Interim analysis of a multicenter study on patient-guided dose reduction of tyrosine kinase inhibitors in chronic myeloid leukemia: the RODEO study

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Abstract

Patient-guided dose reduction, as explored in the RODEO study, offers a promising approach to alleviate the burden of tyrosine kinase inhibitor (TKI) therapy in chronic myeloid leukemia (CML). Supported by shared decision-making (SDM) and a patient decision aid, this strategy aims to reduce TKI toxicity while maintaining effectiveness. This interim analysis evaluates its effectiveness at six months, focusing on intervention failure, i.e., TKI dose re-escalation due to loss of major molecular remission (MMR) of *BCR::ABL1* (>0.1%IS) or expected loss of MMR, and patient-reported health-related quality of life (HRQoL) and symptom burden. The SDM-process and decisional conflict are also evaluated. This is a prospective, single-arm, multicenter trial including 148 patients with chronic-phase CML in at least MMR. Patients and their treating hematologists were engaged in an SDM-process and selected a reduced TKI dose. *BCR::ABL1* monitoring was conducted regularly; HRQoL and symptom burden was assessed using the scores of the QLQ-C30 and QLQ-CML24 questionnaires, and IL 156 item list. of the European Organisation for Research and Treatment of Cancer (EORTC). SDM and decisional conflict were evaluated via SDM-Q-9, SDM-Q-Doc, and the Decisional Conflict Scale. Of 146 patients analyzed, 2.8% experienced intervention failure at six months. Modest statistically significant improvements were seen in multiple symptom scales. SDM was well-evaluated, with low decisional conflict by patients. Patient-guided dose reduction appears safe and beneficial at six months follow-up.

Introduction

Tyrosine kinase inhibitors (TKI) play a crucial role in the treatment of chronic myeloid leukemia (CML), enabling patients to achieve life expectancies similar to those of age-matched peers.[1] Despite their effectiveness, TKI cause drug adverse events that significantly impair health-related quality of life (HRQoL) and tolerability.[2] Common adverse events include fatigue, muscle cramps, pain, edema, skin issues (e.g., rash, dry skin), gastrointestinal symptoms (e.g., diarrhea, constipation, nausea), thrombocytopenia, and headache.[3] This highlights the need for strategies

such as TKI switching or dose modifications to reduce the daily burden of toxicity. Dose optimization strategies are increasingly discussed in recent literature, with studies summarizing investigated dosing regimens and emphasizing the need for prospective trials to evaluate HRQoL in patients with chronic-phase CML after dose reduction.[4-6] Beyond alleviating treatment burden, dose reduction may provide additional benefits, including cost savings and a potential decrease in long-term toxicity. Furthermore, when safety conditions are met, such as more frequent blood monitoring after dose reduction, these strategies are widely endorsed by both patients and healthcare providers.[6-8] However, advice on how to appropriately reduce doses are currently not included in European LeukemiaNet (ELN) recommendations or National Comprehensive Cancer Network (NCCN) guidelines.

Decision-making regarding dose reduction requires careful consideration of various patient-specific factors, including clinical indicators and individual preferences, all of which necessitate active patient engagement, particularly in the context of CML.[9-11] To effectively do this, shared decision-making (SDM) plays a crucial role in ensuring that treatment adjustments align with both medical best practices and patient expectations.[12] SDM involves four steps: 1) the healthcare provider informs the patient about the need for a treatment decision, emphasizing the value of their input; 2) treatment options are assessed including their pros and cons; 3) the patient's preferences are explored, with the healthcare provider offering support; and 4) the healthcare provider and patient discuss the patient's wish to make the decision, leading to either a final decision or a postponement of that decision, followed by a discussion of next steps.[12] To further facilitate patient engagement, the use of patient decision aids (PDA) is advocated.[13] PDA enhance patient knowledge, improve understanding of risks and personal values, and reduce decisional conflict, ultimately fostering more informed and collaborative treatment decisions.[13]

Recent findings from the international CML SUN study, which explored unmet needs among patients with chronic-phase CML and their physicians, underscore the importance of patient-centered approaches in treatment decisions, particularly through SDM and patient education.[11] Highlighting the current relevance of these approaches, the ongoing prospective, multicenter single-arm RODEO study, performed in nine Dutch hospitals, evaluates the effectiveness of patient-guided dose reduction in adult patients with chronic-phase CML on TKI who are in stable major molecular remission (MMR) or deep molecular remission (DMR) (https://doi.org/10.1186/s12885-023-10697-6, EUCT: 2024-516511-24-00).[14] In short, the intervention followed three steps designed to ensure informed and patient-involved decision-making: 1) the patient received a PDA tailored for the decision to reduce the TKI dose; 2) the patient participated in an SDM consult with their trained healthcare provider to discuss their willingness to accept a dose reduction and by how much the dose should be reduced; 3) the patient and healthcare provider together chose a personalized reduced TKI dose.

An interim evaluation is being conducted now that all participants have passed the halfway point of the study's follow-up period, allowing for a meaningful preliminary assessment of outcomes. This interim evaluation of the RODEO study aims to assess the effectiveness of the patient-guided dose reduction intervention at 6-month follow-up by: 1) evaluating the proportion of patients experiencing intervention failure, defined as patients who have restarted their initial dose due to loss of MMR or were expected to lose MMR (re-escalation was initiated in patients with concerning increases in *BCR::ABL1* [% International Scale; IS] to prevent actual loss of MMR), and 2) examining patient-reported HRQoL and symptom burden. Additionally, the decision-making process is evaluated based on the use of the PDA, the level of executed SDM during consultations, and the degree of decisional conflict experienced by patients after deciding to reduce the dose. This analysis will not only provide important clinically relevant insights into TKI dose reduction in real-world settings but will also assess the experiences of a patient-centered approach in achieving this goal.

