Impact of hematopoietic cell transplantation and quizartinib in newly diagnosed patients with acute myeloid leukemia and FMS-like tyrosine kinase 3-internal tandem duplications in the QuANTUM-First trial

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ONLINE SUPPLEMENTARY DATA

Supplementary methods

Patients

Patients aged 18–75 years with morphologically documented primary newly diagnosed AML, or AML secondary to myelodysplastic syndrome or a myeloproliferative neoplasm, with an *FLT3*-ITD identified by central laboratory assessment in bone marrow or peripheral blood at screening and able to receive standard induction chemotherapy were eligible. Patients diagnosed with acute promyelocytic leukemia with t(15;17), *BCR-ABL1*–positive leukemia, or AML secondary to previous chemotherapy or radiotherapy were excluded.[1] The analyses presented in this report focus on patients treated with quizartinib or placebo in the QuANTUM-First trial who achieved CR or CRc by the end of induction per independent review committee assessment, and those who underwent allo-HCT in CR1/CRc1.[1] Patients provided written informed consent before enrollment.[1]

Randomization and masking

Patients were randomly assigned (1:1) to the quizartinib group or the placebo group. Randomization was stratified by region (Europe; North America; or Asia, Australia, and South America), age (<60 years and ≥60 years), and white blood cell count at diagnosis (<40×10^9/L and ≥40×10^9/L). Randomization was managed by an independent biostatistician through an interactive web and voice response system using a stratified permuted block procedure. The investigators enrolled patients, were fully responsible for the management of patients during the trial, and were responsible for the data. Patients, investigators, funders, and contract research organizations were masked to treatments assigned. Masking was achieved as placebo tablets matched the appearance of the quizartinib tablets. The success of blinding was not assessed. In an emergency, unmasking information was restricted to designated study center staff or personnel providing immediate care to the patient.

Safety analyses

Analysis of the frequency and severity of adverse events (AE) was conducted on the safety analysis population (i.e., patients who received at least one dose of quizartinib or placebo). Grading and management of AEs (including GVHD) was as per investigator. Only descriptive analysis was performed on safety, including acute and chronic GVHD, with no statistical analysis.

