ICLUSIG®
(ponatinib) tablets

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ICLUSIG®: Patient profiles

Incyte
EU/ICLG/P/24/0033
Date of preparation: August 2024

ICLUSIG (ponatinib) tablets

Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

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Resistance to 2G TKI

Choose your pathway

Intolerance to 2G TKI

Explore patients with CP-CML who are eligible for and may benefit from ICLUSIG


William


Francine


Thomas


Martha


Agnes


Maria


Peter

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

Incyte

Representative patient cases – not actual patients.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; TKI, tyrosine kinase inhibitor.
1. Incyte Corporation; data on file.

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Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

RESET

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Resistance to 2G TKI

BCR::ABL1 mutation

No known mutation

Find out about Francine

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Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

RESET

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Resistance to 2G TKI

BCR::ABL1^{IS} level:
>1–≤10%

BCR::ABL1^{IS} level:
~1%

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Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

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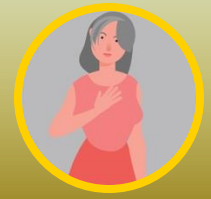
Resistance to 2G TKI

>1–≤10% BCR::ABL1^{IS}
Low CV risk

Find out about William

>1–≤10% BCR::ABL1^{IS}
Medium CV risk



Find out about Agnes

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1. Incyte Corporation; data on file.

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Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

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Resistance to 2G TKI

~1% BCR::ABL1^{IS}
Low CV risk

Find out about Thomas

~1% BCR::ABL1^{IS}
Medium CV risk

Find out about Martha

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

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Representative patient cases – not actual patients.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; TKI, tyrosine kinase inhibitor.
1. Incyte Corporation; data on file.

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Considering patients with CP-CML who are eligible and may benefit from treatment with ICLUSIG

RESET

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Intolerance to 2G TKI

Low CV risk

Find out about Maria

Medium CV risk

Find out about Peter

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

Representative patient cases – not actual patients.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; TKI, tyrosine kinase inhibitor.
1. Incyte Corporation; data on file.

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William: Identifying eligible patients with high resistance and low CV risk

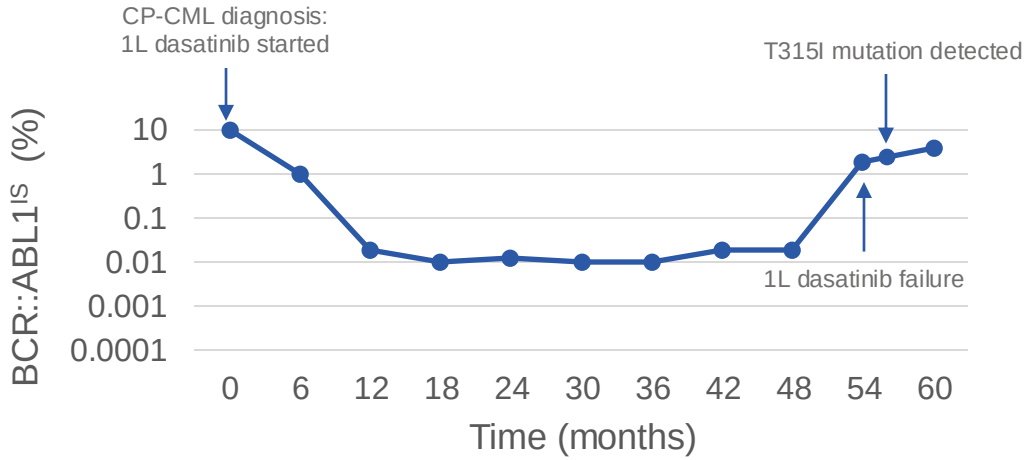
William

- William is a 35-year-old construction worker who owns his own business
- He has 2 children and runs regularly to stay fit for his annual charity race

Clinical background

- William was diagnosed with CP-CML 60 months ago and became resistant to 1L dasatinib after 54 months
- T315I mutation was detected at 56 months
- His BCR::ABL1^{IS} level is 4%
- His ELTS score is low
- William is a former smoker, but he has no previous history of CV events

William was responding to 1L dasatinib until his BCR::ABL1^{IS} level increased to >1% at 54 months



William may have fast, deep and durable responses with ICLUSIG[1]

OPTIC: Patient baseline characteristics[2]

ICLUSIG may benefit patients like William[3,4]

ELN recommendations (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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
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; OPTIC, Optimizing Ponatinib Treatment In CP-CML; SmPC, Summary of Product Characteristics.

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.

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William: Identifying eligible patients with high resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In Chronic-Phase Chronic Myeloid Leukaemia; TKI, tyrosine kinase inhibitor; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

William: Identifying eligible patients with high resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; SmPC, Summary of Product Characteristics.

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

Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[1]

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ICLUSIG may benefit patients like William[2,3]

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

T315I 'gatekeeper' mutation is resistant to imatinib and 2G TKIs (dasatinib, nilotinib, bosutinib)[3]

ICLUSIG is the only approved **BCR::ABL1 inhibitor 3G TKI** designed to potently inhibit BCR::ABL1 with or without any single resistance mutation, including T315I[3]

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

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

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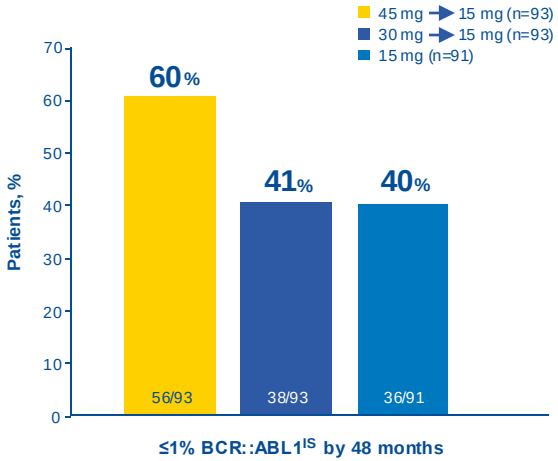
For patients like William, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[3*]



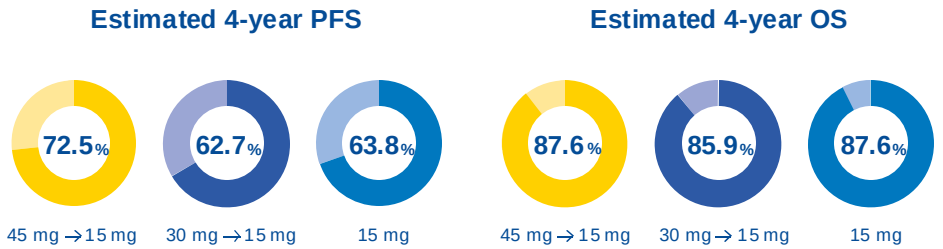
60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months

Figure adapted from Cortes JE, et al.[3] with permission from the author.

Results from the 4-year OPTIC analysis suggest that William may achieve a deep, durable molecular response with ICLUSIG[3]

Patients with a T315I mutation at baseline achieved the greatest clinical benefit in the 45 mg → 15 mg cohort[3]

OPTIC: Estimated 4-year PFS and OS[3*]



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

William may achieve long-term survival with ICLUSIG[3]

- Achieving ≤10% BCR::ABL1^{IS} within 12 months is associated with improved long-term PFS and OS[4]
- Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[5]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 4. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009; 5. Cortes J, et al. *Blood*. 2021;138:2042–50.

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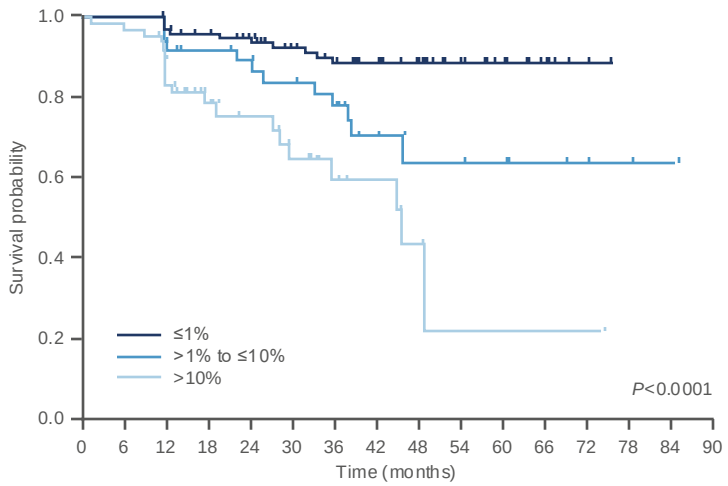
For patients like William, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

OPTIC: Landmark analysis[3]

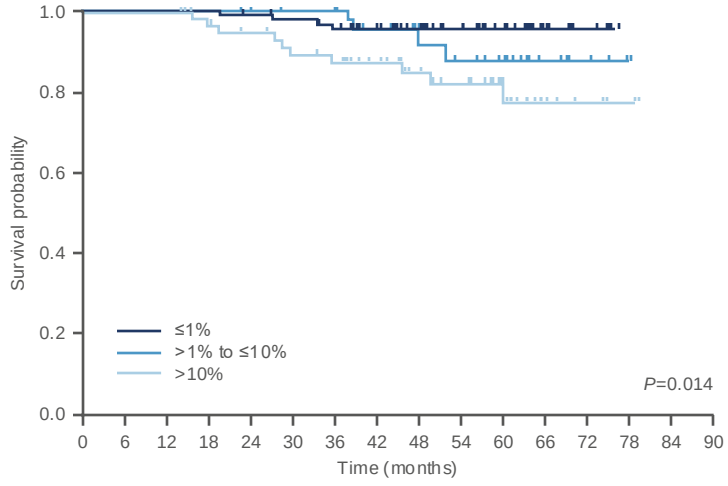
PFS by BCR::ABL1^{IS} response by 12 months



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.,[3] with permission from the author.

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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; SmPC, Summary of Product Characteristics.