Methods

Study design and participants

Adults with chronic-phase CML on imatinib, bosutinib, dasatinib, nilotinib, or ponatinib in least MMR (defined as *BCR::ABL1* levels ≤0.1%) for a minimum of six months were included. The intervention involved a PDA for patients, after which the healthcare provider and patient engaged in SDM to select a reduced dose. Detailed eligibility criteria and intervention information are in the published study protocol.[14] No restrictions were given on the TKI dose at study start; therefore, normal dosages (bosutinib 400 mg, dasatinib 100 mg, imatinib 400 mg, nilotinib 600 mg, ponatinib 45 mg) were standardized to 100%. All participants provided written informed consent in accordance with the Declaration of Helsinki. Ethical approval was granted by Medical Ethical Committee Oost-Nederland (N. 2021-3457). The trial is registered at EUCT: 2024-516511-24-00. Reporting followed the format of the TREND statement (*Online Supplementary Table S1*).[15]

Data collection

To evaluate molecular response, *BCR::ABL1* levels (%IS) were monitored through blood samples. Timing of measurements and detailed questionnaire descriptions are available in the *Online Supplementary Appendix*, *Online Supplementary Table A*, and study protocol.[14] In short, HRQoL and symptom burden were assessed using QLQ-C30 (version

3.0) and QLQ-CML24 questionnaires, and IL 156 item list of the European Organisation for Research and Treatment of Cancer (EORTC).[16-18] The SDM experience was measured using the SDM-Q9 (patients) and SDM-Q-Doc (healthcare providers), alongside the Observer OPTION 5 instrument, independently scored by an SDM expert (Dutch school for shared decision-making; www.schoolvoorsamenbeslissen.nl).[19-23] The impact of the decision to reduce TKI dose on patient's distress was evaluated using the traditional Decisional Conflict Scale (DCS).[24]

Data analysis and outcomes

The proportion of patients with intervention failure, defined as the need to re-escalate the initial dose due to (expected) loss of MMR, was evaluated at six months follow-up as primary outcome. Molecular relapse-free survival was estimated using the Kaplan-Meier method and reported with 95% confidence intervals (CI). A priori sample size calculations for 147 patients are detailed in the *Online Supplementary Appendix*.[14]

EORTC questionnaires were scored following EORTC guidelines. Longitudinal QoL changes from baseline were interpreted using scale-specific thresholds by Cocks *et al.*[25,26] For EORTC QLQ-CML24 and IL156 items, average symptom thresholds were applied in the absence of evidence-based thresholds. Subgroup analyses were conducted by sex, age (< or ≥ 70 years), and TKI type (for groups with N≥30). Symptom prevalence was based on any response other than "not at all" on relevant symptom items. The proportion of missing assessments in patient-reported outcomes (maximum 0.38) supported the validity of a complete case analysis;[27] therefore, no imputation was performed, except for questionnaires with single missing items in scales, which were imputed per scoring manuals. Descriptive statistics were used for categorical (frequencies, percentages) and continuous (mean ± Standard Deviation [SD] or median with interquartile range [IQR]) data. Mean change scores in EORTC QLQ-C30, CML24 and IL156 scales were statistically evaluated using one-sample *t* tests against zero ($\alpha = 0.05$), with 95% CI. $P<0.05$ was considered statistically significant.

Shared decision-making evaluation included PDA uptake and reasons for non-use. Outcomes from SDM-Q9, SDM-Q-Doc, Observer OPTION 5, and DCS were scored as detailed in the *Online Supplementary Appendix*.

Statistical analyses were conducted per protocol using RStudio (version 4.1.3).

Results

A total of 148 patients provided informed consent (Figure 1), of whom 146 were included in this analysis (Table 1). The study started in February 2021 (first patient included) and is expected to be completed in August 2025 (last patient completes follow-up) after achieving the inclusion goal in February 2024. At baseline, 91 patients (62.3%) were on the standard dose, 9 (6.2%) on a higher dose, and 46 (31.5%) on a reduced dose. The median relative dose reduction at 6-month follow-up was 25% (IQR 8.4) of the initial dose.