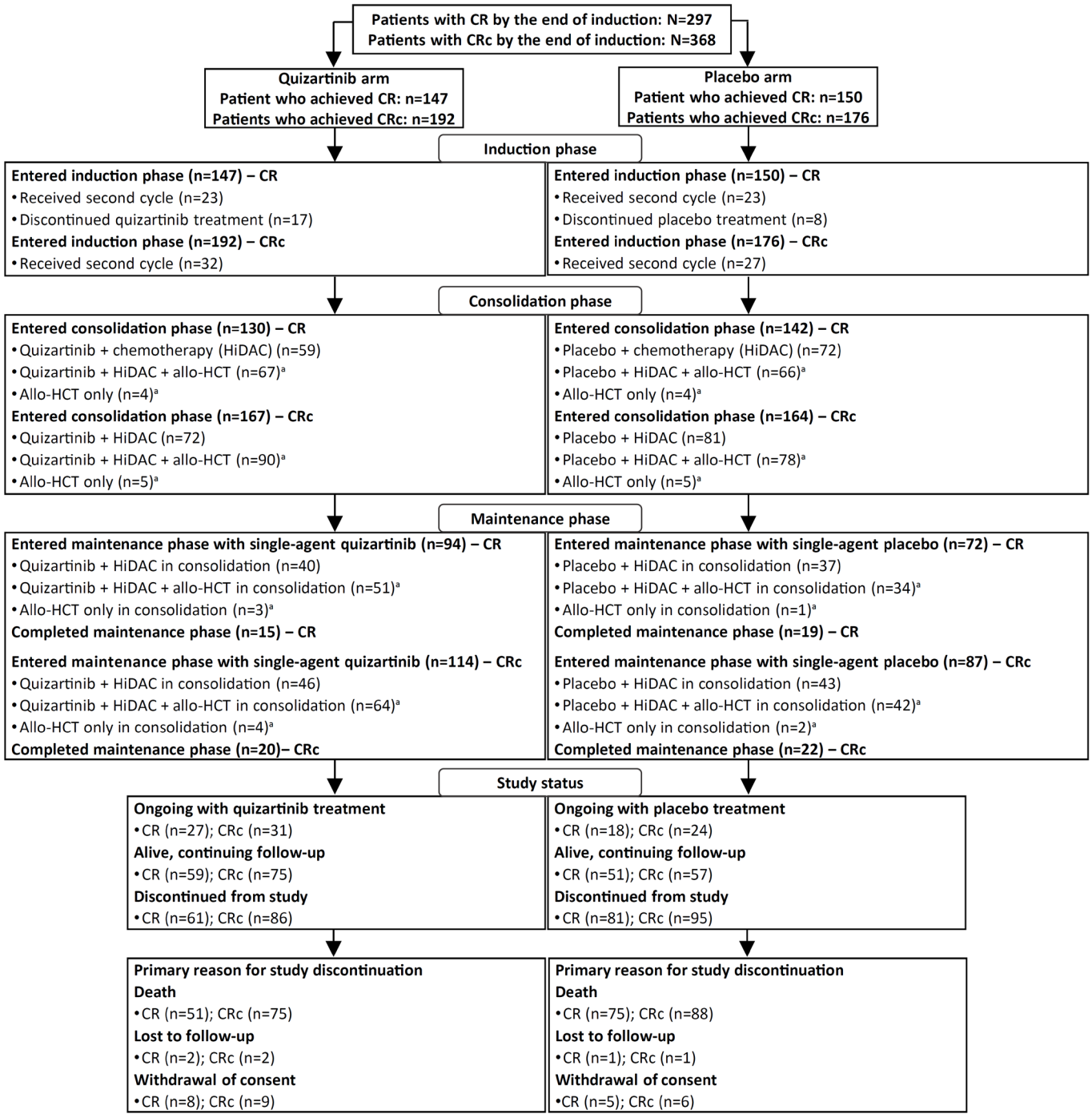
Role of the funding source

Daiichi Sankyo and the study steering committee designed the study. Data were collected by the investigators and monitored by Daiichi Sankyo. Daiichi Sankyo and all authors were responsible for data analysis and interpretation, and for writing this article.

References

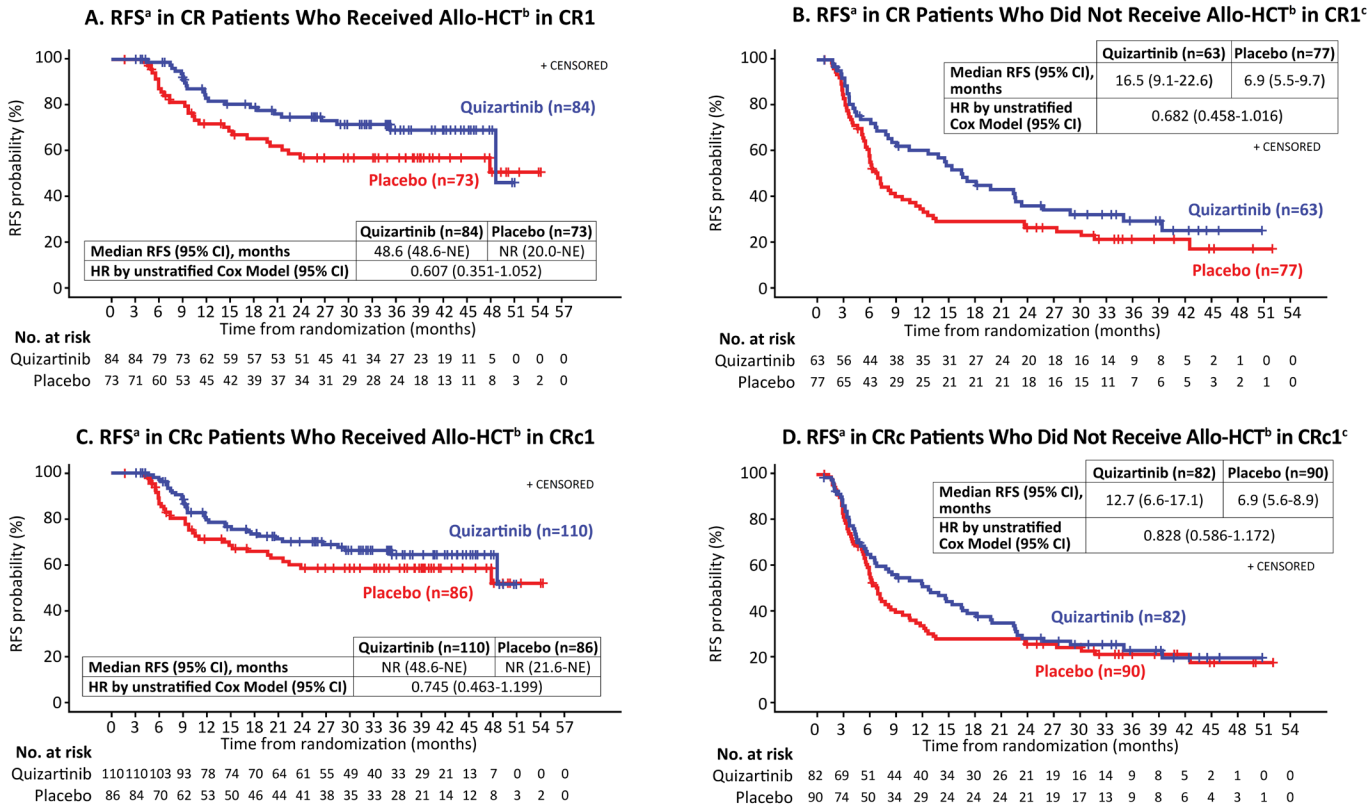
1. Erba HP, Montesinos P, Kim H-J, et al.; on behalf of the QuANTUM-First Study Group. Quizartinib plus chemotherapy in newly diagnosed patients with *FLT3*-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2023;401(10388):1571-1583.

Supplementary Figure S1. Diagram of CR and CRc patient flow.



