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Optimizing treatment of CML in the first-line setting and beyond: Insights from EHA 2024 and ESH–iCMLf 2024

Fact sheet for CML

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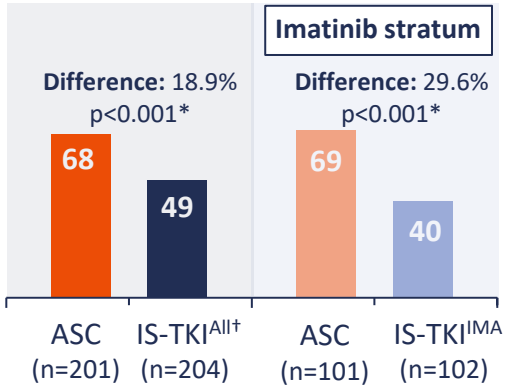
What are the latest data for approved and emerging TKIs for CML in the first-line setting?

ASC4FIRST study of asciminib vs all SoC TKIs in newly diagnosed CML[1]

Patients with MMR at 48 weeks (%)



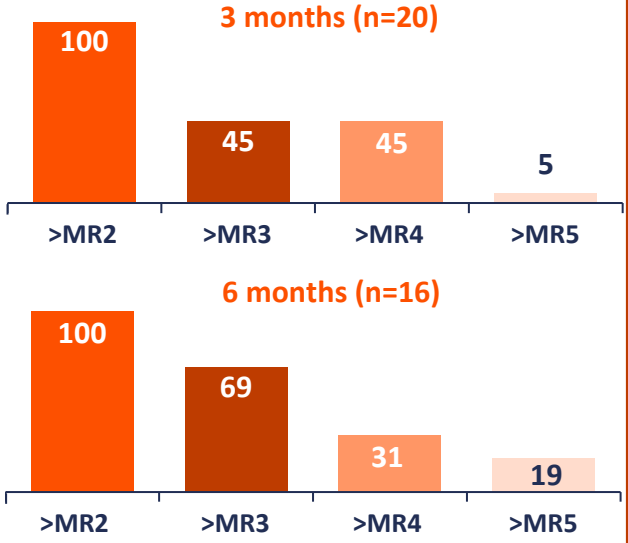
Safety and tolerability

AEs, %	Asciminib (n=200)	2G-TKIs (n=102)	Imatinib (n=99)
Grade ≥3	38	55	44
Leading to discontinuation	5	10	11
Leading to dose adjustment/ interruption	30	53	39

Asciminib demonstrated superior efficacy vs 2G-TKIs and imatinib in newly diagnosed CML, with acceptable safety and tolerability

ALERTCML study of asciminib in newly diagnosed CML-CP[2,3]

Patients achieving an MR‡ (%, N=36)
Median follow-up: 24 weeks[2]



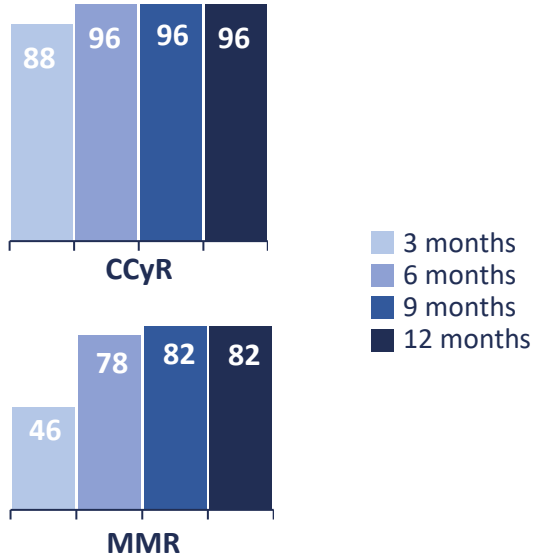
Grade 3 non-haematological toxicities[3]

	No. of patients
Elevated CPK	1
Increased lipase	2

Asciminib is effective and well tolerated in the first-line setting

Study of ponatinib in newly diagnosed CML-CP[4]