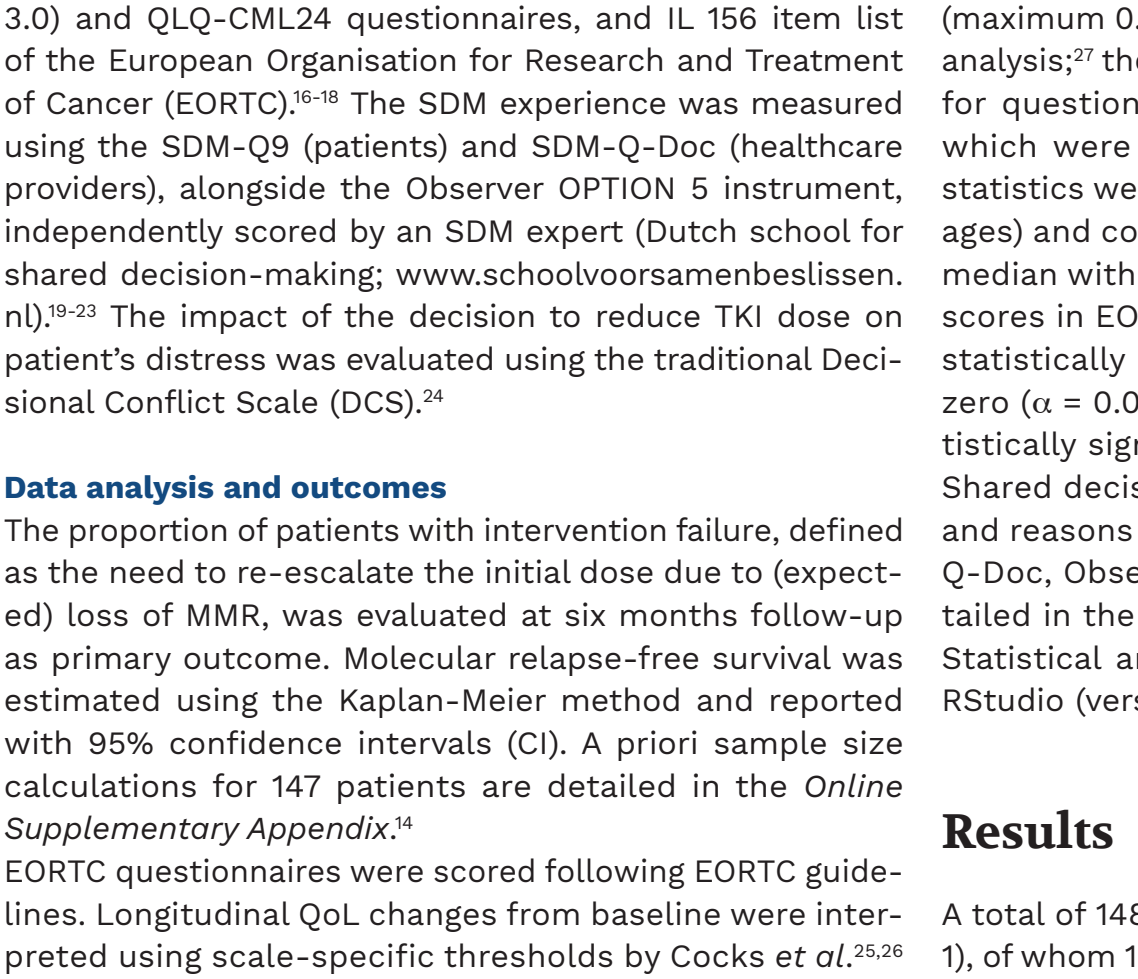

Figure 1. Participant flow-chart.

Intervention failure

At 6-month follow-up, a total of 6 participants re-escalated their dose (4.1%). Of these, 4 patients re-escalated their dose because of expected loss (N=1) or loss (N=3) of MMR and were documented as treatment failure (2.8%), resulting in a molecular relapse-free survival probability of 0.972 (95%CI: 0.946-0.999) at six months (Figure 2). Two patients restarted their initial dose because they wished to do so. Characteristics of patients with (expected) loss of MMR are detailed in *Online Supplementary Table S2*.

Health-related quality of life and symptoms

At baseline, most reported symptoms of any severity among patients were fatigue (82%, N=112/137), followed by aches or pains in muscles or joints (76%, N=105/138), lack of energy (74%, N=87/118), muscle cramps (67%, N=88/132), and drowsiness (60%, N=80/134). After six months, this top five remained largely unchanged, with fatigue the most prevalent problem (82%, N=96/117), followed by lack of energy (69%, N=70/102), aches or pains in muscles or joints (69%, N=84/122), muscle cramps (55%, N=63/115), and eye problems (52%, N=59/114). *Online Supplementary Table S3* shows per timepoint all proportions per severity per symptom along with the number of respondents.

Statistically significant mean changes were observed across eight scales of the EORTC QLQ-C30, CML24, and IL156 after six months (Figure 3). Social functioning demonstrated a medium improvement, while fatigue, nausea / vomiting, diarrhea, impact on daily life, and body image problems showed small improvements. The change in appetite loss and symptom burden was considered trivial. All other changes and corresponding statistical details for the complete set of measurements are presented in *Online Supplementary Table S4*. Median and mean values for all items and measurements are provided in *Online Supplementary Table S5*.

Exploratory subgroup analysis showed that more statistically significant mean changes occurred among females and dasatinib-users (*Online Supplementary Figure S1*). *Online Supplementary Table S6* presents patient characteristics in each subgroup. Females experienced moderate improvements in social functioning, fatigue, dizziness / light-headedness, and coughing, as well as small improvements in nausea / vomiting, diarrhea, and financial difficulties. Males exhibited statistically significant small improvements in body image problems. The only significant (small) deterioration was found in satisfaction with care and information in females. Among the TKI with sufficiently large subgroups (imatinib, dasatinib, and nilotinib) significant mean changes were observed among imatinib- and dasatinib-users. For imatinib, a small improvement in symptom burden and a medium improvement in diarrhea was noted. In the dasatinib group, significant mean changes were observed across ten items. These included small improvements in symptom burden and appetite loss, and medium improvements in role and social functioning, fatigue, constipation, impact on daily life, body image problems, lack of energy, and flatulence. No statistically significant mean changes were found in the elderly group (70+ years).