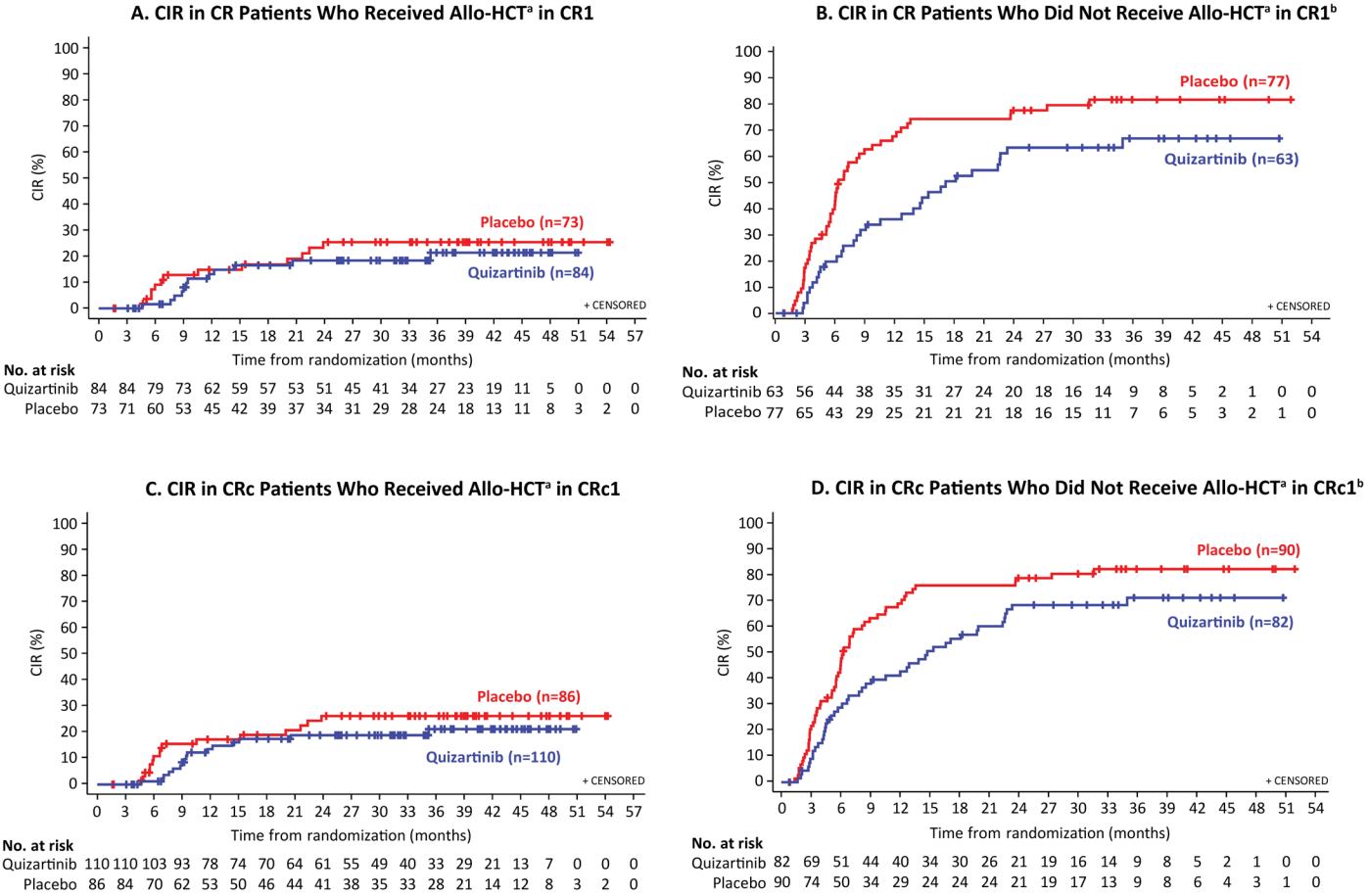
[a]Includes protocol-specified allo-HCT. Allo-HCT: allogeneic hematopoietic cell transplantation; CR: complete remission; CRc: composite complete remission; HiDAC: high-dose cytarabine.

Supplementary Figure S2. Kaplan-Meier plot of RFS by treatment arm in patients who achieved CR/CRc by the end of induction per IRC, by allo-HCT in CR1/CRc1.



[a]RFS was censored at the start date of conditioning regimen for allo-HCT, in patients who underwent allo-HCT. [b]Includes protocol-specified and non-protocol–specified allo-HCT. Some patients had both protocol-specified and non-protocol–specified allo-HCT. [c]Patients who did not receive allo-HCT includes those who did not receive allo-HCT at all during the study and those who received allo-HCT outside of CR1 or CRc1. Allo-HCT: allogeneic hematopoietic cell transplantation; CI: confidence interval; CR: complete remission; CR1: first complete remission; CRc: composite complete remission; CRc1: first composite complete remission; HR: hazard ratio; IRC: independent review committee; NE: not evaluable; NR: not reached; RFS: relapse-free survival.

Supplementary Figure S3. CIR by treatment arm in patients who achieved CR/CRc by the end of induction per IRC, by allo-HCT in CR1/CRc1.



[a]Includes protocol-specified and non-protocol–specified allo-HCT. Some patients had both protocol-specified and non-protocol–specified allo-HCT. [b]Patients who did not receive allo-HCT includes those who did not receive allo-HCT at all during the study and those who received allo-HCT outside of CR1 or CRc1. Allo-HCT: allogeneic hematopoietic cell transplantation; CIR: cumulative incidence of relapse; CR: complete remission; CR1: first complete remission; CRc: composite complete remission; CRc1: first composite complete remission; IRC: independent review committee.

Supplementary Table S1. Baseline demographics and disease characteristics of specific patient cohorts, by treatment arm.

