ICLUSIG®
(ponatinib) tablets

BECAUSE TOMORROW MATTERS TODAY

ICLUSIG (PONATINIB)

A POTENT, PAN-BCR::ABL1 INHIBITOR FOR PATIENTS WITH RESISTANCE TO ONE 2G TKI

ICLUSIG COMBINES EXPERIENCE AND DATA TO IMPROVE PATIENTS' FUTURES: CONSIDER EARLY SWITCH TO ICLUSIG AFTER ONE 2G TKI[1–4]

PATIENT PROFILES

ICLUSIG is indicated in adult patients with chronic phase (CP), accelerated phase (AP) or blast phase (BP) chronic myeloid leukaemia (CML) who are resistant to dasatinib or nilotinib; who are intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation. ICLUSIG is also indicated in patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant to dasatinib; who are intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

Prescribing information can be found on the final slide.

Adverse events should be reported. Reporting forms and information can be found at www.hpra.ie
Adverse events should also be reported to Incyte immediately by phoning the Toll-free phone number 1800-456-748

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood*. 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

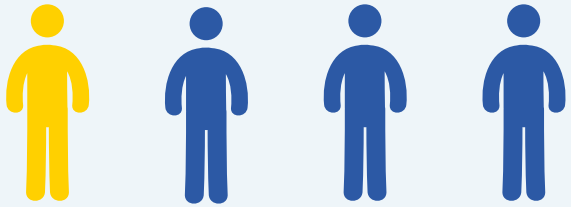
IE/ICLG/P/24/0038
Date of preparation: October 2024

Incyte

CML landscape for patients failing 2G TKIs

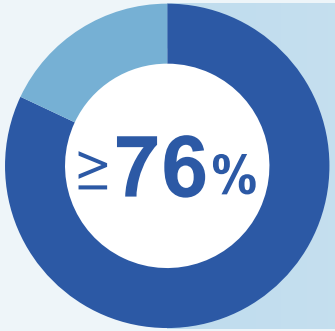
2G TKI failure can be attributed to resistance or intolerance:[1–5]

Up to 1 in 4 patients with CML will become resistant to their first drug treatment[1–3]



Up to 1 in 5 will have side effects that prevent them from continuing initial therapy[4,5]

Cycling 2G TKIs in resistant patients is associated with reduced response rates and poor survival:[6–8]



of patients with CP-CML **resistant to a 2G TKI do not achieve CCyR** with dasatinib, nilotinib or bosutinib in 3L[7,8]

2G, second generation; 3L, third line; CCyR, complete cytogenetic response; CML, chronic myeloid leukaemia; CP, chronic phase; PI, prescribing information; TKI, tyrosine kinase inhibitor.

1. Hochhaus A, et al. *Leukemia*. 2016;30:1044–54; 2. Hughes TP, et al. *Leukemia*. 2015;29:1832–38; 3. Hochhaus A, et al. *Blood*. 2013;121:3703–8; 4. Cortes J, et al. *J Clin Oncol*. 2016;34:2333–40; 5. Brümmendorf TH, et al. *Br J Haematol*. 2015;168:69–81; 6. Ibrahim AR, et al. *Blood*. 2010;116:5497–500; 7. Garg RJ, et al. *Blood*. 2009;114:4361–68; 8. Garcia-Gutierrez V, et al. *Blood*. 2012;120:3764.

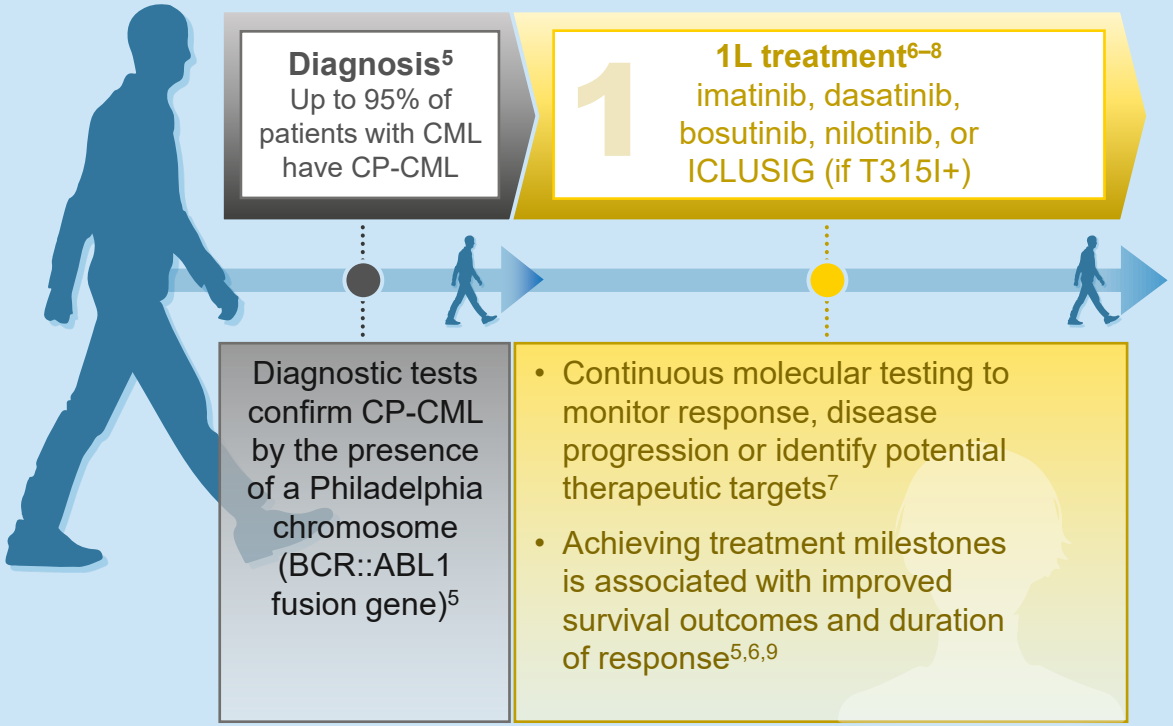
ICLUSIG® (ponatinib) tablets

Exploring the treatment journey of patients with CP-CML

BECAUSE TOMORROW MATTERS TODAY

The discovery of TKIs has transformed CML treatment, allowing patients with CML to have a near-normal life expectancy; however, **treatment failure is still a problem for patients today**[1]

Concern[2,3] › **Hope**[3,4] ····· **Crisis**[3]



Diagnosis[5]
Up to 95% of patients with CML have CP-CML

1L treatment[6–8]
imatinib, dasatinib, bosutinib, nilotinib, or ICLUSIG (if T315I+)

Diagnostic tests confirm CP-CML by the presence of a Philadelphia chromosome (BCR::ABL1 fusion gene)[5]

- Continuous molecular testing to monitor response, disease progression or identify potential therapeutic targets[7]
- Achieving treatment milestones is associated with improved survival outcomes and duration of response[5,6,9]

ELN CML Guidelines 2020 note that TKI change is mandatory in cases of failure or resistance to 1L treatment, and must be accompanied by BCR::ABL1 kinase domain mutation testing[6]

ICLUSIG demonstrates activity against the T315I mutant and is recommended for patients with the T315I mutation[6]

2L treatment in the patient journey

Trust ····· ICLUSIG combines **experience** and **data** to build confidence in treating disease progression in **resistant patients after one 2G TKI treatment**[6,8,10–13] ····· **Confidence**

References & abbreviations

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Exploring the treatment journey of patients with CP-CML

BECAUSE TOMORROW MATTERS TODAY

The discovery of TKIs has transformed CML treatment, allowing patients with CML to have a near-normal life expectancy; however, **treatment failure is still a problem for patients today**[1]

Concern[2,3] › Hope[3,4] ····· Crisis[3] › Adaption[2,4,14] ····· Uncertainty[2–4]

Diagnosis[5]

Up to 95% of patients with CML have CP-CML

Diagnostic tests confirm CP-CML by the presence of a Philadelphia chromosome (BCR::ABL1 fusion gene)[5]

1 1L treatment[6–8]

imatinib, dasatinib, bosutinib, nilotinib, or ICLUSIG (if T315I+)

- Continuous molecular testing to monitor response, disease progression or identify potential therapeutic targets[7]
- Achieving treatment milestones is associated with improved survival outcomes and duration of response[5,6,9]

2 2L treatment[6–8]

dasatinib, bosutinib, nilotinib or ICLUSIG (if T315I+ or after 1L 2G TKI)

- >50% of patients with CP-CML develop resistance or intolerance to imatinib[15]
- 30–40% of patients experience 2G TKI failure by 5 years in the 1L setting[15]

ELN CML Guidelines 2020 note that TKI selection should be guided by the sensitivity profile of specific BCR::ABL1 kinase domain mutations, if possible[6]

ICLUSIG is a 3G potent pan-BCR::ABL1 inhibitor for patients failing 2G TKIs[6,8]

3L treatment in the patient journey

Trust ····· ICLUSIG combines **experience** and **data** to build confidence in treating disease progression in **resistant patients after one 2G TKI treatment**[6,8,10–13] ····· **Confidence**

References & abbreviations

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ICLUSIG®

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Exploring the treatment journey of patients with CP-CML

BECAUSE TOMORROW MATTERS TODAY

The discovery of TKIs has transformed CML treatment, allowing patients with CML to have a near-normal life expectancy; however, **treatment failure is still a problem for patients today**[1]

Concern[2,3] › Hope[3,4] ····· Crisis[3] › Adaption[2,4,14] ····· Uncertainty[2–4] › Reassurance[3] ····· Burden[2]

Diagnosis[5]

Up to 95% of patients with CML have CP-CML

Diagnostic tests confirm CP-CML by the presence of a Philadelphia chromosome (BCR::ABL1 fusion gene)[5]

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- 30–40% of patients experience 2G TKI failure by 5 years in the 1L setting[15]

3 3L treatment[6–8]

dasatinib, bosutinib, nilotinib, ICLUSIG or asciminib

- 1/3 of resistant patients with CP-CML develop resistance due to BCR::ABL1 mutations[6]
- ~50% of patients who relapse show no evidence of secondary BCR::ABL1 mutations or biological progression, suggesting non-adherence as the cause[7]

Trust ····· ICLUSIG combines **experience** and **data** to build confidence in treating disease progression in **resistant patients after one 2G TKI treatment**[6,8,10–13] ····· **Confidence**

References & abbreviations

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Exploring the treatment journey of patients with CP-CML

BECAUSE TOMORROW MATTERS TODAY

The discovery of TKIs has transformed CML treatment, allowing patients with CML to have a near-normal life expectancy; however, **treatment failure is still a problem for patients today**[1]

1L, first line; 2G, second generation; 2L, second line; 3G, third generation; 3L, third line; CML, chronic myeloid leukaemia; CP, chronic phase; ELN, EuropeanLeukemia Net; PI, prescribing information; TKI, tyrosine kinase inhibitor.

1. Senapati J, et al. *Blood Cancer J*. 2023;13:58; 2. Hewison A, et al. *Eur J Oncol Nurs*. 2020;45:101730; 3. Pin A, et al. *Farm Hosp*. 2023;47:T85–92; 4. Leukaemia Care. https://media.leukaemiacare.org.uk/wp-content/uploads/Living-Well-with-Chronic-Myeloid-Leukaemia-CML-Web-Version.pdf (accessed October 2024); 5. Jabbour E, Kantarjian H. *Am J Hematol*. 2020;97:1236–56; 6. Hochhaus A, et al. *Leukemia*. 2020:34;966–84; 7. Cross N, et al. *Leukemia*. 2023;37:2150–67; 8. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 9. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009; 10. Cortes JE, et al. *Blood*. 2018;132:393–404; 11. Cortes J, et al. *Blood*. 2021;138:2042–50; 12. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 13. Incyte, data on file; 14. Borghi L, et al. *Front Psychol*. 2019;10:329; 15. Cortes J, Lang F. *J Hematol Oncol*. 2021;14:44.