Shared decision-making

A total of 85.5% of the patients used the PDA during decision-making. Several factors contributed to the decision not to use the PDA, as outlined in *Online Supplementary Table S7*. The level of SDM was evaluated at a median score of 96 (IQR: 20, N=85) by patients and 82 (IQR: 11, N=7) by healthcare providers. See *Online Supplementary Figure S2* for the proportions of the participants per scale item per question. The median overall score for OPTION5 was 45 (IQR: 10, N=13). Participants had low decisional conflict, with a median score of 12.5 (IQR: 25, N=101). *Online Supplementary Table S8* shows medians per DCS subscore. A total of 7.5% of the patients reported high decisional conflict after the choice for dose reduction (total DCS score ≥ 37.5).

Table 1. Participant baseline characteristics of the study.

Characteristics	Results at baseline
N	146
Gender, male, N (%)	93 (63.7)
Mean age, years, (SD)	59 (13.7)
Median time since diagnosis, years (IQR)	8.2 (9.1)
TKI used, N (%)	
Imatinib	67 (45.9)
High dose	6 (9.0)
Normal dose	49 (73.1)
Low dose	12 (17.9)
Dasatinib	36 (24.7)
High dose	-
Normal dose	18 (50)
Low dose	18 (50)
Nilotinib	32 (21.9)
High dose	3 (8.3)
Normal dose	20 (55.6)
Low dose	9 (25)
Bosutinib	9 (6.2)
High dose	-
Normal dose	4 (44.4)
Low dose	5 (55.6)
Ponatinib (low dose)	2 (1.4)
Molecular response of *BCR::ABL1*, %IS	
Major molecular remission, N (%)	24 (16.4)
Deep molecular remission, N (%)	122 (83.6)
MR4 (≤0.01%)	23 (15.8)
MR4.5 (≤0.0032%)	35 (24.0)
MR5 (≤0.001%)	64 (43.8)
Median time in MMR or DMR, years (IQR)[a]	4.0 (5.1)

[a]N=132. DMR: deep molecular remission; IQR: interquartile range; IS: International Scale; MMR: major molecular remission; MR: molecular response; SD: standard deviation; TKI: tyrosine kinase inhibitor.

Discussion

While survival outcomes for patients with CML have significantly improved in recent years, the focus is increasingly shifting toward optimizing long-term QoL. In this context, recent literature has emphasized the importance of individualized dosing strategies to support both efficacy and tolerability of treatment.[5,6] This interim analysis supports the clinical feasibility and safety of such approaches, demonstrating low rates of intervention failure six months after dose reduction. Moreover, improvements were observed in EORTC HRQoL scores at the 6-month follow-up, with the most significant benefits noted among female patients and those receiving dasatinib. Decision-making in these contexts may benefit from patient involvement and SDM as found by qualitative studies into this topic.[7,28] This was effectively implemented by this study, as the SDM was well-evaluated and has resulted in low decisional conflict. The baseline characteristics of the RODEO study population were comparable to those reported in the DESTINY trial, which served as a reference for intervention failure rates.[29,30] Moreover, compared to data from the Dutch Cancer Registry, the RODEO study population closely reflects the broader Dutch CML population in terms of mean age, gender distribution, and proportional use of the various TKI.[31] The RODEO trial included a higher proportion of patients treated with second-generation TKI compared to the DESTINY trial. This distinction offers valuable insights into

