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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Asciminib

Trial Indication(s)

Chronic myeloid leukemia (CML) and Ph+ Acute lymphoblastic leukemia (ALL)

Protocol Number

CABL001X2101

Protocol Title

A phase I, multicenter, open-label study of oral ABL001 in patients with chronic myelogenous leukemia (CML) or Philadelphia Chromosome-positive acute lymphoblastic leukemia (Ph+ ALL)

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: April 24, 2014 (Actual)
Primary Completion Date: June 03, 2021 (Actual)

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Study Completion Date: March 14, 2023 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a multicenter, open-label dose finding study to define the MTD/RDE(s), safety, tolerability, PK and to provide preliminary evidence of efficacy of asciminib given as single agent or in combination with either nilotinib or imatinib or dasatinib.
The study was designed to include 5 arms:
Arm 1: asciminib as single agent in patients with CML-CP/-AP
Arm 2: asciminib in combination with nilotinib in patients with CML-CP/-AP (introduced with protocol amendment 4)
Arm 3: asciminib in combination with imatinib in patients with CML-CP/-AP (introduced with protocol amendment 6)
Arm 4: asciminib in combination with dasatinib in patients with CML-CP/-AP (introduced with protocol amendment 6)
Arm 5: asciminib as single agent in patients with CML-BP and Ph+ ALL

The study design included the following periods:
Screening period: Inclusion and exclusion criteria were assessed within 28 days prior to the first dose of study treatment.

Treatment period: It commenced on the first day of the first cycle (each cycle was defined as 28 days) of the study treatment and ends after the last dose of the study treatment. Patients were treated with continuous daily dosing of the study treatment until objective evidence of progression of disease or occurrence of unacceptable toxicities occurs.

End of treatment (EOT): Patients who discontinued study treatment were to complete the EOT visit within 14 days of the last dose of study treatment or within 14 days of the decision to discontinue the study treatment due to an adverse event (AE), in the case that the study treatment was already on hold due to the AE.

Follow-up period: All patients had safety evaluations (AEs, serious AEs (SAEs), concomitant medications, including subsequent anti-neoplastic therapy) for 30 days after the last dose of the study treatment.

Each arm began with a dose escalation part to determine the MTD, or the RDE(s) of study treatment followed by an expansion part to further evaluate the safety and tolerability, if deemed appropriate.

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With protocol amendment 9, an additional Arm 1 expansion was incorporated to further assess asciminib as single agent in patients with CML-CP/-AP harboring the T315I mutation.

This study utilized a Bayesian logistic regression model (BLRM) to guide dose escalation and estimate the MTD for asciminib as a single agent in patients with CML-CP/-AP, asciminib in combination with either nilotinib or imatinib or dasatinib in patients with CML-CP/-AP, and asciminib as single agent in patients with CML-BP and Ph+ ALL.

A total of 330 patients were planned; 326 patients were enrolled and analyzed.

Centers

18 centers in 10 countries: Australia(1), Germany(3), Spain(1), France(2), Italy(1), Japan(1), Netherlands(1), Singapore(1), United States(6), Korea, Republic of(1)

Objectives:

Primary objectives:

To determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of:

- asciminib as single agent in patients with CML-Chronic Phase (CP)/-Accelerated Phase (AP)
- asciminib in combination with nilotinib in patients with CML-CP/-AP
- asciminib in combination with imatinib in patients with CML-CP/-AP
- asciminib in combination with dasatinib in patients with CML-CP/-AP
- asciminib as single agent in patients with CML-Blast Phase (BP) and Ph+ ALL

Secondary objectives:

- To characterize the safety and tolerability of asciminib as single agent and in combination with either nilotinib or imatinib or dasatinib
- To assess preliminary anti-CML activity associated with asciminib as single agent and in combination with either nilotinib or imatinib or dasatinib and anti Ph+ ALL activity associated with asciminib as single agent
- To assess the pharmacokinetic profiles of all study drugs in single agent and combination arms in plasma
- To characterize the safety, tolerability, and efficacy of asciminib as single agent in patients with CML-CP/-AP with T315I mutation

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Test Product (s), Dose(s), and Mode(s) of Administration

Asciminib was administered twice daily (b.i.d.) in the fasted state (food was not allowed for at least 2 hours prior and 1 hour after administration) approximately 12 hours apart or was to be taken once daily (q.d.) at around the same time every morning, depending on the dose of the allocated cohort.
Asciminib was administered in the fasted state also when received in combination with nilotinib or dasatinib. When in combination with imatinib, asciminib was administered with a light meal. Nilotinib was to be administered b.i.d. in the fasted state approximately 12 hours apart. Imatinib was to be taken q.d. with a light meal (less than 400 kcal and 20% fat) at around the same time every day. Dasatinib was to be taken q.d. in the fasted state.

Asciminib was supplied as capsules at dose strengths of 5 mg, 20 mg and 50 mg and as tablets of 20 mg, 40 mg and 50 mg (tablets were introduced with protocol amendment 5 (dated 26-Jun-2015). Imatinib was supplied as film coated tablets of 100 mg and 400 mg dose strength. Nilotinib was supplied as hard gelatin capsules in strengths of 150 mg and 200 mg. Dasatinib was supplied as tablets in strengths of 20 mg, 50 mg, 70 mg, 80 mg, and 100 mg.

Asciminib was supplied by Novartis whereas nilotinib, imatinib and dasatinib were procured locally.

Statistical Methods

The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.
Patients were analyzed according to the planned treatment. The FAS was used for all listings of raw data. Unless otherwise specified, the FAS was the default analysis set used for all analyses.

T315I mutation analysis set: subset of FAS consisting of CML-CP patients with centrally confirmed T315I mutation (Sanger sequencing), treated with asciminib 200 mg b.i.d., with evaluable RQ-PCR data (IS) who were not in MMR at baseline.

The Safety set consisted of all patients who received at least one dose of the study treatment. Patients were analyzed according to the study treatment they received.

The dose-determining analysis set (DDS) consisted of all patients from the safety set who either met the following minimum exposure criterion and had sufficient safety evaluations, during the first 28 days (Cycle 1) of dosing or discontinued earlier due to dose limiting toxicity (DLT). Minimum exposure criteria defined as a patient who had received at least 75% of the planned doses of the study treatment in the first 28 days of dosing. For b.i.d. and q.d. schedules, this corresponds to a minimum of 42 out of the 56, and minimum of 21 out of the 28 planned doses, respectively.

The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

The primary analysis was performed when all patients in the monotherapy arms were treated for at least 6 cycles and had their 24-week efficacy evaluation performed, or had discontinued treatment earlier. This report presents the primary analysis results including the safety and PK data from all patients administered with asciminib as a single agent and in combination with nilotinib or imatinib or dasatinib, and efficacy data from all patients who were administered with asciminib as single agent.
The final analysis was done once last patient last visit for the study has been achieved to report final safety and efficacy data at additional time points.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Male or female patients ≥ 18 years of age who present one of the following:

For Arms 1, 2, 3 and 4, either:

-- a. Patients with Ph+ CML in chronic or accelerated phase who were previously treated with at least two different tyrosine kinase inhibitors prior to study entry and are relapsed, refractory to or intolerant of TKIs as determined by investigators

or

-- b. Patients with CML in chronic or accelerated phase who exhibit relapsed disease associated with the presence of the T315I “gatekeeper mutation” after at least one TKI are also eligible provided that no other effective therapy exists

For Arm 5:

-- Patients with CML BP or Ph+ ALL who have a cytopathologically confirmed diagnosis and are relapsed or refractory to at least one prior TKI or intolerant of TKIs. TKI failure for Ph+ ALL and CML-BP patients is defined as at least the loss of Molecular Response (MR) 4.5 (BCR-ABL ≤ 0.0032%)

- Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2

- Willingness and ability to comply with all study procedures
- Written informed consent obtained prior to any screening procedures

Exclusion Criteria:

-Wash-out period:
-- Systemic antineoplastic therapy (including cytotoxic chemotherapy, alfa-interferon and toxin immunoconjugates) or any experimental therapy within 14 days or 5 half-lives, whichever is shorter, before the first dose of study treatment
-- Therapy with TKIs as single agent within 5 half-lives before the first dose of study treatment
-- Unconjugated monoclonal antibody therapies within 28 days or 5 half-lives, whichever is shorter, before the first dose of study treatment

- For patients receiving ABL001 in combination with either nilotinib or imatinib or dasatinib, intolerance to nilotinib, imatinib or dasatinib, respectively
- Radiotherapy with a wide field of radiation within 4 weeks or radiotherapy with a limited field of radiation for palliation within 1 week of the first dose of study treatment.
- CNS irradiation for meningeal leukemia, except if radiotherapy occurred > 3 months previously. At least four weeks must have elapsed since prophylactic CNS irradiation given as part of a front-line therapy regimen for ALL
- Major surgery within 2 weeks before the first dose of study treatment

Participant Flow Table

Overall Study

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	Asciminib as single agent in CML patients (Arm 1)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients	Total
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	
Started	200	26	25	32	43	326
Completed	101	12	10	21	2	146
Not Completed	99	14	15	11	41	180
Adverse Event	22	3	4	3	5	37
Death	5	0	1	0	2	8
Physician Decision	37	8	5	7	8	65
Progressive disease	16	1	2	1	22	42
Subject/Guardian decision	14	2	1	0	4	21
Pregnancy	0	0	1	0	0	1
Lost to Follow-up	2	0	1	0	0	3
Protocol Violation	1	0	0	0	0	1

Technical problems	2	0	0	0	0	2

Baseline Characteristics

	Asciminib as single agent in CML patients (Arm 1)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients	Total
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	
Number of Participants [units: participants]	200	26	25	32	43	326
Baseline Analysis Population Description	Full Analysis Set (FAS): The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.					

Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation	54.5±14.77	56.2±14.18	56.2±16.32	52.9±16.12	56.0±15.60	54.8±15.03
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						
Female	80	10	13	8	20	131
Male	120	16	12	24	23	195
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants						
Black of African American	5	2	1	1	1	10
White	119	20	16	20	27	202
Asian	47	2	4	7	9	69
Other	20	2	2	4	5	33
Unknown	9	0	2	0	1	12
Study Specific Characteristic **ECOG Performance Status** (units: Participants) Description: ECOG performance Status (PS) scale is a standard criterion for measuring how cancer impacts a patient's daily living abilities. It describes a patient's level of functioning in terms of their ability to care for themself, daily activity and physical ability. The scale ranges from 0 to 5 with 0 representing the best possible ability, 4 representing the worst ability to care for oneself and 5 death. Analysis Population Type:						
ECOG performance status of 0	153	19	17	25	13	227
ECOG performance status of 1	44	7	8	7	23	89
ECOG performance status of 2	3	0	0	0	6	9
ECOG performance status - Missing	0	0	0	0	1	1

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Primary Outcome Result(s)

Incidence of dose limiting toxicities (DLTs) during the first cycle of study treatment

Description	Dose-limiting toxicity (DLT) was defined as an adverse event (AE) or abnormal laboratory value assessed by the Investigator as unrelated to disease progression, inter-current illness, or concomitant medications taken within the first 28 days (Cycle 1) of study treatment and that met any of these criteria: Common terminology criteria for AE (CTCAE) grade 4 neutropenia (ANC < 0.5 x 10^9/L) lasting more than 5 days, CTCAE grade 4 thrombocytopenia (platelets < 25 x 10^9/L) or grade 3 thrombocytopenia with bleeding, CTCAE grade 4 febrile neutropenia (fever > 38.3°C), CTCAE grade 4 anemia unexplained by underlying disease or CTCAE grade 3 anemia were not considered a DLT unless judged to be a hemolytic process secondary to study treatment.
Time Frame	First Cycle (28 days)
Analysis Population Description	The dose-determining analysis set (DDS) consisted of all patients from the safety set who either met the following minimum exposure criterion and had sufficient safety evaluations, during the first 28 days (Cycle 1) of dosing or discontinued earlier due to DLT

	Asciminib as single agent in CML patients (Arm 1)	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute

					lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	132	16	25	22	34
Incidence of dose limiting toxicities (DLTs) during the first cycle of study treatment (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Investigations: Lipase increased	2 (1.52%)	0 (%)	1 (4%)	1 (4.55%)	1 (2.94%)
Arthralgia and myalgia	1 (.76%)	0 (%)	0 (%)	0 (%)	0 (%)
Acute coronary syndrome	1 (.76%)	0 (%)	0 (%)	0 (%)	0 (%)
Blood and lymphatic system disorders: Thrombocytopenia	1 (.76%)	0 (%)	0 (%)	1 (4.55%)	0 (%)
Bronchospasm	1 (.76%)	0 (%)	0 (%)	0 (%)	0 (%)
Gastrointestinal disorders: Pancreatitis	2 (1.52%)	0 (%)	2 (8%)	0 (%)	1 (2.94%)
Skin & subcutaneous tissue: Rash maculo-papular	0 (%)	1 (6.25%)	0 (%)	0 (%)	0 (%)
Gastrointestinal disorders: Abdominal pain	0 (%)	0 (%)	1 (4%)	0 (%)	0 (%)
Gastrointestinal disorders: Nausea	0 (%)	0 (%)	1 (4%)	0 (%)	0 (%)
Investigations: Neutrophil count decreased	0 (%)	0 (%)	1 (4%)	0 (%)	0 (%)
Inv: Increased ALT, AST & ALP	0 (%)	0 (%)	0 (%)	0 (%)	1 (2.94%)
Nervous system disorders: Cerebrovascular accident	0 (%)	0 (%)	0 (%)	0 (%)	1 (2.94%)

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Secondary Outcome Result(s)

Major Molecular Response (MMR) rate by 24 weeks of single agent asciminib in CML-CP/-AP not in MMR at screening

Description	Major molecular response was defined as a value of ≤ 0.1% of BCR-ABL1 ratio on the International Scale (IS). The MMR of single agent asciminib in chronic myeloid leukemia in chronic phase/ accelerated phase (CML-CP/-AP) participants not in MMR at screening.
Time Frame	by 24 weeks
Analysis Population Description	These participants were a evaluable for MMR and were a subset of the FAS. The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.

	Asciminib as single agent in CML patients (Arm 1)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	164	22	20	26	18

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Major Molecular Response (MMR) rate by 24 weeks of single agent asciminib in CML-CP/-AP not in MMR at screening
(units: Percentage of articipants)

MMR in CML-CP/-AP participants by 24 weeks	26.2	22.7	35.0	30.8	11.1

Complete Hematologic Response (CHR) rate

Description	A complete hematologic response is when all of the following criteria were present at any assessment and was confirmed by another assessment at least after 4 weeks: WBC count < 10 x 10^9 /L, Platelet count < 450 x 10^9 /L, No extra medullary involvement (spleen, liver, lymph nodes), Myelocytes + metamyelocytes < 5% in peripheral blood, Myelocytes + metamyelocytes < 5% in peripheral blood.
Time Frame	by Weeks 24, 48 & 96
Analysis Population Description	The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment, with participants evaluable for complete hematologic response (CHR).

	Asciminib as single agent in CML patients (Arm 1)	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)

Number of Participants Analyzed [units: participants]	200	26	25	32	43
Complete Hematologic Response (CHR) rate (units: Percentage of participants)					
Complete Hematologic Response (CHR) by Week 24	84.1	71.4	100.0	100.0	23.5
CHR by Week 48	88.6	85.7	100.0	100.0	23.5
CHR by Week 96	88.6	85.7	100.0	100.0	23.5

Percentage of participants with cytogenetic response not in complete cytogenic response (CCyR) at screening

Description	Cytogenetic response was assessed as the percentage of Ph+ metaphases in the bone marrow and included Major cytogenic response (MCyR), Partial cytogenic response (PCyR) and Complete cytogenic response (CCyR). MCyR = 0% and ≤35%Ph+ metaphases; CCyR = 0% Ph+ metaphases and PCyR = > 0% and ≤35% Ph+ metaphases. After screening, bone marrow aspirate was collected to assess cytogenetic response in patients who were not in CCyR. Assesments were on CML CP/AP and CML-BP and PH+ ALL participants..
Time Frame	by Weeks 24, 48 & 96
Analysis Population Description	Participants with who were not in complete cytogenic response (CCyR) at screening. The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.

	Asciminib as single agent in CML patients (Arm 1)	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast

	adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)			Primary Analysis data cut-off.	phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	200	26	25	32	43
Percentage of participants with cytogenetic response not in complete cytogenic response (CCyR) at screening (units: Percentage of participants)					
MCyR: CCyR by week 24	22.8	7.7	18.8	42.9	5.9
MCyR: PCyR by week 24	9.8	15.4	25.0	7.1	5.9
MCyR: CCyR by week 48	27.6	23.1	31.3	42.9	5.9
MCyR: PCyR by week 48	9.8	23.1	25.0	7.1	5.9
MCyR: CCyR by week 96	33.3	30.8	43.8	42.9	5.9
MCyR: PCyR by week 96	8.9	23.1	18.8	7.1	5.9

Molecular response (MR) (Breakpoint cluster region (BCR)-Abelson oncogene (ABL)1 ratio)

Description	Molecular response (MR) rate by scheduled time point was defined as the percentage of participants who achieved MR at the specified time point. Levels of BCR-ABL1 transcripts were determined by real-time quantitative polymerase chain reaction (RQ-PCR) testing of peripheral blood. The percent ratio of BCR-ABL transcripts versus control gene transcripts converted to International Standards (IS) was calculated for each sample. RQ-PCR was monitored monthly for the first three cycles and then every 12 weeks during treatment with ABL001. If during this time the sample was lost or the PCR result is difficult to interpret, or if the PCR sample was not collected, a subsequent unscheduled visit sample had to be collected within 4 weeks. BCR-ABL1 response categories: BCR-ABL <=0.0032% IS BCR-ABL >0.0032% - <=0.01% IS BCR-ABL >0.01% - <=0.1% IS BCR-ABL >0.1% - <=1% IS BCR-ABL >1% - <=10% IS BCR-ABL >10% IS Atypical/p190/Unknown transcripts Missing
Time Frame	at Screening, Weeks 24, 48 and 96
Analysis Population Description	Participants with CML-CP without the T315I mutation at screening as part of FAS. The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.

