Eigene Vorlage

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Ponatinib (Iclusig®)

Incyte Biosciences Germany GmbH

Statistische Analyse

Erwachsene Patienten mit Philadelphia-Chromosom-positiver akuter Lymphoblastenleukämie (Ph+ ALL), die behandlungsresistent gegenüber Dasatinib sind, die Dasatinib nicht vertragen und bei denen eine anschließende Behandlung mit Imatinib klinisch nicht geeignet ist, oder bei denen eine T315I-Mutation vorliegt

Stand: 26.05.2020

STATISTISCHE ANALYSE

zum

Dossier zur Nutzenbewertung

gemäß § 35a SGB V

zu

Ponatinib (Iclusig®)

Incyte Biosciences Germany GmbH

Erwachsene Patienten mit chronischer myeloischer Leukämie (CML) in der chronischen Phase, akzelerierten Phase oder Blastenkrise, die behandlungsresistent gegenüber Dasatinib bzw. Nilotinib sind, die Dasatinib oder Nilotinib nicht vertragen und bei denen eine anschließende Behandlung mit Imatinib klinisch nicht geeignet ist, oder bei denen eine T315I-Mutation vorliegt, sowie erwachsene Patienten mit Philadelphia-Chromosom-positiver akuter Lymphoblastenleukämie (Ph+ ALL), die behandlungsresistent gegenüber Dasatinib sind, die Dasatinib nicht vertragen und bei denen eine anschließende Behandlung mit Imatinib klinisch nicht geeignet ist, oder bei denen eine T315I-Mutation vorliegt.

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Statistische Programmierung:	**Cogitars GmbH**

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2.1 Demographic and other baseline characteristics

2.1.1 Patients with Ph+ ALL

Table 2.1.1.1 (Study 101)
Demographic and Baseline Characteristics
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
T315I mutation	Yes	n (%)	4 (80.0%)
	No	n (%)	1 (20.0%)
Gender	Male	n (%)	5 (100.0%)
	Female	n (%)	0 (0.0%)
Age	(Years)	Mean (SD)	40.0 (15.92)
		Median	36.0
		Min, Max	(27, 67)
ECOG	Grade 0	n (%)	1 (20.0%)
	Grade 1	n (%)	2 (40.0%)
	Grade 2	n (%)	2 (40.0%)
Number of prior TKI(s)	1	n (%)	3 (60.0%)
	2	n (%)	2 (40.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
[1] Percentages are based on the patients previously treated with dasatinib or nilotinib.

Table 2.1.1.1 (Study 101)
Demographic and Baseline Characteristics
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
	>=3	n (%)	0 (0.0%)
Prior Approved TKI	Imatinib	n (%)	3 (60.0%)
	Dasatinib	n (%)	4 (80.0%)
	Nilotinib	n (%)	0 (0.0%)
Time since diagnosis	(Years)	Mean (SD)	1.3 (0.48)
		Median	1.2
		Min, Max	(0.8, 1.9)
Prior dasatinib or nilotinib [1]	All	n	4
	Intolerant	n (%)	0 (0.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
[1] Percentages are based on the patients previously treated with dasatinib or nilotinib.

Table 2.1.1.1 (Study 201)
Demographic and Baseline Characteristics
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
T315I mutation [1]	Yes	n (%)	22 (68.8%)
	No	n (%)	10 (31.3%)
Gender	Male	n (%)	20 (62.5%)
	Female	n (%)	12 (37.5%)
Age	(Years)	Mean (SD)	53.0 (19.15)
		Median	61.5
		Min, Max	(20, 80)
ECOG	Grade 0	n (%)	11 (34.4%)
	Grade 1	n (%)	17 (53.1%)
	Grade 2	n (%)	4 (12.5%)
	Grade 3	n (%)	0 (0.0%)
Number of prior TKI(s)	1	n (%)	6 (18.8%)

Safety Population: All treated patients
Percentages are based on the safety population.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.1.1 (Study 201)
Demographic and Baseline Characteristics
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
	2	n (%)	13 (40.6%)
	>=3	n (%)	13 (40.6%)
Prior approved TKI(s)	No Prior Approved TKI	n (%)	0 (0.0%)
	1 Prior Approved TKI	n (%)	6 (18.8%)
	- Imatinib	n (%)	2 (6.3%)
	- Dasatinib	n (%)	4 (12.5%)
	- Nilotinib	n (%)	0 (0.0%)
	2 Prior Approved TKIs	n (%)	14 (43.8%)
	- Imatinib + 2nd Generation TKI	n (%)	13 (40.6%)
	- Imatinib + Dasatinib	n (%)	13 (40.6%)
	- Imatinib + Nilotinib	n (%)	0 (0.0%)
	- Dasatinib + Nilotinib	n (%)	1 (3.1%)
	3 Prior Approved TKIs	n (%)	12 (37.5%)
	- Imatinib + Dassatinib + Nilotinib	n (%)	12 (37.5%)
Time since diagnosis	(Years)	Mean (SD)	2.3 (1.91)
		Median	1.5

Safety Population: All treated patients
Percentages are based on the safety population.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.1.1 (Study 201)
Demographic and Baseline Characteristics
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
		Min, Max	(0.5, 7.8)
Prior dasatinib or nilotinib	Resistant	n (%)	27 (84.4%)
	Intolerant but not resistant	n (%)	2 (6.3%)
	Not Resistant or intolerant	n (%)	3 (9.4%)

Safety Population: All treated patients
Percentages are based on the safety population.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.1.2 (Study 101)
Follow-up and treatment duration
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
Follow-up duration	(Weeks)	N	5
		Mean (SD)	11.5 (7.35)
		Median	10.1
		Min, Max	(4.3, 23.7)
Follow-up duration	(Months)	N	5
		Mean (SD)	2.6 (1.69)
		Median	2.34
		Min, Max	(0.99, 5.46)
Treatment duration	(Weeks)	N	5
		Mean (SD)	9.3 (6.08)
		Median	7.4
		Min, Max	(4.1, 19.7)
Treatment duration	(Months)	N	5
		Mean (SD)	2.1 (1.40)

Safety Population: All treated patients

Table 2.1.1.2 (Study 101)
Follow-up and treatment duration
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
		Median	1.71
		Min, Max	(0.95, 4.54)

Safety Population: All treated patients

Table 2.1.1.2 (Study 201)
Follow-up and treatment duration
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
Follow-up duration	(Weeks)	N	32
		Mean (SD)	53.1 (66.33)
		Median	23.4
		Min, Max	(0.4, 259.0)
Follow-up duration	(Months)	N	32
		Mean (SD)	12.2 (15.26)
		Median	5.40
		Min, Max	(0.10, 59.61)
Treatment duration	(Weeks)	N	32
		Mean (SD)	21.9 (32.43)
		Median	11.6
		Min, Max	(0.4, 170.7)
Treatment duration	(Months)	N	32
		Mean (SD)	5.0 (7.47)

Safety Population: All treated patients

Table 2.1.1.2 (Study 201)
Follow-up and treatment duration
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
		Median	2.66
		Min, Max	(0.10, 39.31)

Safety Population: All treated patients

2.1.2 Patients with Ph+ ALL by T315I status

No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.1.2.1 (Study 201)
Demographic and Baseline Characteristics by T315I Status
Treated Population - ALL Patients

T315I [1]	*Variable*	*Category*	*Statistic*	*Ph+ ALL (N=32)*
Yes	T315I		n (%)	22 (100%)
No	T315I		n (%)	10 (100%)
Yes	Gender	Male	n (%)	14 (63.6%)
		Female	n (%)	8 (36.4%)
No	Gender	Male	n (%)	6 (60.0%)
		Female	n (%)	4 (40.0%)
Yes	Age	(Years)	Mean (SD)	54.8 (18.78)
			Median	63.0
			Min, Max	(23, 80)
No	Age	(Years)	Mean (SD)	49.2 (20.41)
			Median	53.5

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.2.1 (Study 201)
Demographic and Baseline Characteristics by T315I Status
Treated Population - ALL Patients

T315I [1]	*Variable*	*Category*	*Statistic*	*Ph+ ALL (N=32)*
			Min, Max	(20, 74)
Yes	ECOG	Grade 0	n (%)	8 (36.4%)
		Grade 1	n (%)	11 (50.0%)
		Grade 2	n (%)	3 (13.6%)
No	ECOG	Grade 0	n (%)	3 (30.0%)
		Grade 1	n (%)	6 (60.0%)
		Grade 2	n (%)	1 (10.0%)
		Grade 3	n (%)	0 (0.0%)
Yes	Number of prior TKI(s)	1	n (%)	5 (22.7%)
		2	n (%)	10 (45.5%)
		>=3	n (%)	7 (31.8%)
No	Number of prior TKI(s)	1	n (%)	1 (10.0%)
		2	n (%)	3 (30.0%)
		>=3	n (%)	6 (60.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.2.1 (Study 201)
Demographic and Baseline Characteristics by T315I Status
Treated Population - ALL Patients

T315I [1]	*Variable*	*Category*	*Statistic*	*Ph+ ALL (N=32)*
Yes	Prior approved TKI(s)	No Prior Approved TKI	n (%)	0 (0.0%)
		1 Prior Approved TKI	n (%)	5 (22.7%)
		- Imatinib	n (%)	2 (9.1%)
		- Dasatinib	n (%)	3 (13.6%)
		2 Prior Approved TKIs	n (%)	11 (50.0%)
		- Imatinib + 2nd Generation TKI	n (%)	10 (45.5%)
		- Imatinib + Dasatinib	n (%)	10 (45.5%)
		- Imatinib + Nilotinib	n (%)	0 (0.0%)
		- Dasatinib + Nilotinib	n (%)	1 (4.5%)
		3 Prior Approved TKIs	n (%)	6 (27.3%)
		- Imatinib + Dassatinib + Nilotinib	n (%)	6 (27.3%)
No	Prior approved TKI(s)	1 Prior Approved TKI	n (%)	1 (10.0%)
		- Dasatinib	n (%)	1 (10.0%)
		- Nilotinib	n (%)	0 (0.0%)
		2 Prior Approved TKIs	n (%)	3 (30.0%)
		- Imatinib + 2nd Generation TKI	n (%)	3 (30.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.2.1 (Study 201)
Demographic and Baseline Characteristics by T315I Status
Treated Population - ALL Patients

T315I [1]	*Variable*	*Category*	*Statistic*	*Ph+ ALL (N=32)*
		- Imatinib + Dasatinib	n (%)	3 (30.0%)
		- Imatinib + Nilotinib	n (%)	0 (0.0%)
		- Dasatinib + Nilotinib	n (%)	0 (0.0%)
		3 Prior Approved TKIs	n (%)	6 (60.0%)
		- Imatinib + Dassatinib + Nilotinib	n (%)	6 (60.0%)
Yes	Time since diagnosis	(Years)	Mean (SD)	2.0 (1.56)
			Median	1.4
			Min, Max	(0.5, 6.6)
No	Time since diagnosis	(Years)	Mean (SD)	3.0 (2.45)
			Median	1.9
			Min, Max	(1.0, 7.8)
Yes	Prior dasatinib or nilotinib	Resistant	n (%)	17 (77.3%)
		Intolerant but not resistant	n (%)	2 (9.1%)
		Not Resistant or intolerant	n (%)	3 (13.6%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.2.1 (Study 201)
Demographic and Baseline Characteristics by T315I Status
Treated Population - ALL Patients

T315I [1]	*Variable*	*Category*	*Statistic*	*Ph+ ALL (N=32)*
No	Prior dasatinib or nilotinib	Resistant	n (%)	10 (100.0%)
		Intolerant but not resistant	n (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] T315I Yes: Patients in Cohort F.

Table 2.1.2.2 (Study 201)
Follow-up and treatment duration by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
Follow-up duration	(Weeks)	Yes	N	22
			Mean (SD)	39.6 (54.59)
			Median	22.7
			Min, Max	(0.4, 259.0)
		No	N	10
			Mean (SD)	82.8 (82.31)
			Median	55.7
			Min, Max	(4.7, 244.7)
Follow-up duration	(Months)	Yes	N	22
			Mean (SD)	9.1 (12.56)
			Median	5.23
			Min, Max	(0.10, 59.61)
		No	N	10
			Mean (SD)	19.1 (18.94)
			Median	12.81

Treated Population: All treated patients who were also assigned to a cohort.

