

## SUPPLEMENTARY INFORMATION

### **Real-world effectiveness and safety of blinatumomab in adults with B-cell precursor acute lymphoblastic leukaemia across 13 European countries**

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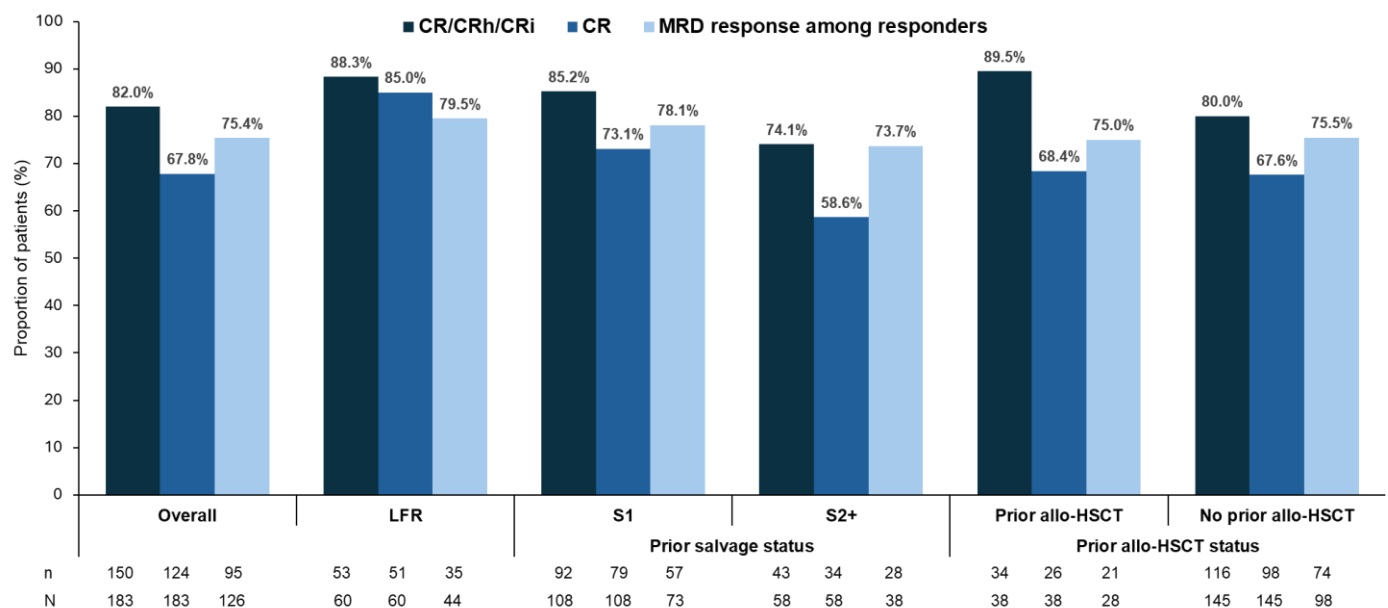
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**Supplementary Figure 1.** Response outcomes for patients with R/R Ph<sup>+</sup> BCP-ALL, overall and by sub-groups within the first two cycles of blinatumomab treatment.

Allo-HSCT, allogeneic haematopoietic stem cell transplantation; CR, complete remission with full recovery of peripheral blood counts; CRh, complete remission with partial recovery of peripheral blood counts; CRi, complete remission with incomplete recovery of peripheral blood counts; LFR, late first relapse; MRD, measurable residual disease; n, number of patients achieving the specified outcome; N, total number of evaluable patients in each subgroup; S1, patients who received blinatumomab as first salvage therapy; S2+, patients who received blinatumomab as subsequent salvage therapy.



**Supplementary Table 1.** Distribution of participating study centres

The study was approved by local institutional review boards/independent ethics committees and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines issued by the International Council for Harmonisation. In countries where patient informed consent was required to access medical records, medical records of patients who did not provide informed consent were excluded.

| Study country   | Number of centres |
|-----------------|-------------------|
| Austria         | 3                 |
| Czech Republic  | 3                 |
| Finland         | 1                 |
| France          | 15                |
| Germany         | 5                 |
| Greece          | 4                 |
| Italy           | 17                |
| Poland          | 6                 |
| Portugal        | 5                 |
| Sweden          | 1                 |
| Switzerland     | 9                 |
| The Netherlands | 3                 |
| United Kingdom  | 6                 |

**Supplementary Table 2.** Effectiveness and safety outcomes in the study

| <b>Outcomes</b>                                                       | <b>Definition</b>                                                                                                         |
|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| <b>Complete remission (CR)</b>                                        | Bone marrow blasts <5%, platelets >100,000 cells/ $\mu$ L, and absolute neutrophil count >1,000 cells/ $\mu$ L            |
| <b>Complete remission with partial haematologic recovery (CRh)</b>    | Bone marrow blasts $\leq$ 5%, platelets >50,000 cells/ $\mu$ L, and absolute neutrophil count >500 cells/ $\mu$ L         |
| <b>Complete remission with incomplete haematologic recovery (CRi)</b> | Bone marrow blasts $\leq$ 5% and incomplete recovery of peripheral blood counts                                           |
| <b>Disease-free survival (DFS)</b>                                    | Time from blinatumomab initiation until relapse or death                                                                  |
| <b>Measurable Residual Disease (MRD) response</b>                     | Evaluated at a level of $<10^{-4}$ , assessed by polymerase chain reaction, flow cytometry, or next-generation sequencing |
| <b>Overall Survival (OS)</b>                                          | Time from blinatumomab initiation until death                                                                             |
| <b>Relapse</b>                                                        | Bone marrow blasts >5% or blasts in peripheral blood after documented CR/CRh/CRi                                          |
| <b>Relapse-free survival (RFS)</b>                                    | Time from CR/CRh/CRi until relapse or death                                                                               |
| <b>Treatment-emergent adverse events (TEAEs)</b>                      | Adverse events occurring between blinatumomab initiation and 30 days after the last infusion                              |
| <b>Treatment-related TEAEs (TR-TEAEs)</b>                             | TEAEs considered by the treating physician to be related to blinatumomab                                                  |