	All patients[a]		Patients who achieved CR		Patients who achieved CR and underwent allo-HCT in CR1[bb]		Patients who achieved CR and did not undergo allo-HCT in CR1[cc]		Patients who achieved CRc		Patients who achieved CRc and underwent allo-HCT in CRc[dd]	
	Quizartinib	**Placebo**	**Quizartinib**	**Placebo**	**Quizartinib**	**Placebo**	**Quizartinib**	**Placebo**	**Quizartinib**	**Placebo**	**Quizartinib**	**Placebo**
Number of patients, N	268	271	147	150	84	73	63	77	192	176	110	86
Patient demographics												
Age, years												
Median (range)	56 (23–75)	56 (20–75)	56 (23–75)	55·5 (20–74)	50 (23–70)	52 (20–69)	62 (23–75)	61 (28–74)	56 (23–75)	55 (20–75)	51 (23–70)	51 (20–69)
<60 years, n (%)	161 (60.1)	162 (59.8)	90 (61.2)	90 (60.0)	64 (76.2)	52 (71.2)	26 (41.3)	38 (49.4)	118 (61.5)	105 (59.7)	78 (70.9)	60 (69.8)
≥60 years, n (%)	107 (39.9)	109 (40.2)	57 (38.8)	60 (40.0)	20 (23.8)	21 (28·8)	37 (58.7)	39 (50.6)	74 (38.5)	71 (40.3)	32 (29.1)	26 (30.2)
60–64 years, n (%)	37 (13.8)	44 (16.2)	22 (15.0)	25 (16.7)	11 (13.1)	15 (20.5)	11 (17.5)	10 (13.0)	27 (14.1)	28 (15.9)	14 (12.7)	17 (19.8)
≥65 years, n (%)	70 (26.1)	65 (24.0)	35 (23.8)	35 (23.3)	9 (10.7)	6 (8.2)	26 (41.3)	29 (37.7)	47 (24.5)	43 (24.4)	18 (16.4)	9 (10.5)
Sex, n (%)												
Male	124 (46.3)	121 (44.6)	65 (44.2)	60 (40.0)	33 (39.3)	34 (46.6)	32 (50.8)	26 (33.8)	87 (45.3)	72 (40.9)	48 (43.6)	41 (47.7)
Female	144 (53.7)	150 (55.4)	82 (55.8)	90 (60.0)	51 (60.7)	39 (53.4)	31 (49.2)	51 (66.2)	105 (54.7)	104 (59.1)	62 (56.4)	45 (52.3)
Race, n (%)												
Asian	80 (29.9)	78 (28.8)	45 (30.6)	42 (28.0)	30 (35.7)	25 (34.2)	15 (23.8)	17 (22.1)	59 (30.7)	50 (28.4)	39 (35.5)	30 (34.9)
Black or African American	2 (0.7)	5 (1.8)	1 (0.7)	3 (2.0)	0	0	1 (1.6)	3 (3.9)	1 (0.5)	3 (1.7)	0	0
American Indian or Alaska Native	0	1 (0.4)	0	1 (0.7)	0	0	0	1 (1.3)	0	1 (0.6)	0	0
Native Hawaiian/Pacific Islander	0	0	0	0	0	0	0	0	0	0	0	0
White	159 (59.3)	163 (60.1)	86 (58.5)	90 (60.0)	46 (54.8)	42 (57.5)	40 (63.5)	48 (62.3)	114 (59.4)	106 (60.2)	62 (56.4)	48 (55.8)
Other	27 (10.1)	24 (8.9)	15 (10.2)	14 (9.3)	8 (9.5)	6 (8.2)	7 (11.1)	8 (10.4)	18 (9.4)	16 (9.1)	9 (8.2)	8 (9.3)
Region, n (%)												
North America	16 (6.0)	18 (6.6)	7 (4.8)	12 (8.0)	6 (7.1)	7 (9.6)	1 (1.6)	5 (6.5)	7 (3.6)	14 (8.0)	6 (5.5)	9 (10.5)
Europe	163 (60.8)	163 (60.1)	94 (63.9)	87 (58.0)	47 (56.0)	39 (53.4)	47 (74.6)	48 (62.3)	122 (63.5)	103 (58.5)	64 (58.2)	44 (51.2)
Asia/other regions	89 (33.2)	90 (33.2)	46 (31.3)	51 (34.0)	31 (36.9)	27 (37.0)	15 (23.8)	24 (31.2)	63 (32.8)	59 (33.5)	40 (36.4)	33 (38.4)
Disease characteristics												
ECOG PS, n (%)[e]												
0	87 (32.5)	98 (36.2)	52 (35.4)	55 (36.7)	33 (39.3)	25 (34.2)	19 (30.2)	30 (39.0)	63 (32.8)	63 (35.8)	40 (36.4)	29 (33.7)
1	134 (50.0)	136 (50.2)	68 (46.3)	75 (50.0)	38 (45.2)	40 (54.8)	30 (47.6)	35 (45.5)	97 (50.5)	91 (51.7)	56 (50.9)	49 (57.0)
2	47 (17.5)	36 (13.3)	27 (18.4)	20 (13.3)	13 (15.5)	8 (11.0)	14 (22.2)	12 (15.6)	32 (16.7)	22 (12.5)	14 (12.7)	8 (9.3)
Cytogenetic risks, n (%)[f]												
Favorable	14 (5.2)	19 (7.0)	5 (3.4)	11 (7.3)	2 (2.4)	5 (6.8)	3 (4.8)	6 (7.8)	8 (4.2)	14 (8.0)	3 (2.7)	7 (8.1)
Intermediate	197 (73.5)	193 (71.2)	112 (76.2)	105 (70.0)	66 (78.6)	56 (76.7)	46 (73.0)	49 (63.6)	148 (77.1)	121 (68.8)	89 (80.9)	65 (75.6)
Unfavorable	19 (7.1)	27 (10.0)	9 (6.1)	14 (9.3)	7 (8.3)	6 (8.2)	2 (3.2)	8 (10.4)	10 (5.2)	17 (9.7)	7 (6.4)	6 (7.0)
Unknown	38 (14.2)	31 (11.4)	21 (14.3)	19 (12·7)	9 (10.7)	5 (6.8)	12 (19.0)	14 (18.2)	26 (13.5)	23 (13.1)	11 (10.0)	7 (8.1)
Missing	0	1 (0.4)	0	1 (0.7)	0	1 (1.4)	0	0	0	1 (0.6)	0	1 (1.2)
Mutated *NPM1*, n (%)[g]	142 (53.0)	140 (51.7)	98 (66.7)	97 (64.7)	57 (67.9)	44 (60.3)	41 (65.1)	53 (68.8)	120 (62.5)	115 (65.3)	71 (64.5)	52 (60.5)
Mutated *CEBPA*, n (%)[g]	61 (22.8)[h]	65 (24.0)[h]	38 (25.9)	35 (23.3)	23 (27.4)	16 (21.9)	15 (23.8)	19 (24.7)	47 (24.5)	41 (23.3)	28 (25.5)	18 (20.9)
***FLT3*-ITD/total *FLT3*, n (%)[i,j]**												
≥3% to ≤25%	94 (35.1)	98 (36.2)	46 (31.3)	50 (33.3)	28 (33.3)	26 (35.6)	18 (28.6)	24 (31.2)	67 (34.9)	60 (34.1)	41 (37.3)	31 (36.0)
>25% to ≤50%	143 (53.4)	138 (50.9)	82 (55.8)	83 (55.3)	44 (52.4)	40 (54.8)	38 (60.3)	43 (55.8)	99 (51.6)	94 (53.4)	53 (48.2)	47 (54.7)
>50%	30 (11.2)	35 (12.9)	19 (12.9)	17 (11.3)	12 (14.3)	7 (9.6)	7 (11.1)	10 (13.0)	25 (13.0)	22 (12.5)	16 (14.5)	8 (9.3)
WBC count at diagnosis of AML, n (%)												
$<40\times10^9$/L	135 (50.4)	137 (50.6)	65 (44.2)	76 (50.7)	36 (42.9)	36 (49.3)	29 (46.0)	40 (51.9)	67 (34.9)	60 (34.1)	41 (37.3)	31 (36.0)
$\geq40\times10^9$/L	133 (49.6)	134 (49.4)	82 (55.8)	74 (49.3)	48 (57.1)	37 (50.7)	34 (54.0)	37 (48.1)	99 (51.6)	94 (53.4)	53 (48.2)	47 (54.7)

