SUPPLEMENTARY MATERIAL

Bosutinib in Japanese patients with newly diagnosed chronic phase chronic myeloid leukemia: final 3-year follow-up results of a phase 2 study

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| Category       | Adverse event criteria                                                                                                                                                                                                                                                                                                                                 |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cardiac        | • HLGTs in cardiac arrhythmias, heart failure, pericardial disorders  
• PTs in cardiac death, sudden cardiac death, sudden death, ejection fraction decreased  
• SMQ (narrow): Torsade de pointes/QT prolongation                                                                                                                                                                                                                      |
| Edema          | • PTs contain edema, weight increased                                                                                                                                                                                                                                                                                                                  |
| Effusion       | • PTs in pleural effusion, pericardial effusion                                                                                                                                                                                                                                                                                                     |
| Gastrointestinal | • PTs in nausea, regurgitation, retching, vomiting, vomiting projectile, diarrhea, defecation urgency, frequent bowel movements, gastrointestinal hypermotility                                                                                                                                                   |
| Hemorrhage     | • PTs in gastric occult blood positive, occult blood positive  
• SMQ (narrow): hemorrhage terms (excluding laboratory terms)                                                                                                                                                                                                                           |
| Hypertension   | • HLGT in vascular hypertensive disorders  
• PTs in BP abnormal, BP ambulatory abnormal, BP ambulatory increased, BP diastolic abnormal, BP diastolic increased, BP increased, BP systolic abnormal, BP systolic increased                                                                                                                                 |
| Infection      | • SOC in infections and infestations                                                                                                                                                                                                                                                                                                                   |
| Liver function | • Sub SMQs (narrow): cholestasis and jaundice of hepatic origin; hepatic failure, fibrosis and cirrhosis and other liver damage–related conditions; hepatitis, non-infectious; liver-related investigations, signs and symptoms (selected relevant)  
• PTs in ALT abnormal, ALT increased, AST abnormal, AST increased, bilirubin conjugated abnormal, bilirubin conjugated
increased, blood bilirubin abnormal, blood bilirubin increased, blood bilirubin unconjugated increased, hepatic enzyme abnormal, hepatic enzyme increased, hepatic function abnormal, hyperbilirubinemia, hypertransaminasemia, liver function test abnormal, transaminases abnormal, transaminases increased, blood ALP abnormal, blood ALP increased, liver function test increased

| Myelosuppression | • SMQs (narrow): hematopoietic cytopenias affecting >1 type of blood cell, hematopoietic erythropenia, hematopoietic leukopenia, hematopoietic thrombocytopenia
• PTs in bone marrow toxicity, hematocrit decreased, hemoglobin decreased, hematotoxicity, anemia |

| Rash | • HLTs in rashes, eruptions, and exanthem NEC; erythema; acne; dermatitis and eczema |

| Renal | • HLT in renal failure and impairment
• PTs in blood creatinine abnormal, blood creatinine increased, creatinine renal clearance abnormal, creatinine renal clearance decreased, glomerular filtration rate abnormal, glomerular filtration rate decreased |

| Vascular | • HLG Ts in coronary artery disorders; arteriosclerosis, stenosis, vascular insufficiency, and necrosis; embolism and thrombosis
• HLTs in arterial therapeutic procedures (excluding aortic), CNS hemorrhages and cerebrovascular accidents, CNS vascular disorders NEC, non–site specific vascular disorders NEC, peripheral vascular disorders NEC (excluding the 2 PTs flushing |
and hot flush), transient cerebrovascular events, vascular imaging procedures NEC, vascular therapeutic procedures NEC

*The following clustered terms for cytopenias including lymphopenia (PT = lymphopenia; lymphocyte count decreased), thrombocytopenia (PT = thrombocytopenia; platelet count decreased), anemia (PT = anemia; hemoglobin decreased), neutropenia (PT = neutropenia; neutrophil count decreased), leukopenia (PT = leukopenia; white blood cell count decreased) are used