**Supplementary Table 3.** Disease and treatment characteristics in patients with R/R Ph-  
BCP-ALL with prior allo-HSCT

|                                                                 | <b>Adult R/R Ph- BCP-<br/>ALL<br/>(N=38)</b> | <b>Adult R/R Ph- BCP-<br/>ALL LFR<br/>(N=17)</b> |
|-----------------------------------------------------------------|----------------------------------------------|--------------------------------------------------|
| Age at ALL diagnosis (years), median (min–max)                  | 33.5<br>(16.0–62.0)                          | 31.0<br>(18.0–55.0)                              |
| <b>Disease Characteristics</b>                                  |                                              |                                                  |
| <b>BCP-ALL subtype, n (%)</b>                                   |                                              |                                                  |
| Pro-BCP-ALL                                                     | 8 (21.1)                                     | 4 (23.5)                                         |
| Pre-BCP-ALL                                                     | 11 (28.9)                                    | 5 (29.4)                                         |
| C-ALL                                                           | 7 (18.4)                                     | 3 (17.6)                                         |
| BCP-ALL with recurrent genetic abnormality                      | 8 (21.1)                                     | 3 (17.6)                                         |
| Missing                                                         | 4 (10.5)                                     | 2 (11.8)                                         |
| <b>WBC, n (%)</b>                                               |                                              |                                                  |
| <30,000/ $\mu$ L                                                | 19 (50.0)                                    | 8 (47.1)                                         |
| $\geq$ 30,000/ $\mu$ L                                          | 12 (31.6)                                    | 8 (47.1)                                         |
| Unknown                                                         | 7 (18.4)                                     | 1 (5.9)                                          |
| <b>Extramedullary disease, n (%)</b>                            | 4 (10.5)                                     | 1 (5.9)                                          |
| CNS                                                             | 3 (7.9)                                      | 1 (5.9)                                          |
| Testis                                                          | 0 (0.0)                                      | 0 (0.0)                                          |
| Other                                                           | 1 (2.6)                                      | 0 (0.0)                                          |
| <b>Disease status at time of blinatumomab initiation, n (%)</b> |                                              |                                                  |
| Primary refractory                                              | 0 (0.0)                                      | 0 (0.0)                                          |
| Refractory to salvage therapy                                   | 3 (7.9)                                      | 0 (0.0)                                          |
| Missing                                                         | 0 (0.0)                                      | 0 (0.0)                                          |

|                                                                                    |                     |                    |
|------------------------------------------------------------------------------------|---------------------|--------------------|
| Late first relapse (duration of prior remission >12 months)                        | 17 (44.7)           | 17 (100.0)         |
| Untreated second or greater relapse                                                | 11 (28.9)           | 0 (0.0)            |
| Missing                                                                            | 0 (0.0)             | 0 (0.0)            |
| Morphological CR MRD+                                                              | 0 (0.0)             | 0 (0.0)            |
| Missing                                                                            | 2 (5.3)             | 1 (5.9)            |
| Untreated ALL in CNS                                                               | 0 (0.0)             | 0 (0.0)            |
| Missing                                                                            | 6 (15.8)            | 3 (17.6)           |
| <b>Prior Treatment History</b>                                                     |                     |                    |
| <b>Previous HSCT, n (%)</b>                                                        | 38 (100.0)          | 17 (100.0)         |
| Autologous                                                                         | 0 (0.0)             | 0 (0.0)            |
| Allogeneic                                                                         | 38 (100.0)          | 17 (100.0)         |
| <b>Time from previous HSCT to start of blinatumomab (months), median (min–max)</b> | 12.1<br>(2.4–137.7) | 17.3<br>(8.5–77.1) |
| <b>Prior lines of anti-cancer therapy for ALL, n (%)</b>                           |                     |                    |
| Frontline chemotherapy                                                             | 16 (42.1)           | 11 (64.7)          |
| First salvage chemotherapy                                                         | 8 (21.1)            | 0 (0.0)            |
| Second salvage chemotherapy                                                        | 3 (7.9)             | 0 (0.0)            |
| Third or later salvage chemotherapy                                                | 1 (2.6)             | 0 (0.0)            |
| Conditioning regimen for HSCT                                                      | 8 (21.1)            | 5 (29.4)           |
| Other                                                                              | 2 (5.3)             | 1 (5.9)            |
| <b>Treatment Characteristics</b>                                                   |                     |                    |
| Number of cycles started, median (min–max)                                         | 2.5 (1–9)           | 2 (1–9)            |
| Duration of treatment (days), median (min–max)                                     | 67<br>(12.0–215.0)  | 61<br>(13.0–215.0) |

ALL, acute lymphoblastic leukaemia; allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic leukaemia; C-ALL, common acute lymphoblastic leukaemia; CNS, central nervous system; CR, complete remission; HSCT, haematopoietic stem cell transplant; max, maximum; min, minimum; NA, not applicable; Ph, Philadelphia chromosome; WBC, white blood cell.