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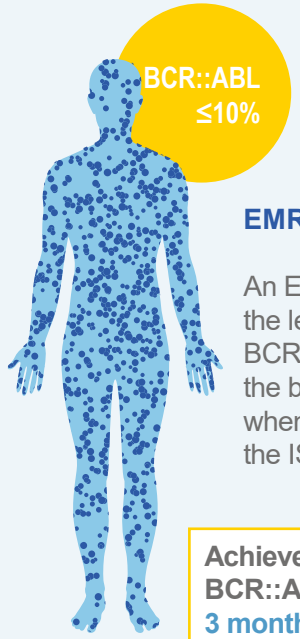
ELN CML Guidelines clinical milestones

A change of treatment is recommended when molecular milestones are not reached or tolerability cannot be improved[1]

AT DIAGNOSIS

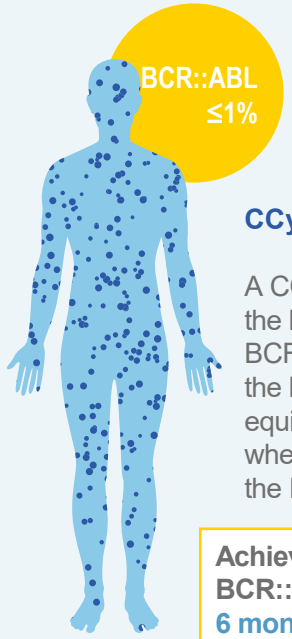
The level of BCR::ABL gene in the body is different for every patient at diagnosis, as measured on the IS



EMR

An EMR means that the level of BCR::ABL gene in the blood is ≤10% when measured on the IS

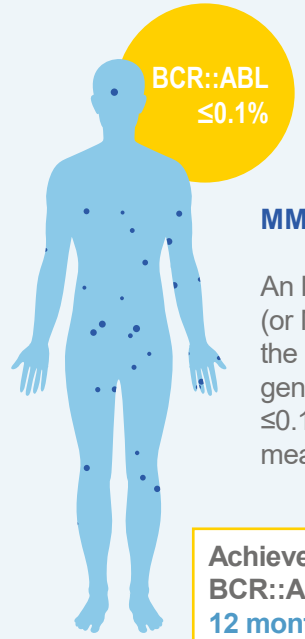
Achievement of BCR::ABL ≤10% by 3 months is considered an optimal response



CCyR

A CCyR means that the level of BCR::ABL gene in the blood is equivalent to 1% when measured on the IS

Achievement of BCR::ABL ≤1% by 6 months is considered an optimal response



MMR

An MMR (or MR3) means that the level of BCR::ABL gene in the blood is ≤0.1% when measured on the IS

Achievement of BCR::ABL ≤0.1% by 12 months is considered an optimal response

ELN CML Guidelines (2020) recommend that **patients who are resistant to one 2G TKI should be treated with ICLUSIG** instead of another 2G TKI, unless CV risk factors preclude its use[1]

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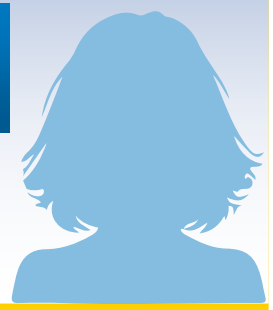
2G, second-generation; CCyR, complete cytogenetic response; CML, chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; EMR, early molecular response; IS, international scale; MMR, major molecular response; MR, molecular response; PI, prescribing information; TKI, tyrosine kinase inhibitor.

1. Hochhaus A, et al. *Leukemia*. 2020;34:966–84.

Patients with CP-CML who are clinically eligible for treatment with ICLUSIG after 2G TKIs and beyond

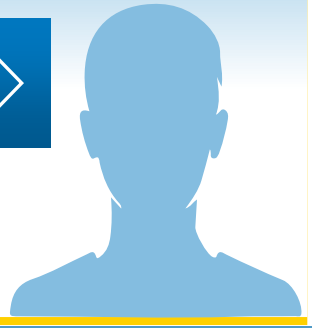
Highly resistant with no mutations or history of CV events

Resistant to 1L imatinib and 2L dasatinib



Highly resistant with no history of CV events

Resistant to 1L dasatinib; T315I+



Highly resistant with well-controlled dyslipidaemia

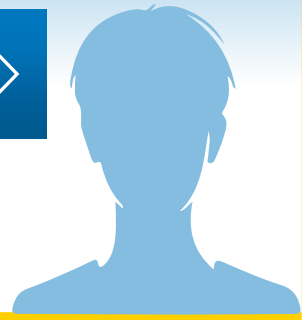
Resistant to 1L dasatinib; V299L+

Resistant with no history of CV events

Resistant to 1L nilotinib; E255K+

Resistant with well-controlled hypertension* and hypercholesterolaemia

Resistant to 1L imatinib and 2L dasatinib; F317L+



Over 15,000 patients have been treated with ICLUSIG within the first 10 years since launch in Europe, combining experience and data to build confidence in your patient's future[1]

Prescribing information and adverse event reporting information can be found on the final slide.

All patient profiles are fictional and intended for demonstrative purposes.

*Hypertension may contribute to the risk of arterial occlusive events. ICLUSIG treatment should be temporarily interrupted if hypertension is not medically controlled.

2G, second generation; 1L, first line; 2L, second line; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; TKI, tyrosine kinase inhibitor.

1. Incyte Corporation; data on file.

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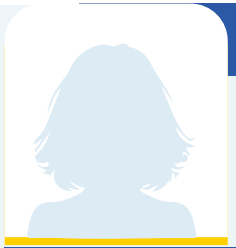
Identifying eligible patients with high degree of TKI resistance and no mutations



Personal information

Age: 69 years

Sex: Female

Clinical background

CP-CML diagnosis: 36 months ago

Treatment history: 1L imatinib for 24 months (resistant), 2L dasatinib until 36 months (resistant)

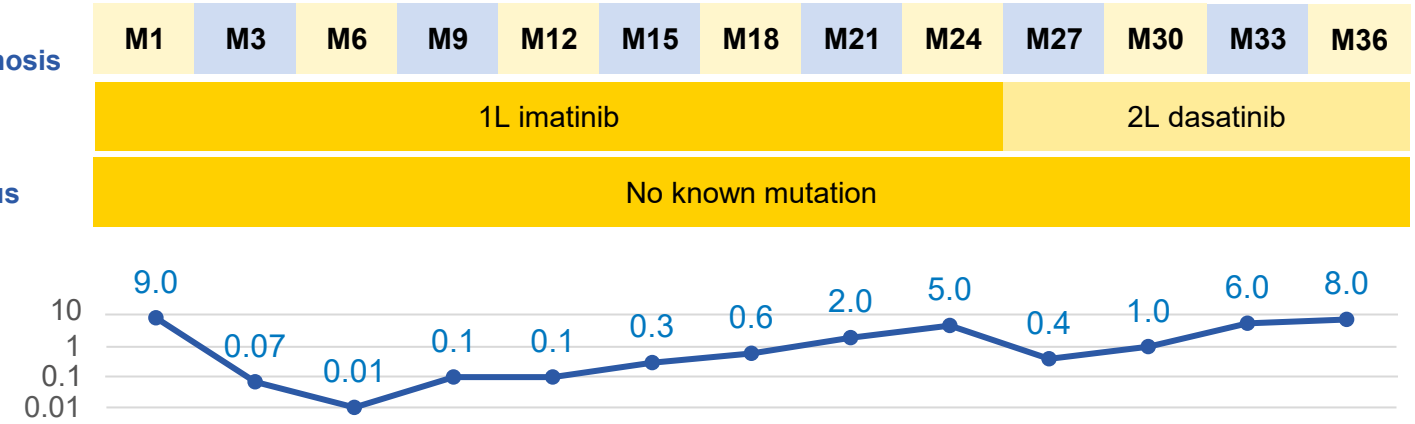
BCR::ABL1^{IS} level: 8%

Mutation status: No known mutation

ELTS score: Low

CV risk factors: No history of CV events

Treatment history



Patients may have deep and durable responses with ICLUSIG[1]

OPTIC and PACE: Patient baseline characteristics[1,2]

Why might this patient benefit from treatment with ICLUSIG?[3,4]

ELN CML Guidelines (2020) recommend that patients who are resistant to a 2G TKI should be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[4]

Representative patient case – not an actual patient.

1L, first line; 2G, second generation; 2L, second line; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; M, month(s); OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood.* 2018;132:393–404; 2. Cortes J, et al. *Blood.* 2021;138:2042–50; 3. De Santis S, et al. *Onco Targets Ther.* 2022;15:103–16; 4. Hochhaus A, et al. *Leukemia.* 2020;34:966–84.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and no mutations

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Age, years, median (range)	46 (19–81)	51 (21–77)	49 (18–81)
Male, n (%)	50 (53)	38 (40)	53 (56)
Prior TKIs, n (%)			
2	43 (46)	37 (39)	42 (45)
≥3	50 (53)	56 (60)	48 (51)
Reason prior therapy stopped, n (%)			
Resistant	92 (98)	94 (100)	94 (100)
BCR::ABL1 mutation, n (%)			
No mutation	51 (54)	58 (62)	54 (57)
T315I	25 (27)	21 (22)	21 (22)
Other	15 (16)	12 (13)	18 (19)
BMI, kg/m^2, median (range)	27 (17–45)	26 (17–49)	26 (18–49)

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and no mutations

PACE: Patient baseline characteristics[1]

The PACE study was a Phase 2, single-arm, open-label, international, multicentre trial

Characteristic	CP-CML (n=270)	AP-CML (n=85)	BP-CML (n=62)	Ph+ ALL (n=32)	Total (N=449)
Age, years, median (range)	60 (18–94)	60 (23–82)	53 (18–74)	62 (20–80)	59 (18–94)
Female, n (%)	126 (47)	48 (56)	25 (40)	12 (38)	211 (47)
Prior TKIs, n (%)					
≥2	251 (93)	80 (94)	60 (97)	26 (81)	417 (93)
≥3	154 (57)	47 (55)	37 (60)	12 (38)	250 (56)
Reason prior therapy stopped, n (%)					
Resistant	215 (80)	74 (87)	59 (95)	27 (84)	375 (84)
Intolerant only	39 (14)	6 (7)	2 (3)	2 (6)	49 (11)
Both resistant and intolerant	52 (19)	11 (13)	13 (21)	5 (16)	81 (18)
BCR::ABL1 mutation, n (%)	64 (24)	18 (21)	24 (39)	22 (69)	128 (29)

Representative patient case – not an actual patient.
ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood*. 2018;132:393–404.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and no mutations

Why might this patient benefit from treatment with ICLUSIG?[1]

The most frequent mechanisms of resistance in CP-CML are **BCR::ABL1-independent**[1]

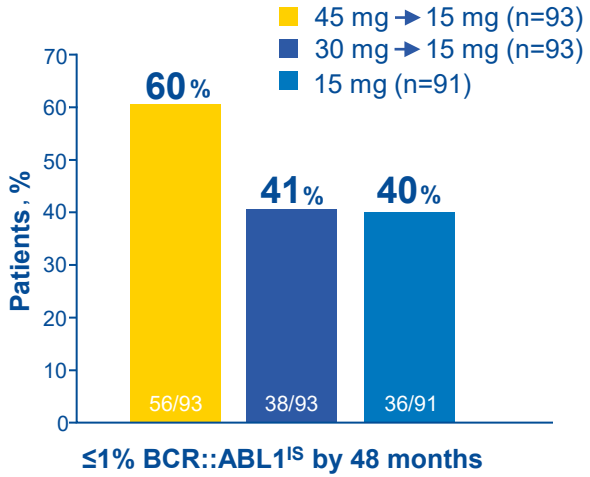
In CP-CML, **60–70%** of patients with unsatisfactory response to TKI therapy are negative for mutations or transcript overexpression[1]

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. De Santis S, et al. *Onco Targets Ther*. 2022;15:103–16.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[4*]



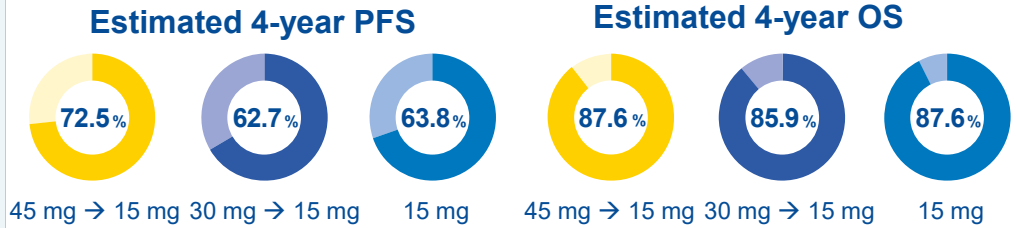
60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months[4]

Figure adapted from Cortes JE, et al.[4] with permission from the author.

