For CP-CML patients right after the first 2G TKI failure[1]

ICLUSIG® (PONATINIB) COMBINES EXPERIENCE AND DATA THAT MAY HELP IMPROVE THEIR FUTURE[2–4]

WE'VE COME A LONG WAY IN CML TREATMENT, BUT WE STILL HAVE WORK TO DO

We know that treatment failure in CML can be devastating for the 1 in 3 patients who experience failure in the 1L setting (on imatinib or a 2G TKI).[5,6]

Failure of the first 2G TKI is still a problem today: 30–40% of patients experience 2G TKI failure by 5 years in the 1L setting, and there is a low likelihood of response to an alternative 2G TKI (regardless of treatment line).[7]

Read on to learn more about why you should consider switching to ICLUSIG after one 2G TKI, for eligible patients.

10 YEARS OF ICLUSIG — ICLUSIG HAS BEEN WITH YOU SINCE 2014!*

TOGETHER, WE'VE BUILT EXPERIENCE AND CONFIDENCE WITH ICLUSIG IN PATIENTS WITH CML[1–4]

Over the last decade, ICLUSIG has proudly demonstrated responses that are:

Fast

Median time to MCyR in CP-CML patients who achieved MCyR in PACE: **2.8 months** (range: 1.6 to 11.3 months)[1]

Median time to MMR in CP-CML patients who achieved MMR in PACE: **5.5 months** (range: 1.8 to 55.5 months)[1]

Deep

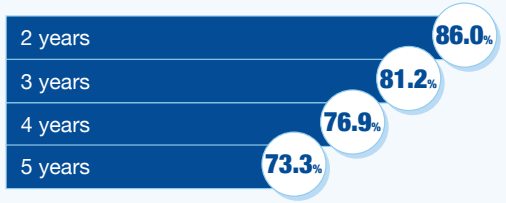
MMR rate in CP-CML patients in PACE at **5-year follow-up**:[2]

40% of patients

Durable

Among CP-CML patients in PACE, at **5 years**:
59% of patients who achieved MMR at any time maintained their response[2]
82% of patients who achieved MCyR by 12 months maintained their response (Kaplan-Meier estimates)[2]

For patients with CP-CML, the probability of overall survival from PACE is estimated at:[1]



Recently, data from the OPTIC trial affirmed efficacy outcomes, demonstrating clinical benefit in patients with CP-CML[3,4]

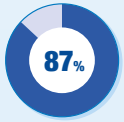
MR2 (≤1% BCR::ABL1^{IS}) by **3 years** in OPTIC:[3]

60% of patients — 45 mg → 15 mg regimen

75% of patients with a response-based dose-reduction from 45 mg or 30 mg to 15 mg **maintained response**.[4†]

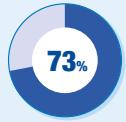
(primary analysis‡)

Estimated 3-year OS[3]



45 mg → 15 mg regimen

Estimated 3-year PFS[3]



45 mg → 15 mg regimen

The OPTIC trial now provides clear evidence to induce, reduce and maintain ICLUSIG dose to manage your patients with CP-CML[3,4]

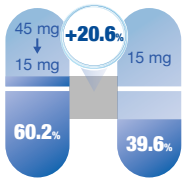
Induce
with 45 mg orally, once daily

Reduce
to 15 mg orally, once daily, upon achievement of ≤1% BCR::ABL1[IS†]

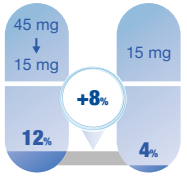
Maintain
with 15 mg dose†

The results from the OPTIC trial support an ICLUSIG regimen of a starting dose of 45 mg reduced to 15 mg upon response, to maximise response while minimising toxicity[3]

Improvement in response rate (by 3 years)



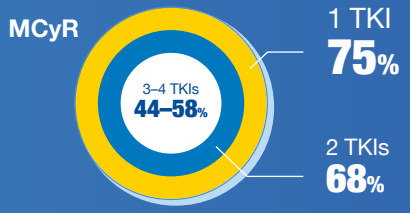
AOE rate (by 3 years)



UNDERSTANDING OF HOW TO OPTIMISE USE OF CURRENT TKIs TO IMPROVE PATIENT OUTCOMES CONTINUES TO GROW

Early use of ICLUSIG leads to the deepest responses[1]

The **deepest response with ICLUSIG** was achieved when used after 1 or 2 TKIs compared to after 3 or 4.[1]