Patients achieving CCyR and MMR (%, N=51)
Median time on therapy: 13 months



Safety and tolerability	%
CV SAEs	16
Dose reduction due to CV AEs	16
Permanent discontinuation due to CV AEs	10

Ponatinib was associated with high CCyR and MR rates in newly diagnosed CML-CP but CV toxicity posed a challenge for its first-line use

*Estimated using the Mantel–Haenszel method after stratifying for prerandomization-selected TKI and baseline ELTS risk groups (both IRT data). Adjusted 1-sided p-value calculated based on the graphical gatekeeping procedure. †Imatinib (n=102) + 2G-TKI (n=102; nilotinib, 48%; dasatinib, 41%; and bosutinib, 11%). ‡MR2, BCR::ABL ≤1%; MR3, BCR::ABL ≤0.1%; MR4, BCR::ABL ≤0.01%; MR5, BCR::ABL ≤0.001%.

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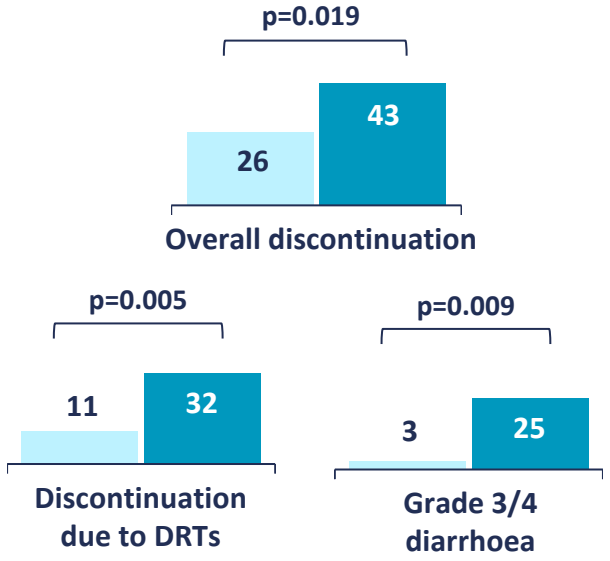
What are the latest data for approved and emerging TKIs for CML in the second- and later-line settings?

BOGI trial of lower initiating bosutinib dose in second/third-line CML-CP[5]

Patients discontinuing bosutinib at 12 months (%)

This study: 200 mg starting dose (n=35)[5]
Previous study: 500 mg starting dose (n=28)[6]



Cumulative incidence of response at 12 months

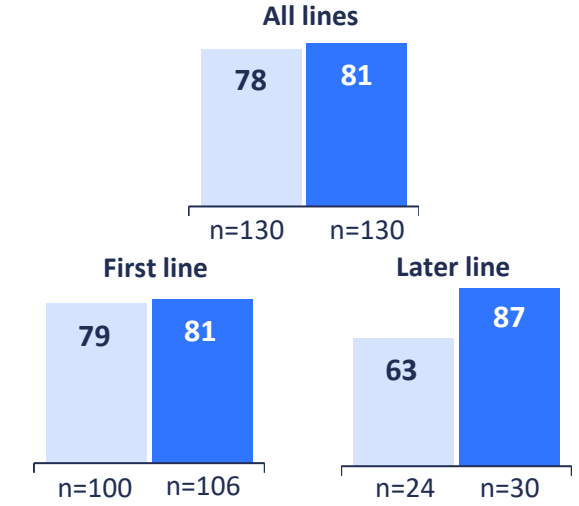
MMR: 23 (66%)
DMR: 15 (43%)

The lower initiating bosutinib dose reduced the drug discontinuation rate due to severe DRTs, while maintaining clinical efficacy

DasaHIT trial of dasatinib tolerability with weekend holidays vs 7-day dosing[7]

Patients achieving MMR at 24 months (%)