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Table 2.1.2.2 (Study 201)
Follow-up and treatment duration by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
			Min, Max	(1.09, 56.32)
Treatment duration	(Weeks)	Yes	N	22
			Mean (SD)	20.7 (36.25)
			Median	10.9
			Min, Max	(0.4, 170.7)
		No	N	10
			Mean (SD)	24.6 (23.36)
			Median	13.4
			Min, Max	(4.7, 67.7)
Treatment duration	(Months)	Yes	N	22
			Mean (SD)	4.8 (8.35)
			Median	2.52
			Min, Max	(0.10, 39.31)
		No	N	10
			Mean (SD)	5.7 (5.38)

Treated Population: All treated patients who were also assigned to a cohort.

Table 2.1.2.2 (Study 201)
Follow-up and treatment duration by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
			Median	3.08
			Min, Max	(1.09, 15.59)

Treated Population: All treated patients who were also assigned to a cohort.

2.2. Results

2.2.1 Efficacy

2.2.1.1 Mortality

2.2.1.1.1 Patients with Ph+ ALL

2.2.1.1.1.1 Deaths

Table 2.2.1.1.1.1 (Study 101)
Deaths
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
Patient status	Deaths at 24 months	N (%)	3 (60.0%)
		95% CI (Clopper-Pearson)	(14.7%, 94.7%)
Patient status	Deaths at 48 months	N (%)	3 (60.0%)
		95% CI (Clopper-Pearson)	(14.7%, 94.7%)
Patient status	Deaths at end of trial	N (%)	3 (60.0%)
		95% CI (Clopper-Pearson)	(14.7%, 94.7%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.1.1.1.1 (Study 201)
Deaths
Treated Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
Patient status	Deaths at 24 months	N (%)	24 (75.0%)
		95% CI (Clopper-Pearson)	(56.6%, 88.5%)
Patient status	Deaths at 48 months	N (%)	25 (78.1%)
		95% CI (Clopper-Pearson)	(60.0%, 90.7%)
Patient status	Deaths at end of trial	N (%)	25 (78.1%)
		95% CI (Clopper-Pearson)	(60.0%, 90.7%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the treated population.

2.2.1.1.1.2 Overall Survival, OS

Figure 2.2.1.1.1.2 (Study 101)
Overall Survival (OS)
Safety Population - Ph+ ALL Patients

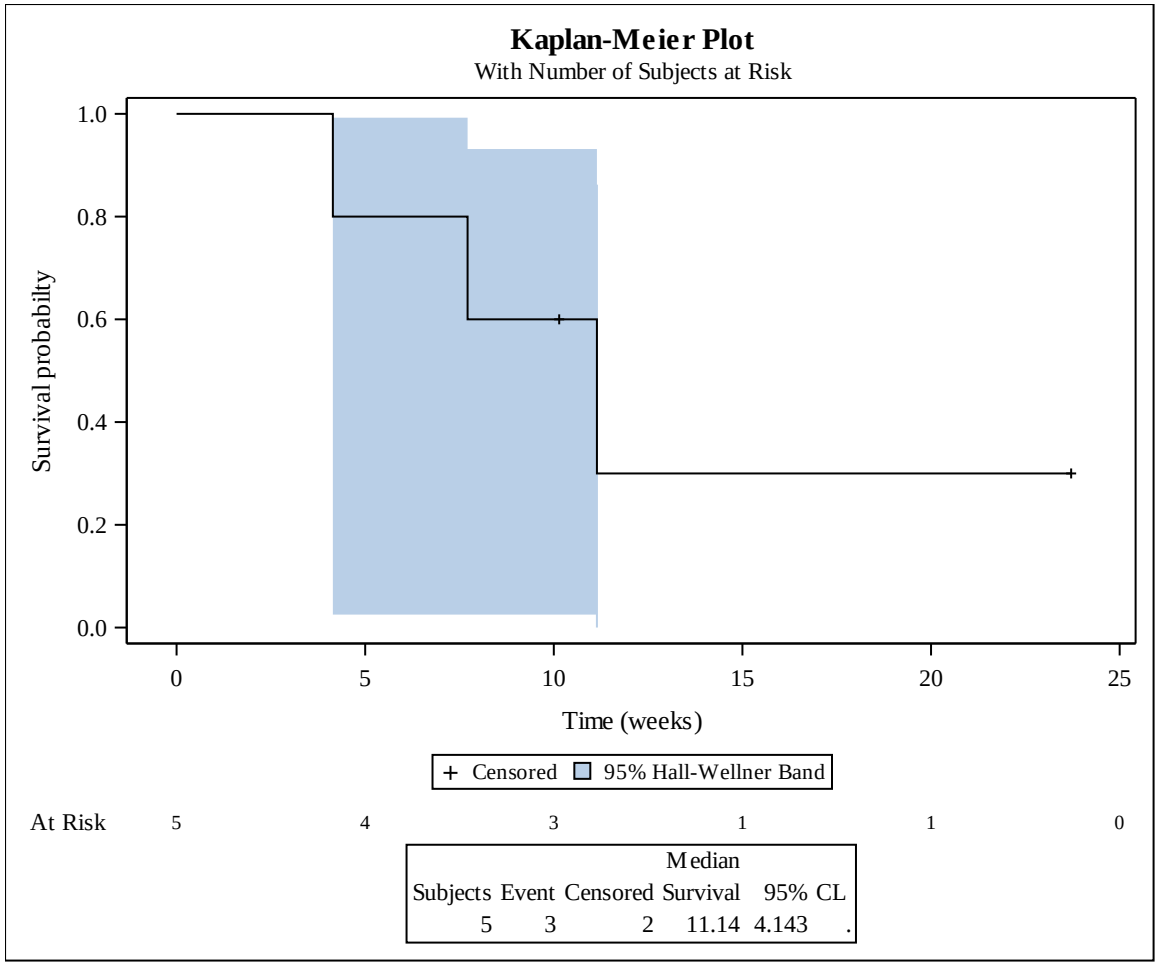

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Figure 2.2.1.1.1.2 (Study 201)
Overall Survival (OS)
Treated Population - Ph+ ALL Patients

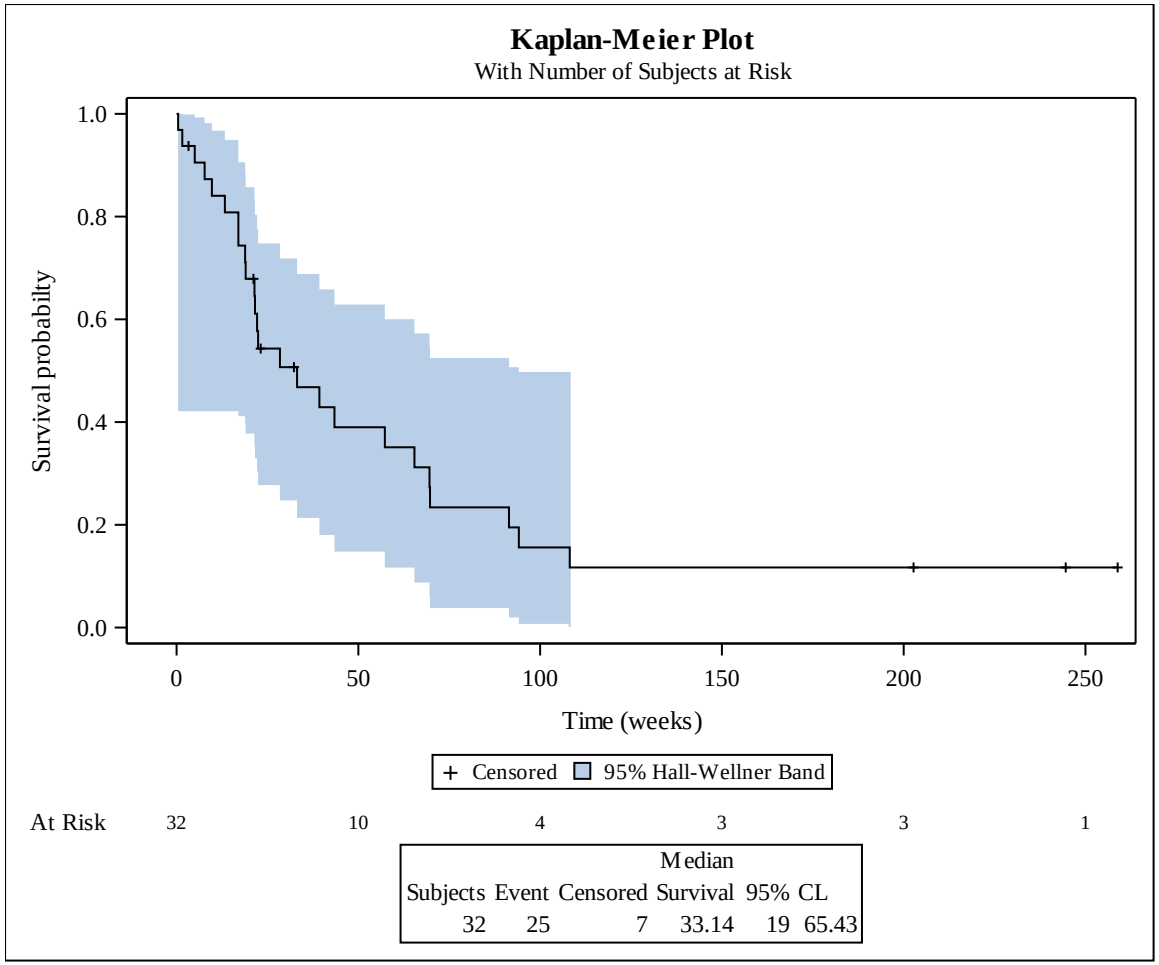

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Table 2.2.1.1.1.3 (Study 101)
Overall Survival (OS) at 24 and 48 Months
Safety Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*OS (%)*	*95% CI*
ALL Ph+ (N=5)	24	104	.	.%	(.%, .%)
	48	208	.	.%	(.%, .%)

Safety Population: All treated patients
Estimates were derived using the Kaplan-Meier method.

Table 2.2.1.1.1.3 (Study 201)
Overall Survival (OS) at 24 and 48 Months
Treated Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*OS (%)*	*95% CI*
ALL Ph+ (N=32)	24	104	4	15.6%	(5.0%, 31.6%)
	48	208	2	11.7%	(3.0%, 26.9%)

Treated Population: All treated patients who were also assigned to a cohort.
Estimates were derived using the Kaplan-Meier method.

2.2.1.1.2 Patients with Ph+ ALL by T315I status

No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.2.1.1.2.1 (Study 201)
Deaths by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
Patient status	Deaths at 24 months	Yes	N total	22
			N (%)	17 (77.3%)
			95% CI (Clopper-Pearson)	(54.6%, 92.2%)
		No	N total	10
			N (%)	7 (70.0%)
			95% CI (Clopper-Pearson)	(34.8%, 93.3%)
			p-value Fisher's exact test	0.6808
	Deaths at 48 months	Yes	N total	22
			N (%)	17 (77.3%)
			95% CI (Clopper-Pearson)	(54.6%, 92.2%)
		No	N total	10
			N (%)	8 (80.0%)
			95% CI (Clopper-Pearson)	(44.4%, 97.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.

Table 2.2.1.1.2.1 (Study 201)
Deaths by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
			p-value Fisher's exact test	1.0000
Patient status	Deaths at end of trial	Yes	N total	22
			N (%)	17 (77.3%)
			95% CI (Clopper-Pearson)	(54.6%, 92.2%)
		No	N total	10
			N (%)	8 (80.0%)
			95% CI (Clopper-Pearson)	(44.4%, 97.5%)
			p-value Fisher's exact test	1.0000

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.

