S142

QuANTUM-First: Efficacy in Newly Diagnosed Patients With FMS-Like Tyrosine Kinase 3-Internal Tandem Duplication–Positive Acute Myeloid Leukemia Who Received Continuation Therapy

Mikkael A. Sekeres,[1] Harry P. Erba,[2] Pau Montesinos,[3] Elżbieta Patkowska,[4] Jorge Cortes,[5] Alexander E. Perl,[6] Hervé Dombret,[7] Sergio Amadori,[8] Jianxiang Wang,[9] Richard F. Schlenk,[10] Li Liu,[11] Yasser Mostafa Kamel,[11] Karima Imadalou,[11] Abderrahmane Laadem,[11] Arnaud Lesegretain,[11] Mark J. Levis[12]

[1]Sylvester Cancer Center, University of Miami Health System, Miami, FL, USA; [2]Duke Cancer Institute, Durham, NC, USA; [3]La Fe University and Polytechnic Hospital, Valencia, Spain; [4]Institute of Hematology and Blood Transfusion, Warsaw, Poland; [5]Augusta University Medical Center, Augusta, GA, USA; [6]Division of Hematology/Oncology, University of Pennsylvania, Philadelphia, PA, USA; [7]Saint Louis Hospital, University of Paris, Paris, France; [8]Tor Vergata Polyclinic Hospital Rome, Rome, Italy; [9]Institute of Hematology and Blood Diseases Hospital, Tianjin, China; [10]National Center of Tumor Diseases Trial Center, German Cancer Research Center, Department of Internal Medicine V, Heidelberg University Hospital, Heidelberg, Germany; [11]Daiichi Sankyo, Basking Ridge, NJ, USA; [12]Division of Hematologic Malignancies, Johns Hopkins University, Baltimore, MD, USA

QuANTUM-FIRST STUDY

Disclosures

- ***Participation on a Data Safety Monitoring Board or Advisory Board:*** Bristol Myers Squibb, Kurome Therapeutics, and Schrödinger

- ***Stock options:*** Kurome Therapeutics

Background and Objectives

BACKGROUND

- The addition of quizartinib to intensive induction, consolidation, and continuation therapy improved OS in the QuANTUM-First phase 3 study (NCT02668653)[1]
  - The HR for OS was 0.78 (95% CI, 0.62-0.98), with a decrease in the relative risk of death by 22% versus placebo[1]
- Based on these data[1]:
  - Quizartinib has been approved in the US,[2] EU,[3] UK,[4] and Japan[5] in combination with chemotherapy across induction, consolidation, and as continuation monotherapy (but not after transplantation in the US) for the treatment of adult patients with newly diagnosed *FLT3*-ITD–positive AML

OBJECTIVES

- To evaluate the impact of continuation therapy on quizartinib efficacy in patients with newly diagnosed *FLT3*-ITD–positive AML treated in the QuANTUM-First study, by analyzing OS, RFS (prespecified exploratory analyses), and CIR in patients who entered continuation

AML, acute myeloid leukemia; CIR, cumulative incidence of relapse; EU, European Union; *FLT3*-ITD, FMS-like tyrosine kinase 3–internal tandem duplication; HR, hazard ratio; OS, overall survival; RFS, relapse-free survival; UK, United Kingdom; US, United States. 1. Erba HP, et al. *Lancet*. 2023;401(10388):1571-1583. 2. VANFLYTA® (quizartinib). Package insert. Daiichi Sankyo, Inc.; July 2023. 3. VANFLYTA® (quizartinib). Summary of product characteristics. Daiichi Sankyo Europe GmbH; November 2023. 4. VANFLYTA® (quizartinib). Summary of product characteristics. Daiichi Sankyo UK Ltd; March 2024. 5. VANFLYTA® first FLT3 inhibitor approved in Japan for patients with newly diagnosed *FLT3*-ITD positive AML. Press release. May 25, 2023. Accessed May 1, 2024. https://www.daiichisankyo.com/files/news/pressrelease/pdf/202305/20230525_E.pdf.

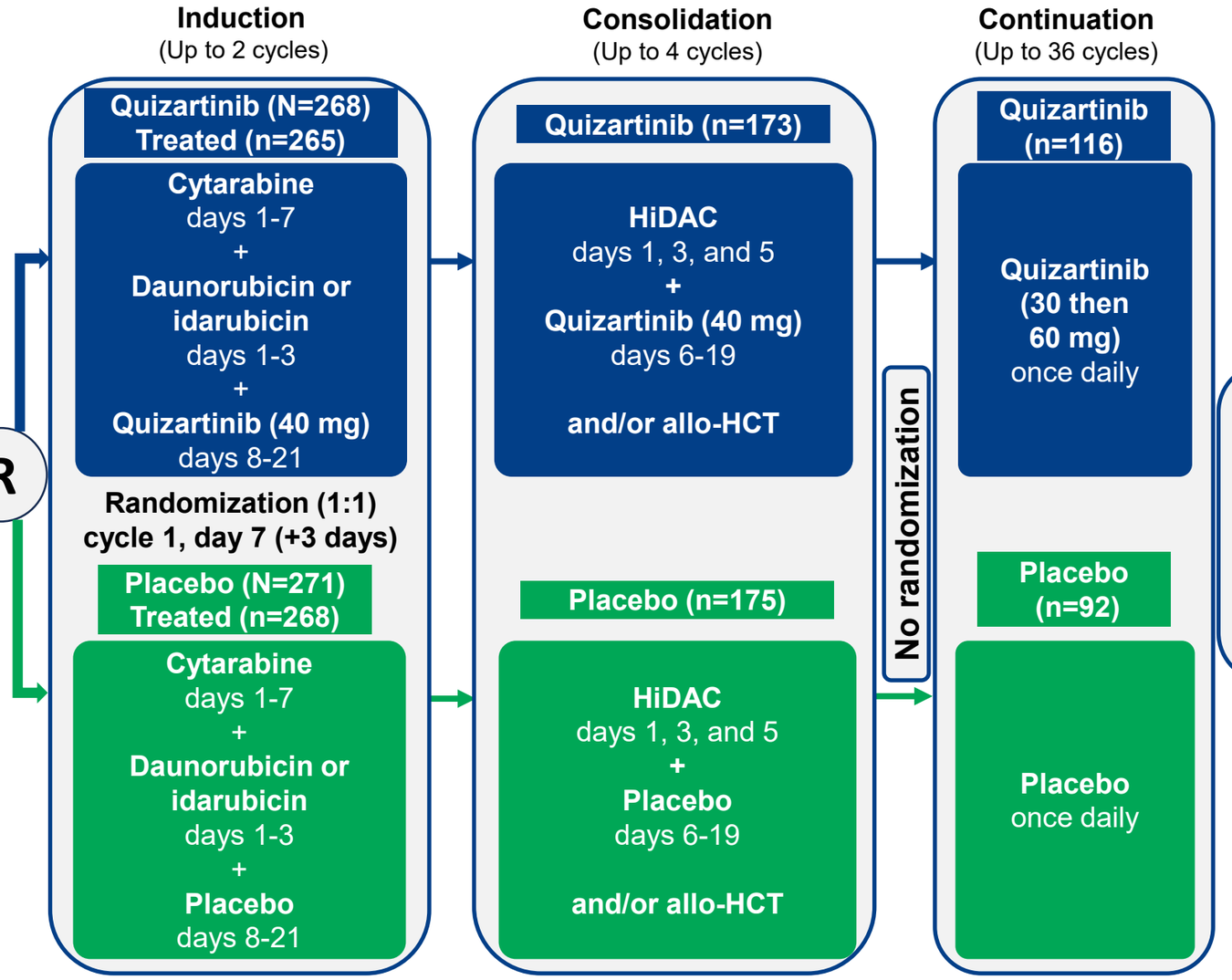
QuANTUM-First Phase 3 Study: Quizartinib Plus Standard Induction Chemotherapy and Consolidation Followed by Single-Agent Quizartinib[1]

Stratification Factors
- **Region:** NA, EU, and Asia/other regions
- **Patient age:** <60 years, ≥60 years
- **WBC[a]:** <40×10^9/L, ≥40×10^9/L

- Newly diagnosed *FLT3*-ITD–positive AML
- 18-75 years of age
- ≥3% *FLT3*-ITD allelic frequency
- Patients begin 7+3 chemotherapy during screening

Screened (N=3468)
Randomized 1:1 (N=539)

Key Endpoints[a]
- **Primary endpoint**: OS
- **Secondary endpoints**: EFS, CR, CRc, CR/CRc with MRD negativity by end of induction, safety
- **Exploratory endpoints**: RFS, DOCR, CIR[b], OS in continuation, and RFS in continuation



[a]A hierarchical testing procedure was used to test the primary endpoint of OS, followed by EFS, CR, CRc, CR with *FLT3*-ITD MRD negativity, and CRc with *FLT3*-ITD MRD negativity. [b]CIR was assessed post hoc.
AML, acute myeloid leukemia; allo-HCT, allogeneic hematopoietic cell transplantation; CR, complete remission; CRc, composite complete remission; DOCR, duration of complete remission; EFS, event-free survival; EU, Europe; *FLT3*-ITD, FMS-like tyrosine kinase 3–internal tandem duplication; HiDAC, high-dose cytarabine; MRD, measurable residual disease; NA, North America; R, randomization; OS, overall survival; RFS, relapse-free survival; WBC, white blood cell. 1. Erba HP, et al. *Lancet*. 2023;401(10388):1571-1583. NCT02668653.

