Bleximenib in Combination With Intensive Chemotherapy: A Phase 1b Study in Newly Diagnosed Acute Myeloid Leukemia With *KMT2A* or *NPM1* Alterations

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Supplementary Material

Supplementary Table 1: Baseline demographics and clinical characteristics: safety population[a]

Characteristic	Safety population N=44
Age, median (range), years	57.0 (19–71)
Female, n (%)	23 (52.3)
ECOG PS score, n (%)	
0	16 (36.4)
1	27 (61.4)
2	1 (2.3)
Leukocyte count, median (range), × 10^9/L	3.4 (0.8–20.1)
Bone marrow blasts, median (range), %	63.0 (0.0–98.0)
Genetic alterations, n (%)	
KMT2A	19 (43.2)
NPM1	25 (56.8)
Clinically relevant comutations, n (%)	
DNMT3a	9 (20.5)
FLT3	8 (18.2)
ITD	4 (9.1)
TKD	4 (9.1)
IDH2	6 (13.6)
TET2	5 (11.4)

BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance status; ITD, internal tandem duplication; TKD, tyrosine kinase domain.
Data cutoff: October 2025.
[a]Safety population comprised all dosed participants who received bleximenib at 30 mg BID (n=2), 50 mg BID (n=17), or 100 mg BID (n=25).

Supplementary Table 2: TEAEs occurring in ≥30% of participants, regardless of relatedness to study treatment, with onset during continuation phase

TEAE, n (%)	Participants across all dose levels who initiated continuation phase n=20	
	Any grade	Grade ≥3
Participants with ≥1 TEAE	18 (90.0)	6 (30.0)
Hematologic TEAEs		
Thrombocytopenia	6 (30.0)	2 (10.0)
Neutropenia	8 (40.0)	2 (10.0)

TEAE, treatment-emergent adverse event.
Data cutoff: October 2025.

Supplementary Table 3: TEAEs occurring in ≥30% of participants, regardless of relatedness to study treatment