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	Asciminib as single agent in CML patients (Arm 1)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	115	26	25	32	43
Molecular response (MR) (Breakpoint cluster region (BCR)-Abelson oncogene (ABL)1 ratio) (units: % IS)					
Screening: BCR-ABL <=0.0032% IS (n = 115, 26, 25, 32, 43)	0.9	3.8	0.0	0.0	0.0
Week 24: BCR-ABL >0.0032 - 0.01% IS (n = 115, 26, 25, 32, 43)	3.5	3.8	0.0	0.0	0.0
Screening: BCR-ABL >0.01 - 0.1% IS (n = 115, 26, 25, 32, 43)	13.0	7.7	12.0	12.2	0.0
Screening: BCR-ABL >0.1 - 1% IS (n = 115, 26, 25, 32, 43)	20.9	15.4	20.0	21.5	0.

Screening: BCR-ABL >1 - 10% IS (n = 115, 26, 25, 32, 43)	18.3	19.2	20.0	18.8	0.0
Screening: CR-ABL >10% IS (n = 115, 26, 25, 32, 43)	35.7	50.0	40.0	40.6	0.0
Screening: Atypical/p190/Unknown transcripts (n = 115, 26, 25, 32, 43)	7.8	0.0	8.0	6.3	0.0
Screening: Missing (n = 115, 26, 25, 32, 43)	0.0	0.0	0.0	0.0	11.6
Week 24: BCR-ABL <=0.0032% IS(MR4.5) (n = 115, 26, 25, 32, 43)	13.2	7.7	13.0	3.3	5.3
Week 24: BCR-ABL <=0.01% IS (MR4) (n = 115, 26, 25, 32, 43)	18.9	11.5	17.4	6.7	5.3
Week 24: BCR-ABL <=0.1% IS (MMR) (n = 115, 26, 25, 32, 43)	33.0	30.8	43.5	36.7	5.3
Week 24: BCR-ABL <=10% IS (MR1) (n = 115, 26, 25, 32, 43)	77.4	69.2	73.9	70.0	5.3
Week 24: BCR-ABL >10% IS (n = 115, 26, 25, 32, 43)	13.2	19.2	26.1	10.0	5.3
Week 24: Missing (n = 115, 26, 25, 32, 43)	9.4	11.5	0.0	20.0	89.5
Week 48: BCR-ABL <=0.0032% IS (MR4.5) (n = 115, 26, 25, 32, 43)	15.1	7.7	4.3	0.0	5.3
Week 48: BCR-ABL <=0.01% IS (MR4) (n = 115, 26, 25, 32, 43)	17.9	15.4	17.4	10.0	5.3
Week 48: BCR-ABL <=0.1% IS (MMR) (n = 115, 26, 25, 32, 43)	36.8	26.9	26.1	36.7	5.3

Week 48: BCR-ABL <=10% IS (MR1) (n = 115, 26, 25, 32, 43)	75.5	61.5	47.8	66.7	5.3
Week 48: BCR-ABL >10% IS (n = 115, 26, 25, 32, 43)	6.6	19.2	21.7	13.3	5.3
Week 48: Missing (n = 115, 26, 25, 32, 43)	17.9	19.2	30.4	20.0	89.5
Week 96: BCR-ABL <=0.0032% IS (MR4.5) (n = 115, 26, 25, 32, 43)	18.9	7.7	17.4	10.0	5.3
Week 96: BCR-ABL <=0.01% IS (MR4) (n = 115, 26, 25, 32, 43)	23.6	11.5	30.4	16.7	5.3
Week 96: BCR-ABL <=0.1% IS (MMR) (n = 115, 26, 25, 32, 43)	47.2	30.8	34.8	33.3	5.3
Week 96: BCR-ABL <=10% IS (MR1) (n = 115, 26, 25, 32, 43)	69.8	50.0	52.2	50.0	5.3
Week 96: BCR-ABL >10% IS (n = 115, 26, 25, 32, 43)	6.6	11.5	4.3	6.7	5.3
Week 96: Missing (n = 115, 26, 25, 32, 43)	23.6	38.5	43.5	43.3	89.5

Time to molecular response (MR)

Description	Time to first MMR among patients who achieved MMR – single agent ABL001 in CML CP not in MMR at screening - MMR evaluable.
Time Frame	approx. 360 weeks
Analysis Population Description	Participants with CML-CP/-AP who achieved major molecular response (MMR) after starting treatment with single agent asciminib in FAS. The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.

	Asciminib as single agent in	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+

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	CML patients (Arm 1)				ALL (Arm 5) patients
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	164	22	20	26	0
Time to molecular response (MR) (units: Weeks)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	28.2 (2 to 360)	20.1 (12 to 132)	20.9 (8 to 192)	22.1 (4 to 224)	

Kaplan -Meier estimates of duration of first major molecular response (MMR) at 24 weeks

Description	Duration of first MMR was defined as the period of time between the time-point when the first BCR-ABL1 ratio ≤0.1 % (IS) was observed until and the time-point of confirmed loss of major molecular response (MMR).
Time Frame	24 weeks
Analysis Population Description	Participants with CML-CP/-AP who achieved major molecular response (MMR) after starting treatment with single agent asciminib in FAS. The Full analysis set (FAS) consisted of all patients who received at least one dose of study treatment.

	Asciminib as single agent in CML patients (Arm 1)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)	Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	164	22	20	26	0
Kaplan -Meier estimates of duration of first major molecular response (MMR) at 24 weeks (units: Weeks)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	99 (96.5 to 100.0)	88 (64.6 to 100.0)	100 (100.0 to 100.0)	93 (80.7 to 100.0)	

Pharmacokinetics (PK): Plasma concentration (Tmax) of asciminib (ABL001), single agent Asciminib in CML patients (Arm 1)

Description	Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose

Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML patients (Arm 1: ABL001 40 mg b.i.d.)	**Asciminib as single agent in CML patients (Arm 1: ABL001 200 mg b.i.d.)**	**Asciminib as single agent in CML patients (Arm 1: ABL001 80 mg q.d.)**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)
Number of Participants Analyzed [units: participants]	32	62	18
Pharmacokinetics (PK): Plasma concentration (Tmax) of asciminib (ABL001), single agent Asciminib in CML patients (Arm 1) (units: hr)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n = 30, 61, 18)	2.10 (1.95 to 5.62)	2.03 (0.95 to 7.28)	2.06 (1.13 to 6.00)
Cycle 2 Day 1 (n = 30, 54, 17)	2.01 (1.00 to 6.00)	2.00 (0.90 to 7.03)	2.00 (0.95 to 4.10)

PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)

Description	Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose

Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 20 mg b.i.d. + NIL 300 mg b.i.d.)	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 40 mg b.i.d. + NIL 300 mg b.i.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	12	14
PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) (units: hr)	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n = 11, 14)	2.25 (1.98 to 3.03)	2.08 (0.92 to 3.08)
Cycle 2 Day 1 (n = 10, 12)	2.00 (1.00 to 4.00)	2.02 (1.00 to 4.00)

PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)

Description	Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Imatinib in CML-CP/-AP patients	**Asciminib+Imatinib in CML-CP/-AP patients**	**Asciminib+Imatinib in CML-CP/-AP patients**	**Asciminib+Imatinib in CML-CP/-AP patients**

	(Arm 3: ABL001 40 mg b.i.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 40 mg q.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 60 mg q.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 80 mg q.d. + IMA 400 mg q.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	6	9	6	4
PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) (units: hr)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n = 6, 9, 6, 4)	4.03 (2.00 to 4.13)	2.08 (1.00 to 4.13)	2.75 (1.08 to 4.13)	2.03 (2.00 to 2.13)
Cycle 2 Day 1 (n = 5, 8, 5, 2)	3.87 (2.00 to 4.00)	1.50 (1.00 to 4.00)	3.00 (1.00 to 4.08)	1.37 (0.92 to 1.83)

PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)