Results from the 4-year OPTIC analysis suggest that patients may achieve a deep, durable molecular response with ICLUSIG[4]

Consider dose optimisation for a favourable benefit-risk profile with a 45 mg starting dose reduced to 15 mg upon achievement of response (≤1% BCR::ABL1^{IS})[3,4]

OPTIC: Estimated 4-year PFS and OS[4*]



Estimated 4-year PFS was 72.5% and OS was 87.6% for patients receiving 45 mg → 15 mg ICLUSIG[4]

Patients may achieve long-term survival with ICLUSIG[4]

Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

Representative patient case – not an actual patient. *Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

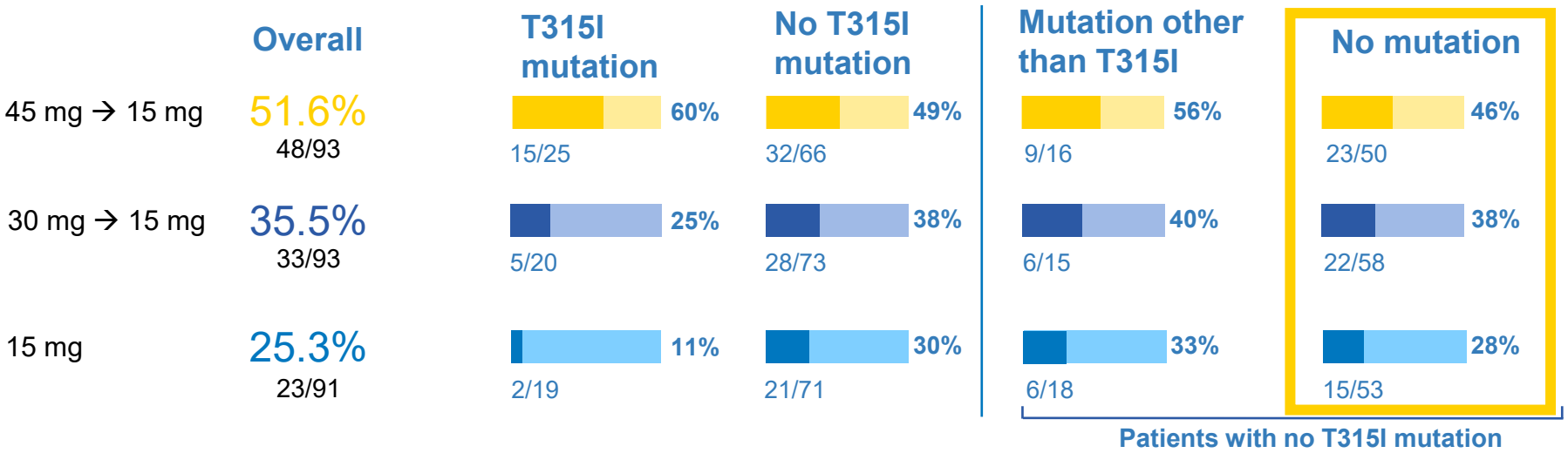
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Mutational subgroup analysis[3]

≤1% BCR::ABL1^{IS} by 12 months by baseline mutation status*



Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

Representative patient case – not an actual patient. *4 patients did not have a mutation test result at baseline.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

OPTIC: Dose-reduction regimen[2,3]

- Faster dose reductions vs PACE
- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
- Dose can be re-escalated if patients experience loss of response

Patients may regain MMR or achieve a deep MR (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain response following dose reduction[2,3]

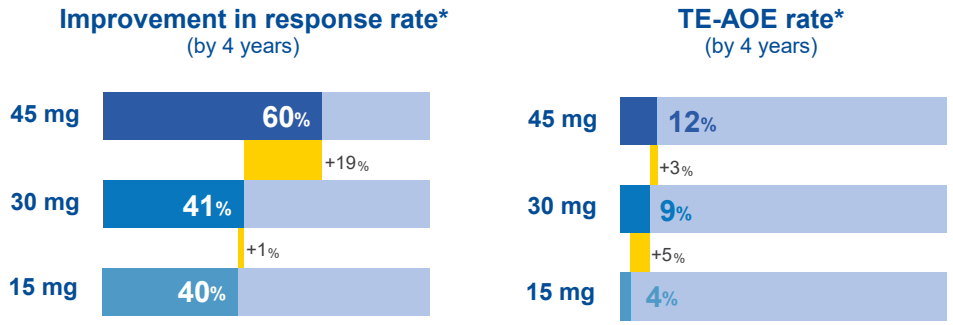
Reducing the dose of ICLUSIG to 15 mg should be considered for patients with CP-CML who have achieved MCyR taking the following individual factors into account: CV risk, side effects, time to response, and BCR::ABL transcript levels. If dose reduction is undertaken, close monitoring of response is recommended. In patients with loss of response the dose of ICLUSIG can be re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily

Representative patient case – not an actual patient.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[2]

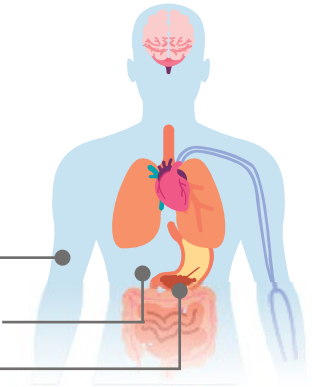


In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Patients without baseline CV risk factors should be at minimal risk of having CV adverse events[2–4*]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4 years[2]

Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards[2]



- Hypertension (10%)
- Increased ALT (3%)
- Increased lipase (7%)

ICLUSIG had a manageable safety profile in the OPTIC trial with no new events; tolerability should be manageable for patients[1,2,5]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and AOE rate; †Response rate of ≤1% BCR::ABL1^{IS} by 48 months when compared with the 15-mg cohort after 4 years of exposure.

ALT, alanine transaminase; AOE, arterial occlusive event; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Jabbour E, et al. *Leukemia.* 2024;38:475–81; 4. Januzzi JL, et al. *J Hematol Oncol.* 2022;15:1; 5. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Considering ICLUSIG

For patients with highly resistant CP-CML and have no known mutations or history of CV events:

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI[1–4]

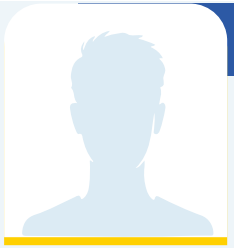
ELN CML Guidelines (2020) recommend that patients who are resistant to a 2G TKI with no mutation detected should be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[5]

Representative patient case – not an actual patient.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50; 4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. Hochhaus A, et al. *Leukemia.* 2020;34:966–84.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and low CV risk



Personal information

Age: 55 years

Sex: Male

Clinical background

CP-CML diagnosis: 60 months ago

Previous treatments: 1L dasatinib for 60 months (resistant)

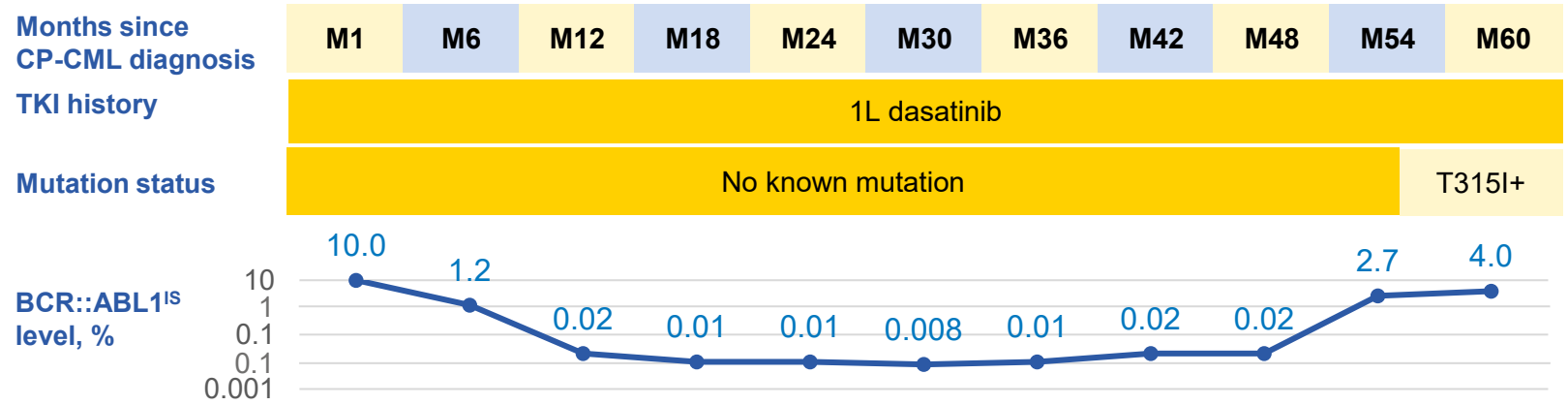
Mutation status: T315I+ (detected at 56 months)

BCR::ABL1^{IS} level: 4%

ELTS score: Low

CV risk factors: Former smoker, but no history of CV events

Treatment history



Patients may have deep and durable responses with ICLUSIG[1]

OPTIC: Patient baseline characteristics[2]

Why might this patient benefit from treatment with ICLUSIG?[3,4]

ELN CML Guidelines (2020) note that ICLUSIG is the only TKI with activity against the T315I mutant, and recommend ICLUSIG in patients with T315I, unless CV risk factors preclude its use[3]

Representative patient case – not an actual patient.

1L, first line; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; M, month(s); OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood.* 2018;132:393–404; 2. Cortes J, et al. *Blood.* 2021;138:2042–50; 3. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 4. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Age, years, median (range)	46 (19–81)	51 (21–77)	49 (18–81)
Male, n (%)	50 (53)	38 (40)	53 (56)
Prior TKIs, n (%)			
2	43 (46)	37 (39)	42 (45)
≥3	50 (53)	56 (60)	48 (51)
Reason prior therapy stopped, n (%)			
Resistant	92 (98)	94 (100)	94 (100)
BCR::ABL1 mutation, n (%)			
No mutation	51 (54)	58 (62)	54 (57)
T315I	25 (27)	21 (22)	21 (22)
Other	15 (16)	12 (13)	18 (19)

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
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Identifying eligible patients with high degree of TKI resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Patients with CV risk factors, n (%)			
Hypertension	26 (28)	25 (27)	22 (23)
Diabetes mellitus	5 (5)	3 (3)	7 (7)
Hyperlipidaemia	19 (20)	14 (15)	16 (17)
Patients with ≥1 CV risk factor	32 (34)	30 (32)	32 (34)
Patients with >1 CV risk factor	5 (5)	4 (4)	4 (4)
Current or former smokers	29 (31)	37 (39)	33 (35)
BMI, kg/m^2, median (range)	27 (17–45)	26 (17–49)	26 (18–49)

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and low CV risk

Why might this patient benefit from treatment with ICLUSIG?[1,2]

Mutations account for resistance in approximately **1** in **3** of patients with CP-CML[1]

T315I 'gatekeeper' mutation is resistant to imatinib and 2G TKIs (dasatinib, nilotinib, bosutinib)[2]

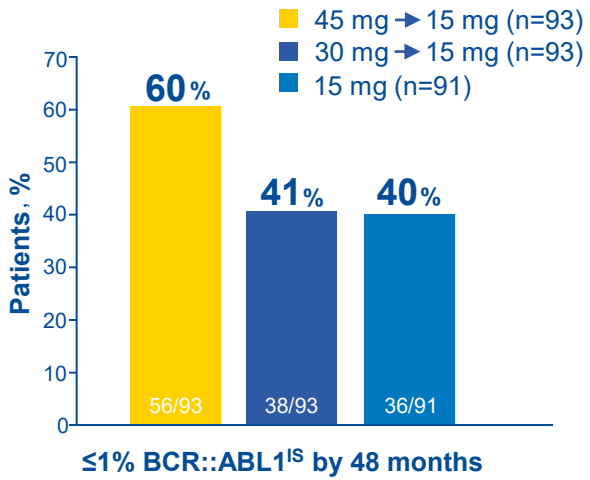
ICLUSIG, a **3G TKI**, is the **only approved BCR::ABL1 inhibitor in Europe** designed to be effective in CML patients with or without resistance mutations, including T315I[2]

Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 2. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[4*]



60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months[4]

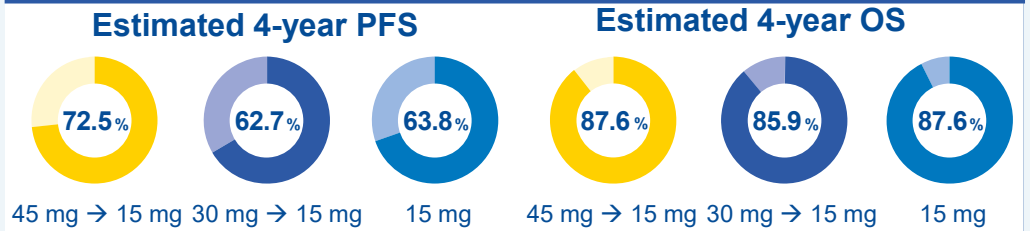
Figure adapted from Cortes JE, et al.[4] with permission from the author.

Results from the 4-year OPTIC analysis suggest that patients may achieve a deep, durable molecular response with ICLUSIG[4]

Patients with a T315I mutation at baseline achieved the greatest clinical benefit in the 45 mg → 15 mg cohort[4]

Consider dose optimisation for a favourable benefit-risk profile with a 45 mg starting dose reduced to 15 mg upon achievement of response (≤1% BCR::ABL1^{IS})[3,4]

OPTIC: Estimated 4-year PFS and OS[4*]



Estimated 4-year PFS was 72.5% and OS was 87.6% for patients receiving 45 mg → 15 mg ICLUSIG[4]

Patients may achieve long-term survival with ICLUSIG[4]

- Achieving ≤10% BCR::ABL1^{IS} within 12 months is associated with improved long-term PFS and OS[5]
- Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

Representative patient case – not an actual patient. *Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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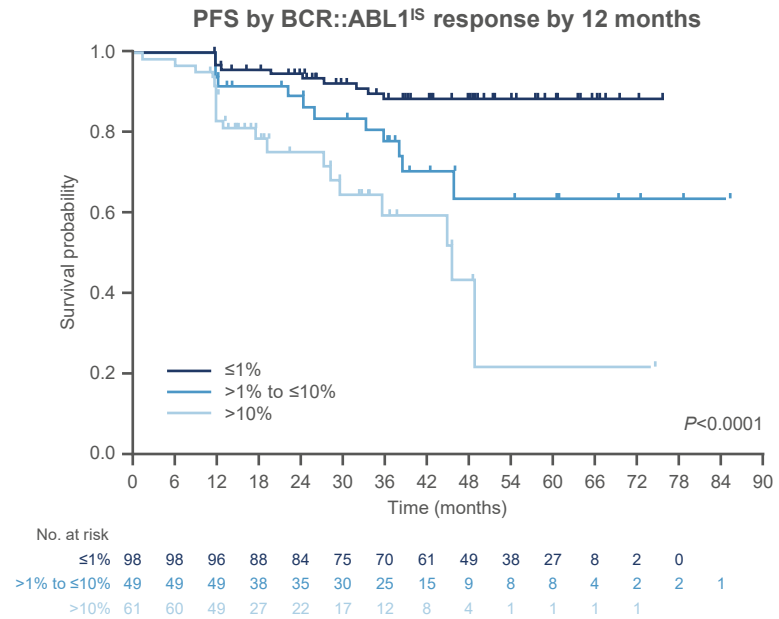
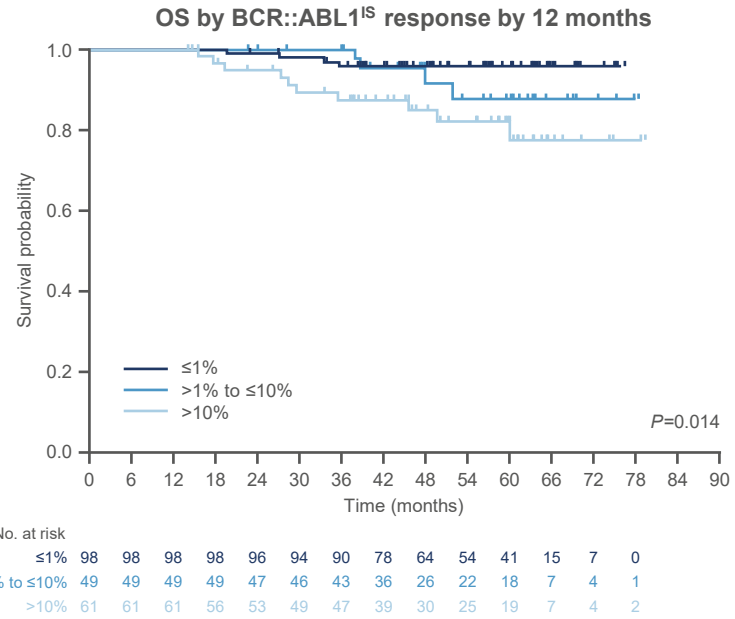
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Landmark analysis[5]





Achieving ≤10% BCR::ABL1IS within 12 months is associated with improved long-term PFS and OS

Figures adapted from Apperley J, et al.[5] with permission from the author.