Figure 2.2.1.1.2.2 (Study 201)
Overall Survival by T315I status
Treated Population - ALL Ph+ Patients

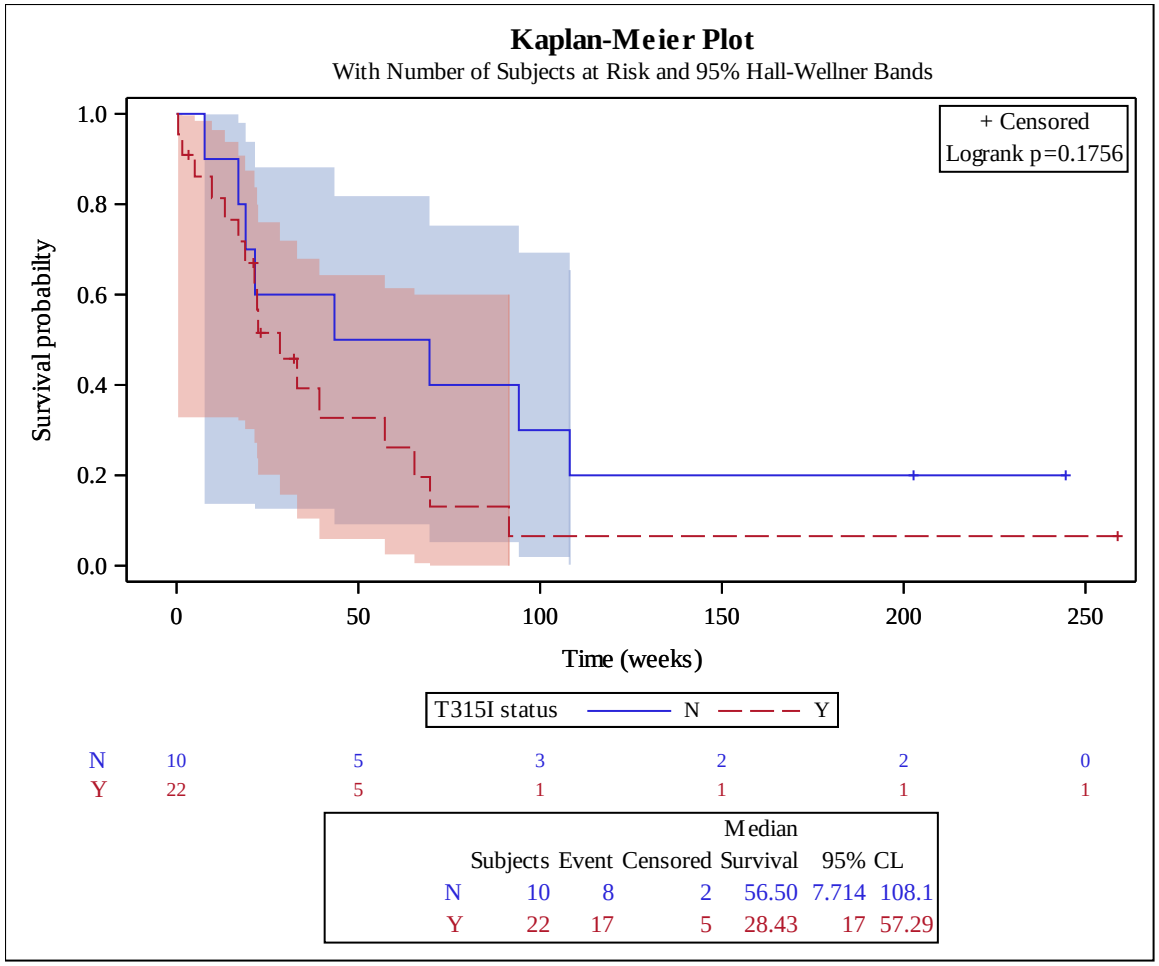

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Table 2.2.1.1.2.3 (Study 201)
Overall Survival (OS) at 24 and 48 Months by T315I Status
Treated Population - ALL Patients

Diagnosis	*T315I*	*Month*	*Week*	*Number at risk*	*OS (%)*	*95% CI*
ALL Ph+ (T315I Yes: N=22, No: N=10)	Yes	24	104	1	6.5%	(0.4%, 25.4%)
		48	208	1	6.5%	(0.4%, 25.4%)
	No	24	104	3	30.0%	(7.1%, 57.8%)
		48	208	1	20.0%	(3.1%, 47.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Estimates were derived using the Kaplan-Meier method.

2.2.1.2 Major Molecular Response, MMR

2.2.1.2.1 Patients with Ph+ ALL

Table 2.2.1.2.1.1 (Study 101)
MMR
Safety Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=5)*
MMR	MMR reached before 12 months	N (%)	1 (20.0%)
		95% CI (Clopper-Pearson)	(0.5%, 71.6%)
MMR	MMR reached before 24 months	N (%)	1 (20.0%)
		95% CI (Clopper-Pearson)	(0.5%, 71.6%)
MMR	MMR reached at any time during trial	N (%)	1 (20.0%)
		95% CI (Clopper-Pearson)	(0.5%, 71.6%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.1.2.1.1 (Study 201)
MMR
Treated Population - Ph+ ALL Patients

Variable	*Category*	*Statistic*	*Ph+ ALL (N=32)*
MMR	MMR reached before 12 months	N (%)	3 (9.4%)
		95% CI (Clopper-Pearson)	(2.0%, 25.0%)
MMR	MMR reached before 24 months	N (%)	3 (9.4%)
		95% CI (Clopper-Pearson)	(2.0%, 25.0%)
MMR	MMR reached at any time during trial	N (%)	3 (9.4%)
		95% CI (Clopper-Pearson)	(2.0%, 25.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the treated population.

Figure 2.2.1.2.1.2 (Study 101)
Time to MMR
Safety Population - Ph+ ALL Patients

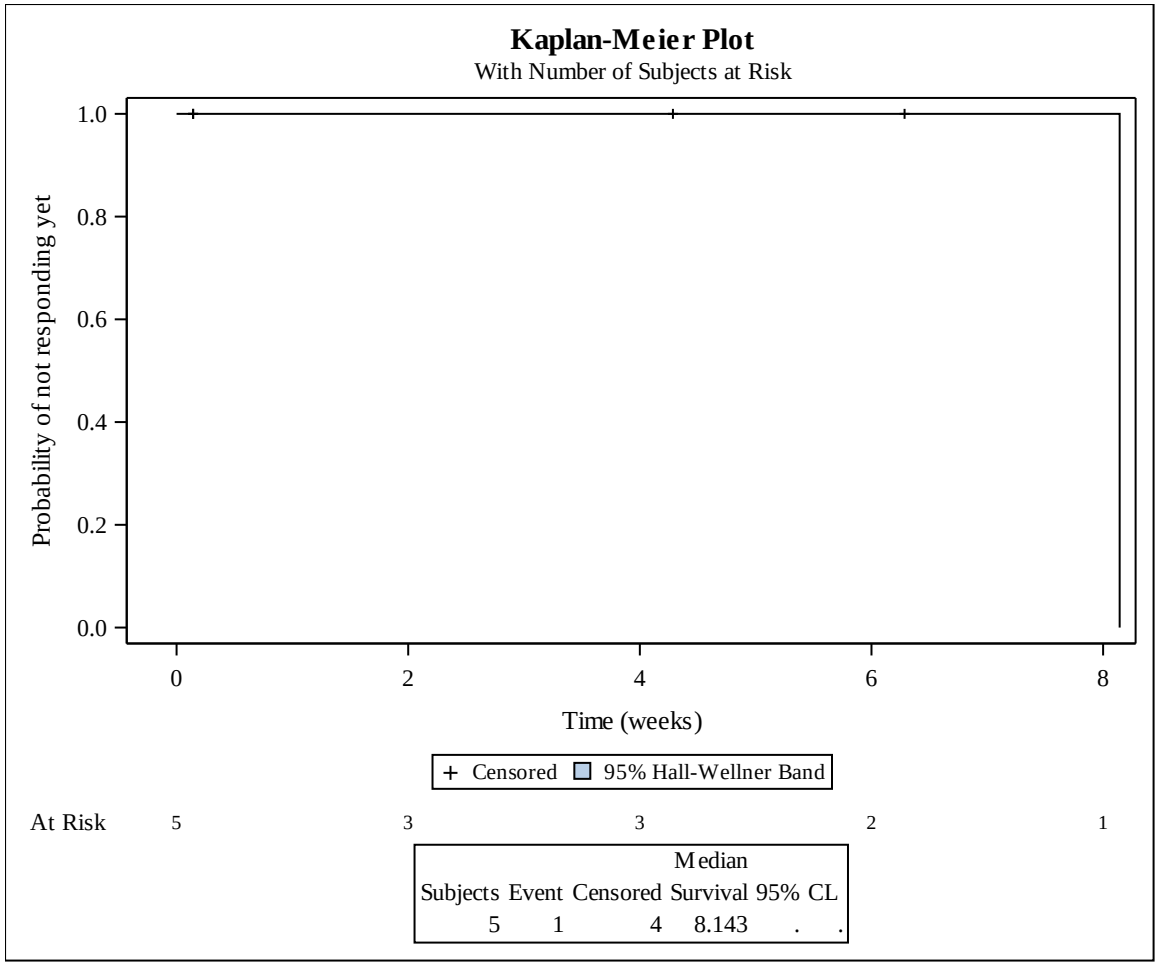

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Figure 2.2.1.2.1.2 (Study 201)
Time to MMR
Treated Population - Ph+ ALL Patients

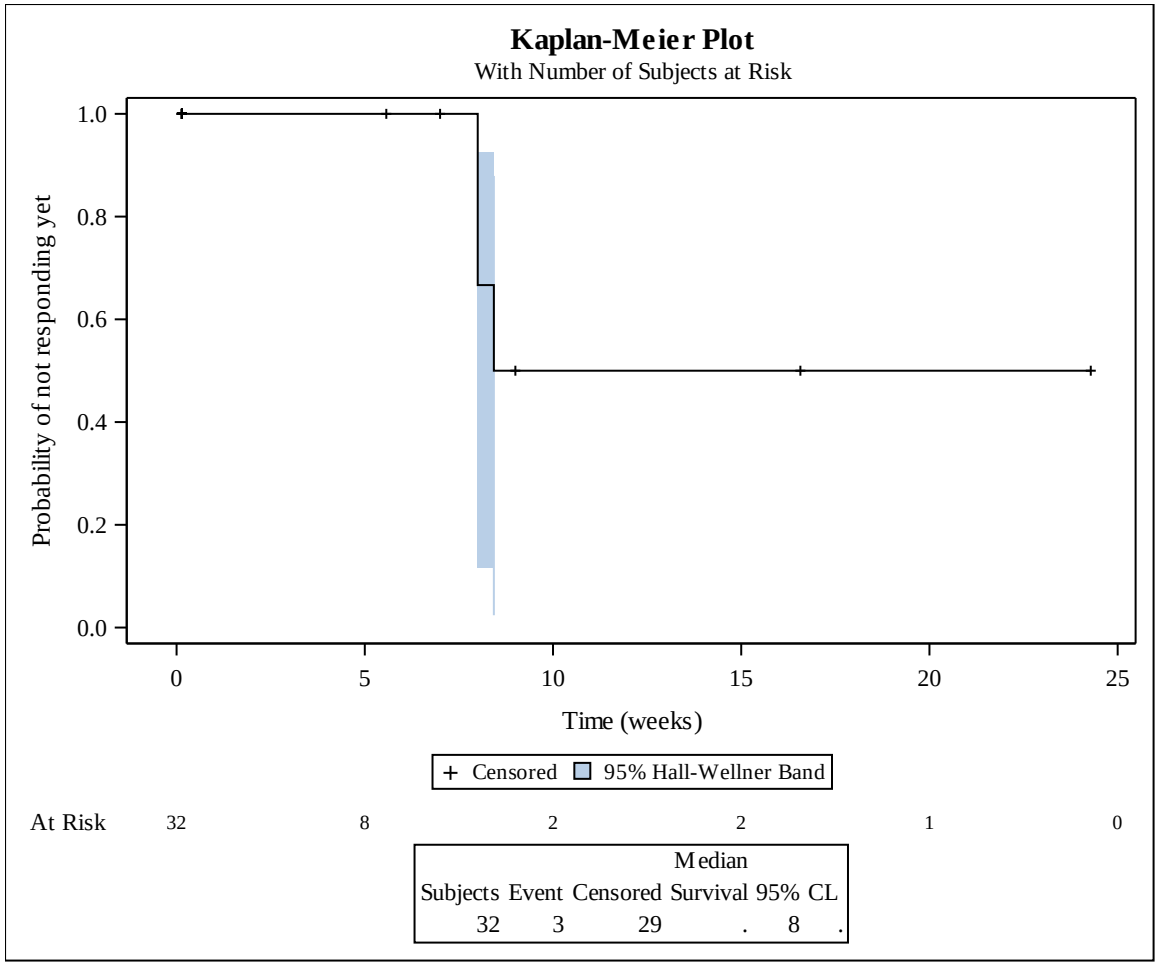

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Table 2.2.1.2.1.3 (Study 101)
Time to MMR in responders
Safety Population - Ph+ ALL Patients

Variable	*Statistic*	*Ph+ ALL (N=5)*
Time to MMR (weeks), responders only	N	1
	Median	8.1
	Min, Max	8.1, 8.1

Safety Population: All treated patients

Table 2.2.1.2.1.3 (Study 201)
Time to MMR in responders
Treated Population - Ph+ ALL Patients

Variable	*Statistic*	*Ph+ ALL (N=32)*
Time to MMR (weeks), responders only	N	3
	Median	8.0
	Min, Max	8.0, 8.4

Treated Population: All treated patients who were also assigned to a cohort.