**Supplementary Table 4.** Treatment characteristics

| Characteristics                                                                                              | Entire Study<br>Cohort<br>(N=264) | Adult R/R Ph- BCP-ALL<br>(N=183) |                      | Adult MRD+<br>Ph- BCP-ALL<br>(N=46) |
|--------------------------------------------------------------------------------------------------------------|-----------------------------------|----------------------------------|----------------------|-------------------------------------|
|                                                                                                              |                                   | Overall<br>(N=183)               | LFR<br>(N=60)        |                                     |
| Number of cycles started,<br>median (min–max)                                                                | 2.0<br>(1.0–9.0)                  | 2.0<br>(1.0–9.0)                 | 2.0<br>(1.0–9.0)     | 2.0<br>(1.0–6.0)                    |
| Duration of treatment (days),<br>median (min–max)                                                            | 57.0<br>(6.0–215.0)               | 57.0<br>(6.0–215.0)              | 58.0<br>(13.0–215.0) | 57.0<br>(16.0–172.0)                |
| Duration of treatment in patients with HSCT<br>prior to blinatumomab (days), median (min–<br>max)            | 59.0<br>(12.0–215.0)              | 67.0<br>(13.0–215.0)             | 61.0<br>(13.0–215.0) | 56.5<br>(29.0–57.0)                 |
| Duration of treatment in patients who did not<br>have HSCT prior to blinatumomab (days),<br>median (min–max) | 56.5<br>(6.0–172.0)               | 56.0<br>(6.0–156.0)              | 58.0<br>(25.0–149.0) | 57.5<br>(16.0–172.0)                |
| <b>Dose interruptions, n (%)</b>                                                                             |                                   |                                  |                      |                                     |
| None                                                                                                         | 150 (56.8)                        | 95 (51.9)                        | 37 (61.7)            | 31 (67.4)                           |
| Adverse event                                                                                                | 86 (32.6)                         | 68 (37.2)                        | 17 (28.3)            | 10 (21.7)                           |
| Dose administration error                                                                                    | 2 (0.8)                           | 1 (0.5)                          | 0 (0.0)              | 1 (2.2)                             |
| Patient request                                                                                              | 2 (0.8)                           | 2 (1.1)                          | 0 (0.0)              | 0 (0.0)                             |
| Device complaint                                                                                             | 2 (0.8)                           | 1 (0.5)                          | 0 (0.0)              | 0 (0.0)                             |
| Infusion bag emptied prematurely                                                                             | 1 (0.4)                           | 1 (0.5)                          | 0 (0.0)              | 0 (0.0)                             |
| Other                                                                                                        | 37 (14.0)                         | 27 (14.8)                        | 10 (16.7)            | 6 (13.0)                            |

BCP-ALL, B-cell precursor acute lymphoblastic leukaemia; HSCT, haematopoietic stem cell transplant; LFR, late first relapse; max, maximum; min, minimum; MRD, measurable residual disease; Ph, Philadelphia chromosome; R/R, relapsed/refractory.

**Supplementary Table 5.** Disease-free survival outcomes in patients with MRD+ Ph- BCP-ALL by subgroups

|                                  | Adult MRD+ Ph- BCP-ALL (N=46) |                |                                                    |                                      |
|----------------------------------|-------------------------------|----------------|----------------------------------------------------|--------------------------------------|
|                                  | Death, n (%)                  | Relapse, n (%) | Time to Death or Relapse (Months), Median (95% CI) | KM Estimate at 24 Months, % (95% CI) |
| <b>All patients (N=46)</b>       | 5 (10.9)                      | 18 (39.1)      | 31.2 (5.9–NE)                                      | 54 (39–67)                           |
| <b>CR1 (n=28)</b>                | 2 (7.1)                       | 10 (35.7)      | NE (11.4–NE)                                       | 64 (44–79)                           |
| <b>CR2+ (n=13)</b>               | 2 (15.4)                      | 4 (30.8)       | NE (2.8–NE)                                        | 54 (25–76)                           |
| <b>Prior allo-HSCT (n=4)</b>     | 1 (25.0)                      | 3 (75.0)       | 2.7 (1.4–NE)                                       | 0 (NE–NE)                            |
| <b>No prior allo-HSCT (n=42)</b> | 4 (9.5)                       | 15 (35.7)      | NE (11.4–NE)                                       | 60 (43–73)                           |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic

leukaemia; CI, confidence interval; CR1, patients who received blinatumomab as the first remission; CR2, patients

who received blinatumomab as subsequent remissions; KM, Kaplan–Meier; MRD, measurable residual disease; NE,

not estimable; Ph, Philadelphia chromosome.

**Supplementary Table 6.** Overall survival outcomes in patients with MRD+ Ph- BCP-ALL by subgroups

|                                      | Adult MRD+ Ph- BCP-ALL (N=46) |                                                  |                                            |                                                         |                                                  |                                            |
|--------------------------------------|-------------------------------|--------------------------------------------------|--------------------------------------------|---------------------------------------------------------|--------------------------------------------------|--------------------------------------------|
|                                      | Overall survival              |                                                  |                                            | Overall survival<br>(Censored at the time of allo-HSCT) |                                                  |                                            |
|                                      | Death,<br>n (%)               | Time to death<br>(months),<br>median (95%<br>CI) | KM estimate<br>at 24 months,<br>% (95% CI) | Death,<br>n (%)                                         | Time to death<br>(months),<br>median (95%<br>CI) | KM estimate<br>at 24 months,<br>% (95% CI) |
| <b>All patients (N=46)</b>           | 17 (37.0)                     | NE (36.0–NE)                                     | 67 (51–79)                                 | 8 (17.4)                                                | NE (13.7–NE)                                     | 54 (24–77)                                 |
| <b>CR1 (n=28)</b>                    | 7 (25.0)                      | NE (39.3–NE)                                     | 82 (62–92)                                 | 2 (7.1)                                                 | NE (23.2–NE)                                     | 73 (24–93)                                 |
| <b>CR2+ (n=13)</b>                   | 5 (38.5)                      | NE (12.2–NE)                                     | 62 (31–82)                                 | 2 (15.4)                                                | NE (4.2–NE)                                      | 76 (31–94)                                 |
| <b>Prior allo-HSCT<br/>(n=4)</b>     | 4 (100.0)                     | 5.4 (1.4–NE)                                     | 0 (NE–NE)                                  | 3 (75.0)                                                | 4.5 (1.4–NE)                                     | 0 (NE–NE)                                  |
| <b>No prior allo-HSCT<br/>(n=42)</b> | 13 (31.0)                     | NE (39.3–NE)                                     | 73 (57–84)                                 | 5 (11.9)                                                | NE (13.7–NE)                                     | 62 (26–84)                                 |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic

leukaemia; CI, confidence interval; CR1, patients who received blinatumomab as the first remission; CR2+, patients who received blinatumomab as subsequent remissions; KM, Kaplan–Meier; MRD, measurable residual disease; NE, not estimable; Ph, Philadelphia chromosome.

**Supplementary Table 7.** Relapse-free survival outcomes among CR/CRh/CRi responders in patients with R/R Ph<sup>+</sup> BCP-ALL by subgroups

|                           | Adult R/R Ph <sup>+</sup> BCP-ALL (N=183) |                 |                   |                                                          |                                            |
|---------------------------|-------------------------------------------|-----------------|-------------------|----------------------------------------------------------|--------------------------------------------|
|                           | N                                         | Death,<br>n (%) | Relapse,<br>n (%) | Time to death or<br>relapse (months),<br>median (95% CI) | KM estimate at<br>24 months, %<br>(95% CI) |
| <b>Overall</b>            | 150                                       | 29 (19.3)       | 61 (40.7)         | 15.9 (8.7–41.3)                                          | 43 (35–51)                                 |
| MRD response              | 102                                       | 18 (17.6)       | 38 (37.3)         | 20.5 (10.5–NE)                                           | 50 (39–59)                                 |
| No MRD response           | 28                                        | 5 (17.9)        | 15 (53.6)         | 6.5 (1.8–22.5)                                           | 29 (14–47)                                 |
| <b>LFR</b>                | 53                                        | 5 (9.4)         | 19 (35.8)         | NE (11.3–NE)                                             | 58 (43–70)                                 |
| <b>S1</b>                 | 92                                        | 16 (17.4)       | 38 (41.3)         | 16.0 (8.9–45.4)                                          | 42 (32–52)                                 |
| <b>S2+</b>                | 41                                        | 5 (12.2)        | 16 (39.0)         | 8.7 (6.5–73.3)                                           | 42 (27–56)                                 |
| <b>Prior allo-HSCT</b>    | 34                                        | 4 (11.8)        | 18 (52.9)         | 11.3 (6.0–73.3)                                          | 41 (25–57)                                 |
| <b>No prior allo-HSCT</b> | 116                                       | 25 (21.6)       | 43 (37.1)         | 18.5 (8.9–41.4)                                          | 44 (34–53)                                 |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic

leukaemia; CI, confidence interval; CR, complete remission with full recovery of peripheral blood counts; CRh,

complete remission with partial recovery of peripheral blood counts; CRi, complete remission with incomplete

recovery of peripheral blood counts; KM, Kaplan–Meier; LFR, late first relapse; MRD, measurable residual disease;

NE, not estimable; Ph, Philadelphia chromosome; R/R, relapsed/refractory; S1, patients who received blinatumomab

as first salvage therapy; S2+, patients who received blinatumomab as subsequent salvage therapy.

**Supplementary Table 8.** Overall survival outcomes in patients with R/R Ph- BCP-ALL by subgroups

|                           | Adult R/R Ph- BCP-ALL (N=183) |              |                                         |                                      |                                                 |              |                                         |                                      |
|---------------------------|-------------------------------|--------------|-----------------------------------------|--------------------------------------|-------------------------------------------------|--------------|-----------------------------------------|--------------------------------------|
|                           | Overall survival              |              |                                         |                                      | Overall Survival (Censored at the Time of HSCT) |              |                                         |                                      |
|                           | N                             | Death, n (%) | Time to death (months), median (95% CI) | KM estimate at 24 months, % (95% CI) | N                                               | Death, n (%) | Time to death (months), median (95% CI) | KM estimate at 24 months, % (95% CI) |
| <b>Overall</b>            | 183                           | 97 (53.0)    | 29.9 (17.8–NE)                          | 52 (44–59)                           | 183                                             | 57 (31.1)    | 20.1 (11.9–58.2)                        | 41 (30–53)                           |
| <b>LFR</b>                | 60                            | 19 (31.7)    | NE (NE–NE)                              | 71 (58–81)                           | 60                                              | 10 (16.7)    | NE (14.6–NE)                            | 57 (34–75)                           |
| <b>S1</b>                 | 108                           | 55 (50.9)    | 31.7 (17.8–NE)                          | 53 (43–62)                           | 108                                             | 33 (30.6)    | 14.6 (9.6–NE)                           | 36 (22–50)                           |
| <b>S2+</b>                | 58                            | 33 (56.9)    | 13.0 (8.6–NE)                           | 48 (35–60)                           | 58                                              | 19 (32.8)    | 20.4 (4.4–NE)                           | 41 (19–63)                           |
| <b>Prior allo-HSCT</b>    | 38                            | 16 (42.1)    | 74.7 (22.1–NE)                          | 65 (48–78)                           | 38                                              | 9 (23.7)     | NE (12.3–NE)                            | 72 (49–86)                           |
| <b>No prior allo-HSCT</b> | 145                           | 81 (55.9)    | 22.6 (12.7–NE)                          | 49 (40–57)                           | 145                                             | 48 (33.1)    | 12.2 (8.7–20.4)                         | 28 (16–42)                           |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic

leukaemia; CI, confidence interval; KM, Kaplan–Meier; LFR, late first relapse; NE, not estimable; Ph, Philadelphia

chromosome; R/R, relapsed/refractory; S1, patients who received blinatumomab as first salvage therapy; S2+,

patients who received blinatumomab as subsequent salvage therapy.

