oncology/Hematology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

NCRI Advancing Cancer Research Together

Sunnybrook HEALTH SCIENCES CENTRE

AIL Roma Vanessa Verdecchia ODV
ROMAIL • ASSOCIAZIONE ITALIANA CONTRO LEUCEMIE - LINFOMI E MIELOMA

PROACTIVE Project: >6000 patients (AML/MDS)

Create a **large international dataset** with **clinical, survival and QoL data**, which will allow us to answer several unique research clinical questions

	APL	AML	MDS	TOTAL
Italy	520	1017	1146	2683
UK	206	816	810	1832
Canada	-	-	1500	1500
Total	726	1833	3456	**>6000 pts**

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Take-home messages

- **Notable advances** have been made in recent years in the **treatment of AML** with several **new drugs** approved and under development.
- **Quality of Life (QoL)** data provides unique information that can **facilitate clinical decision-making** for AML patients
- **Early integration of palliative care** in patients with AML has a number of clinical and QoL benefits

Acknowledgments

GIMEMA Health Outcomes Research Unit
GIMEMA Working Party on Quality of Life

Francesca Tartaglia, Laura Cannella, Francesco Sparano

AIL Roma
Vanessa Verdecchia • ODV
ROMAIL • ASSOCIAZIONE ITALIANA
CONTRO LEUCEMIE - LINFOMI E MIELOMA

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