Experimental arm: 100 mg QD, 5 + 2 days' rest
Standard arm: 100 mg QD, 7 days



Safety and tolerability

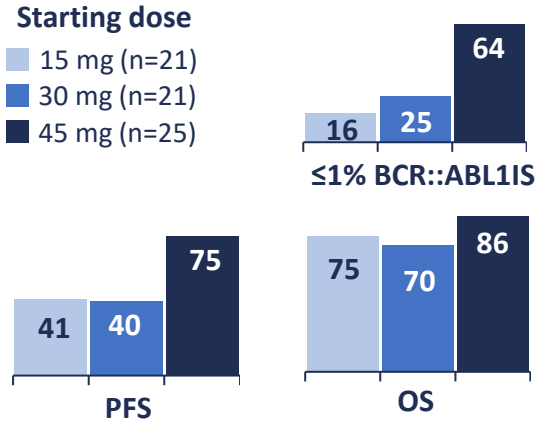
	Exp. arm	Stand. arm
Median cTS, n	2	2
Pleural and pericardial effusions, %	8	16

Dose modification of dasatinib improved safety. While efficacy was maintained in the first line; later-line patients benefitted more from continuous dosing

OPTIC trial of ponatinib in patients with CML-CP and the T315I mutation[8]

Efficacy in patients with the T315I mutation (%, N=67)[9]

Median follow-up 60.6–63.5 months[8]



Safety and tolerability[8]

AEs, %	15 mg (n=21)	30 mg (n=21)	45 mg (n=25)
Grade ≥3 TEAE	38	38	60
TEAEs leading to discontinuation	5	14	8
TE-AOE	5	14	8

The optimal ponatinib benefit:risk ratio was achieved with a starting dose of 45 mg QD, reducing to 15 mg QD on attaining ≤1% BCR::ABL1IS

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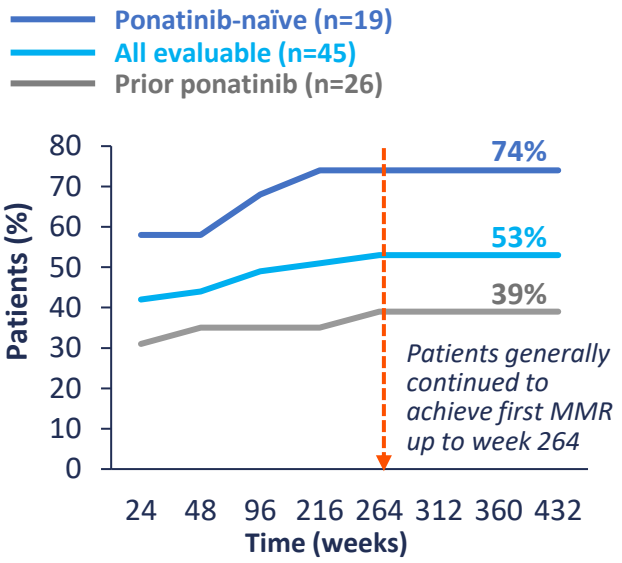
What are the emerging findings from clinical trials and real-world studies?

First-in-human trial of asciminib in T315I-mutated CML-CP: Final analysis[10]

Cumulative MMR over time with asciminib 200 mg BID (n=45)
Median exposure, 3.5 years

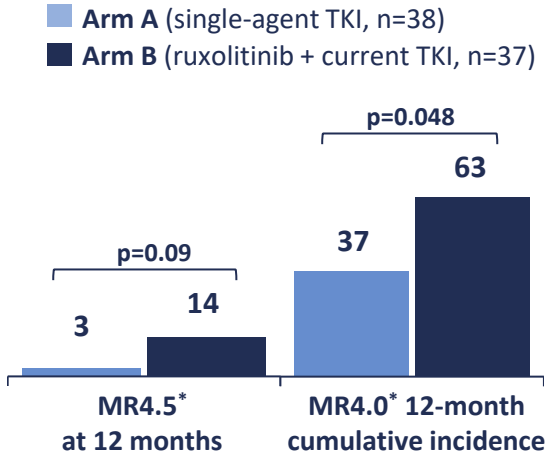


AEs, %	All patients (N=48)
Leading to dose adj./interrupt.	44
Leading to discontinuation	10