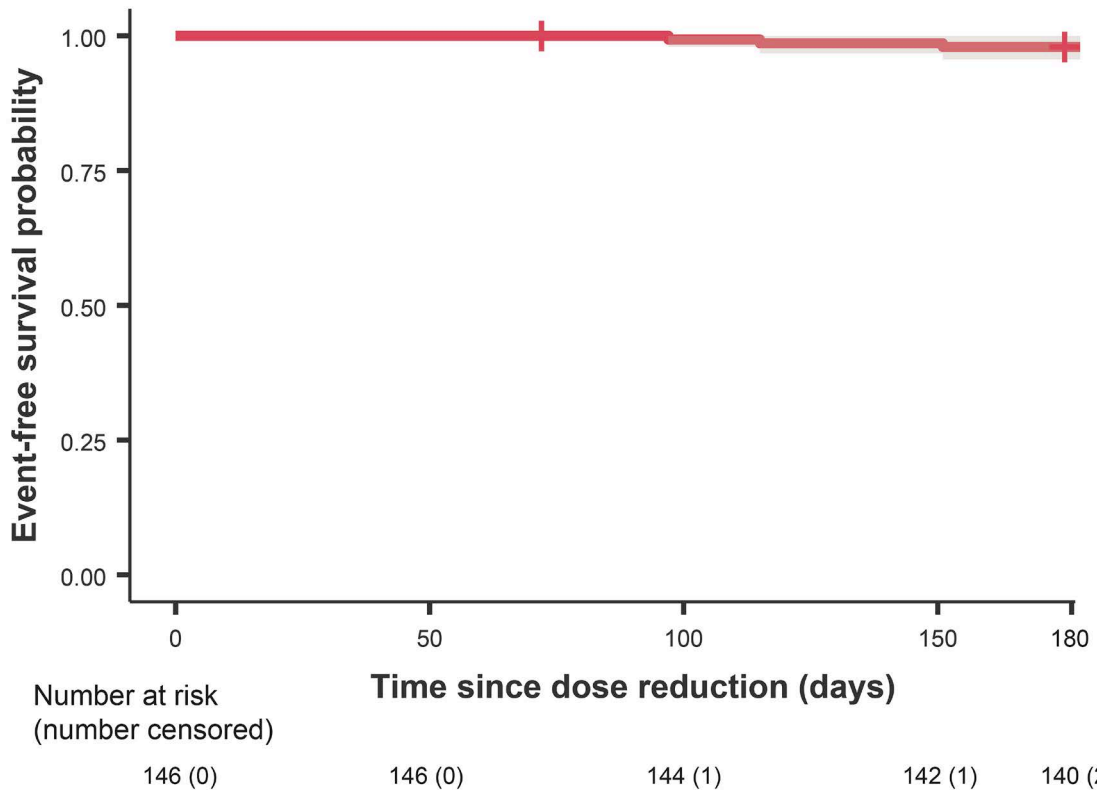

Figure 2. Event-free survival curve for major molecular remission over six months following dose reduction.

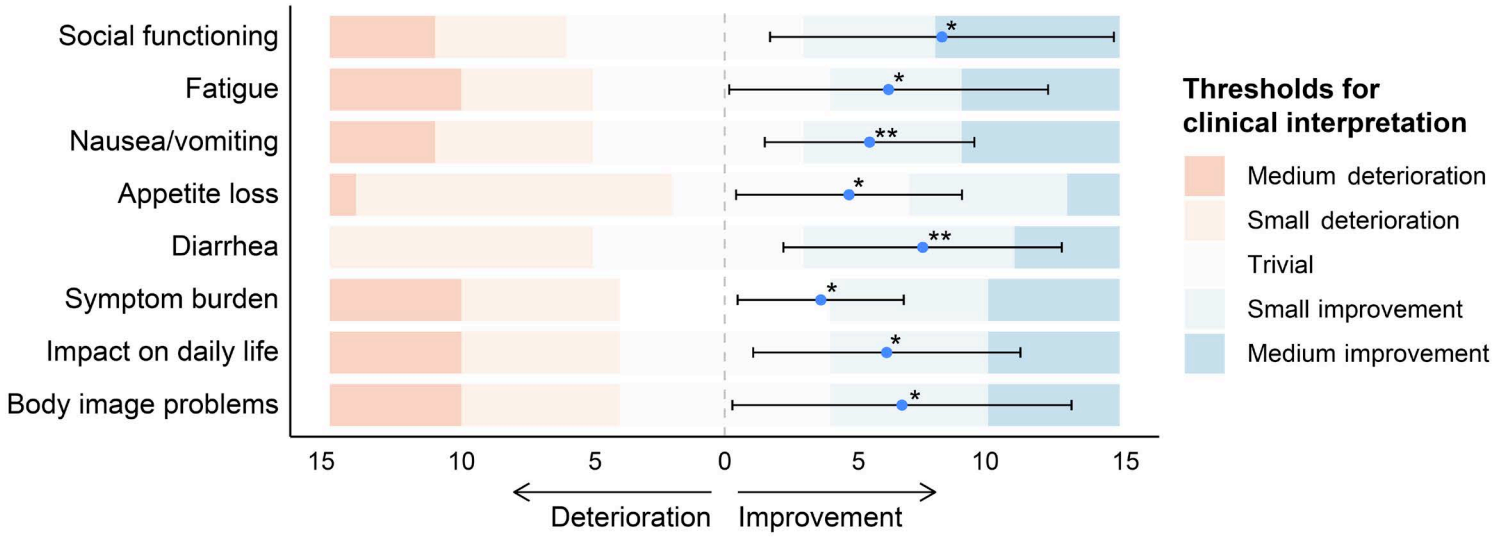

Figure 3. Statistically significant mean changes in the scores of the QLQ C30 and QLQ 24 questionnaires, and IL 156 item list of the European Organisation for Research and Treatment of Cancer after six months. Dots with 95% confidence intervals represent the observed mean changes in European Organisation for Research and Treatment of Cancer (EORTC) scores. Colored bars indicate evidence-based thresholds for meaningful differences on the EORTC scales, based on the criteria established by Cocks *et al.*[26] *$P \leq 0.05$; **$P \leq 0.01$.

the differential outcomes associated with various TKI. Furthermore, the RODEO study population includes a greater number of patients in DMR, a factor previously associated with improved outcomes in both dose reduction and treatment-free remission settings.[6] Nonetheless, after six months of follow-up following a 50% dose reduction, the probability of event-free survival was 0.88 in the MR3 cohort and 0.99 in the MR4 cohort in DESTINY, compared to 0.97 (95%CI: 0.946-0.999) observed in the RODEO population. Notably, all patients in RODEO who experienced (or were expected to experience) intervention failure, were in deep molecular remission (≥MR4) (*Online Supplementary Table S2*). The slightly higher rate of intervention failure observed may be attributed to the sample size, or the design of the DESTINY study, which required patients to actually lose MMR before intervention, whereas in the RODEO study, dose re-escalation also occurred pre-emptively when loss of MMR was anticipated. While the latter approach may be considered more patient-friendly, it could also lead to a higher probability of intervention failure.