ALP alkaline phosphatase; ALT alanine aminotransferase; AST aspartate aminotransferase; BP blood pressure; CNS central nervous system; HLGT High Level Group Term; HLT High Level Term; NEC not elsewhere classified; PT Preferred Term; SMQ standardized Medical Dictionary for Regulatory Activities query; SOC system organ class
Table S2  Major molecular response before and after dose escalation/reduction

|                              | Bosutinib (N = 60) |
|------------------------------|---------------------|
|                              | No escalation to ≥500 mg | Dose escalation to 500 mg | Dose escalation to 600 mg |
| Patients with/without escalation | 50 (83.3) | 10 (16.7) | 1 (1.7) |
| Attained/maintained MMR       | 33 (66.0) | 9 (90.0) | 1 (100) |
| First MMR following escalation | NA | 2 (22.2) | 1 (100) |
| MMR before and after escalation | NA | 7 (77.8) | 0 |
| MMR before but not after escalation | NA | 0 | 0 |

|                              | No reduction to ≤300 mg | Dose reduction to 300 mg | Dose reduction to 200 mg |
|------------------------------|------------------------|------------------------|-------------------------|
| Patients with/without reduction | 24 (40.0) | 36 (60.0) | 9 (15.0) |
| Attained/maintained MMR       | 19 (79.2) | 23 (63.9) | 3 (33.3) |
| First MMR following reduction | NA | 17 (73.9) | 2 (66.7) |
| MMR before and after reduction | NA | 6 (26.1) | 1 (33.3) |
| MMR before but not after reduction | NA | 0 | 0 |

Modified as-treated population. Only first dose escalation/reduction to the dose level for the patient is considered in this table. MMR = ≤0.1%

BCR::ABL1 on the IS with ≥3000 ABL1 transcripts assessed

IS international scale; MMR major molecular response; NA not applicable
### Table S3
Cumulative molecular response rates any time on treatment by Sokal score, age, and modified Charlson comorbidity index

| n (%) | Low-risk | Intermediate-risk | High-risk | <65 years | ≥65 years | mCCI ≤2 | mCCI >2 | Total |
|-------|----------|-------------------|----------|-----------|-----------|---------|---------|-------|
|       | Sokal score | Sokal score | Sokal score | (n = 41) | (n = 19) | (n = 42) | (n = 18) | (N = 60) |
| MMR   | (n = 28)   | (n = 25)         | (n = 7)  |           |           |         |         |       |
| 16 (57.1) | 22 (88.0) | 4 (57.1) | 30 (73.2) | 12 (63.2) | 29 (69.0) | 13 (72.2) | 42 (70.0) |
| 90% CI | 41.8–72.5 | 77.3–98.7 | 26.4–87.9 | 61.8–84.6 | 45.0–81.4 | 57.3–80.8 | 54.9–89.6 | 60.3–79.7 |
| MR⁴   | (n = 28)   | (n = 25)         | (n = 7)  |           |           |         |         |       |
| 13 (46.4) | 16 (64.0) | 3 (42.9) | 21 (51.2) | 11 (57.9) | 19 (45.2) | 13 (72.2) | 32 (53.3) |
| 90% CI | 30.9–61.9 | 48.2–79.8 | 12.1–73.6 | 38.4–64.1 | 39.3–76.5 | 32.6–57.9 | 54.9–89.6 | 42.7–63.9 |
| MR⁴.⁵ | (n = 28)   | (n = 25)         | (n = 7)  |           |           |         |         |       |
| 11 (39.3) | 15 (60.0) | 3 (42.9) | 19 (46.3) | 10 (52.6) | 18 (42.9) | 11 (61.1) | 29 (48.3) |
| 90% CI | 24.1–54.5 | 43.9–76.1 | 12.1–73.6 | 33.5–59.2 | 33.8–71.5 | 30.3–55.4 | 42.2–80.0 | 37.5–58.9 |

