Supplemental Material

Phase 1/2 study of uproleselan added to chemotherapy in patients with relapsed or refractory acute myeloid leukemia

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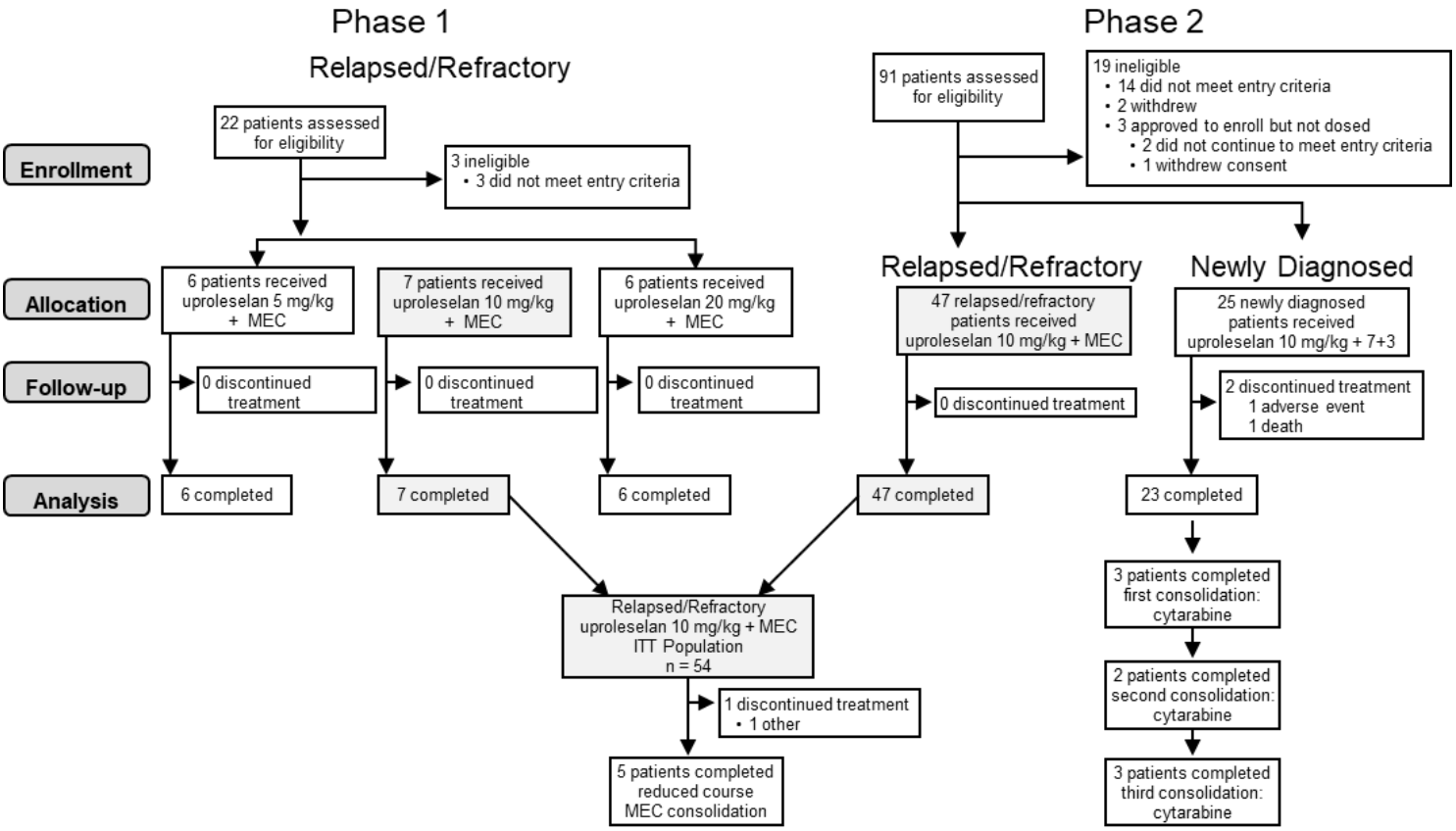
Supplemental Figure 1. Patient disposition during phase 1 and phase 2. ITT, intention to treat; MEC, combination regimen mitoxantrone, etoposide, cytarabine; 7+3, combination regimen cytarabine/idarubicin.