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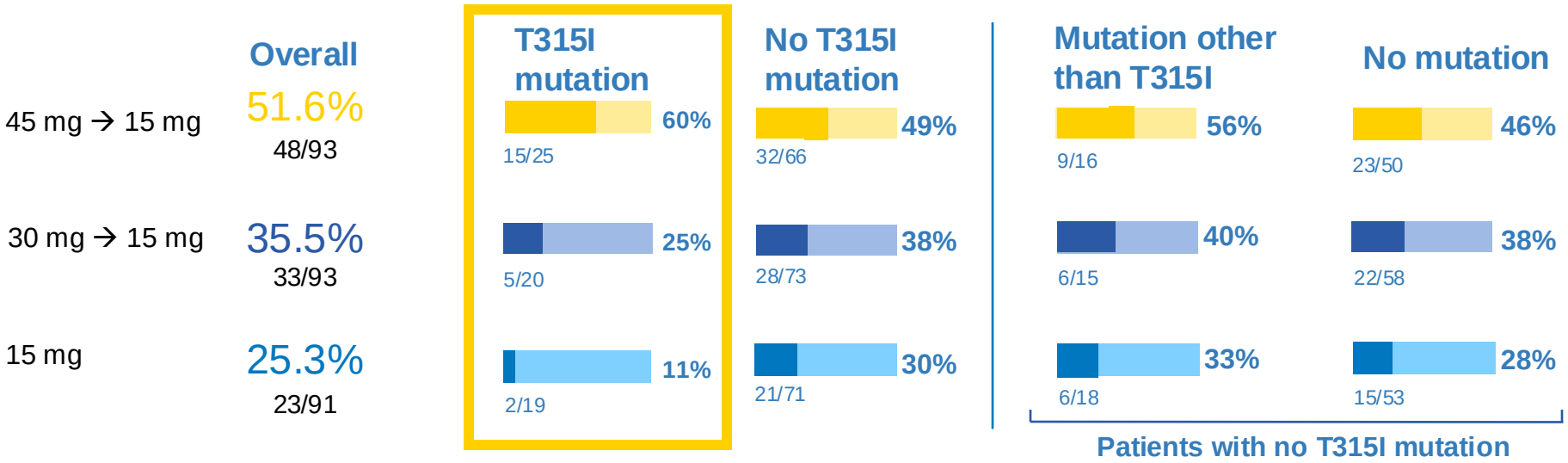
For patients like William, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes J, et al. *Blood*. 2021;138:2042–50.

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Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like William[1,2]

OPTIC: Dose-reduction regimen[3,4]

- 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

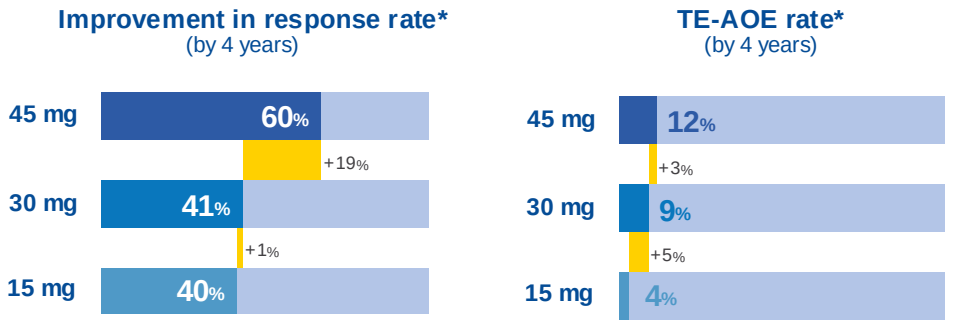
William may regain MMR or achieve a deep molecular response (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain his response following dose reduction[3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
AE, adverse event; IS, international scale; MMR, major molecular response; OPTIC, Optimizing Ponatinib Treatment In In Chronic-Phase Chronic Myeloid Leukaemia; PACE, Ponatinib Philadelphia Chromosome Positive Acute Lymphoblastic Leukaemia and Chronic Myeloid Leukaemia Evaluation; SmPC, Summary of Product Characteristics.

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

Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[1]

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



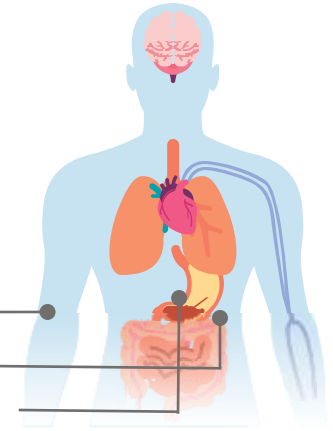
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

William 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



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

You may be confident that ICLUSIG tolerability will be manageable for William[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; SmPC, Summary of Product Characteristics; TE, treatment-emergent; AE, 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.

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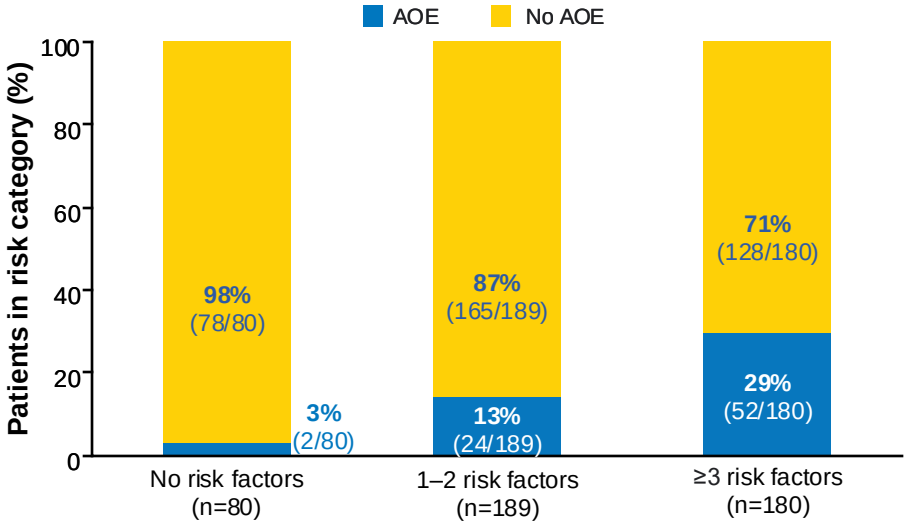
Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[1]

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]

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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; SmPC, Summary of Product Characteristics.

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Considering ICLUSIG for William

William has highly resistant CP-CML and he has no history of CV events

- ICLUSIG may offer patients like William a better future[1–3]
- **Together, we've built experience and confidence in treating patients, like William, with ICLUSIG over the last decade[1,2]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including T315I[1,3–5]

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CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Cortes J, Lang F. *J Hematol Oncol.* 2021;14:44;
4. O'Hare T, et al. *Cancer Cell.* 2009;16:401–12; 5. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

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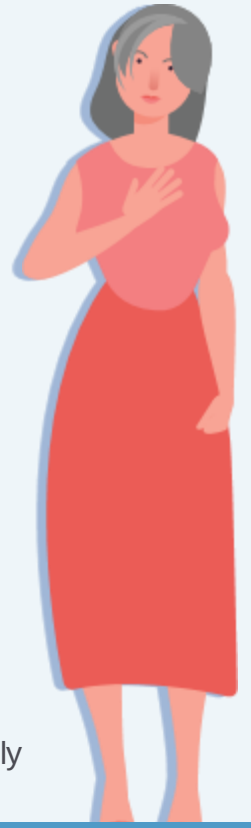
Agnes: Identifying eligible patients with high resistance and medium CV risk

Agnes

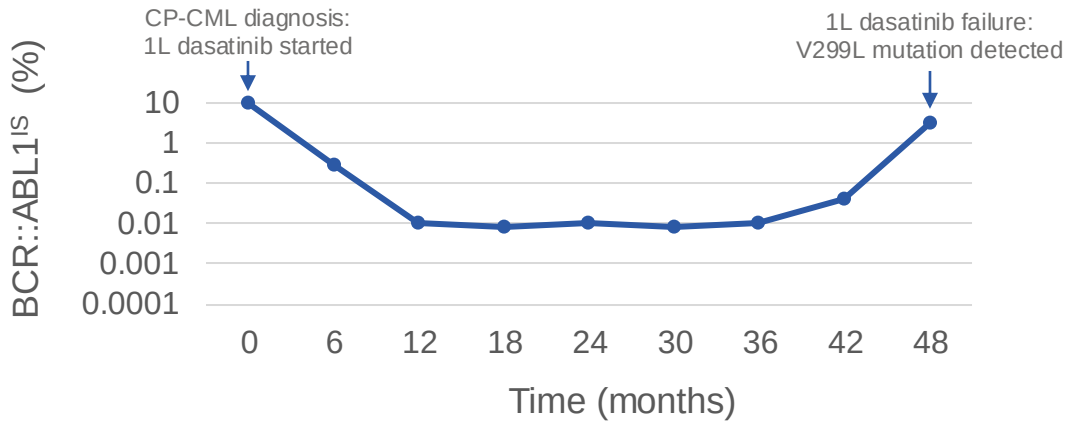
- Agnes is 68 years old and was a paramedic before retiring a few years ago
- She volunteers to teach first-aid classes in the local community and is looking forward to seeing her son get married

Clinical background

- Agnes was diagnosed with CP-CML 48 months ago and became resistant to 1L dasatinib after 48 months
- V299L mutation was detected at 48 months
- Her BCR::ABL1^{IS} level is 3%
- Her ELTS score is intermediate
- Agnes has a family history of dyslipidaemia and, after lifestyle changes were ineffective, was recently prescribed statins to balance her lipid levels



Agnes was responding to 1L dasatinib until her BCR::ABL1^{IS} level increased to 3% at 48 months



Agnes may have fast, deep and durable responses with ICLUSIG[1]

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

ICLUSIG may benefit patients like Agnes[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.

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; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; SmPC, Summary of Product Characteristics. 1. Cortes JE, et al. *Blood*. 2018;132:393–404; 2. Cortes J, et al. *Blood*. 2021;138:2042–50; 3. Jabbour E, et al. *Leukemia*. 2024;38:475–81; 4. Hochhaus A, et al. *Leukemia*. 2020;34:966–84; 5. Cross N, et al. *Leukemia*. 2023;37:2150–67; 6. Elnair E. Galal A. *BMC Cancer*. 2018;18:1097.

Agnes: Identifying eligible patients with high resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

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 (%)			
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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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; TKI, tyrosine kinase inhibitor; SmPC, Summary of Product Characteristics.

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

Agnes: Identifying eligible patients with high resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

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)

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BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; SmPC, Summary of Product Characteristics.

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

BECAUSE TOMORROW MATTERS TODAY

Agnes: Identifying eligible patients with high resistance and medium CV risk

PACE: Patient baseline characteristics[1]

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)

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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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

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ICLUSIG®

Agnes: Identifying eligible patients with high resistance and medium CV risk

ICLUSIG may benefit patients like Agnes[1–3]

ICLUSIG is the only approved **BCR::ABL1 inhibitor 3G TKI** designed to potently inhibit BCR::ABL1 with or without any single resistance mutation, including V299L[1–3]

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

ELN recommendations (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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; 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.