[a]Three patients in the intent-to-treat set were randomized but not treated in each arm. [b]Includes protocol-specified allo-HCT and non-protocol–specified allo-HCT that occurred after the CR1 without evidence of relapse by IRC assessment. [c]Includes 118 patients who achieved CR and did not undergo allo-HCT at all (55 in the quizartinib arm and 63 in the placebo arm), and 22 patients who achieved CR and underwent allo-HCT outside CR1 (after relapse; 8 in the quizartinib arm and 12 in the placebo arm). [d]Includes protocol-specified allo-HCT and non-protocol–specified allo-HCT that occurred after the composite CR1 without evidence of relapse by IRC assessment. [e]One patient in the placebo group was missing an ECOG PS. [f]Favorable: inv(16), t(16;16), t(8;21), t(15;17); intermediate: normal, +8, +6, −Y; unfavorable: del(5q), −5, del(7q), −7, complex karyotype. [g]Based on the Navigate BioPharma central data. [h]In a *post-hoc* analysis, 18 (6.7%) and 20 (7.4%) patients in the quizartinib and placebo arms, respectively, had *CEBPA* single mutations and 9 (3.4%) and 4 (1.5%) patients, respectively, had *CEBPA* double mutations. [i]Variant allele frequency was assessed by central lab testing. [j]One patient with unknown *FLT3*-ITD/total *FLT3* by central laboratory testing was positive per local laboratory testing. Allo-HCT: allogeneic hematopoietic cell transplantation; AML: acute myeloid leukemia; *CEBPA*: CCAAT enhancer-binding protein alpha; CR: complete remission; CR1: first complete remission; CRc: composite complete remission; ECOG PS: Eastern Cooperative Oncology Group performance status; *FLT3*-ITD: FMS-like tyrosine kinase 3–internal tandem duplication; IRC: independent review committee; *NPM1*: nucleophosmin 1; WBC: white blood cell.

Supplementary Table S2. Post–allo-HCT GVHD score for each organ system in patients who underwent protocol-specified allo-HCT (safety analysis set).