Table 2.2.1.2.1.4 (Study 101)
Probability of no MMR yet at 12 and 24 months
Safety Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*No MMR yet (%)*	*95% CI*
ALL Ph+ (N=5)	12	52	0	0.0%	(0.0%, 0.0%)
	24	104	0	0.0%	(0.0%, 0.0%)

Safety Population: All treated patients
Total numbers refer to the patients with an MMR.
Estimates were derived using the Kaplan-Meier method.

Table 2.2.1.2.1.4 (Study 201)
Probability of no MMR yet at 12 and 24 months
Treated Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*No MMR yet (%)*	*95% CI*
ALL Ph+ (N=32)	12	52	.	.%	(.%, .%)
	24	104	.	.%	(.%, .%)

Treated Population: All treated patients who were also assigned to a cohort.
Estimates were derived using the Kaplan-Meier method.

2.2.1.2.2 Patients with Ph+ ALL by T315I status

No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.2.1.2.2.1 (Study 201)
MMR by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
MMR	MMR reached before 12 months	Yes	N total	22
			N (%)	1 (4.5%)
			95% CI (Clopper-Pearson)	(0.1%, 22.8%)
		No	N total	10
			N (%)	2 (20.0%)
			95% CI (Clopper-Pearson)	(2.5%, 55.6%)
			p-value Fisher's exact test	0.2238
MMR	MMR reached before 24 months	Yes	N total	22
			N (%)	1 (4.5%)
			95% CI (Clopper-Pearson)	(0.1%, 22.8%)
		No	N total	10
			N (%)	2 (20.0%)
			95% CI (Clopper-Pearson)	(2.5%, 55.6%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.

Table 2.2.1.2.2.1 (Study 201)
MMR by T315I status
Treated Population - ALL Patients

Variable	*Category*	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
			p-value Fisher's exact test	0.2238
MMR	MMR reached at any time during trial	Yes	N total	22
			N (%)	1 (4.5%)
			95% CI (Clopper-Pearson)	(0.1%, 22.8%)
		No	N total	10
			N (%)	2 (20.0%)
			95% CI (Clopper-Pearson)	(2.5%, 55.6%)
			p-value Fisher's exact test	0.2238

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.

Figure 2.2.1.2.2.2 (Study 201)
Time to MMR by T315I status
Treated Population - ALL Ph+ Patients

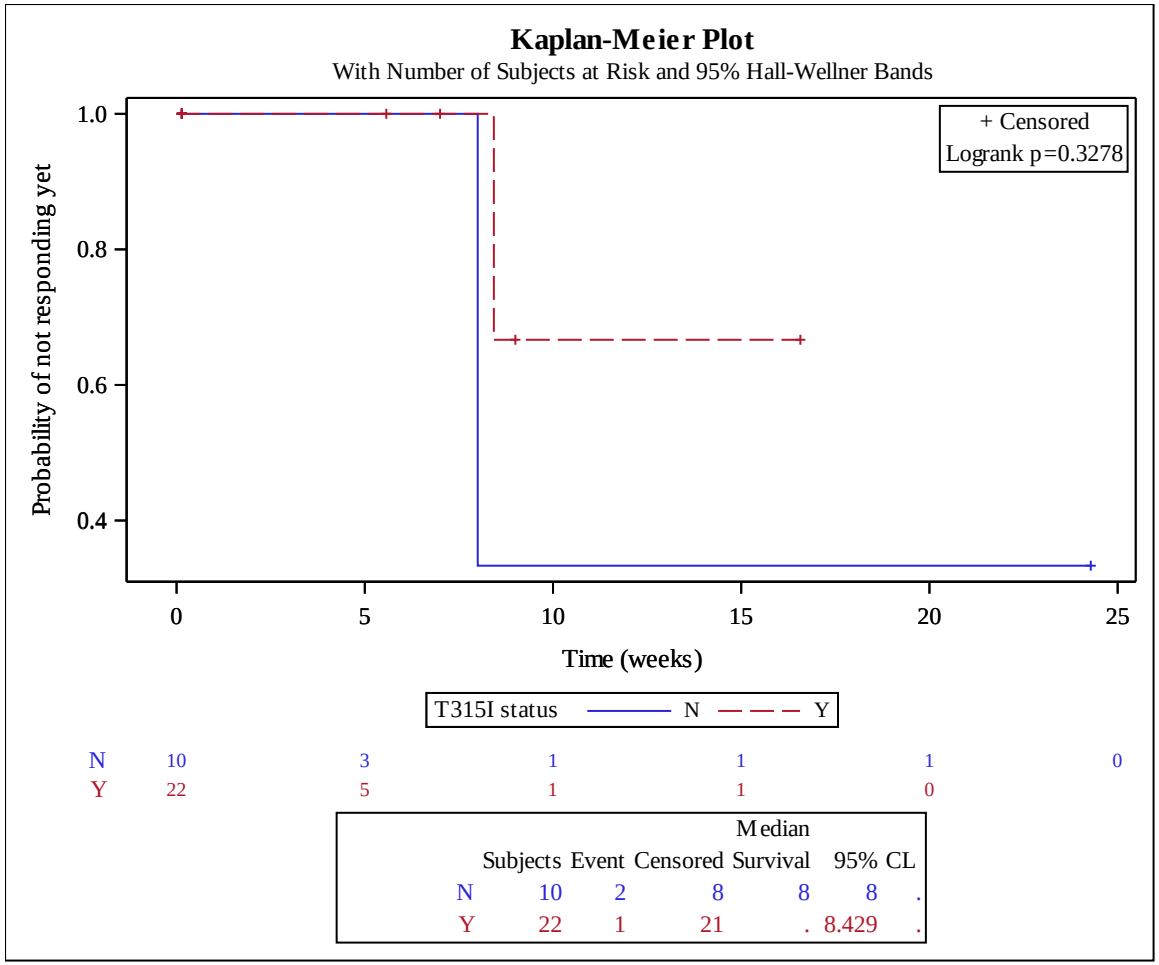

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Table 2.2.1.2.2.3 (Study 201)
Time to MMR in responders by T315I status
Treated Population - ALL Patients

Variable	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
Time to MMR (weeks), responders only	Yes	N	1
		Median	8.4
		Min, Max	8.4, 8.4
	No	N	2
		Median	8.0
		Min, Max	8.0, 8.0

Treated Population: All treated patients who were also assigned to a cohort.

Table 2.2.1.2.2.4 (Study 201)
Probability of no MMR yet at 12 and 24 months by T315I Status
Treated Population - ALL Patients

Diagnosis	*T315I*	*Month*	*Week*	*Number at risk*	*No MMR yet (%)*	*95% CI*
ALL Ph+ (T315I Yes: N=22, No: N=10)	Yes	12	52	.	.%	(.%, .%)
		24	104	.	.%	(.%, .%)
	No	12	52	.	.%	(.%, .%)
		24	104	.	.%	(.%, .%)

Treated Population: All treated patients who were also assigned to a cohort.
Estimates were derived using the Kaplan-Meier method.

2.2.1.3 Duration of MMR

2.2.1.3.1 Patients with Ph+ ALL

Table 2.2.1.3.1.1 (Study 101)
Duration of MMR
Safety Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*Remaining in response (%)*	*95% CI*
ALL Ph+ (N=1)	6	26	0	0.0%	(0.0%, 0.0%)
	12	52	0	0.0%	(0.0%, 0.0%)
	36	156	0	0.0%	(0.0%, 0.0%)
	48	208	0	0.0%	(0.0%, 0.0%)
	60	260	0	0.0%	(0.0%, 0.0%)

Safety Population: All treated patients
Total numbers refer to the patients with an MMR.
Estimates were derived using the Kaplan-Meier method.

Table 2.2.1.3.1.1 (Study 201)
Duration of MMR
Treated Population - Ph+ ALL Patients

Diagnosis	*Month*	*Week*	*Number at risk*	*Remaining in response (%)*	*95% CI*
ALL Ph+ (N=3)	6	26	0	0.0%	(0.0%, 0.0%)
	12	52	0	0.0%	(0.0%, 0.0%)
	36	156	0	0.0%	(0.0%, 0.0%)
	48	208	0	0.0%	(0.0%, 0.0%)
	60	260	0	0.0%	(0.0%, 0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Total numbers refer to the patients with an MMR.
Estimates were derived using the Kaplan-Meier method.

Figure 2.2.1.3.1.2 (Study 101)
Duration of MMR
Safety Population - Ph+ ALL Patients