Representative patient case – not an actual patient.

2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

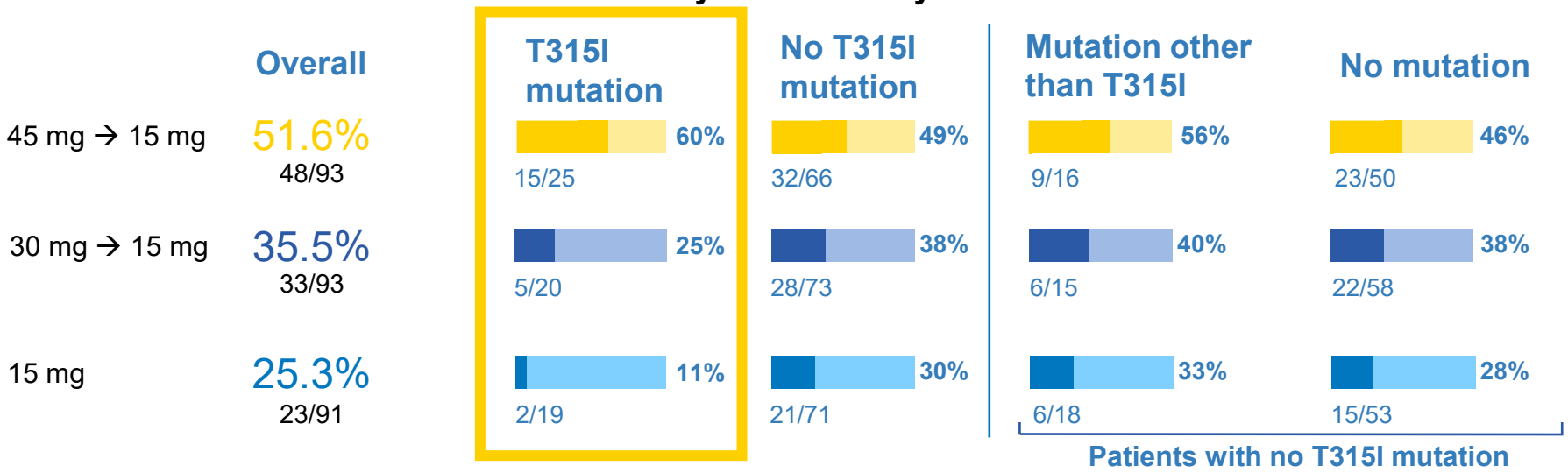
Incyte

ICLUSIG®

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Mutational subgroup analysis[3]

≤1% BCR::ABL1^{IS} by 12 months by baseline mutation status*



Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

Representative patient case – not an actual patient. *4 patients did not have a mutation test result at baseline.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

OPTIC: Dose-reduction regimen[2,3]

- Faster dose reductions vs PACE
- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
- Dose can be re-escalated if patients experience loss of response

Patients may regain MMR or achieve a deep MR (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain response following dose reduction[2,3]

Reducing the dose of ICLUSIG to 15 mg should be considered for patients with CP-CML who have achieved MCyR taking the following individual factors into account: CV risk, side effects, time to response, and BCR::ABL transcript levels. If dose reduction is undertaken, close monitoring of response is recommended. In patients with loss of response the dose of ICLUSIG can be re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily

Representative patient case – not an actual patient.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.

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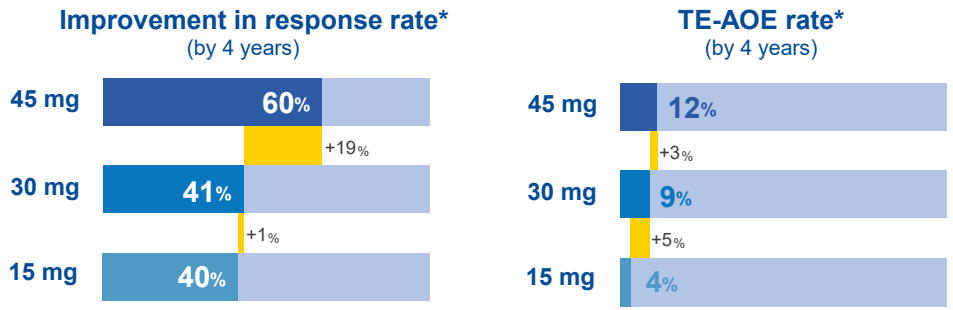
The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[2]



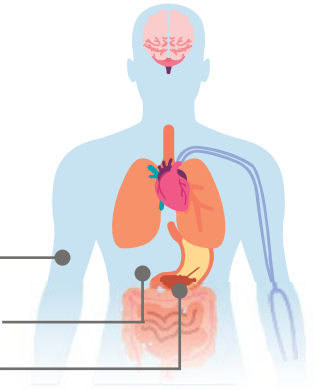
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Patients without baseline CV risk factors should be at minimal risk of having CV adverse events[2–4*]

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[3]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4 years[2]

Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards[2]



- Hypertension (10%)
- Increased ALT (3%)
- Increased lipase (7%)

ICLUSIG had a manageable safety profile in the OPTIC trial with no new events; tolerability should be manageable for patients[1,2,5]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and AOE rate; †Response rate of ≤1% BCR::ABL1^{IS} by 48 months when compared with the 15-mg cohort after 4 years of exposure.

ALT, alanine transaminase; AOE, arterial occlusive event; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

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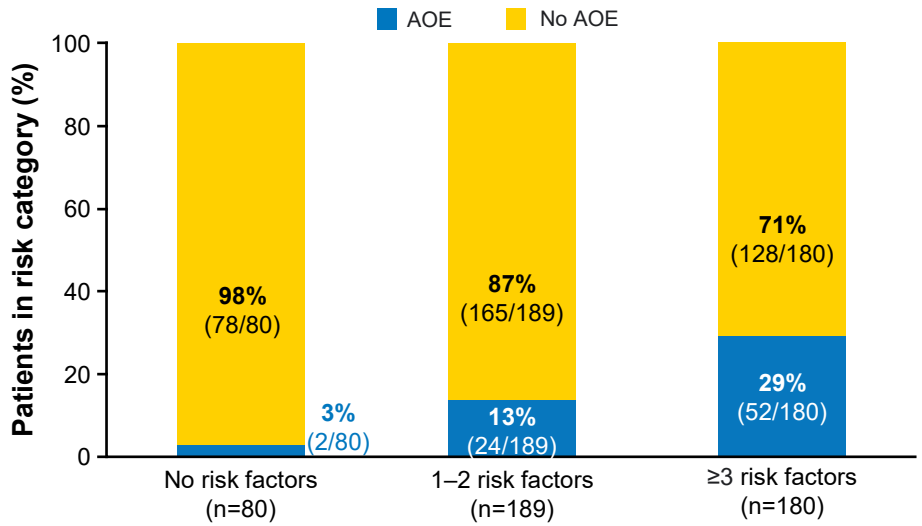
The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

PACE: Adjudicated AOEs[2]



- 98% of patients with no CV risk factors did not experience an AOE
- Rate of AOEs may not increase with treatment duration

Figure adapted from Januzzi JL, et al.[2] Freely distributed under the Creative Commons Attribution License (CC-BY 4.0).

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.

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Considering ICLUSIG

For patients with highly resistant CP-CML who are T315I+ and have no history of CV events:

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI[1–4]

ICLUSIG, a 3G TKI, is the only approved BCR::ABL1 inhibitor in Europe designed to be effective in CML patients with or without resistance mutations, including T315I[1,5–7]

Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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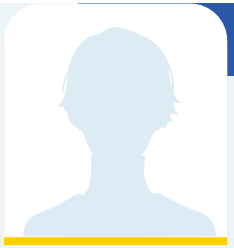
The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and medium CV risk



Personal information

Age: 72 years

Sex: Female

Clinical background

CP-CML diagnosis: 48 months ago

Previous treatments: 1L dasatinib for 48 months (resistant)

Mutation status: V299L+ (detected at 48 months)

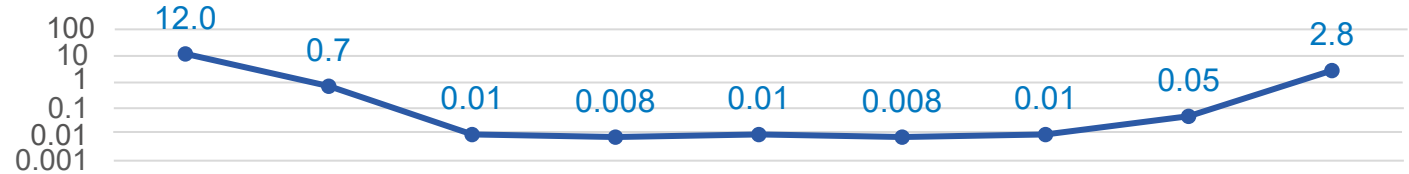
BCR::ABL1^{IS} level: 2.8%

ELTS score: Intermediate

CV risk factors: Family history of dyslipidaemia - prescribed statins to balance lipid levels after lifestyle changes were ineffective

Treatment history

Months since CP-CML diagnosis	M1	M6	M12	M18	M24	M30	M36	M42	M48
TKI history	1L dasatinib								
Mutation status	No known mutation								V299L+



Patients may have deep and durable responses with ICLUSIG[1]

OPTIC and PACE: Patient baseline characteristics[1,2]

Why might this patient benefit from treatment with ICLUSIG?[3–5]

V299L single resistance mutation has been shown to confer resistance to both bosutinib and dasatinib[6]

Representative patient case – not an actual patient.