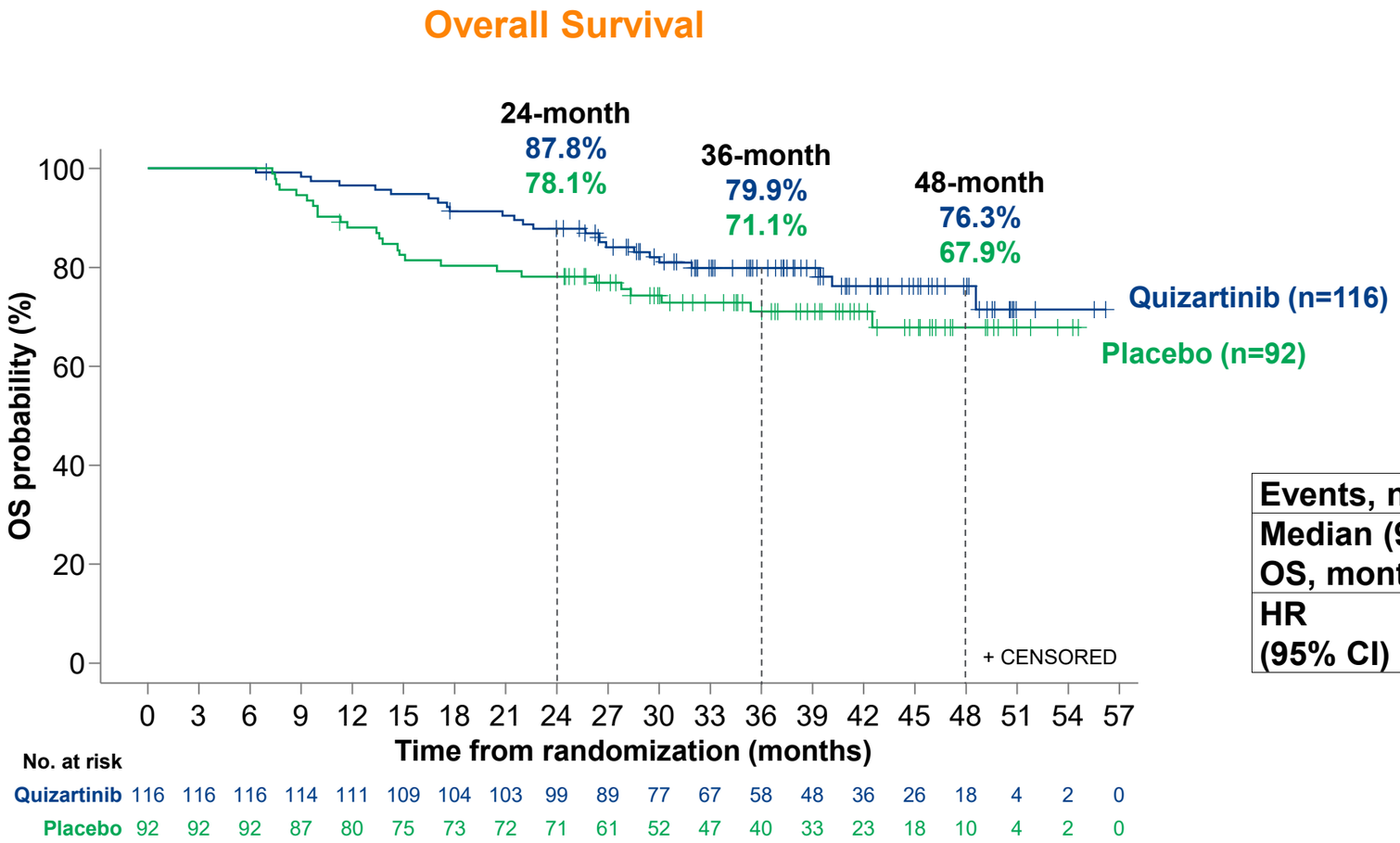
Demographics and Disease Characteristics in Patients Who Received Continuation Therapy by Treatment Arm

Baseline characteristics	Patients who received continuation therapy		ITT population	
	Quizartinib (n=116)	Placebo (n=92)	Quizartinib (n=268)	Placebo (n=271)
Age				
Median (range), years	53 (23-73)	56.5 (20-74)	56 (23-75)	56 (20-75)
<60 years, %	66.4	54.3	60.1	59.8
≥60 years, %	33.6	45.7	39.9	40.2
Sex, %				
Male	45.7	41.3	46.3	44.6
Female	54.3	58.7	53.7	55.4
ECOG PS, %				
0	36.2	38.0	32.5	36.2
1	49.1	54.3	50.0	50.2
2	14.7	7.6	17.5	13.3
Missing	0	0	0	0.4
Cytogenetic risk status, %				
Favorable	4.3	10.9	5.2	7.0
Intermediate	72.4	65.2	73.5	71.2
Unfavorable	6.9	9.8	7.1	10.0
Unknown/Missing	16.4	14.1	14.2	11.8
Mutated *NPM1*,[b] %	59.5	65.2	53.0	51.7
Mutated *CEBPA*,[b] %	25.0	27.2	22.8	24.0
***FLT3*-ITD/total *FLT3* (VAF), %**				
≥3 to ≤25%	37.9	45.7	35.1	36.2
>25% to ≤50%	50.9	45.7	53.4	50.9
>50%	10.3	8.7	11.2	12.9
>25%	61.2	54.3	64.6	63.8
Unknown	0.9	0	0.4	0
WBC count at AML diagnosis, %				
$<40\times10^9$/L	49.1	63.0	50.4	50.6
$\geq40\times10^9$/L	50.9	37.0	49.6	49.4
***FLT3*-ITD MRD negativity ($<10^{-4}$ leukemia cells) in induction, n/n (%)**	NA	NA	78/162 (48.1)	61/159 (38.4)

AML, acute myeloid leukemia; C, cycle; *CEBPA*, CCAAT enhancer-binding protein alpha; D, day; ECOG PS, ECOG PS, Eastern Cooperative Oncology Group performance status; *FLT3*-ITD, FMS-like tyrosine kinase 3–internal tandem duplication; ITT, intent-to-treat; MRD, measurable residual disease; NA, not applicable; *NPM1*, nucleophosmin 1; VAF, variant allele frequency; WBC, white blood cell.

OS in Patients Who Received Continuation Therapy

Quizartinib Provided a Numerical OS Benefit Over Placebo in Patients Who Received Continuation Therapy



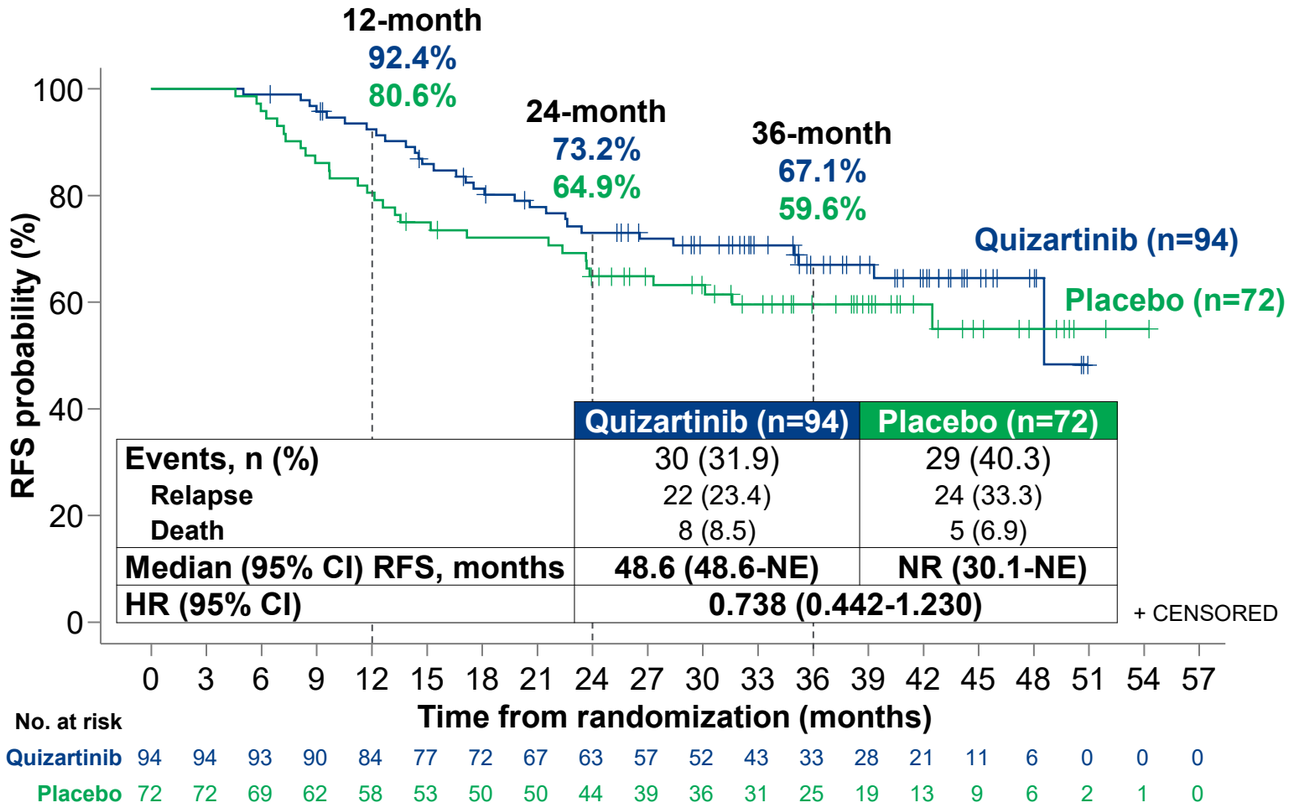
	Quizartinib (n=116)	Placebo (n=92)
Events, n (%)	25 (21.6)	26 (28.3)
Median (95% CI) OS, months	**NR (NE-NE)**	**NR (NE-NE)**
HR (95% CI)	**0.683 (0.395-1.183)**	

CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached; OS, overall survival.

RFS and CIR in Patients Who Achieved CR in Induction by IRC and Received Continuation Therapy

Numerically Higher RFS Rates Were Observed in the Quizartinib Arm Versus the Placebo Arm

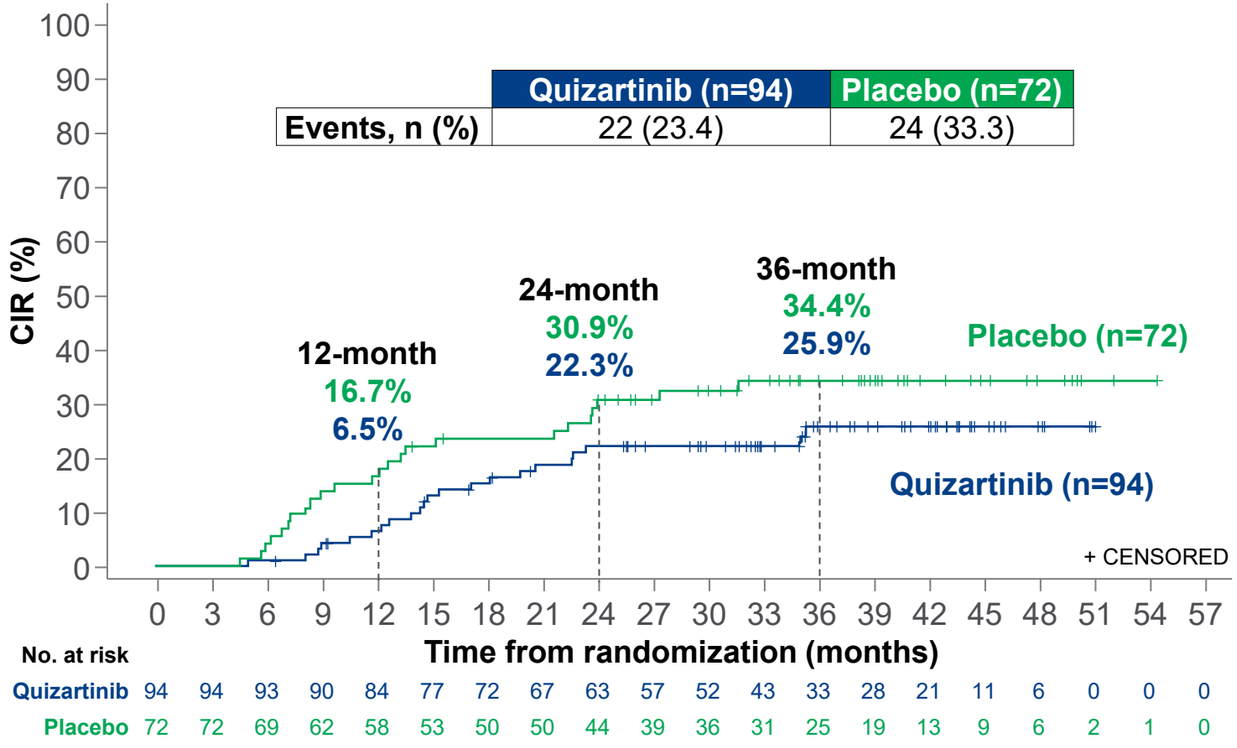
Relapse-Free Survival



	Quizartinib (n=94)	Placebo (n=72)
Events, n (%)	30 (31.9)	29 (40.3)
Relapse	22 (23.4)	24 (33.3)
Death	8 (8.5)	5 (6.9)
Median (95% CI) RFS, months	48.6 (48.6-NE)	NR (30.1-NE)
HR (95% CI)	0.738 (0.442-1.230)	

CIR Decreased at 12, 24, and 36 Months in the Quizartinib Arm Versus the Placebo Arm

Cumulative Incidence of Relapse



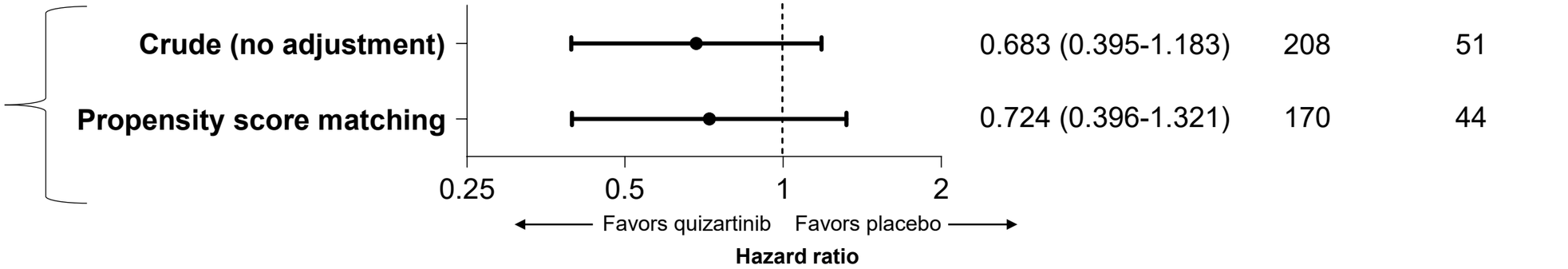
	Quizartinib (n=94)	Placebo (n=72)
Events, n (%)	22 (23.4)	24 (33.3)

CI, confidence interval; CIR, cumulative incidence of relapse; CR, complete remission; HR, hazard ratio; IRC, independent review committee; NE, not estimable; NR, not reached; RFS, relapse-free survival.

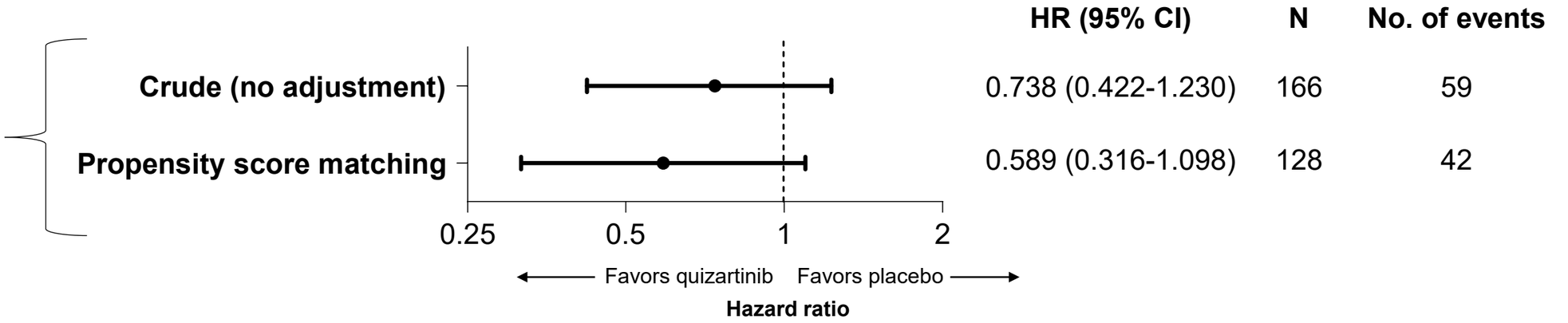
Propensity Score-Based Analyses of OS and RFS in Patients Who Received Continuation Therapy