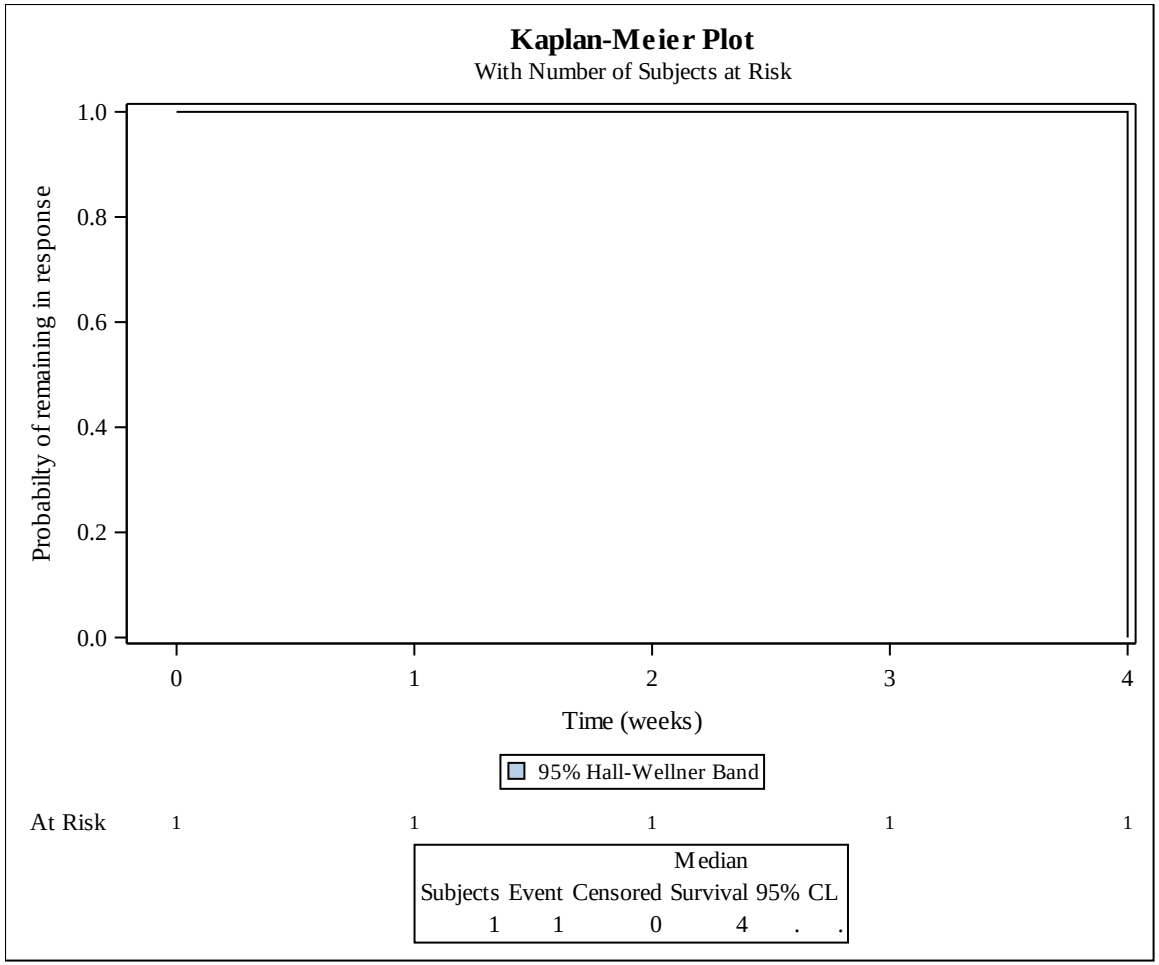

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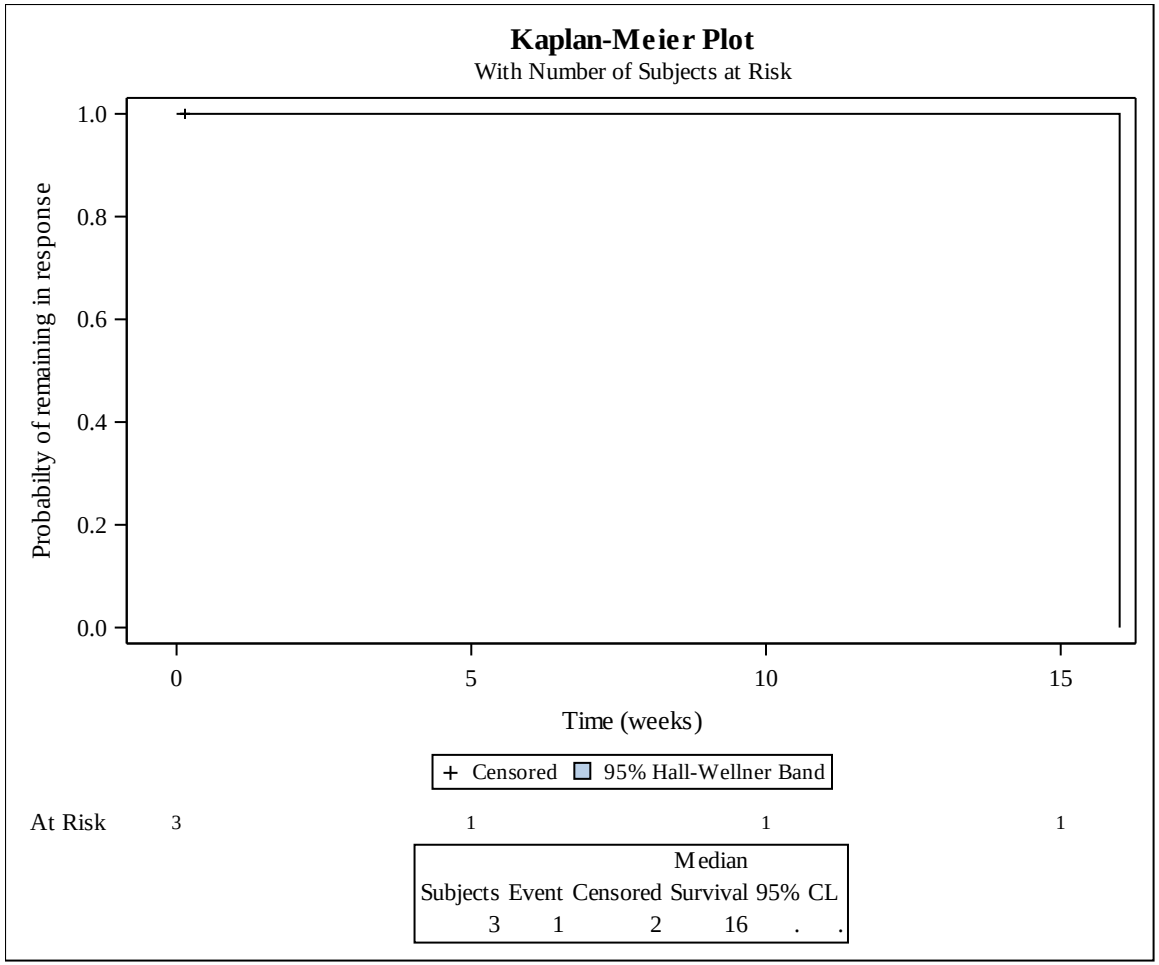
Figure 2.2.1.3.1.2 (Study 201)
Duration of MMR
Treated Population - Ph+ ALL Patients



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2.2.1.3.2 Patients with Ph+ ALL by T315I status

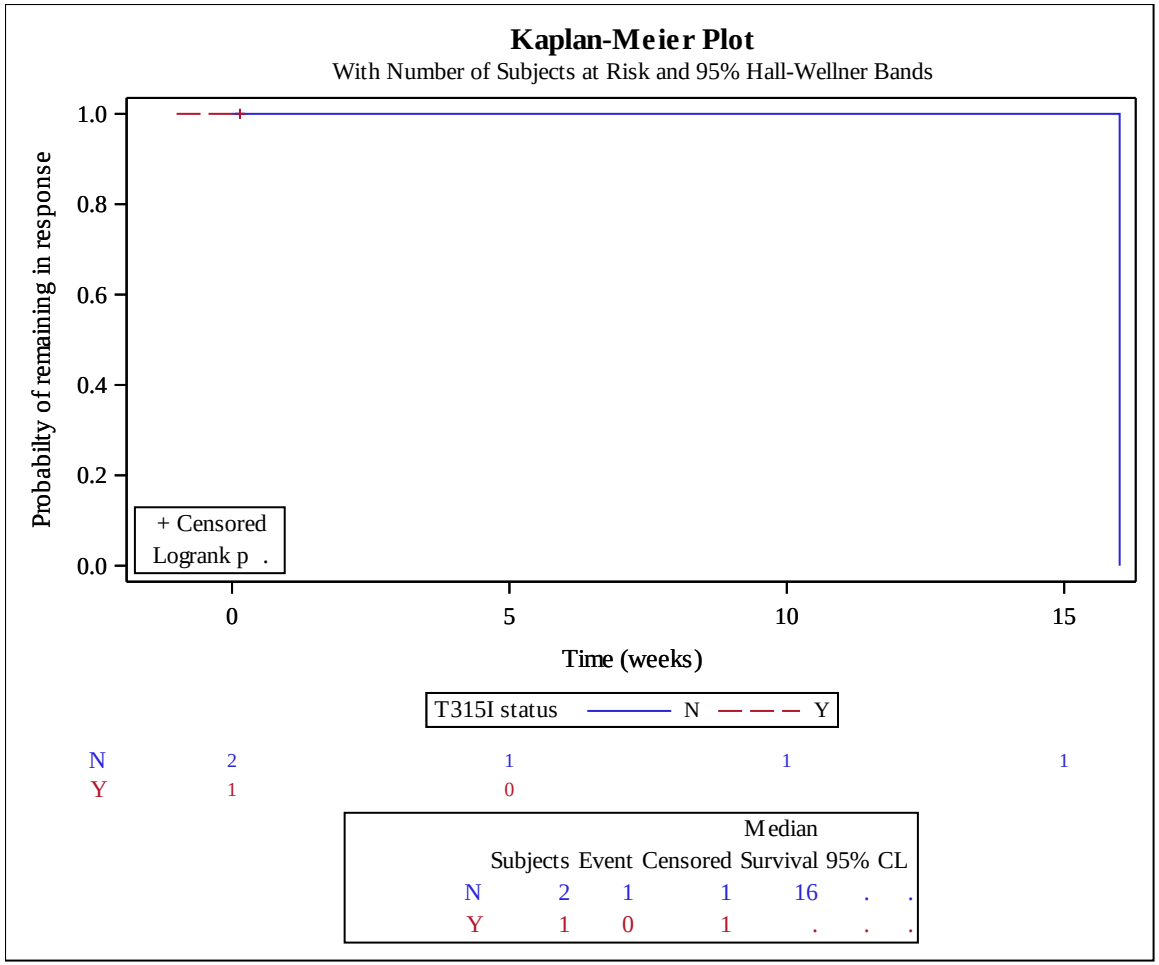
No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.2.1.3.2.1 (Study 201)
Duration of MMR by T315I status
Treated Population - ALL Patients

Diagnosis	*T315I*	*Month*	*Week*	*Number at risk*	*Remaining in response (%)*	*95% CI*
ALL Ph+ (T315I Yes: N=1, No: N=2)	Yes	6	26	.	.%	(.%, .%)
		12	52	.	.%	(.%, .%)
		36	156	.	.%	(.%, .%)
		48	208	.	.%	(.%, .%)
		60	260	.	.%	(.%, .%)
	No	6	26	0	0.0%	(0.0%, 0.0%)
		12	52	0	0.0%	(0.0%, 0.0%)
		36	156	0	0.0%	(0.0%, 0.0%)
		48	208	0	0.0%	(0.0%, 0.0%)
		60	260	0	0.0%	(0.0%, 0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Total numbers refer to the patients with an MMR.
Estimates were derived using the Kaplan-Meier method.

Figure 2.2.1.3.2.2 (Study 201)
Duration of MMR by T315I status
Treated Population - ALL Ph+ Patients



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2.2.1.4 Disease progression in blast crisis

2.2.1.4.1 Patients with Ph+ ALL

Table 2.2.1.4.1 (Study 101)
Blast crisis
Safety Population - Ph+ ALL Patients

Variable	*Statistic*	*Ph+ ALL (N=5)*
Blast crisis [1]	N (%)	0 (0.0%)
	95% CI (Clopper-Pearson)	(0.0%, 52.2%)

Safety Population: All treated patients
Percentages are based on the safety population.
[1] Patients with any TEAE of BLAST CRISIS IN MYELOGENOUS LEUKAEMIA.

Table 2.2.1.4.1 (Study 201)
Blast crisis
Safety Population - Ph+ ALL Patients

Variable	*Statistic*	*Ph+ ALL (N=32)*
Blast crisis [1]	N (%)	0 (0.0%)
	95% CI (Clopper-Pearson)	(0.0%, 10.9%)

Safety Population: All treated patients
Percentages are based on the Safety Population.
[1] Patients with any TEAE of BLAST CRISIS IN MYELOGENOUS LEUKAEMIA.

2.2.1.4.2 Patients with Ph+ ALL by T315I status

No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.2.1.4.2 (Study 201)
Blast crisis by T315I Status
Treated Population - ALL Patients

Variable	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
Blast crisis [1]	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
[1] Patients with any TEAE of BLAST CRISIS IN MYELOGENOUS LEUKAEMIA.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

2.2.2 Safety and Tolerability

2.2.2.1 Overview TEAE

2.2.2.1.1 Patients with Ph+ ALL

Table 2.2.2.1.1 (Study 101)
Overview of Adverse Events
Safety Population - Ph+ ALL Patients

Patients with any		*Ph+ ALL (N=5)*
Treatment-emergent AE (TEAE)		5 (100.0%)
Serious TEAE (SAE)		5 (100.0%)
TEAE leading to permanent discontinuation		1 (20.0%)
TEAE of Grade 3 & 4		2 (40.0%)
TEAE of Grade 5		3 (60.0%)
TEAE of Grade >=3		5 (100.0%)
TEAE of special interest (AESI)	Hepatoxicity	3 (60.0%)
	Skin and subcutaneous tissue disorders	4 (80.0%)
	Infections and infestations	5 (100.0%)
	Myelosuppression	4 (80.0%)
	Edema and Fluid Retention	2 (40.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.1.1 (Study 101)
Overview of Adverse Events
Safety Population - Ph+ ALL Patients

Patients with any		*Ph+ ALL (N=5)*
	Hypertension	1 (20.0%)
	Eye disorder	2 (40.0%)
	Bleeding Events	2 (40.0%)
	Cardiac Arrhythmias	3 (60.0%)
SAE of special interest (Serious AESI)	Skin and subcutaneous tissue disorders	2 (40.0%)
	Infections and infestations	4 (80.0%)
	Myelosuppression	4 (80.0%)
	Bleeding Events	2 (40.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.1.1 (Study 201)
Overview of Adverse Events
Safety Population - Ph+ ALL Patients

Patients with any		*Ph+ ALL (N=32)*
Treatment-emergent AE (TEAE)		32 (100.0%)
Serious TEAE (SAE)		25 (78.1%)
TEAE leading to permanent discontinuation		3 (9.4%)
TEAE of Grade 3 & 4		19 (59.4%)
TEAE of Grade 5		9 (28.1%)
TEAE of Grade >=3		28 (87.5%)
TEAE of special interest (AESI)	Arterial Occlusive Events	3 (9.4%)
	Cardiovascular Arterial Occlusive Events	1 (3.1%)
	Cerebrovascular Arterial Occlusive Events	1 (3.1%)
	Peripheral Vascular Arterial Occlusive Events	3 (9.4%)
	Venous Thrombotic/Embolic Events	3 (9.4%)

Safety Population: All treated patients
Percentages are based on the Safety Population.