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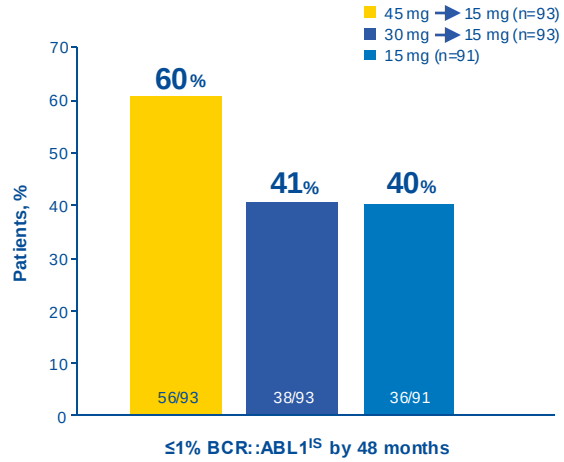
For patients like Agnes, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[3]*

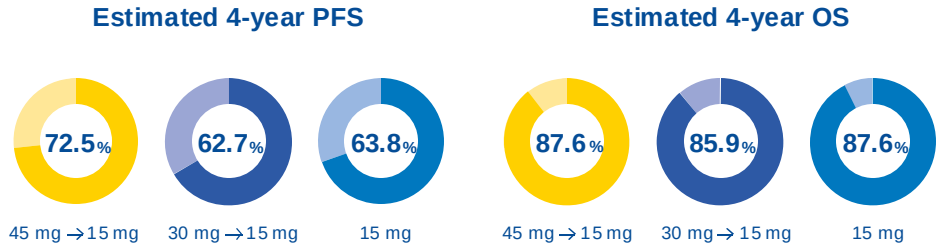


60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months

Figure adapted from Cortes JE, et al.[3] with permission from the author.

Results from the 4-year OPTIC analysis suggest that Agnes may achieve a deep, durable molecular response with ICLUSIG[3]

OPTIC: Estimated 4-year PFS and OS[3]*



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

Agnes may achieve long-term survival with ICLUSIG[3]

Achieving ≤10% BCR::ABL1^{IS} within 12 months is associated with improved long-term PFS and OS[4]

Most patients in the 45 mg → 15 mg cohort achieved ≤1% BCR::ABL1^{IS} by 4 years regardless of baseline mutation status[3]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 4. Apperley J, et al. Poster presentation at ASH 2022; Abstract 3009.

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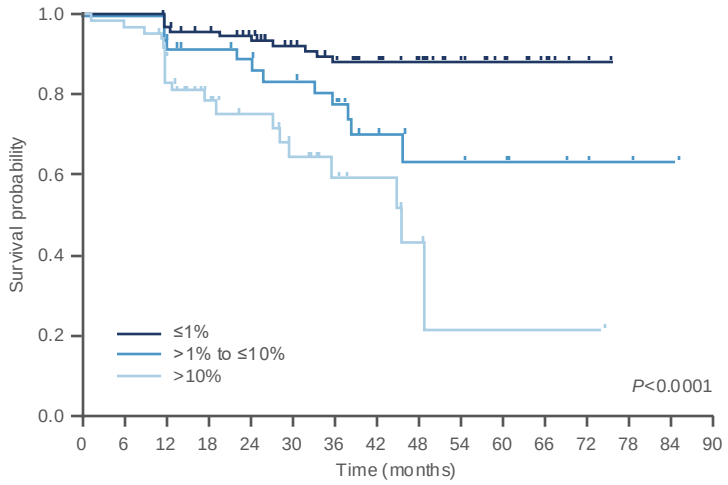
BECAUSE TOMORROW MATTERS TODAY

For patients like Agnes, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

OPTIC: Landmark analysis[3]

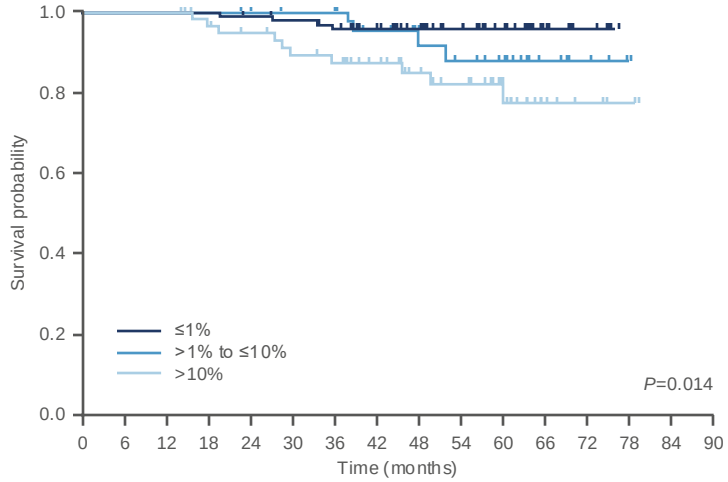
PFS by BCR::ABL1^{IS} response by 12 months



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.,[3] with permission from the author.

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
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; SmPC, Summary of Product Characteristics.

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Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Agnes[1,2]

OPTIC: Dose-reduction regimen[3,4]

- 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

Agnes may regain MMR or achieve a deep molecular response (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain her response following dose reduction[3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; IS, international scale; MMR, major molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; SmPC, Summary of Product Characteristics.

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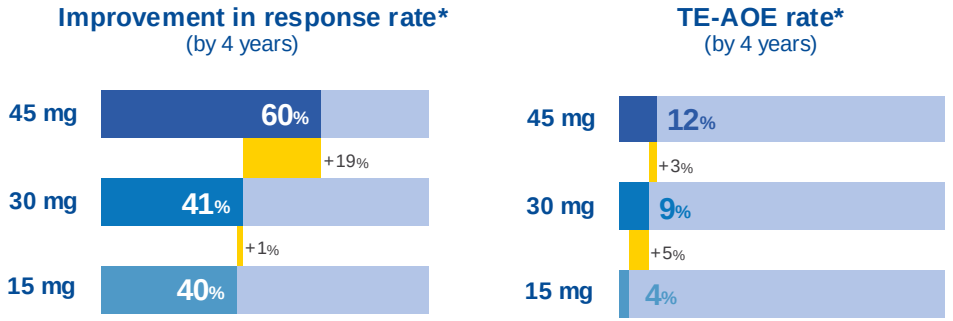
Together, we've built experience and confidence in treating patients like Agnes with ICLUSIG over the last decade[1]

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



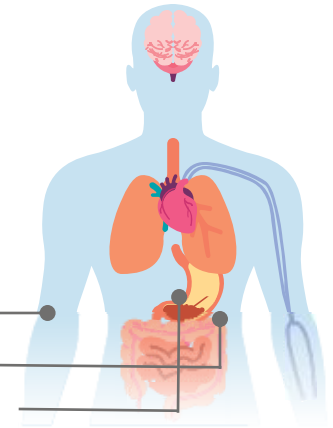
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Agnes's hyperlipidaemia is well-controlled, so she 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



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

You may be confident that ICLUSIG tolerability will be manageable for Agnes[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; 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.

Incyte

Together, we've built experience and confidence in treating patients like Agnes with ICLUSIG over the last decade[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; PY, patient-years; SmPC, Summary of Product Characteristics.

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

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Considering ICLUSIG for Agnes

Agnes has highly resistant CP-CML and her CV risk factors are well controlled

- ICLUSIG may offer patients like Agnes a better future[1,2]
- **Together, we've built experience and confidence in treating patients, like Agnes, with ICLUSIG over the last decade[1,2]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including V299L[1,3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

Francine: Identifying eligible patients with high resistance and no mutations

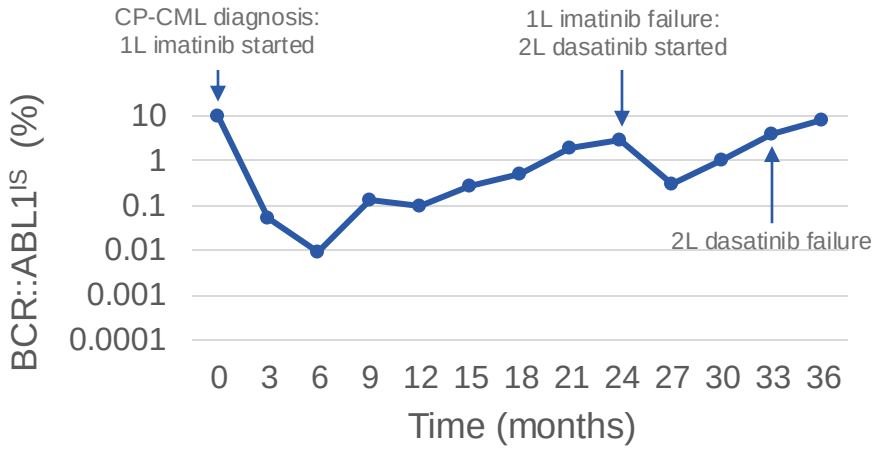
Francine

- Francine is 69 years old. She was a nurse for over 40 years before retiring to spend more time with her family
- She likes to stay active and is a member of her local walking club

Clinical background

- Francine was diagnosed with CP-CML 36 months ago and became resistant to 1L imatinib after 24 months and 2L dasatinib at 33 months
- Her BCR::ABL1^{IS} level is 8% and she has no known mutation
- Her ELTS score is low
- Francine has no previous history of CV events

Francine was responding to 2L dasatinib until her BCR::ABL1^{IS} level increased to 4% at 33 months



Francine may have fast, deep and durable responses with ICLUSIG[1]

- OPTIC and PACE: Patient baseline characteristics[1,2]
- ICLUSIG may benefit patients like Francine[3]

ELN recommendations (2020) note 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]

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1L, first line; 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; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

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Francine: Identifying eligible patients with high resistance and no mutations

OPTIC: Patient baseline characteristics[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

Francine: Identifying eligible patients with high resistance and no mutations

ICLUSIG may benefit patients like Francine[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]

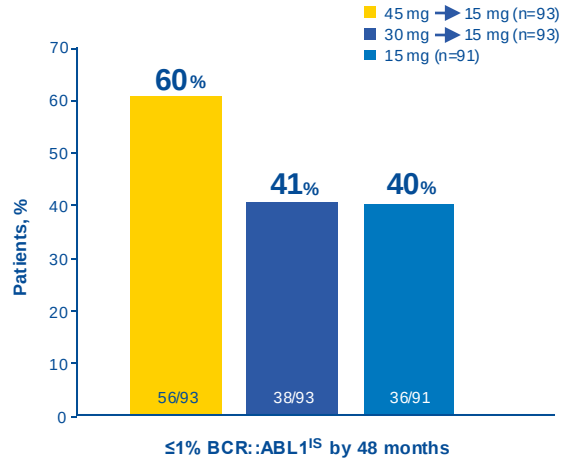
Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. De Santis S, et al. *Onco Targets Ther*. 2022;15:103–16.

