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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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Interim analysis of TKI dose reduction in CML

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Authors' contributions

DNL contributed to conceptualization, methodology, formal analysis, investigation, data curation, writing – original draft, and visualization. YS contributed to funding acquisition, conceptualization, methodology, supervision, and writing – review & editing. BJFB and RPMH were involved in conceptualization, methodology, and writing – review & editing. MRN, AKSJ, LGMD, SKK, EFMP, PEW, MD, and MH contributed resources (patient inclusion) and writing – review & editing. CLB and NMAB contributed equally to this work and were involved in conceptualization, methodology, writing – review & editing, supervision, and funding acquisition, with CLB also responsible for project administration.

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 its supplementary files.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used ChatGPT to enhance language and improve readability. All content was thoroughly reviewed and edited as needed, and the authors take full responsibility for the final version of the publication.

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Competing Interests statement

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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 EORTC QLQ-C30, QLQ-CML24, and IL156. 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.

1. Introduction

Tyrosine kinase inhibitors (TKIs) 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, TKIs cause drug adverse events that significantly impair health-related quality of life (HRQoL) and tolerability [2]. Common adverse events include fatigue, muscle cramps, pain, oedema, 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 and 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 (PDAs) is advocated [13]. PDAs 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 TKIs 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 the willingness and extent of dose reduction; (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 six months 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* (%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 also assess the experiences of a patient-centered approach in achieving this goal.

2. Methods

2.1. 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, norm 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 (No. 2021–3457). The TREND statement was followed during reporting (see Supplementary Table S1)[15].

2.2. Data collection

To evaluate molecular response, *BCR::ABL1* levels (%IS) were monitored through blood samples. Timing of measurements and detailed questionnaire descriptions are in the Supplementary Information, Supplemental Table A, and study protocol[14]. In short, HRQoL and symptom burden were assessed using the EORTC QLQ-C30 (version 3.0), QLQ-CML24, and IL156[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 (www.schoolvoorsamenbeslissen.nl *Dutch school for shared decision-making*)[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].

2.3. 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 Supplementary Information[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 (</≥ 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 (max 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 data (mean ± SD or median with IQR). 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. A p-value of <0.05 was considered statistically significant.

SDM 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 Supplementary Information.

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

3. Results

A total of 148 patients provided informed consent (see Figure 1), of whom 146 were included in this analysis (see 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 six months follow-up was 25% (IQR 8.4) of the initial dose.

3.1. Intervention failure

At six months follow-up, a total of six participants re-escalated their dose (4.1%). Of these, four patients re-escalated their dose because of expected (n=1) or loss of MMR (n=3) 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 (see 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 Table S2.

3.2. 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). Table S3 depicts 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 (see 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 Table S4. Median and mean values for all items and measurements are provided in Table S5.

Exploratory subgroup analysis showed that more statistically significant mean changes occurred among females and dasatinib-users (see Figure S1). 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 TKIs 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).

3.3. 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 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 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). Table S8 depicts medians per DCS subscore. A total of 7.5% of the patients reported to have a high decisional conflict after the choice for dose reduction (total DCS score ≥ 37.5).

4. Discussion

While survival outcomes for patients with CML have significantly improved in recent years, 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 six-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.

4.1. Study population and intervention failure

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 TKIs [31]. The RODEO trial included a higher proportion of patients treated with second-generation TKIs compared to the DESTINY trial. This distinction offers valuable insights into the differential outcomes associated with various TKIs. 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) (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.

4.2. HRQoL and symptom burden

Baseline EORTC mean and median scores in the RODEO population are comparable to those reported in previous studies of patients with CML (see 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 form moderate/severe to mild problems with fatigue (Table S3). Interestingly, subgroup analysis suggests that women and dasatinib-users (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, 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 (Table S3).

In this interim analysis, only a limited number of subgroup analyses were performed, focusing on sex, age (</≥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.

4.3. SDM and decisional conflict

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 five 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 (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 underrepresented, possibly underestimating SDM performance compared to routine, non-trial settings.

4.4. Limitations

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.

4.5. Future perspectives and conclusions

In light of the ultimate treatment goal of CML: 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 (NCT04147533) [30]. However, these studies do not incorporate SDM and PDAs 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 PDAs 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.

