Check for updates

ELSEVIER

Blood 142 (2023) 2854–2856

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Outcome of Intensively Treated Elderly AML Patients Reported to the Harmony Alliance Compares Well to Outcome of Control Patients of the Prospective Randomized HOVON 103 Study in Elderly AML

Sjoerd J.F. Hermans, MD[1], *Jurjen Versluis, MD PhD*[1], *Yvette van Norden, PhD*[1,2], *Erik D. van Werkhoven, MSc*[1,2], *Jeroen J.W.M. Janssen, MD PhD*[3], *Gerwin A. Huls, Prof.*[4], *Bob Lowenberg, MDPhD*[1], *Thomas Pabst*[5], *Dimitri A. Breems, MD PhD*[6], *Elizabeth Berkx, PhD*[7], *Avinash G. Dinmohamed, PhD*[7], *Peter C. Huijgens, Prof.*[7], *Eric Sträng*[8], *Jesús María Hernández-Rivas, PhD*[9], *Hartmut Döhner, MD*[10], *Marta Sobas, MDPhD*[11], *Lars Bullinger*[12], *Rosa Ayala, MD PhD*[13], *Joaquin Martinez-Lopez, MD PhD*[13], *Klaus H Metzeler, MD*[14], *Torsten Haferlach, MD PhD*[15], *Christian Thiede, MD*[16], *Carin A. Uyl-De Groot, Prof.*[17], *Gert J. Ossenkoppele, MD PhD*[18], *Francesco Pignatti*[19], *Jan J. Cornelissen, MD PhD*[1]

[1] Erasmus University Medical Center Cancer Institute, Rotterdam, Netherlands
[2] HOVON Foundation, Rotterdam, Netherlands
[3] Department of Hematology, University Medical Centre Nijmegen, Nijmegen, Netherlands
[4] Dept. of Hematology, University Medical Center Groningen (UMCG), Groningen, Netherlands
[5] Department of Medical Oncology, Inselspital, Bern University Hospital, Bern, Switzerland
[6] Ziekenhuis Netwerk Antwerpen, Antwerp, Belgium
[7] Department of Research and Development, Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, Netherlands
[8] Department of Hematology, Oncology, Tumor Immunology, Charité University Medicine, Berlin, Germany
[9] Servicio de Hematología, Hospital Universitario de Salamanca, Universidad de Salamanca, Salamanca, Spain
[10] Department of Internal Medicine III, University Hospital of Ulm, Ulm, Germany
[11] Wroclaw Medical University, Wroclaw, Poland
[12] Department of Hematology, Oncology, and Cancer Immunology, Charité-Universitätsmedizin Berlin, Berlin, Germany
[13] Hematology Department, Hospital 12 de Octubre (i+12), Centro Nacional de Investigaciones Oncológicas (CNIO), Complutense University, Madrid, Spain
[14] Department of Hematology, Cellular Therapy, Hemostaseology and Infectious Diseases, University Leipzig Medical Center, Leipzig, Germany
[15] MLL Munich Leukemia Laboratory, Munich, Germany
[16] Department of Medicine I, University Hospital Carl Gustav Carus, Dresden, Germany
[17] Erasmus School of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, Netherlands
[18] Department of Hematology, Cancer Center Amsterdam, Amsterdam University Medical Centers, Vrije Universiteit University Medical Center, Amsterdam, Netherlands
[19] Oncology and Hematology Office, European Medicines Agency, Amsterdam, Netherlands

Introduction: The evaluation of novel drugs in hemato-oncology is hampered by relatively large sample sizes needed for sufficiently powered, randomized controlled trials (RCT). External control data are increasingly applied in prospective phase II and III studies, and might be derived from Real-World Data (RWD) sources, such as national cancer registries. The HARMONY Alliance recently reported on a big data platform, consisting of data that were generated by cooperative European acute myeloid leukemia (AML) study groups (*Lang et al., Trials, 2020*). HARMONY or cancer registry data might supplement prospectively collected trial control data. Here, we investigated whether and to what extent data included in the HARMONY AML database and RWD from the Netherlands Cancer Registry (NCR) compare to the control arm of the recently reported prospective randomized HOVON-103 (H103) study in elderly AML (*Ossenkoppele et al., Leukemia, 2020; Janssen et al., Leukemia, 2022*).
Methods: The H103 trial consecutively randomized newly diagnosed AML patients aged >65 years between standard induction chemotherapy with or without lenalidomide, tosedostat, or selinexor. External control patients concerned newly diagnosed (HARMONY: 2010-2018; NCR: 2014-2018) and intensively treated (intensified cytarabine/anthracycline) elderly AML patients aged >60 years. H103 were matched 1:1 using nearest neighbor propensity scores with NCR and HARMONY pa-