- Propensity score-based analysis of OS and RFS favored quizartinib over placebo
- These analyses were conducted considering baseline covariates (age, sex, WBC count at AML diagnosis, *NPM1* mutational status, percent of bone marrow blasts), and also allo-HCT before continuation and type of anthracycline

Propensity score–based analyses of OS

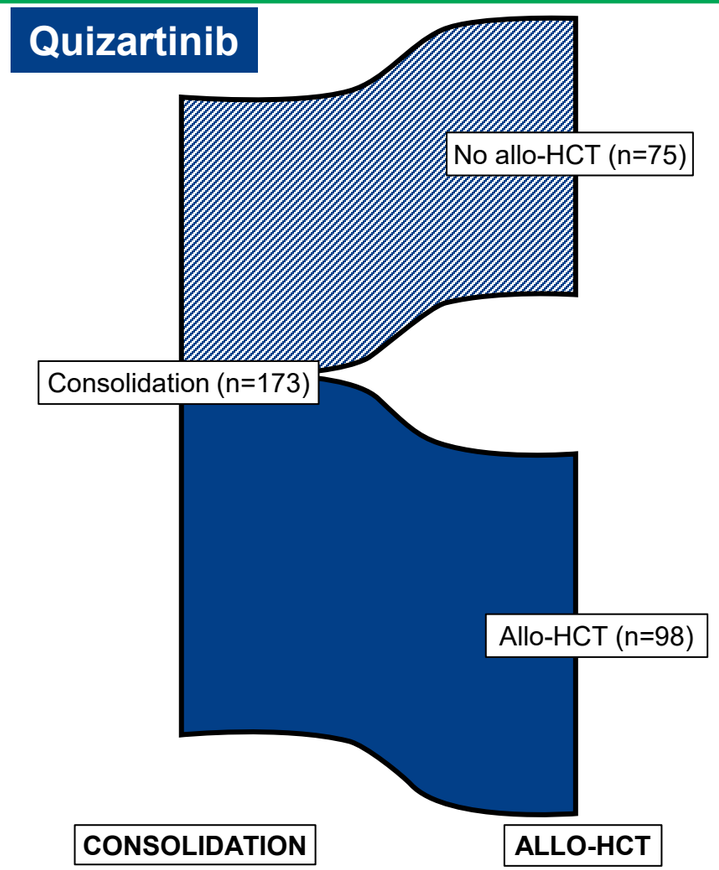


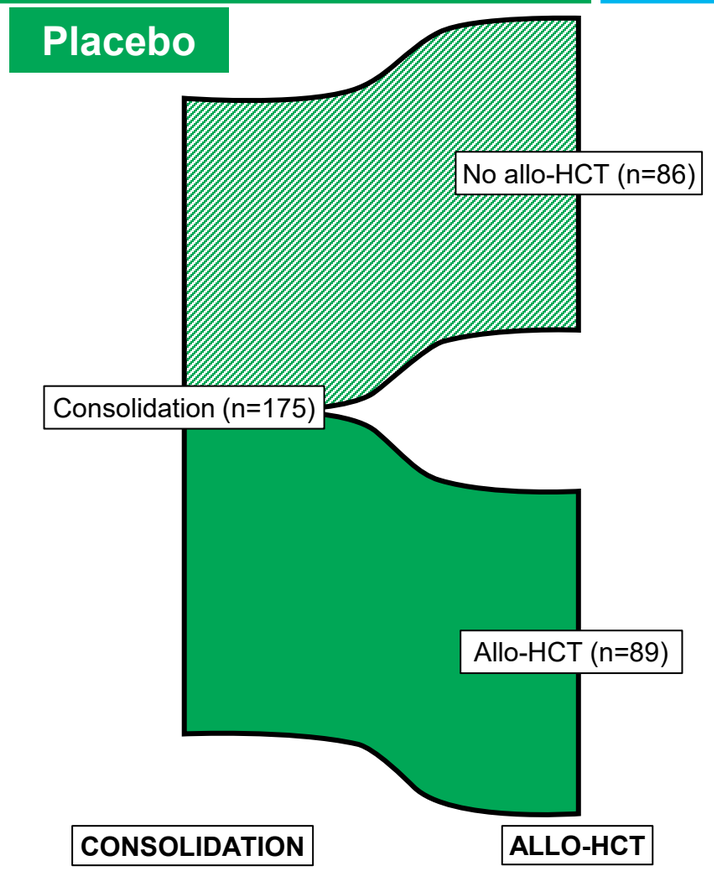
Propensity score–based analyses of RFS in patients who achieved CR in induction by IRC



Allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; CR, complete remission; HR, hazard ratio; IRC, independent review committee; *NPM1*, nucleophosmin 1; OS, overall survival; RFS, relapse-free survival; WBC, white blood cell.

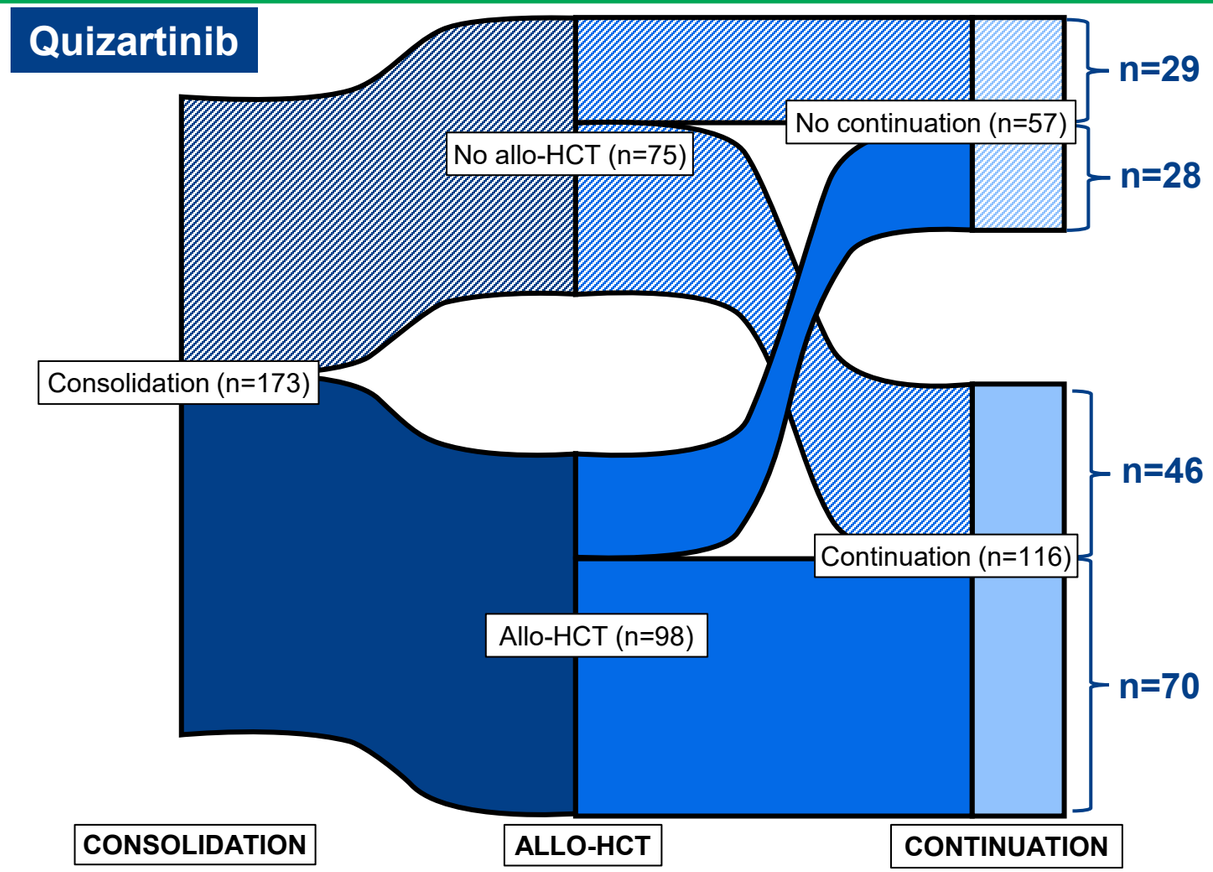
Patients Who Received Continuation Therapy by Allo-HCT and by Treatment Arm