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. 2025 Jul 10. doi: 10.3324/haematol.2025.287772. [Epub ahead of print.]

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 Edition). Published by: 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 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.

Tables

Participants (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 (%)	67 (45.9)
Imatinib	6 (9.0)
High dose	49 (73.1)
Norm dose	12 (17.9)
Low dose	36 (24.7)
Dasatinib	-
High dose	18 (50)
Norm dose	18 (50)
Low dose	32 (21.9)
Nilotinib	3 (8.3)
High dose	20 (55.6)
Norm dose	9 (25)
Low dose	9 (6.2)
Bosutinib	-
High dose	4 (44.4)
Norm dose	5 (55.6)
Low dose	2 (1.4)
Ponatinib (low dose)	
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)

Table 1. Participant baseline characteristics of the study

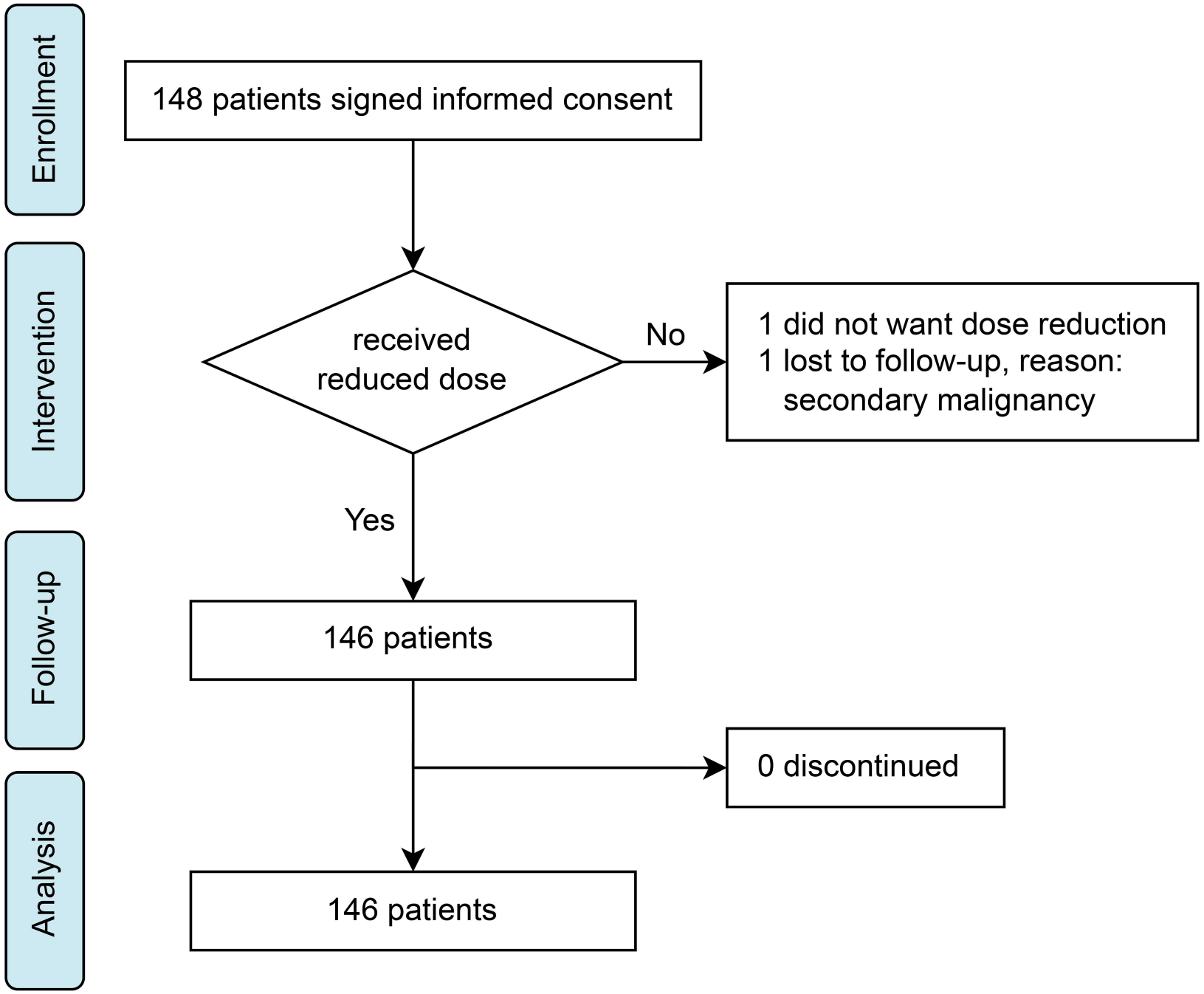
[a] n=132. Abbreviations; SD: standard deviation; IQR: Interquartile range; TKI: tyrosine kinase inhibitor; IS: international scale; MR: molecular response; MMR: major molecular remission; DMR: deep molecular remission.

