ICLUSIG®
(ponatinib) tablets

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ICLUSIG®: Patient profiles

Incyte
CH/ICLG/P/24/0020
Date of preparation: September 2024

ICLUSIG (ponatinib) tablets

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

RESET

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Resistance to 2G TKI

Choose your pathway

Intolerance to 2G TKI

Explore how eligible CP-CML patients may benefit from ICLUSIG


William

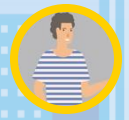

Francine


Thomas


Martha


Agnes


Maria


Peter

ICLUSIG combines experience and data to improve patients' futures – consider early switch to ICLUSIG after just one 2G TKI[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.

ICLUSIG (ponatinib) tablets

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 mutation detected

Find out about Francine

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

Incyte

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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

BCR::ABL1^{IS} level:
>1–<10%

BCR::ABL1^{IS} level:
≥10%

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

Incyte

ICLUSIG®

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.

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

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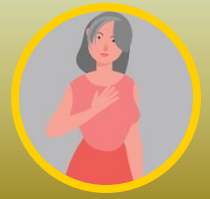
Resistance to 2G TKI

>1–<10% BCR::ABL1^{IS}
Low CV risk

Find out about William

>1–<10% BCR::ABL1^{IS}
Medium CV risk



Find out about Agnes

ICLUSIG combines experience and data to improve patients' futures – consider early switch to ICLUSIG after just one 2G TKI[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.

ICLUSIG (ponatinib) tablets

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

RESET

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Resistance to 2G TKI

≥10% BCR::ABL1^{IS}
Low CV risk

Find out about Thomas

≥10% BCR::ABL1^{IS}
Medium CV risk

Find out about Martha

ICLUSIG combines experience and data to improve patients' futures – consider early switch to ICLUSIG after just one 2G TKI[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.

ICLUSIG (ponatinib) tablets

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

ICLUSIG combines experience and data to improve patients' futures – consider early switch to ICLUSIG after just one 2G TKI[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.

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

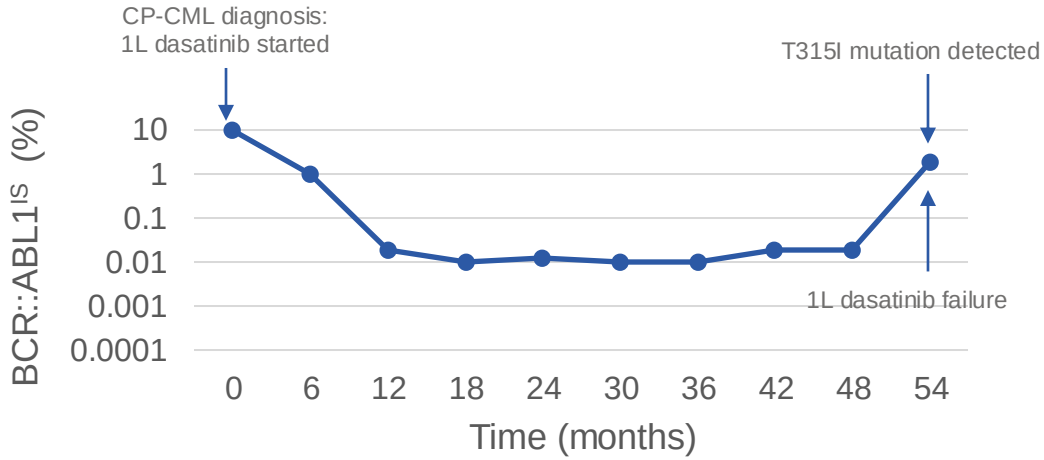
William

- 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 54 months ago and became resistant to 1L dasatinib after 54 months
- T315I mutation was detected at 54 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[2]

OPTIC: Patient baseline characteristics[3]

ICLUSIG may benefit patients like William[4,5]

ELN recommendations (2020) note that ICLUSIG is the only TKI with activity against the T315I mutation and recommend ICLUSIG in patients with T315I, unless CV risk factors preclude its use[4]

Representative patient case – not an actual patient.
1L, first line; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

References

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Age, years, median (range)	46 (19–81)
Male, n (%)	50 (53)
Prior TKIs, n (%)	
2	43 (46)
≥3	50 (53)
Reason prior therapy stopped, n (%)	
Resistant	92 (98)
BCR::ABL1 mutation, n (%)	
No mutation	51 (54)
T315I	25 (27)
Other	15 (16)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.

CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In chronic-phase chronic myeloid leukaemia; TKI, tyrosine kinase inhibitor; SmPC, Summary of Product Characteristics.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.

CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In Chronic-Phase Chronic Myeloid Leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Patients with CV risk factors, n (%)	
Hypertension	26 (28)
Diabetes mellitus	5 (5)
Hyperlipidaemia	19 (20)
Patients with ≥1 CV risk factor	32 (34)
Patients with >1 CV risk factor	5 (5)
Current or former smokers	29 (31)
BMI, kg/m^2, median (range)	27 (17–45)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

OPTIC: Patient baseline characteristics[3]

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

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[2]

ICLUSIG may benefit patients like William[4,5]

Mutations account for resistance in approximately **1/3** of patients with CP-CML[4]

T315I 'gatekeeper' mutation is resistant to imatinib and 2G TKIs (dasatinib, nilotinib, bosutinib)[5]

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[5]

References

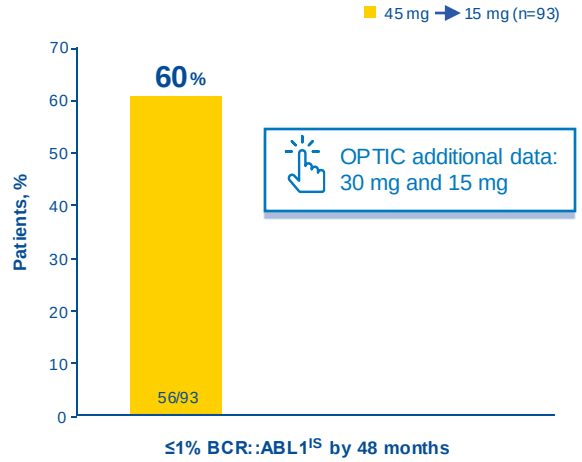
Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

For patients like William who remain in CP at the time of T315I mutation, early use of ICLUSIG may lead to an indolent disease course[5,6]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg



OPTIC additional data: 30 mg and 15 mg

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

Figure adapted from Cortes JE, et al.[7] with permission from the author.

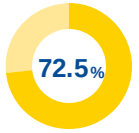
Results from the 4-year OPTIC analysis suggest that William may achieve a deep, durable molecular response with ICLUSIG[7]

Patients with a T315I mutation at baseline achieved the greatest clinical benefit in the 45 mg → 15 mg cohort[7]

OPTIC: Estimated 4-year PFS and OS[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

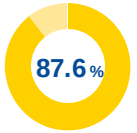
Estimated 4-year PFS



45 mg → 15 mg

OPTIC additional data: 30 mg and 15 mg

Estimated 4-year OS



45 mg → 15 mg

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[7]

- In OPTIC, patients with the T315I mutation had similar survival outcomes to the overall population[5]
- Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

References

Representative patient case – not an actual patient.

*Median follow-up: 63 months in the 45-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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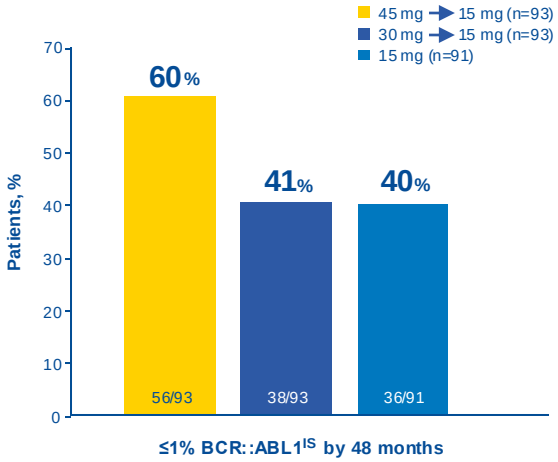
For patients like William who remain in CP at the time of T315I mutation, early use of ICLUSIG may lead to an indolent disease course[5,6]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*



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

Figure adapted from Cortes JE, et al.[7] with permission from the author.

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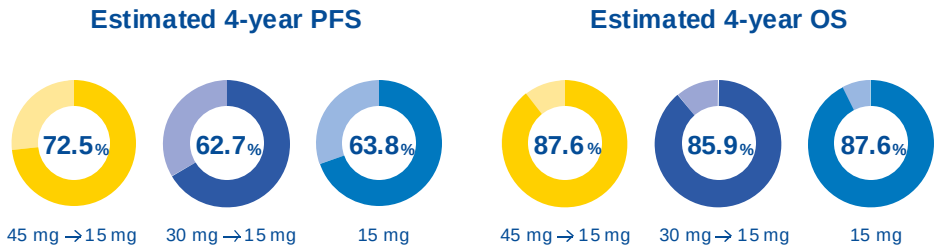

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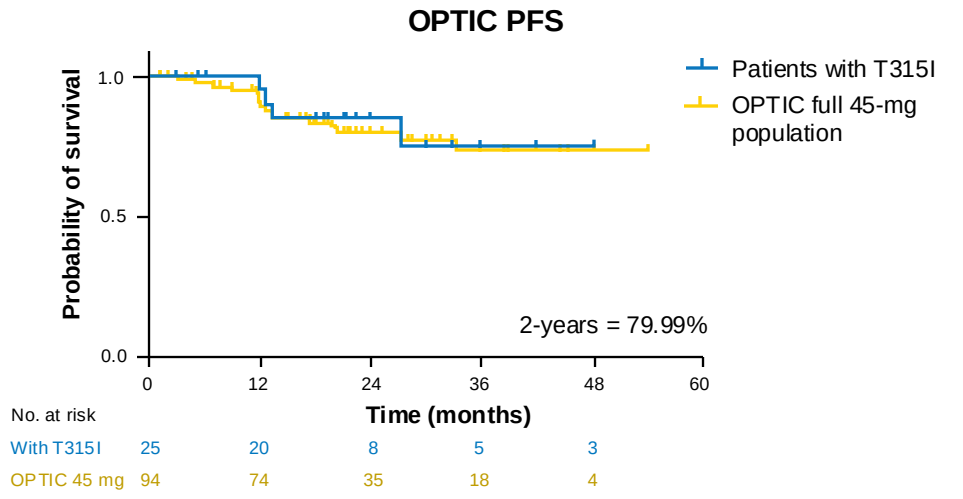
- In OPTIC, patients with the T315I mutation had similar survival outcomes to the overall population[5]
- Subgroup analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months in patients with and without T315I[3]

References

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

For patients like William who remain in CP at the time of T315I mutation, early use of ICLUSIG may lead to an indolent disease course[5,6]

OPTIC: Survival outcomes by mutation status[5]



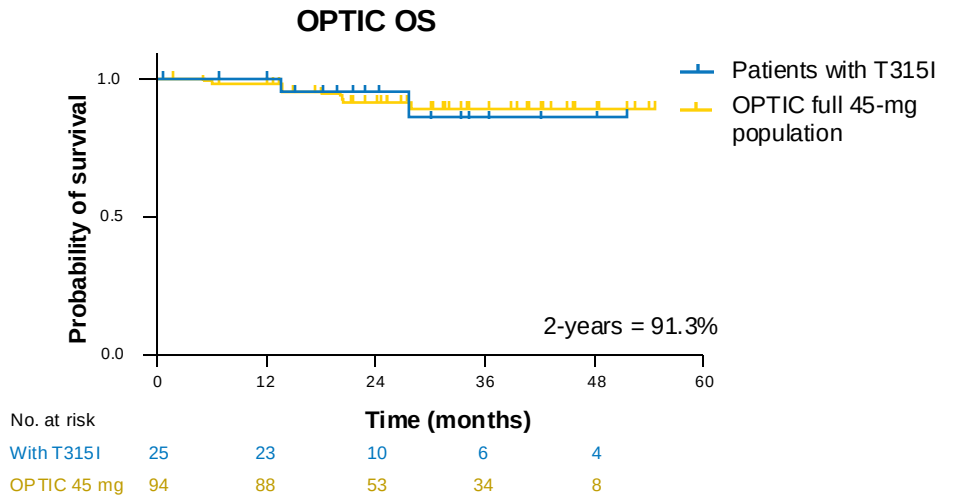


Figure adapted from Jabbour E, et al.[5] Freely distributed under the Creative Commons Attribution License (CC-BY 4.0).