BECAUSE TOMORROW MATTERS TODAY

For patients like Francine, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[3]*

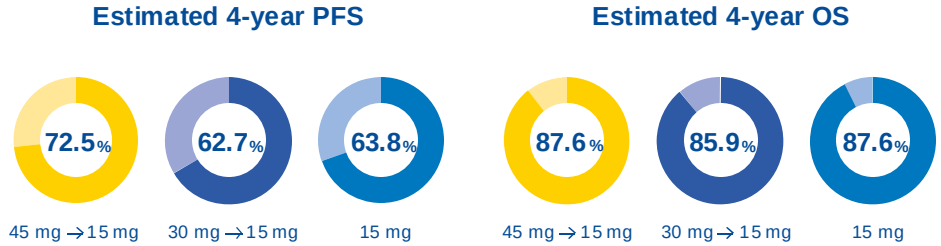


60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months

Figure adapted from Cortes JE, et al.[3] with permission from the author.

Results from the 4-year OPTIC analysis suggest that Francine may achieve a deep, durable molecular response with ICLUSIG[3]

OPTIC: Estimated 4-year PFS and OS[3]*



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

Francine may achieve long-term survival with ICLUSIG[3]

Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[4]

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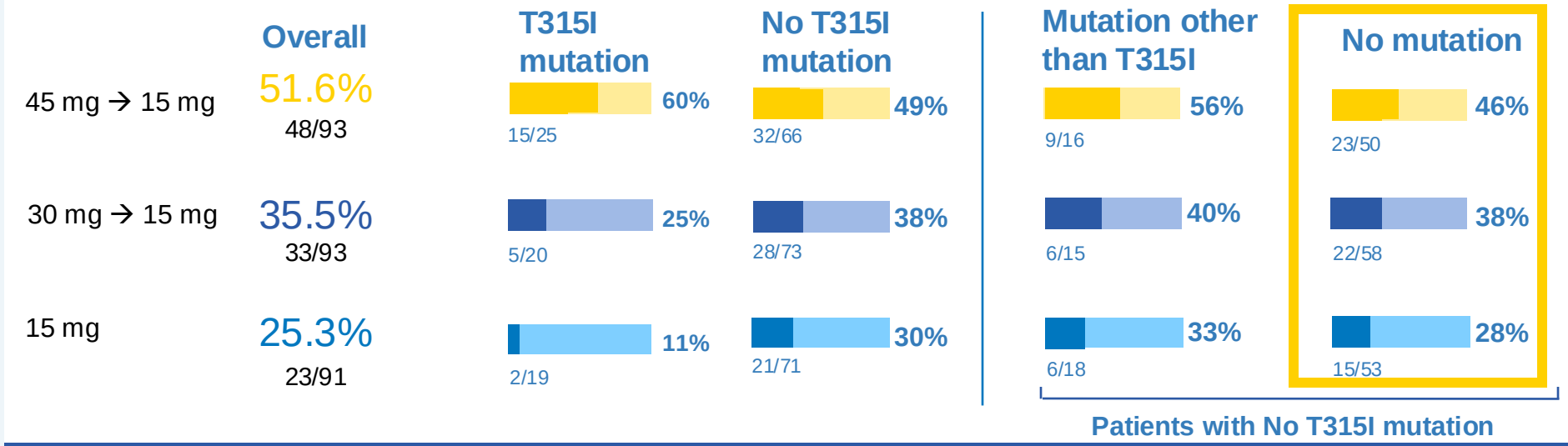
For patients like Francine, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics.

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- Fewer AE-related dose reductions vs PACE
- Lower median dose intensity vs PACE
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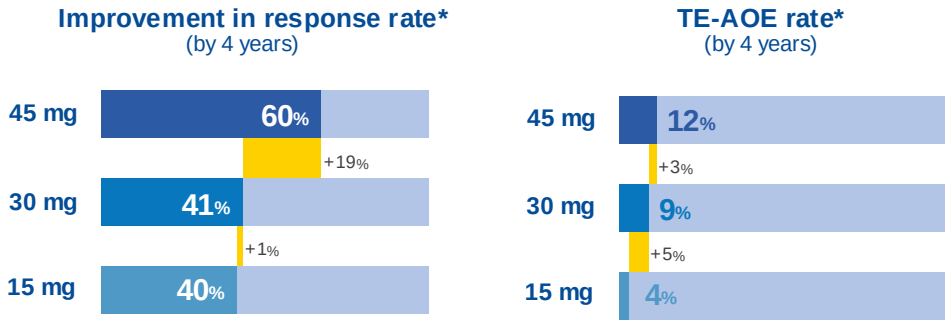
BECAUSE TOMORROW MATTERS TODAY

Together, we've built experience and confidence in treating patients like Francine with ICLUSIG over the last decade[1]

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

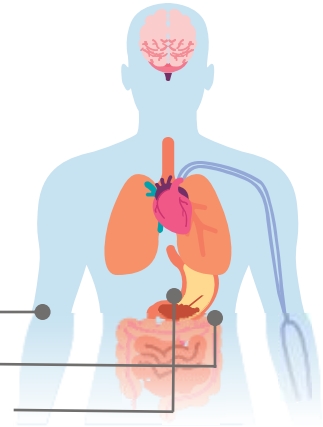


In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Francine 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



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

You may be confident that ICLUSIG tolerability will be manageable for Francine[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; 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.

Incyte

Considering ICLUSIG for Francine

Francine has highly resistant CP-CML and no known mutations or history of CV events

- ICLUSIG may offer patients like Francine a better future[1,2]
- **Together, we've built experience and confidence in treating patients, like Francine, with ICLUSIG over the last decade[1,2]**
- ELN recommendations (2020) note that patients like Francine 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[3]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Hochhaus A, et al. *Leukemia.* 2020;34:966–84.

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Thomas: Identifying eligible patients with low resistance and low CV risk

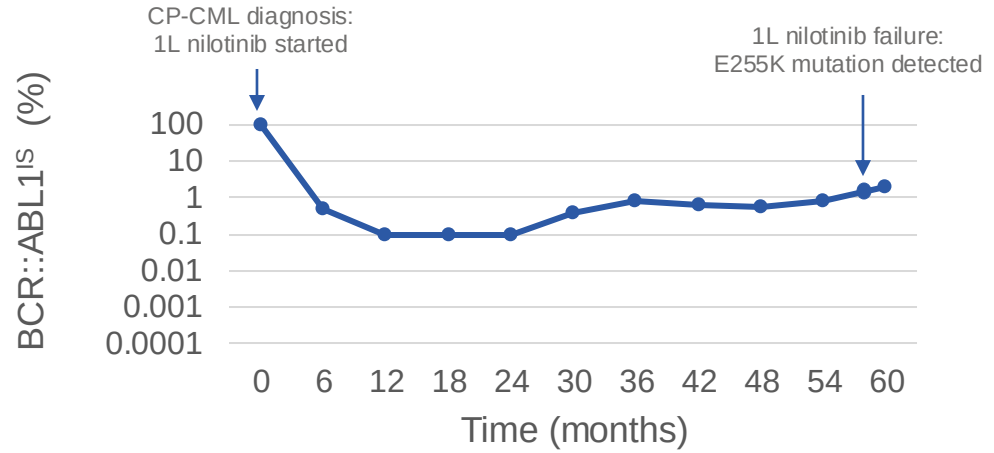
Thomas

- Thomas is 66 years old and teaches biology at the local school
- He walks his dog regularly with his family and is looking forward to becoming a grandfather next year

Clinical background

- Thomas was diagnosed with CP-CML 60 months ago and became resistant to 1L nilotinib after 56 months
- E255K mutation was detected at 56 months
- His BCR::ABL1^{IS} level is 2%
- His ELTS score is low
- Thomas has no history of CV events

Thomas was responding to 1L nilotinib until 56 months when his BCR::ABL1^{IS} level increased to 2%



Thomas may have fast, deep and durable responses with ICLUSIG[1]

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

ICLUSIG may benefit patients like Thomas[3–6]

ELN recommendations (2020) note 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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
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; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; 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.

Thomas: Identifying eligible patients with low resistance and low CV risk

OPTIC: Patient baseline characteristics[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML;
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OPTIC: Patient baseline characteristics[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
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1. Cortes J, et al. *Blood.* 2021;138:2042–50.

Thomas: Identifying eligible patients with low resistance and low CV risk

PACE: Patient baseline characteristics[1]

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)

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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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

BECAUSE TOMORROW MATTERS TODAY

Thomas: Identifying eligible patients with low resistance and low CV risk

ICLUSIG may benefit patients like Thomas[1–4]

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

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

ICLUSIG is the only approved **BCR::ABL1 inhibitor 3G TKI** designed to potently inhibit BCR::ABL1 with or without any single resistance mutation, including E255K[1–4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; 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;
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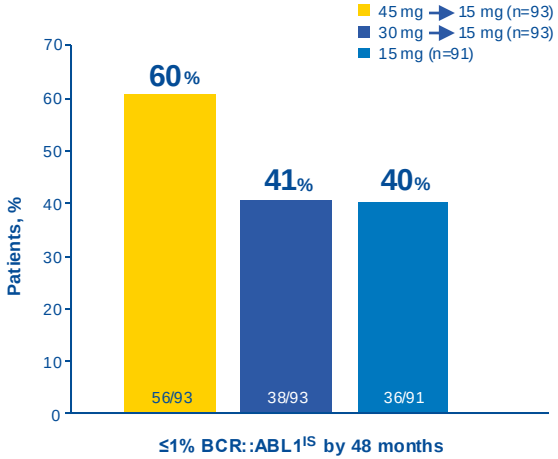
A delay means that patients like Thomas may miss the opportunity to have the deepest response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,2]

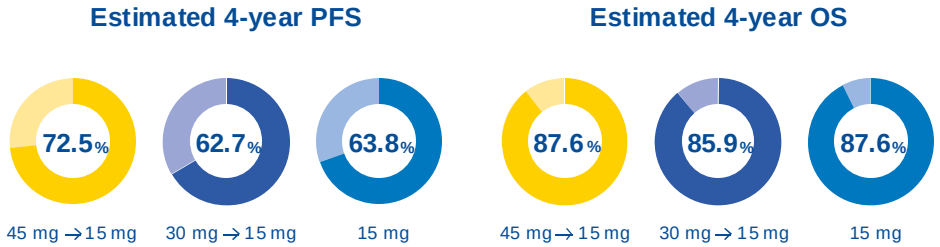
OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[3]*



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

Figure adapted from Cortes JE, et al.[3] with permission from the author.