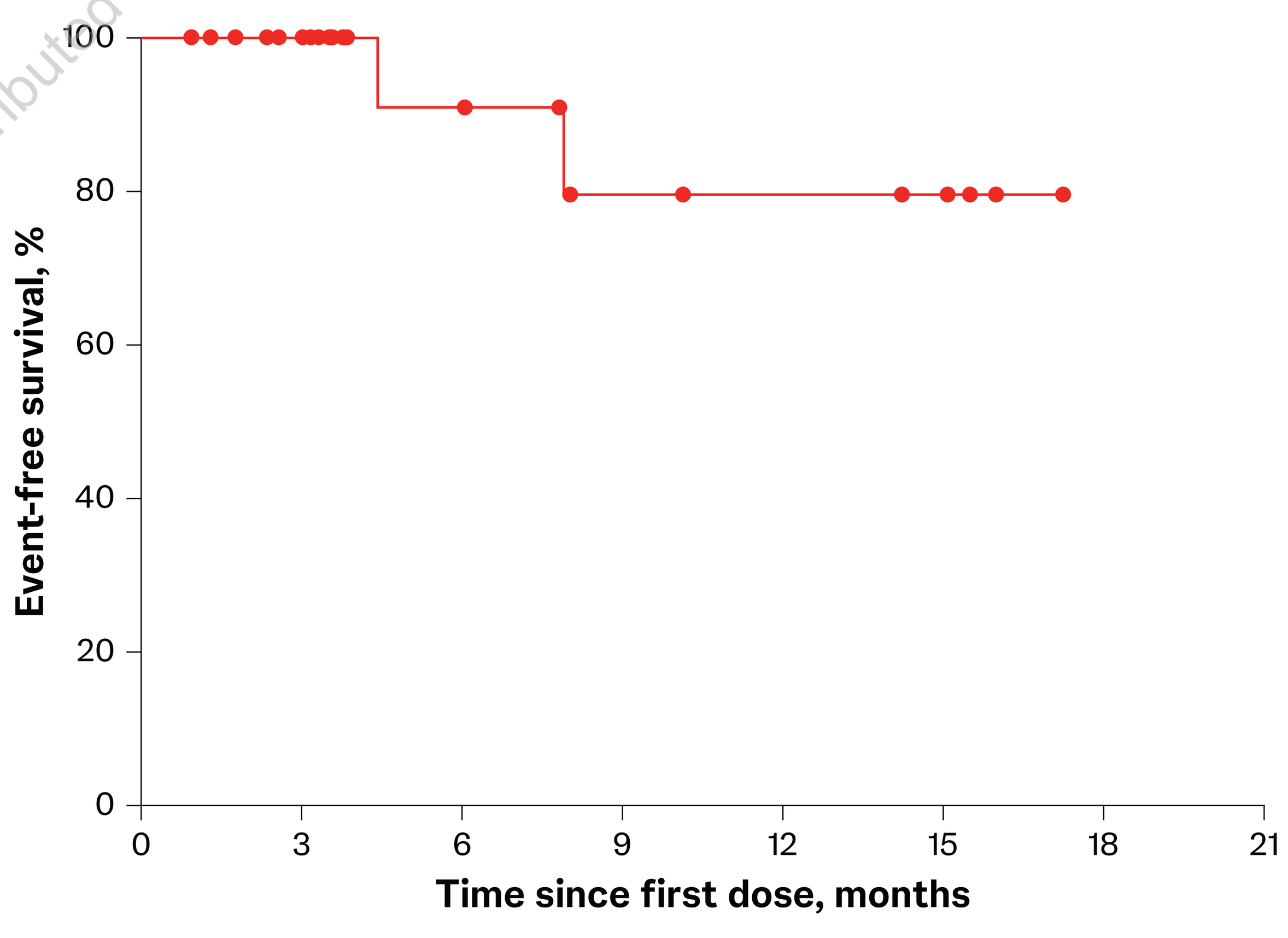
TEAE, n (%)	Safety population N=44	
	Any grade	Grade ≥3
Participants with ≥1 TEAE	**44 (100.0)**	**44 (100.0)**
Hematologic TEAEs		
Thrombocytopenia	36 (81.8)	36 (81.8)
Neutropenia	31 (70.5)	30 (68.2)
Anemia	29 (65.9)	29 (65.9)
Febrile neutropenia	30 (68.2)	30 (68.2)
Leukopenia	17 (38.6)	17 (38.6)
Nonhematologic TEAEs		
Diarrhea	31 (70.5)	2 (4.5)
Nausea	30 (68.2)	3 (6.8)
Pyrexia	26 (59.1)	2 (4.5)
Stomatitis	19 (43.2)	6 (13.6)
ALT increased	18 (40.9)	3 (6.8)
Vomiting	17 (38.6)	2 (4.5)
Peripheral edema	15 (34.1)	0
Hypokalemia	17 (38.6)	3 (6.8)
AST increased	14 (31.8)	3 (6.8)
Constipation	15 (34.1)	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.
Data cutoff: October 2025.