Modified as-treated population. Sokal score = low risk (≤0.8); intermediate risk (0.8–1.2); and high risk (>1.2). MMR = ≤0.1% BCR::ABL1 on the IS with ≥3000 ABL1 transcripts assessed; MR⁴ = ≤0.01% BCR::ABL1 on the IS with ≥9800 ABL1 transcripts assessed; MR⁴.⁵ = ≤0.0032%

IS international scale; mCCI modified Charlson comorbidity index; MMR major molecular response; MR molecular response
Table S4 Summary of treatment-emergent adverse events

|                        | Bosutinib (N = 60) |
|------------------------|---------------------|
|                        | All-causality       | Treatment-related |
| **n (%)**              |                     |                    |
| **All patients**       |                     |                    |
| Patients with TEAEs    | 60 (100)            | 60 (100)           |
| Patients with serious TEAEs | 15 (25.0)        | 13 (21.7)          |
| Patients with maximum grade ≥3 TEAEs | 49 (81.7) | 47 (78.3) |
| Patients with maximum grade 5 TEAEs | 0 | 0 |
| Patients with TEAEs leading to discontinuation of bosutinib\(^a\) | 21 (35.0) | 20 (33.3) |
| Patients with TEAEs leading to dose reduction of bosutinib\(^b\) | 37 (61.7) | 36 (60.0) |
| Patients with TEAEs leading to temporary discontinuation of bosutinib\(^c\) | 44 (73.3) | 41 (68.3) |
| **Patients <65 years of age** |                     |                    |
| Patients with TEAEs    | 41 (100.0)          | 41 (100.0)         |
| Patients with serious TEAEs | 10 (24.4)       | 8 (19.5)           |
| Patients with maximum grade ≥3 TEAEs | 31 (75.6) | 30 (73.2) |
| Patients with maximum grade 5 TEAEs | 0 | 0 |
| Category                                                                 | Patients with TEAEs leading to discontinuation of bosutinib | Patients with TEAEs leading to dose reduction of bosutinib | Patients with TEAEs leading to temporary discontinuation of bosutinib |
|-------------------------------------------------------------------------|------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|
| Patients with TEAEs                                                     | 10 (24.4)                                                  | 10 (24.4)                                                |                                                              |
| Patients with TEAEs leading to dose reduction of bosutinib              | 22 (53.7)                                                  | 21 (51.2)                                                |                                                              |
| Patients with TEAEs leading to temporary discontinuation of bosutinib   | 26 (63.4)                                                  | 24 (58.5)                                                |                                                              |

**Patients ≥65 years of age**

| Category                                                                 | Patients with TEAEs | Patients with TEAEs leading to discontinuation of bosutinib | Patients with TEAEs leading to dose reduction of bosutinib | Patients with TEAEs leading to temporary discontinuation of bosutinib |
|-------------------------------------------------------------------------|---------------------|------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|
| Patients with TEAEs                                                     | 19 (100.0)         | 19 (100.0)                                                |                                                          |                                                              |
| Patients with serious TEAEs                                             | 5 (26.3)           | 5 (26.3)                                                  |                                                          |                                                              |
| Patients with maximum grade ≥3 TEAEs                                    | 18 (94.7)          | 17 (89.5)                                                |                                                          |                                                              |
| Patients with maximum grade 5 TEAEs                                     | 0                  | 0                                                         |                                                          |                                                              |
| Patients with TEAEs leading to discontinuation of bosutinib             | 11 (57.9)          | 10 (52.6)                                                |                                                          |                                                              |
| Patients with TEAEs leading to dose reduction of bosutinib              | 15 (78.9)          | 15 (78.9)                                                |                                                          |                                                              |
| Patients with TEAEs leading to temporary discontinuation of bosutinib   | 18 (94.7)          | 17 (89.5)                                                |                                                          |                                                              |