Description	Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 40 mg b.i.d. + DAS 100 mg q.d.)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 80 mg q.d. + DAS 100 mg q.d.)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 160 mg q.d. + DAS 100 mg q.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in

	patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off
Number of Participants Analyzed [units: participants]	11	14	6
PK: Plasma concentration (Tmax) of asciminib administered in combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) (units: hr)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n = 11, 14, 5),	2.07 (1.83 to 4.28)	1.99 (1.08 to 2.22)	1.97 (0.97 to 2.00)
Cycle 2 Day 1 (n = 9, 10, 5)	2.00 (1.00 to 4.03)	2.00 (0.78 to 3.02)	2.03 (1.88 to 3.03)

PK: Plasma concentration (Tmax) of asciminib administered as single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5)

Description	Tmax is the time to reach maximum (peak) plasma drug concentration after single dose administration (time).
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 40 mg b.i.d.)	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 80 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 160 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 200 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 280 mg b.i.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of	Dose escalation study estimated the MTD and/or RDE of	Dose escalation study estimated the MTD and/or RDE of	Dose escalation study estimated the MTD and/or RDE of	Dose escalation study estimated the MTD and/or RDE of

	asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	4	9	16	6	5
PK: Plasma concentration (Tmax) of asciminib administered as single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5) (units: hr)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n = 4, 9, 15, 6, 4)	3.07 (2.00 to 8.00)	2.22 (2.00 to 8.17)	2.07 (1.15 to 5.78)	2.58 (1.90 to 4.05)	2.08 (2.03 to 2.17)
Cycle 2 Day 1 (n = 3, 5, 11, 6, 3)	2.00 (1.05 to 2.00)	2.03 (1.92 to 3.87)	2.02 (1.17 to 7.08)	2.12 (0.83 to 3.05)	3.00 (2.00 to 8.02)

PK: Cmax and Cmin of asciminib as measured in plasma with single agent Asciminib in CML patients (Arm 1)

Description	Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1). Only PK blood samples with date and time and for which the last prior dose dates and times are adequately recorded were included in the PK analyses. Samples taken from patients who vomited within 4 hours of dosing were excluded from the analysis. Cmin is the minimum blood plasma concentration reached by a drug during a dosing interval.
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs pre-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML patients (Arm 1: ABL001 40 mg b.i.d.)	Asciminib as single agent in CML patients (Arm 1: ABL001 200 mg b.i.d.)	Asciminib as single agent in CML patients (Arm 1: ABL001 80 mg q.d.)
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)
Number of Participants Analyzed [units: participants]	32	62	18
PK: Cmax and Cmin of asciminib as measured in plasma with single agent Asciminib in CML patients (Arm 1) (units: ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 30, 61, 18)	536.85 (74.29%)	3467.70 (33.60%)	1157.54 (46.46%)
Cmax: Cycle 2 Day 1 (n = 30, 54, 17)	793.26 (48.92%)	5641.84 (39.86%)	1780.98 (23.34%)
Cmin: Cycle 1 Day 1 (n = 0, 0, 0)			
Cmin: Cycle 2 Day 1 (n = 30, 55, 16)	262.50 (67.53%)	2715.38 (57.65%)	193.26 (39.58%)

PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)

Description	Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1). Only PK blood samples with date and time and for which the last prior dose dates and times are adequately recorded were included in the PK analyses. Samples taken from patients who vomited within 4 hours of dosing were excluded from the analysis. Cmin is the minimum blood plasma concentration reached by a drug during a dosing interval.
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 20 mg b.i.d. + NIL 300 mg b.i.d.)	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 40 mg b.i.d. + NIL 300 mg b.i.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	12	14
PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) (units: ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 11, 14)	383.37 (26.71%)	744.59 (76.99%)
Cmax: Cycle 2 Day 1 (n = 10, 12)	447.28 (701.82%)	1158.92 (86.71%)
Cmin: Cycle 1 Day 1 (n = 0, 0)		
Cmin: Cycle 2 Day 1 (n = 10, 12)	168.02 (420.83%)	503.45 (84.45%)

PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)

Description	Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1). Only PK blood samples with date and time and for which the last prior dose dates and times are adequately recorded were included in the PK analyses. Samples taken from patients who vomited within 4 hours of dosing were excluded from the analysis. Cmin is the minimum blood plasma concentration reached by a drug during a dosing interval.
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Imatinib in CML-CP/-AP patients	Asciminib+Imatinib in CML-CP/-AP patients	Asciminib+Imatinib in CML-CP/-AP patients	Asciminib+Imatinib in CML-CP/-AP patients

	(Arm 3: ABL001 40 mg b.i.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 40 mg q.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 60 mg q.d. + IMA 400 mg q.d.)	(Arm 3: ABL001 80 mg q.d. + IMA 400 mg q.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	6	9	6	4
PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) (units: ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 6, 9, 6, 4)	496.81 (31.79%)	693.04 (26.01%)	1093.86 (22.26%)	1363.00 (34.75%)
Cmax: Cycle 2 Day 1 (n = 5, 8, 5, 2)	980.71 (51.41%)	717.38 (42.05%)	1185.38 (58.07%)	1524.50 (26.27%)
Cmin: Cycle 1 Day 1 (n = 0, 0, 0, 0)				
Cmin: Cycle 2 Day 1 (n = 5, 8, 5, 2)	435.39 (56.53%)	143.24 (81.69%)	186.29 (98.61%)	218.96 (142.48%)

PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)

Description	Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1). Only PK blood samples with date and time and for which the last prior dose dates and times are adequately recorded were included in the PK analyses. Samples taken from patients who vomited within 4 hours of dosing were excluded from the analysis. Cmin is the minimum blood plasma concentration reached by a drug during a dosing interval.
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 40 mg b.i.d. + DAS 100 mg q.d.)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 80 mg q.d. + DAS 100 mg q.d.)	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 160 mg q.d. + DAS 100 mg q.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off
Number of Participants Analyzed [units: participants]	11	14	6
PK: Cmax and Cmin of asciminib as measured in plasma with combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) (units: ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 11, 14, 5)	472.13 (37.31%)	1154.98 (61.49%)	4148.86 (35.59%)
Cmax: Cycle 2 Day 1 (n = 9, 10, 5)	823.16 (43.41%)	1473.22 (40.86%)	3780.20 (19.25%)
Cmin: Cycle 1 Day 1 (n = 0, 0, 0)			
Cmin: Cycle 2 Day 1 (n = 9, 10, 5)	308.69 (62.70%)	114.97 (196.47%)	489.80 (26.82%)

PK: Cmax and Cmin of asciminib as measured in plasma with single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5)

Description	Cmax is the maximum (peak) observed plasma drug concentration after single dose administration (mass x volume-1). Only PK blood samples with date and time and for which the last prior dose dates and times are adequately recorded were included in the PK analyses. Samples taken from patients who vomited within 4 hours of dosing were excluded from the analysis. Cmin is the minimum blood plasma concentration reached by a drug during a dosing interval.
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 40 mg b.i.d.)	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 80 mg b.i.d.)	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 160 mg b.i.d.)	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 200 mg b.i.d.)	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 280 mg b.i.d.)
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	4	9	16	6	5
PK: Cmax and Cmin of asciminib as measured in plasma with single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5) (units: ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 4, 9, 15, 6, 4)	423.05 (47.46%)	1472.08 (59.26%)	3210.31 (46.77%)	3287.27 (37.03%)	6450.88 (46.15%)
Cmax: Cycle 2 Day 1 (n = 3, 5, 11, 6, 3)	1297.39 (35.16%)	1750.54 (71.45%)	4784.45 (66.54%)	5976.30 (41.22%)	6695.48 (31.68%)
Cmin: Cycle 1 Day 1 (n = 0, 0, 0, 0, 0)					
Cmin: Cycle 2 Day 1 (n = 3, 5, 11, 6, 2)	464.42 (93.17%)	754.63 (153.92%)	1955.91 (127.63%)	3194.86 (70.62%)	4164.76 (1.53%)

NOVARTIS

PK: AUClast and AUCtau of asciminb as measured in plasma with single agent Asciminib in CML patients (Arm 1)

Description	AUClast is the area under the plasma concentration-time curve from time zero to the last measurable concentration (mass x time x volume-1). AUCtau is the area under the concentration-time curve during a dosing interval [mass x time x volume-1] (i.e. 12 h for BID dosing and 24 h for QD dosing)
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs pre-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML patients (Arm 1: ABL001 40 mg b.i.d.)	**Asciminib as single agent in CML patients (Arm 1: ABL001 200 mg b.i.d.)**	**Asciminib as single agent in CML patients (Arm 1: ABL001 80 mg q.d.)**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)
Number of Participants Analyzed [units: participants]	32	62	18
PK: AUClast and AUCtau of asciminb as measured in plasma with single agent Asciminib in CML patients (Arm 1) (units: hr*ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
AUClast: Cycle 1 Day 1 (n = 30, 61, 18)	2247.11 (69.26%)	14869.9 (33.42%)	10752.4 (42.90%)
AUClast: Cycle 2 Day 1 (n = 30, 54, 17)	3967.03 (49.64%)	29924.6 (41.27%)	15001.3 (28.27%)
AUCtau: Cycle 1 Day 1 (n = 23, 51, 17)	2724.65 (59.63%)	19745.7 (29.33%)	11228.7 (39.82%)
AUCtau: Cycle 2 Day 1 (n = 23, 34, 17)	5262.32 (48.49%)	37547.0 (41.00%)	15112.4 (27.85%)