Bleximenib exposure and dose modifications

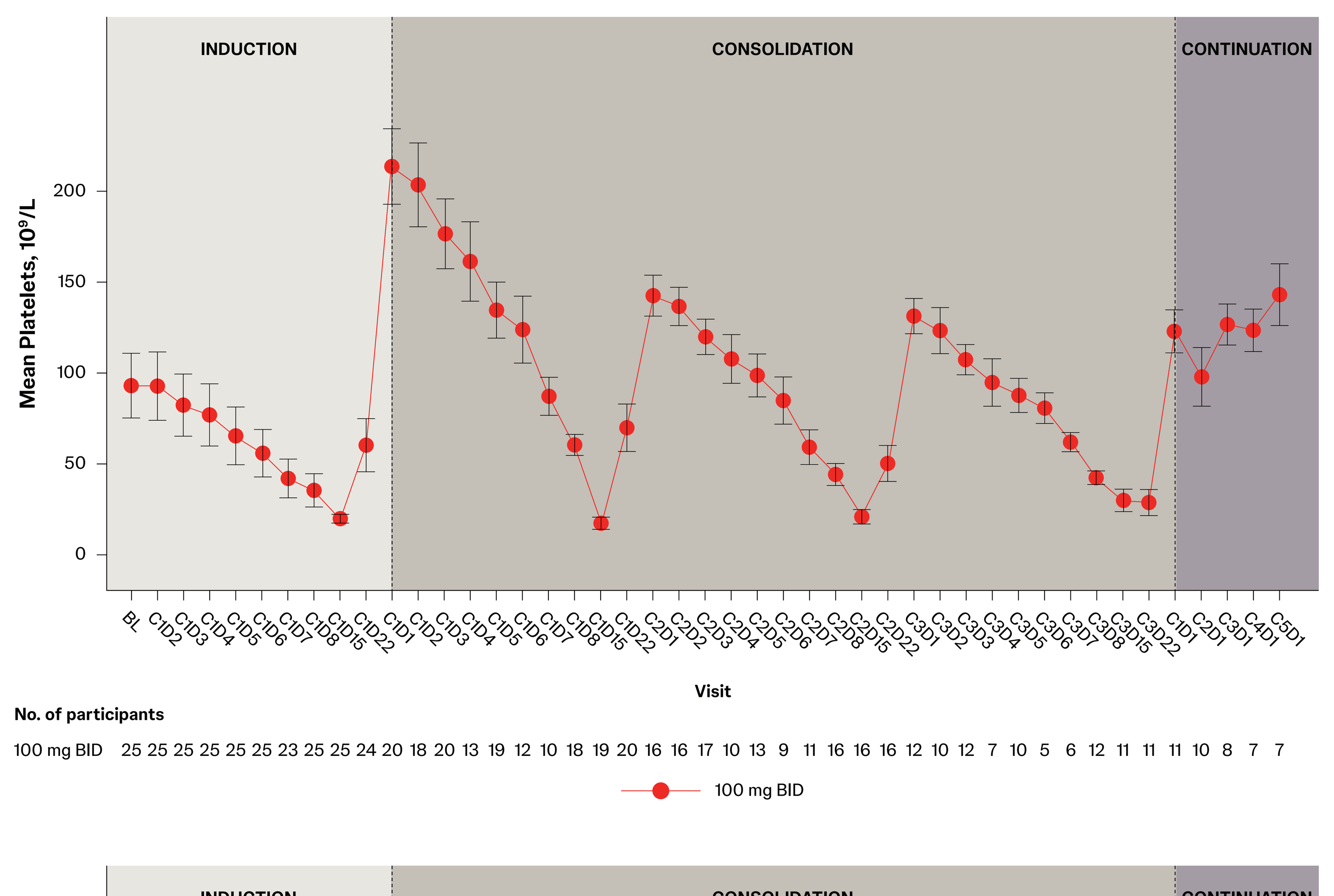
- TEAEs led to bleximenib dose reduction in 1 participant (2.3%), dose interruption in 23 participants (52.3%), and discontinuation in 4 participants (9.1%)
- The median (range) relative dose intensity of bleximenib during cycles 1 and 2 of the consolidation phase was 100% (0–100%) and 100% (0–100%), respectively