**Supplementary Table 9.** HSCT following blinatumomab treatment in adult patients with MRD+ Ph- BCP-ALL

|                                                                                             | <b>Adult MRD+ Ph-<br/>BCP-ALL (N=46)</b> |
|---------------------------------------------------------------------------------------------|------------------------------------------|
| <b>Allo-HSCT status, n (%)</b>                                                              |                                          |
| Received after blinatumomab therapy                                                         | 33 (71.7)                                |
| Without anti-cancer therapy prior to allo-HSCT                                              | 28 (84.8)                                |
| With anti-cancer therapy prior to allo-HSCT                                                 | 5 (15.2)                                 |
| Did not receive                                                                             | 3 (6.5)                                  |
| Not available                                                                               | 10 (21.7)                                |
| <b>Intensity of conditioning regimen, n (%)</b>                                             |                                          |
| Myeloablative                                                                               | 23 (69.7)                                |
| Reduced intensity/non-myeloablative                                                         | 4 (12.1)                                 |
| Not available                                                                               | 6 (18.2)                                 |
| <b>Time to transplant, median in months (min–max)</b>                                       |                                          |
| Among patients (n=28) without anti-cancer therapy prior to allo-HSCT                        | 2.4 (0.3–6.4)                            |
| Among patients (n=5) with anti-cancer therapy prior to allo-HSCT                            | 6.2 (1.4–8.7)                            |
| <b>Mortality after allo-HSCT (overall)</b>                                                  | <b>N=33</b>                              |
| Death, n (%)                                                                                | 9 (27.3)                                 |
| Time to death (months), median (min–max)                                                    | NE (1.4–32.3)                            |
| <b>Mortality after allo-HSCT in patients without anti-cancer therapy prior to allo-HSCT</b> | <b>N=28</b>                              |
| Death, n (%)                                                                                | 5 (17.9)                                 |
| Relapse-related                                                                             | 4 (14.3)                                 |
| Non-relapse-related                                                                         | 1 (3.6)                                  |
| Time to death (months), median (min–max)                                                    | NE (1.6–32.3)                            |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic leukaemia; max, maximum; min, minimum; NE, not estimable; Ph, Philadelphia chromosome; R/R, relapsed/refractory.

**Supplementary Table 10.** HSCT following blinatumomab treatment in adult patients with R/R

Ph- B-ALL

|                                                                                        | <b>Adult R/R Ph-<br/>BCP-ALL<br/>(N=183)</b> | <b>Adult R/R Ph-<br/>BCP-ALL LFR<br/>(N=60)</b> |
|----------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------|
| <b>Allo-HSCT status after blinatumomab, n (%)</b>                                      |                                              |                                                 |
| Received                                                                               | 101 (55.2)                                   | 39 (65.0)                                       |
| As first allo-HSCT                                                                     | 83 (82.2)                                    | 29 (74.4)                                       |
| In patients who achieved CR/CRh/CRi and received                                       | 76 (75.2)                                    | 25 (64.1)                                       |
| First allo-HSCT without anti-cancer therapy                                            | 56                                           | 23                                              |
| First allo-HSCT with anti-cancer therapy                                               | 20                                           | 2                                               |
| After a prior allo-HSCT                                                                | 18 (17.8)                                    | 10 (25.6)                                       |
| In patients who achieved CR/CRh/CRi and received                                       | 16 (88.9)                                    | 8 (80)                                          |
| Allo-HSCT without anti-cancer therapy                                                  | 8                                            | 4                                               |
| Allo-HSCT with anti-cancer therapy                                                     | 8                                            | 4                                               |
| Did not receive                                                                        | 31 (16.9)                                    | 10 (16.7)                                       |
| Not available                                                                          | 51 (27.9)                                    | 11 (18.3)                                       |
| <b>Intensity of conditioning regimen among patients receiving<br/>allo-HSCT, n (%)</b> |                                              |                                                 |
| Myeloablative                                                                          | 66 (65.3)                                    | 25 (64.1)                                       |
| Reduced intensity/non-myeloablative                                                    | 16 (15.8)                                    | 4 (10.3)                                        |
| Not available                                                                          | 21 (20.8)                                    | 10 (25.6)                                       |
| <b>Allo-HSCT procedure in patients achieving CR/CRh/CRi, n (%)</b>                     |                                              |                                                 |
| Without anti-cancer therapy prior to allo-HSCT                                         | 64 (68.8)                                    | 27 (79.4)                                       |
| With anti-cancer therapy prior to allo-HSCT                                            | 28 (30.1)                                    | 6 (17.6)                                        |
| <b>Allo-HSCT procedure in patients without CR/CRh/CRi, n (%)</b>                       |                                              |                                                 |
| With anti-cancer therapy prior to allo-HSCT                                            | 8 (100%)                                     | 5 (100%)                                        |