Supplemental Table 1. Overview of treatment-emergent adverse events

	Patients, n (%)				
	Uproleselan				
				RP2D 10 mg/kg	
	Phase 1 relapsed/refractory			Relapsed/ refractory	Newly diagnosed in patients aged ≥60 years
Parameter	5 mg/kg + MEC (n = 6)	10 mg/kg + MEC (n = 7)	20 mg/kg + MEC (n = 6)	+ MEC (n = 54)	+ 7+3 (n = 25)
Any TEAE	6 (100)	7 (100)	6 (100)	54 (100)	25 (100)
Serious adverse event	3 (50)	0	2 (33)	18 (33)	9 (36)
Severe adverse event	1 (17)	3 (43)	3 (50)	15 (28)	8 (32)
Deaths	0	0	0	0	2 (8)
Drug-related adverse event	4 (67)	4 (57)	3 (50)	28 (52)	16 (64)
Mild	1 (17)	1 (14)	0	6 (11)	2 (8)
Moderate	1 (17)	0	0	4 (7)	6 (24)
Severe	0	1 (14)	1 (17)	9 (17)	4 (16)
Life-threatening	2 (33)	2 (29)	2 (33)	9 (17)	4 (16)
Fatal	0	0	0	0	0
AE leading to drug discontinuation	0	0	0	0	0

AE, adverse event; MEC, mitoxantrone/etoposide/cytarabine; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event; 7+3, combination regimen cytarabine/idarubicin.

Supplemental Table 2. Grade 3 or 4 treatment-emergent adverse events reported in ≥10% of patients in the overall MEC and 7+3-treated populations

	Phase 1			Phase 1/2	
System organ class / preferred term, n (%)	R/R 5 mg + MEC (n = 6)	R/R 10 mg + MEC (n = 7)	R/R 20 mg + MEC (n = 6)	R/R + MEC* (n = 66)	Newly diagnosed† 10 mg + 7+3 (n = 25)
Blood and lymphatic system disorders	5 (83)	5 (71)	4 (67)	52 (79)	23 (92)
Anemia	4 (67)	1 (14)	1 (17)	17 (26)	6 (24)
Febrile neutropenia	1 (17)	4 (57)	3 (50)	39 (59)	22 (88)
Neutropenia	2 (33)	0 (0)	0 (0)	11 (17)	3 (12)
Thrombocytopenia	3 (50)	1 (14)	1 (17)	23 (35)	6 (24)
Infections and infestations	4 (67)	4 (57)	5 (83)	31 (47)	9 (36)
Sepsis	1 (17)	1 (14)	3 (50)	8 (12)	1 (4)
Investigations	4 (67)	1 (14)	0 (0)	23 (35)	12 (48)
Neutrophil count decreased	1 (17)	1 (14)	0 (0)	4 (6)	4 (16)
Platelet count decreased	3 (50)	1 (14)	0 (0)	12 (18)	6 (24)
WBC count decreased	1 (17)	0 (0)	0 (0)	7 (11)	5 (20)
Metabolism and nutrition disorders	3 (50)	0 (0)	2 (33)	18 (27)	10 (40)
Hypokalemia	0 (0)	0 (0)	0 (0)	2 (3)	4 (16)
Hypophosphatemia	1 (17)	0 (0)	2 (33)	6 (9)	3 (12)
Respiratory, thoracic, and mediastinal disorders	0 (0)	1 (14)	1 (17)	6 (9)	7 (28)
Pulmonary edema	0 (0)	0 (0)	0 (0)	1 (2)	3 (12)
Respiratory failure	0 (0)	0 (0)	0 (0)	0 (0)	4 (16)