Asciminib is a treatment option for T315I-mutated CML-CP; it potentially provides sustained efficacy and tolerability, regardless of prior ponatinib treatment

SWOG S1712: Efficacy of ruxolitinib plus BCR::ABL1 TKIs in CML[11]

Patients with MR at 12 months (%)
Median time on TKI prior to enrolment: 3.2 years



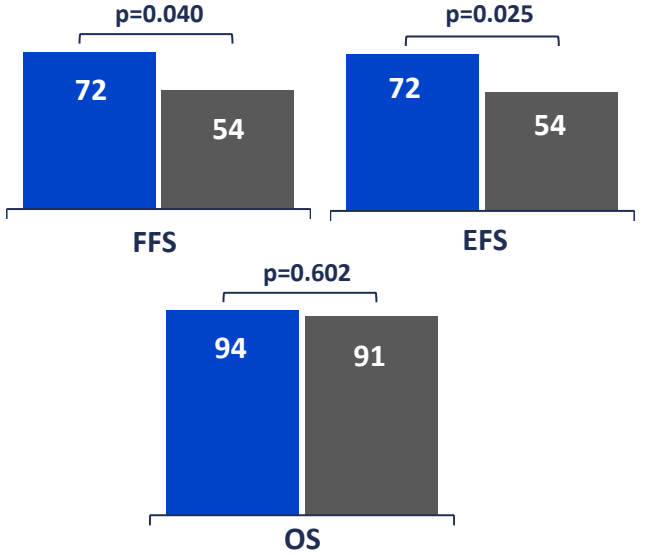
Proportion of patients who met NCCN criteria to discontinue TKI therapy: **29%** (**Arm B**) vs **11%** (**Arm A**), p=0.08

Safety	Arm A	Arm B
Grade 3 AEs, n	2	3

The ruxolitinib plus TKI combination warrants further investigation to determine if it could lead to higher TFR rates

INFINITY Czech CML database: Real-world efficacy of first-line nilotinib vs imatinib[12]

TKI efficacy (%)



No difference in **disease-specific survival** between matched groups or all four groups,† due to older age and comorbidities in the imatinib-unmatched groups

First-line nilotinib demonstrated higher FFS and EFS but did not show any benefit for OS. Imatinib is still an effective choice for first-line treatment of CML-CP

*MR4.0, BCR::ABL ≤0.01%; MR4.5, BCR::ABL ≤0.0032%. †The four groups: imatinib (all, n=821); nilotinib (n=163); imatinib matched (n=163); imatinib unmatched (n=658).

Abbreviations and references

Abbreviations

2G, second generation; AE, adverse event; adj., adjustment; ASC, asciminib; BCR::ABL1IS, BCR::ABL1 International Scale; BID, twice daily; CCyR, complete cytogenetic response; CML, chronic myeloid leukaemia; CML-CP, CML-chronic phase; CPK, creatine phosphokinase; cTS, cumulative toxicity score; CV, cardiovascular; DMR, deep molecular response; DRT, drug-related toxicity; EFS, event-free survival; EHA, European Hematology Association; ELTS, European Treatment and Outcome Study long-term survival score; ESH, European School of Haematology; Exp., experimental; FFS, failure-free survival; G, generation; iCMLf, International Chronic Myeloid Leukaemia Foundation; IMA, imatinib; interrupt., interruption; IRT, interactive response technology; IS, investigator-selected; MMR, major molecular response; MR, molecular response; NCCN, National Comprehensive Cancer Network; OS, overall survival; PFS, progression-free survival; QD, once daily; SAE, serious AE; SoC, standard of care; Stand., standard; TE-AOE, TE arterial occlusive event; TEAE, treatment-emergent AE; TFR, treatment-free remission; TKI, tyrosine kinase inhibitor.

References

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