In OPTIC, patients with the T315I mutation had similar survival outcomes to the overall population

References

Representative patient case – not an actual patient.
2G, second generation; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, Professional Information.

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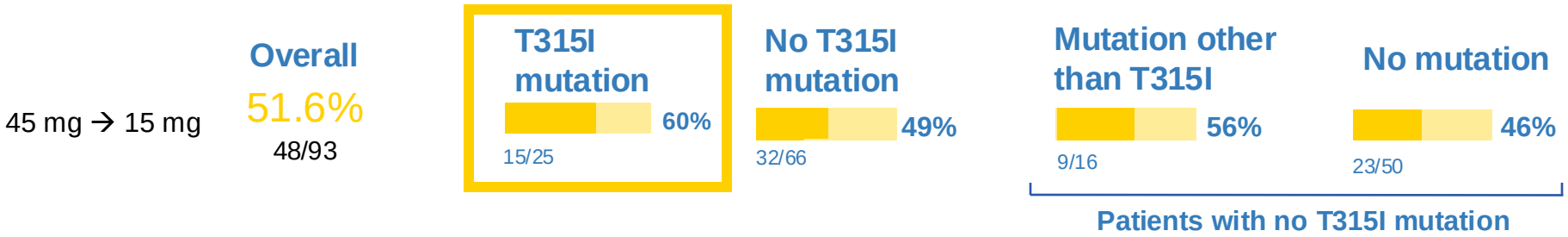
For patients like William who remain in CP at the time of T315I mutation, early use of ICLUSIG may lead to an indolent disease course[5,6]

OPTIC: Mutational subgroup analysis[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

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



OPTIC additional data: 30 mg and 15 mg

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

Representative patient case – not an actual patient.
*4 patients did not have a mutation test result at baseline. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

References

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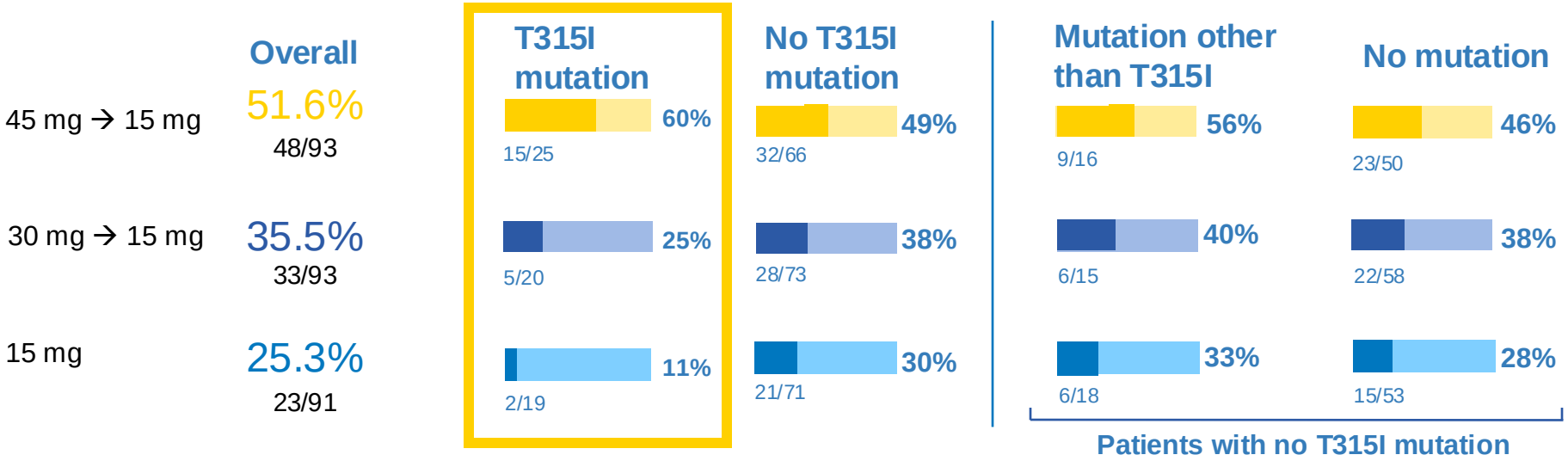
For patients like William who remain in CP at the time of T315I mutation, early use of ICLUSIG may lead to an indolent disease course[5,6]

OPTIC: Mutational subgroup analysis[3]

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



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

Representative patient case – not an actual patient.
*4 patients did not have a mutation test result at baseline. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

References

Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like William[1,3]

OPTIC: Dose-reduction regimen[5,7]

- 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[5,7]

References

Representative patient case – not an actual patient. *The OPTIC comparison group started with an ICLUSIG dose of 45 mg which was reduced to 15 mg following a response.
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; PI, Professional Information.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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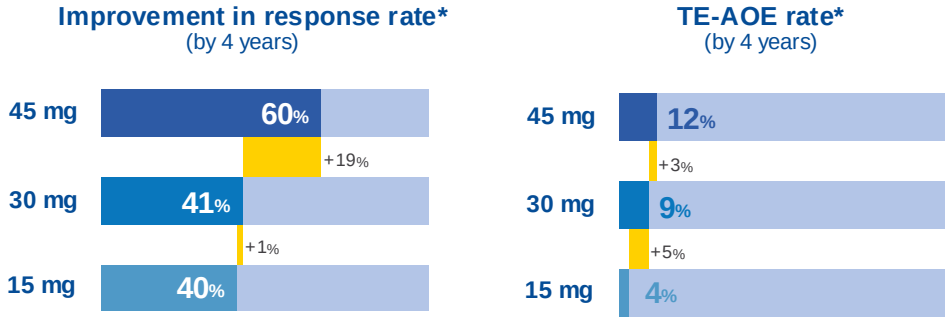
Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[1]

OPTIC: 4-year BCR::ABL1^{IS} and TE-AOE rates by dosing regimen[7]



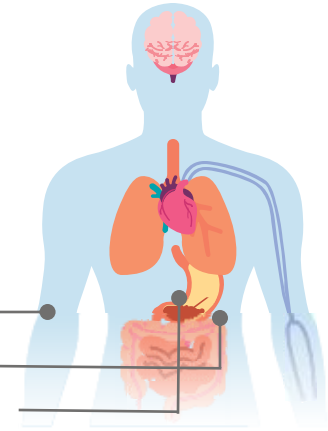
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the TE-AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[7†]

William should be at minimal risk of having CV adverse events[5,7,8*]

Adjudicated TE-AOEs in PACE were more likely in patients with multiple CV factors[8]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4-years[7]

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[1,3,7]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[7]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and TE-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; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; TE-AOE, treatment-emergent arterial occlusive event; TEAE, treatment-emergent adverse event.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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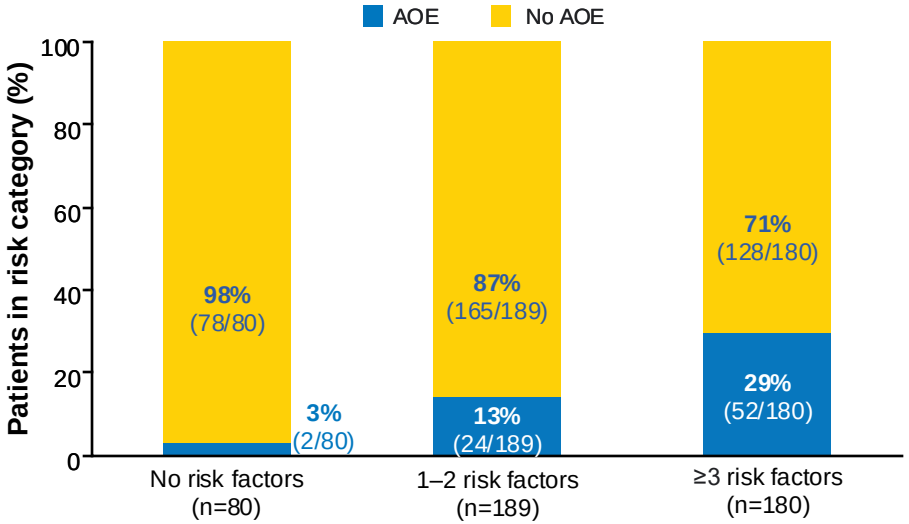
Together, we've built experience and confidence in treating patients like William with ICLUSIG over the last decade[1]

PACE: Adjudicated AOEs[8]



- 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.[8] 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[8]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information.

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[1,7,9]
- **Together, we've built experience and confidence in treating patients, like William, with ICLUSIG over the last decade[1,7]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including T315I[1,9,10]

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

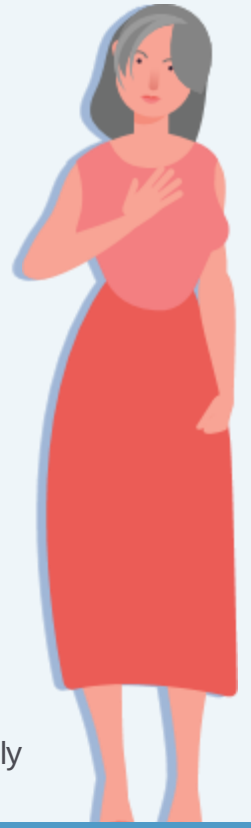
Agnes: Identifying eligible patients with high resistance and medium CV risk

Agnes

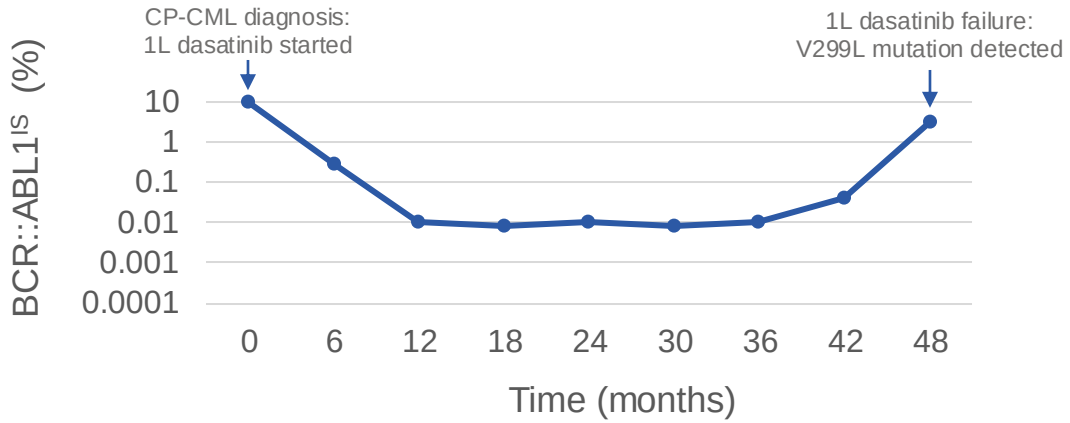
- Agnes is 68 years old and was a paramedic before retiring a few years ago
- She volunteers to teach first-aid classes in the local community and is looking forward to seeing her son get married

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[2]

OPTIC and PACE: Patient baseline characteristics[2,3]

ICLUSIG may benefit patients like Agnes[4,5,11]

V299L single resistance mutation has been shown to confer resistance to both bosutinib and dasatinib[12]

References

Representative patient case – not an actual patient.
1L, first line; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

ICLUSIG®

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 **mg**

Characteristic	45 mg → 15 mg (n=94)
Age, years, median (range)	46 (19–81)
Male, n (%)	50 (53)
Prior TKIs, n (%)	
2	43 (46)
≥3	50 (53)
Reason prior therapy stopped, n (%)	
Resistant	92 (98)
BCR::ABL1 mutation, n (%)	
No mutation	51 (54)
T315I	25 (27)
Other	15 (16)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 **mg**

Characteristic	45 mg → 15 mg (n=94)
Patients with CV risk factors, n (%)	
Hypertension	26 (28)
Diabetes mellitus	5 (5)
Hyperlipidaemia	19 (20)
Patients with ≥1 CV risk factor	32 (34)
Patients with >1 CV risk factor	5 (5)
Current or former smokers	29 (31)
BMI, kg/m^2, median (range)	27 (17–45)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

PACE: Patient baseline characteristics[2]

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)

References

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

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

ICLUSIG may benefit patients like Agnes[4,5,11]

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[4,5,11]

Mutations account for resistance in approximately **1/3** of patients with CP-CML[5]

References

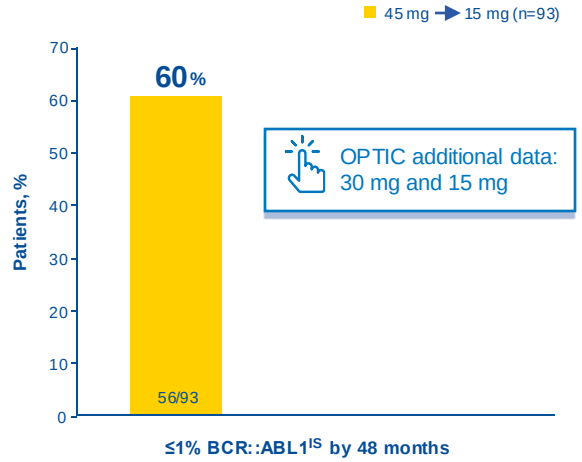
Representative patient case – not an actual patient.
2G, second generation; 3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

For patients like Agnes, early use of ICLUSIG after one 2G TKI may lead to very deep responses[1,13]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg



OPTIC additional data: 30 mg and 15 mg

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

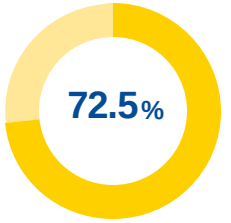
Figure adapted from Cortes JE, et al.[7] with permission from the author.