NOVARTIS

PK: AUlast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2)

Description	AUClast is the area under the plasma concentration-time curve from time zero to the last measurable concentration (mass x time x volume-1). AUCtau is the area under the concentration-time curve during a dosing interval [mass x time x volume-1] (i.e. 12 h for BID dosing and 24 h for QD dosing)
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 20 mg b.i.d. + NIL 300 mg b.i.d.)	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2: ABL001 40 mg b.i.d. + NIL 300 mg b.i.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	12	14
PK: AUlast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) (units: hr*ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cmax: Cycle 1 Day 1 (n = 11, 14)	383.37 (26.71%)	744.59 (76.99%)
Cmax: Cycle 2 Day 1 (n = 10, 12)	447.28 (701.82%)	1158.92 (86.71%)
Cmin: Cycle 1 Day 1 (n = 0, 0)		
Cmin: Cycle 2 Day 1 (n = 10, 12)	168.02 (420.83%)	503.45 (84.45%)

NOVARTIS

PK: AUClast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3)

Description	AUClast is the area under the plasma concentration-time curve from time zero to the last measurable concentration (mass x time x volume-1). AUCtau is the area under the concentration-time curve during a dosing interval [mass x time x volume-1] (i.e. 12 h for BID dosing and 24 h for QD dosing)
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Imatinib in CML-CP/-AP patients (Arm 3: ABL001 40 mg b.i.d. + IMA 400 mg q.d.)	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3: ABL001 40 mg q.d. + IMA 400 mg q.d.)**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3: ABL001 60 mg q.d. + IMA 400 mg q.d.)**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3: ABL001 80 mg q.d. + IMA 400 mg q.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP
Number of Participants Analyzed [units: participants]	6	9	6	4
PK: AUClast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) (units: hr*ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
AUClast: Cycle 1 Day 1 (n = 6, 9, 6, 4)	2581.58 (38.87%)	6556.20 (28.13%)	10810.6 (37.98%)	12246.3 (27.16%)
AUClast: Cycle 2 Day 1 (n = 5, 8, 5, 2)	5652.32 (58.67%)	6948.59 (51.93%)	11424.4 (62.93%)	9932.87 (42.70%)
AUCtau: Cycle 1 Day 1 (n = 4, 8, 6, 4)	3746.59 (17.90%)	6590.30 (30.97%)	10841.6 (38.14%)	12407.8 (25.53%)

AUCtau: Cycle 2 Day 1 (n = 3, 8, 5, 2)	9840.61 (22.07%)	6995.18 (52.05%)	11383.5 (61.99%)	14002.0 (6.45%)

PK: AUClast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4)

Description	AUClast is the area under the plasma concentration-time curve from time zero to the last measurable concentration (mass x time x volume-1). AUCtau is the area under the concentration-time curve during a dosing interval [mass x time x volume-1] (i.e. 12 h for BID dosing and 24 h for QD dosing)
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 40 mg b.i.d. + DAS 100 mg q.d.)	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 80 mg q.d. + DAS 100 mg q.d.)**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4: ABL001 160 mg q.d. + DAS 100 mg q.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off
Number of Participants Analyzed [units: participants]	11	14	6
PK: AUClast and AUCtau of asciminib as measured in plasma in combination arm, Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) (units: hr*ng/ml)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
AUClast: Cycle 1 Day 1 (n = 11, 14, 5)	1885.11 (42.54%)	5706.30 (78.20%)	28738.0 (41.85%)
AUClast: Cycle 2 Day 1 (n = 9, 10, 5)	3910.65 (38.11%)	8734.56 (44.82%)	33816.6 (23.78%)

AUCtau: Cycle 1 Day 1 (n = 6, 13, 5)	2266.79 (55.15%)	7041.92 (71.29%)	28976.2 (42.29%)
AUCtau: Cycle 2 Day 1 (n = 7, 9, 5)	5242.86 (42.98%)	10813.9 (41.39%)	33965.4 (23.88%)

PK: AUClast and AUCtau of asciminib as measured in plasma with single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5)

Description	AUClast is the area under the plasma concentration-time curve from time zero to the last measurable concentration (mass x time x volume-1). AUCtau is the area under the concentration-time curve during a dosing interval [mass x time x volume-1] (i.e. 12 h for BID dosing and 24 h for QD dosing)
Time Frame	0hr pre-dose, (12hrs pre-dose, Japan only as patients were housed overnight), 0.5, 1, 2, 3, 4, 6, 8hrs post-dose
Analysis Population Description	The pharmacokinetic analysis set (PAS) consisted of all patients who had at least one blood sample providing an evaluable full PK profile (Cycle 1 Day 1, Cycle 1 Day 15 or Cycle 2 Day 1).

	Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 40 mg b.i.d.)	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 80 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 160 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 200 mg b.i.d.)**	**Asciminib as single agent in CML-BP and Ph+ ALL participants (Arm 5: ABL001 280 mg b.i.d.)**
Arm/Group Description	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Number of Participants Analyzed [units: participants]	4	9	16	6	5

PK: AUClast and AUCtau of asciminib as measured in plasma with single agent Asciminib in CML-BP and Ph+ ALL patients (Arm 5) (units: hr*ng/ml)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)
AUClast: Cycle 1 Day 1 (n = 4, 9, 15, 6, 4)	2173.66 (45.68%)	6926.15 (54.71%)	14177.3 (44.21%)	15091.6 (42.56%)	3569.7 (29.43%)
AUClast: Cycle 2 Day 1 (n =3, 5, 11, 6, 3)	6588.31 (26.84%)	9462.88 (86.55%)	25821.7 (83.95%)	32017.1 (36.99%)	40212.1 (22.76%)
AUCtau: Cycle 1 Day 1 (n = 2, 5, 13, 4, 2)	2187.40 (65.54%)	10525.7 (53.48%)	20156.5 (34.81%)	16199.3 (27.12%)	39869.3 (34.95%)
AUCtau: Cycle 2 Day 1 (n = 3, 3, 8, 5, 1)	9106.45 (39.75%)	9650.85 (50.97%)	34477.6 (69.25%)	44766.3 (43.67%)	73405.2 (NA%)[1]

[1] NA = Geometric Coefficient of Variation could not be calculated as there was only 1 participant analyzed for this arm

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Commented [AP1]: Still waiting for safety from the stats programmer

Time Frame	Adverse events were collected from first dose of study treatment up to at least 64 weeks in the study treatment with a median duration of exposure to crizanlizumab of ??? weeks.
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Other Adverse Event: An adverse event that is not a serious adverse event, meaning that it does not result in death, is not life-threatening, does not require inpatient hospitalization or

	extend a current hospital stay, does not result in an ongoing or significant incapacity or interfere substantially with normal life functions, and does not cause a congenital anomaly or birth defect.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Asciminib as single agent in CML patients (Arm 1) N = 200	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) N = 26**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) N = 25**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) N = 32**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients N = 43**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)
Total Number Affected	12	1	1	0	10
Total Number At Risk	200	26	25	32	43

NOVARTIS

Serious Adverse Events

Time Frame	Adverse events were collected from first dose of study treatment up to at least 64 weeks in the study treatment with a median duration of exposure to crizanlizumab of ??? weeks.
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Other Adverse Event: An adverse event that is not a serious adverse event, meaning that it does not result in death, is not life-threatening, does not require inpatient hospitalization or extend a current hospital stay, does not result in an ongoing or significant incapacity or interfere substantially with normal life functions, and does not cause a congenital anomaly or birth defect.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

	Asciminib as single agent in CML patients (Arm 1) N = 200	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) N = 26**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) N = 25**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) N = 32**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients N = 43**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute

	CP)/Accelerated Phase (-AP)				lymphoblastic leukemia (ALL)
Total # Affected by any Serious Adverse Event	96	15	13	14	29
Total # at Risk by any Serious Adverse Event	200	26	25	32	43
Blood and lymphatic system disorders					
Anaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Febrile neutropenia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (9.30%)
Haemolytic anaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leukocytosis	1 (0.50%)	1 (3.85%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Neutropenia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders					
Acute coronary syndrome	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acute myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Angina pectoris	2 (1.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aortic valve stenosis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Arrhythmia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Atrial fibrillation	5 (2.50%)	2 (7.69%)	1 (4.00%)	1 (3.13%)	0 (0.00%)
Atrial flutter	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Atrioventricular block	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac arrest	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Cardiac dysfunction	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac failure	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Cardiac failure acute	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Cardiac failure congestive	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiovascular disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Coronary artery disease	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mitral valve incompetence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Myocardial infarction	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myocardial ischaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pericardial effusion	1 (0.50%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Sinus node dysfunction	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ventricular tachycardia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders					
Vestibular disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders					
Cataract	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diplopia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Ectropion	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eyelid cyst	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neovascular age-related macular degeneration	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Visual impairment	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders					
Abdominal pain	3 (1.50%)	1 (3.85%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Abdominal pain upper	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Anal prolapse	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Colitis	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	2 (1.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)

Diarrhoea	2 (1.00%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Duodenal ulcer	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Duodenal ulcer haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Enteritis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Enterocolitis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastric ulcer	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastritis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ileus paralytic	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intestinal obstruction	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intra-abdominal haematoma	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Melaena	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pancreatitis	2 (1.00%)	1 (3.85%)	1 (4.00%)	0 (0.00%)	2 (4.65%)
Pancreatitis acute	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	2 (1.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Vomiting	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
General disorders and administration site conditions					
Asthenia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chest discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Chest pain	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Facial pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Fatigue	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	1 (2.33%)

General physical health deterioration	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Multiple organ dysfunction syndrome	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	3 (1.50%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pyrexia	3 (1.50%)	1 (3.85%)	1 (4.00%)	1 (3.13%)	1 (2.33%)
Hepatobiliary disorders					
Cholecystitis	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholecystitis acute	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatitis	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Liver disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders					
Hypersensitivity	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iodine allergy	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations					
Abdominal abscess	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acinetobacter bacteraemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Appendicitis	2 (1.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Appendicitis perforated	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Atypical pneumonia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchiolitis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Candida infection	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cellulitis	1 (0.50%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)

Clostridium difficile infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Corynebacterium bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
COVID-19	4 (2.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19 pneumonia	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus infection reactivation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Device related infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Escherichia bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Gastroenteritis viral	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Infected bite	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Infectious pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Influenza	1 (0.50%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Kidney infection	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Localised infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Meningitis aseptic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Parotitis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	7 (3.50%)	3 (11.54%)	0 (0.00%)	2 (6.25%)	8 (18.60%)
Pneumonia bacterial	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia fungal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pneumonia klebsiella	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Postoperative wound infection	1 (0.50%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (2.33%)
Pseudomonal bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Respiratory syncytial virus infection	1 (0.50%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Sepsis	3 (1.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)

Septic shock	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Serratia infection	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Sinusitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Upper respiratory tract infection	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Viral hepatitis carrier	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Wound infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Injury, poisoning and procedural complications					
Ankle fracture	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fall	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fibula fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Gastrointestinal anastomotic leak	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Overdose	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Poisoning deliberate	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural complication	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Post procedural haemorrhage	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural inflammation	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Procedural haemorrhage	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Subdural haematoma	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Vascular graft occlusion	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations					
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)

Amylase increased	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Blood creatine phosphokinase increased	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gamma-glutamyltransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders					
Diabetes mellitus inadequate control	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperuricaemia	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypervolaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	1 (0.50%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tetany	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders					
Arthralgia	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Bone pain	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Fibromyalgia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Intervertebral disc protrusion	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Muscular weakness	1 (0.50%)	1 (3.85%)	1 (4.00%)	1 (3.13%)	0 (0.00%)
Myalgia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myopathy	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Osteonecrosis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhabdomyolysis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Spinal stenosis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Systemic lupus erythematosus	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Blast cell crisis	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Blast crisis in myelogenous leukaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Breast cancer	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic myeloid leukaemia	3 (1.50%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Colon cancer	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Malignant melanoma	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myelodysplastic syndrome	1 (0.50%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Prostate cancer	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Squamous cell carcinoma of the vulva	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Thyroid cancer metastatic	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vulval neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Nervous system disorders					

Bell's palsy	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebellar infarction	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebrovascular accident	4 (2.00%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	1 (2.33%)
Chronic inflammatory demyelinating polyradiculoneuropathy	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Facial nerve disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Hemiparesis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
IIIrd nerve paralysis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ischaemic stroke	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neurological symptom	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Sciatica	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Subarachnoid haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Transient ischaemic attack	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
VIth nerve disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders					
Alcohol abuse	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Burnout syndrome	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Completed suicide	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Depression	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Suicide attempt	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders					
Acute kidney injury	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)

Anuria	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nephrolithiasis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal failure	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Renal impairment	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders					
Acute pulmonary oedema	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acute respiratory failure	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchospasm	2 (1.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic obstructive pulmonary disease	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Dyspnoea	1 (0.50%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Interstitial lung disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pleural effusion	9 (4.50%)	1 (3.85%)	0 (0.00%)	3 (9.38%)	0 (0.00%)
Pleurisy	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleuritic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pulmonary alveolar haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pulmonary embolism	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Pulmonary haematoma	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary mass	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary oedema	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stridor	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders					

Angioedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Stasis dermatitis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urticaria	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders					
Aortic stenosis	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Arteriosclerosis	0 (0.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Circulatory collapse	1 (0.50%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cyanosis	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematoma	0 (0.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Hypertension	2 (1.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	2 (4.65%)
Hypertensive emergency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
May-Thurner syndrome	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral arterial occlusive disease	2 (1.00%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral ischaemia	1 (0.50%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (2.33%)
Peripheral vascular disorder	1 (0.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events were collected from first dose of study treatment up to at least 64 weeks in the study treatment with a median duration of exposure to crizanlizumab of ??? weeks.
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Other Adverse Event: An adverse event that is not a serious adverse event, meaning that it does not result in death, is not life-threatening, does not require inpatient hospitalization or

	extend a current hospital stay, does not result in an ongoing or significant incapacity or interfere substantially with normal life functions, and does not cause a congenital anomaly or birth defect.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Asciminib as single agent in CML patients (Arm 1) N = 200	**Asciminib+Nilotinib in CML-CP/-AP patients (Arm 2) N = 26**	**Asciminib+Imatinib in CML-CP/-AP patients (Arm 3) N = 25**	**Asciminib+Dasatinib in CML-CP/-AP patients (Arm 4) N = 32**	**Asciminib as single agent in CML-BP * Ph+ ALL (Arm 5) patients N = 43**
Arm/Group Description	Dose escalation study estimated the maximum tolerated dose (MTD) and/or recommended dose for expansion (RDE) of asciminib as a single agent in adult patients with chronic myeloid leukemia chronic phase (CML-CP)/Accelerated Phase (-AP)	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with nilotinib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in adult patients with CML-CP/-AP	Dose escalation study estimated the MTD and/or RDE of asciminib in combination with dasatinib in patients with CML-CP/-APs. This arm includes 9 new patients enrolled in the expansion cohort after Primary Analysis data cut-off.	Dose escalation study estimated the MTD and/or RDE of asciminib asciminib as single agent in patients with CML-BP (blast phase) and Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia (ALL)

Total # Affected by any Other Adverse Event	199	26	25	32	39
Total # at Risk by any Other Adverse Event	200	26	25	32	43
Blood and lymphatic system disorders					
Anaemia	29 (14.50%)	5 (19.23%)	4 (16.00%)	5 (15.63%)	16 (37.21%)
Leukocytosis	4 (2.00%)	1 (3.85%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Leukopenia	5 (2.50%)	1 (3.85%)	1 (4.00%)	0 (0.00%)	6 (13.95%)
Lymphopenia	4 (2.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Neutropenia	26 (13.00%)	2 (7.69%)	3 (12.00%)	3 (9.38%)	9 (20.93%)
Thrombocytopenia	46 (23.00%)	7 (26.92%)	6 (24.00%)	11 (34.38%)	9 (20.93%)
Cardiac disorders					
Atrial fibrillation	8 (4.00%)	2 (7.69%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Cardiac failure	2 (1.00%)	1 (3.85%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Palpitations	13 (6.50%)	1 (3.85%)	1 (4.00%)	0 (0.00%)	2 (4.65%)
Ear and labyrinth disorders					
Tinnitus	11 (5.50%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (2.33%)
Eye disorders					
Diplopia	5 (2.50%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (2.33%)
Dry eye	18 (9.00%)	1 (3.85%)	4 (16.00%)	4 (12.50%)	4 (9.30%)
Eye irritation	5 (2.50%)	3 (11.54%)	1 (4.00%)	0 (0.00%)	2 (4.65%)
Eyelid oedema	0 (0.00%)	0 (0.00%)	2 (8.00%)	1 (3.13%)	0 (0.00%)
Lacrimation increased	6 (3.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	3 (6.98%)
Photophobia	4 (2.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)