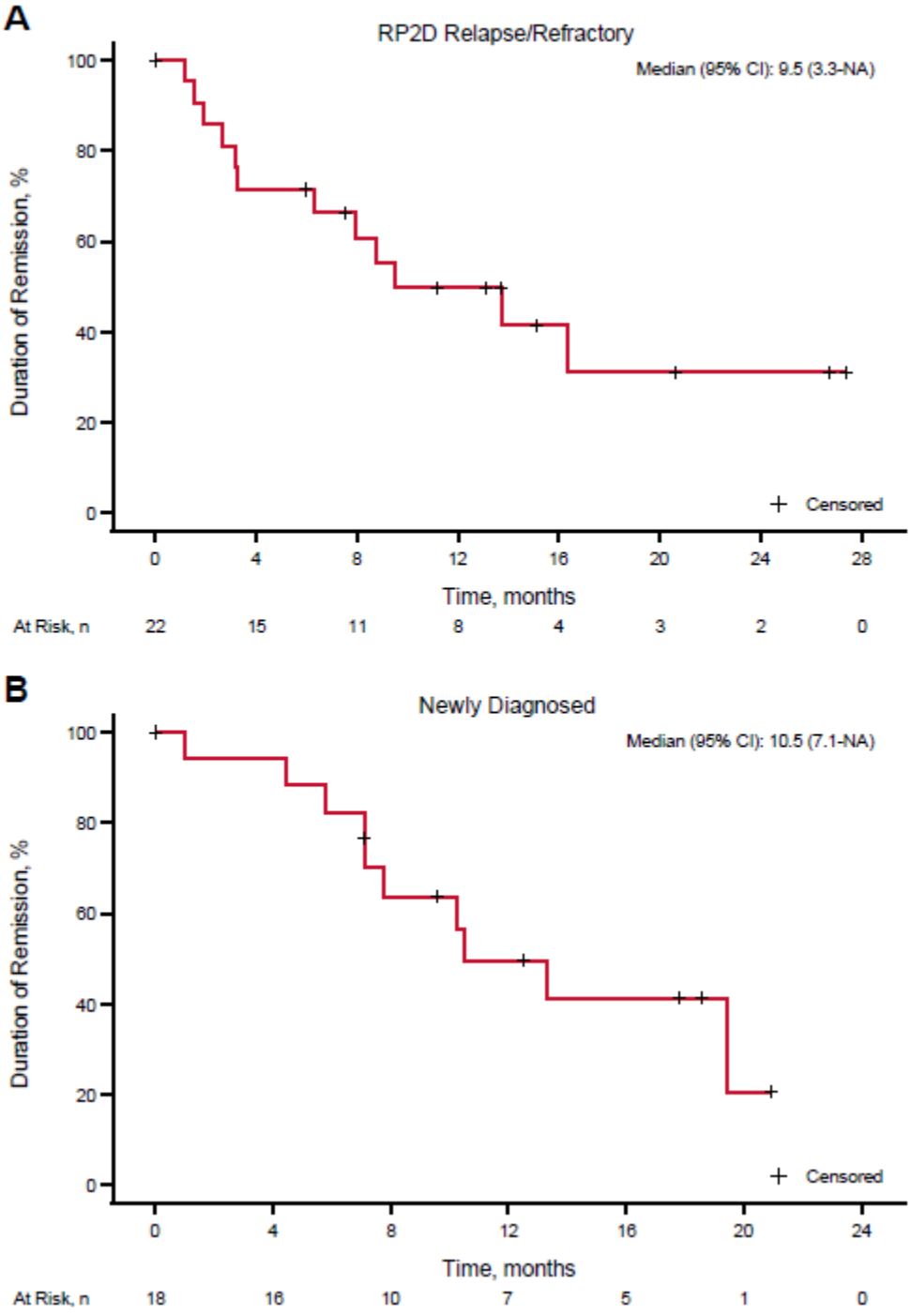
Patients were counted once in each category; if a patient experienced the same coded event more than once, only the greatest severity is presented.

*Includes 7 patients from the phase 1 dose-escalation phase.