Results from the 4-year OPTIC analysis suggest that Agnes may achieve a deep, durable molecular response with ICLUSIG[7]

OPTIC: Estimated 4-year PFS and OS[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

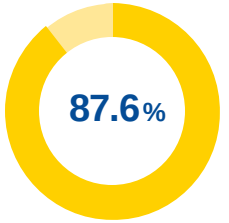
Estimated 4-year PFS



45 mg ⟶ 15 mg

OPTIC additional data: 30 mg and 15 mg

Estimated 4-year OS



45 mg ⟶ 15 mg

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[7]

Most patients in the 45 mg → 15 mg cohort achieved ≤1% BCR::ABL1^{IS} by 4 years regardless of baseline mutation status[7]

References

Representative patient case – not an actual patient.
*Median follow-up: 63 months in the 45-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, Professional Information.

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BECAUSE TOMORROW MATTERS TODAY

For patients like Agnes, early use of ICLUSIG after one 2G TKI may lead to very deep responses[1,13]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

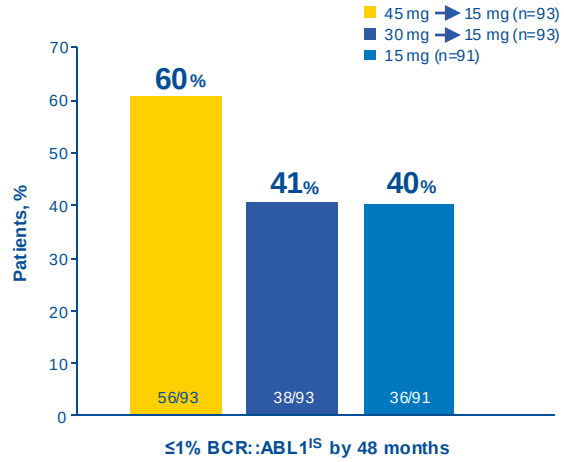

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Figure adapted from Cortes JE, et al.[7] with permission from the author.

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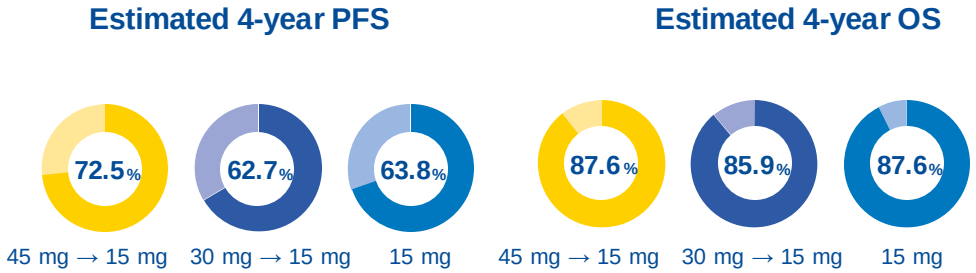

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References

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

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Agnes[1,3]

OPTIC: Dose-reduction regimen[5,7]

- 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[5,7]

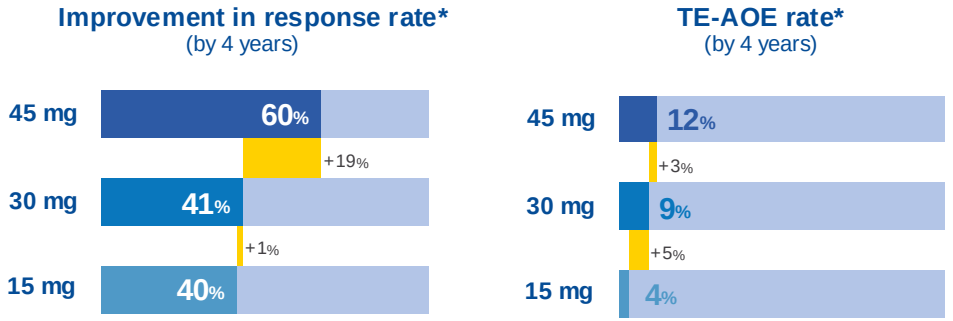
References

Representative patient case – not an actual patient.
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; PI, Professional Information.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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[7]



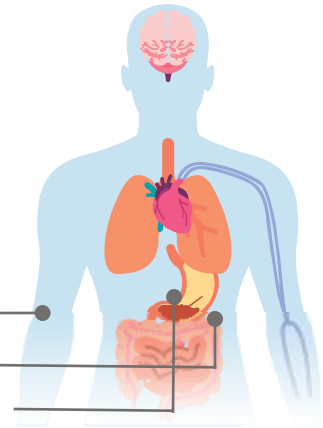
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the TE-AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[7†]

Agnes's hyperlipidaemia is well-controlled, so she should be at minimal risk of CV adverse events[5,7,8*]

Rate of TE-AOEs may not increase with treatment duration[5]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4-years[7]

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[1,3,7]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[7]

References

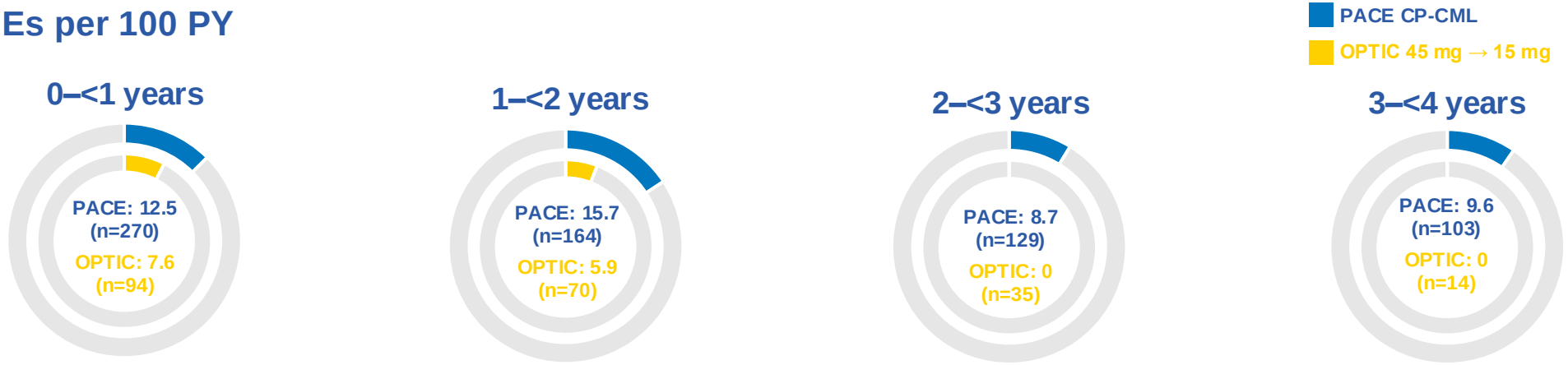
Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI.
*The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and TE-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; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TE-AOE, treatment-emergent arterial occlusive event; TEAE, treatment-emergent adverse event.

BECAUSE TOMORROW MATTERS TODAY

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[5]

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[5]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; PY, patient-years.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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[1,7]
- **Together, we've built experience and confidence in treating patients, like Agnes, with ICLUSIG over the last decade[1,7]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including V299L[1,10,13]

References

Incyte

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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Francine: Identifying eligible patients with high resistance and no mutations

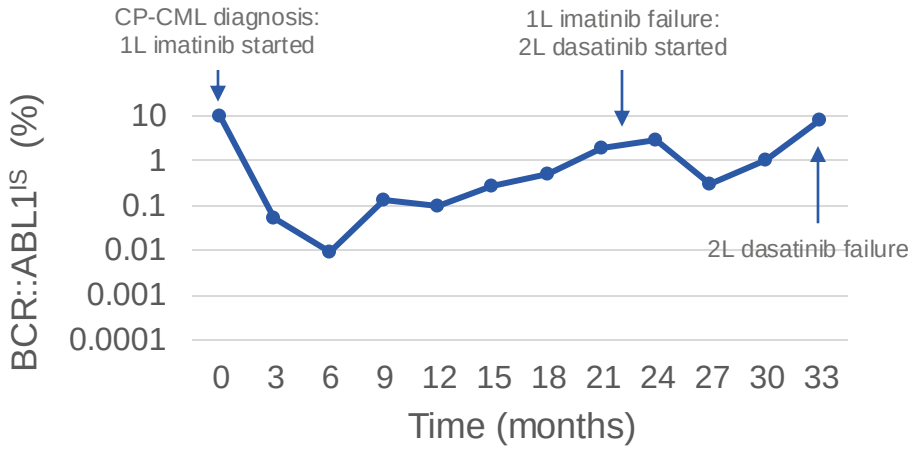
Francine

- 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 33 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 mutations detected
- 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 8% at 33 months



Francine may have fast, deep and durable responses with ICLUSIG[2]

OPTIC and PACE: Patient baseline characteristics[2,3]

ICLUSIG may benefit patients like Francine[14]

ELN recommendations (2020) note that patients who are resistant to a 2G TKI without specific mutations should preferably be treated with ICLUSIG instead of another 2G TKI, unless CV risk factors preclude its use[4]

References

Representative patient case – not an actual patient.
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; PI, Professional Information; TKI, tyrosine kinase inhibitor.

Francine: Identifying eligible patients with high resistance and no mutations

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Age, years, median (range)	46 (19–81)
Male, n (%)	50 (53)
Prior TKIs, n (%)	
2	43 (46)
≥3	50 (53)
Reason prior therapy stopped, n (%)	
Resistant	92 (98)
BCR::ABL1 mutation, n (%)	
No mutation	51 (54)
T315I	25 (27)
Other	15 (16)
BMI, kg/m^2, median (range)	27 (17–45)

OPTIC additional data: 30 mg and 15 mg

References

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BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

BECAUSE TOMORROW MATTERS TODAY

Francine: Identifying eligible patients with high resistance and no mutations

OPTIC: Patient baseline characteristics[3]

Characteristic	45 mg → 15 mg (n=94)	30 mg → 15 mg (n=94)	15 mg (n=94)
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Prior TKIs, n (%)			
2	43 (46)	37 (39)	42 (45)
≥3	50 (53)	56 (60)	48 (51)
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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)

References

Incyte

Representative patient case – not an actual patient.
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BECAUSE TOMORROW MATTERS TODAY

Francine: Identifying eligible patients with high resistance and no mutations

PACE: Patient baseline characteristics[2]

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)
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Francine: Identifying eligible patients with high resistance and no mutations

ICLUSIG may benefit patients like Francine[14]

The most frequent mechanisms of resistance in CP-CML are **BCR::ABL1-independent**[14]

In CP-CML, **60–70%** of patients with unsatisfactory response to TKI therapy are negative for mutations or transcript overexpression[14]

References

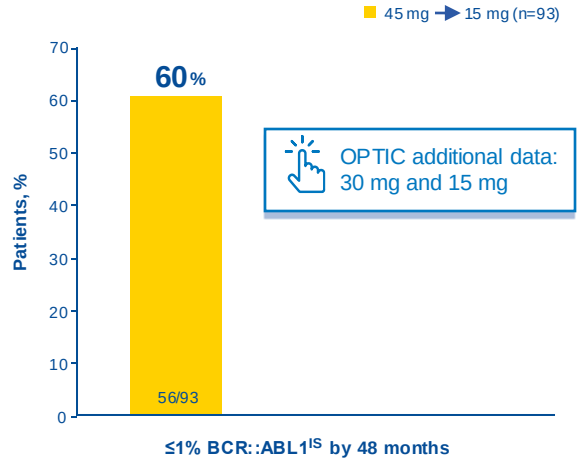
Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

BECAUSE TOMORROW MATTERS TODAY

For patients like Francine, early use of ICLUSIG after one 2G TKI may lead to very deep responses[1,13]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg



OPTIC additional data: 30 mg and 15 mg

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Figure adapted from Cortes JE, et al.[7] with permission from the author.