**Patients with an mCCI score ≤2**

| Category                                                                 | Patients with TEAEs | Patients with TEAEs leading to discontinuation of bosutinib | Patients with TEAEs leading to dose reduction of bosutinib | Patients with TEAEs leading to temporary discontinuation of bosutinib |
|-------------------------------------------------------------------------|---------------------|------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|
| Patients with TEAEs                                                     | 42 (100.0)         | 42 (100.0)                                                |                                                          |                                                              |
| Patients with serious TEAEs                                             | 12 (28.6)          | 11 (26.2)                                                |                                                          |                                                              |
| Patients with maximum grade ≥3 TEAEs                                    | 34 (81.0)          | 34 (81.0)                                                |                                                          |                                                              |
| Patients with maximum grade 5 TEAEs                                     | 0                  | 0                                                         |                                                          |                                                              |
| Patients with TEAEs leading to discontinuation of bosutinib\textsuperscript{a} | 14 (33.3) | 14 (33.3) |
|---|---|---|
| Patients with TEAEs leading to dose reduction of bosutinib\textsuperscript{b} | 28 (66.7) | 27 (64.3) |
| Patients with TEAEs leading to temporary discontinuation of bosutinib\textsuperscript{c} | 29 (69.0) | 29 (69.0) |

| Patients with an mCCI score \(>2\) |
|---|---|---|
| Patients with TEAEs | 18 (100.0) | 18 (100.0) |
| Patients with serious TEAEs | 3 (16.7) | 2 (11.1) |
| Patients with maximum grade \(\geq 3\) TEAEs | 15 (83.3) | 13 (72.2) |
| Patients with maximum grade 5 TEAEs | 0 | 0 |
| Patients with TEAEs leading to discontinuation of bosutinib\textsuperscript{a} | 7 (38.9) | 6 (33.3) |
| Patients with TEAEs leading to dose reduction of bosutinib\textsuperscript{b} | 9 (50.0) | 9 (50.0) |
| Patients with TEAEs leading to temporary discontinuation of bosutinib\textsuperscript{c} | 15 (83.3) | 12 (66.7) |

As-treated population. Serious TEAEs were according to the investigator’s assessment. \textsuperscript{a}Patients whose record indicated that the TEAE caused them to be discontinued from bosutinib treatment; \textsuperscript{b}Patients whose record indicated that action taken with bosutinib was dose reduction; \textsuperscript{c}Patients whose record indicated that action taken with bosutinib was temporary discontinuation

*TEAE* treatment-emergent adverse event
| MedDRA PT, n (%) | Year 1 (N = 60) | Year 2 (N = 42) | Year 3 (N = 39) | ≥Year 4 (N = 31) | Total (N = 60) |
|----------------|-----------------|-----------------|-----------------|-----------------|---------------|
| Any TEAE       | 17 (28.3)       | 3 (7.1)         | 1 (2.6)         | 0               | 21 (35.0)     |
| ALT increased  | 6 (10.0)        | 0               | 0               | 0               | 6 (10.0)      |
| AST increased  | 5 (8.3)         | 0               | 0               | 0               | 5 (8.3)       |
| Drug eruption  | 2 (3.3)         | 0               | 0               | 0               | 2 (3.3)       |
| Erythema multiforme | 2 (3.3)       | 0               | 0               | 0               | 2 (3.3)       |
| Lipase increased | 2 (3.3)        | 0               | 0               | 0               | 2 (3.3)       |
| Neutropenia    | 1 (1.7)         | 0               | 0               | 0               | 1 (1.7)       |
| Thrombocytopenia | 1 (1.7)        | 0               | 0               | 0               | 1 (1.7)       |
| Drug-induced liver injury | 1 (1.7)   | 0               | 0               | 0               | 1 (1.7)       |
| Liver disorder | 1 (1.7)         | 0               | 0               | 0               | 1 (1.7)       |
| Pneumonia      | 1 (1.7)         | 0               | 0               | 0               | 1 (1.7)       |
| Blood creatinine increased | 0      | 0               | 1 (2.6)         | 0               | 1 (1.7)       |
| Event                          | Count | | | | Count |
|-------------------------------|-------|---|---|---|-------|
| Hepatic enzyme increased      | 1 (1.7) | 0 | 0 | 0 | 0 | 1 (1.7) |
| Pancreatic enzymes increased  | 1 (1.7) | 0 | 0 | 0 | 0 | 1 (1.7) |
| Breast cancer                 | 0     | 1 (2.4) | 0 | 0 | 0 | 1 (1.7) |
| Nephropathy toxic             | 0     | 1 (2.4) | 0 | 0 | 0 | 1 (1.7) |
| Pleural effusion              | 0     | 1 (2.4) | 0 | 0 | 0 | 1 (1.7) |