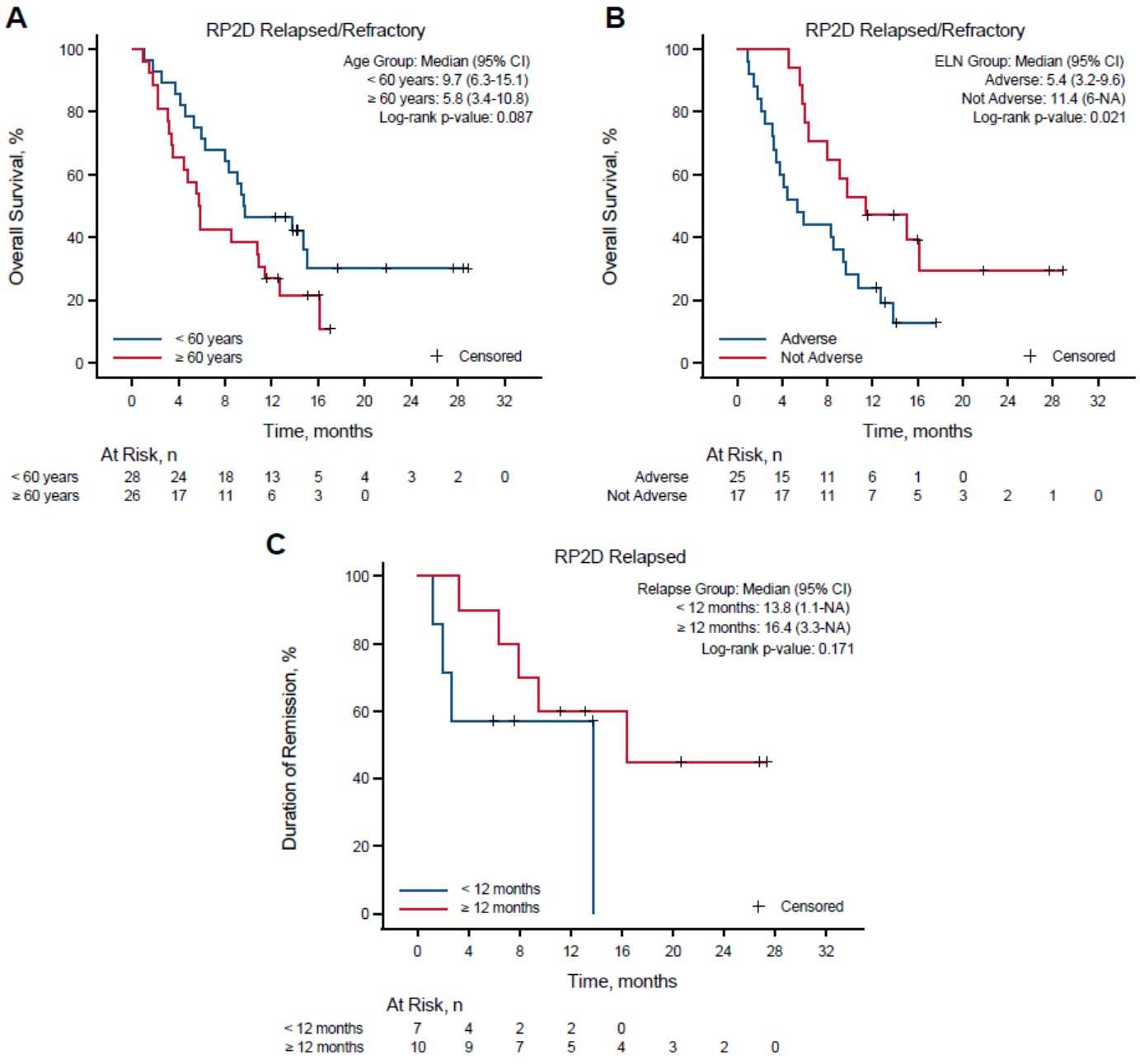
†Patients aged ≥60 years.

MEC, mitoxantrone/etoposide/cytarabine; R/R, relapsed/refractory; WBC, white blood cells; 7+3, combination regimen cytarabine/idarubicin.