Table 2.2.2.1.1 (Study 201)
Overview of Adverse Events
Safety Population - Ph+ ALL Patients

Patients with any		*Ph+ ALL (N=32)*
	Vascular Occlusive Events	6 (18.8%)
	Hepatoxicity	5 (15.6%)
	Cardiac Failure	2 (6.3%)
	Skin and subcutaneous tissue disorders	19 (59.4%)
	Infections and infestations	23 (71.9%)
	Myelosuppression	19 (59.4%)
	Edema and Fluid Retention	13 (40.6%)
	Hypertension	8 (25.0%)
	Eye disorder	9 (28.1%)
	Bleeding Events	10 (31.3%)
	Pancreatitis	3 (9.4%)
	Chemical Pancreatitis	3 (9.4%)
	Cardiac Arrhythmias	8 (25.0%)
	QT Prolongation	2 (6.3%)
SAE of special interest (Serious AESI)	Arterial Occlusive Events	3 (9.4%)
	Cerebrovascular Arterial Occlusive Events	1 (3.1%)
	Peripheral Vascular Arterial Occlusive Events	3 (9.4%)
	Venous Thrombotic/Embolic Events	2 (6.3%)

Safety Population: All treated patients
Percentages are based on the Safety Population.

Table 2.2.2.1.1 (Study 201)
Overview of Adverse Events
Safety Population - Ph+ ALL Patients

Patients with any		*Ph+ ALL (N=32)*
	Vascular Occlusive Events	5 (15.6%)
	Cardiac Failure	2 (6.3%)
	Skin and subcutaneous tissue disorders	1 (3.1%)
	Infections and infestations	10 (31.3%)
	Myelosuppression	8 (25.0%)
	Edema and Fluid Retention	2 (6.3%)
	Bleeding Events	3 (9.4%)
	Cardiac Arrhythmias	5 (15.6%)
	QT Prolongation	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the Safety Population.

2.2.2.1.2 Patients with Ph+ ALL by T315I status

No subgroup analyses were performed for Ph+ ALL patients in Study AP24534-07-101 due to small sample size.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
Treatment-emergent AE (TEAE)	Yes	N total	22
		N (%)	22 (100.0%)
		95% CI (Clopper-Pearson)	(84.6%, 100.0%)
	No	N total	10
		N (%)	10 (100.0%)
		95% CI (Clopper-Pearson)	(69.2%, 100.0%)
Serious TEAE (SAE)	Yes	N total	22
		N (%)	17 (77.3%)
		95% CI (Clopper-Pearson)	(54.6%, 92.2%)
	No	N total	10
		N (%)	8 (80.0%)
		95% CI (Clopper-Pearson)	(44.4%, 97.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		p-value Fisher's exact test	1.0000
TEAE leading to permanent discontinuation	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	1.0000
TEAE of Grade 3 & 4	Yes	N total	22
		N (%)	12 (54.5%)
		95% CI (Clopper-Pearson)	(32.2%, 75.6%)
	No	N total	10
		N (%)	7 (70.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(34.8%, 93.3%)
		p-value Fisher's exact test	0.4673
TEAE of Grade 5	Yes	N total	22
		N (%)	7 (31.8%)
		95% CI (Clopper-Pearson)	(13.9%, 54.9%)
	No	N total	10
		N (%)	2 (20.0%)
		95% CI (Clopper-Pearson)	(2.5%, 55.6%)
		p-value Fisher's exact test	0.6808
TEAE of Grade >=3	Yes	N total	22
		N (%)	19 (86.4%)
		95% CI (Clopper-Pearson)	(65.1%, 97.1%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		No	N total	10
			N (%)	9 (90.0%)
			95% CI (Clopper-Pearson)	(55.5%, 99.7%)
			p-value Fisher's exact test	1.0000
TEAE of special interest (AESI)	Arterial Occlusive Events	Yes	N total	22
			N (%)	2 (9.1%)
			95% CI (Clopper-Pearson)	(1.1%, 29.2%)
		No	N total	10
			N (%)	1 (10.0%)
			95% CI (Clopper-Pearson)	(0.3%, 44.5%)
			p-value Fisher's exact test	1.0000
	Cardiovascular Arterial Occlusive Events	Yes	N total	22
			N (%)	1 (4.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Cerebrovascular Arterial Occlusive Events	Yes	N total	22
		N (%)	1 (4.5%)
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	Peripheral Vascular Arterial Occlusive Events	Yes	N total	22
			N (%)	2 (9.1%)
			95% CI (Clopper-Pearson)	(1.1%, 29.2%)
		No	N total	10
			N (%)	1 (10.0%)
			95% CI (Clopper-Pearson)	(0.3%, 44.5%)
			p-value Fisher's exact test	1.0000
	Venous Thrombotic/Embolic Events	Yes	N total	22
			N (%)	3 (13.6%)
			95% CI (Clopper-Pearson)	(2.9%, 34.9%)
		No	N total	10
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 30.8%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		p-value Fisher's exact test	0.5343
Vascular Occlusive Events	Yes	N total	22
		N (%)	5 (22.7%)
		95% CI (Clopper-Pearson)	(7.8%, 45.4%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	0.6367
Hepatoxicity	Yes	N total	22
		N (%)	3 (13.6%)
		95% CI (Clopper-Pearson)	(2.9%, 34.9%)
	No	N total	10
		N (%)	2 (20.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(2.5%, 55.6%)
		p-value Fisher's exact test	0.6367
Cardiac Failure	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Skin and subcutaneous tissue disorders	Yes	N total	22
		N (%)	13 (59.1%)
		95% CI (Clopper-Pearson)	(36.4%, 79.3%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	No	N total	10
		N (%)	6 (60.0%)
		95% CI (Clopper-Pearson)	(26.2%, 87.8%)
		p-value Fisher's exact test	1.0000
Infections and infestations	Yes	N total	22
		N (%)	15 (68.2%)
		95% CI (Clopper-Pearson)	(45.1%, 86.1%)
	No	N total	10
		N (%)	8 (80.0%)
		95% CI (Clopper-Pearson)	(44.4%, 97.5%)
		p-value Fisher's exact test	0.6808
Myelosuppression	Yes	N total	22
		N (%)	11 (50.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(28.2%, 71.8%)
	No	N total	10
		N (%)	8 (80.0%)
		95% CI (Clopper-Pearson)	(44.4%, 97.5%)
		p-value Fisher's exact test	0.1408
Edema and Fluid Retention	Yes	N total	22
		N (%)	6 (27.3%)
		95% CI (Clopper-Pearson)	(10.7%, 50.2%)
	No	N total	10
		N (%)	7 (70.0%)
		95% CI (Clopper-Pearson)	(34.8%, 93.3%)
		p-value Fisher's exact test	0.0494

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	Hypertension	Yes	N total	22
			N (%)	5 (22.7%)
			95% CI (Clopper-Pearson)	(7.8%, 45.4%)
		No	N total	10
			N (%)	3 (30.0%)
			95% CI (Clopper-Pearson)	(6.7%, 65.2%)
			p-value Fisher's exact test	0.6808
	Eye disorder	Yes	N total	22
			N (%)	5 (22.7%)
			95% CI (Clopper-Pearson)	(7.8%, 45.4%)
		No	N total	10
			N (%)	4 (40.0%)
			95% CI (Clopper-Pearson)	(12.2%, 73.8%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		p-value Fisher's exact test	0.4072
Bleeding Events	Yes	N total	22
		N (%)	7 (31.8%)
		95% CI (Clopper-Pearson)	(13.9%, 54.9%)
	No	N total	10
		N (%)	3 (30.0%)
		95% CI (Clopper-Pearson)	(6.7%, 65.2%)
		p-value Fisher's exact test	1.0000
Pancreatitis	Yes	N total	22
		N (%)	1 (4.5%)
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	2 (20.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(2.5%, 55.6%)
		p-value Fisher's exact test	0.2238
Clinical Pancreatitis	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Chemical Pancreatitis	Yes	N total	22
		N (%)	1 (4.5%)
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	No	N total	10
		N (%)	2 (20.0%)
		95% CI (Clopper-Pearson)	(2.5%, 55.6%)
		p-value Fisher's exact test	0.2238
Cardiac Arrhythmias	Yes	N total	22
		N (%)	5 (22.7%)
		95% CI (Clopper-Pearson)	(7.8%, 45.4%)
	No	N total	10
		N (%)	3 (30.0%)
		95% CI (Clopper-Pearson)	(6.7%, 65.2%)
		p-value Fisher's exact test	0.6808
QT Prolongation	Yes	N total	22
		N (%)	1 (4.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	0.5343
Hypothyroidism	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	Tumour lysis syndrome	Yes	N total	22
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 15.4%)
		No	N total	10
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 30.8%)
			p-value Fisher's exact test	
SAE of special interest (Serious AESI)	Arterial Occlusive Events	Yes	N total	22
			N (%)	2 (9.1%)
			95% CI (Clopper-Pearson)	(1.1%, 29.2%)
		No	N total	10
			N (%)	1 (10.0%)
			95% CI (Clopper-Pearson)	(0.3%, 44.5%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		p-value Fisher's exact test	1.0000
Cardiovascular Arterial Occlusive Events	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Cerebrovascular Arterial Occlusive Events	Yes	N total	22
		N (%)	1 (4.5%)
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Peripheral Vascular Arterial Occlusive Events	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	1.0000
Venous Thrombotic/Embolic Events	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Vascular Occlusive Events	Yes	N total	22
		N (%)	4 (18.2%)
		95% CI (Clopper-Pearson)	(5.2%, 40.3%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	1.0000
Hepatoxicity	Yes	N total	22
		N (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Cardiac Failure	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	Skin and subcutaneous tissue disorders	Yes	N total	22
			N (%)	1 (4.5%)
			95% CI (Clopper-Pearson)	(0.1%, 22.8%)
		No	N total	10
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 30.8%)
			p-value Fisher's exact test	1.0000
	Infections and infestations	Yes	N total	22
			N (%)	6 (27.3%)
			95% CI (Clopper-Pearson)	(10.7%, 50.2%)
		No	N total	10
			N (%)	4 (40.0%)
			95% CI (Clopper-Pearson)	(12.2%, 73.8%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
			p-value Fisher's exact test	0.6828
	Myelosuppression	Yes	N total	22
			N (%)	4 (18.2%)
			95% CI (Clopper-Pearson)	(5.2%, 40.3%)
		No	N total	10
			N (%)	4 (40.0%)
			95% CI (Clopper-Pearson)	(12.2%, 73.8%)
			p-value Fisher's exact test	0.2182
	Edema and Fluid Retention	Yes	N total	22
			N (%)	2 (9.1%)
			95% CI (Clopper-Pearson)	(1.1%, 29.2%)
		No	N total	10
			N (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Hypertension	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Eye disorder	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Bleeding Events	Yes	N total	22
		N (%)	2 (9.1%)
		95% CI (Clopper-Pearson)	(1.1%, 29.2%)
	No	N total	10
		N (%)	1 (10.0%)
		95% CI (Clopper-Pearson)	(0.3%, 44.5%)
		p-value Fisher's exact test	1.0000
Pancreatitis	Yes	N total	22
		N (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	
Clinical Pancreatitis	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any		*T315I*	*Statistic*	*Ph+ ALL (N=32)*
	Chemical Pancreatitis	Yes	N total	22
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 15.4%)
		No	N total	10
			N (%)	0 (0.0%)
			95% CI (Clopper-Pearson)	(0.0%, 30.8%)
			p-value Fisher's exact test	
	Cardiac Arrhythmias	Yes	N total	22
			N (%)	3 (13.6%)
			95% CI (Clopper-Pearson)	(2.9%, 34.9%)
		No	N total	10
			N (%)	2 (20.0%)
			95% CI (Clopper-Pearson)	(2.5%, 55.6%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		p-value Fisher's exact test	0.6367
QT Prolongation	Yes	N total	22
		N (%)	1 (4.5%)
		95% CI (Clopper-Pearson)	(0.1%, 22.8%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	1.0000
Hypothyroidism	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

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Table 2.2.2.1.2 (Study 201)
Overview of Adverse Events by T315I Status
Treated Population - ALL Patients

Patients with any	*T315I*	*Statistic*	*Ph+ ALL (N=32)*
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
Tumour lysis syndrome	Yes	N total	22
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 15.4%)
	No	N total	10
		N (%)	0 (0.0%)
		95% CI (Clopper-Pearson)	(0.0%, 30.8%)
		p-value Fisher's exact test	

Treated Population: All treated patients who were also assigned to a cohort.
Percentages are based on the patients with the respective T315I status.
Note: Fisher's exact test is not performed if AE frequencies are 0% or 100% in both groups.