As-treated population. One year = 365.25 days. Patients were counted only once per event. MedDRA version 23.1 coding dictionary applied.

The following clustered terms for cytopenias are used: neutropenia (PT = neutropenia; neutrophil count decreased), and thrombocytopenia (PT = thrombocytopenia; platelet count decreased)

*ALT* alanine aminotransferase; *AST* aspartate aminotransferase; *MedDRA* Medical Dictionary for Regulatory Activities; *PT* Preferred Term; *TEAE* treatment-emergent adverse event
**Table S6** Follow-up CML treatment

|                      | Bosutinib (N = 60) |
|----------------------|---------------------|
| Any follow-up CML treatment | 24 (40.0)          |
| Bosutinib            | 4 (6.7)             |
| Dasatinib            | 11 (18.3)           |
| Imatinib             | 7 (11.7)            |
| Nilotinib            | 9 (15.0)            |
| Ponatinib            | 2 (3.3)             |

Three patients out of 24 above discontinued bosutinib due to reasons other than adverse events: one patient due to change hospital (subsequent bosutinib), one patient due to breast cancer (subsequent bosutinib), and one patient due to physician decision (subsequent dasatinib, nilotinib and ponatinib).

*CML* chronic myeloid leukemia
Table S7 Characteristics of treatment-emergent adverse events of special interest

| Bosunib (N = 60) |
|------------------|
| **n (%)**        | Liver | Increased | Increased | Gastro-intestinal | Diarrhea<sup>b</sup> | Myelo-suppression | Rash | Cardiac | Vascular | Hypertension | Renal |
|                  | ALT<sup>b</sup> | AST<sup>b</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> | TEAEs<sup>a</sup> |
| Total patients with event | 48 (80.0) | 33 (55.0) | 28 (46.7) | 52 (86.7) | 52 (86.7) | 27 (45.0) | 34 (56.7) | 5 (8.3) | 1 (1.7) | 4 (6.7) | 10 (16.7) |
| Medical history of event | 4 (8.3) | 2 (6.1) | 1 (3.6) | 0 | 0 | 7 (25.9) | 5 (14.7) | 0 | 0 | 2 (50.0) | 1 (10.0) |
| Time to first event, median (range),<sup>c</sup> days | 15.0 | 15.0 | 15.0 | 1.0 | 1.0 | 21.0 | 24.5 | 505.0 | 41.0 | 598.0 | 671.0 |
| Duration of any grade event, median (range), days | 14.0 | 14.0 | 14.0 | 3.0 | 3.0 | 14.0 | 27.0 | 42.0 | 91.0 | 56.0 |
| Duration of treatment stop events, median (range), days | 18.5 | 14.0 | 20.0 (13–497) | 9.0 | 8.0 | 14.0 | 6.0 | 0 | 0 | 0 | 53.0 |
| Treatment change<sup>f</sup> | Dose reduction | 17 (35.4) | 13 (39.4) | 8 (28.6) | 6 (11.5) | 3 (5.8) | 7 (25.9) | 4 (11.8) | 4 (80.0) | 0 | 0 | 1 (10.0) |
| Temporary interruption | 29 (60.4) | 17 (51.5) | 10 (35.7) | 8 (15.4) | 7 (13.5) | 10 (37.0) | 4 (11.8) | 0 | 0 | 0 | 1 (10.0) |
| Treatment rechallenge<sup>a</sup> | 28 (96.6) | 17 (100) | 9 (90.0) | 8 (100) | 7 (100) | 10 (100) | 4 (100) | 0 | 0 | 0 | 1 (100.0) |
| Successful treatment rechallenge<sup>b</sup> | 20 (71.4) | 13 (76.5) | 6 (66.7) | 8 (100) | 7 (100) | 10 (100) | 4 (100) | 0 | 0 | 0 | 0 |
| Permanent treatment discontinuation | 10 (16.7) | 6 (10.0) | 5 (8.3) | 0 | 0 | 2 (3.3) | 0 | 0 | 0 | 0 | 1 (1.7) |
| Treated with concomitant medication | 27 (56.3) | 16 (48.5) | 14 (50.0) | 50 (96.2) | 50 (96.2) | 2 (7.4) | 28 (82.4) | 2 (40.0) | 1 (100.0) | 4 (100.0) | 3 (30.0) |