|                                                                                                           | <b>Adult R/R Ph-<br/>BCP-ALL<br/>(N=183)</b> | <b>Adult R/R Ph-<br/>BCP-ALL LFR<br/>(N=60)</b> |
|-----------------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------------------|
| <b>Time to transplant, median in months (min–max)</b>                                                     |                                              |                                                 |
| In CR/CRh/CRi and no anti-cancer therapy prior to allo-HSCT                                               | 2.4 (0.2–10.1)                               | 2.6 (0.3–4.6)                                   |
| In CR/CRh/CRi and anti-cancer therapy prior to allo-HSCT                                                  | 8.4 (0.3–36.8)                               | NE (2.8–36.8)                                   |
| CR/CRh/CRi not achieved and anti-cancer therapy prior to allo-HSCT                                        | 8.5 (2.5–8.5)                                | 5.0 (2.5–7.3)                                   |
| <b>Mortality after allo-HSCT overall</b>                                                                  |                                              |                                                 |
| Death, n (%)                                                                                              | 40 (39.6)                                    | 9 (23.1)                                        |
| Time to death, median in months (min–max)                                                                 | NE (0.5–72.0)                                | NE (0.5–37.9)                                   |
| <b>Mortality after allo-HSCT in patients in CR/CRh/CRi without anti-cancer therapy prior to allo-HSCT</b> |                                              |                                                 |
|                                                                                                           | <b>N=64</b>                                  | <b>N=27</b>                                     |
| Death, n (%)                                                                                              | 22/64 (34.4)                                 | 6/27 (22.2)                                     |
| In patients with prior allo-HSCT                                                                          | 3/8 (37.5)                                   | 1/4 (25.0)                                      |
| Relapse-related                                                                                           | 1/8 (12.5)                                   | 1/4 (25.0)                                      |
| Non-relapse-related                                                                                       | 2/8 (25.0)                                   | 0/4 (0.0)                                       |
| In patients with no prior allo-HSCT                                                                       | 19/56 (33.9)                                 | 5/23 (21.7)                                     |
| Relapse-related                                                                                           | 8/56 (14.3)                                  | 3/23 (13.0)                                     |
| Non-relapse-related                                                                                       | 11/56 (19.6)                                 | 2/23 (8.7)                                      |
| Time to death, median in months (min–max)                                                                 | NE (0.5–37.9)                                | NE (0.5–37.9)                                   |
| Among patients with prior allo-HSCT                                                                       | NE (3.7–18.6)                                | NE (18.6–18.6)                                  |
| Among patients with no prior allo-HSCT                                                                    | NE (0.5–37.9)                                | NE (0.5–37.9)                                   |

allo-HSCT, allogeneic haematopoietic stem cell transplant; BCP-ALL, B-cell precursor acute lymphoblastic

leukaemia; CR, complete remission with full recovery of peripheral blood counts; CRh, complete remission with partial recovery of peripheral blood counts; CRi, complete remission with incomplete recovery of peripheral blood counts; LFR, late first relapse; max, maximum; min, minimum; NE, not estimable; Ph, Philadelphia chromosome; R/R, relapsed/refractory.

**Supplementary Table 11. Safety outcomes**

| AEs, n (%)                             | Full analysis set <sup>a</sup><br>(N=264) |            | Adult MRD+ Ph-<br>BCP-ALL (N=46) |           | Adult R/R Ph-<br>BCP-ALL (N=183) |            |
|----------------------------------------|-------------------------------------------|------------|----------------------------------|-----------|----------------------------------|------------|
|                                        | TEAE                                      | TR-TEAE    | TEAE                             | TR-TEAE   | TEAE                             | TR-TEAE    |
| <b>Any grade</b>                       | 240 (90.9)                                | 182 (68.9) | 39 (84.8)                        | 32 (69.6) | 170 (92.9)                       | 127 (69.4) |
| <b>Grade ≥3</b>                        | 153 (58.0)                                | 91 (34.5)  | 18 (39.1)                        | 12 (26.1) | 111 (60.7)                       | 64 (35.0)  |
| <b>Grade ≥4</b>                        | 71 (26.9)                                 | 31 (11.7)  | 7 (15.2)                         | 4 (8.7)   | 55 (30.1)                        | 24 (13.1)  |
| <b>Serious</b>                         | 139 (52.7)                                | 77 (29.2)  | 17 (37.0)                        | 12 (26.1) | 98 (53.6)                        | 50 (27.3)  |
| <b>Fatal</b>                           | 20 (7.6)                                  | 2 (0.8)    | 3 (6.5)                          | 1 (2.2)   | 15 (8.2)                         | 1 (0.5)    |
| <b>Leading to drug interruption</b>    | 83 (31.4)                                 | 66 (25.0)  | 10 (21.7)                        | 8 (17.4)  | 65 (35.5)                        | 52 (28.4)  |
| <b>Leading to drug discontinuation</b> | 26 (9.8)                                  | 13 (4.9)   | 2 (4.3)                          | 0 (0)     | 20 (10.9)                        | 10 (5.5)   |
| <b>AEs of interest, n (%)</b>          |                                           |            |                                  |           |                                  |            |
| <b>Neurologic AEs</b>                  | 110 (41.7)                                | 74 (28.0)  | 19 (41.3)                        | 16 (34.8) | 77 (42.1)                        | 47 (25.7)  |
| Grade ≥3                               | 28 (10.6)                                 | 21 (8.0)   | 4 (8.7)                          | 4 (8.7)   | 22 (12.0)                        | 15 (8.2)   |
| Grade ≥4                               | 4 (1.5)                                   | 3 (1.1)    | 0 (0)                            | 0 (0)     | 3 (1.6)                          | 2 (1.1)    |
| Serious                                | 26 (9.8)                                  | 21 (8.0)   | 3 (6.5)                          | 3 (6.5)   | 20 (10.9)                        | 15 (8.2)   |
| Fatal                                  | 1 (0.4)                                   | 1 (0.4)    | 0 (0)                            | 0 (0)     | 1 (0.5)                          | 1 (0.5)    |
| Leading to drug interruption           | 31 (11.7)                                 | 30 (11.4)  | 6 (13.0)                         | 6 (13.0)  | 22 (12.0)                        | 21 (11.5)  |
| Leading to drug discontinuation        | 8 (3.0)                                   | 7 (2.7)    | 0 (0)                            | 0 (0)     | 6 (3.3)                          | 5 (2.7)    |
| <b>Cytokine release syndrome</b>       | 39 (14.8)                                 | 38 (14.4)  | 5 (10.9)                         | 5 (10.9)  | 30 (16.4)                        | 29 (15.8)  |
| Grade ≥3                               | 10 (3.8)                                  | 10 (3.8)   | 0 (0)                            | 0 (0)     | 10 (5.5)                         | 10 (5.5)   |
| Grade ≥4                               | 0 (0)                                     | 0 (0)      | 0 (0)                            | 0 (0)     | 0 (0)                            | 0 (0)      |
| Serious                                | 25 (9.5)                                  | 24 (9.1)   | 2 (4.3)                          | 2 (4.3)   | 19 (10.4)                        | 18 (9.8)   |
| Fatal                                  | 0 (0)                                     | 0 (0)      | 0 (0)                            | 0 (0)     | 0 (0)                            | 0 (0)      |
| Leading to drug interruption           | 14 (5.3)                                  | 14 (5.3)   | 0 (0)                            | 0 (0)     | 14 (7.7)                         | 14 (7.7)   |