Baseline EORTC mean and median scores in the RODEO population are comparable to those reported in previous studies of patients with CML (*Online Supplementary Table S5*).[32-35] Notably, for CML-specific scales, baseline median scores in the RODEO population indicate better health status compared to those in an earlier cohort with similar patient characteristics.[34] Fatigue was the most prevalent problem that patients reported at baseline. This aligns with recent findings from a meta-analysis of patient-reported TKI toxicities in CML.[36] Although its prevalence remained stable over six months, the mean score on the EORTC QLQ-C30 fatigue scale decreased by 6 points, indicating a small improvement in fatigue severity across all patients. Indeed, a small proportion (2%) of patients shifted from moderate / severe to mild problems with fatigue (*Online Supplementary Table S3*). Interestingly, subgroup analysis suggests that women and dasatinib-users (*Online Supplementary Figure S1*) may experience greater benefit from dose reduction regarding fatigue problems. However, this study cannot determine whether these differences are due to biological factors or socio-cultural or psychological influences, and further research is needed to clarify the underlying causes.

A phenomenon often observed after TKI discontinuation is TKI withdrawal syndrome, primarily musculoskeletal pain, which affects at least 23% of patients within the first three months after discontinuation.[37] In contrast, no increase in musculoskeletal problems was observed in this study following dose reduction (*Online Supplementary Table S3*). In this interim analysis, only a limited number of subgroup analyses were performed, focusing on sex, age (< or ≥70 years), and TKI type. The 70+ age group was specifically examined considering findings by Efficace *et al.*, who reported worsening fatigue in this age group following TKI discontinuation compared to an opposite trend in the younger age groups.[32] However, no statistically significant differences were observed in this study population. Nonetheless, future analyses of the complete follow-up data may benefit from longitudinal modelling stratified by age and other baseline characteristics, to better identify which patient groups are most likely to benefit from TKI dose reduction.

Overall, patient experience on SDM was rated positively and exceeded national averages, suggesting that the patient-guided dosing approach was well received.[38] The high rate of PDA use further reflects strong engagement with the decision-making process. Importantly, reasons for non-use were largely related to logistical aspects of the trial rather than a lack of relevance or acceptance. Both patients and healthcare providers reported high levels of SDM, though patients rated the experience higher, reflecting possible differences in perception or potentially reflecting critical self-evaluation from healthcare providers.

In line with the overall positive SDM ratings, patients reported low decisional conflict, with only a small proportion experiencing high conflict following the decision. This suggests the combined use of a PDA and structured SDM approach can support informed and confident decision-making. Interestingly, among patients with high decisional conflict, only one had a below-average SDM-Q9 score, implying that inadequate SDM was not the primary cause of conflict in most cases. In fact, the 5 patients who completed the SDM-Q9, all rated their experience at the maximum score, further supporting this interpretation. Further analysis revealed that 88% of patients experiencing high decisional conflict were female, with greater representation from the MMR group (38%) and a shorter median time since diagnosis (6.2 years; IQR: 5.0). These patterns suggest that gender and a recent diagnosis may contribute to increased uncertainty, even within the context of high-quality SDM. Supporting this, results from the EORTC QLQ-CML24 indicated that women reported lower satisfaction with care and information six months after dose reduction (*Online Supplementary Figure S1*), highlighting a potential role of gender on this process. Follow-up data on decisional regret at twelve months will provide additional insight into the long-term effects of the decision-making process.

The observed OPTION5 score exceeds the commonly reported benchmark of 25 and national averages, suggesting a potential added benefit of the e-learning intervention for healthcare providers.[39,40] It is important to recognize that some healthcare providers had already addressed key decision-making elements during the informed consent consultation and only briefly referenced them during the SDM consult. This may have led to certain SDM behaviors being under-represented, possibly underestimating SDM performance compared to routine, non-trial settings.

An important limitation of this study is the absence of a screening log. Consequently, there is no information on the number of patients assessed for eligibility, reasons for exclusion, or the proportion of eligible patients who declined

participation. Additionally, as with all single-arm trials, there is an inherent risk of overattributing observed effects to the intervention due to the absence of a randomized control group. This limitation is relevant when interpreting patient-reported outcomes, as it introduces a risk of overestimating QoL and underestimating symptom burden.[41] Nonetheless, more statistically significant changes were observed across sex and TKI usage subgroups, suggesting an intervention effect.

Although widely used, the SDM-Q9 and SDM-Q-Doc have limitations. Prior studies have shown discrepancies between observer and patient-reported SDM, with the latter often showing ceiling effects, i.e., scores clustered at the top with limited variability.[42,43] These effects may result from patients' unfamiliarity with SDM or difficulty distinguishing it from general care satisfaction (halo effects), reducing the sensitivity of these tools to detect meaningful differences. In the light of the ultimate treatment goal of CML, i.e., treatment-free remission, TKI dose reduction is increasingly being used as a step toward eventual treatment discontinuation. This approach has been explored in studies such as the DESTINY trial and is currently being further investigated in the HALF trial (*clinicaltrials.gov NCT04147533*).[30] However, these studies do not incorporate SDM and PDA to decide on dose reduction steps, elements that were identified as highly important by patients and healthcare providers.[44] Future research should, therefore, focus on integrating SDM and PDA into these treatment decisions. Evaluating these components may not only enhance the decision-making process but also contribute to greater patient satisfaction in CML care.[9,10]

To conclude, patient-guided dose reduction, supported by SDM and a PDA, appears to be a safe and well-accepted approach for patients with CML in stable remission. At six months, the strategy was associated with low rates of intervention failure, improvements in specific domains of HRQoL, a positively evaluated SDM process, and minimal decisional conflict. These findings suggest that this approach may effectively reduce treatment burden without compromising clinical outcomes. Ongoing follow-up will be essential to determine which patient subgroups derive the greatest benefit from TKI dose reduction.