As-treated population. n (%) unless otherwise stated. <sup>a</sup>TEAE cluster; <sup>b</sup>MedDRA PT; <sup>c</sup>Time to event for a given patient was calculated as (start date of first TEAE – date of first bosutinib dose) + 1 for non-missing or non-partial dates; <sup>d</sup>Duration was defined as (stop date of TEAE – start date of TEAE) + 1 for non-missing or non-partial dates; <sup>e</sup>Duration is based on distinct treatment stop events from bosutinib data that were triggered by the TEAE under consideration; <sup>f</sup>Patients with multiple TEAEs reported were counted in each category; <sup>g</sup>Rechallenge is defined as patients who had any grade toxicity TEAEs leading to temporary stop of bosutinib and who were subsequently redosed; <sup>h</sup>Successful is defined as patients redosed after the specific TEAE type who have no subsequent TEAE of that type or are not discontinued permanently due to that type of TEAE.

ALT alanine aminotransferase; AST aspartate aminotransferase; MedDRA Medical Dictionary for Regulatory Activities; PT Preferred Term; TEAE treatment-emergent adverse event
Table S8 Cardiac, vascular, hypertension, and renal adverse events of special interest

| n (%)                     | Bosutinib (N = 60) |                      |                      |
|---------------------------|--------------------|----------------------|----------------------|
|                           | All-causality      | Treatment-related    |                      |
|                           | Any grade          | Grade ≥3             | Any grade            | Grade ≥3             |
| Cardiac TEAEs             | 5 (8.3)            | 0                    | 5 (8.3)              | 0                    |
| Pericardial effusion      | 3 (5.0)            | 0                    | 3 (5.0)              | 0                    |
| Cardiac failure           | 2 (3.3)            | 0                    | 2 (3.3)              | 0                    |
| Vascular TEAEs            | 1 (1.7)            | 0                    | 0                    | 0                    |
| Peripheral coldness       | 1 (1.7)            | 0                    | 0                    | 0                    |
| Hypertension TEAEs        | 4 (6.7)            | 1 (1.7)              | 3 (5.0)              | 1 (1.7)              |
| Hypertension              | 4 (6.7)            | 1 (1.7)              | 3 (5.0)              | 1 (1.7)              |
| Renal TEAEs               | 10 (16.7)          | 1 (1.7)              | 9 (15.0)             | 0                    |
| Increased blood creatinine| 6 (10.0)           | 0                    | 5 (8.3)              | 0                    |
| Acute kidney injury       | 2 (3.3)            | 0                    | 2 (3.3)              | 0                    |
| Chronic kidney disease    | 1 (1.7)            | 1 (1.7)              | 0                    | 0                    |
| Renal impairment          | 1 (1.7)            | 0                    | 1 (1.7)              | 0                    |
| Renal injury              | 1 (1.7)            | 0                    | 1 (1.7)              | 0                    |

As-treated population.

