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

| 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         | 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

| System organ class / preferred term, n (%) | Phase 1 | Phase 1/2 |
|-----------------------------------------|---------|-----------|
|                                        | 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.