Results from the 4-year OPTIC analysis suggest that Francine may achieve a deep, durable molecular response with ICLUSIG[7]

OPTIC: Estimated 4-year PFS and OS[7]*

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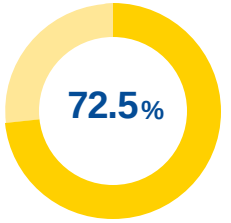
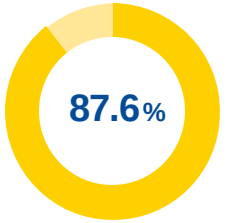
Estimated 4-year PFS



45 mg ⟶ 15 mg

OPTIC additional data: 30 mg and 15 mg

Estimated 4-year OS



45 mg ⟶ 15 mg

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[7]

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

References

Representative patient case – not an actual patient.
*Median follow-up: 63 months in the 45-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, Professional Information.

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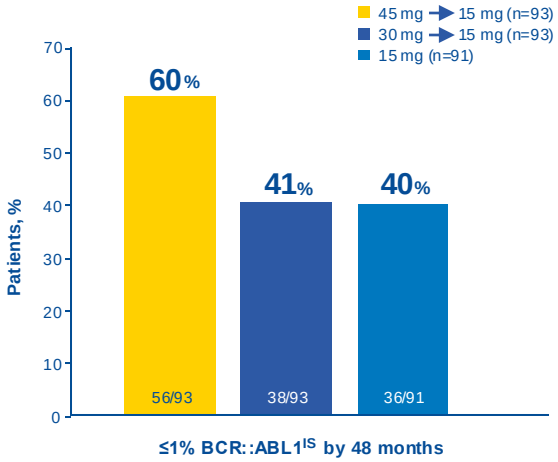
OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

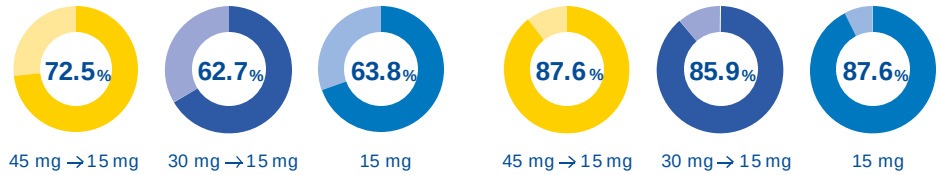


60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months

Figure adapted from Cortes JE, et al.[7] with permission from the author.

Results from the 4-year OPTIC analysis suggest that Francine may achieve a deep, durable molecular response with ICLUSIG[7]

OPTIC: Estimated 4-year PFS and OS[7]*



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[7]

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

References

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*Median follow-up: 63 months in the 45-mg cohort and 15-mg cohort; 65 months in the 30-mg cohort. 2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PFS, progression-free survival; PI, Professional Information.

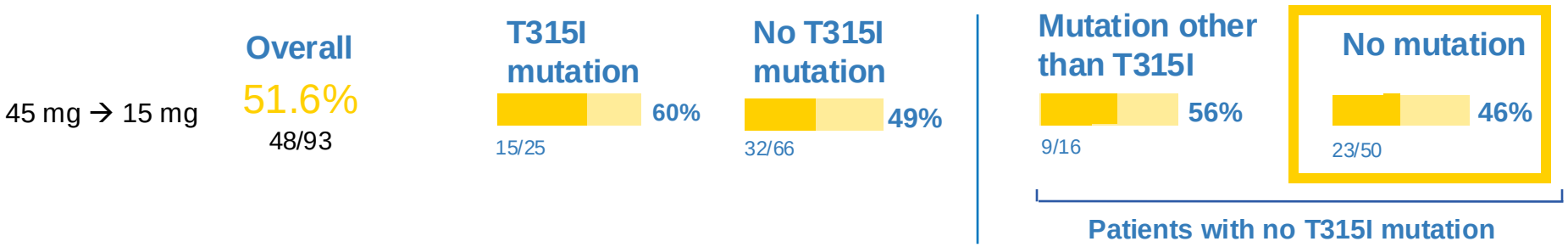
BECAUSE TOMORROW MATTERS TODAY

For patients like Francine, early use of ICLUSIG after one 2G TKI may lead to very deep responses[1,13]

OPTIC: Mutational subgroup analysis[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

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



OPTIC additional data: 30 mg and 15 mg

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

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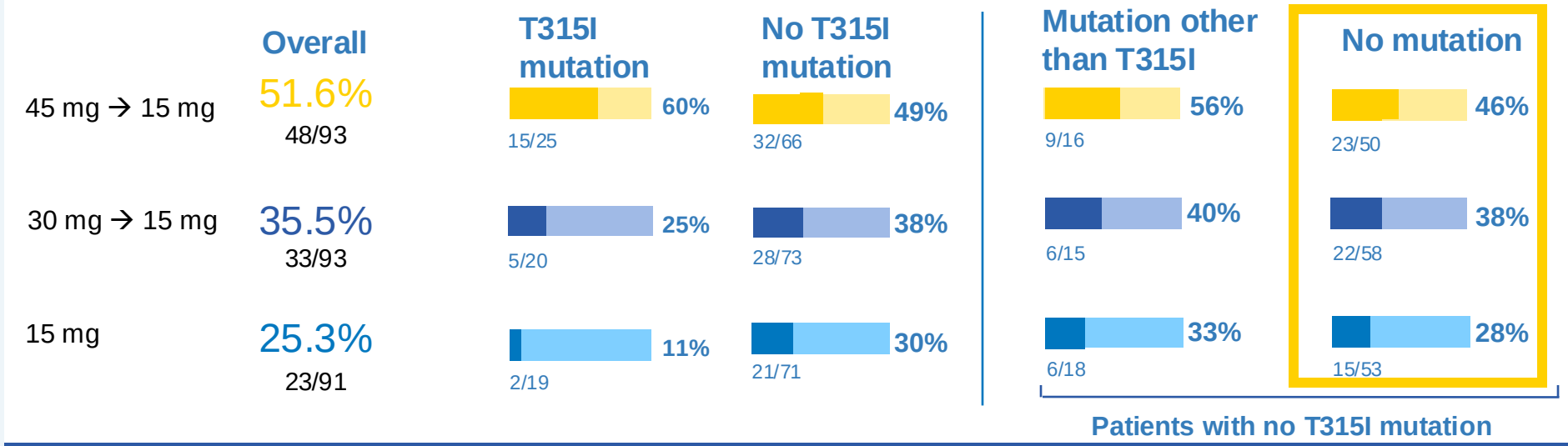

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Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Francine[1,3]

OPTIC: Dose-reduction regimen[5,7]

- 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

Francine may regain MMR or achieve a deep molecular response (≤0.01% BCR::ABL1^{IS}) with ICLUSIG and may maintain her response following dose reduction[5,7]

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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; PI, Professional Information.

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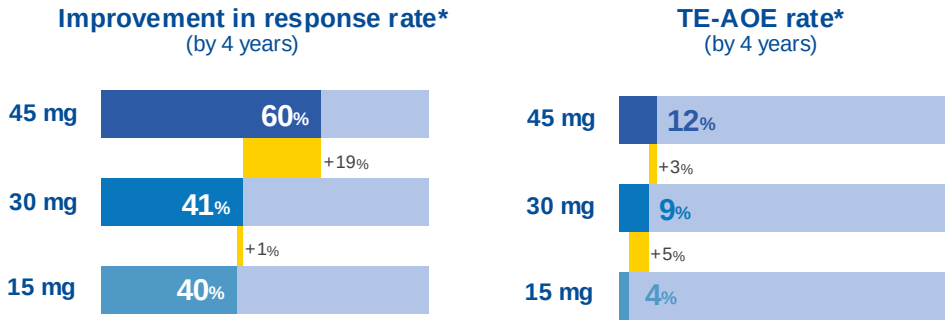
BECAUSE TOMORROW MATTERS TODAY

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[7]

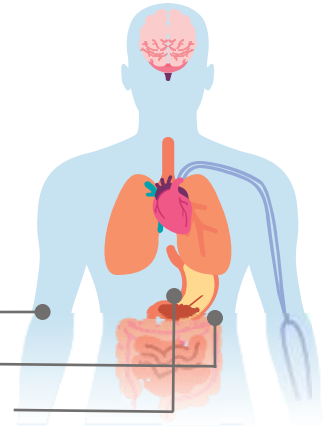


In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the TE-AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[7†]

Francine should be at minimal risk of having CV adverse events[5,7,8*]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4-years[7]

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[1,3,7]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[7]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and TE-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; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TE-AOE, treatment-emergent arterial occlusive event; TEAE, treatment-emergent adverse event.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

Considering ICLUSIG for Francine

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

- ICLUSIG may offer patients like Francine a better future[1,7]
- **Together, we've built experience and confidence in treating patients, like Francine, with ICLUSIG over the last decade[1,7]**

References

Representative patient case – not an actual patient.
2G, second generation; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; ELN, European LeukemiaNet; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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

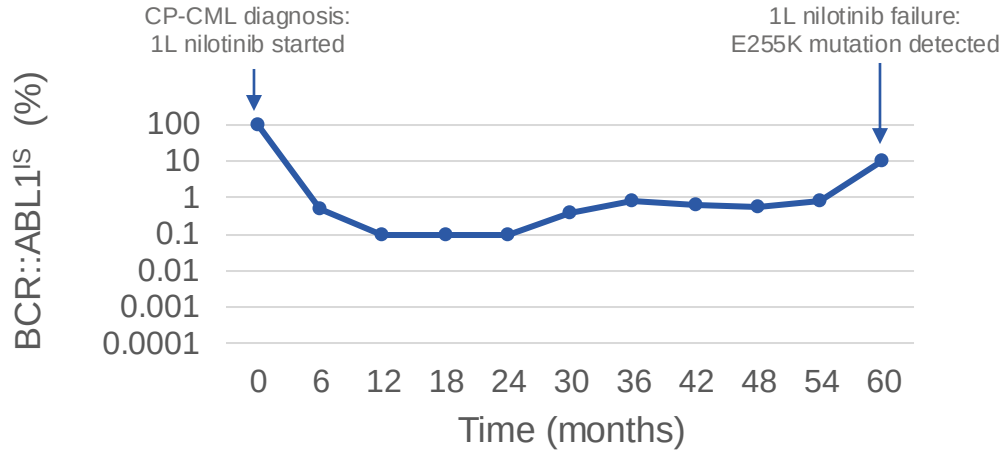
Thomas

- 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 60 months
- E255K mutation was detected at 60 months
- His BCR::ABL1^{IS} level is 10%
- His ELTS score is low
- Thomas has no history of CV events

Thomas was responding to 1L nilotinib until 60 months when his BCR::ABL1^{IS} level increased to 10%



Thomas may have fast, deep and durable responses with ICLUSIG[2]

OPTIC and PACE: Patient baseline characteristics[2,3]

ICLUSIG may benefit patients like Thomas[4,5,11,13]

References

Representative patient case – not an actual patient.
1L, first line; 2G, second generation; ALL, acute lymphoblastic leukaemia; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; ELN, European LeukemiaNet; ELTS, EUTOS Long Term Survival; EUTOS, European Treatment and Outcome Study; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Age, years, median (range)	46 (19–81)
Male, n (%)	50 (53)
Prior TKIs, n (%)	
2	43 (46)
≥3	50 (53)
Reason prior therapy stopped, n (%)	
Resistant	92 (98)
BCR::ABL1 mutation, n (%)	
No mutation	51 (54)
T315I	25 (27)
Other	15 (16)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.

CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Patients with CV risk factors, n (%)	
Hypertension	26 (28)
Diabetes mellitus	5 (5)
Hyperlipidaemia	19 (20)
Patients with ≥1 CV risk factor	32 (34)
Patients with >1 CV risk factor	5 (5)
Current or former smokers	29 (31)
BMI, kg/m^2, median (range)	27 (17–45)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

PACE: Patient baseline characteristics[2]

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)

References

Representative patient case – not an actual patient.

ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

ICLUSIG may benefit patients like Thomas[4,5,11,13]

Mutations account for resistance in approximately **1/3** of patients with CP-CML[4]

The **E255K** single resistance mutation has been shown to confer resistance to both bosutinib and nilotinib[11]

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[4,5,11,13]

References

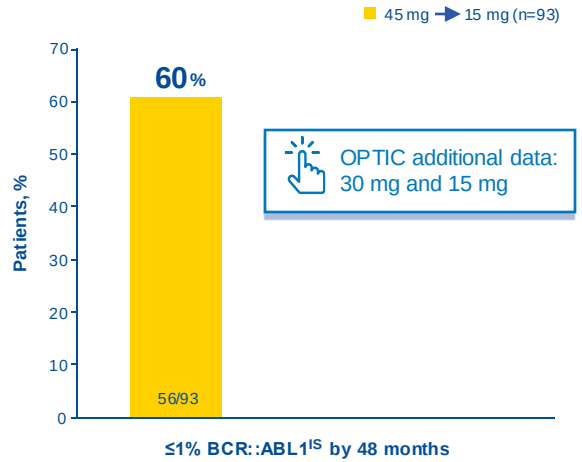
Representative patient case – not an actual patient.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

A delay means that patients like Thomas may miss the opportunity to have a very deep response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,13]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7]*

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg



OPTIC additional data: 30 mg and 15 mg

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

Figure adapted from Cortes JE, et al.[7] with permission from the author.

OPTIC: Estimated 4-year PFS and OS[7]*

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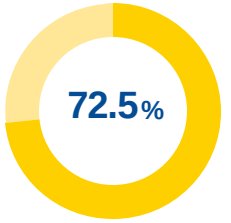
Estimated 4-year PFS



45 mg → 15 mg

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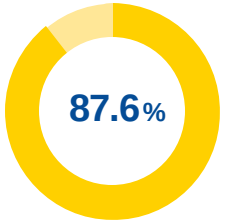
Estimated 4-year OS



45 mg → 15 mg

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[3]

Today, we know that treatment with a pan-inhibitor without delay may offer Thomas a better future[1,7,13]

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ICLUSIG®

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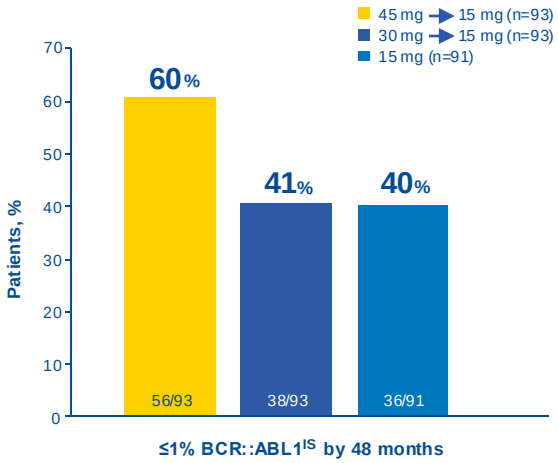

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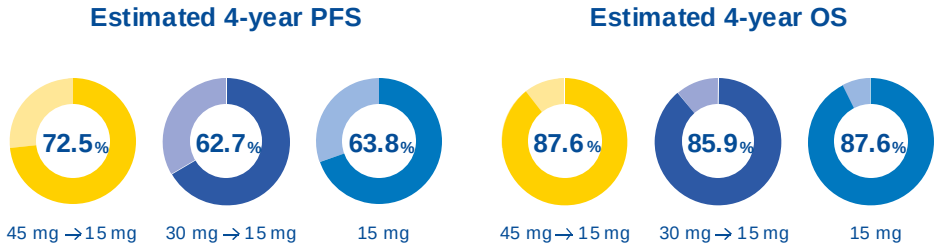

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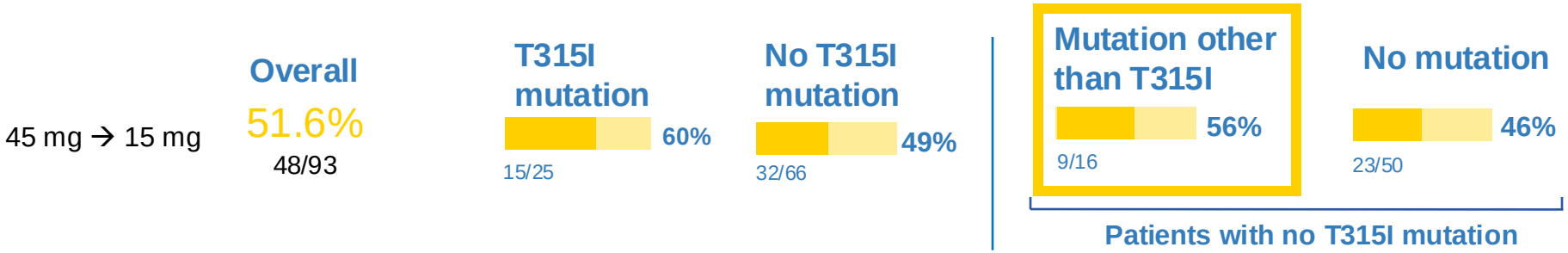

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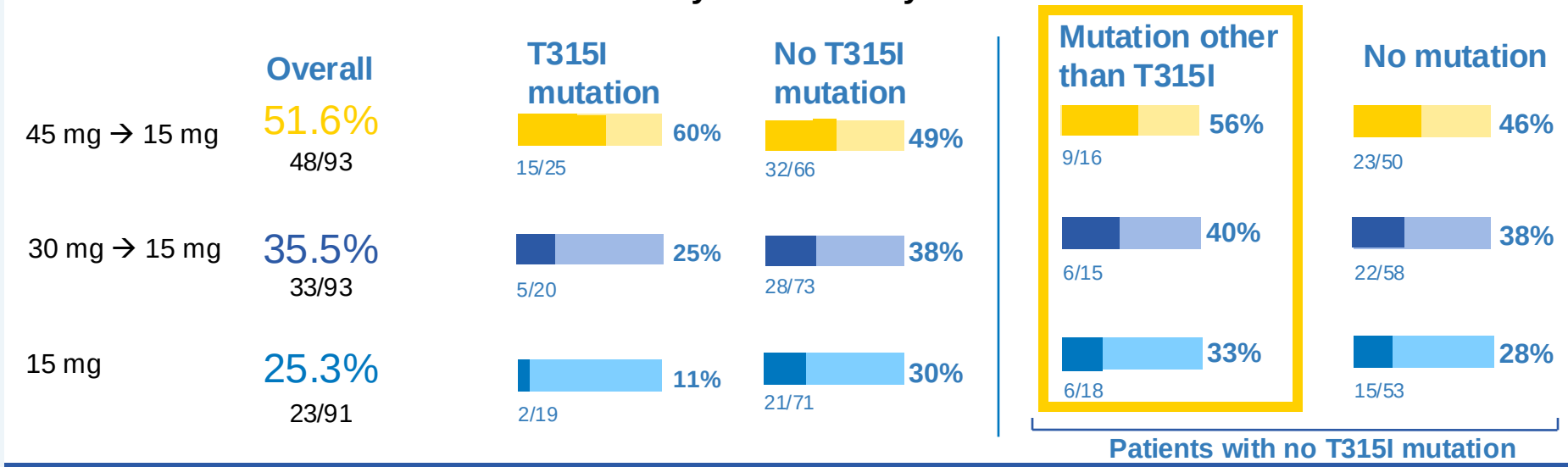

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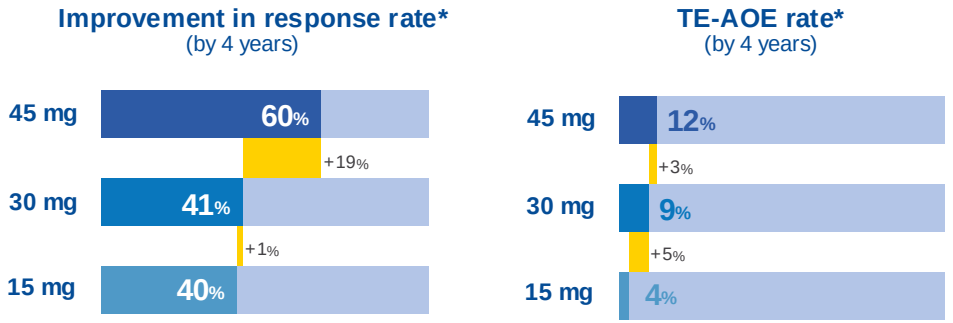

In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the TE-AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[7†]

Thomas' hypertension is well-controlled so he should be at minimal risk of CV adverse events[5,7,8*]

Adjudicated TE-AOEs in PACE were more likely in patients with multiple CV factors[8]

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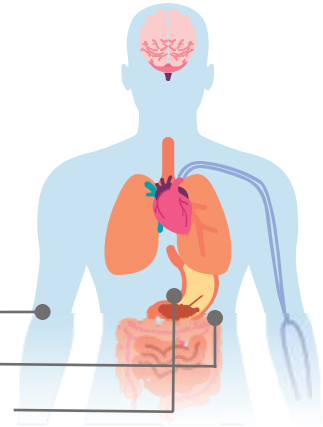
Across the most common TEAEs, the number of TEAEs decreased from year 1 onwards



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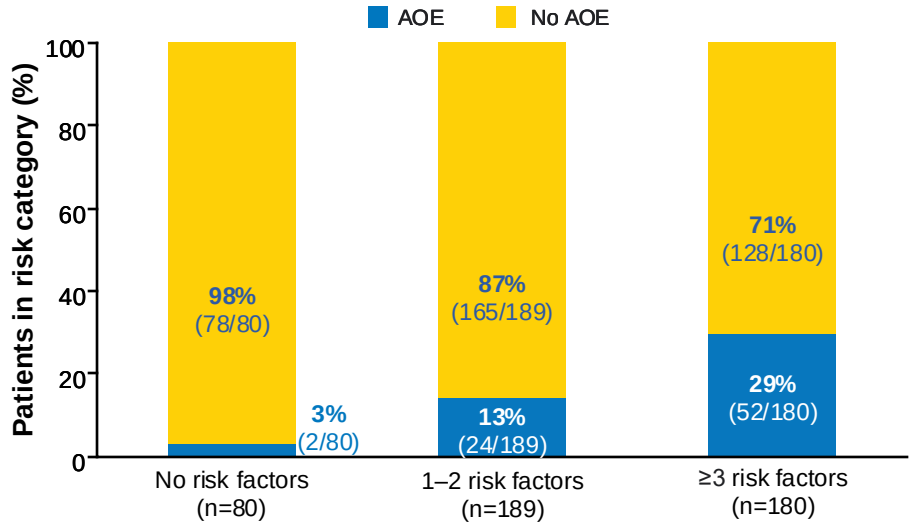
PACE: Adjudicated AOEs[8]



- 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.[8] 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[8]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information.