1L, first line; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; M, month(s); OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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Identifying eligible patients with high degree of TKI resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

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Prior TKIs, n (%)			
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≥3	50 (53)	56 (60)	48 (51)
Reason prior therapy stopped, n (%)			
Resistant	92 (98)	94 (100)	94 (100)
BCR::ABL1 mutation, n (%)			
No mutation	51 (54)	58 (62)	54 (57)
T315I	25 (27)	21 (22)	21 (22)
Other	15 (16)	12 (13)	18 (19)

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Patients with CV risk factors, n (%)			
Hypertension	26 (28)	25 (27)	22 (23)
Diabetes mellitus	5 (5)	3 (3)	7 (7)
Hyperlipidaemia	19 (20)	14 (15)	16 (17)
Patients with ≥1 CV risk factor	32 (34)	30 (32)	32 (34)
Patients with >1 CV risk factor	5 (5)	4 (4)	4 (4)
Current or former smokers	29 (31)	37 (39)	33 (35)
BMI, kg/m^2, median (range)	27 (17–45)	26 (17–49)	26 (18–49)

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and medium CV risk

PACE: Patient baseline characteristics[1]

The PACE study was a Phase 2, single-arm, open-label, international, multicentre trial

Characteristic	CP-CML (n=270)	AP-CML (n=85)	BP-CML (n=62)	Ph+ ALL (n=32)	Total (N=449)
Age, years, median (range)	60 (18–94)	60 (23–82)	53 (18–74)	62 (20–80)	59 (18–94)
Female, n (%)	126 (47)	48 (56)	25 (40)	12 (38)	211 (47)
Prior TKIs, n (%)					
≥2	251 (93)	80 (94)	60 (97)	26 (81)	417 (93)
≥3	154 (57)	47 (55)	37 (60)	12 (38)	250 (56)
Reason prior therapy stopped, n (%)					
Resistant	215 (80)	74 (87)	59 (95)	27 (84)	375 (84)
Intolerant only	39 (14)	6 (7)	2 (3)	2 (6)	49 (11)
Both resistant and intolerant	52 (19)	11 (13)	13 (21)	5 (16)	81 (18)
BCR::ABL1 mutation, n (%)	64 (24)	18 (21)	24 (39)	22 (69)	128 (29)

Representative patient case – not an actual patient.
ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood*. 2018;132:393–404.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with high degree of TKI resistance and medium CV risk

Why might this patient benefit from treatment with ICLUSIG?[1–3]

ICLUSIG, a **3G TKI**, is the **only approved BCR::ABL1 inhibitor** in Europe designed to be effective in CML patients with or without resistance mutations, including V299L[1–3]

Mutations account for resistance in approximately **1** in **3** of patients with CP-CML[2]

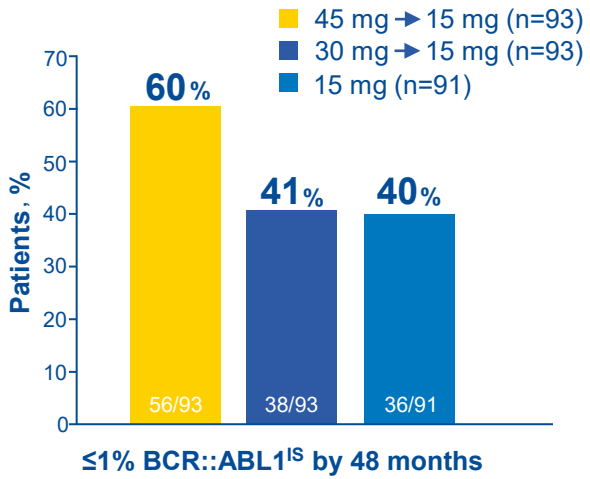
ELN CML Guidelines (2020) recommend that patients who are resistant to a 2G TKI should be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[2]

Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELN, European LeukemiaNet; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. Jabbour E, et al. *Leukemia*. 2024;38:475–81; 2. Hochhaus A, et al. *Leukemia*. 2020;34:966–84; 3. Cross N, et al. *Leukemia*. 2023;37:2150–67.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[4*]



60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months[4]

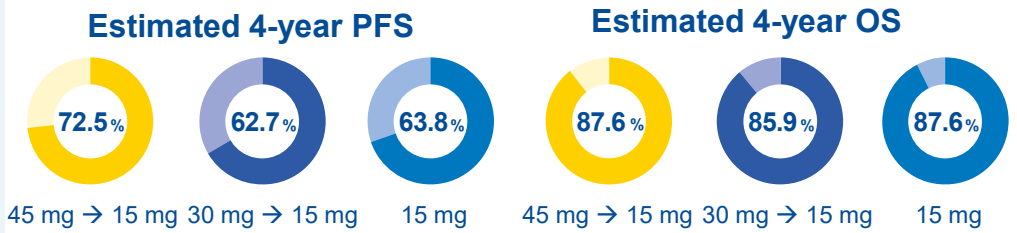
Figure adapted from Cortes JE, et al.[4] with permission from the author.

Results from the 4-year OPTIC analysis suggest that patients may achieve a deep, durable molecular response with ICLUSIG[4]

Most patients in the 45 mg → 15 mg cohort achieved ≤1% BCR::ABL1^{IS} by 4 years regardless of baseline mutation status[4]

Consider dose optimisation for a favourable benefit-risk profile with a 45 mg starting dose reduced to 15 mg upon achievement of response (≤1% BCR::ABL1^{IS})[3,4]

OPTIC: Estimated 4-year PFS and OS[4*]



Estimated 4-year PFS was 72.5% and OS was 87.6% for patients receiving 45 mg → 15 mg ICLUSIG[4]

Patients may achieve long-term survival with ICLUSIG[4]

Achieving ≤10% BCR::ABL1^{IS} within 12 months is associated with improved long-term PFS and OS[5]

Representative patient case – not an actual patient. *Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

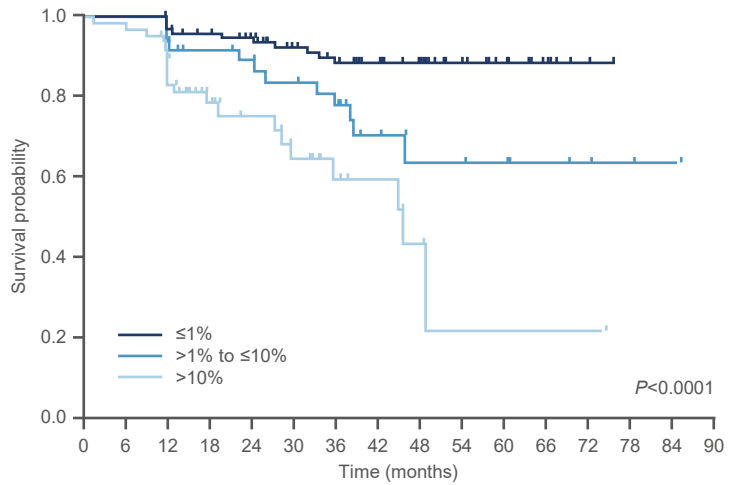
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Landmark analysis[5]

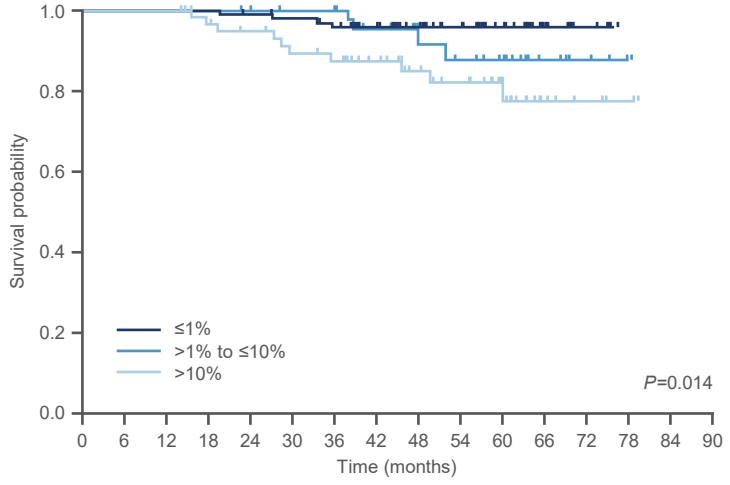
PFS by BCR::ABL1^{IS} response by 12 months



No. at risk

≤1%	98	98	96	88	84	75	70	61	49	38	27	8	2	0
>1% to ≤10%	49	49	49	38	35	30	25	15	9	8	8	4	2	2	1
>10%	61	60	49	27	22	17	12	8	4	1	1	1	1		

OS by BCR::ABL1^{IS} response by 12 months



No. at risk

≤1%	98	98	98	98	96	94	90	78	64	54	41	15	7	0
>1% to ≤10%	49	49	49	49	47	46	43	36	26	22	18	7	4	1
>10%	61	61	61	56	53	49	47	39	30	25	19	7	4	2

Achieving ≤10% BCR::ABL1^{IS} within 12 months is associated with improved long-term PFS and OS

Figures adapted from Apperley J, et al.[5] with permission from the author.

Representative patient case – not an actual patient.

2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Incyte

ICLUSIG®

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

OPTIC: Dose-reduction regimen[2,3]

- Faster dose reductions vs PACE
- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
- Dose can be re-escalated if patients experience loss of response

Patients may regain MMR or achieve a deep MR (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain response following dose reduction[2,3]

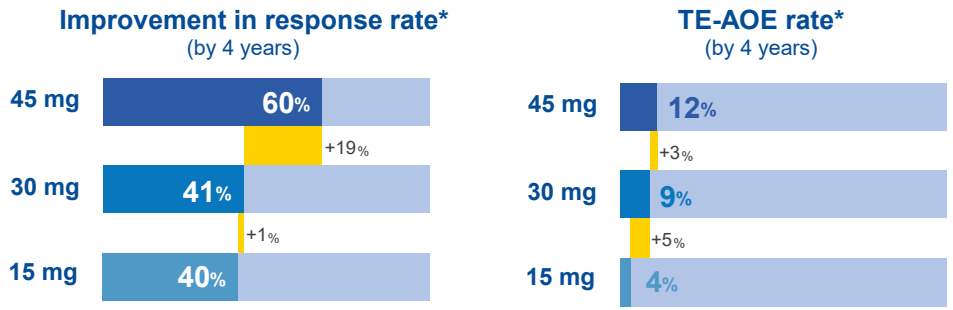
Reducing the dose of ICLUSIG to 15 mg should be considered for patients with CP-CML who have achieved MCyR taking the following individual factors into account: CV risk, side effects, time to response, and BCR::ABL transcript levels. If dose reduction is undertaken, close monitoring of response is recommended. In patients with loss of response the dose of ICLUSIG can be re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily

Representative patient case – not an actual patient.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[2]



In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

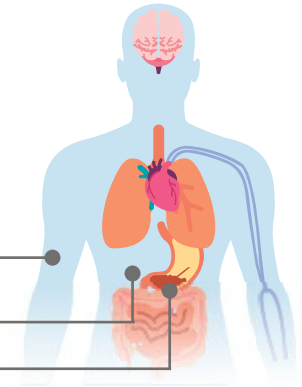
Patients with well-controlled dyslipidaemia should be at minimal risk of CV adverse events[2–4*]

Rate of AOEs may not increase with treatment duration[3]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4 years[2]

Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards[2]

- Hypertension (10%)
- Increased ALT (3%)
- Increased lipase (7%)



ICLUSIG had a manageable safety profile in the OPTIC trial with no new events; tolerability should be manageable for patients[1,2,5]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and AOE rate; †Response rate of ≤1% BCR::ABL1^{IS} by 48 months when compared with the 15-mg cohort after 4 years of exposure.

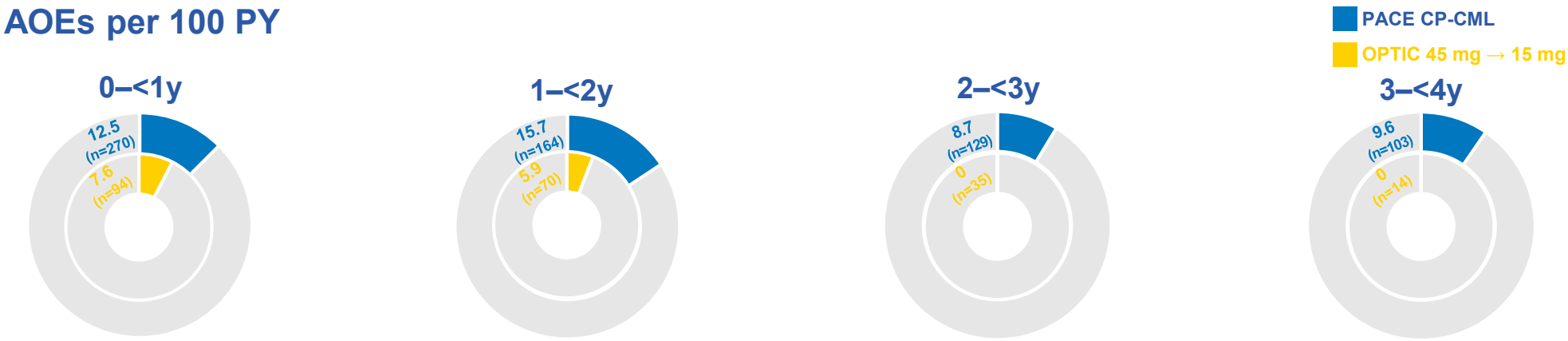
ALT, alanine transaminase; AOE, arterial occlusive event; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Jabbour E, et al. *Leukemia.* 2024;38:475–81; 4. Januzzi JL, et al. *J Hematol Oncol.* 2022;15:1; 5. Cortes J, et al. *Blood.* 2021;138:2042–50.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC vs PACE: Exposure-adjusted AOEs[2]

AOEs per 100 PY



Patients in OPTIC had a lower exposure-adjusted incidence of AOEs vs PACE and no AOEs occurred from Year 3 onwards, demonstrating that response-based dosing for ICLUSIG improves treatment tolerance and mitigates CV risk

Rate of AOEs may not increase with treatment duration[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; PY, patient-years; SmPC, Summary of Product Characteristics; y, year(s).