	Quizartinib	Placebo
Number of patients, N	102	91
Maximum score for each organ system (up to 24 months post–allo-HCT), n (%)		
Skin (BSA)		
Score 0	15 (14.7)	7 (7.7)
Score 1	7 (6.9)	8 (8.8)
Score 2	3 (2.9)	1 (1.1)
Score 3	2 (2.0)	0
Unknown	3 (2.9)	2 (2.2)
Skin (features)		
Score 0	21 (20.6)	14 (15.4)
Score 1	4 (3.9)	1 (1.1)
Score 2	2 (2.0)	0
Score 3	1 (1.0)	0
Unknown	2 (2.0)	3 (3.3)
Mouth		
Score 0	12(11.8)	11 (12.1)
Score 1	12 (11.8)	2 (2.2)
Score 2	2 (2.0)	2 (2.2)
Score 3	1 (1.0)	0
Unknown	3 (2.9)	3 (3.3)
Eyes		
Score 0	19 (18.6)	9 (9.9)
Score 1	3 (2.9)	4 (4.4)
Score 2	4 (3.9)	2 (2.2)
Score 3	1 (1.0)	0
Unknown	3 (2.9)	3 (3.3)
GI tract		
Score 0	23 (22.5)	10 (11.0)

Score 1	3 (2.9)	2 (2.2)
Score 2	1 (1.0)	4 (4.4)
Score 3	2 (2.0)	0
Unknown	1 (1.0)	2 (2.2)
Liver		
Score 0	20 (19.6)	14 (15.4)
Score 1	1 (1.0)	1 (1.1)
Score 2	3 (2.9)	0
Score 3	3 (2.9)	1 (1.1)
Unknown	3 (2.9)	2 (2.2)
Lung (symptom score)		
Score 0	25 (24.5)	15 (16.5)
Score 1	1 (1.0)	1 (1.1)
Score 2	1 (1.0)	0
Score 3	0	0
Unknown	3 (2.9)	2 (2.2)
Lung (lung score)		
Score 0	25 (24.5)	15 (16.5)
Score 1	2 (2.0)	0
Score 2	0	1 (1.1)
Score 3	0	0
Unknown	3 (2.9)	2 (2.2)
Joints and fascia		
Score 0	25 (24.5)	14 (15.4)
Score 1	1 (1.0)	2 (2.2)
Score 2	0	0
Score 3	0	0
Unknown	4 (3.9)	2 (2.2)
Genital tract		
Score 0	24 (23.5)	13 (14.3)
Score 1	3 (2.9)	2 (2.2)
Score 2	0	1 (1.1)
Score 3	0	0
Unknown	3 (2.9)	2 (2.2)

Other features		
Score 0	26 (25.5)	15 (16.5)
Score 1	0	0
Score 2	0	1 (1.1)
Score 3	0	0
Unknown	4 (3.9)	2 (2.2)

Allo-HCT: allogeneic hematopoietic cell transplantation; BSA: body surface area; GI: gastrointestinal; GVHD: graft-versus-host disease.

Supplementary Table S3. Post–allo-HCT medical conditions that occurred in ≥3% of patients in either arm among patients who underwent protocol-specified allo-HCT (safety analysis set).

	Quizartinib	Placebo
Number of patients, N	102	91
Any medical condition, n (%)	85 (83.3)	68 (74.7)
Stomatitis	24 (23.5)	15 (16.5)
Pyrexia	15 (14.7)	7 (7.7)
Diarrhea	13 (12.7)	7 (7.7)
Nausea	12 (11.8)	14 (15.4)
Cytomegalovirus infection	12 (11.8)	5 (5.5)
Rash	12 (11.8)	5 (5.5)
Vomiting	10 (9.8)	9 (9.9)
Hypertension	10 (9.8)	7 (7.7)
Febrile neutropenia	9 (8.8)	12 (13.2)
Headache	9 (8.8)	4 (4.4)
Dyspepsia	9 (8.8)	4 (4.4)
GVHD in skin	8 (7.8)	8 (8.8)
GVHD in gastrointestinal tract	8 (7.8)	3 (3.3)
GVHD	7 (6.9)	8 (8.8)
Hypomagnesemia	6 (5.9)	6 (6.6)
Pneumonia	6 (5.9)	2 (2.2)
Oedema peripheral	6 (5.9)	1 (1.1)
Acute GVHD	5 (4.9)	6 (6.6)
Abdominal pain	5 (4.9)	4 (4.4)
Erythema	5 (4.9)	3 (3.3)
Abdominal pain upper	5 (4.9)	2 (2.2)
Acute GVHD in skin	5 (4.9)	1 (1.1)
Alanine aminotransferase increased	5 (4.9)	1 (1.1)
Hemorrhoids	5 (4.9)	0
Back pain	4 (3.9)	5 (5.5)
Hypogammaglobulinemia	4 (3.9)	3 (3.3)
Epistaxis	4 (3.9)	2 (2.2)
Dysuria	4 (3.9)	2 (2.2)
Cytomegalovirus test positive	4 (3.9)	2 (2.2)
Pain in extremity	4 (3.9)	1 (1.1)