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Contributions

DNL contributed to study conceptualization, methodology, formal analysis, investigation, data curation, and wrote and visualized the original draft. YS contributed to funding acquisition, study conceptualization, methodology and supervision, and reviewing and editing the manuscript. BJFB and RPMH were involved in conceptualization, methodology, and reviewing and editing the manuscript. MRN, AKSJ, LGMD, SKK, EFMP, PEW, MD and MH contributed resources (patient inclusion), and reviewed and edited the manuscript. NMAB was involved in conceptualization, methodology, reviewing and editing the manuscript, supervision, and funding acquisition. CLB was involved in conceptualization, methodology, reviewing and editing the manuscript, supervision, funding acquisition, and was responsible for project administration.

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Data-sharing statement

The datasets generated and/or analyzed during the current study are not publicly available due to ongoing follow-up in the RODEO trial but will become available upon publication of the final results. The data on SDM results are presented in the manuscript or in the Online Supplementary Appendix..

References

1. Bower H, Björkholm M, Dickman PW, Höglund M, Lambert PC, Andersson TM-L. Life expectancy of patients with chronic myeloid leukemia approaches the life expectancy of the general population. J Clin Oncol. 2016;34(24):2851-2857.
2. Schoenbeck KL, Flynn KE. Health-related quality of life of patients with chronic myeloid leukemia as measured by patient-reported outcomes: current state and future directions. Curr Hematol Malig Rep. 2021;16(6):491-499.
3. Lipton JH, Brümmendorf TH, Gambacorti-Passerini C, Garcia-Gutiérrez V, Deininger MW, Cortes JE. Long-term safety review of tyrosine kinase inhibitors in chronic myeloid leukemia - What to look for when treatment-free remission is not an option. Blood Rev. 2022;56:100968.
4. Chen J, Zhu Y, Zhao Y, et al. Dose optimization of tyrosine