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Jabbour E, et al. *Leukemia.* 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Considering ICLUSIG

For patients with highly resistant CP-CML who are V299L+ and have well-controlled dyslipidaemia:

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI[1–4]

ICLUSIG, a 3G TKI, is the only approved BCR::ABL1 inhibitor in Europe designed to be effective in CML patients with or without resistance mutations, including V299L[1,5,6]

Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. O'Hare T, et al. *Cancer Cell.* 2009;16:401–12; 6. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and low CV risk

Personal information

Age: 47 years

Sex: Male

Clinical background

CP-CML diagnosis: 60 months ago

Treatment history: 1L nilotinib for 60 months (resistant)

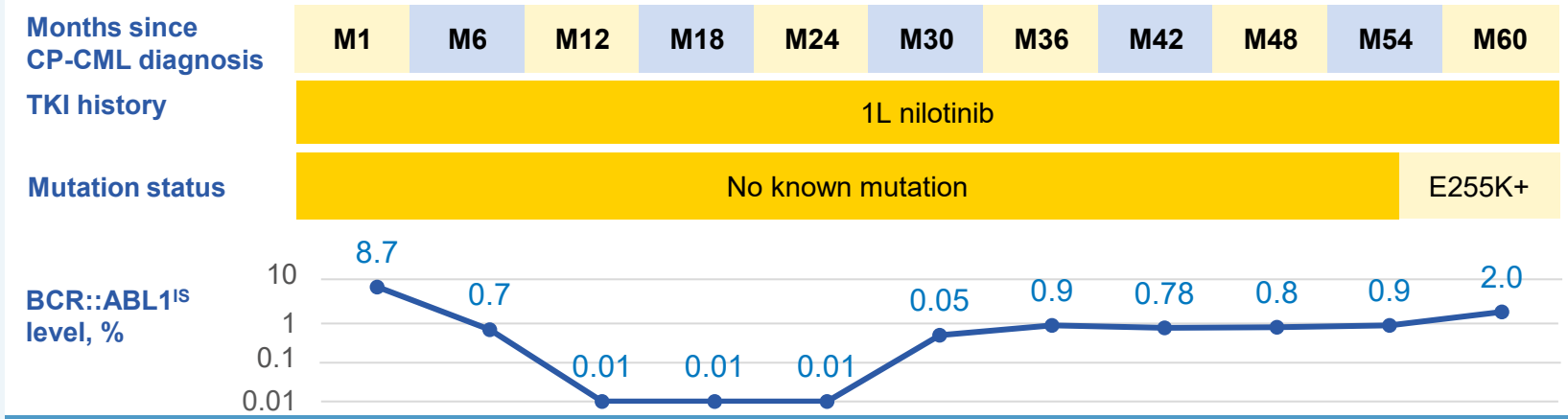
Mutation status: E255K+ (detected at 56 months)

BCR::ABL1^{IS} level: 2%

ELTS score: Low

CV risk factors: No history of CV events

Treatment history



Patients may have deep and durable responses with ICLUSIG[1]

OPTIC and PACE: Patient baseline characteristics[1,2]

Why might this patient benefit from treatment with ICLUSIG?[3–6]

ELN CML Guidelines (2020) recommend that patients who are resistant to a 2G TKI should be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[3]

Representative patient case – not an actual patient.

1L, first line; 2G, second generation; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; M, month(s); OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood.* 2018;132:393–404; 2. Cortes J, et al. *Blood.* 2021;138:2042–50; 3. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 4. Cross N, et al. *Leukemia.* 2023;37:2150–67; 5. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 6. Jabbour E, et al. *Leukemia.* 2024;38:475–81.

Incyte

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Age, years, median (range)	46 (19–81)	51 (21–77)	49 (18–81)
Male, n (%)	50 (53)	38 (40)	53 (56)
Prior TKIs, n (%)			
2	43 (46)	37 (39)	42 (45)
≥3	50 (53)	56 (60)	48 (51)
Reason prior therapy stopped, n (%)			
Resistant	92 (98)	94 (100)	94 (100)
BCR::ABL1 mutation, n (%)			
No mutation	51 (54)	58 (62)	54 (57)
T315I	25 (27)	21 (22)	21 (22)
Other	15 (16)	12 (13)	18 (19)

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
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Identifying eligible patients with low degree of TKI resistance and low CV risk

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Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Patients with CV risk factors, n (%)			
Hypertension	26 (28)	25 (27)	22 (23)
Diabetes mellitus	5 (5)	3 (3)	7 (7)
Hyperlipidaemia	19 (20)	14 (15)	16 (17)
Patients with ≥1 CV risk factor	32 (34)	30 (32)	32 (34)
Patients with >1 CV risk factor	5 (5)	4 (4)	4 (4)
Current or former smokers	29 (31)	37 (39)	33 (35)
BMI, kg/m^2, median (range)	27 (17–45)	26 (17–49)	26 (18–49)

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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Identifying eligible patients with low degree of TKI resistance and low CV risk

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The PACE study was a Phase 2, single-arm, open-label, international, multicentre trial

Characteristic	CP-CML (n=270)	AP-CML (n=85)	BP-CML (n=62)	Ph+ ALL (n=32)	Total (N=449)
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Female, n (%)	126 (47)	48 (56)	25 (40)	12 (38)	211 (47)
Prior TKIs, n (%)					
≥2	251 (93)	80 (94)	60 (97)	26 (81)	417 (93)
≥3	154 (57)	47 (55)	37 (60)	12 (38)	250 (56)
Reason prior therapy stopped, n (%)					
Resistant	215 (80)	74 (87)	59 (95)	27 (84)	375 (84)
Intolerant only	39 (14)	6 (7)	2 (3)	2 (6)	49 (11)
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BCR::ABL1 mutation, n (%)	64 (24)	18 (21)	24 (39)	22 (69)	128 (29)

Representative patient case – not an actual patient.
ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood*. 2018;132:393–404.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and low CV risk

Why might this patient benefit from treatment with ICLUSIG?[1–4]

Mutations account for resistance in approximately **1** in **3** of patients with CP-CML[1]

The **E255K** single resistance mutation has been shown to confer resistance to both bosutinib and nilotinib[2]

ICLUSIG, a **3G TKI**, is the **only approved BCR::ABL1 inhibitor** in Europe designed to be effective in CML patients with or without resistance mutations, including E255K[1–4]

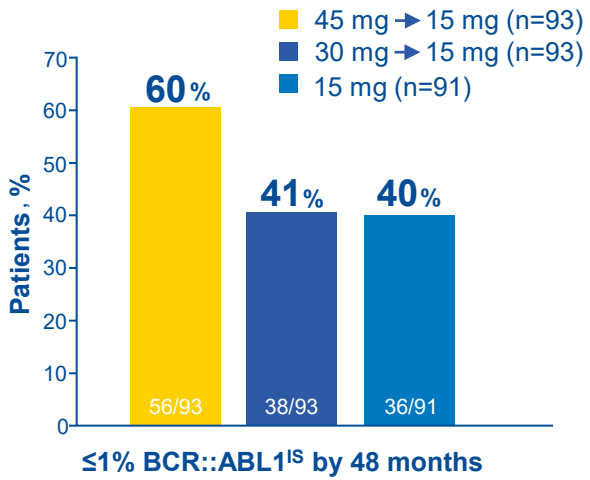
Representative patient case – not an actual patient.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 2. Cross N, et al. *Leukemia*. 2023;37:2150–67; 3. Kantarjian HM, et al. *Am J Hematol*. 2022;97:1419–26; 4. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[4*]



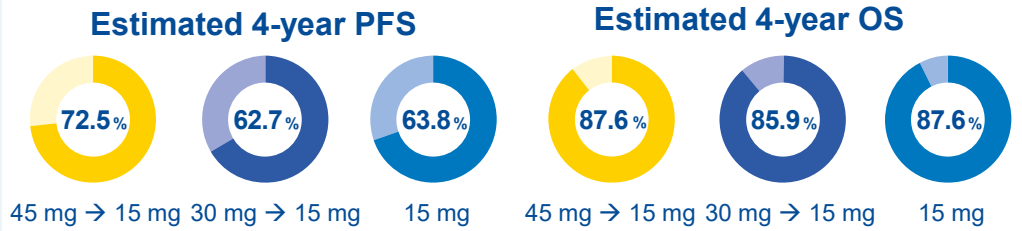
60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months[4]

Figure adapted from Cortes JE, et al.[4] with permission from the author.

Results from the 4-year OPTIC analysis suggest that patients may achieve a deep, durable molecular response with ICLUSIG[4]

Consider dose optimisation for a favourable benefit-risk profile with a 45 mg starting dose reduced to 15 mg upon achievement of response (≤1% BCR::ABL1^{IS})[3,4]

OPTIC: Estimated 4-year PFS and OS[4*]



Estimated 4-year PFS was 72.5% and OS was 87.6% for patients receiving 45 mg → 15 mg ICLUSIG[4]

Patients may achieve long-term survival with ICLUSIG[4]

Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with or without mutations[3]

Representative patient case – not an actual patient. *Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

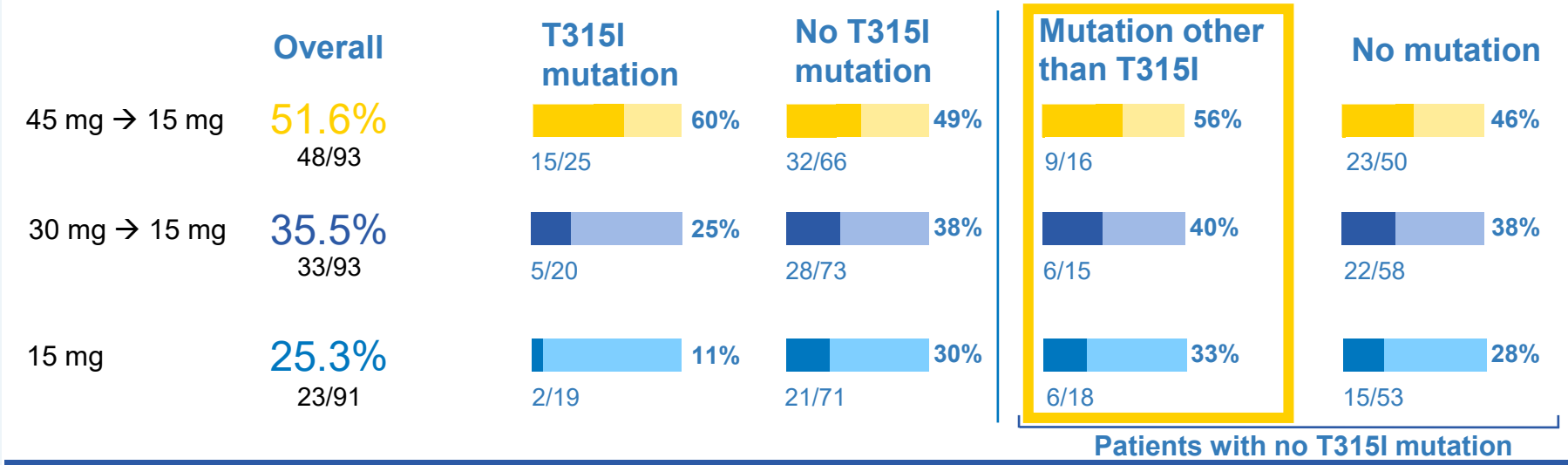
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Mutational subgroup analysis[3]

≤1% BCR::ABL1^{IS} by 12 months by baseline mutation status*



Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with or without mutations[3]

Representative patient case – not an actual patient. *4 patients did not have a mutation test result at baseline.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Incyte

ICLUSIG®

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

OPTIC: Dose-reduction regimen[2,3]

- Faster dose reductions vs PACE
- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
- Dose can be re-escalated if patients experience loss of response

Patients may regain MMR or achieve a deep MR (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain response following dose reduction[2,3]

Reducing the dose of ICLUSIG to 15 mg should be considered for patients with CP-CML who have achieved MCyR taking the following individual factors into account: CV risk, side effects, time to response, and BCR::ABL transcript levels. If dose reduction is undertaken, close monitoring of response is recommended. In patients with loss of response the dose of ICLUSIG can be re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily

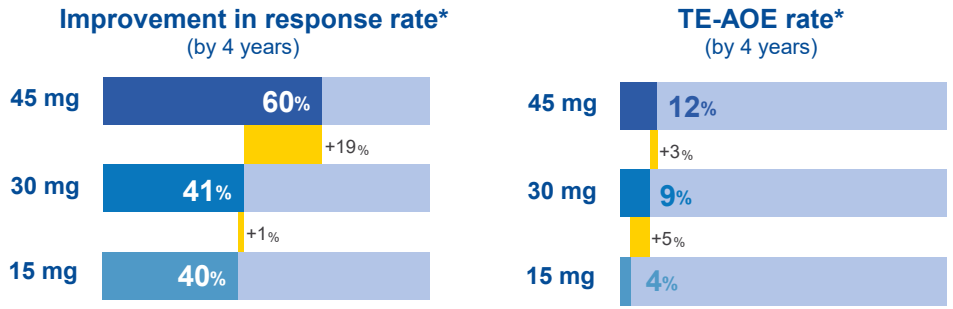
Representative patient case – not an actual patient.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[2]



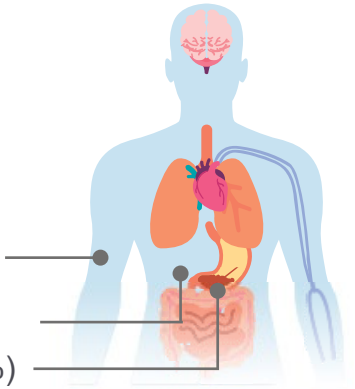
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Patients without baseline CV risk factors should be at minimal risk of CV adverse events[2–4*]

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[3]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4 years[2]

Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards[2]



- Hypertension (10%)
- Increased ALT (3%)
- Increased lipase (7%)

ICLUSIG had a manageable safety profile in the OPTIC trial with no new events; tolerability should be manageable for patients[1,2,5]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and AOE rate; †Response rate of ≤1% BCR::ABL1^{IS} by 48 months when compared with the 15-mg cohort after 4 years of exposure.