Decreased appetite	3 (2.9)	11 (12.1)
Hypokalemia	3 (2.9)	3 (3.3)
Cough	3 (2.9)	3 (3.3)
Dyspnea	3 (2.9)	2 (2.2)
Asthenia	3 (2.9)	2 (2.2)
BK virus infection	3 (2.9)	1 (1.1)
Sepsis	3 (2.9)	1 (1.1)
Hyperglycemia	3 (2.9)	1 (1.1)
Sinus tachycardia	3 (2.9)	1 (1.1)
Hepatic function abnormal	3 (2.9)	1 (1.1)
Hematuria	3 (2.9)	1 (1.1)
Aspartate aminotransferase increased	3 (2.9)	1 (1.1)
Gamma-glutamyl transferase increased	3 (2.9)	1 (1.1)
Hypocalcemia	3 (2.9)	0
Pleural effusion	3 (2.9)	0
Oral pain	3 (2.9)	0
Anemia	2 (2.0)	5 (5.5)
Thrombocytopenia	2 (2.0)	5 (5.5)
Constipation	2 (2.0)	5 (5.5)
Proctalgia	2 (2.0)	4 (4.4)
Hyponatremia	2 (2.0)	3 (3.3)
Blood creatinine increased	2 (2.0)	3 (3.3)
Cytomegalovirus infection reactivation	1 (1.0)	8 (8.8)
Neutropenia	1 (1.0)	4 (4.4)
Dysgeusia	1 (1.0)	4 (4.4)
Gastrointestinal inflammation	1 (1.0)	4 (4.4)
Tremor	1 (1.0)	3 (3.3)
Fatigue	0	5 (5.5)
Oral herpes	0	3 (3.3)
Chills	0	3 (3.3)
Weight decreased	0	3 (3.3)

Note: for patients who underwent allo-HCT, updated medical history was collected, including clinically relevant medical conditions that had onset and resolution during the allo-HCT duration, and any medical condition with onset during the allo-HCT period that was still ongoing on day 1 of the maintenance phase. Allo-HCT: allogeneic hematopoietic cell transplantation; GVHD, graft-versus-host disease.

Supplementary Table S4. Summary of overall safety in patients who underwent protocol-specified allo-HCT (safety analysis set).[a]

	Quizartinib	Placebo
Number of patients, N	102	91
Overview of AEs, n (%)		
AEs[b]	102 (100.0)	91 (100.0)
AEs of ECG QT prolonged	13 (12.7)	4 (4.4)
Drug-related[c] AEs	67 (65.7)	38 (41.8)
Grade ≥3 AEs[b] (including grade 5)	98 (96.1)	86 (94.5)
Drug-related[c] grade ≥3 AEs (including grade 5)	55 (53.9)	24 (26.4)
AEs[b] associated with fatal outcome	3 (2.9)	2 (2.2)
Grade 5 infections and infestations	2 (2.0)	0
Grade 5 ECG QT prolonged	0	0
Drug-related[c] AEs associated with fatal outcome	0	1 (1.1)
SAEs[b]	57 (55.9)	40 (44.0)
SAEs occurring in ≥3% of patients in either arm		
Febrile neutropenia	14 (13.7)	7 (7.7)
Pneumonia	10 (9.8)	4 (4.4)
Herpes zoster	4 (3.9)	1 (1.1)
GVHD in gastrointestinal tract	4 (3.9)	0
Sepsis	3 (2.9)	2 (2.2)
Neutrophil count decreased	3 (2.9)	0
Septic shock	3 (2.9)	0
Colitis	1 (1.0)	3 (3.3)
Thrombocytopenia	0	3 (3.3)
Drug-related[c] SAEs	13 (12.7)	11 (12.1)
Grade 3/4 pancytopenia[b]	3 (2.9)	0
Grade 3/4 myelosuppression[b]	1 (1.0)	0
Dose modifications, n (%)[d]		
AEs[b] associated with discontinuation	14 (13.7)	6 (6.6)
AEs[b] associated with dose interruption	51 (50.0)	23 (25.3)
AEs[b] associated with dose reduction	33 (32.4)	10 (11.0)
Dose reductions due to any AEs[b] of ECG QT prolonged	5 (4.9)	0

[a]The safety analysis set includes all patients who received at least one dose of quizartinib or placebo (3 patients in each arm were not treated and are not included in the safety analysis set). If a patient had more than one event, the patient was counted only once. [b]Regardless of causality. [c]Based on investigator-reported causality. [d]Patients may be included in more than one category. AE: adverse event; allo-HCT: allogeneic hematopoietic cell transplantation; ECG, electrocardiogram; GVHD: graft-versus-host disease; SAE: serious adverse event.

Supplementary Table S5. Exposure to quizartinib/placebo during maintenance therapy in patients who underwent allo-HCT.

	Patients with allo-HCT who received maintenance (N=119)[a]	
	Quizartinib	**Placebo**
Number of patients, N	70	49
Number of cycles		
Median (range), months	18.90 (0.09–38.41)	19.96 (0.07–38.52)
<12 cycles, n (%)	22 (31.4)	13 (26.5)
≥12 cycles, n (%)	48 (68.6)	36 (73.5)
Adjusted treatment duration[b]		
Median (range), months	18.90 (0.09–35.21)	19.96 (0.07–34.61)
Dose intensity[c]		
Median (range), mg/day	36.69 (14.79–59.50)	57.54 (16.67–59.68)
Relative dose intensity[d]		
Median (range), %	82.35 (29.88–190.48)	99.95 (39.35–173.89)

[a]Includes protocol-specified allo-HCT. [b]Adjusted treatment duration (days) = sum of treatment duration (days) minus the planned off-drug days in the maintenance phase. [c]Dose intensity (mg/day) = cumulative dose / adjusted treatment duration in days. [d]Relative dose intensity (%) = dose intensity / planned dose intensity × 100. Allo-HCT: allogeneic hematopoietic cell transplantation.