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/2854/2190221/blood-9456-main.pdf by guest on 01 June 2024

© 2023 by The American Society of Hematology

tients for age, European Leukemia Net (ELN) 2022 risk classification, and leukocyte count at diagnosis, while HARMONY patients were additionally matched for WHO performance score. Patients with missing values for propensity score factors were excluded from that analysis. The primary endpoint was overall survival (OS), calculated by the Kaplan-Meier method.
Results: 67% of HARMONY patients (n=510) concerned trial patients. Median age was lower for HARMONY patients compared with H103-controls (n=279) (67 vs. 69 years, P<0.01), with also a preponderance of male patients in the H103 cohort (54% vs. 62%, P=0.03). Age and male sex did not differ between H103-controls and NCR patients (n=320) (69 vs. 69 years, P=0.46; 62% vs. 62%, P=1.0) (Table 1). WHO performance score of 0 or 1 was reported in 49% and 41% of H103-controls which was less frequent in HARMONY and NCR data (8% and 31%, P<0.01; 26% and 18%, P<0.01, respectively). Unknown WHO status was more prevalent in the external cohorts than in H103, at 43%, 54%, and 1% for the HARMONY, NCR, and H103 cohorts, respectively. ELN 2022 risk (favorable vs. non-favorable) was reported in 24% vs. 76% of H103 patients, which was similar in HARMONY patients (26% vs. 74%; P=0.73). ELN 2022 risk differed, however, for NCR patients (17% vs 83%; P=0.03). The median leukocyte count at diagnosis was lower for H103-controls than for HARMONY and NCR patients (3.65 vs. 17.1, P<0.01; 3.65 vs. 13.1, P<0.01, respectively). Propensity scores matched 278 HARMONY patients and 278 NCR patients to H103-controls. The 2-year OS (estimate±SE) was 40±3% for H103-controls vs. 35±3% for HARMONY patients (P=0.22), and vs. 30±3% for NCR patients (P=0.052), respectively (Figure 1).
Conclusion: Characteristics of H103-controls and HARMONY patients appeared largely comparable, while NCR patients were more frequently ELN 2022 non-favorable risk. Following matching, OS was similar between H103-controls and HARMONY patients, while NCR patients showed inferior OS. The inclusion of a large proportion of trial patients in the HARMONY cohort, adhering to strict inclusion and exclusion criteria and fewer comorbidities compared to RWD patients, might explain these observations. These results suggest that matched data of the HARMONY Alliance might supplement prospectively collected control data in studies evaluating intensive therapy in elderly AML.

Disclosures Versluis: *ExCellThera:* Consultancy; *AbbVie:* Honoraria. **Hernández-Rivas:** *GSK:* Consultancy, Honoraria, Speakers Bureau; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene/BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding. **Döhner:** *Janssen:* Consultancy, Honoraria; *Syndax:* Honoraria; *Novartis:* Consultancy, Honoraria, Research Funding; *Kronos-Bio:* Research Funding; *AstraZeneca:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria, Research Funding; *Bristol Myers Squibb:* Consultancy, Honoraria, Research Funding; *Berlin-Chemie:* Consultancy, Honoraria; *Jazz Pharmaceuticals:* Consultancy, Honoraria, Research Funding; *Celgene:* Consultancy, Honoraria, Research Funding; *Daiichi Sankyo:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria; *Pfizer:* Research Funding; *Servier:* Consultancy, Honoraria; *Stemline:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria, Research Funding; *Agios:* Consultancy, Honoraria, Research Funding; *Abbvie:* Consultancy, Honoraria, Research Funding. **Bullinger:** *Amgen:* Honoraria; *Janssen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bayer Oncology:* Research Funding; *Jazz Pharmaceuticals:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Gilead:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Astellas:* Honoraria; *Celgene/BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol-Myers Squibb:* Honoraria; *Daiichi Sankyo:* Honoraria; *Sanofi:* Honoraria. **Ayala:** *Novartis:* Consultancy, Speakers Bureau; *Incyte:* Consultancy; *Astellas, BMS:* Speakers Bureau. **Haferlach:** *MLL Munich Leukemia Laboratory:* Current Employment, Other: Equity Ownership.