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[1,7]
- **Together, we've built experience and confidence in treating patients, like Thomas, with ICLUSIG over the last decade[1,7]**
- ICLUSIG was the first and remains the only TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including E255K[1,10,13]

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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

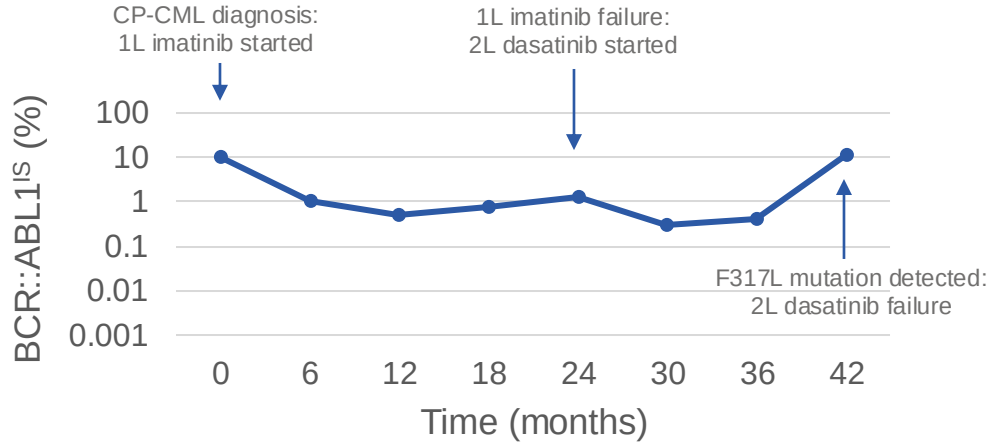
Martha

- 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 36 months and 2L dasatinib at 42 months
- F317L mutation was detected at 42 months
- Her BCR::ABL1^{IS} level is 12%
- 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 demonstrated an initial response to 1L imatinib and 2L dasatinib. However, results at 36 and 42 months confirmed rising BCR::ABL1^{IS} levels



Martha may have fast, deep and durable responses with ICLUSIG[2]

- OPTIC and PACE: Patient baseline characteristics[2,3]
- ICLUSIG may benefit patients like Martha[4,5,11,13]

References

Representative patient case – not an actual patient.
1L, first line; 2L, second 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; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Age, years, median (range)	46 (19–81)
Male, n (%)	50 (53)
Prior TKIs, n (%)	
2	43 (46)
≥3	50 (53)
Reason prior therapy stopped, n (%)	
Resistant	92 (98)
BCR::ABL1 mutation, n (%)	
No mutation	51 (54)
T315I	25 (27)
Other	15 (16)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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

OPTIC: Patient baseline characteristics[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

Characteristic	45 mg → 15 mg (n=94)
Patients with CV risk factors, n (%)	
Hypertension	26 (28)
Diabetes mellitus	5 (5)
Hyperlipidaemia	19 (20)
Patients with ≥1 CV risk factor	32 (34)
Patients with >1 CV risk factor	5 (5)
Current or former smokers	29 (31)
BMI, kg/m^2, median (range)	27 (17–45)

OPTIC additional data: 30 mg and 15 mg

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

BECAUSE TOMORROW MATTERS TODAY

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

OPTIC: Patient baseline characteristics[3]

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)

References

Representative patient case – not an actual patient.
BMI, body mass index; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information.

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

PACE: Patient baseline characteristics[2]

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)

References

Representative patient case – not an actual patient.

ALL, acute lymphoblastic leukaemia; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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

ICLUSIG may benefit patients like Martha[4,5,11,13]

Mutations account for resistance in approximately **1/3** of patients with CP-CML[4]

F317L single resistance mutation has been shown to confer resistance to dasatinib[11]

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[4,5,11,13]

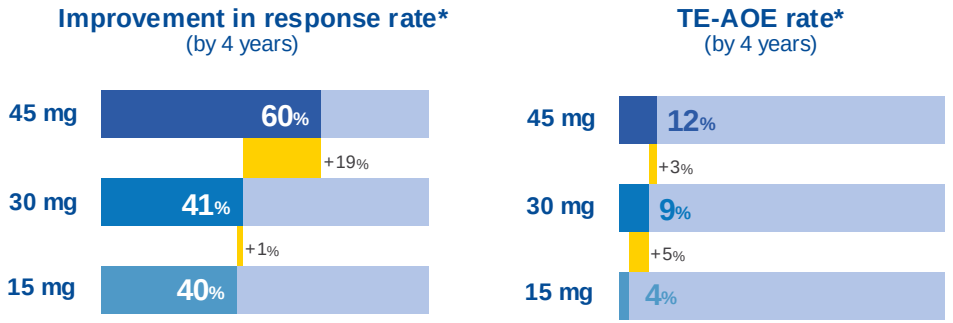
References

Representative patient case – not an actual patient.
3G, third generation; CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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[7]



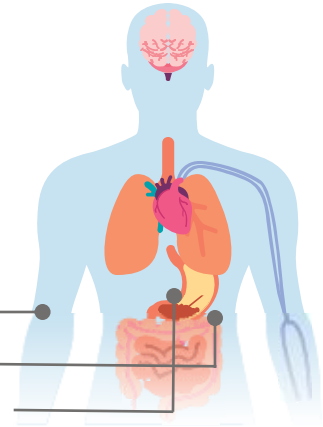
In OPTIC, a starting dose of 45 mg was associated with an 8% increase in the TE-AOE rate (12% vs 4%) but with a 20% improvement in the response rate (60% vs 40%)[7†]

Response-based dosing with ICLUSIG should maximise Martha's response while minimising toxicity[5,7,8*]

Rate of TE-AOEs may not increase with treatment duration[5]

OPTIC: Non-haematologic Grade ≥3 TEAEs by 4-years[7]

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[1,3,7]

The OPTIC 4-year analysis established the consistency of the ICLUSIG safety profile over this prolonged period[7]

References

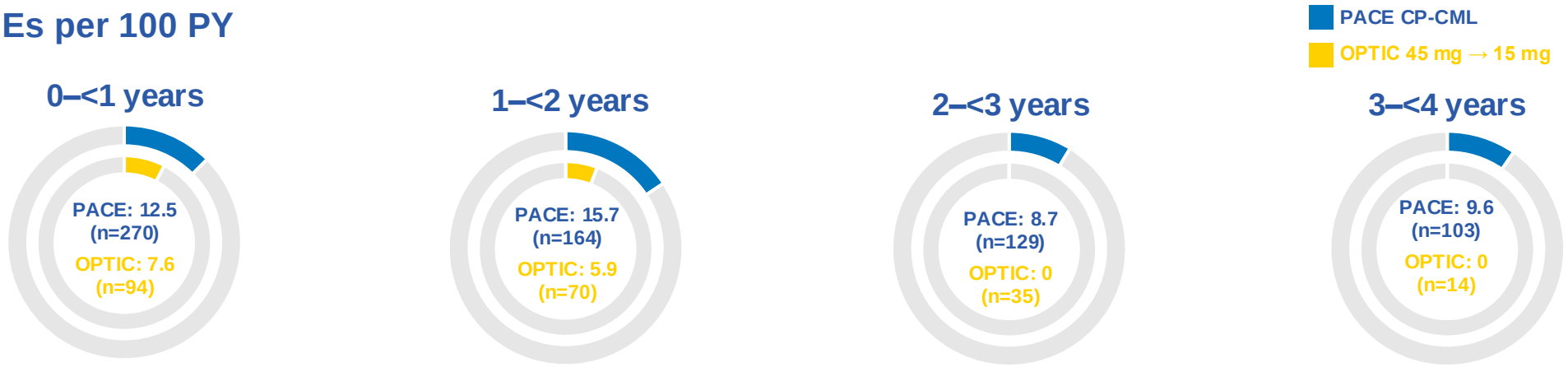
Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI. *The analysis above is a descriptive clinical summary of the data to illustrate the relationship between the efficacy and TE-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; CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; IS, international scale; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PI, Professional Information; TE-AOE, treatment-emergent arterial occlusive event; TEAE, treatment-emergent adverse event.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

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[5]

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[5]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI.

ALL, acute lymphoblastic leukaemia; AOE, arterial occlusive event; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OPTIC, Optimizing Ponatinib Treatment In CP-CML; PACE, Ponatinib Ph+ ALL and CML Evaluation; Ph+, Philadelphia chromosome positive; PI, Professional Information; PY, patient-years.

Thanks to OPTIC, there's now clear evidence to induce response, reduce dose and maintain response with ICLUSIG to safely manage patients like Martha[1,3]

OPTIC: Dose-reduction regimen[5,7]

- 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[5,7]

References

Representative patient case – not an actual patient. *The OPTIC comparison group started with an ICLUSIG dose of 45 mg which was reduced to 15 mg following a response.
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; PI, Professional Information.

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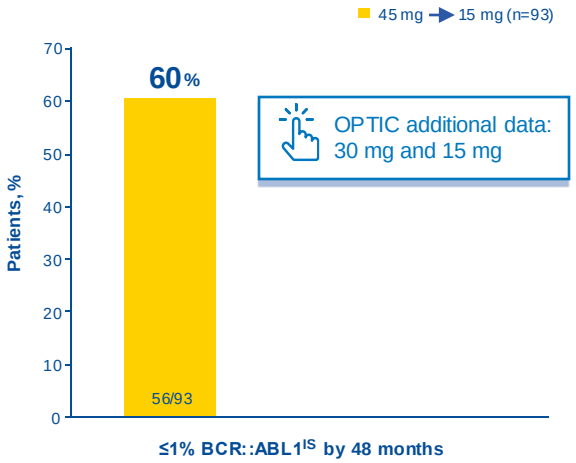
A delay means that patients like Martha may miss the opportunity to have a very deep response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,13]

OPTIC: ≤1% BCR::ABL1^{IS} by 48 months[7*]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg



OPTIC additional data: 30 mg and 15 mg

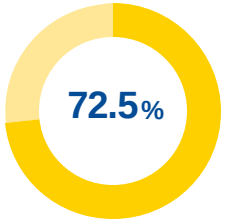
60% of patients receiving 45 mg → 15 mg ICLUSIG achieved ≤1% BCR::ABL1^{IS} by 48 months

Figure adapted from Cortes JE, et al.[7] with permission from the author.

OPTIC: Estimated 4-year PFS and OS[7*]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

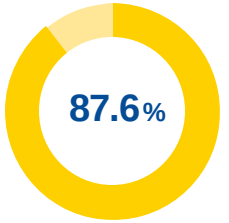
Estimated 4-year PFS



45 mg ⟶ 15 mg

OPTIC additional data: 30 mg and 15 mg

Estimated 4-year OS



45 mg ⟶ 15 mg

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[3]

Today, we know that treatment with a pan-inhibitor without delay may offer Martha a better future[1,7,13]

References

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

A delay means that patients like Martha may miss the opportunity to have a very deep response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,13]

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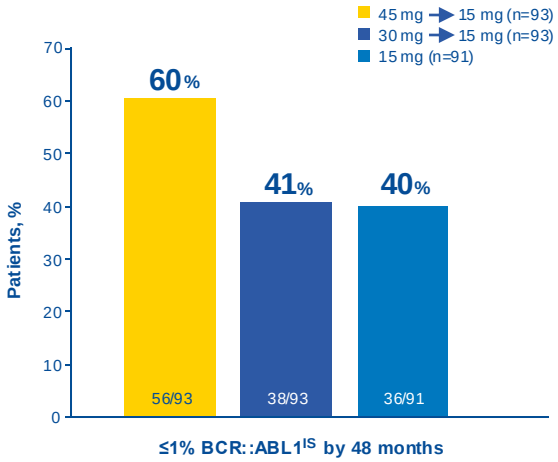

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Figure adapted from Cortes JE, et al.[3] with permission from the author.