OPTIC: Estimated 4-year PFS and OS[3]*



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

Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with or without mutations[4]

Today, we know that treatment with a pan-inhibitor without delay may offer Thomas a better future[1–3]

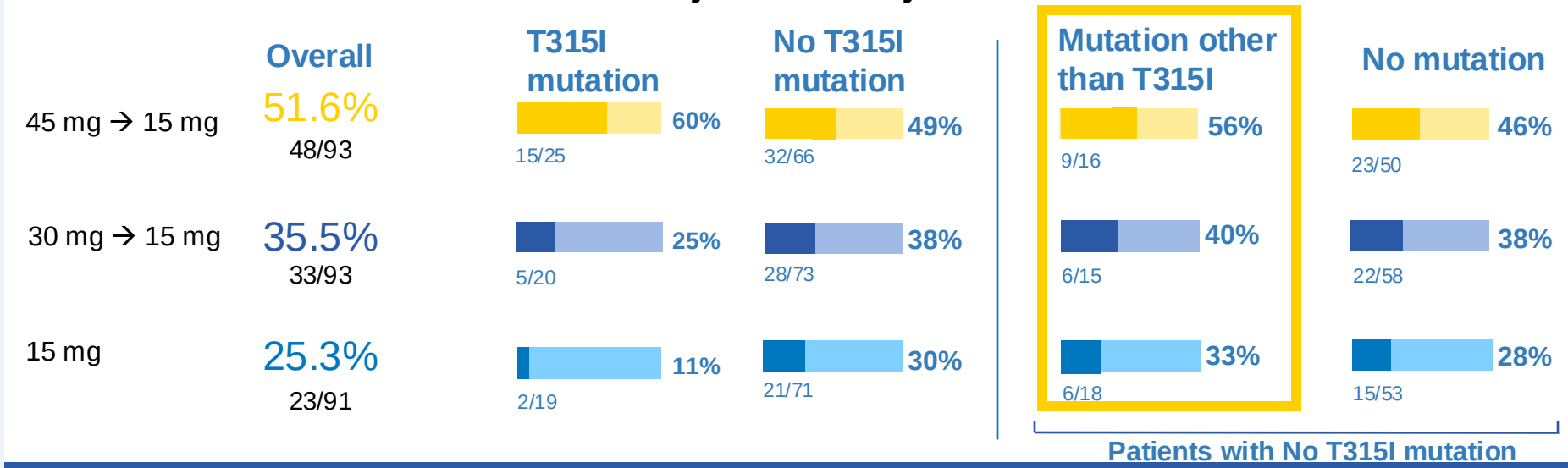
Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 4. Cortes J, et al. *Blood*. 2021;138:2042–50.

A delay means that patients like Thomas may miss the opportunity to have the deepest response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,2]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Thomas[1,2]

OPTIC: Dose-reduction regimen[3,4]

- 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

Thomas may regain MMR or achieve a deep molecular response (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain his response following dose reduction[3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
AE, adverse event; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; IS, international scale; MMR, major molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; SmPC, Summary of Product Characteristics.

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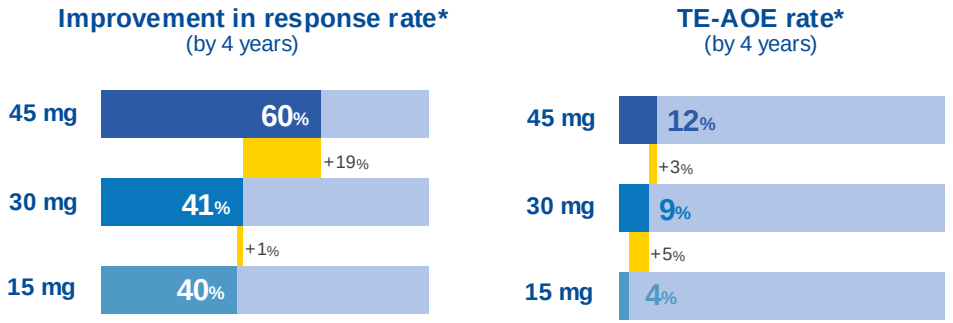
Together, we've built experience and confidence in treating patients like Thomas with ICLUSIG over the last decade[1]

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



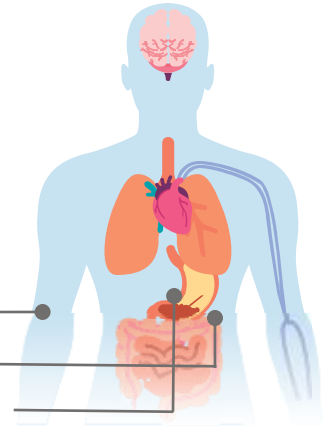
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Thomas' hypertension is well-controlled so he 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



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

You may be confident that ICLUSIG tolerability will be manageable for Thomas[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; SmPC, Summary of Product Characteristics; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

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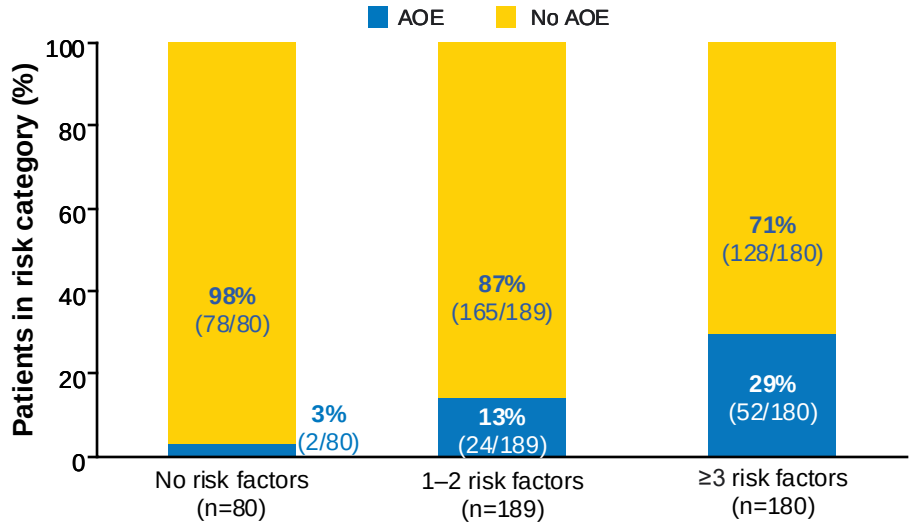
Together, we've built experience and confidence in treating patients like Thomas with ICLUSIG over the last decade[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; SmPC, Summary of Product Characteristics.

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Incyte

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Considering ICLUSIG for Thomas

Thomas has resistant CP-CML and he has no history of CV events

- ICLUSIG may offer patients like Thomas a better future[1,2]
- **Together, we've built experience and confidence in treating patients, like Thomas, with ICLUSIG over the last decade[1,2]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including E255K[1,3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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4. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

Incyte

ICLUSIG®

Martha: Identifying eligible patients with low resistance and medium CV risk

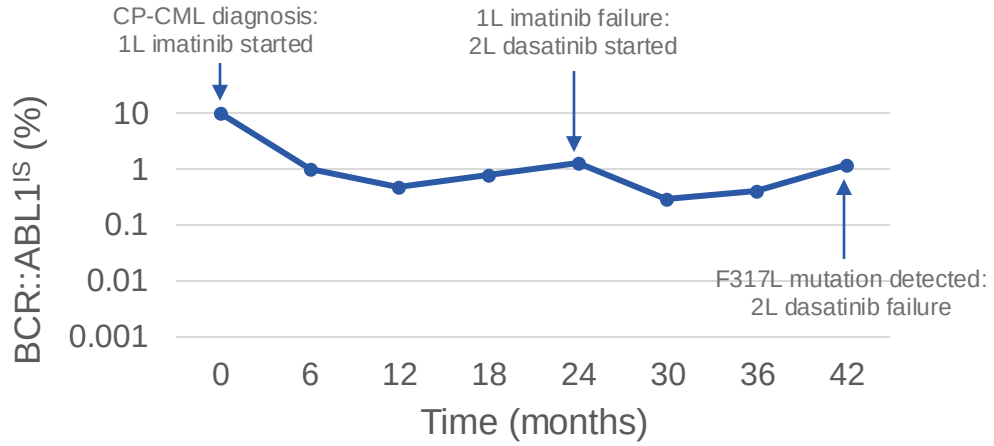
Martha

- Martha is a semi-retired, 65 year old who works in the neighbourhood café
- She lives with her daughter and is looking forward to their holiday abroad together

Clinical background

- Martha was diagnosed with CP-CML 42 months ago and became resistant to 1L imatinib at 24 months and 2L dasatinib at 42 months
- F317L mutation was detected at 42 months
- Her BCR::ABL1^{IS} level is 1.2%
- Her ELTS score is intermediate
- Martha takes beta blockers and statins to keep her hypertension and hypercholesterolaemia under control

Martha's BCR::ABL1^{IS} level was stable and responding to 2L dasatinib treatment until 42 months



Martha may have fast, deep and durable responses with ICLUSIG[1]

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

ICLUSIG may benefit patients like Martha[3–6]

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Martha: Identifying eligible patients with low resistance and medium CV risk

OPTIC: Patient baseline characteristics[1]

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)
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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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

Martha: Identifying eligible patients with low resistance and medium CV risk

BECAUSE TOMORROW MATTERS TODAY

ICLUSIG may benefit patients like Martha[1–4]

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

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

ICLUSIG is the only approved **BCR::ABL1 inhibitor 3G TKI** designed to potently inhibit BCR::ABL1 with or without any single resistance mutation, including F317L[1–4]

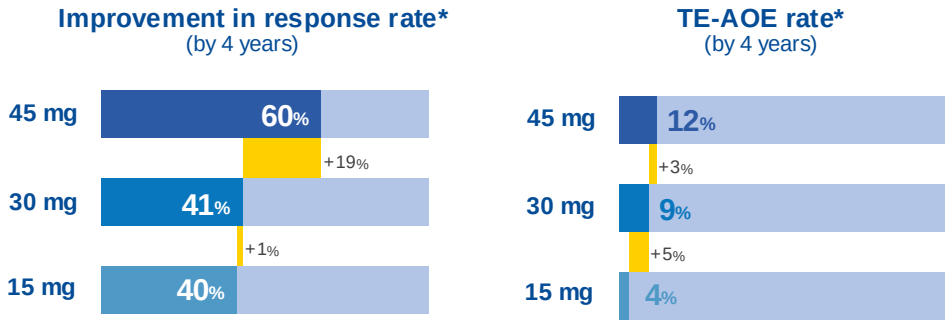
Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase 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.