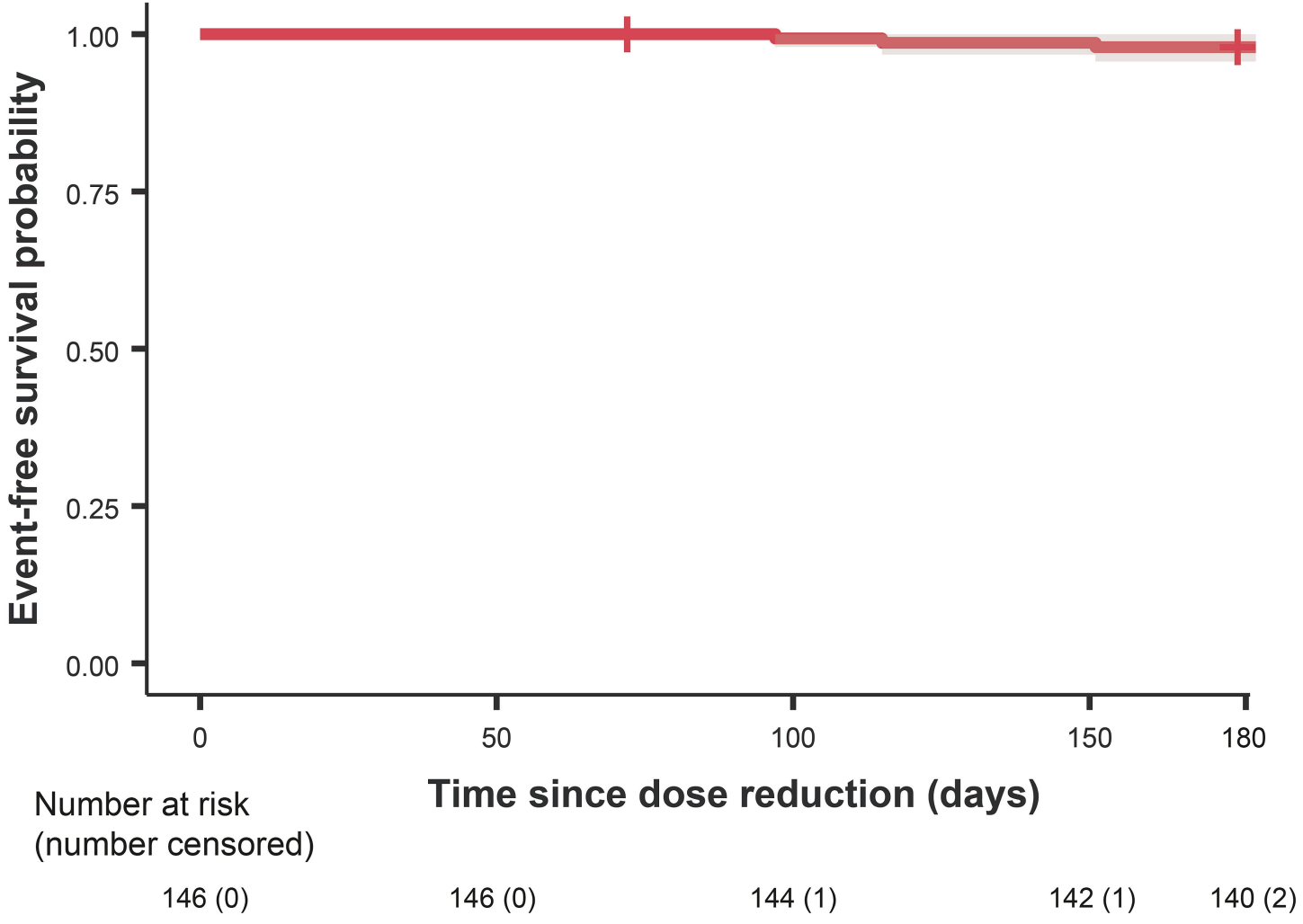
Figure legends

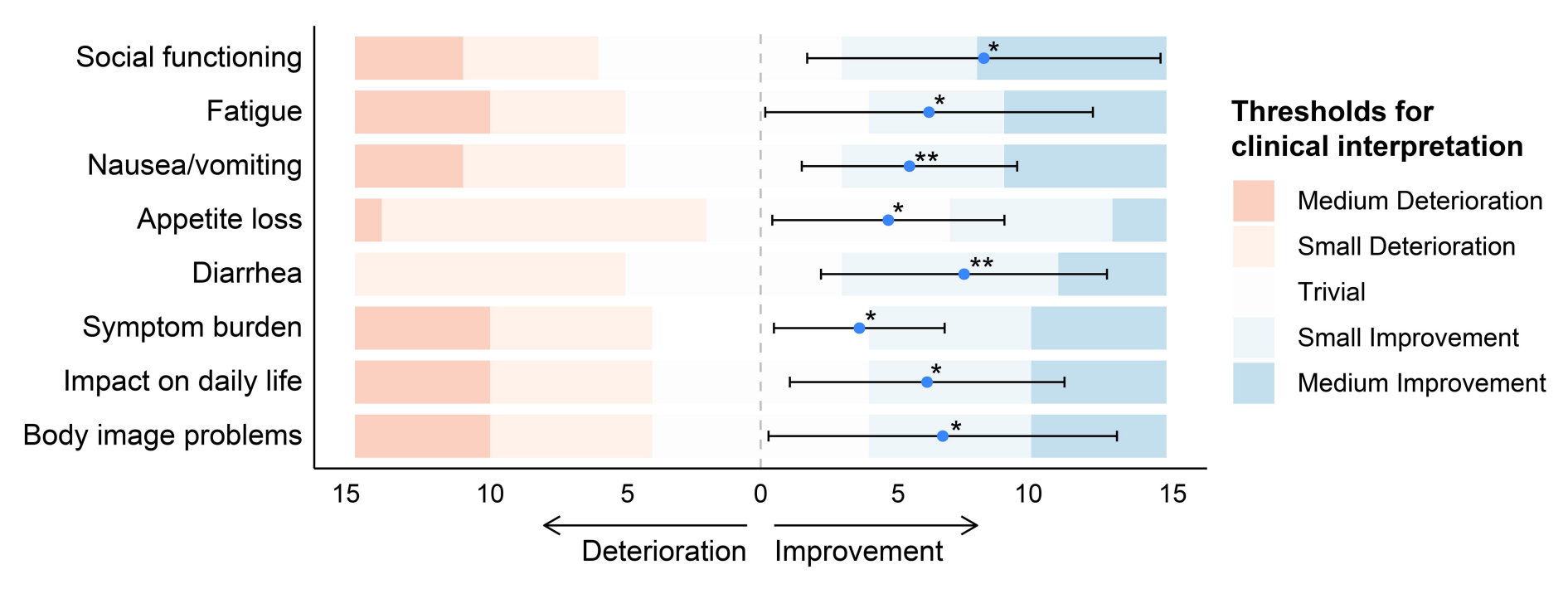
Figure 1. Participant flow

Figure 2. Event-free survival curve for MMR over six months following dose reduction.

Figure 3. Statistically significant mean changes in EORTC QLQ-C30, CML24, and IL156 scales after six months. Dots with 95% confidence intervals represent the observed mean changes in EORTC scores. Asterisks indicate levels of statistical significance: $p \leq 0.05$ (*) and $p \leq 0.01$ (**). Colored bars indicate evidence-based thresholds for meaningful differences on the EORTC scales, based on the criteria established by Cocks et al. (26).