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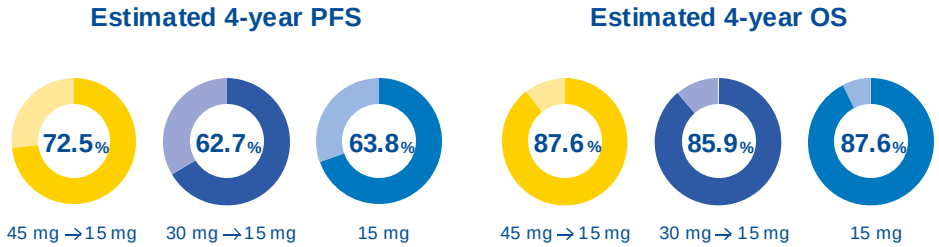

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Analysis showed similar ≤1% BCR::ABL1^{IS} rates at 12 months across all mutation subgroups[3]

Today, we know that treatment with a pan-inhibitor without delay may offer Martha a better future[1,7,13]

References

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

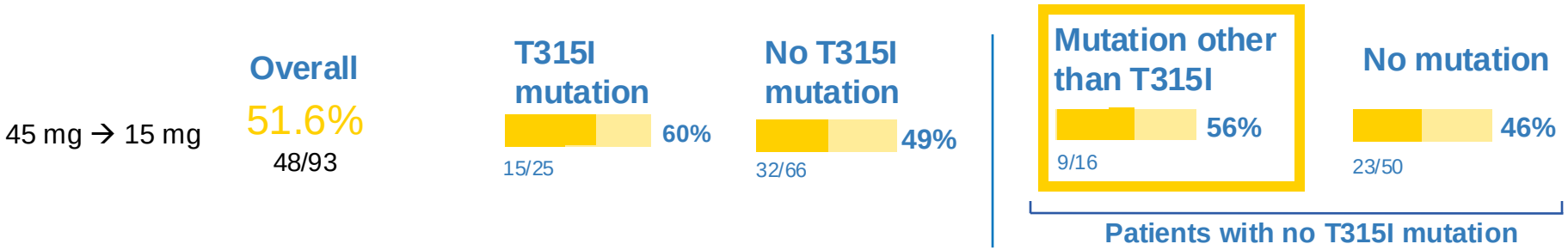
BECAUSE TOMORROW MATTERS TODAY

A delay means that patients like Martha may miss the opportunity to have a very deep response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,13]

OPTIC: Mutational subgroup analysis[3]

Only the 45 mg → 15 mg cohort data are displayed to align with the PI recommended starting dose of 45 mg

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



OPTIC additional data: 30 mg and 15 mg

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

References

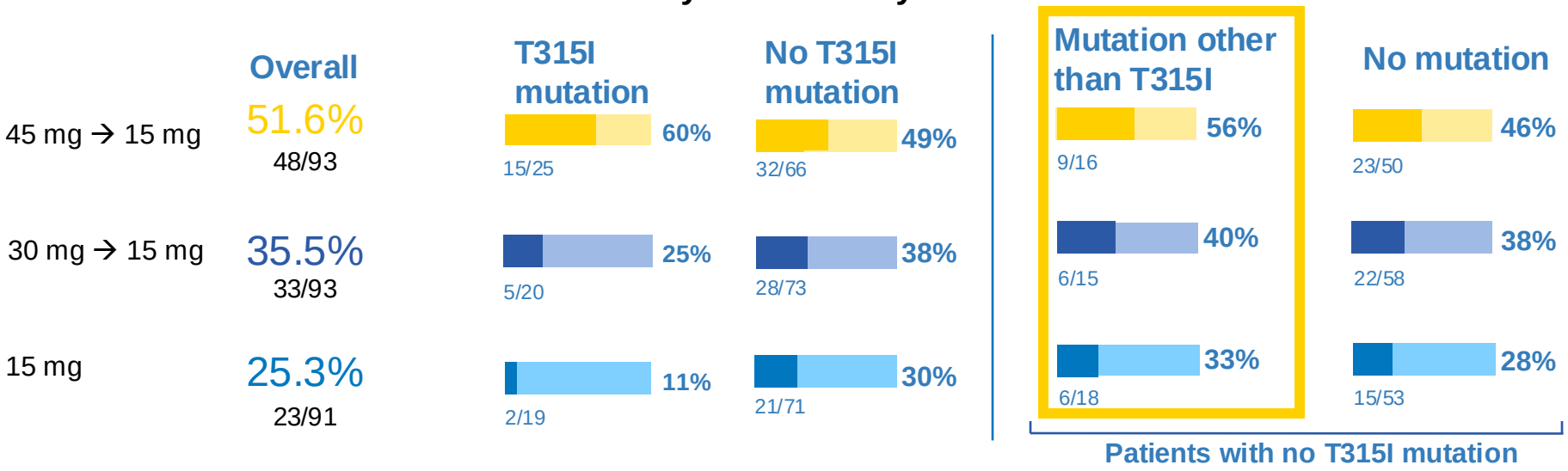
Incyte

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

A delay means that patients like Martha may miss the opportunity to have a very deep response with ICLUSIG – consider early switch to ICLUSIG after just one 2G TKI[1,13]

OPTIC: Mutational subgroup analysis[3]

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



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

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

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

References

BECAUSE TOMORROW MATTERS TODAY

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[1,7]
- **Together, we've built experience and confidence in treating patients, like Martha, with ICLUSIG over the last decade[1,7]**
- ICLUSIG was the first, and remains the only, TKI approved in Europe capable of inhibiting all single BCR::ABL1 resistance mutations, including F317L[1,10,13]

References

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

ICLUSIG®

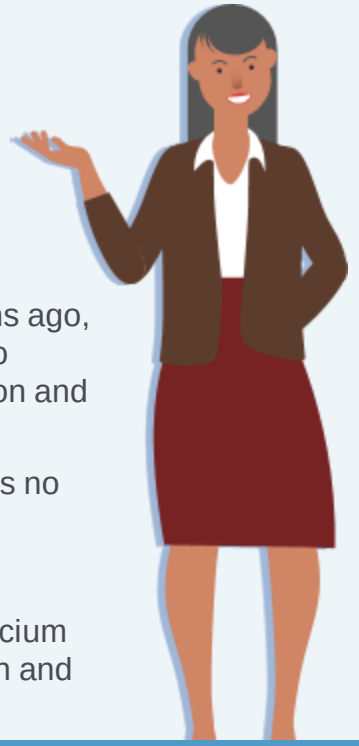
Maria: Identifying eligible patients with intolerance and medium CV risk

Maria

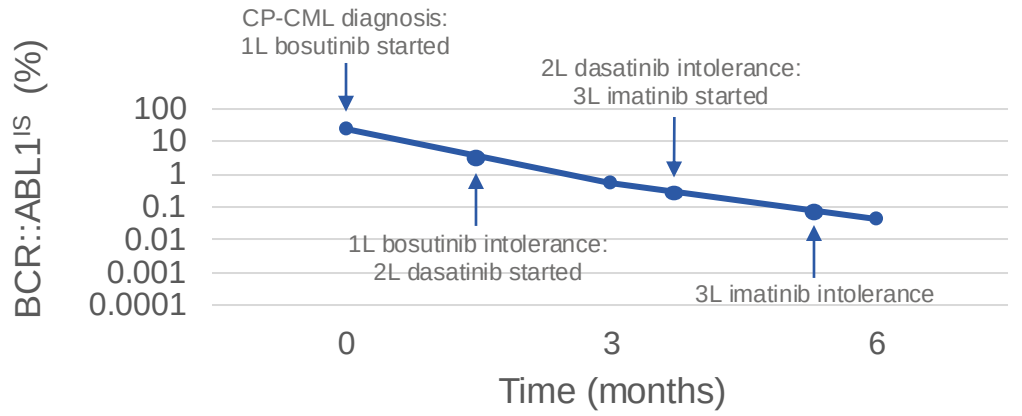
- Maria is a 67-year-old museum curator who has worked in exhibits across Europe
- Maria and her husband enjoy spending quality time together when gardening

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[2]

RWE: Patient baseline characteristics[15,16]

ELN recommendations (2020) recommend starting ICLUSIG at a lower dose in the case of intolerance to previous TKIs[4]

References

Representative patient case – not an actual patient.
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; PI, Professional Information; RWE, real-world evidence; TKI, tyrosine kinase inhibitor.

Maria: Identifying eligible patients with intolerance and medium CV risk

RWE: Patient baseline characteristics[15]

Characteristic	Belgian Registry (N=50)
Age, years, median (range)	58 (19–83)
CP-CML, n (%)	30 (60)
Prior TKIs, n (%)	
1	4 (8)
2	23 (46)
≥3	23 (46)
Reason for starting ponatinib, n (%)	
Intolerance to prior TKI	20 (40)
Relapse or refractoriness to prior TKI	14 (28)
Patients with CV risk factors, n (%)	
History of CV events	-
Hypertension	17 (34)
Hyperlipidaemia	5 (10)
Starting dose of ponatinib, n (%)	
45 mg	36 (72)
30 mg	6 (12)
15 mg	7 (14)

References

Incyte

Representative patient case – not an actual patient.
CP-CML, chronic-phase chronic myeloid leukaemia; CV, cardiovascular; PI, Professional Information; RWE, real-world evidence; TKI, tyrosine kinase inhibitor.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

Maria: Identifying eligible patients with intolerance and medium CV risk

RWE: Patient baseline characteristics[16]

OITI

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

- 1/2 of patients were in **2L**
- **More than** 1/2 of patients changed TKI for a reason **other than resistance***
- 1/2 of patients had a **CV history**

Starting dose of ponatinib, n (%)

45 mg	44 (37)
30 mg	49 (41)
15 mg	26 (22)

TOPASE

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

- 2/3 of patients were in **2L or 3L**
- 1/3 of patients changed TKI for a reason **other than resistance***
- **Up to** 1/2 of patients had a **CV history**

Starting dose of ponatinib, n (%)†

45 mg	21 (20)
30 mg	46 (44)
15 mg	37 (36)

Representative patient case – not an actual patient.
*Reasons include intolerance or in search of a deeper response; †CP-CML population. 2L, second-line; 3L, third-line; AP, accelerated phase; BP, blast phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; PI, Professional Information; TKI, tyrosine kinase inhibitor; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy.

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[8]

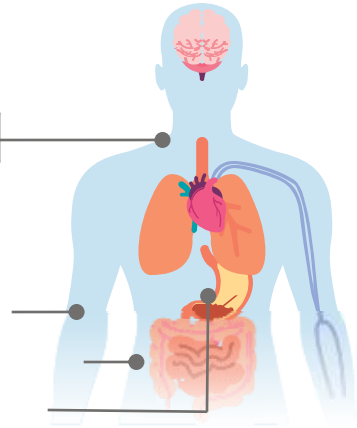
AOEs were reported in 4 patients in the OITI study[16]

Rate of new AOEs may not increase with longer treatment duration[2,5,8]

RWE: AEs and TRAEs[15,16]*

68% of patients experienced AEs in the Belgian registry:[15]

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



27% of patients in TOPASE discontinued treatment due to AEs (CV events in 4 patients)[16]

62% of patients in OITI underwent dose modifications, of which 41% were due to AEs in the 45 mg and 30 mg cohorts[16]

You may be confident that ICLUSIG tolerability will be manageable for Maria[15,16]

The PACE 5-year analysis and RWE studies established the consistency of the ICLUSIG safety profile over a prolonged period[2,15,16]

References

Representative patient case – not an actual patient. Please refer to the ICLUSIG PI for guidance on close monitoring of CV status.[1] Please refer to the safety slide for more information about the most common adverse events listed in the PI. *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; PI, Professional Information; RWE, real-world evidence; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy; TRAE, treatment-related adverse event.

The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the ICLUSIG Swiss PI for further information.[1]

Incyte

ICLUSIG®

ICLUSIG's response-based dosing regimen should improve Maria's treatment tolerability[5,7]

Patients with intolerance:

Maria's intolerance may contribute to nonadherence which could lead to loss of response, or biological progression to AP-/BP-CML[11,17,18]

Death attributed to disease progression is approximately 10 times that due to TRAEs in patients with CP-CML receiving 2L or 3L therapy[19]

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2L, second line; 3L, third line; AP, accelerated phase; BP, blastic phase; CML, chronic myeloid leukaemia; CP, chronic phase; PI, Professional Information; TRAE, treatment-related adverse events.

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BECAUSE TOMORROW MATTERS TODAY

For patients like Maria, early use of ICLUSIG after one 2G TKI may lead to very deep responses[1,13]

RWE: Response rates and estimated survival[15,16]

OITI[16]

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

CP-CML: 93%

1-year response rate:[16] CP-CML (N=111)[16]

MMR: 44%

3-year KM estimates:[15,16]

OS: 87%

PFS: 83%

Belgian registry[15]

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

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

3-year response rates:[15] Intolerant CP-CML (n=14)[15]

MMR–MR2: 71%

MR2: ≤1% BCR::ABL1[IS]

CML (N=33)[15]

OS: 85%

PFS: 82%

TOPASE[16]

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

CP-CML: 87%

CP-CML (non-responders at baseline; n=70):[16]

MMR: 60%

Median time to response:[16] 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[15,16]

References

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BECAUSE TOMORROW MATTERS TODAY

Considering ICLUSIG for Maria

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

- ICLUSIG may offer patients like Maria a better future[7,20]
- **Together, we've built experience and confidence in treating patients, like Maria, with ICLUSIG over the last decade[1,7,20]**
- 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[9,20,21]
- Considering an early switch to ICLUSIG after one 2G TKI for patients like Maria may improve their outcomes[9,20,21]

References

Representative patient case – not an actual patient.
2G, second generation; AE, adverse event; CML, chronic myeloid leukaemia; PI, Professional Information; TKI, tyrosine kinase inhibitor.