2.2.2.2 TEAE by SOC/PT and grade

2.2.2.2.1 Patients with Ph+ ALL

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (40.0%)	3 (60.0%)	5 (100.0%)	5 (100.0%)
Blood and lymphatic system disorders	All	2 (40.0%)	1 (20.0%)	3 (60.0%)	3 (60.0%)
	Febrile neutropenia	2 (40.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)
	Neutropenia	2 (40.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)
	Anaemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Bone marrow failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Cardiac disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	3 (60.0%)
	Tachycardia	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Sinus bradycardia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Ear and labyrinth disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Tinnitus	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Eye disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Conjunctival pallor	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Pupil fixed	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Gastrointestinal disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (80.0%)
	Nausea	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Abdominal pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Abdominal pain upper	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Dyspepsia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
General disorders and administration site conditions	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (80.0%)
	Oedema peripheral	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Chills	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Fatigue	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Peripheral swelling	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Pyrexia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Infections and infestations	All	2 (40.0%)	2 (40.0%)	4 (80.0%)	5 (100.0%)
	Clostridium difficile colitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Device related infection	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Meningitis bacterial	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Mucormycosis	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Pneumonia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Septic shock	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal bacteraemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Investigations	All	3 (60.0%)	0 (0.0%)	3 (60.0%)	4 (80.0%)
	Alanine aminotransferase increased	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
	Aspartate aminotransferase increased	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
	Blood triglycerides increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Breath sounds abnormal	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Platelet count decreased	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Metabolism and nutrition disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (80.0%)
	Decreased appetite	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Dehydration	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Hyperuricaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Hypocalcaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Hypokalaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Hypophosphataemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Musculoskeletal and connective tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Bone pain	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Arthralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Nervous system disorders	All	0 (0.0%)	1 (20.0%)	1 (20.0%)	4 (80.0%)
	Headache	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Depressed level of consciousness	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Dizziness	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Dysgeusia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Haemorrhage intracranial	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Psychiatric disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Anger	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Depression	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Respiratory, thoracic and mediastinal disorders	All	1 (20.0%)	1 (20.0%)	2 (40.0%)	4 (80.0%)
	Cough	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Dysphonia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Pneumonia aspiration	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Respiratory failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Skin and subcutaneous tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	4 (80.0%)
	Dermatitis acneiform	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 101)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Ecchymosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Exfoliative rash	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Night sweats	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Nodular rash	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash follicular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash macular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash maculo-papular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Vascular disorders	All	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
	Hypotension	2 (40.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)
	Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 201)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		19 (59.4%)	9 (28.1%)	28 (87.5%)	32 (100.0%)
Blood and lymphatic system disorders	All	17 (53.1%)	0 (0.0%)	17 (53.1%)	20 (62.5%)
	Anaemia	6 (18.8%)	0 (0.0%)	6 (18.8%)	8 (25.0%)
	Febrile neutropenia	8 (25.0%)	0 (0.0%)	8 (25.0%)	8 (25.0%)
	Neutropenia	6 (18.8%)	0 (0.0%)	6 (18.8%)	7 (21.9%)
	Thrombocytopenia	6 (18.8%)	0 (0.0%)	6 (18.8%)	6 (18.8%)
Cardiac disorders	All	2 (6.3%)	2 (6.3%)	4 (12.5%)	12 (37.5%)
	Atrial fibrillation	2 (6.3%)	0 (0.0%)	2 (6.3%)	5 (15.6%)
Eye disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	9 (28.1%)
Gastrointestinal disorders	All	6 (18.8%)	1 (3.1%)	7 (21.9%)	27 (84.4%)
	Constipation	1 (3.1%)	0 (0.0%)	1 (3.1%)	17 (53.1%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 201)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
	Abdominal pain upper	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (21.9%)
	Nausea	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (21.9%)
	Abdominal pain	2 (6.3%)	0 (0.0%)	2 (6.3%)	6 (18.8%)
	Diarrhoea	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
General disorders and administration site conditions	All	3 (9.4%)	0 (0.0%)	3 (9.4%)	23 (71.9%)
	Fatigue	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (28.1%)
	Oedema peripheral	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
	Pyrexia	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
Infections and infestations	All	12 (37.5%)	2 (6.3%)	14 (43.8%)	23 (71.9%)
	Sepsis	4 (12.5%)	0 (0.0%)	4 (12.5%)	4 (12.5%)
Investigations	All	5 (15.6%)	0 (0.0%)	5 (15.6%)	14 (43.8%)
	Alanine aminotransferase increased	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
	Weight decreased	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 201)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Metabolism and nutrition disorders	All	7 (21.9%)	0 (0.0%)	7 (21.9%)	16 (50.0%)
	Decreased appetite	0 (0.0%)	0 (0.0%)	0 (0.0%)	10 (31.3%)
Musculoskeletal and connective tissue disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	20 (62.5%)
	Arthralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
	Back pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
	Muscle spasms	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
	Pain in extremity	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	All	2 (6.3%)	3 (9.4%)	5 (15.6%)	8 (25.0%)
	Neoplasm progression	1 (3.1%)	3 (9.4%)	4 (12.5%)	4 (12.5%)
Nervous system disorders	All	1 (3.1%)	1 (3.1%)	2 (6.3%)	14 (43.8%)
	Headache	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

Table 2.2.2.2.1 (Study 201)
Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Psychiatric disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	11 (34.4%)
	Insomnia	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (12.5%)
Renal and urinary disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (18.8%)
Respiratory, thoracic and mediastinal disorders	All	4 (12.5%)	0 (0.0%)	4 (12.5%)	15 (46.9%)
	Pleural effusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	6 (18.8%)
Skin and subcutaneous tissue disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	19 (59.4%)
	Dry skin	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
	Rash erythematous	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
Vascular disorders	All	5 (15.6%)	1 (3.1%)	6 (18.8%)	12 (37.5%)
	Hypertension	3 (9.4%)	0 (0.0%)	3 (9.4%)	8 (25.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 10% patients are listed.

2.2.2.3 Serious TEAE by SOC/PT and grade

2.2.2.3.1 Patients with Ph+ ALL

Table 2.2.2.3.1 (Study 101)
Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (40.0%)	3 (60.0%)	5 (100.0%)	5 (100.0%)
Blood and lymphatic system disorders	All	2 (40.0%)	1 (20.0%)	3 (60.0%)	3 (60.0%)
	Bone marrow failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Febrile neutropenia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Neutropenia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Gastrointestinal disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Nausea	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Infections and infestations	All	2 (40.0%)	2 (40.0%)	4 (80.0%)	4 (80.0%)
	Device related infection	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Mucormycosis	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 5% patients are listed.

Table 2.2.2.3.1 (Study 101)
Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Pneumonia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Septic shock	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal bacteraemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Musculoskeletal and connective tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Bone pain	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Nervous system disorders	All	0 (0.0%)	1 (20.0%)	1 (20.0%)	2 (40.0%)
	Haemorrhage intracranial	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Headache	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Respiratory, thoracic and mediastinal disorders	All	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Respiratory failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Skin and subcutaneous tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Exfoliative rash	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 5% patients are listed.

Table 2.2.2.3.1 (Study 201)
Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		13 (40.6%)	9 (28.1%)	22 (68.8%)	25 (78.1%)
Blood and lymphatic system disorders	All	8 (25.0%)	0 (0.0%)	8 (25.0%)	8 (25.0%)
	Febrile neutropenia	7 (21.9%)	0 (0.0%)	7 (21.9%)	7 (21.9%)
Cardiac disorders	All	2 (6.3%)	2 (6.3%)	4 (12.5%)	7 (21.9%)
	Atrial fibrillation	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
Gastrointestinal disorders	All	5 (15.6%)	1 (3.1%)	6 (18.8%)	6 (18.8%)
Infections and infestations	All	7 (21.9%)	2 (6.3%)	9 (28.1%)	10 (31.3%)
	Sepsis	2 (6.3%)	0 (0.0%)	2 (6.3%)	2 (6.3%)
	Septic shock	0 (0.0%)	2 (6.3%)	2 (6.3%)	2 (6.3%)
Metabolism and nutrition disorders	All	3 (9.4%)	0 (0.0%)	3 (9.4%)	3 (9.4%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 5% patients are listed.

Table 2.2.2.3.1 (Study 201)
Treatment-Emergent Serious Adverse Events by System Organ Class, Preferred Term and Maximum Grade
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Dehydration	2 (6.3%)	0 (0.0%)	2 (6.3%)	2 (6.3%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	All	2 (6.3%)	3 (9.4%)	5 (15.6%)	5 (15.6%)
	Neoplasm progression	1 (3.1%)	3 (9.4%)	4 (12.5%)	4 (12.5%)
Respiratory, thoracic and mediastinal disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
Vascular disorders	All	3 (9.4%)	1 (3.1%)	4 (12.5%)	5 (15.6%)

Safety Population: All treated patients
Percentages are based on the safety population.
Note: Only AEs occuring in at least 5% patients are listed.

2.2.2.4 TEAE leading to discontinuation by SOC/PT

2.2.2.4.1 Patients with Ph+ ALL

Table 2.2.2.4.1 (Study 101)
Treatment-Emergent Adverse Events Leading to Premature Discontinuation by System Organ Class and Preferred Term
Safety Population - Ph+ ALL Patients

SOC	*Preferred term*	*Ph+ ALL (N=5)*
Any AE		1 (20.0%)
Musculoskeletal and connective tissue disorders	All	1 (20.0%)
	Bone pain	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.4.1 (Study 201)
Treatment-Emergent Adverse Events Leading to Premature Discontinuation by System Organ Class and Preferred Term
Safety Population - Ph+ ALL Patients

SOC	*Preferred term*	*Ph+ ALL (N=32)*
Any AE		3 (9.4%)
Infections and infestations	All	1 (3.1%)
	Haematoma infection	1 (3.1%)
Vascular disorders	All	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)
Skin and subcutaneous tissue disorders	All	1 (3.1%)
	Rash erythematous	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the Safety Population.