Incyte

Together, we've built experience and confidence in treating patients like Martha with ICLUSIG over the last decade[1]

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



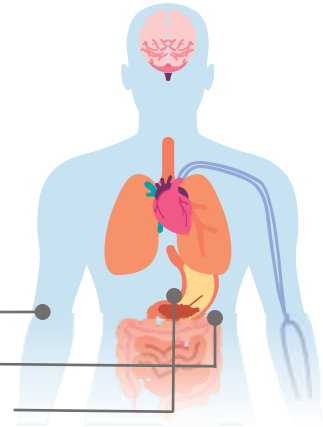
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[2†]

Response-based dosing with ICLUSIG should maximise Martha's 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



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

You may be confident that ICLUSIG tolerability will be manageable for Martha[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; 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.

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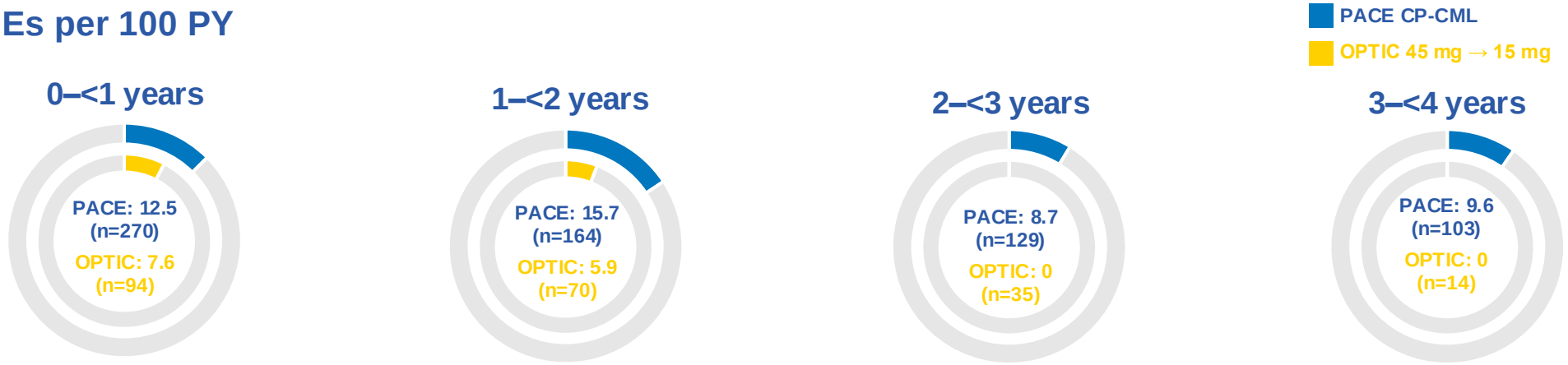
ICLUSIG®

BECAUSE TOMORROW MATTERS TODAY

Together, we've built experience and confidence in treating patients like Martha with ICLUSIG over the last decade[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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; PY, patient-years; SmPC, Summary of Product Characteristics.

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

Incyte

Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Martha[1,2]

OPTIC: Dose-reduction regimen[3,4]

- 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

Martha may regain MMR or achieve a deep molecular response (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain her response following dose reduction; ICLUSIG's response-based dosing regimen should mitigate Martha's CV risk[3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
AE, adverse event; ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; MMR, major molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; SmPC, Summary of Product Characteristics.

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

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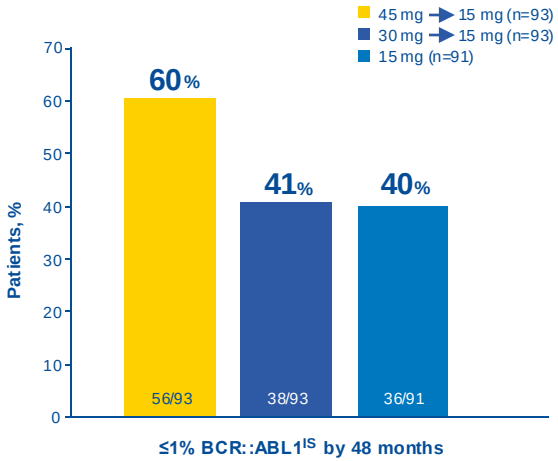
A delay means that patients like Martha may miss the opportunity to have the deepest response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,2]

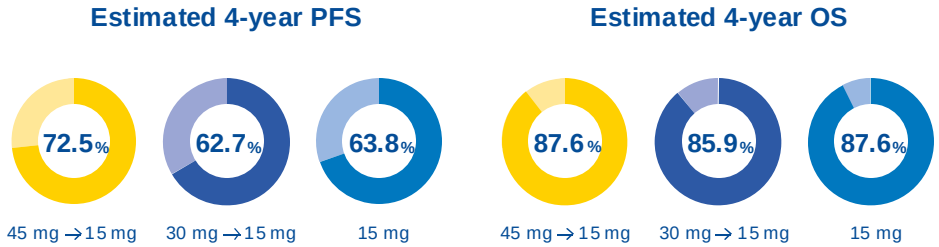
OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[3*]



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

Figure adapted from Cortes JE, et al.[3] with permission from the author.

OPTIC: Estimated 4-year PFS and OS[3*]



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

Analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months across all mutation subgroups[4]

Today, we know that treatment with a pan-inhibitor without delay may offer Martha a better future[1–3]

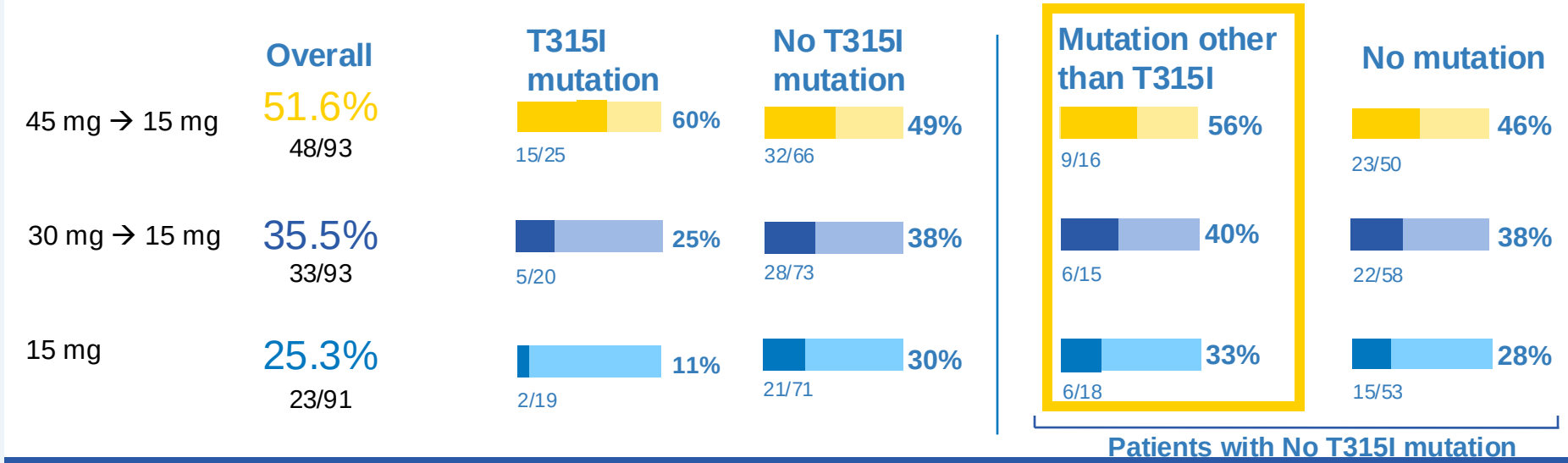
Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 4. Cortes J, et al. *Blood*. 2021;138:2042–50.

A delay means that patients like Martha may miss the opportunity to have the deepest response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,2]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*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; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Cortes J, et al. *Blood*. 2021;138:2042–50.

Incyte

ICLUSIG®

Considering ICLUSIG for Martha

Martha has resistant CP-CML; her hypertension and hypercholesterolaemia are well controlled

- ICLUSIG may offer patients like Martha a better future[1,2]
- **Together, we've built experience and confidence in treating patients, like Martha, with ICLUSIG over the last decade[1,2]**
- ICLUSIG was the first, and remains the only, TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including F317L[1,3,4]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
CP-CML, chronic-phase chronic myeloid leukaemia; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

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

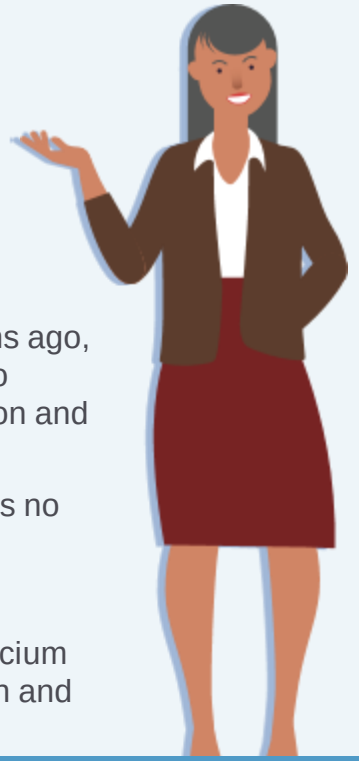
Maria: Identifying eligible patients with intolerance and medium CV risk

Maria

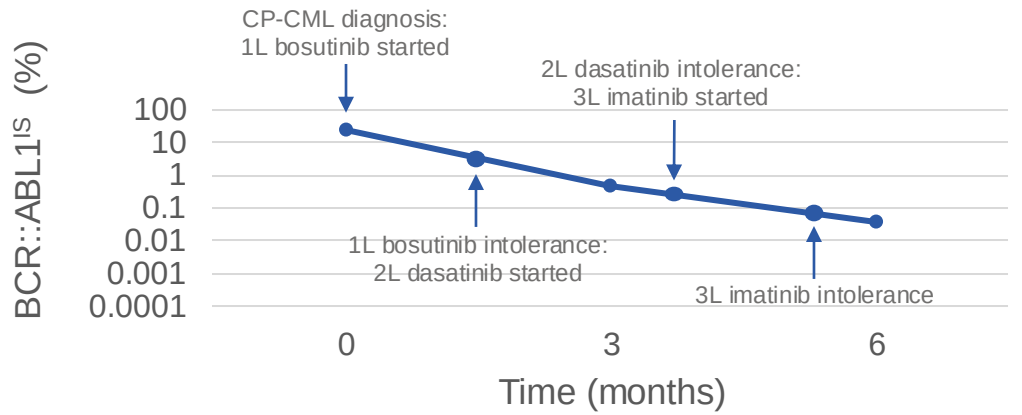
- Maria is a 67-year-old museum curator who has worked in exhibits across Europe
- Maria and her husband enjoy spending quality time together when gardening