kinase inhibitors for chronic myeloid leukemia. Clin Pharmacol. 2025;17:211-225.
5. Dalgetty M, Cortes J. Considerations on the dose and schedule of tyrosine kinase inhibitors for chronic myeloid leukemia: does dose matter? Blood. 2025;145(23):2701-2708.
6. Oehler VG, Huang IJ, Siu C, et al. Dose modifications in the management of chronic phase chronic myeloid leukemia: who, what, and when. J Natl Compr Canc Netw. 2024;22(9):e247044.
7. Lou J, Huang J, Wang Z, et al. Chronic myeloid leukemia patients and treatment-free remission attitudes: a multicenter survey. Patient Prefer Adherence. 2018;12:1025-1032.
8. Sharf G, Marin C, Bradley JA, et al. Treatment-free remission in chronic myeloid leukemia: the patient perspective and areas of unmet needs. Leukemia. 2020;34(8):2102-2112.
9. Clements J, Fleischman A, Lerner V, Ruiz C. The importance of developing open communication and a professional, long-term relationship between patients with chronic myeloid leukemia and their oncologist. Future Oncol. 2023;19(17):1197-1208.
10. Geerts PAF, van der Weijden T, Moser A, Bos GMJ. The perception of shared decision-making in hematology by patients and physicians seems satisfactory, but important steps are still ahead of us. Hemasphere. 2020;4(4):e417.
11. Lang F, Pemberton-Whiteley Z, Clements J, et al. Improving chronic myeloid leukemia management and quality of life: patient and physician survey on unmet needs from the CML SUN survey. Haematologica. 2026;111(2):597-608.
12. Stiggelbout AM, Pieterse AH, De Haes JC. Shared decision making: concepts, evidence, and practice. Patient Educ Couns. 2015;98(10):1172-1179.
13. Stacey D, Lewis KB, Smith M, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev. 2024;1(1):CD001431.
14. Djodikromo MF, Hermens RP, Bemt B, et al. Patient-guided dose reduction of tyrosine kinase inhibitors in chronic myeloid leukaemia (RODEO study): study protocol for a prospective, multicentre, single-arm trial. BMC Cancer. 2023;23(1):231.
15. Des Jarlais DC, Lyles C, Crepaz N. Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. Am J Public Health. 2004;94(3):361-366.
16. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365-376.
17. Efficace F, Cardoni A, Cottone F, Vignetti M, Mandelli F. Tyrosine-kinase inhibitors and patient-reported outcomes in chronic myeloid leukemia: a systematic review. Leuk Res. 2013;37(2):206-213.
18. Efficace F, Iurlo A, Patriarca A, et al. Validation and reference values of the EORTC QLQ-CML24 questionnaire to assess health-related quality of life in patients with chronic myeloid leukemia. Leuk Lymphoma. 2021;62(3):669-678.
19. Kriston L, Scholl I, Hölzel L, Simon D, Loh A, Härter M. The 9-item Shared Decision Making Questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample. Patient Educ Couns. 2010;80(1):94-99.
20. Rodenburg-Vandenbussche S, Pieterse AH, Kroonenberg PM, et al. Dutch translation and psychometric testing of the 9-item Shared Decision Making Questionnaire (SDM-Q-9) and Shared Decision Making Questionnaire-Physician Version (SDM-Q-Doc) in primary and secondary care. PLoS One. 2015;10(7):e0132158.
21. Scholl I, Kriston L, Dirmaier J, Buchholz A, Härter M. Development and psychometric properties of the Shared Decision Making Questionnaire--physician version (SDM-Q-Doc). Patient Educ Couns. 2012;88(2):284-290.
22. Barr PJ, O'Malley AJ, Tsulukidze M, Gionfriddo MR, Montori V, Elwyn G. The psychometric properties of Observer OPTION(5), an observer measure of shared decision making. Patient Educ Couns. 2015;98(8):970-976.
23. Elwyn G, Hutchings H, Edwards A, et al. The OPTION scale: measuring the extent that clinicians involve patients in decision-making tasks. Health Expect. 2005;8(1):34-42.
24. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making. 1995;15(1):25-30.
25. Fayers P, Aaronson NK, Bjordal K, et al. The EORTC QLQ-C30 scoring manual (3rd ed). European Organisation for Research and Treatment of Cancer, Brussels, 2001.
26. Cocks K, King MT, Velikova G, et al. Evidence-based guidelines for interpreting change scores for the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. Eur J Cancer. 2012;48(11):1713-1721.
27. Janssen KJ, Donders AR, Harrell FE Jr, et al. Missing covariate data in medical research: to impute is better than to ignore. J Clin Epidemiol. 2010;63(7):721-727.
28. Tromp VNMF, Timmers L, Koningen L, et al. Tyrosine kinase inhibitor treatment discontinuation in chronic myeloid leukemia: patient views. Leuk Lymphoma. 2021;62(3):649-658.
29. Clark RE, Polydoros F, Apperley JF, et al. De-escalation of tyrosine kinase inhibitor dose in patients with chronic myeloid leukaemia with stable major molecular response (DESTINY): an interim analysis of a non-randomised, phase 2 trial. Lancet Haematol. 2017;4(7):e310-e316.
30. Clark RE, Polydoros F, Apperley JF, et al. De-escalation of tyrosine kinase inhibitor therapy before complete treatment discontinuation in patients with chronic myeloid leukaemia (DESTINY): a non-randomised, phase 2 trial. Lancet Haematol. 2019;6(7):e375-e383.
31. Netherlands Comprehensive Cancer Organisation (IKNL), Netherlands Cancer Registry (NKR). Data from: Zorgpadanalyse CML [restricted dataset]. Deposited 2024. Accessed February 20, 2025.
32. Efficace F, Mahon F-X, Richter J, et al. Health-related quality of life and symptoms of chronic myeloid leukemia patients after discontinuation of tyrosine kinase inhibitors: results from the EURO-SKI Trial. Leukemia. 2024;38(8):1722-1730.
33. Bostan H, Toptas T, Tanrikulu FP, et al. Quality of life and symptom burden with first- and second-generation tyrosine kinase inhibitors in patients with chronic-phase chronic myeloid leukemia. Clin Lymphoma Myeloma Leuk. 2020;20(12):836-842.
34. Foulon S, Cony-Makhoul P, Guerci-Bresler A, et al. Health state utility and quality of life measures in patients with chronic myeloid leukemia in France. Qual Life Res. 2021;30(7):2021-2032.
35. Malagola M, Iurlo A, Abruzzese E, et al. Molecular response and quality of life in chronic myeloid leukemia patients treated with intermittent TKIs: first interim analysis of OPTkIMA study. Cancer Med. 2021;10(5):1726-1737.
36. Smit Y, Scheuter P, Lange MPM, et al. Patient-reported toxicity symptoms during tyrosine kinase inhibitor treatment in chronic myeloid leukemia: a systematic review and meta-analysis. Support Care Cancer. 2025;33(5):446.
37. Berger MG, Pereira B, Rousselot P, et al. Longer treatment duration and history of osteoarticular symptoms predispose to tyrosine kinase inhibitor withdrawal syndrome. Br J Haematol. 2019;187(3):337-346.
38. van der Weijden T, van der Kraan J, Brand PLP, et al. Shared

decision-making in the Netherlands: progress is made, but not for all. Time to become inclusive to patients. Z Evid Fortbild Qual Gesundhwes. 2022;171:98-104.
39. Couët N, Desroches S, Robitaille H, et al. Assessments of the extent to which health-care providers involve patients in decision making: a systematic review of studies using the OPTION instrument. Health Expect. 2015;18(4):542-561.
40. Driever EM, Stiggelbout AM, Brand PLP. Patients' preferred and perceived decision-making roles, and observed patient involvement in videotaped encounters with medical specialists. Patient Educ Couns. 2022;105(8):2702-2707.
41. Di Maio M. The value of patient-reported outcomes in single-arm cancer trials. Cancer Invest. 2023;41(5):491-494.
42. Baghus A, Giroldi E, van Geel J, et al. Shared decision-making performance of general practice residents: an observational study combining observer, resident, and patient perspectives. Fam Pract. 2024;41(1):50-59.
43. Kunneman M, LaVecchia CM, Singh Ospina N, et al. Reflecting on shared decision making: a reflection-quantification study. Health Expect. 2019;22(5):1165-1172.
44. Rood JAJ, Nauta IH, Witte BI, et al. Shared decision-making and providing information among newly diagnosed patients with hematological malignancies and their informal caregivers: not "one-size-fits-all". Psychooncology. 2017;26(12):2040-2047.