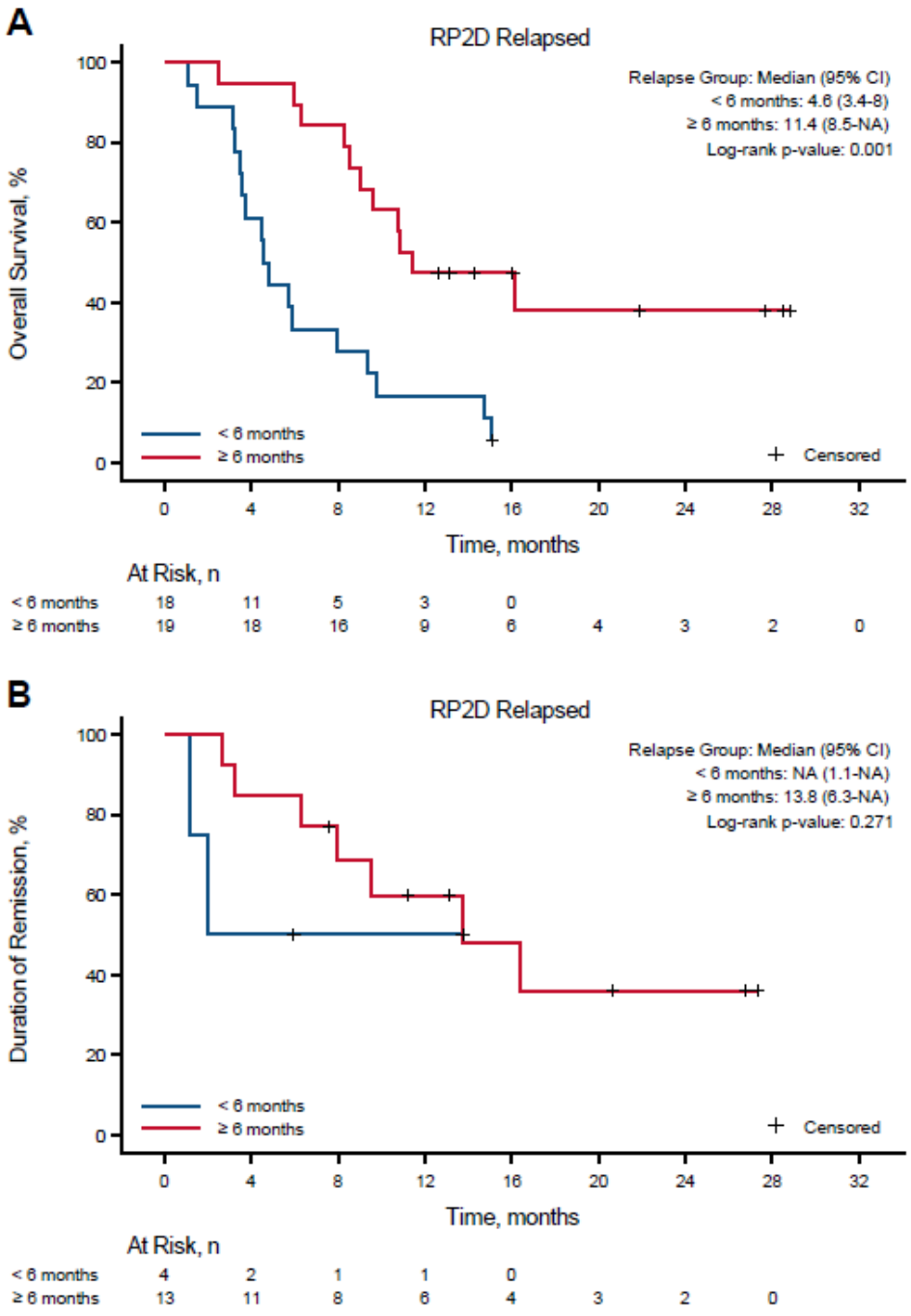
Supplemental Figure 2. Duration of remission with uproleselan in combination with chemotherapy in patients with acute myeloid leukemia among those (A) with relapsed/refractory disease and (B) aged ≥60 years with newly diagnosed disease. NA, not applicable; RP2D, recommended phase 2 dose.



Supplemental Figure 3. Overall survival with uproleselan in (A) patients according to age, and (B) patients with an adverse risk according to ELN (N = 42) and (C) duration of remission for relapsed patients with an initial complete response duration of <12 months or ≥12 months. ELN, European Leukemia Net; RP2D, recommended phase 2 dose.



Supplemental Figure 4. (A) Overall survival in patients with relapsed AML among those with an initial remission duration of <6 months or ≥6 months and (B) duration of remission in patients with relapsed AML among those with an initial remission duration of <6 months or ≥6 months. MEC, mitoxantrone/etoposide/cytarabine; NA, not applicable; RP2D, recommended phase 2 dose.



Supplemental Figure 5. Correlation of E-selectin ligand expression between leukemic stem cells and myeloblasts in bone marrow of patients with AML among those with (A) relapsed/refractory disease and (B) those aged ≥60 years with newly diagnosed disease.
E-selectin ligand expression detected by a fit-for-purpose flow cytometric evaluation of bone marrow and peripheral blood samples from patients with AML. E-selectin ligand expression was identified in the leukemic blast population using FITC-HECA-452. The HECA-452 antibody recognizes the E-selectin carbohydrate binding ligand shared by sLea and sLea/x. The backbone panel to identify the AML population and leukemic stem cells from non-leukemic cells was composed of fluorochrome-labeled antibodies to CD45, CD34, CD38, and CD123.
AML, acute myeloid leukemia; E-sel-L, E-selectin ligand; LCS, leukemic stem cells.