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Peter: Identifying eligible patients with intolerance and low CV risk

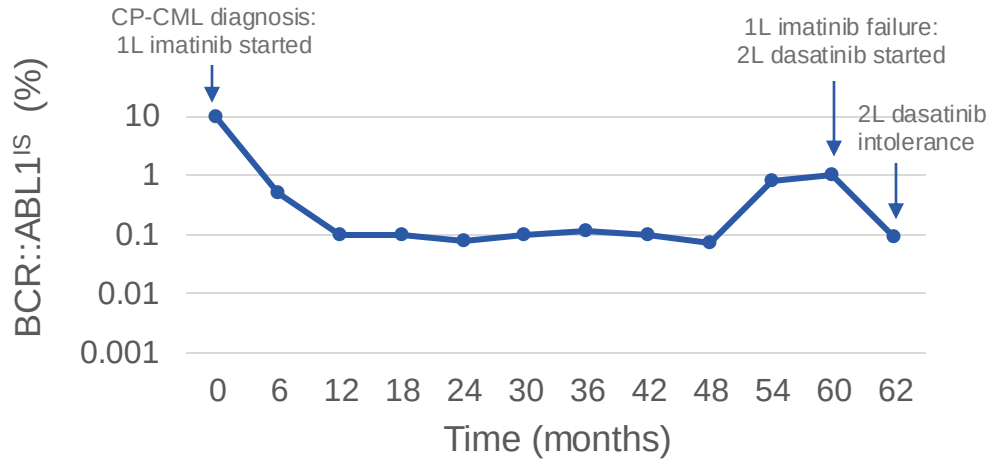
Peter

- 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[2]

RWE: Patient baseline characteristics[15,16]

ELN recommendations (2020) recommend starting ICLUSIG at a lower dose in the case of intolerance to previous TKIs[4]

Representative patient case – not an actual patient.
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; PI, Professional Information; RWE, real-world evidence; TKI, tyrosine kinase inhibitor.

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Peter: Identifying eligible patients with intolerance and low CV risk

RWE: Patient baseline characteristics[15]

Characteristic	Belgian Registry (N=50)
Age, years, median (range)	58 (19–83)
CP-CML, n (%)	30 (60)
Prior TKIs, n (%)	
1	4 (8)
2	23 (46)
≥3	23 (46)
Reason for starting ponatinib, n (%)	
Intolerance to prior TKI	20 (40)
Relapse or refractoriness to prior TKI	14 (28)
Patients with CV risk factors, n (%)	
History of CV events	-
Hypertension	17 (34)
Hyperlipidaemia	5 (10)
Starting dose of ponatinib, n (%)	
45 mg	36 (72)
30 mg	6 (12)
15 mg	7 (14)

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OITI

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

- **1/2** of patients were in **2L**
- **More than 1/2** of patients changed TKI for a reason **other than resistance***
- **1/2** of patients had a **CV history**

Starting dose of ponatinib, n (%)

45 mg	44 (37)
30 mg	49 (41)
15 mg	26 (22)

TOPASE

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

- **2/3** of patients were in **2L or 3L**
- **1/3** of patients changed TKI for a reason **other than resistance***
- **Up to 1/2** of patients had a **CV history**

Starting dose of ponatinib, n (%)†

45 mg	21 (20)
30 mg	46 (44)
15 mg	37 (36)

Representative patient case – not an actual patient.
*Reasons include intolerance or in search of a deeper response; †CP-CML population. 2L, second-line; 3L, third-line; AP, accelerated phase; BP, blast phase; CML, chronic myeloid leukaemia; CP, chronic phase; CV, cardiovascular; OITI, Observational study of Iclusig (ponatinib) Treatment in patients with CML in Italy; PI, Professional Information; TKI, tyrosine kinase inhibitor; TOPASE, Therapeutic Observatory of Ponatinib About Safety and Efficacy.

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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[16]

Peter should be at minimal risk of having CV adverse events[2,5,8]

Adjudicated AOEs in PACE were more likely in patients with multiple CV factors[8]

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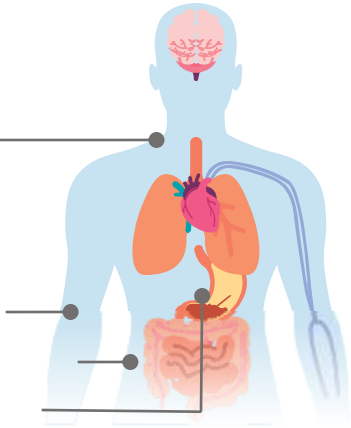

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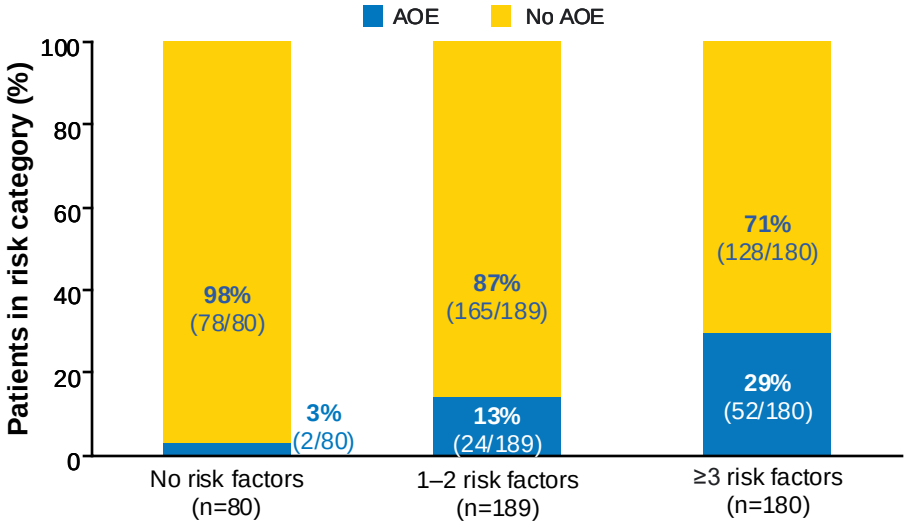
PACE: Adjudicated AOEs[8]



- 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.[8] Freely distributed under the Creative Commons Attribution License (CC-BY 4.0).

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Considering ICLUSIG for Peter

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

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ICLUSIG (ponatinib) tablets

BECAUSE TOMORROW MATTERS TODAY

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 PI[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 PI[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; PI, Professional Information.

References (1/2)

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Prescribing Information for Switzerland

ICLUSIG (ponatinib hydrochloride), 15 mg, 30 mg and 45 mg film-coated tablets

I: In adult patients suffering from: 1) T315I-positive Philadelphia-chromosome positive (Ph+) chronic myeloid leukemia (chronic phase, accelerated phase or blast phase) or T315I-positive Ph+ acute lymphoblastic leukemia or 2) Ph+ chronic myeloid leukemia (chronic phase, accelerated phase or blast phase) or Ph+ acute lymphoblastic leukemia for whom a treatment with other BCR-ABL tyrosine kinase inhibitors is not appropriate. **P:** Therapy should be initiated by a physician experienced in the diagnosis and treatment of patients with leukemia. The recommended starting dose for CP-CML is 45 mg once daily with a reduction to 15 mg once daily upon achievement of ≤1% BCR-ABL1^{IS}. The risk of arterial occlusive events is dose-related.-When dose is reduced, close monitoring of response is recommended. In patients with loss of response, dose of Iclusig can be re-escalated to previously tolerated dosage. Consider treatment discontinuation if a complete haematologic response has not occurred by 3 months. AP-CML, BP-CML and Ph+ALL: The recommended starting dose of Iclusig is 45 mg once daily. Consider discontinuing Iclusig if a complete haematologic response has not occurred by 3 months. Treatment should be continued as long as the patient does not show evidence of disease progression or unacceptable toxicity. Dose modifications should be considered for the management of treatment toxicity (e.g. for myelosuppression, arterial occlusion and venous thromboembolism, congestive heart failure, neuropathy, pancreatitis and hepatic impairment). **CI:** Hypersensitivity to the active substance or to any of the excipients. Prior myocardial infarction or stroke unless the potential benefit of treatment outweighs the potential risk. **W/P:** Before starting treatment with ponatinib, the risk of aneurysms and/or artery dissections and the cardiovascular status should be assessed in patients with risk factors such as hypertension or history of aneurysm; patients should be tested for HBV infection. Cardiovascular risk factors should be actively managed. Cardiovascular status should continue to be monitored and medical and supportive therapy for conditions that contribute to cardiovascular risk should be optimized during treatment with ponatinib. Monitoring for evidence of thromboembolism, arterial occlusion, blood pressure elevations and monitoring of cardiac functions should be performed. Immediately interrupt Iclusig in case of arterial occlusion or if hypertension is not medically controlled. In the event of significant worsening, labile or treatment-resistant hypertension, interrupt treatment and consider evaluating for renal artery stenosis. Dose modification or discontinuation of Iclusig in patients who develop serious venous thromboembolism should be considered. Comprehensive eye exams at baseline and periodically should be conducted during treatment. Monitoring should be performed for symptoms of neuropathy and if symptoms occur, consider interrupting Iclusig and evaluate for evidence of neuropathy. Iclusig is associated with pancreatitis. Check serum lipase every 2 weeks for the first 2 months and then periodically thereafter. Dose interruption/reduction or treatment withdrawal may be required. Patients with severe or very severe hypertriglyceridaemia should be appropriately managed to reduce the risk of pancreatitis. Hepatic failure has been observed. Perform liver function tests and measure transaminase level periodically. Myelosuppression is generally reversible and usually managed by withholding Iclusig temporarily or reducing the dose. A complete blood count should be performed every 2 weeks for the first 3 months and then monthly or as clinically indicated. If Posterior Reversible Encephalopathy Syndrome (PRES) is diagnosed, interrupt Iclusig treatment and resume treatment only once the event is resolved and if the benefit of treatment outweighs the risk of PRES. Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic purpura (TTP), has been associated with the use of VEGF receptor tyrosine kinase inhibitors. Iclusig treatment should be discontinued in patients who develop TMA and immediate treatment is necessary. Monitor for signs and symptoms suggestive of slow heart rate (fainting, dizziness) or rapid heart rate (chest pain, palpitations or dizziness) and manage patients as clinically indicated. Interrupt, then resume at the same or reduced dose or discontinue Iclusig if there is recurrence or severity. **IA:** Caution should be exercised and a reduction of the starting dose of ponatinib to 30 mg should be considered with concurrent use of Iclusig and strong CYP3A inhibitors. Co-administration of Iclusig with strong CYP3A inducers should be avoided unless the benefit outweighs the possible risk of ponatinib underexposure. Close clinical surveillance is recommended when ponatinib is administered with substrates of P-glycoprotein. **Preg./Lact.:** Iclusig should not be used during pregnancy. Stop breast-feeding during treatment. **UEs:** The most common serious adverse reactions >2% were 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 and increased lipase levels. Serious arterial cardiovascular, cerebrovascular, peripheral vascular occlusive adverse reactions and serious venous occlusive reactions occurred in 10%, 7%, 9% and 5% of patients treated with Iclusig. Very common UEs (≥20%): platelet or neutrophil counts, anaemia, hypertension, abdominal pain, constipation, nausea, diarrhea, rash, dry skin, arthralgia, myalagia, pain in extremity, back pain, fatigue, pyrexia and headache. For further information on UEs, see www.swissmedicinfo.ch. **Disp. cat.:** A. **Revision date:** November 2023. **Marketing authorization holder:** Incyte Biosciences International Sàrl, 1110 Morges. Refer to www.swissmedicinfo.ch for detailed information