TEAE treatment-emergent adverse event
Fig. S1 Cumulative incidence of molecular response: (a) MMR, (b) MR², and (c) MR²⁻. Modified as-treated population. Molecular response was analyzed using cumulative incidence, adjusting for the competing risk without response. MMR = ≤0.1% BCR:ABL1 on the IS with ≥3000 ABL1 transcripts assessed. MR² = ≤0.01% BCR:ABL1 on the IS with ≥8600 ABL1 transcripts assessed. MR²⁻ = ≤0.0032% BCR:ABL1 on the IS with ≥30,990 ABL1 transcripts assessed. 90% CIs based on delta method with the log-log transformation. CI confidence interval; IS international scale; MMR major molecular response; MR molecular response

(a) MMR

Cumulative incidence of response:
Week 48: 81.7% (90% CI: 51.3–72.0)
Week 66: 66.7% (90% CI: 56.7–76.7)
Week 144: 70.0% (90% CI: 60.3–79.7)

(b) MR²

Cumulative incidence of response:
Week 48: 33.3% (90% CI: 23.3–43.3)
Week 66: 46.7% (90% CI: 36.1–57.3)
Week 144: 50.0% (90% CI: 39.4–60.6)

(c) MR²⁻

Cumulative incidence of response:
Week 48: 28.3% (90% CI: 18.8–37.9)
Week 66: 35.0% (90% CI: 24.9–45.1)
Week 144: 46.7% (90% CI: 36.1–57.3)
**Fig. S2** Cumulative incidence of event-free survival on treatment. Modified as-treated population. Event-free survival was analyzed using cumulative incidence, adjusting for the competing risk events (treatment discontinuation for reasons other than progressive disease). 90% CIs based on delta method with the log(-log) transformation. CI confidence interval; EFS event-free survival

Cumulative incidence of EFS events:
- Week 48: 1.7% (90% CI: 0.2–6.4)
- Week 96: 1.7% (90% CI: 0.2–6.4)
- Week 144: 1.7% (90% CI: 0.2–6.4)

Number at risk

| Time (weeks) | 60 | 56 | 46 | 44 | 41 | 41 | 40 | 39 | 38 | 37 | 37 | 36 | 29 | 19 | 11 | 1 |
|--------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|
**Fig. S3** Kaplan–Meier plot of overall survival. Modified as-treated population. 90% CIs based on Greenwood’s log(-log) transformation. CI confidence interval

Overall survival rate:
- Week 48: 100.0% (90% CI: 100.0–100.0)
- Week 96: 98.3% (90% CI: 91.7–99.7)
- Week 144: 96.7% (90% CI: 89.7–98.9)
Fig. S4 Cumulative incidence of molecular response by Sokal score: (a) MMR, (b) MR1, and (c) MR1+. Modified as-treated population. Molecular response was analyzed using cumulative incidence, adjusting for the competing risk without response. MMR = ≤0.1% BCR-ABL1 on the IS with ≥3000 ABL1 transcripts assessed, MR1 = ≤0.01% BCR-ABL1 on the IS with ≥8000 ABL1 transcripts assessed. MR1+ = ≤0.0032% BCR-ABL1 on the IS with ≥30,990 ABL1 transcripts assessed. IS international scale; MMR major molecular response; MR molecular response.

(a) MMR

(b) MR1

(c) MR1+
Fig. S5 All grade and grade ≥3 treatment-emergent adverse events (≥20%) by subgroup: (a) age and (b) modified Charlson comorbidity index. As-treated population. ALT alanine aminotransferase; AST aspartate aminotransferase; GGT gamma-glutamyltransferase; mCCI modified Charlson comorbidity index. TEAE treatment-emergent adverse event

(a) Age

- <65 years (n = 41) Any grade
- ≥65 years (n = 18) Any grade
- <65 years (n = 41) Grade ≥3
- ≥65 years (n = 18) Grade ≥3

(b) mCCI

- ≤2 mCCI (n = 42) Any grade
- >2 mCCI (n = 18) Any grade
- ≤2 mCCI (n = 42) Grade ≥3
- >2 mCCI (n = 18) Grade ≥3