Supplementary Table S6. Summary of overall safety during maintenance therapy by allo-HCT status.

	Patients with allo-HCT who received maintenance (N=119)[a]	
	Quizartinib	**Placebo**
Number of patients, N	70	49
AEs, n (%)		
Any TEAEs	68 (97.1)	45 (91.8)
Any TRAEs	53 (75.7)	19 (38.8)
Grade ≥3 TEAEs (including grade 5)	58 (82.9)	27 (55.1)
Grade ≥3 TRAEs (including grade 5)	42 (60.0)	9 (18.4)
TESAEs	25 (35.7)	16 (32.7)
TRSAEs	5 (7.1)	4 (8.2)
AEs associated with fatal outcome	2 (2.9)	1 (2.0)
TRAEs associated with fatal outcome	0	0
Dose modifications, n (%)		
TEAEs associated with discontinuation	14 (20.0)	5 (10.2)
TRAEs associated with discontinuation	9 (12.9)	3 (6.1)
TEAEs associated with dose interruption	41 (58.6)	13 (26.5)
TRAEs associated with dose interruption	29 (41.4)	8 (16.3)
TEAEs associated with dose reduction	28 (40.0)	8 (16.3)
TRAEs associated with dose reduction	19 (27.1)	4 (8.2)

[a]Includes protocol-specified allo-HCT. AE: adverse event; allo-HCT: allogeneic hematopoietic cell transplantation; TEAE: treatment-emergent adverse event; TESAE: treatment-emergent serious adverse event; TRAE: treatment-related adverse event; TRSAE: treatment-related serious adverse event.

Supplementary Table S7. TEAEs occurring in ≥10% of patients in either arm during maintenance therapy by allo-HCT status.

	Patients with allo-HCT who received maintenance (N=119)[a]			
	Quizartinib		Placebo	
Number of patients, N	70		49	
TEAEs, n (%)	**All grades[a]**	**Grade ≥3**	**All grades[a]**	**Grade ≥3**
Any TEAEs, n (%)	68 (97.1)	58 (82.9)	45 (91.8)	27 (55.1)
Neutropenia	24 (34.3)	21 (30.0)	3 (6.1)	2 (4.1)
Nausea	20 (28.6)	2 (2.9)	6 (12.2)	1 (2.0)
Anemia	17 (24.3)	6 (8.6)	4 (8.2)	2 (4.1)
Diarrhea	16 (22.9)	1 (1.4)	6 (12.2)	0
Vomiting	15 (21.4)	0	4 (8.2)	0
Pyrexia	14 (20.0)	0	9 (18.4)	2 (4.1)
Cough	14 (20.0)	1 (1.4)	7 (14.3)	0
Neutrophil count decreased	14 (20.0)	12 (17.1)	3 (6.1)	0
Upper respiratory tract infection	12 (17.1)	0	6 (12.2)	0
Thrombocytopenia	12 (17.1)	6 (8.6)	3 (6.1)	2 (4.1)
Decreased appetite	12 (17.1)	3 (4.3)	2 (4.1)	0
Rash	11 (15.7)	2 (2.9)	9 (18.4)	0
Fatigue	11 (15.7)	1 (1.4)	5 (10.2)	0
Arthralgia	10 (14.3)	0	8 (16.3)	0
Edema peripheral	10 (14.3)	1 (1.4)	8 (16.3)	2 (4.1)
Alanine aminotransferase increased	9 (12.9)	2 (2.9)	7 (14.3)	3 (6.1)
Headache	9 (12.9)	0	5 (10.2)	1 (2.0)
Dry eye	9 (12.9)	0	4 (8.2)	0
Pneumonia	9 (12.9)	7 (10.0)	2 (4.1)	0
Platelet count decreased	9 (12.9)	4 (5.7)	0	0
Pruritus	8 (11.4)	1 (1.4)	8 (16.3)	0
Pain in extremity	8 (11.4)	1 (1.4)	4 (8.2)	0
Hypokalemia	7 (10.0)	1 (1.4)	2 (4.1)	2 (4.1)
Herpes zoster	7 (10.0)	3 (4.3)	1 (2.0)	0
ECG QT prolonged	7 (10.0)	0	0	0
Aspartate aminotransferase increased	6 (8.6)	2 (2.9)	5 (10.2)	2 (4.1)
Constipation	6 (8.6)	0	5 (10.2)	0
Gamma-glutamyltransferase increased	6 (8.6)	5 (7.1)	5 (10.2)	4 (8.2)
Dyspnea	4 (5.7)	0	5 (10.2)	0
Hyperkalemia	3 (4.3)	0	5 (10.2)	0

Influenza-like illness	2 (2.9)	0	5 (10.2)	0
Febrile neutropenia	1 (1.4)	1 (1.4)	1 (2.0)	1 (2.0)
Muscle spasms	3 (4.3)	0	3 (6.1)	0

[a]The 10% threshold is based on all-grade TEAEs. Allo-HCT: allogeneic hematopoietic cell transplantation; ECG: electrocardiogram; TEAE: treatment-emergent adverse event.