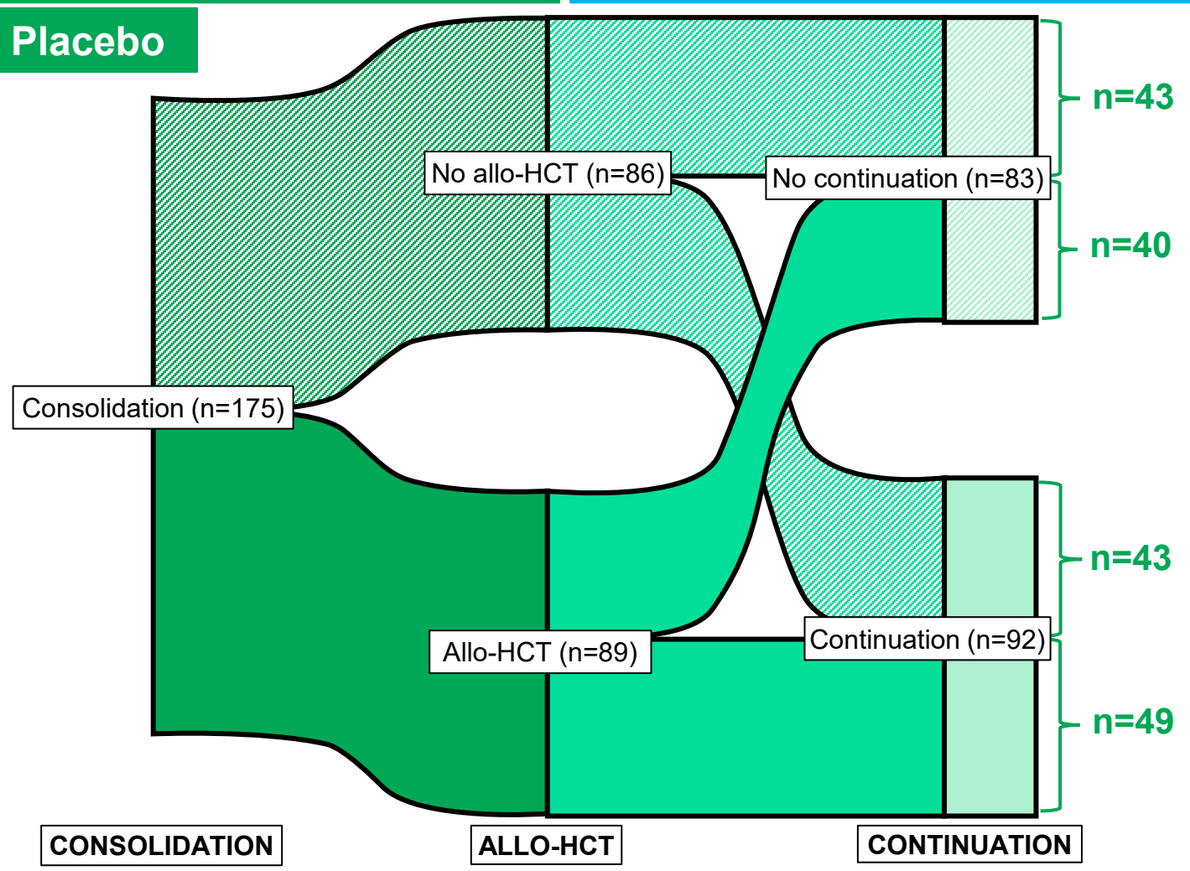




The thickness of each flow path is proportional to the number of patients. Allo-HCT, allogeneic hematopoietic cell transplantation.

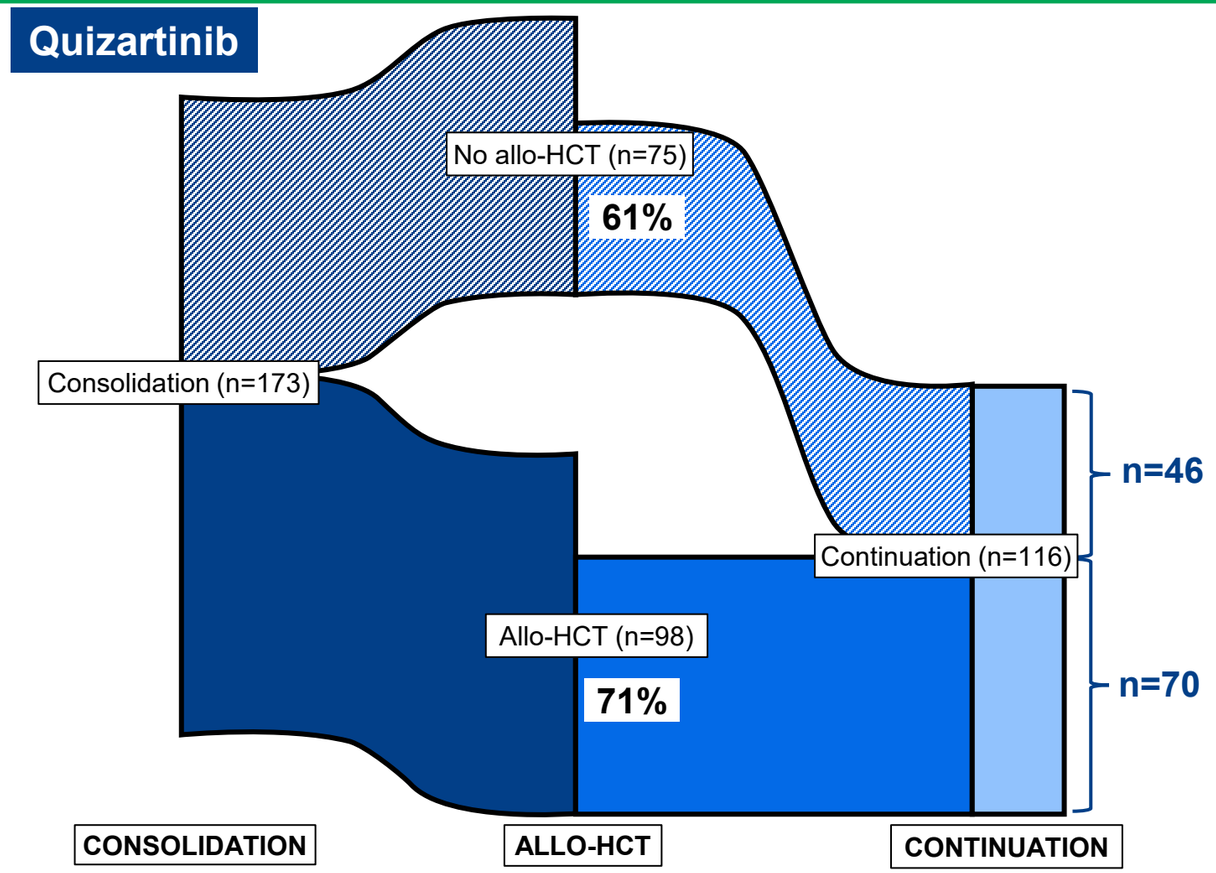
Patients Who Received Continuation Therapy by Allo-HCT and by Treatment Arm