Clinical background

- Maria was diagnosed with CP-CML 6 months ago, and became intolerant to 1L bosutinib due to diarrhoea, 2L dasatinib due to pleural effusion and 3L imatinib due to muscle cramps
- Her BCR::ABL1^{IS} level is 0.04% and she has no BCR::ABL1 mutations
- Her ELTS score is intermediate
- Maria is prescribed an ACE inhibitor and calcium channel blocker to manage her hypertension and her BMI is 31.0 kg/m^2



Maria's BCR::ABL1^{IS} level is responding to 3L imatinib



Maria may have fast, deep and durable responses with ICLUSIG[1]

RWE: Patient baseline characteristics[3–6]

ELN recommendations (2020) recommend starting ICLUSIG at a lower dose in the case of intolerance to previous TKIs[2]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
1L first line; 2L, second line; 3L, third line; ACE, angiotensin-converting enzyme; BMI, body mass index; 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; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood.* 2018;132:393–404; 2. Hochhaus A, et al. *Leukemia.* 2020;34:966–84; 3. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 4. Lurlo A, et al. *Blood*. 2019;134(Suppl 1):1652; 5. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 6. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

Maria: Identifying eligible patients with intolerance and medium CV risk

RWE: Patient baseline characteristics[1–4]

Characteristic	OITI[1] (N=120)	Belgian Registry[3] (N=50)	TOPASE[4] (N=120)
Age, years, median (range) [Q1, Q3]	60 (19–93)	58 (19–83)	58 [45,69]
CP-CML, n (%)	111 (93)	30 (60)	104 (87)
Prior TKIs, n (%)			
1	60 (50)	4 (8)	17 (14)
2	42 (35)	23 (46)	59 (49)
≥3	18 (15)	23 (46)	42 (35)
Reason for starting ponatinib, n (%)			
Intolerance to prior TKI	40 (33)	20 (40)	72 (60)
Relapse or refractoriness to prior TKI	48 (40)*	14 (28)	30 (25)†
Patients with CV risk factors, n (%)			
History of CV events	20 (36)[2]	-	56 (47)
Hypertension	23 (41)[2]	17 (34)	39 (33)
Hyperlipidaemia	-	5 (10)	-
Starting dose of ponatinib, n (%)			
45 mg	43 (36)	36 (72)	21 (20)‡
30 mg	49 (41)	6 (12)	46 (44)‡
15 mg	28 (23)	7 (14)	37 (36)‡

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Primary resistance: 29 (24%), secondary resistance: 19 (16%); †Reported as 'poor response to previous therapies'; ‡CP-CML population.
CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy.

1. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 2. Lurlo A, et al. *Blood*. 2019;134(Suppl 1):1652; 3. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 4. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

BECAUSE TOMORROW MATTERS TODAY

Together, we've built experience and confidence in treating patients like Maria with ICLUSIG over the last decade[1]

PACE: Incidence rates of newly occurring AOEs[2]

Number of CP-CML patients with events per patient-years:

0 to <1 year	1 to <2 years	2 to <3 years	3 to <4 years	4 to <5 years
15.8	15.6	13.4	9.8	4.9

Median dose intensity (mg/d):

0 to <1 year	1 to <2 years	2 to <3 years	3 to <4 years	4 to <5 years
32.1	31.4	24.8	19.0	20.4

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

Only 2 treatment-related AOEs were reported in the RWE study OITI[6]

Rate of new AOEs may not increase with longer treatment duration[2–4]

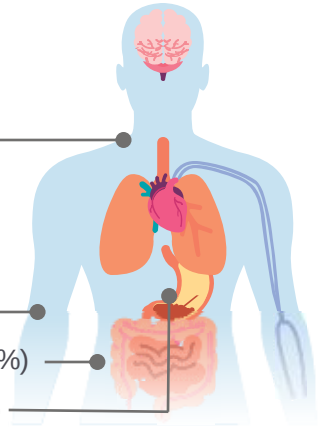
RWE: AEs and TRAEs[5–7]*

68% of patients experienced AEs in the Belgian registry:[5]

Most common AEs (≥10%) in the Belgian registry:
- Rash (26%)
- Dry skin (10%)

53–57% of patients in OITI and TOPASE experienced ≥1 TRAE[6,7]

Most common TRAEs in OITI were:[6]
- Hypertension (8%)
- Thrombocytopenia (6%)
- Increased lipase (5%)



You may be confident that ICLUSIG tolerability will be manageable for Maria[5–7]

The PACE 5-year analysis and RWE studies established the consistency of the ICLUSIG safety profile over a prolonged period[2,5–7]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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.

*Includes both intolerant and resistant patients. AE, adverse event; ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy; TRAE, treatment-related adverse event.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Cortes JE, et al. *Blood.* 2018;132:393–404; 3. Januzzi JL, et al. *J Hematol Oncol.* 2022;15:1; 4. Jabbour E, et al. *Leukemia.* 2024;38:475–81; 5. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 6. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 7. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

Incyte

ICLUSIG's response-based dosing regimen should improve Maria's treatment tolerability[1,2]

BECAUSE TOMORROW MATTERS TODAY

Patients with intolerance:

Maria's intolerance may contribute to nonadherence which could lead to loss of response, or biological progression to AP-/BP-CML[3–5]

Death attributed to disease progression is approximately 10 times that due to TRAEs in patients with CP-CML receiving 2L or 3L therapy[6]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2L, second line; 3L, third line; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase;
SmPC, Summary of Product Characteristics; TRAE, treatment-related adverse events.

1. Jabbour E, et al. *Leukemia*. 2024;38:475–81; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Cross N, et al. *Leukemia*. 2023;37:2150–67;
4. Shanmuganathan N. Hughes TP. *Am Soc Hematol Educ Program*. 2018;1:168–76; 5. García-Gutiérrez V, et al. *J Hematol Oncol*. 2022;15:90;
6. Pearson E, et al. *Leuk Res.* 2016;43:1–8.

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BECAUSE TOMORROW MATTERS TODAY

For patients like Maria, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

RWE: Response rates and estimated survival[3–5]

OITI[3]

Prospective and retrospective, observational study (CP-, AP-, BP-CML; N=120)*

CP-CML: 93% | Intolerance: 33%

3-year response rates:[3,4] CP-CML (N=111)[3]

MMR: 31%

MR4–MR5: 50%

MR4: ≤0.01% BCR::ABL1^{IS}; MR5: ≤0.001% BCR::ABL1^{IS}

3-year KM estimates:[3,4] CP-CML (N=111)[3]

OS: 87%
(95% CI: 80.2–93.8)

PFS: 83%
(95% CI: 75.9–90.8)

Belgian registry[4]

Prospective, observational study (CP-, AP-, BP-CML or Ph+ ALL; N=50)†

CP-CML: 60% | Intolerance (CML): 42%

Intolerant CP-CML (n=14)[4]

MMR–MR2: 71%

MR2: ≤1% BCR::ABL1^{IS}

CML (N=33)[4]

OS: 85%

PFS: 82%

TOPASE[5]

Ambispective, observational study (CP-, AP-, BP-CML; N=120)‡

CP-CML: 87% | Intolerance (CML): 60%

Of the patients with CP-CML who were non-responders at baseline (n=70):[5]

60% achieved **MMR**

Median time to response:[5]

4.8 months

Results from real-world, observational studies suggest that Maria may achieve a deep, durable molecular response and long-term survival with ICLUSIG[3–5]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Median follow-up in all patients: 41 months; †Median follow-up in patients with CML: 15 months; ‡Median follow-up in patients with CP-CML: 18.2 months. 2G, second generation; ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CI, confidence interval; CML, chronic myeloid leukaemia; CP, chronic phase; IS, international scale; KM, Kaplan Meier; MR, molecular response; MMR, major molecular response; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; OS, overall survival; PFS, progression-free survival; Ph+, Philadelphia chromosome positive; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 4. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 5. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

Incyte

Considering ICLUSIG for Maria

Maria has a history of intolerance; her hypertension is well controlled

- ICLUSIG may offer patients like Maria a better future[1–3]
- **Together, we've built experience and confidence in treating patients, like Maria, with ICLUSIG over the last decade[1–3]**
- Approximately 25% of patients with CML change TKIs because of AEs. We know that cycling TKIs may lead to mutations, lowering the likelihood of response to an alternative TKI[1,4,5]
- Considering an early switch to ICLUSIG after one 2G TKI for patients like Maria may improve their outcomes[1,4,5]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2G, second generation; AE, adverse event; CML, chronic myeloid leukaemia; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Claudiani S, et al. *Leukemia*. 2024;38:796–802; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. ICLUSIG® (ponatinib) SmPC; Incyte, 2022;
4. Braun TP, et al. *Cancer Cell*. 2020;37:530–42; 5. Cortes J, Lang F. *J Hematol Oncol*. 2021;14:44.

Peter: Identifying eligible patients with intolerance and low CV risk

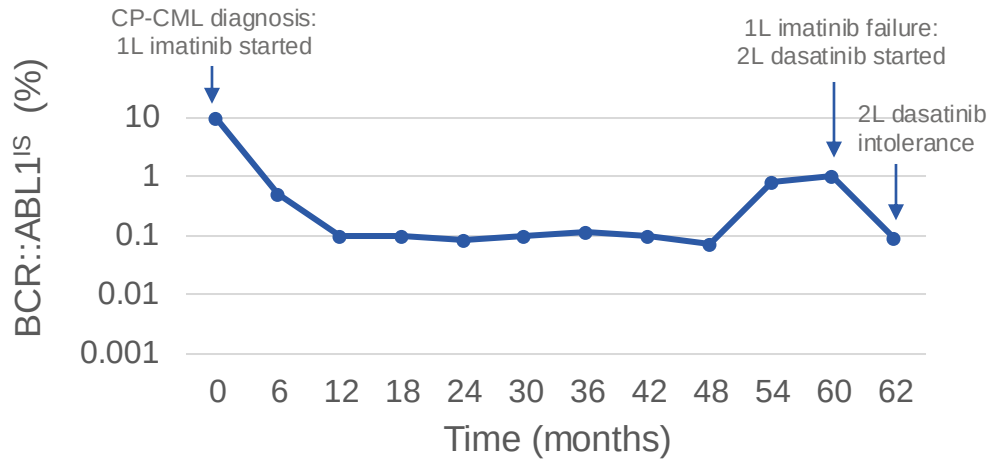
Peter

- Peter is a 52-year-old journalist for the local newspaper
- He is an amateur photographer and is excited for his next travelling adventure

Clinical background

- Peter was diagnosed with CP-CML 62 months ago, becoming resistant to 1L imatinib after 60 months and developed intolerance to 2L dasatinib after 2 months of treatment
- His BCR::ABL1^{IS} level is 0.09% after 2 months of dasatinib treatment
- His ELTS score is low
- Peter has no BCR::ABL1 mutations or previous history of CV events
- He has some gastrointestinal issues following treatment with dasatinib but no other comorbidities

Peter's BCR::ABL1^{IS} level is 0.09% after 2 months of 2L dasatinib treatment



Peter may have fast, deep and durable responses with ICLUSIG[1]

RWE: Patient baseline characteristics[2–4]

ELN recommendations (2020) recommend starting ICLUSIG at a lower dose in the case of intolerance to previous TKIs[5]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
1L, first line, 2L, second 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; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.