Vision blurred	14 (7.00%)	2 (7.69%)	0 (0.00%)	2 (6.25%)	0 (0.00%)
Gastrointestinal disorders					
Abdominal distension	9 (4.50%)	2 (7.69%)	1 (4.00%)	2 (6.25%)	1 (2.33%)
Abdominal pain	41 (20.50%)	9 (34.62%)	9 (36.00%)	7 (21.88%)	8 (18.60%)
Abdominal pain upper	24 (12.00%)	2 (7.69%)	2 (8.00%)	0 (0.00%)	4 (9.30%)
Constipation	34 (17.00%)	5 (19.23%)	3 (12.00%)	3 (9.38%)	5 (11.63%)
Diarrhoea	59 (29.50%)	6 (23.08%)	10 (40.00%)	7 (21.88%)	9 (20.93%)
Dyspepsia	16 (8.00%)	2 (7.69%)	1 (4.00%)	2 (6.25%)	1 (2.33%)
Gastrooesophageal reflux disease	9 (4.50%)	2 (7.69%)	2 (8.00%)	2 (6.25%)	1 (2.33%)
Inguinal hernia	1 (0.50%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)
Nausea	56 (28.00%)	6 (23.08%)	12 (48.00%)	9 (28.13%)	15 (34.88%)
Oral pain	4 (2.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (2.33%)
Pancreatitis	7 (3.50%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Stomatitis	5 (2.50%)	1 (3.85%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Vomiting	50 (25.00%)	5 (19.23%)	8 (32.00%)	3 (9.38%)	12 (27.91%)
General disorders and administration site conditions					
Asthenia	8 (4.00%)	1 (3.85%)	2 (8.00%)	1 (3.13%)	1 (2.33%)
Chills	9 (4.50%)	1 (3.85%)	1 (4.00%)	3 (9.38%)	4 (9.30%)
Face oedema	2 (1.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Fatigue	62 (31.00%)	4 (15.38%)	3 (12.00%)	13 (40.63%)	12 (27.91%)
Gait disturbance	2 (1.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Influenza like illness	8 (4.00%)	1 (3.85%)	1 (4.00%)	3 (9.38%)	1 (2.33%)
Localised oedema	2 (1.00%)	2 (7.69%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Non-cardiac chest pain	20 (10.00%)	0 (0.00%)	1 (4.00%)	4 (12.50%)	1 (2.33%)

Oedema peripheral	25 (12.50%)	4 (15.38%)	5 (20.00%)	4 (12.50%)	4 (9.30%)
Pain	7 (3.50%)	0 (0.00%)	1 (4.00%)	2 (6.25%)	1 (2.33%)
Pyrexia	31 (15.50%)	1 (3.85%)	5 (20.00%)	5 (15.63%)	11 (25.58%)
Hepatobiliary disorders					
Hepatomegaly	1 (0.50%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations					
Bronchitis	8 (4.00%)	0 (0.00%)	1 (4.00%)	2 (6.25%)	2 (4.65%)
Cellulitis	4 (2.00%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Conjunctivitis	8 (4.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Coronavirus infection	0 (0.00%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	42 (21.00%)	6 (23.08%)	6 (24.00%)	7 (21.88%)	2 (4.65%)
Ear infection	1 (0.50%)	0 (0.00%)	1 (4.00%)	2 (6.25%)	0 (0.00%)
Folliculitis	7 (3.50%)	1 (3.85%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Influenza	11 (5.50%)	0 (0.00%)	2 (8.00%)	2 (6.25%)	1 (2.33%)
Nasopharyngitis	25 (12.50%)	4 (15.38%)	3 (12.00%)	4 (12.50%)	3 (6.98%)
Oral herpes	6 (3.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	3 (6.98%)
Pneumonia	10 (5.00%)	2 (7.69%)	1 (4.00%)	4 (12.50%)	4 (9.30%)
Respiratory tract infection	5 (2.50%)	2 (7.69%)	2 (8.00%)	0 (0.00%)	2 (4.65%)
Sinusitis	6 (3.00%)	1 (3.85%)	0 (0.00%)	2 (6.25%)	1 (2.33%)
Upper respiratory tract infection	36 (18.00%)	1 (3.85%)	4 (16.00%)	7 (21.88%)	6 (13.95%)
Urinary tract infection	11 (5.50%)	2 (7.69%)	1 (4.00%)	1 (3.13%)	2 (4.65%)
Injury, poisoning and procedural complications					
Contusion	7 (3.50%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)

Fall	14 (7.00%)	1 (3.85%)	1 (4.00%)	2 (6.25%)	4 (9.30%)
Procedural pain	5 (2.50%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	3 (6.98%)
Investigations					
Alanine aminotransferase increased	32 (16.00%)	3 (11.54%)	4 (16.00%)	4 (12.50%)	9 (20.93%)
Amylase increased	33 (16.50%)	7 (26.92%)	4 (16.00%)	5 (15.63%)	3 (6.98%)
Aspartate aminotransferase increased	27 (13.50%)	3 (11.54%)	4 (16.00%)	4 (12.50%)	7 (16.28%)
Blood alkaline phosphatase increased	10 (5.00%)	1 (3.85%)	2 (8.00%)	0 (0.00%)	7 (16.28%)
Blood bilirubin increased	11 (5.50%)	2 (7.69%)	2 (8.00%)	0 (0.00%)	1 (2.33%)
Blood creatine phosphokinase increased	8 (4.00%)	0 (0.00%)	3 (12.00%)	2 (6.25%)	2 (4.65%)
Blood creatinine increased	18 (9.00%)	1 (3.85%)	5 (20.00%)	2 (6.25%)	5 (11.63%)
Gamma-glutamyltransferase increased	19 (9.50%)	4 (15.38%)	2 (8.00%)	2 (6.25%)	10 (23.26%)
Lipase increased	61 (30.50%)	10 (38.46%)	8 (32.00%)	8 (25.00%)	8 (18.60%)
Neutrophil count decreased	11 (5.50%)	3 (11.54%)	2 (8.00%)	1 (3.13%)	3 (6.98%)
Platelet count decreased	12 (6.00%)	2 (7.69%)	2 (8.00%)	1 (3.13%)	3 (6.98%)
SARS-CoV-2 test negative	3 (1.50%)	2 (7.69%)	1 (4.00%)	1 (3.13%)	1 (2.33%)
Weight decreased	13 (6.50%)	4 (15.38%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Weight increased	20 (10.00%)	1 (3.85%)	2 (8.00%)	1 (3.13%)	2 (4.65%)
White blood cell count decreased	9 (4.50%)	2 (7.69%)	2 (8.00%)	1 (3.13%)	3 (6.98%)
Metabolism and nutrition disorders					
Decreased appetite	18 (9.00%)	2 (7.69%)	4 (16.00%)	5 (15.63%)	6 (13.95%)
Fluid retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)

Hyperglycaemia	18 (9.00%)	2 (7.69%)	2 (8.00%)	1 (3.13%)	1 (2.33%)
Hyperkalaemia	5 (2.50%)	2 (7.69%)	2 (8.00%)	0 (0.00%)	1 (2.33%)
Hypertriglyceridaemia	20 (10.00%)	3 (11.54%)	4 (16.00%)	1 (3.13%)	2 (4.65%)
Hyperuricaemia	23 (11.50%)	2 (7.69%)	3 (12.00%)	3 (9.38%)	2 (4.65%)
Hypocalcaemia	6 (3.00%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	2 (4.65%)
Hypokalaemia	10 (5.00%)	2 (7.69%)	2 (8.00%)	2 (6.25%)	5 (11.63%)
Hypomagnesaemia	5 (2.50%)	2 (7.69%)	1 (4.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	9 (4.50%)	4 (15.38%)	3 (12.00%)	1 (3.13%)	4 (9.30%)
Hypophosphataemia	21 (10.50%)	1 (3.85%)	6 (24.00%)	3 (9.38%)	4 (9.30%)
Vitamin D deficiency	3 (1.50%)	1 (3.85%)	1 (4.00%)	2 (6.25%)	2 (4.65%)
Musculoskeletal and connective tissue disorders					
Arthralgia	64 (32.00%)	6 (23.08%)	6 (24.00%)	7 (21.88%)	5 (11.63%)
Back pain	34 (17.00%)	2 (7.69%)	6 (24.00%)	4 (12.50%)	5 (11.63%)
Bone pain	18 (9.00%)	4 (15.38%)	0 (0.00%)	4 (12.50%)	3 (6.98%)
Flank pain	14 (7.00%)	0 (0.00%)	1 (4.00%)	1 (3.13%)	2 (4.65%)
Joint swelling	6 (3.00%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	0 (0.00%)
Muscle spasms	17 (8.50%)	0 (0.00%)	4 (16.00%)	0 (0.00%)	2 (4.65%)
Muscular weakness	4 (2.00%)	3 (11.54%)	1 (4.00%)	0 (0.00%)	3 (6.98%)
Musculoskeletal chest pain	8 (4.00%)	3 (11.54%)	1 (4.00%)	3 (9.38%)	2 (4.65%)
Musculoskeletal pain	15 (7.50%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Myalgia	33 (16.50%)	9 (34.62%)	3 (12.00%)	5 (15.63%)	4 (9.30%)
Neck pain	13 (6.50%)	1 (3.85%)	2 (8.00%)	3 (9.38%)	1 (2.33%)
Pain in extremity	36 (18.00%)	5 (19.23%)	3 (12.00%)	6 (18.75%)	4 (9.30%)
Nervous system disorders					
Dizziness	39 (19.50%)	4 (15.38%)	1 (4.00%)	7 (21.88%)	6 (13.95%)