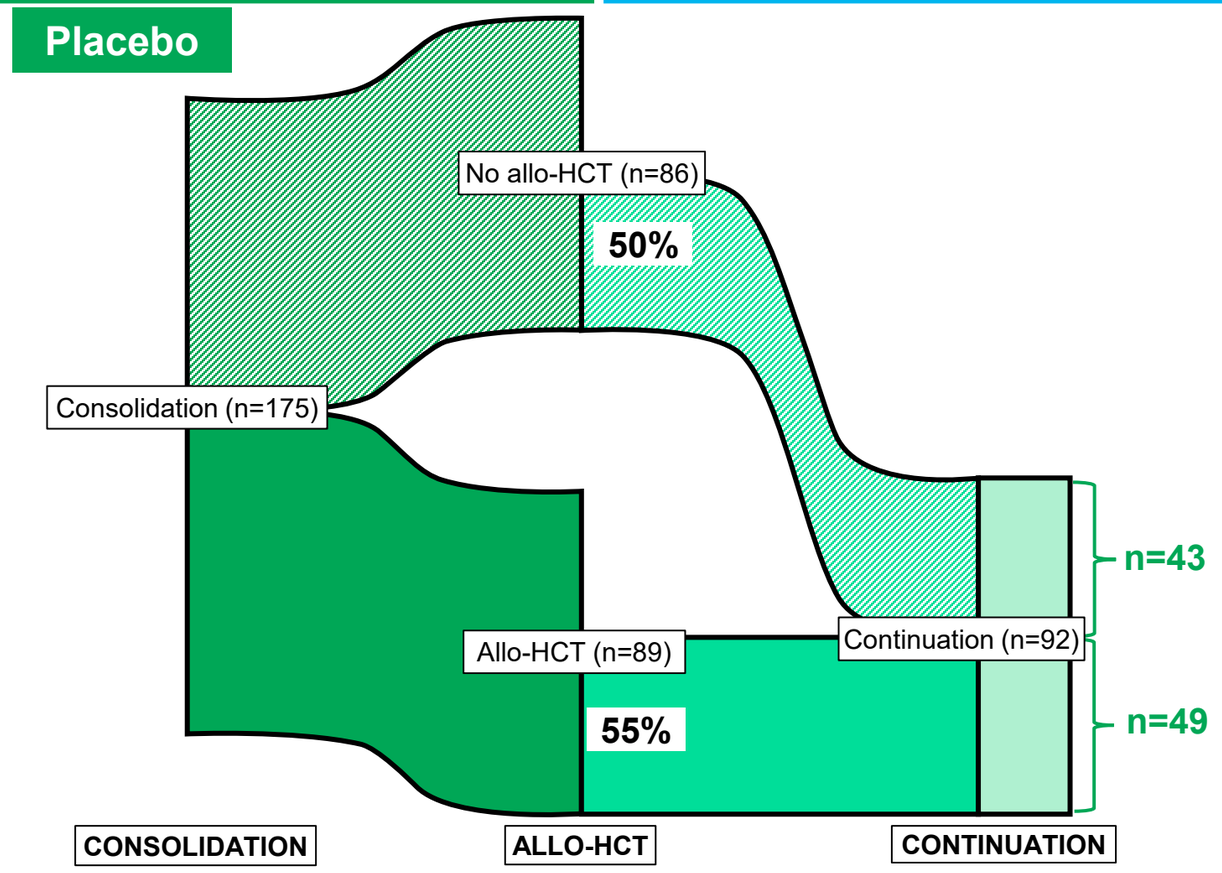




The thickness of each flow path is proportional to the number of patients. Allo-HCT, allogeneic hematopoietic cell transplantation.

Patients Who Received Continuation Therapy by Allo-HCT and by Treatment Arm

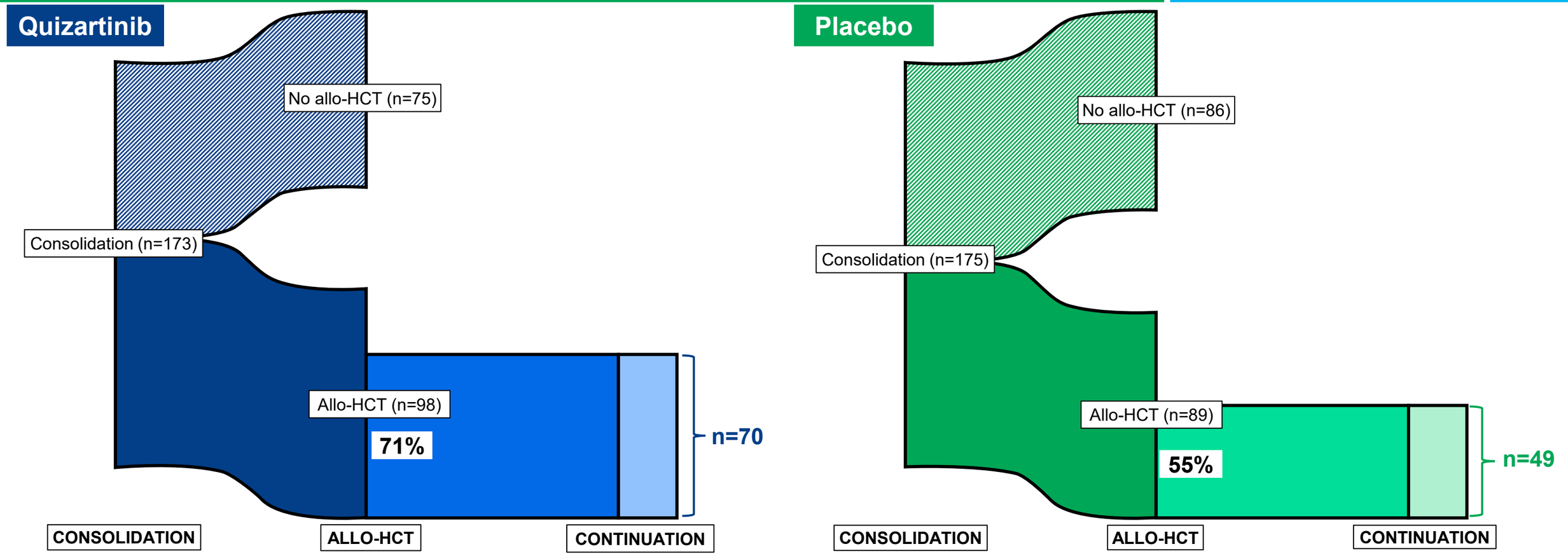




- Of the patients who had allo-HCT in consolidation, 71% (70/98) of those in the quizartinib arm versus 55% (49/89) in the placebo arm proceeded to continuation
- More transplanted patients in the placebo arm could not proceed to continuation because of relapse or failure to meet continuation criteria

The thickness of each flow path is proportional to the number of patients. Allo-HCT, allogeneic hematopoietic cell transplantation.

Patients Who Received Continuation Therapy by Allo-HCT and by Treatment Arm

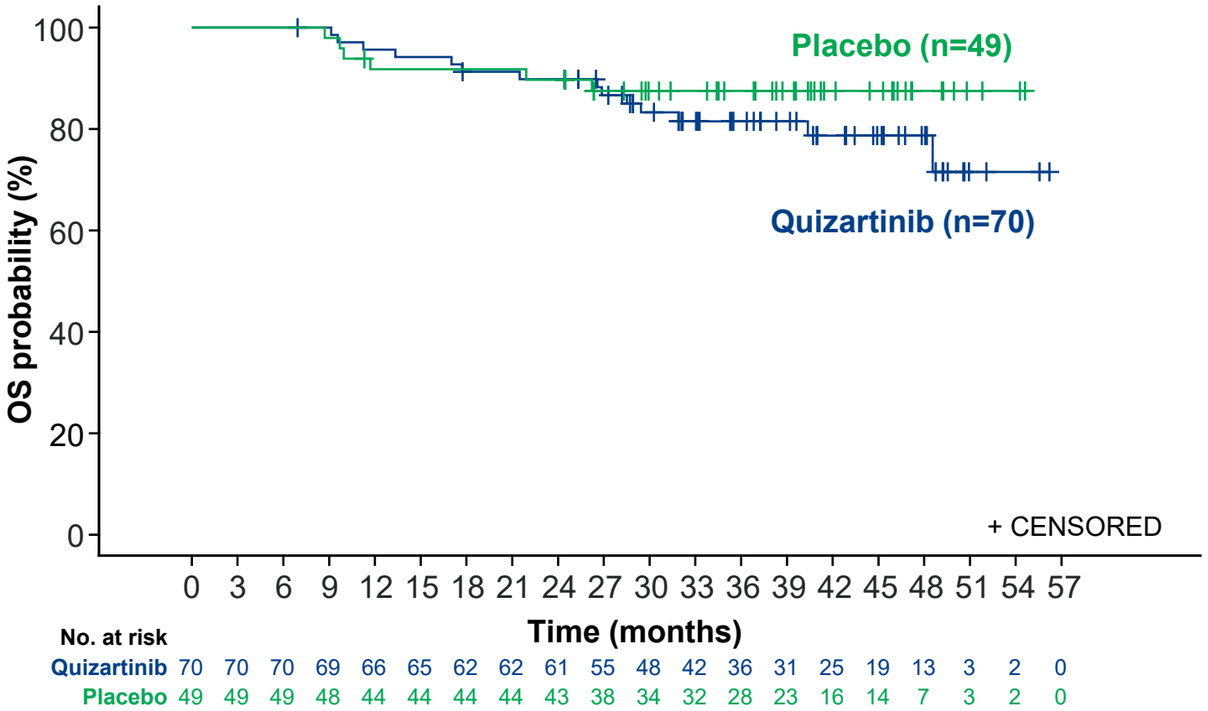


- Of the patients who had allo-HCT in consolidation, 71% (70/98) of those in the quizartinib arm versus 55% (49/89) in the placebo arm proceeded to continuation
- More transplanted patients in the placebo arm could not proceed to continuation because of relapse or failure to meet continuation criteria

The thickness of each flow path is proportional to the number of patients. Allo-HCT, allogeneic hematopoietic cell transplantation.