| AEs, n (%)                      | Full analysis set <sup>a</sup><br>(N=264) |         | Adult MRD+ Ph-<br>BCP-ALL (N=46) |         | Adult R/R Ph-<br>BCP-ALL (N=183) |         |
|---------------------------------|-------------------------------------------|---------|----------------------------------|---------|----------------------------------|---------|
|                                 | TEAE                                      | TR-TEAE | TEAE                             | TR-TEAE | TEAE                             | TR-TEAE |
| Leading to drug discontinuation | 0 (0)                                     | 0 (0)   | 0 (0)                            | 0 (0)   | 0 (0)                            | 0 (0)   |
| <b>Opportunistic infections</b> | 9 (3.4)                                   | 4 (1.5) | 2 (4.3)                          | 1 (2.2) | 6 (3.3)                          | 3 (1.6) |
| Grade ≥3                        | 4 (1.5)                                   | 1 (0.4) | 1 (2.2)                          | 0 (0)   | 3 (1.6)                          | 1 (1.7) |
| Grade ≥4                        | 1 (0.4)                                   | 0 (0)   | 0 (0)                            | 0 (0)   | 1 (0.5)                          | 0 (0)   |
| Serious                         | 7 (2.7)                                   | 3 (1.1) | 2 (4.3)                          | 1 (2.2) | 4 (2.2)                          | 2 (1.1) |
| Fatal                           | 1 (0.4)                                   | 0 (0)   | 0 (0)                            | 0 (0)   | 1 (0.5)                          | 0 (0)   |
| Leading to drug interruption    | 0 (0)                                     | 0 (0)   | 0 (0)                            | 0 (0)   | 0 (0)                            | 0 (0)   |
| Leading to drug discontinuation | 1 (0.4)                                   | 0 (0)   | 0 (0)                            | 0 (0)   | 1 (0.5)                          | 0 (0)   |

AE, adverse event; BCP-ALL, B-cell precursor acute lymphoblastic leukaemia; MRD, measurable residual disease;

Ph, Philadelphia chromosome; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event; TR-TEAE, treatment-related treatment-emergent adverse event.

<sup>a</sup>The full analysis set included an additional 35 patients with Ph+ BCP-ALL: nine with Ph+ R/R BCP-ALL (eight adult patients, one paediatric patient), five adult patients with Ph+ MRD+ BCP-ALL, and 21 with other ALL diagnoses.

**Supplementary Table 12.** Incidence of adverse events by age

|                                  | <b>≥18 and &lt;65 Years<br/>(N=227)</b> | <b>≥65 Years<br/>(N=36)</b> |
|----------------------------------|-----------------------------------------|-----------------------------|
| <b>Any-grade TEAEs, n (%)</b>    | <b>203 (89.4)</b>                       | <b>36 (100.0)</b>           |
| Grade ≥3                         | 125 (55.1)                              | 27 (75.0)                   |
| Grade ≥4                         | 58 (25.6)                               | 13 (36.1)                   |
| Serious                          | 111 (48.9)                              | 27 (75.0)                   |
| Fatal                            | 14 (6.2)                                | 6 (16.7)                    |
| Leading to drug interruption     | 64 (28.2)                               | 19 (52.8)                   |
| Leading to drug discontinuation  | 21 (9.3)                                | 5 (13.9)                    |
| <b>Any-grade TR-TEAEs, n (%)</b> | <b>150 (66.1)</b>                       | <b>31 (86.1)</b>            |
| Grade ≥3                         | 73 (32.2)                               | 18 (50.0)                   |
| Grade ≥4                         | 26 (11.5)                               | 5 (13.9)                    |
| Serious                          | 58 (25.6)                               | 19 (52.8)                   |
| Fatal                            | 1 (0.4)                                 | 1 (2.8)                     |
| Leading to drug interruption     | 51 (22.5)                               | 15 (41.7)                   |
| Leading to drug discontinuation  | 10 (4.4)                                | 3 (8.3)                     |
| <b>TEAEs of interest, n (%)</b>  |                                         |                             |
| <b>Neurologic adverse events</b> | <b>92 (40.5)</b>                        | <b>18 (50.0)</b>            |
| Grade ≥3                         | 23 (10.1)                               | 5 (13.9)                    |
| Grade ≥4                         | 2 (0.9)                                 | 2 (5.6)                     |
| Serious                          | 18 (7.9)                                | 8 (22.2)                    |
| Fatal                            | 0 (0.0)                                 | 1 (2.8)                     |
| Leading to drug interruption     | 22 (9.7)                                | 9 (25.0)                    |
| Leading to drug discontinuation  | 6 (2.6)                                 | 2 (5.6)                     |
| <b>Cytokine release syndrome</b> | <b>33 (14.5)</b>                        | <b>6 (16.7)</b>             |
| Grade ≥3                         | 9 (4.0)                                 | 1 (2.8)                     |