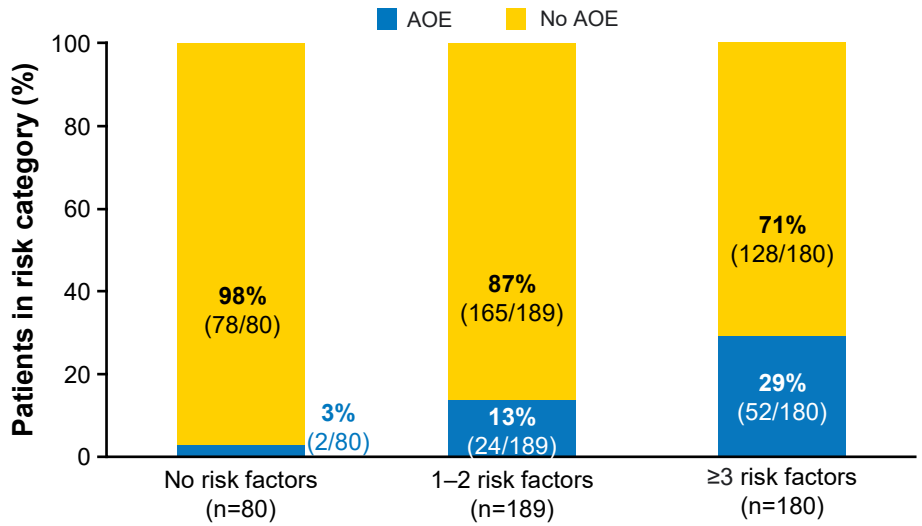
ALL, acute lymphoblastic leukaemia; ALT, alanine transaminase; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Januzzi JL, et al. *J Hematol Oncol.* 2022;15:1; 4. Jabbour E, et al. *Leukemia.* 2024;38:475–81; 5. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

PACE: Adjudicated AOEs[2]



- 87% of patients with 1–2 risk factors did not experience an AOE
- Rate of AOEs may not increase with treatment duration

Figure adapted from Januzzi JL, et al.[2] Freely distributed under the Creative Commons Attribution License (CC-BY 4.0).

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Januzzi JL, et al. *J Hematol Oncol.* 2022;15:1.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Considering ICLUSIG

For patients with resistant CP-CML and no history of CV events:

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI[1–4]

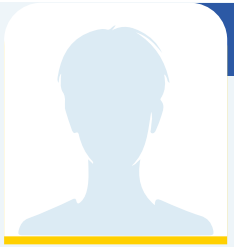
ICLUSIG, a 3G TKI, is the only approved BCR::ABL1 inhibitor in Europe designed to be effective in CML patients with or without resistance mutations, including E255K[1,5,6]

Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. O'Hare T, et al. *Cancer Cell.* 2009;16:401–12;
6. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and medium CV risk



Personal information

Age: 65 years

Sex: Female

Clinical background

CP-CML diagnosis: 42 months ago

Treatment history: 1L imatinib for 24 months (resistant), 2L dasatinib for 18 months (resistant)

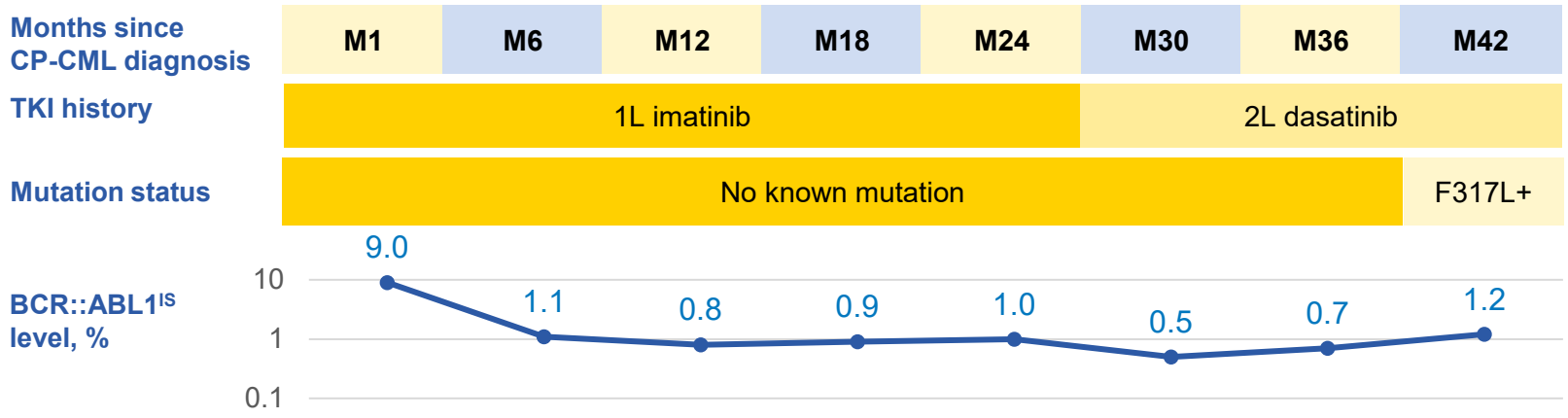
Mutation status: F317L+ (detected at 42 months)

BCR::ABL1^{IS} level: 1.2%

ELTS score: Intermediate

CV risk factors: well-controlled hypertension and hypercholesterolaemia

Treatment history



Patients may have deep and durable responses with ICLUSIG[1]

OPTIC and PACE: Patient baseline characteristics[1,2]

Why might this patient benefit from treatment with ICLUSIG?[3–6]

ELN CML Guidelines (2020) recommend that patients who are resistant to a 2G TKI should be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[3]

Representative patient case – not an actual patient.

1L, first line; 2L, second line; 2G, second generation; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; M, month(s); OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia-chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood.* 2018;132:393–404; 2. Cortes J, et al. *Blood.* 2021;138:2042–50; 3. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 4. Cross N, et al. *Leukemia.* 2023;37:2150–67; 5. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 6. Jabbour E, et al. *Leukemia.* 2024;38:475–81.

Identifying eligible patients with low degree of TKI resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Age, years, median (range)	46 (19–81)	51 (21–77)	49 (18–81)
Male, n (%)	50 (53)	38 (40)	53 (56)
Prior TKIs, n (%)			
2	43 (46)	37 (39)	42 (45)
≥3	50 (53)	56 (60)	48 (51)
Reason prior therapy stopped, n (%)			
Resistant	92 (98)	94 (100)	94 (100)
BCR::ABL1 mutation, n (%)			
No mutation	51 (54)	58 (62)	54 (57)
T315I	25 (27)	21 (22)	21 (22)
Other	15 (16)	12 (13)	18 (19)

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

The OPTIC study was a Phase 2, open-label, randomized, dose-optimisation trial

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
Patients with CV risk factors, n (%)			
Hypertension	26 (28)	25 (27)	22 (23)
Diabetes mellitus	5 (5)	3 (3)	7 (7)
Hyperlipidaemia	19 (20)	14 (15)	16 (17)
Patients with ≥1 CV risk factor	32 (34)	30 (32)	32 (34)
Patients with >1 CV risk factor	5 (5)	4 (4)	4 (4)
Current or former smokers	29 (31)	37 (39)	33 (35)
BMI, kg/m^2, median (range)	27 (17–45)	26 (17–49)	26 (18–49)

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes J, et al. *Blood.* 2021;138:2042–50.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and medium CV risk

PACE: Patient baseline characteristics[1]

The PACE study was a Phase 2, single-arm, open-label, international, multicentre trial

Characteristic	CP-CML (n=270)	AP-CML (n=85)	BP-CML (n=62)	Ph+ ALL (n=32)	Total (N=449)
Age, years, median (range)	60 (18–94)	60 (23–82)	53 (18–74)	62 (20–80)	59 (18–94)
Female, n (%)	126 (47)	48 (56)	25 (40)	12 (38)	211 (47)
Prior TKIs, n (%)					
≥2	251 (93)	80 (94)	60 (97)	26 (81)	417 (93)
≥3	154 (57)	47 (55)	37 (60)	12 (38)	250 (56)
Reason prior therapy stopped, n (%)					
Resistant	215 (80)	74 (87)	59 (95)	27 (84)	375 (84)
Intolerant only	39 (14)	6 (7)	2 (3)	2 (6)	49 (11)
Both resistant and intolerant	52 (19)	11 (13)	13 (21)	5 (16)	81 (18)
BCR::ABL1 mutation, n (%)	64 (24)	18 (21)	24 (39)	22 (69)	128 (29)

Representative patient case – not an actual patient.
ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood*. 2018;132:393–404.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Identifying eligible patients with low degree of TKI resistance and medium CV risk

Why might this patient benefit from treatment with ICLUSIG?[1–4]

Mutations account for resistance in approximately **1** in **3** of patients with CP-CML[1]

F317L single resistance mutation has been shown to confer resistance to dasatinib[2]

ICLUSIG, a **3G TKI**, is the **only approved BCR::ABL1 inhibitor** in Europe designed to be effective in CML patients with or without resistance mutations, including F317L[1–4]

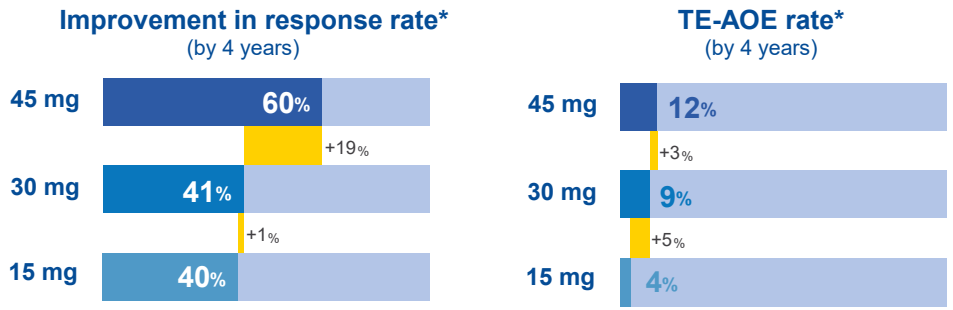
Representative patient case – not an actual patient.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 2. Cross N, et al. *Leukemia*. 2023;37:2150–67; 3. Kantarjian HM, et al. *Am J Hematol*. 2022;97:1419–26; 4. Jabbour E, et al. *Leukemia*. 2024;38:475–81.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[2]



In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

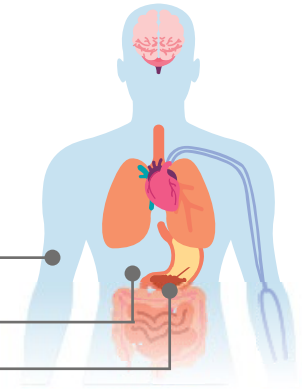
The response-based dosing with ICLUSIG should maximise patients' response while minimising toxicity[2–4*]

Rate of AOEs may not increase with treatment duration[3]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4 years[2]

Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards[2]

- Hypertension (10%)
- Increased ALT (3%)
- Increased lipase (7%)



ICLUSIG had a manageable safety profile in the OPTIC trial with no new events; tolerability should be manageable for patients[1,2,5]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and AOE rate; †Response rate of ≤1% BCR::ABL1^{IS} by 48 months when compared with the 15-mg cohort after 4 years of exposure.

ALT, alanine transaminase; AOE, arterial occlusive event; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

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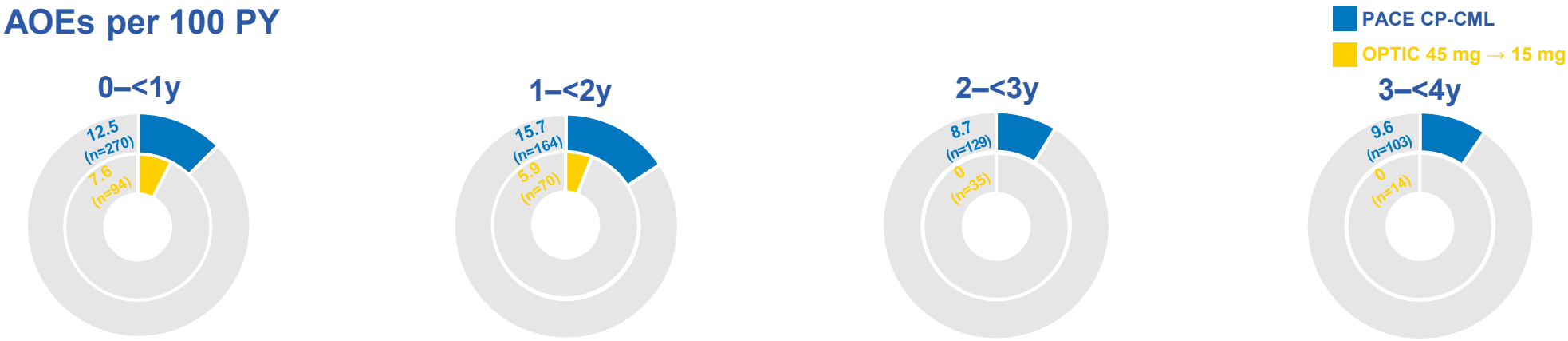
The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

ICLUSIG combines experience and data to improve patients' futures[1]

OPTIC vs PACE: Exposure-adjusted AOEs[2]

AOEs per 100 PY



Patients in OPTIC had a lower exposure-adjusted incidence of AOEs vs PACE and no AOEs occurred from Year 3 onwards, demonstrating that response-based dosing for ICLUSIG improves treatment tolerance and mitigates CV risk

Rate of AOEs may not increase with treatment duration[2]

Representative patient case – not an actual patient. Please refer to the SmPC for guidance on close monitoring of CV status. Please refer to the safety slide for more information about the most common adverse events listed in the SmPC.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; PY, patient-years; SmPC, Summary of Product Characteristics; y, year(s).