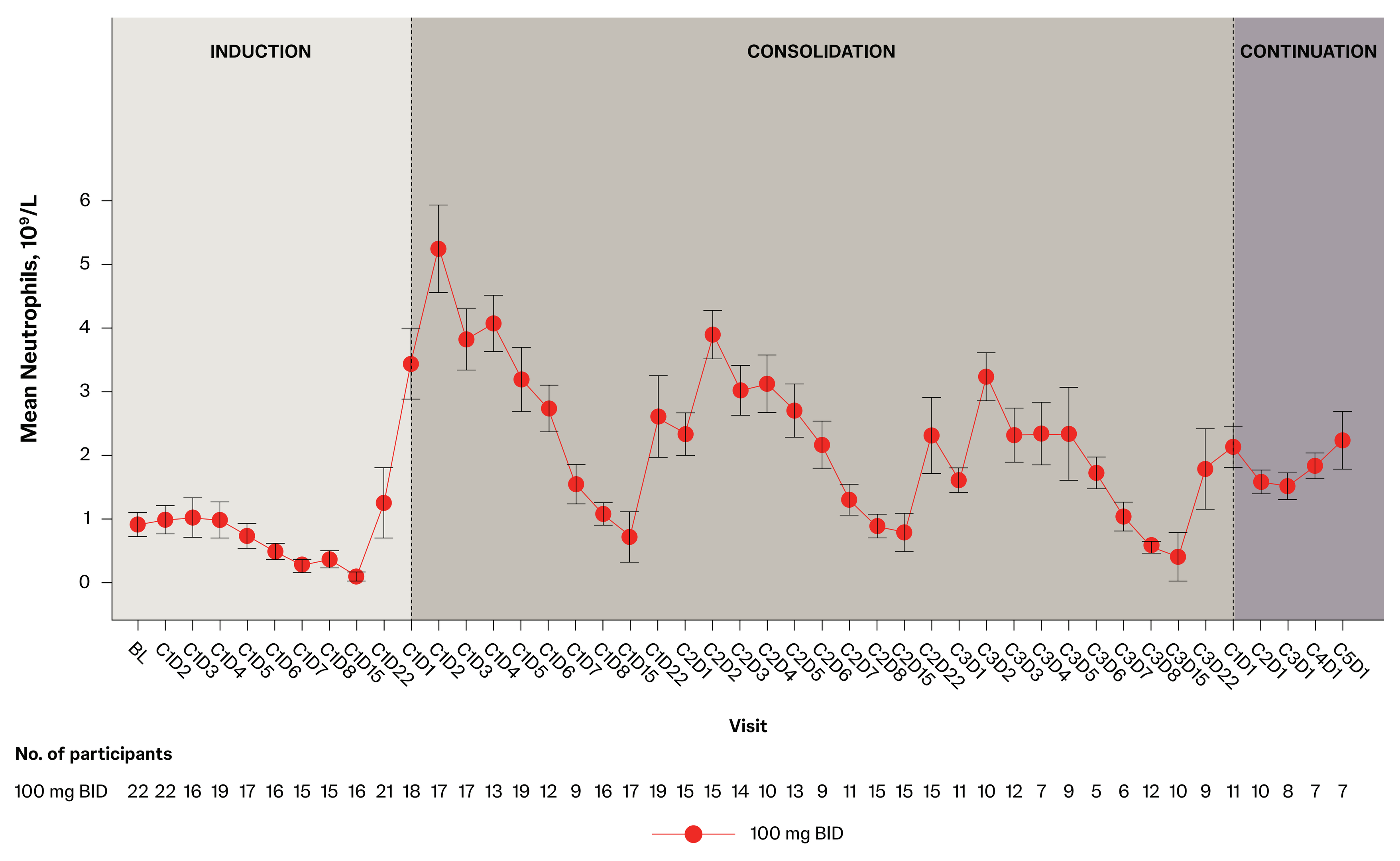
Supplementary Figure 1: Kaplan-Meier plot of event-free survival per investigator assessment in the ITT efficacy population[a]