Dysgeusia	8 (4.00%)	0 (0.00%)	1 (4.00%)	3 (9.38%)	1 (2.33%)
Headache	64 (32.00%)	3 (11.54%)	7 (28.00%)	8 (25.00%)	14 (32.56%)
Memory impairment	12 (6.00%)	0 (0.00%)	1 (4.00%)	1 (3.13%)	0 (0.00%)
Neuralgia	1 (0.50%)	2 (7.69%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Paraesthesia	9 (4.50%)	1 (3.85%)	1 (4.00%)	4 (12.50%)	3 (6.98%)
Peripheral sensory neuropathy	3 (1.50%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	0 (0.00%)
Sciatica	9 (4.50%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	3 (6.98%)
Psychiatric disorders					
Anxiety	18 (9.00%)	0 (0.00%)	1 (4.00%)	0 (0.00%)	1 (2.33%)
Depression	15 (7.50%)	1 (3.85%)	0 (0.00%)	1 (3.13%)	0 (0.00%)
Insomnia	22 (11.00%)	2 (7.69%)	2 (8.00%)	0 (0.00%)	4 (9.30%)
Sleep disorder	6 (3.00%)	3 (11.54%)	2 (8.00%)	1 (3.13%)	1 (2.33%)
Renal and urinary disorders					
Dysuria	4 (2.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Renal failure	1 (0.50%)	0 (0.00%)	2 (8.00%)	0 (0.00%)	2 (4.65%)
Reproductive system and breast disorders					
Benign prostatic hyperplasia	4 (2.00%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders					
Cough	41 (20.50%)	6 (23.08%)	4 (16.00%)	7 (21.88%)	8 (18.60%)
Dyspnoea	27 (13.50%)	3 (11.54%)	4 (16.00%)	5 (15.63%)	12 (27.91%)
Dyspnoea exertional	3 (1.50%)	0 (0.00%)	0 (0.00%)	2 (6.25%)	1 (2.33%)
Nasal congestion	13 (6.50%)	0 (0.00%)	1 (4.00%)	1 (3.13%)	0 (0.00%)
Oropharyngeal pain	20 (10.00%)	1 (3.85%)	2 (8.00%)	1 (3.13%)	3 (6.98%)

Pleural effusion	15 (7.50%)	2 (7.69%)	0 (0.00%)	8 (25.00%)	2 (4.65%)
Rhinorrhoea	8 (4.00%)	0 (0.00%)	1 (4.00%)	2 (6.25%)	1 (2.33%)
Skin and subcutaneous tissue disorders					
Alopecia	9 (4.50%)	2 (7.69%)	2 (8.00%)	1 (3.13%)	0 (0.00%)
Dry skin	17 (8.50%)	7 (26.92%)	4 (16.00%)	4 (12.50%)	2 (4.65%)
Erythema	7 (3.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.98%)
Hyperhidrosis	18 (9.00%)	0 (0.00%)	0 (0.00%)	1 (3.13%)	1 (2.33%)
Keratosis pilaris	0 (0.00%)	0 (0.00%)	2 (8.00%)	1 (3.13%)	0 (0.00%)
Night sweats	5 (2.50%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	4 (9.30%)
Pruritus	37 (18.50%)	8 (30.77%)	4 (16.00%)	2 (6.25%)	9 (20.93%)
Rash	44 (22.00%)	5 (19.23%)	6 (24.00%)	4 (12.50%)	5 (11.63%)
Rash maculo-papular	11 (5.50%)	3 (11.54%)	2 (8.00%)	5 (15.63%)	2 (4.65%)
Vascular disorders					
Haematoma	3 (1.50%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	1 (2.33%)
Hot flush	9 (4.50%)	1 (3.85%)	0 (0.00%)	2 (6.25%)	0 (0.00%)
Hypertension	49 (24.50%)	6 (23.08%)	4 (16.00%)	9 (28.13%)	2 (4.65%)
Hypotension	4 (2.00%)	1 (3.85%)	0 (0.00%)	2 (6.25%)	3 (6.98%)
Peripheral arterial occlusive disease	4 (2.00%)	2 (7.69%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Relevant Findings

Definition: *Important finding not meeting the criteria for efficacy/safety results (ie, notable change in laboratory or drug trough values that posed no safety issue, but is of medical interest).*

Example: *Mean (SD) parameters of company product*

Commented [PA2]: Anything needed here?

Not Applicable

Conclusion:

- Based on the BLRM modeling, emerging safety and tolerability data, PK and preliminary efficacy observed, the RDEs/RP2Ds were determined as follows:
    - In patients with CML-CP/-AP treated with asciminib single agent, asciminib at 40 mg b.i.d. was determined as the RDE/RP2D in patients with CML-CP/-AP not harboring the T315I mutation, and at 200 mg b.i.d. in patients with CML-CP/-AP harboring the T315I mutation.
    - In patients with CML-CP/-AP treated with asciminib in combination with nilotinib, asciminib 40 mg b.i.d. + nilotinib 300 mg b.i.d. was determined as the RDE.
    - In patients with CML-CP/-AP treated with asciminib in combination with imatinib, two doses of asciminib 40 mg or 60 mg administered daily in combination with imatinib 400 mg q.d. were identified as RP2Ds providing pharmacologically active exposures. Both dose levels are being evaluated in the Phase II trial.
    - In patients with CML-CP/-AP treated with asciminib in combination with dasatinib, asciminib 80 mg q.d. + dasatinib 100 mg q.d. was determined as the RDE.
    - In patients with CML-BP or Ph+ ALL the RDE has not been determined and due to scarce anti-leukemic activity observed across doses tested, this cohort was not further assessed
- In patients with CML-CP/-AP, asciminib as single agent after single or multiple doses was rapidly absorbed with the Tmax of 2-3 hours, and was independent of dose. Asciminib exposure increased slightly more than proportionally for b.i.d. doses analyzed and dose proportional increase for q.d. dosing.
    - There was no apparent difference in PK between the patients with CML-CP harboring the T315I mutation compared to the patients with disease not harboring the T315I mutation.
- When comparing to the asciminib single agent exposure, the exposure of asciminib appeared to be increased moderately when administered in combination with nilotinib or imatinib at steady state (Cycle 2 Day 1; AUCtau increased by 1.5-fold and 1.9-fold for nilotinib and imatinib, respectively). Dasatinib had no apparent effect on the PK of asciminib 40 mg b.i.d. and at 80 mg q.d. the Cmax and AUCtau was 1.2 to 1.4-fold higher when compared to the monotherapy. There was no relevant difference in nilotinib, imatinib and dasatinib exposure across the different dose groups.
- Overall, asciminib as single agent was well tolerated and AEs reported were manageable with dose adjustment/interruption, concomitant medication or supportive therapy. The safety profile was similar across the doses and regimens tested.
    - Overall, patients with CML-CP harboring the T315I mutation showed similar safety profile to that of all CML-CP/-AP patients treated at 200 mg b.i.d. in Arm 1
- Overall, the safety of asciminib in combination with nilotinib or imatinib or dasatinib was similar among the different treatment groups and was consistent with the safety of individual agents.

- Asciminib as single agent was demonstrated to be efficacious in achieving optimal disease control with durable MMR in most of the patients with CML-CP/-AP or even improved to a deeper level of response across dose levels and regimens (b.i.d. and q.d.) tested. Further, asciminib showed clinically meaningful anti-leukemic activity in patients with CML-CP harboring the T315I mutation who were treated at 200 mg b.i.d. (RDE) regardless of prior ponatinib treatment.

The overall data from the study supports use of asciminib as a therapeutic treatment option which is efficacious and safe for heavily pre-treated patients with CML including those harboring the T315I mutation. These populations represent patients with a high unmet medical need for alternative therapies.

Date of Clinical Trial Report

Primary CSR Published Date: 30 April 2021

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