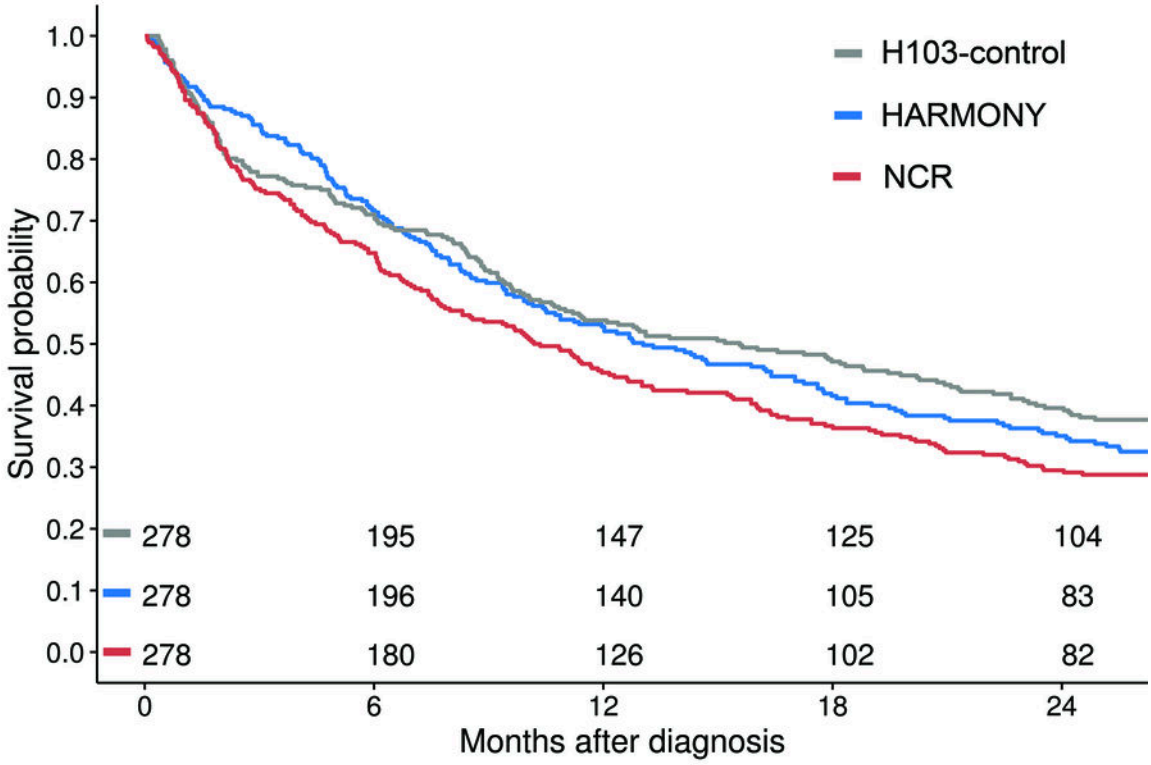
Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/2854/2190221/blood-9456-main.pdf by guest on 01 June 2024

Table 1. Patient characteristics of H103-control patients, HARMONY patients, and NCR patients in the unmatched cohorts

Parameter	H103-controls (n=279)	HARMONY (n=510)	NCR (n=320)	P-value	
				vs. HARMONY	vs. NCR
Age, median (range)	69 (65-84)	67 (60-86)	69 (66-89)	<0.01	0.46
Male sex, n (%)	172 (62)	273 (54)	197 (62)	0.03	1.00
WHO performance score, n (%)				<0.01	<0.01
0	136 (49)	43 (8)	84 (26)		
1	114 (41)	158 (31)	58 (18)		
2	25 (9)	91 (18)	7 (2)		
Unknown	4 (1)	218 (43)	171 (54)		
Favorable ELN 2022 risk classification, n (%)	68 (24)	131 (26)	55 (17)	0.73	0.03
White blood cell count (10^9/L), median (range)	3.65 (0-301)	17.1 (0.5-466)	13.1 (0.3-437)	<0.01	<0.01
Missing	1 (0.4)	21 (4)	1 (0.3)		

Abbreviations: NCR: Netherlands Cancer Registry

Figure 1. Overall survival for H103-control patients vs. HARMONY patients, and H103-control patients vs. NCR patients in the matched cohorts



Patients with missing values for propensity score factors were excluded from the analysis. The 2-year OS (estimate±SE) was 40±3% vs. 35±3% vs. 30±3%, for H103-controls, HARMONY-controls (P=0.22), and NCR patients (P=0.052), respectively. Abbreviations: NCR: Netherlands Cancer Registry; OS: overall survival

Figure 1

https://doi.org/10.1182/blood-2023-186277

Downloaded from http://ashpublications.net/blood/article-pdf/142/Supplement 1/2854/2190221/blood-9456-main.pdf by guest on 01 June 2024