1. Cortes JE, et al. *Blood*. 2018;132:393–404; 2. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 3. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 4. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77; 5. Hochhaus A, et al. *Leukemia*. 2020;34:966–84.

Peter: Identifying eligible patients with intolerance and low CV risk

RWE: Patient baseline characteristics[1–3]

Characteristic	OITI[1] (N=120)	Belgian Registry[2] (N=50)	TOPASE[3] (N=120)
Age, years, median (range) [Q1, Q3]	60 (19–93)	58 (19–83)	58 [45,69]
CP-CML, n (%)	111 (93)	30 (60)	104 (87)
Prior TKIs, n (%)			
1	60 (50)	4 (8)	17 (14)
2	42 (35)	23 (46)	59 (49)
≥3	18 (15)	23 (46)	42 (35)
Reason for starting ponatinib, n (%)			
Intolerance to prior TKI	40 (33)	20 (40)	72 (60)
Relapse or refractoriness to prior TKI	48 (40)*	14 (28)	30 (25)†
Starting dose of ponatinib, n (%)			
45 mg	43 (36)	36 (72)	21 (20)‡
30 mg	49 (41)	6 (12)	46 (44)‡
15 mg	28 (23)	7 (14)	37 (36)‡

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Primary resistance: 29 (24%), secondary resistance: 19 (16%); †Reported as 'poor response to previous therapies'; ‡CP-CML population. CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy.

1. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 2. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 3. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

ICLUSIG's response-based dosing regimen should improve Peter's treatment tolerability[1,2]

Patients with intolerance:

Peter's intolerance may contribute to nonadherence which could lead to loss of response, or biological progression to AP-/BP-CML[3–5]

Death attributed to disease progression is approximately 10 times that due to TRAEs in patients with CP-CML receiving 2L or 3L therapy[6]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2L, second line; 3L, third line; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; SmPC, Summary of Product Characteristics; TRAE, treatment-related adverse event.

1. Jabbour E, et al. *Leukemia*. 2024;38:475–81; 2. Cortes JE, et al. Poster presentation at ASH 2023; Abstract 3164; 3. Cross N, et al. *Leukemia*. 2023;37:2150–67;
4. Shanmuganathan N. Hughes TP. *Am Soc Hematol Educ Program*. 2018;1:168–76; 5. García-Gutiérrez V, et al. *J Hematol Oncol*. 2022;15:90;
6. Pearson E, et al. *Leuk Res*. 2016;43:1–8.

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For patients like Peter, early use of ICLUSIG after one 2G TKI may lead to the deepest responses[1,2]

RWE: Response rates and estimated survival[3–5]

OITI[3]

Prospective and retrospective, observational study (CP-, AP-, BP-CML; N=120)*

CP-CML: 93% | Intolerance: 33%

3-year response rates:[3,4] CP-CML (N=111)[3]

MMR: 31%

MR4–MR5: 50%

MR4: ≤0.01% BCR::ABL1^{IS}; MR5: ≤0.001% BCR::ABL1^{IS}

3-year KM estimates:[3,4] CP-CML (N=111)[3]

OS: 87%
(95% CI: 80.2–93.8)

PFS: 83%
(95% CI: 75.9–90.8)

Belgian registry[4]

Prospective, observational study (CP-, AP-, BP-CML or Ph+ ALL; N=50)†

CP-CML: 60% | Intolerance (CML): 42%

Intolerant CP-CML (n=14)[4]

MMR–MR2: 71%

MR2: ≤1% BCR::ABL1^{IS}

CML (N=33)[4]

OS: 85%

PFS: 82%

TOPASE[5]

Ambispective, observational study (CP-, AP-, BP-CML; N=120)‡

CP-CML: 87% | Intolerance (CML): 60%

Of the patients with CP-CML who were non-responders at baseline (n=70):[5]

60% achieved **MMR**

Median time to response:[5]

4.8 months

Results from real-world, observational studies suggest that Peter may achieve a deep, durable molecular response and long-term survival with ICLUSIG[3–5]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
*Median follow-up in all patients: 41 months; †Median follow-up in patients with CML: 15 months; ‡Median follow-up in patients with CP-CML: 18.2 months. 2G, second generation; ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CI, confidence interval; CML, chronic myeloid leukaemia; CP, chronic phase; IS, international scale; KM, Kaplan Meier; MR, molecular response; MMR, major molecular response; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; OS, overall survival; PFS, progression-free survival; Ph+, Philadelphia chromosome positive; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy.

1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26; 3. Breccia M, et al. *Hemasphere*. 2023;7(Suppl):e8949080; 4. Devos T, et al. *Ann Hematol*. 2021;100:1723–32; 5. Cayssials E, et al. *Blood*. 2022;140(Suppl 1):6776–77.

Incyte

Together, we've built experience and confidence in treating patients like Peter with ICLUSIG over the last decade[1]

PACE: Incidence rates of newly occurring AOEs[2]

Number of CP-CML patients with events per patient-years:

0 to <1 year	1 to <2 years	2 to <3 years	3 to <4 years	4 to <5 years
15.8	15.6	13.4	9.8	4.9

Median dose intensity (mg/d):

0 to <1 year	1 to <2 years	2 to <3 years	3 to <4 years	4 to <5 years
32.1	31.4	24.8	19.0	20.4

Only 2 treatment-related AOEs were reported in the RWE study OITI[3]

Peter should be at minimal risk of having CV adverse events[2,4,5]

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[4]

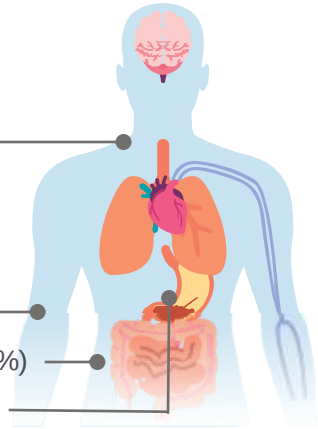
RWE: AEs and TRAEs[3,6,7]*

68% of patients experienced AEs in the Belgian registry:[6]

Most common AEs (≥10%) in the Belgian registry:
- Rash (26%)
- Dry skin (10%)

53–57% of patients in OITI and TOPASE experienced ≥1 TRAE[3,7]

Most common TRAEs in OITI were:[3]
- Hypertension (8%)
- Thrombocytopenia (6%)
- Increased lipase (5%)



You may be confident that ICLUSIG tolerability will be manageable for Peter[3,6,7]

The PACE 5-year analysis and RWE studies established the consistency of the ICLUSIG safety profile over a prolonged period[2,3,6,7]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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.
*Includes both intolerant and resistant patients. AE, adverse event; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; PACE, Ponatinib Ph+ ALL and CML Evaluation; RWE, real-world evidence; SmPC, Summary of Product Characteristics; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy; TRAE, treatment-related adverse event.

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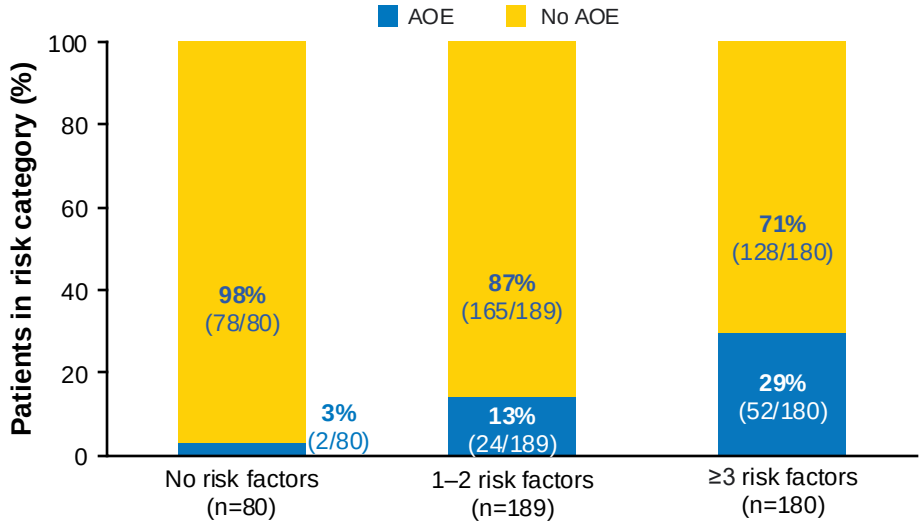
Together, we've built experience and confidence in treating patients like Peter with ICLUSIG over the last decade[1]

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. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information and 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; SmPC, Summary of Product Characteristics.

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

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ICLUSIG®

Considering ICLUSIG for Peter

Peter has a history of intolerance and no history of CV events

- ICLUSIG may offer patients like Peter a better future[1]
- **Together, we've built experience and confidence in treating patients, like Peter, with ICLUSIG over the last decade[1]**
- Approximately 25% of patients with CML change TKIs because of AEs. We know that cycling TKIs may lead to mutations, lowering the likelihood of response to an alternative[1–3]
- Considering an early switch to ICLUSIG after one 2G TKI for patients like Peter may improve their outcomes[1–3]

Representative patient case – not an actual patient. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the local SmPC for further information.
2G, second generation; AE, adverse event; CML, chronic myeloid leukaemia; CV, cardiovascular; SmPC, Summary of Product Characteristics; TKI, tyrosine kinase inhibitor.
1. ICLUSIG® (ponatinib) SmPC; Incyte, 2022; 2. O'Hare T, et al. *Cancer Cell.* 2009;16:401–12; 3. Kantarjian HM, et al. *Am J Hematol.* 2022;97:1419–26.

ICLUSIG (ponatinib) tablets

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Most common AEs and serious AEs

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 transferase 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]

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

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

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