Enrollment
Intervention
Follow-up
Analysis
148 patients signed informed consent
received reduced dose
No
1 did not want dose reduction
1 lost to follow-up, reason: secondary malignancy
Yes
146 patients
0 discontinued
146 patients


Event-free survival probability
1.00
0.75
0.50
0.25
0.00
0
50
100
150
180
Time since dose reduction (days)
Number at risk
(number censored)
146 (0)
146 (0)
144 (1)
142 (1)
140 (2)


Social functioning
Fatigue
Nausea/vomiting
Appetite loss
Diarrhea
Symptom burden
Impact on daily life
Body image problems
*
*
**
*
**
*
*
*
15
10
5
0
5
10
15
Deterioration
Improvement
Thresholds for clinical interpretation
Medium Deterioration
Small Deterioration
Trivial
Small Improvement
Medium Improvement

Supplementary Information

The Supplementary Information is divided into two parts: Part 1 provides detailed methodological information, and Part 2 (starting on page 5) contains all supplementary tables and figures referenced in the main text.

Part 1: Supplementary Information on Methods

2.2. Data collection

Table A. Timing of assessments at six months follow-up in the RODEO study.

Assessment	Baseline	Start dose reduction	Follow-up		
			Week 6	Month 3	Month 6
BCR::ABL1 (%IS)	X		X	X	X
HRQoL and symptom burden (EORTC QLQ30, CML24 & IL156)	X		X	X	X
Process of SDM (Observer OPTION 5)		X (during first SDM consult)			
Process of SDM (SDM-Q9)		X (directly after SDM consult)			
Process of SDM (SDM-Q-doc)		X (after the healthcare provider's third consult)			
Decisional conflict (DCS)			X		

Abbreviations; IS: international scale; HRQoL: health related quality of life; EORTC: European Organisation for Research and Treatment of Cancer; QLQ: quality of life questionnaire; CML: chronic myeloid leukemia; IL: item library; SDM: shared decision making; DCS: decisional conflict scale.

To assess HRQoL, the EORTC QLQ-C30 (version 3.0) and its CML-specific module, QLQ-CML24, were used. The EORTC QLQ-C30 is widely utilized for measuring QoL in various malignancies, including CML [1, 2]. It evaluates five functional scales (physical, role, emotional, social, and cognitive), three symptom scales (fatigue, nausea/vomiting, and pain), global health status/QoL, and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) on a 4-point scale. Similarly, the EORTC QLQ-CML24 is a validated 24-item CML-specific scale including four multi-item scales (symptom burden, impact on worry/mood, impact on daily life, and satisfaction with social life) and two single items (body image problems and satisfaction with social life) [3]. To examine symptom burden, the symptom scales and individual symptom items of the EORTC QLQ-CML24 and QLQ-C30

questionnaire were evaluated, as well as the EORTC IL156, accessible via the EORTC Item Library. The IL156 complements existing HRQoL measures, specifically addressing symptoms of TKI use in CML. The EORTC QLQ-C30, CML24, and IL156 were used on prespecified timepoints as detailed in Table A.

Directly after the SDM consultation, patients completed the Shared Decision-Making Questionnaire (SDM-Q9) to evaluate their experience [4, 5]. Similarly, healthcare providers filled out the SDM-Q-Doc following their consultation with the third participant they enrolled in the study [5, 6]. Both tools are concise self-assessment questionnaires: the SDM-Q-9 captures the patient's perspective on the decision-making process, while the SDM-Q-Doc reflects the provider's self-assessed effectiveness in supporting and guiding that process. Each questionnaire contains nine items, rated on a six-point Likert scale ranging from 'completely disagree' (0 points) to 'completely agree' (5 points). In addition, an independent expert in SDM (www.schoolvoorsamenbeslissen.nl *Dutch school for shared decision-making)* evaluated consultations with the Observer OPTION 5 instrument using audio recordings of the healthcare providers' first SDM session in the RODEO trial [7]. This instrument is considered well-suited for use in oncology practice and assesses five key decision-making behaviors, each rated on a scale from 0 (no effort made) to 4 (exemplary effort made) [8].