2.2.2.5 Adverse Event of Special Interest, AESI

2.2.2.5.1 Patients with Ph+ ALL

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Hepatoxicity
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
Investigations	All	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
	Alanine aminotransferase increased	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)
	Aspartate aminotransferase increased	2 (40.0%)	0 (0.0%)	2 (40.0%)	3 (60.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Skin and subcutaneous tissue disorders
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (20.0%)	0 (0.0%)	1 (20.0%)	4 (80.0%)
Skin and subcutaneous tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	4 (80.0%)
	Dermatitis acneiform	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Ecchymosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Exfoliative rash	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Night sweats	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Nodular rash	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash follicular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash macular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Rash maculo-papular	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Infections and infestations
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (40.0%)	2 (40.0%)	4 (80.0%)	5 (100.0%)
Infections and infestations	All	2 (40.0%)	2 (40.0%)	4 (80.0%)	5 (100.0%)
	Clostridium difficile colitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Device related infection	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Meningitis bacterial	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Mucormycosis	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Pneumonia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Septic shock	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal bacteraemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Myelosuppression
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		3 (60.0%)	1 (20.0%)	4 (80.0%)	4 (80.0%)
Blood and lymphatic system disorders	All	2 (40.0%)	1 (20.0%)	3 (60.0%)	3 (60.0%)
	Febrile neutropenia	2 (40.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)
	Neutropenia	2 (40.0%)	0 (0.0%)	2 (40.0%)	2 (40.0%)
	Anaemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Bone marrow failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Infections and infestations	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Investigations	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Platelet count decreased	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Edema and Fluid Retention
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
General disorders and administration site conditions	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Oedema peripheral	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Peripheral swelling	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Hypertension
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
Vascular disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Hypertension	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Eye disorder
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
Eye disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Conjunctival pallor	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Pupil fixed	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Bleeding Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (20.0%)	1 (20.0%)	2 (40.0%)
Nervous system disorders	All	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Haemorrhage intracranial	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Skin and subcutaneous tissue disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (40.0%)
	Ecchymosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 101)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiac Arrhythmias
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (20.0%)	0 (0.0%)	1 (20.0%)	3 (60.0%)
Cardiac disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	3 (60.0%)
	Tachycardia	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Sinus bradycardia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)
Cardiac disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Coronary artery stenosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	2 (6.3%)	1 (3.1%)	3 (9.4%)	3 (9.4%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiovascular Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Cardiac disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Coronary artery stenosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cerebrovascular Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Peripheral Vascular Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	2 (6.3%)	1 (3.1%)	3 (9.4%)	3 (9.4%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Venous Thrombotic/Embolic Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	0 (0.0%)	1 (3.1%)	3 (9.4%)
Vascular disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	3 (9.4%)
	Deep vein thrombosis	1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
	Embolism venous	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Vascular Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	2 (6.3%)	4 (12.5%)	6 (18.8%)
Cardiac disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Coronary artery stenosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	3 (9.4%)	1 (3.1%)	4 (12.5%)	6 (18.8%)
	Deep vein thrombosis	1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Embolism venous	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Vascular Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Hepatoxicity
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		3 (9.4%)	0 (0.0%)	3 (9.4%)	5 (15.6%)
Eye disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Ocular icterus	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Hepatobiliary disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Hepatotoxicity	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Investigations	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	4 (12.5%)
	Alanine aminotransferase increased	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
	Aspartate aminotransferase increased	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	International normalised ratio increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiac Failure
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	1 (3.1%)	2 (6.3%)	2 (6.3%)
Cardiac disorders	All	1 (3.1%)	1 (3.1%)	2 (6.3%)	2 (6.3%)
	Cardiac failure congestive	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Cardiopulmonary failure	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Skin and subcutaneous tissue disorders
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	0 (0.0%)	2 (6.3%)	19 (59.4%)
Skin and subcutaneous tissue disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	19 (59.4%)
	Dry skin	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
	Rash erythematous	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
	Alopecia	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Erythema	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Rash	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Rash papular	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Rash pruritic	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Blood blister	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Dermatitis exfoliative	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Erythema multiforme	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Hair disorder	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Hyperhidrosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Keratosis pilaris	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Skin and subcutaneous tissue disorders
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Night sweats	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Pityriasis rubra pilaris	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Psoriasis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Skin mass	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Infections and infestations
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		12 (37.5%)	2 (6.3%)	14 (43.8%)	23 (71.9%)
Infections and infestations	All	12 (37.5%)	2 (6.3%)	14 (43.8%)	23 (71.9%)
	Sepsis	4 (12.5%)	0 (0.0%)	4 (12.5%)	4 (12.5%)
	Pneumonia	1 (3.1%)	0 (0.0%)	1 (3.1%)	3 (9.4%)
	Urinary tract infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (9.4%)
	Bacteraemia	2 (6.3%)	0 (0.0%)	2 (6.3%)	2 (6.3%)
	Bronchitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Folliculitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Septic shock	0 (0.0%)	2 (6.3%)	2 (6.3%)	2 (6.3%)
	Atypical pneumonia	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Bronchopulmonary aspergillosis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Device related infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Device related sepsis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Diarrhoea infectious	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Endophthalmitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Infections and infestations
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
	Erysipelas	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Haematoma infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Laryngitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Lower respiratory tract infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Lower respiratory tract infection bacterial	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Lung infection	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Nasopharyngitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Oral herpes	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Otitis externa	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Pneumonia influenzal	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Rhinitis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Skin infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Staphylococcal infection	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Staphylococcal sepsis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Tooth abscess	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Upper respiratory tract infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Myelosuppression
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		17 (53.1%)	0 (0.0%)	17 (53.1%)	19 (59.4%)
Blood and lymphatic system disorders	All	17 (53.1%)	0 (0.0%)	17 (53.1%)	18 (56.3%)
	Anaemia	6 (18.8%)	0 (0.0%)	6 (18.8%)	8 (25.0%)
	Febrile neutropenia	8 (25.0%)	0 (0.0%)	8 (25.0%)	8 (25.0%)
	Neutropenia	6 (18.8%)	0 (0.0%)	6 (18.8%)	7 (21.9%)
	Thrombocytopenia	6 (18.8%)	0 (0.0%)	6 (18.8%)	6 (18.8%)
Investigations	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
	Neutrophil count decreased	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Platelet count decreased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	White blood cell count decreased	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Edema and Fluid Retention
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	0 (0.0%)	2 (6.3%)	13 (40.6%)
Cardiac disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (9.4%)
	Pericardial effusion	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (9.4%)
General disorders and administration site conditions	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
	Oedema peripheral	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (25.0%)
Metabolism and nutrition disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Fluid retention	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Respiratory, thoracic and mediastinal disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	6 (18.8%)
	Pleural effusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	6 (18.8%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Hypertension
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		3 (9.4%)	0 (0.0%)	3 (9.4%)	8 (25.0%)
Vascular disorders	All	3 (9.4%)	0 (0.0%)	3 (9.4%)	8 (25.0%)
	Hypertension	3 (9.4%)	0 (0.0%)	3 (9.4%)	8 (25.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Eye disorder
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	0 (0.0%)	1 (3.1%)	9 (28.1%)
Eye disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	9 (28.1%)
	Dry eye	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Eye pain	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Conjunctival oedema	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Episcleritis	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Exophthalmos	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Eye irritation	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Ocular hyperaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Ocular icterus	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Bleeding Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		4 (12.5%)	0 (0.0%)	4 (12.5%)	10 (31.3%)
Blood and lymphatic system disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Disseminated intravascular coagulation	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Spontaneous haematoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Gastrointestinal disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	5 (15.6%)
	Mouth haemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Gastric haemorrhage	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Gastrointestinal haemorrhage	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Gingival bleeding	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Rectal haemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Infections and infestations	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Haematoma infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Bleeding Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Injury, poisoning and procedural complications	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Contusion	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Respiratory, thoracic and mediastinal disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	Epistaxis	1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
	Haemoptysis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Skin and subcutaneous tissue disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Blood blister	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Vascular disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Haematoma	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Pancreatitis
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
Investigations	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	Lipase increased	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	Amylase increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Chemical Pancreatitis
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
Investigations	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	Lipase increased	2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
	Amylase increased	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiac Arrhythmias
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	1 (3.1%)	3 (9.4%)	8 (25.0%)
Cardiac disorders	All	2 (6.3%)	1 (3.1%)	3 (9.4%)	7 (21.9%)
	Atrial fibrillation	2 (6.3%)	0 (0.0%)	2 (6.3%)	5 (15.6%)
	Tachycardia	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (6.3%)
	Cardiac arrest	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Extrasystoles	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
Investigations	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Electrocardiogram QT prolonged	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.1 (Study 201)
Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
QT Prolongation
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (3.1%)	1 (3.1%)	2 (6.3%)
Cardiac disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cardiac arrest	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Investigations	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Electrocardiogram QT prolonged	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 101)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Skin and subcutaneous tissue disorders
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
Skin and subcutaneous tissue disorders	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	2 (40.0%)
	Exfoliative rash	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 101)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Infections and infestations
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (40.0%)	2 (40.0%)	4 (80.0%)	4 (80.0%)
Infections and infestations	All	2 (40.0%)	2 (40.0%)	4 (80.0%)	4 (80.0%)
	Device related infection	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Mucormycosis	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Pneumonia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Septic shock	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Staphylococcal bacteraemia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 101)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Myelosuppression
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		3 (60.0%)	1 (20.0%)	4 (80.0%)	4 (80.0%)
Blood and lymphatic system disorders	All	2 (40.0%)	1 (20.0%)	3 (60.0%)	3 (60.0%)
	Bone marrow failure	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Febrile neutropenia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Neutropenia	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
Infections and infestations	All	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)
	Neutropenic sepsis	1 (20.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 101)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Bleeding Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=5)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (20.0%)	1 (20.0%)	2 (40.0%)
Nervous system disorders	All	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
	Haemorrhage intracranial	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)
Skin and subcutaneous tissue disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)
	Petechiae	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	2 (6.3%)	1 (3.1%)	3 (9.4%)	3 (9.4%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cerebrovascular Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Peripheral Vascular Arterial Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	2 (6.3%)	3 (9.4%)	3 (9.4%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	2 (6.3%)	1 (3.1%)	3 (9.4%)	3 (9.4%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Venous Thrombotic/Embolic Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
Vascular disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
	Deep vein thrombosis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Embolism venous	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Vascular Occlusive Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	2 (6.3%)	4 (12.5%)	5 (15.6%)
Gastrointestinal disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Mesenteric arterial occlusion	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Nervous system disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cerebral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Vascular disorders	All	3 (9.4%)	1 (3.1%)	4 (12.5%)	5 (15.6%)
	Coeliac artery occlusion	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Deep vein thrombosis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Embolism venous	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Peripheral arterial occlusive disease	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Peripheral ischaemia	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiac Failure
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	1 (3.1%)	2 (6.3%)	2 (6.3%)
Cardiac disorders	All	1 (3.1%)	1 (3.1%)	2 (6.3%)	2 (6.3%)
	Cardiac failure congestive	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Cardiopulmonary failure	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Skin and subcutaneous tissue disorders
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Skin and subcutaneous tissue disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Dermatitis exfoliative	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Infections and infestations
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		7 (21.9%)	2 (6.3%)	9 (28.1%)	10 (31.3%)
Infections and infestations	All	7 (21.9%)	2 (6.3%)	9 (28.1%)	10 (31.3%)
	Sepsis	2 (6.3%)	0 (0.0%)	2 (6.3%)	2 (6.3%)
	Septic shock	0 (0.0%)	2 (6.3%)	2 (6.3%)	2 (6.3%)
	Atypical pneumonia	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Device related sepsis	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Haematoma infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Lung infection	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Otitis externa	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Pneumonia	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Pneumonia influenzal	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Myelosuppression
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		8 (25.0%)	0 (0.0%)	8 (25.0%)	8 (25.0%)
Blood and lymphatic system disorders	All	8 (25.0%)	0 (0.0%)	8 (25.0%)	8 (25.0%)
	Febrile neutropenia	7 (21.9%)	0 (0.0%)	7 (21.9%)	7 (21.9%)
	Thrombocytopenia	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Edema and Fluid Retention
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	0 (0.0%)	1 (3.1%)	2 (6.3%)
Metabolism and nutrition disorders	All	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Fluid retention	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Respiratory, thoracic and mediastinal disorders	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Pleural effusion	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Bleeding Events
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		2 (6.3%)	0 (0.0%)	2 (6.3%)	3 (9.4%)
Gastrointestinal disorders	All	2 (6.3%)	0 (0.0%)	2 (6.3%)	2 (6.3%)
	Gastric haemorrhage	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
	Gastrointestinal haemorrhage	1 (3.1%)	0 (0.0%)	1 (3.1%)	1 (3.1%)
Infections and infestations	All	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)
	Haematoma infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
Cardiac Arrhythmias
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		1 (3.1%)	1 (3.1%)	2 (6.3%)	5 (15.6%)
Cardiac disorders	All	1 (3.1%)	1 (3.1%)	2 (6.3%)	5 (15.6%)
	Atrial fibrillation	1 (3.1%)	0 (0.0%)	1 (3.1%)	4 (12.5%)
	Cardiac arrest	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.

Table 2.2.2.5.2 (Study 201)
Serious Adverse Events of Special Interest (AESI) by System Organ Class, Preferred Term and Maximum Grade
QT Prolongation
Safety Population - Ph+ ALL Patients

		Ph+ ALL Patients (N=32)			
System Organ Class	*Preferred term*	*Grade 3 & 4*	*Grade 5*	*Grade >=3*	*All grades*
Any AE		0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
Cardiac disorders	All	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Cardiac arrest	0 (0.0%)	1 (3.1%)	1 (3.1%)	1 (3.1%)

Safety Population: All treated patients
Percentages are based on the safety population.