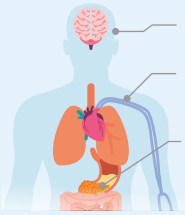
In the PACE trial, patients with CP-CML who received **fewer prior TKIs** attained **higher cytogenetic, haematological and molecular responses.**[1]

10 years

With a decade of ICLUSIG experience, the safety profile is well characterised and tolerability is manageable[1]

ICLUSIG had a manageable safety profile in the OPTIC trial, with no new safety signals[4]

The most common non-haematological TEAEs for all cohorts combined in the OPTIC trial were:[4]



18% Headache

28% Arterial Hypertension

17% Lipase Increase

(primary analysis†)

AOEs have occurred in:[1]

Iclusig-treated patients

25% PACE (≥64 mo follow up) including arterial cardiovascular **(13%)**, cerebrovascular **(9%)** and peripheral vascular occlusive **(11%)** adverse reactions

10% OPTIC (45 mg cohort, median follow up: 31.1 mo) including arterial cardiovascular **(4%)**, cerebrovascular **(2%)** and peripheral vascular occlusive **(3%)** adverse reactions

Common AEs

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

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

- A comprehensive list of AEs can be found in the PI[1]

ICLUSIG combines experience and data to improve patients' futures – consider early switch to ICLUSIG after just one 2G TKI[8]

A decade of building patients' futures

ICLUSIG is indicated in adult patients suffering from T315I-positive Philadephia-positive (Ph+) chronic myeloid leukemia (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ acute lymphoblastic leukemia, or Ph+ chronic myeloid leukemia (chronic phase, accelerated phase or blast phase) or Ph+ acute lymphoblastic leukemia for whom a treatment with other c-abl tyrosine kinase inhibitors is not appropriate. The recommended starting dose of ICLUSIG is 45 mg once daily. Please refer to the latest version of the Swiss ICLUSIG Professional Information (PI) at www.swissmedicinfo.ch.

*ICLUSIG was approved for the European market in 2013 and by Swissmedic in 2014. †Patients with loss of response can re-escalate the dose of ICLUSIG to a previously tolerated dosage of 30 mg or 45 mg orally once daily. Continue ICLUSIG until loss of response at the re-escalated dose or unacceptable toxicity. Consider discontinuing ICLUSIG if a complete haematological response has not occurred by 3 months.† ‡Data not reported in the 3-year OPTIC update presented at ASH 2022.

1L, first-line; 2G, second-generation; ADR, adverse drug reaction; AE, adverse event; AOE, arterial occlusive event; AP, accelerated phase; BP, blast phase; CML, chronic myeloid leukaemia; CP, chronic phase; IS, International Scale; MCyR, major cytogenetic response; MMR, major molecular response; mo, months; MR, molecular response; OPTIC, Optimizing Ponatinib Treatment In CP-CML; OS, overall survival; PACE, Ponatinib Ph+ ALL and CML Evaluation; PFS, progression-free survival; Ph+ ALL, Philadelphia chromosome–positive acute lymphoblastic leukaemia; PI, Professional Information; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor.

1. ICLUSIG® Professional Information, see www.swissmedicinfo.ch. **2.** Cortes JE, et al. Ponatinib efficacy and safety in Philadelphia chromosome–positive leukemia: final 5-year results of the phase 2 PACE trial. *Blood*. 2018;132:393–404; **3.** Cortes JE, et al. Three-year update from the OPTIC trial: A doseoptimization study of 3 starting doses of ponatinib. *Blood*. 2022;140(Supplement 1):1495–97; Presentation at ASH 2022; Abstract 620; accessed at: https://doi.org/10.1182/blood-2022-157822; **4.** Cortes JE, et al. Ponatinib dose-ranging study in chronic-phase chronic myeloid leukemia: a randomized, open-label phase 2 clinical trial. *Blood*. 2021;138:2042–50; **5.** Miller GD, et al. Resistant mutations in CML and Ph+ ALL – role of ponatinib. *Biologics*. 2014;8:243–54; **6.** Borghi L, et al. Chronic Myeloid Leukemia Patient's Voice About the Experience of Treatment-Free Remission Failure: Results From the Italian Sub-Study of ENESTPath Exploring the Emotional Experience of Patients During Different Phases of a Clinical Trial. *Front Psychol*. 2019;10:329; **7.** Cortes JE, Lang F. Third-line therapy for chronic myeloid leukemia: current status and future directions. *J Hematol Oncol*. 2021;14:44; **8.** Hochhaus A, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia*. 2020;34:966–84.

All references are available upon request.

EXPO code: CH/ICLG/P/24/0010
Date of preparation: 02/2024
Date of expiry: 12/2024

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-ABL1IS. 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