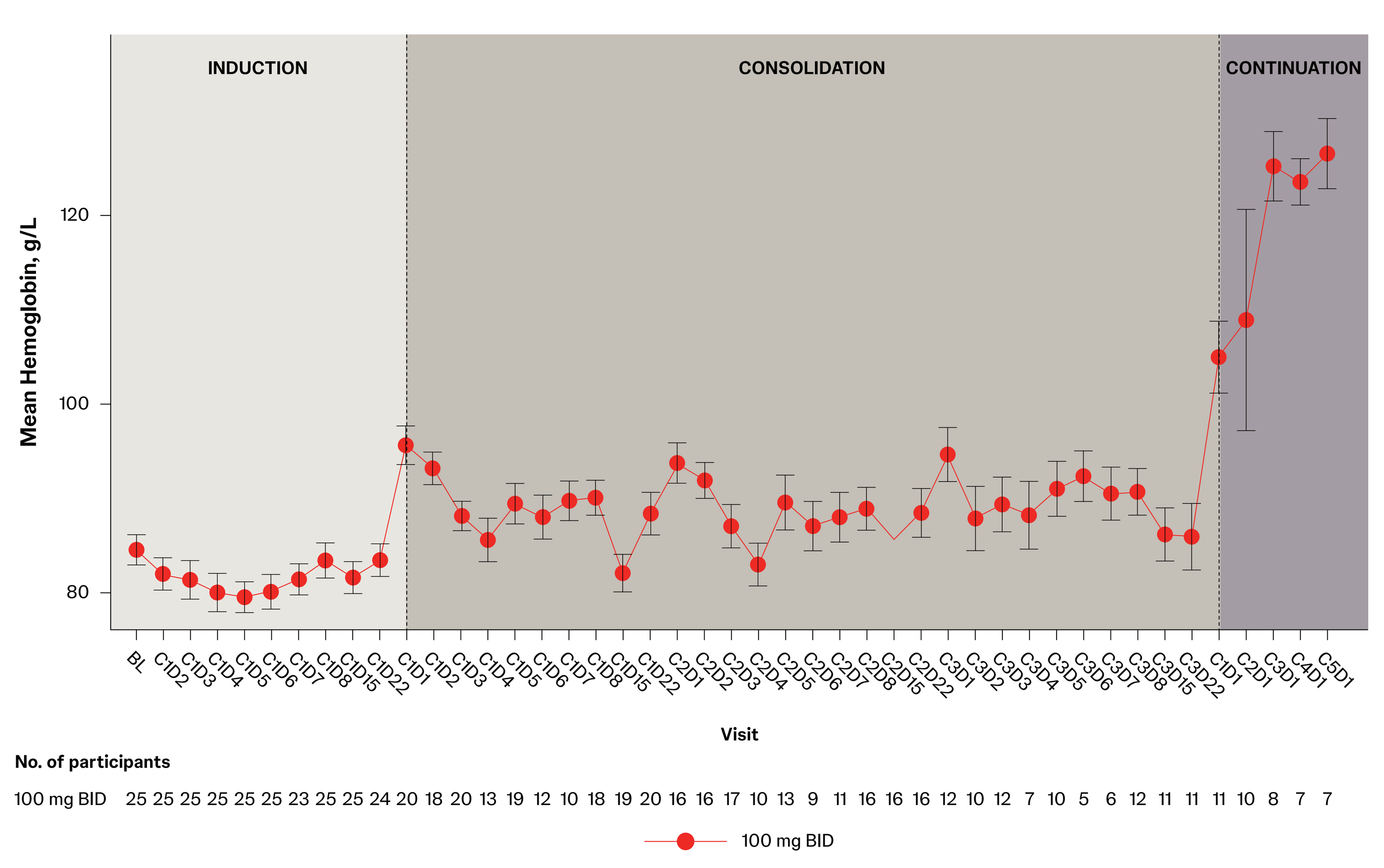


AML, acute myeloid leukemia; IC, intensive chemotherapy; ITT, intention to treat; *KMT2Ar*, *KMT2A* rearranged, ND, newly diagnosed; *NPM1m*, *NPM1* mutated.
Data cutoff: October 2025.
[a]ITT population comprised participants with *KMT2Ar* or *NPM1m* ND AML who were eligible for IC, and who received bleximenib 100 mg BID in combination with '7+3' IC, including those who discontinued prior to the first disease evaluation; 1 participant with *KMT2A* amplification was excluded from the analysis.

Supplementary Figure 2: Hematologic parameters over time







BL, baseline; C, cycle; D, day.
Data cutoff: October 2025.

Study treatment disposition

- Of 24 participants in the ITT efficacy population, 15 participants (62.5%) discontinued
  - Reasons for discontinuation were transplantation (7 participants; 29.2%), adverse event (3 participants; 12.5%), consent withdrawal (2 participants; 8.3%), relapsed disease (2 participants, 8.3%), and refractory disease (1 participant; 4.2%)

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