OS in Patients Who Had Prior Allo-HCT and Received Continuation Therapy

OS in Patients Who Received Continuation Therapy With Allo-HCT[a]

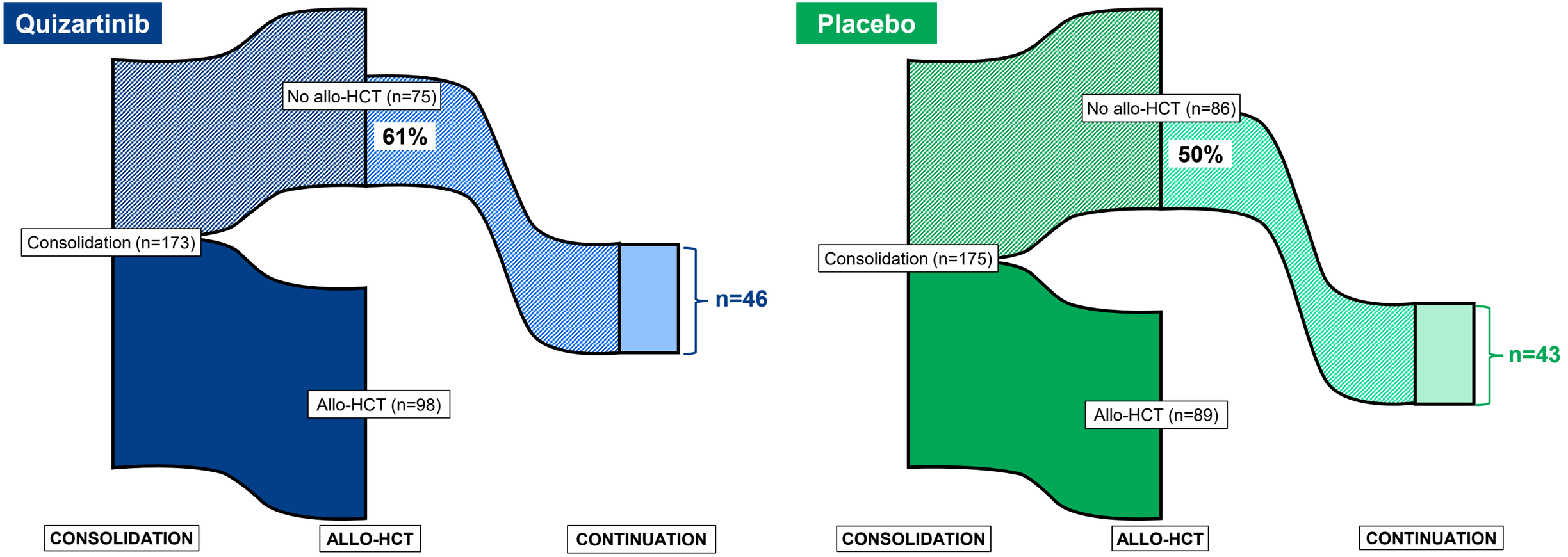


- More patients on quizartinib who received allo-HCT in consolidation were able to reach continuation, explaining the imbalance in the number of patients in the quizartinib arm versus the placebo arm (70 vs 49)
- The total number of OS events was 20
- The median follow-up was 39.2 months

	Quizartinib (n=70)	Placebo (n=49)
Median OS, months	**NR**	**NR**
HR (95% CI)	**1.622 (0.623-4.220)**	

[a]Includes protocol-specified allo-HCT. Allo-HCT, allogeneic hematopoietic cell transplantation; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.

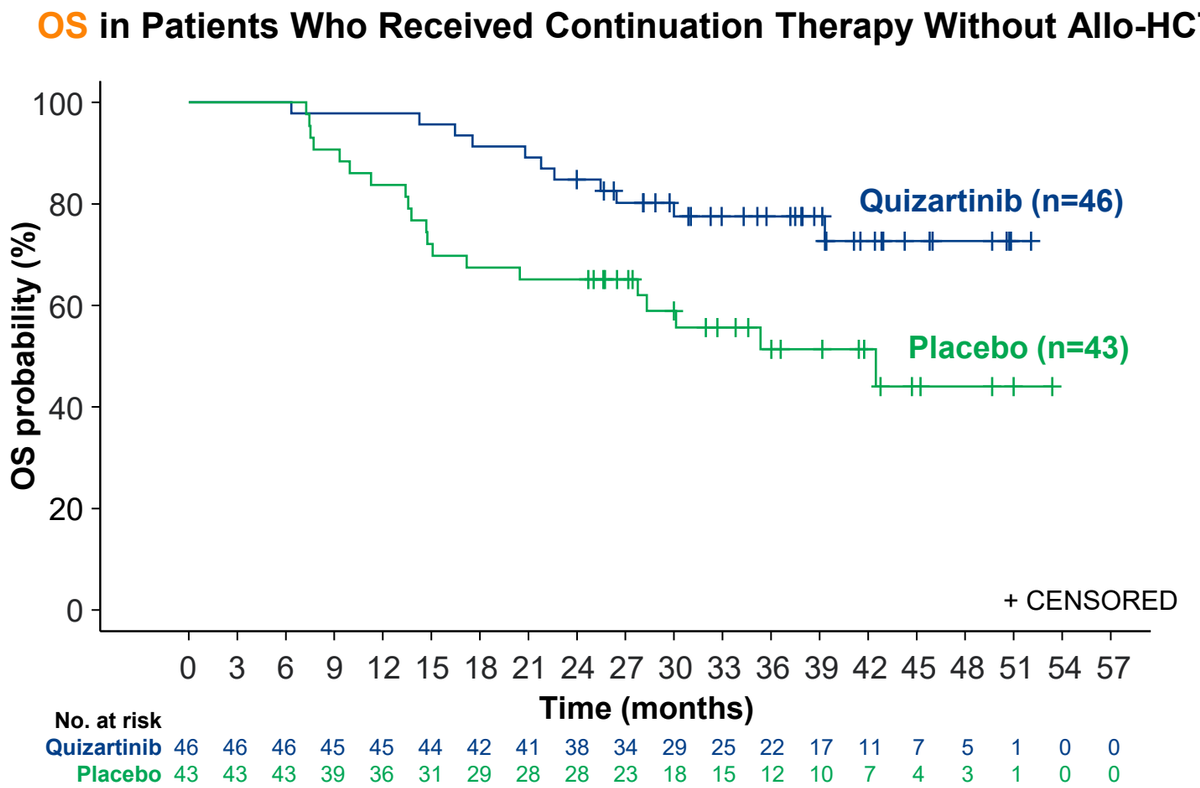
Patients Who Received Continuation Therapy by Allo-HCT and by Treatment Arm



- Of the patients who did not undergo allo-HCT before consolidation, a similar proportion of patients proceeded to continuation in either arms

The thickness of each flow path is proportional to the number of patients. Allo-HCT, allogeneic hematopoietic cell transplantation.

OS in Patients Who Received Continuation Therapy Without Allo-HCT



- Similar number of patients without allo-HCT in both groups were able to reach continuation
- An OS benefit was observed with quizartinib over placebo with a 60% reduction in the risk of death

	Quizartinib (n=46)	Placebo (n=43)
Median OS, months	**NR**	**42.5**
HR (95% CI)	**0.401 (0.192-0.838)**	

Allo-HCT, allogeneic hematopoietic cell transplantation; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.

Exposure and Summary of Overall Safety During Continuation Therapy

EXPOSURE

- Median (range) number of cycles:
  - 16 (1-36) in the quizartinib arm
  - 17 (1-36) in the placebo arm
- Median (range) adjusted treatment durations:
  - 67.36 weeks (0.4-164.1) in the quizartinib arm
  - 67.71 weeks (0.3-150.4) in the placebo arm
- A total of 64.4% of patients who received continuation therapy had ≥12 cycles:
  - 75/116 (64.7%) patients in the quizartinib arm
  - 59/92 (64.1%) patients in the placebo arm

- During continuation, rates of grade ≥3 TEAEs, TRAEs, and AEs leading to dose interruptions/reductions were more common with quizartinib compared with placebo

	Quizartinib (n=116)	Placebo (n=92)
AEs, n (%)		
Any TEAEs	109 (94.0)	84 (91.3)
Any TRAEs	85 (73.3)	34 (37.0)
Grade ≥3 TEAEs (including grade 5)	91 (78.4)	53 (57.6)
Grade ≥3 TRAEs (including grade 5)	62 (53.4)	16 (17.4)
Serious TEAEs	39 (33.6)	34 (37.0)
TRSAEs	8 (6.9)	5 (5.4)
AEs associated with fatal outcome	3 (2.6)	7 (7.6)
TRAEs associated with fatal outcome	0	0
Dose modifications, n (%)		
TEAEs associated with discontinuation	18 (15.5)	7 (7.6)
TRAEs associated with discontinuation	12 (10.3)	3 (3.3)
TEAEs associated with dose interruption	65 (56.0)	22 (23.9)
TRAEs associated with dose interruption	46 (39.7)	11 (12.0)
TEAEs associated with dose reduction	42 (36.2)	14 (15.2)
TRAEs associated with dose reduction	32 (27.6)	8 (8.7)

AE, adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; TRSAE, treatment-related serious adverse event.

