Relapses and treatment-related events contributed equally to poor prognosis in children with ABL-class fusion positive B-cell acute lymphoblastic leukemia treated according to AIEOP-BFM protocols

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Supplementary Material
Supplementary Tables and Figures

Table S1. Type of ABL class fusion and TKI treatment

| Type of fusion and fusion partner | ABL-class fusion pos. cases | Treatment without additional TKI | Treatment with additional TKI |
|----------------------------------|----------------------------|----------------------------------|-------------------------------|
| **Total**                        | 46                        | 33                               | 13                            |
| ABL1                             | 15                        | 10                               | 5                             |
| ETV6                             | 5                         | 3                                | 2                             |
| NUB214                           | 1                         | 0                                | 1                             |
| RANBP2                           | 1                         | 1                                | 0                             |
| RCSD1                            | 2                         | 2                                | 0                             |
| SHIP1                            | 1                         | 0                                | 1                             |
| ZMIZ1                            | 4                         | 4                                | 0                             |
| Not known                        | 1                         | 0                                | 1                             |
| **ABL2**                         | 5                         | 4                                | 1                             |
| RCSD1                            | 2                         | 2                                | 0                             |
| ZC3HAV                           | 2                         | 2                                | 0                             |
| Not known                        | 1                         | 0                                | 1                             |
| **CSF1R**                        | 3                         | 2                                | 1                             |
| MEF2D                            | 1                         | 1                                | 0                             |
| SSBP2                            | 2                         | 1                                | 1                             |
| **PDGFRB**                       | 23                        | 17                               | 6                             |
| EBF1                             | 19                        | 14                               | 5                             |
| ZNF608                           | 1                         | 1                                | 0                             |
| not known                        | 3                         | 2                                | 1                             |

¹TKI, tyrosine kinase inhibitor
Supplementary Figures

Figure S1: Type of fusion, treatment performed, type of TKI and EFS/follow-up time of those 13 patients treated with TKI in addition to chemotherapy. FLA(G), FLudarabin, Arabinosid C, (Granuloyte-Colony stimulating factor), HSCT, Hematopoietic stem cell transplantation.

Figure S2. Treatment outcome of patients with pediatric ABL-class fusion positive ALL. Cumulative incidence (CI) of relapses (CIR) and of treatment related mortality (CI-TRM) at 5 years. A) in PDGFRB-fusion pos. cases, B) in ABL1-fusion positive cases and C) in others (ABL2 n=5, CSFR n=2) at 5 years.

Figure S3. Treatment outcome of patients with pediatric ABL-class fusion positive ALL comparing patients treated without tyrosine kinase inhibitor (TKI, no-TKI) and with TKI (TKI). Kaplan-Meier estimates: A) cumulative incidence (CI) of relapses (CIR) at 5 years, B) of treatment related mortality (TRM) at 5 years.

Figure S4. Treatment outcome of patients with pediatric ABL-class fusion positive ALL comparing patients receiving hematopoietic stem cell transplantation (HSCT) to those not transplanted (No-HSCT). In the No-HSCT group, only those patients were considered without an event until the median waiting time to HSCT within the group receiving HSCT. Kaplan-Meier estimates: A) event free survival (EFS) at 5 years, B) overall survival (OS) at 5 years for the entire cohort. C) Cumulative incidence of relapses (CIR) at 5 years, D) of treatment related mortality (CI-TRM) at 5 years for the No-TKI group.

Figure S5. Treatment outcome of patients with pediatric ABL-class fusion positive ALL according to End of Induction Minimal residual disease (EoI-MRD). Kaplan-Meier estimates: A) event free survival (EFS) at 5 years, B) Cumulative incidence of relapses (CIR) and of treatment related mortality (CI-TRM) at 5 years.

Figure S6. Treatment outcome of patients with pediatric ABL-class fusion positive ALL according to End of Consolidation Minimal residual disease (EoC-MRD). Kaplan-Meier estimate of the event free survival (EFS) at 5 years. The proportion of patients who received hematopoietic stem cell transplantation is shown.
Figure S1
Figure S2
Figure S3

A

\[ P = 0.60 \]

- No-TKI: 5 y-CIR = 28.0 \pm 9.4\% (N=33, 8 events)
- TKI: 5 y-CIR = 12.6 \pm 12.8\% (N=13, 1 event)

B

\[ P = 0.34 \]

- No-TKI: 5 y-CI-TRM = 17.9 \pm 7.5\% (N=33, 5 events)
- TKI: 5 y-CI-TRM = 24.5 \pm 12.9\% (N=13, 3 events)
Figure S4
Figure S5
Figure S6

- **EoC-MRD ≥5×10^-4; 5 y-pEFS=46.2±12.1\% (N= 21, 11 events); HSCT: 19/21**
- **EoC-MRD <5×10^-4; 5 y-pEFS=56.7±15.4\% (N= 20, 6 events); HSCT: 3/20**

*P= .31*