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Jabbour E, et al. *Leukemia.* 2024;38:475–81.

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

OPTIC: Dose-reduction regimen[2,3]

- Faster dose reductions vs PACE
- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
- Dose can be re-escalated if patients experience loss of response
- ~60% reduction in AOE risk in OPTIC vs PACE

Patients may regain MMR or achieve a deep MR (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain response following dose reduction; ICLUSIG's response-based dosing regimen should mitigate this patients' CV risk[2,3]

Reducing the dose of ICLUSIG to 15 mg should be considered for patients with CP-CML who have achieved MCyR taking the following individual factors into account: CV risk, side effects, time to response, and BCR::ABL transcript levels. If dose reduction is undertaken, close monitoring of response is recommended. In patients with loss of response the dose of ICLUSIG can be re-escalated to a previously tolerated dosage of 30 mg or 45 mg orally once daily

Representative patient case – not an actual patient.
AE, adverse event; ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MCyR, major cytogenetic response; MMR, major molecular response; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.
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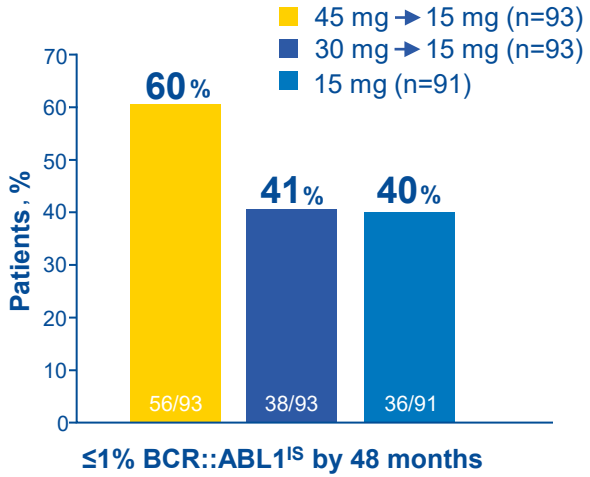
Incyte

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[4*]



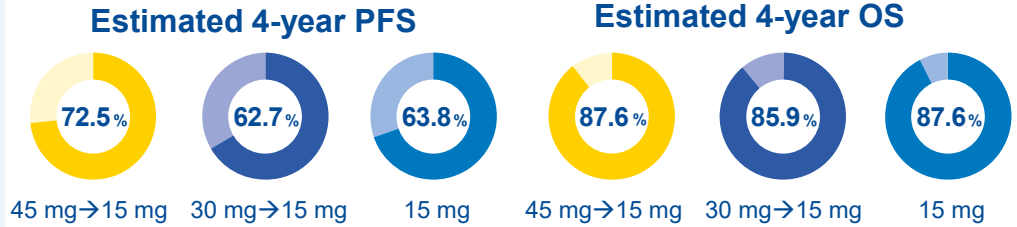
60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months[4]

Figure adapted from Cortes JE, et al.[4] with permission from the author.

Results from the 4-year OPTIC analysis suggest that patients may achieve a deep, durable molecular response with ICLUSIG[4]

Consider dose optimisation for a favourable benefit-risk profile with a 45 mg starting dose reduced to 15 mg upon achievement of response (≤1% BCR::ABL1^{IS})[3,4]

OPTIC: Estimated 4-year PFS and OS[4*]



Estimated 4-year PFS was 72.5% and OS was 87.6% for patients receiving 45 mg → 15 mg ICLUSIG[4]

Patients may achieve long-term survival with ICLUSIG[4]

Analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months across all mutation subgroups[3]

Representative patient case – not an actual patient. *Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Consider early switch to ICLUSIG after one 2G TKI[1–4]

OPTIC: Mutational subgroup analysis[3]

≤1% BCR::ABL1^{IS} by 12 months by baseline mutation status*

	Overall	T315I mutation	No T315I mutation	Mutation other than T315I	No mutation
45 mg → 15 mg	51.6% (48/93)	60% (15/25)	49% (32/66)	56% (9/16)	46% (23/50)
30 mg → 15 mg	35.5% (33/93)	25% (5/20)	38% (28/73)	40% (6/15)	38% (22/58)
15 mg	25.3% (23/91)	11% (2/19)	30% (21/71)	33% (6/18)	28% (15/53)

Patients with no T315I mutation

Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with or without mutations[3]

Representative patient case – not an actual patient. *4 patients did not have a mutation test result at baseline.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50;
4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

Considering ICLUSIG

For patients with resistant CP-CML who have well-controlled hypertension and hypercholesterolaemia

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI[1–4]

ICLUSIG, a 3G TKI, is the only approved BCR::ABL1 inhibitor in Europe designed to be effective in CML patients with or without resistance mutations, including F317L[1,5,6]

Representative patient case – not an actual patient.

2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, prescribing information; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Cortes J, et al. *Blood*. 2021;138:2042–50; 4. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 5. O'Hare T, et al. *Cancer Cell.* 2009;16:401–12; 6. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the SmPC for further information.

SUMMARY: A POTENT, PAN-BCR::ABL1 INHIBITOR FOR PATIENTS WITH RESISTANCE TO ONE 2G TKI

ICLUSIG combines experience and data to improve patients' futures: consider early switch to ICLUSIG after one 2G TKI

ICLUSIG dose can be reduced to 15 mg for patients who have achieved an MR, taking individual patient factors into account[1]

ICLUSIG – trusted since licensed over 10 years ago and counting

Incyte Oncology

Our Commitment

- to people living with CML
- to healthcare professionals fighting for their patients' health
- to continuing clinical evidence

To be kept up to date on relevant information from Incyte scan here

This QR code leads to a promotional Incyte website

2G, second generation; CML, chronic myeloid leukaemia; MR, molecular response; PI, prescribing information; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022.

Most common AEs and serious AEs

Very common AEs

- AEs occurring in ≥10% of CML and Ph+ ALL patients in PACE:[1]

Upper respiratory tract infection, anaemia, platelet count decreased, neutrophil count decreased, decreased appetite, insomnia, headache, dizziness, hypertension, dyspnoea, cough, abdominal pain, diarrhoea, vomiting, constipation, nausea, lipase increased, alanine aminotransferase increased, aspartate aminotransferase increased, rash, dry skin, pruritis, bone pain, arthralgia, myalgia, pain in extremity, back pain, muscle spasm, fatigue, asthenia, oedema peripheral, pyrexia, pain.

- A full list of ADRs can be found in the SmPC[1]

Serious AEs

- Serious AEs occurring in >2% of CML and Ph+ ALL patients in PACE:[1]

Pneumonia, pancreatitis, abdominal pain, atrial fibrillation, pyrexia, myocardial infarction, peripheral arterial occlusive disease, anaemia, angina pectoris, platelet count decreased, febrile neutropenia, hypertension, coronary artery disease, cardiac failure congestive, cerebrovascular accident, sepsis, cellulitis, acute kidney injury, urinary tract infection, lipase increased.

- A full list of serious ADRs can be found in the SmPC[1]

ADR, adverse drug reaction; AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+ ALL, Philadelphia chromosome positive; PI, prescribing information; SmPC, Summary of Product Characteristics.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022.

PRESCRIBING INFORMATION – Iclusig® (ponatinib) film coated tablets

15 mg, 30 mg or 45 mg ponatinib (as hydrochloride)

Contains lactose monohydrate

Legal Category: POM. See Summary of Product Characteristics (SmPC) before prescribing.

Indications:

Adult patients with

- Chronic phase (CP), accelerated phase (AP), or blast phase (BP) chronic myeloid leukaemia (CML) who are resistant/intolerant to dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.
- Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) who are resistant/intolerant to dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or who have the T315I mutation.

Dosage and administration:

Recommended starting dose 45 mg once daily; swallow tablets whole.

Assess and actively manage cardiovascular (CV) risk factors before starting treatment and continue throughout treatment; consider other treatment options in patients with prior myocardial infarction (MI), revascularisation or stroke (CVA).

The risk of Arterial Occlusive Events is likely to be dose-related. Consider dose reduction to 15 mg for CP-CML patients who achieve a Major Cytogenetic Response. If patients lose response, dose can be re-escalated; consult the SmPC for full details of risk:benefit and recommended monitoring of response.

Discontinue in case of disease progression or severe adverse reactions (ADRs); also, if Complete Haematological Response does not occur by 3 months.

Dose modifications, or interruptions, should be considered for haematological and non-haematological toxicities; consult the SmPC for full details of all recommended dose modifications.

Contraindications: Hypersensitivity to ponatinib or excipients.

Warnings and precautions: *Important ADRs: refer to SmPC for full details of recommended monitoring and management.*

Myelosuppression: Perform Full Blood Count every 2 weeks for the first 3 months and then monthly as clinically indicated. Most severe events occurred in first 3 months; overall, events occurred more frequently in AP-CML, BP-CML or Ph+ ALL than CP-CML.

Arterial Occlusion: Interrupt treatment immediately. Serious reactions including MI, CVA and retinal artery occlusion have occurred in 20% of patients in the PACE Phase 2 trial of Iclusig including patients <50 years and without CV risk factors; events occurred more frequently with increasing age and those with history of ischaemia, hypertension, diabetes, or hyperlipidaemia. Serious reactions have occurred in 4.3% of patients in the OPTIC Phase 2 trial (45 mg cohort).

Venous thromboembolism: Interrupt treatment immediately. Serious reactions have occurred in 5% of patients in the PACE trial including retinal vein occlusion.

Hypertension: Monitor and manage throughout treatment; may increase risk of arterial thrombotic events including renal artery stenosis.

Treatment-emergent events have occurred, including hypertensive crisis.

Aneurysms and artery dissections: This risk should be considered in patients with hypertension or history of aneurysm. VEGF pathway inhibitors may promote the formation of aneurysms and/or artery dissections.

Congestive Heart Failure: Consider discontinuing treatment if severe.

Fatal events have occurred, some related to prior vascular occlusive events.

Pancreatitis and serum lipase: Check serum lipase fortnightly for 2 months and then periodically.

Frequency of events is greater in the first 2 months. Caution in patients with history of pancreatitis or alcohol abuse.

Hepatotoxicity: Perform liver function tests (LFTs) before and during treatment.

Hepatic failure (including fatal outcome) has been observed, mostly in first year of treatment.

Haemorrhage: Interrupt treatment if serious or severe. Most severe events, including gastrointestinal haemorrhage and subdural haematoma, occurred more frequently in AP-CML, BP-CML or Ph+ ALL. Caution with use of anti-clotting agents.

Risk of Hepatitis B reactivation: Test for HBV before treatment. Reactivation has occurred following Iclusig treatment. Consult with hepatologist if serology is positive.

Severe Cutaneous Adverse Reaction (SCARs). Severe skin reactions (such as Stevens-Johnson Syndrome) have been reported with some BCR-ABL TKIs.

Posterior Reversible Encephalopathy Syndrome (PRES).

Post-marketing cases of PRES have been reported in Iclusig-treated patients.

Effects on ability to drive and use machines.

Lethargy, dizziness and blurred vision have occurred.

QT prolongation.

A clinically significant effect on QT cannot be excluded.

Iclusig contains lactose. Avoid treatment with patients having rare hereditary problems of galactose intolerance.

Drug Interactions: See SmPC for details of all interactions. **Avoid treatment with Iclusig and strong CYP3A4 inducers if possible.**

Caution when treating with strong CYP3A inhibitors; consider 30 mg starting dose of Iclusig.

Pregnancy and breastfeeding: Advise patients not to become pregnant or father a child during treatment; use effective contraception.

Studies in animals have shown reproductive toxicity. Breastfeeding should be discontinued.

Undesirable effects:

Most common serious ADRs (see SmPC for details of all ADRs).

Pneumonia, CVA, coronary artery disease, peripheral arterial occlusive disease, pancreatitis, pyrexia, abdominal pain, anaemia, angina, decreased platelet count, febrile neutropaenia, hypertension, MI, atrial fibrillation, CCF, sepsis, cellulitis, acute kidney injury, UTI, increased lipase.

Other very common ADRs.

Upper respiratory tract infection, decreased neutrophil count, dyspnoea, cough, diarrhoea, decreased appetite, nausea, vomiting, constipation, increased ALT/AST, peripheral oedema, rash, dry skin, pruritis, pain incl. back, bone & extremities, arthralgia, myalgia, muscle spasms, fatigue, headache, dizziness, asthenia.

Quantities and Marketing Authorisation numbers:

45 mg dose

30 tablets EU/1/13/839/003

30 mg dose:

30 tablets EU/1/13/839/006

15 mg dose:

30 tablets EU/1/13/839/005

Cost: 45mg x 30 tablets €6426; 30mg x 30 tablets €6426 ; 15mg x 30 tablets €3213.

Marketing Authorisation Holder: Incyte Biosciences Distribution B.V., Paasheuvelweg 25, 1105 BP Amsterdam, Netherlands.

For further information phone 1800-456-748

Date of preparation: September 2024 IE/ICLG/P/24/0033

Adverse events should be reported.
Reporting forms and information can be found at www.hpra.ie
Adverse events should also be reported to Incyte immediately by phoning the Toll-free phone number 1800-456-748