TEAEs Occurring in ≥15% of Patients During Continuation Therapy

- The most common (≥15%) TEAEs of all grades during continuation were:
  - Neutropenia (36%), nausea (23%), and diarrhea (21%) in the quizartinib arm
  - Pyrexia (17%) and arthralgia (17%) in the placebo arm

TEAEs, %	Quizartinib (n=116)		Placebo (n=92)	
	All grade[a]	Grade ≥3	All grade[a]	Grade ≥3
Any TEAEs	**109 (94.0)**	**91 (78.4)**	**84 (91.3)**	**53 (57.6)**
Neutropenia	42 (36.2)	36 (31.0)	6 (6.5)	4 (4.3)
Nausea	27 (23.3)	2 (1.7)	8 (8.7)	1 (1.1)
Diarrhea	24 (20.7)	3 (2.6)	10 (10.9)	1 (1.1)
Thrombocytopenia	20 (17.2)	10 (8.6)	8 (8.7)	4 (4.3)
Upper respiratory tract infection	20 (17.2)	1 (0.9)	9 (9.8)	0
Anemia	19 (16.4)	6 (5.2)	4 (4.3)	2 (2.2)
Cough	19 (16.4)	1 (0.9)	11 (12.0)	0
Neutrophil count decreased	17 (14.7)	14 (12.1)	4 (4.3)	0
Vomiting	17 (14.7)	0	7 (7.6)	0
Pyrexia	16 (13.8)	0	16 (17.4)	2 (2.2)
Arthralgia	13 (11.2)	0	16 (17.4)	0

[a]The 15% threshold is based on all-grade TEAEs. TEAE, treatment-emergent adverse event.

Conclusions

- Quizartinib is part of a treatment regimen that includes induction, consolidation, and continuation; for the entire study population, in patients who received continuation, a numerical longer OS, higher RFS rates, and lower CIR rates were observed among those treated with quizartinib
- More patients in the quizartinib arm could proceed to continuation compared with placebo, especially in those who underwent transplantation
  - Among the transplanted patients, the K-M OS curves for quizartinib and placebo overlapped; a wide confidence interval and a limited number of OS events precluded a meaningful assessment of efficacy
  - Among the patients who received continuation but did not undergo transplantation, quizartinib provided an OS benefit over placebo
- This exploratory analysis in patients who received continuation together with the positive benefit-risk profile in the ITT population support the use of quizartinib in patients with newly diagnosed *FLT3*-ITD–positive AML, across the whole treatment regimen
- Future analysis of measurable residual disease may help identifying which patients would benefit the most from continuation therapy

Allo-HCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; CIR, cumulative incidence of relapse; *FLT3*-ITD, FMS-like tyrosine kinase 3–internal tandem duplication; ITT, intent-to-treat; K-M, Kaplan-Meier; OS, overall survival; RFS, relapse-free survival.

Acknowledgments

We would like to thank the patients, their families, and caregivers for their participation in the QuANTUM-First study. We would further like to thank the QuANTUM-First steering committee members, the investigators, the study staff, and independent review committee and data monitoring committee members for their important contributions.

This study is sponsored by Daiichi Sankyo, Inc.

Medical writing support was provided by, Mohamed Abdelmegeed, MD, PhD, CMPP, and Francesca Balordi, PhD, CMPP, of The Lockwood Group (Stamford, CT, USA), in accordance with Good Publication Practice (GPP 2022) guidelines, with funding by Daiichi Sankyo, Inc.

QuANTUM-First Investigators

Australia
- Paul Cannell
- Anoop Enjeti
- Georgina Hodges
- Paula Marlton

Belgium
- Carlos Graux
- Ine Moors
- Dominik Selleslag

Brazil
- Jordana Ramires Aragao
- Jaisson Bortolini
- Denise Ramos De Almeida
- Fernando Duarte
- Carlos Eugenio Santiago Escovar
- Laura Fogliatto
- Ederson Mattos
- Vanderson Rocha

Bulgaria
- Vasko Graklanov
- Nikolay Tzvetkov

Canada
- Joseph Brandwein
- Michelle Geddes
- Donna Hogge
- Mark Minden

China
- Xin Du
- Sujun Gao
- Jianda Hu
- Jian Li

China (cont)
- Junmin Li
- Li Liu
- Hanyun Ren
- Jianxiang Wang*
- Yu Wu
- Kang Yu
- Li Yu
- Liansheng Zhang
- Xinghu Zhu

Croatia
- Vlatko Pejsa
- Radovan Vrhovac

Czechia
- Roman Hajek
- Pavel Jindra
- Tomas Szotkowski
- Jan Vydra
- Pavel Zak

France
- Hervé Dombret*
- Olliver Legrand
- Emilie Lemasle
- Arnaud Pigneux
- Bruno Quesnel
- Christian Recher
- Philippe Rousselot
- Xavier Thomas

Germany
- Alwin Krämer
- Juergen Krauter
- Richard F. Schlenk*
- Kathrin Rieger
- Sebastian Schwind
- Felicitas Thol
- Maxi Wass

Hungary
- Zita Borbenyi
- Judit Demeter
- Arpad Illes
- Janos Laszlo Ivanyi
- Agnes Nagy

Israel
- Maya Koren-Michowitz
- David Lavie
- Yishai Ofran
- Ron Ram
- Ofir Wolach

Italy
- Sergio Amadori*
- Ernesta Audisio
- Germana Beltrami
- Monica Bocchia
- Alberto Bosi
- Roberto Cairoli
- Fabio Ciceri
- Alessandro Cignetti
- Daniela Cilloni
- Matteo Giovanni Della Porta
- Lorella Depaoli
- Felicetto Ferrara
- Piero Galieni
- Francesco Lanza
- Monia Lunghi
- Antonino Mule
- Fabrizio Pane
- Stefania Paolini
- Francesco Passamonti
- Mario Petrini
- Simona Sica
- Adriano Venditti
- Patrizia Zappasodi

Japan
- Naohito Fujishima
- Hiroshi Handa
- Takayuki Ishikawa
- Yuna Katsuoka
- Toru Kiguchi
- Hitoshi Kiyoi
- Shingo Kurahashi
- Kosei Matsue
- Toshihiro Miyamoto
- Yuho Najima
- Hideaki Nakajima
- Hitoshi Ohno
- Satoru Takada
- Takahiro Yamauchi
- Akira Yokota

Korea
- Sung-Hwa Bae
- Chul-Won Choi
- Yunsuk Choi
- Seong Hyun Jeong
- Chul-Won Jung
- Hee-Je Kim
- Hyeoung-Joon Kim
- Il-Hwan Kim
- MinKyoung Kim
- Jeong-Ok Lee
- Kyoo-Hyung Lee
- Yoo Hong Min
- Jinny Park
- Ho-Jin Shin
- Sang Kyun Sohn
- Jong Ho Won
- Sung-Soo Yoon

Poland
- Wojciech Homenda
- Elżbieta Patkowska*
- Aleksander Skotnicki
- Tomasz Wrobel

Portugal
- Ana Crisóstomo
- Aida Botelho de Sousa
- Angelo Martins
- Ricardo Pinto

Romania
- Gabriela Borsaru
- Horia Bumbea
- Catalin-Doru Danaila
- Delia-Monica Dima
- Viola-Maria Popov

Russia
- Tatiana Chagorova
- Alexandr Myasnikov
- Alexander Pristupa
- Olga Samoilova
- Tatiana Shelekhova
- Olga Uspenskaya

Singapore
- Liang Piu Koh
- Zhentang Lao

Serbia
- Lana Macukanovic-Golubovic
- Aleksandar Savic
- Dragana Stamatovic
- Ana Vidovic

Spain
- Antonio Romero-Aguilar
- Jesús Lorenzo Algarra
- María-Luz Amigo
- Maria Angeles Ardaiz
- Montserrat Arnan
- Lissette Costilla Barriga
- Guiomar Bautista
- Teresa Bernal
- Juan Miguel Bergua Burgués
- Marta Cervera
- Carmen Martinez Chamorro
- Maria de las Mercedes Colorado
- Victor Noriega Concepcion
- Cristina Gil Cortes
- Manuel Pérez Encinas
- Juan Ignacio Rodriguez Gutierrez
- Pilar Herrera
- José Luis Lopez Lorenzo
- Maria del Pilar Martinez-Sanchez
- Antonia Sampol Mayol
- Pau Montesinos*
- Maite Olave
- Marta Polo
- Gabriela Rodriguez-Macias
- Olga Salamero
- Josefina Serrano
- José Antonio Perez Simón
- Mar Tormo
- Maria-Belen Vidriales
- Susana Vives-Polo

Taiwan
- Tsai-Yun Chen
- Jyh-Pyng Gau
- Bor-Sheng Ko
- Ming-Chun Ma
- Po-Nan Wang
- Su-Peng Yeh

Ukraine
- Galyna Pylypenko
- Igor Skrypnyk

United Kingdom
- Evangelia Dimitriadou

United States
- Michael Craig
- Brenda Cooper
- Jorge Cortes*
- Carlos de Castro
- Harry Paul Erba*
- Gerhard Hildebrandt
- Jack Hsu
- Margaret Kasner
- Jamie Koprivnikar
- Richard Larson
- Mark James Levis*
- Alexander Edward Perl*
- Mikkael A. Sekeres*
- Anand Tandra

*Investigator members of steering committee.