|                                 | <b>≥18 and &lt;65 Years<br/>(N=227)</b> | <b>≥65 Years<br/>(N=36)</b> |
|---------------------------------|-----------------------------------------|-----------------------------|
| Grade ≥4                        | 0 (0.0)                                 | 0 (0.0)                     |
| Serious                         | 20 (8.8)                                | 5 (13.9)                    |
| Fatal                           | 0 (0.0)                                 | 0 (0.0)                     |
| Leading to drug interruption    | 12 (5.3)                                | 2 (5.6)                     |
| Leading to drug discontinuation | 0 (0.0)                                 | 0 (0.0)                     |
| <b>Opportunistic infections</b> | 9 (4.0)                                 | 0 (0.0)                     |
| Grade ≥3                        | 4 (1.8)                                 | 0 (0.0)                     |
| Grade ≥4                        | 1 (0.4)                                 | 0 (0.0)                     |
| Serious                         | 7 (3.1)                                 | 0 (0.0)                     |
| Fatal                           | 1 (0.4)                                 | 0 (0.0)                     |
| Leading to drug interruption    | 0 (0.0)                                 | 0 (0.0)                     |
| Leading to drug discontinuation | 1 (0.4)                                 | 0 (0.0)                     |

TEAE, treatment-emergent adverse event; TR-TEAE, treatment-related treatment-emergent adverse event.

**Supplementary Table 13.** Description of medication errors in the study

|                                                                          | <b>Full Analysis<br/>Set<sup>a</sup><br/>(N=264)</b> | <b>Adult MRD+<br/>Ph- BCP-ALL<br/>(N=46)</b> | <b>Adult R/R Ph-<br/>BCP-ALL<br/>(N=183)</b> | <b>Adult R/R Ph-<br/>BCP-ALL LFR<br/>(N=60)</b> |
|--------------------------------------------------------------------------|------------------------------------------------------|----------------------------------------------|----------------------------------------------|-------------------------------------------------|
| <b>≥1 medication error, n (%)</b>                                        | 26 (9.8)                                             | 6 (13.0)                                     | 15 (8.2)                                     | 7 (11.7)                                        |
| 1 medication error                                                       | 22 (8.34)                                            | 4 (8.7)                                      | 13 (7.1)                                     | 6 (10.0)                                        |
| 2 medication errors                                                      | 3 (1.1)                                              | 2 (4.3)                                      | 1 (0.5)                                      | 0 (0.0)                                         |
| 3 medication errors                                                      | 1 (0.4)                                              | 0 (0)                                        | 1 (0.5)                                      | 1 (1.7)                                         |
| <b>Total medication errors, n</b>                                        | 31                                                   | 8                                            | 18                                           | 9                                               |
| <b>Where did the error occur, n (%)</b>                                  |                                                      |                                              |                                              |                                                 |
| Inpatient                                                                | 16 (51.6)                                            | 5 (62.5)                                     | 10 (55.6)                                    | 7 (77.8)                                        |
| Outpatient clinic                                                        | 6 (19.4)                                             | 3 (37.5)                                     | 2 (11.1)                                     | 1 (11.1)                                        |
| Outside a medical facility                                               | 9 (29.0)                                             | 0 (0.0)                                      | 6 (33.3)                                     | 1 (11.1)                                        |
| <b>Type of medication error, n (%)</b>                                   |                                                      |                                              |                                              |                                                 |
| Preparation                                                              | 1 (3.2)                                              | 0 (0)                                        | 1 (5.6)                                      | 0 (0)                                           |
| Administration                                                           | 22 (71.0)                                            | 6 (75.0)                                     | 12 (66.7)                                    | 6 (66.7)                                        |
| Product storage                                                          | 0 (0)                                                | 0 (0)                                        | 0 (0)                                        | 0 (0)                                           |
| Accidental exposure                                                      | 0 (0)                                                | 0 (0)                                        | 0 (0)                                        | 0 (0)                                           |
| Other                                                                    | 8 (25.8)                                             | 2 (25.0)                                     | 5 (27.8)                                     | 3 (33.3)                                        |
| <b>If administration error, who was responsible for the error, n (%)</b> |                                                      |                                              |                                              |                                                 |
| Operator use error                                                       | 12 (38.7)                                            | 4 (50.0)                                     | 6 (33.3)                                     | 4 (44.4)                                        |
| Pump malfunction                                                         | 7 (22.6)                                             | 1 (12.5)                                     | 5 (27.8)                                     | 2 (22.2)                                        |
| Line flush                                                               | 0 (0)                                                | 0 (0)                                        | 0 (0)                                        | 0 (0)                                           |
| Other                                                                    | 2 (6.5)                                              | 0 (0)                                        | 0 (0)                                        | 0 (0)                                           |
| Unknown                                                                  | 1 (3.2)                                              | 0 (0)                                        | 1 (5.6)                                      | 0 (0)                                           |

BCP-ALL, B-cell precursor acute lymphoblastic leukaemia; LFR, late first relapse; MRD, measurable residual disease; Ph, Philadelphia chromosome; R/R, relapsed/refractory.

<sup>a</sup>The full analysis set included an additional 35 patients with Ph+ BCP-ALL: nine with Ph+ R/R BCP-ALL (eight adult patients, one paediatric patient), five adult patients with Ph+ MRD+ BCP-ALL, and 21 with other ALL diagnoses.