The impact of the decision to reduce TKI dose on patient's distress was evaluated at six week follow-up using the traditional Decisional Conflict Scale (DCS). This is a 16-item validated questionnaire that evaluates levels of uncertainty in decision-making, factors contributing to this uncertainty, and the effectiveness of the decision-making process [9]. The scale includes a total score and five subscales: informed, support, values clarity, uncertainty, and effective decision. Responses are recorded on a five-point Likert scale ranging from 0 (strongly disagree) to 4 (strongly agree).

2.3. Data analysis and outcomes

The targeted sample size of 140 patients was determined based on a priori statistical calculations. Specifically, a sample of this size would allow estimation of the treatment failure rate with a two-sided 90% Clopper-Pearson confidence interval, ensuring the upper limit remains below 28%, assuming a

treatment failure probability of 19% and a statistical power of at least 80%. To account for an anticipated dropout rate of approximately 5%, the final required sample size was adjusted to 147 patients opting for TKI dose reduction.

The scores for the nine items on the SDM questionnaires were linearly transformed to a 0 (no SDM) to 100 (maximum SDM) score. If a maximum of two items were missing, their values were imputed using the average of the scored items; questionnaires with more than two missing items were excluded from analysis [4]. Similarly, the Observer OPTION 5 scores per healthcare provider were expressed on a scale from 0 to 100. This score reflects the degree to which the healthcare provider demonstrated the communication behaviors necessary to involve patients in the decision-making process [10].

Scores for each DCS scale were calculated following the guidelines provided in the manual, with higher scores indicating greater decisional conflict [11]. The scores range from 0 (extremely low decisional conflict) to 100 (extremely high decisional conflict). No imputation was performed; therefore, total scores and subscores with missing values were excluded from the analysis.

References Part 1: Supplementary Information on Methods

1. 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.

2. Efficace F, Cardoni A, Cottone F, Vignetti M, Mandelli F. Tyrosine-kinase inhibitors and patient-reported outcomes in chronic myeloid leukemia: A systematic review. Leukemia Research. 2013;37(2):206-213.

3. 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. Leukemia & Lymphoma. 2021;62(3):669-678.

4. 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.

5. 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.

6. 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.

7. 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.

8. Butow P, Juraskova I, Chang S, Lopez AL, Brown R, Bernhard J. Shared decision making coding systems: how do they compare in the oncology context? Patient Educ Couns. 2010;78(2):261-268.

9. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making. 1995;15(1):25-30.

10. 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.

11. O'connor A. User manual-decisional conflict scale. Ottawa: Ottawa Hospital Research Institute. 1993;1993

Part 2: Supplementary Tables and Figures

Table S1. TREND statement checklist [1].

TREND Statement Checklist

Paper Section/ Topic	Item No	Descriptor	Reported? ✓	Reported? section Pg #
Title and Abstract				
Title and Abstract	1	• Information on how unit were allocated to interventions	Yes	abstract
		• Structured abstract recommended	NA	
		• Information on target population or study sample	Yes	abstract
Introduction				
Background	2	• Scientific background and explanation of rationale	Yes	1.
		• Theories used in designing behavioral interventions	NA	
Methods				
Participants	3	• Eligibility criteria for participants, including criteria at different levels in recruitment/sampling plan (e.g., cities, clinics, subjects)	Yes	2.1
		• Method of recruitment (e.g., referral, self-selection), including the sampling method if a systematic sampling plan was implemented	Yes	ref
		• Recruitment setting	Yes	ref
		• Settings and locations where the data were collected	Yes	2.1
Interventions	4	• Details of the interventions intended for each study condition and how and when they were actually administered, specifically including:	Yes	ref
		○ Content: what was given?	Yes	ref
		○ Delivery method: how was the content given?	Yes	ref
		○ Unit of delivery: how were the subjects grouped during delivery?	Yes	ref
		○ Deliverer: who delivered the intervention?	Yes	ref
		○ Setting: where was the intervention delivered?	Yes	ref
		○ Exposure quantity and duration: how many sessions or episodes or events were intended to be delivered? How long were they intended to last?	NA	
		○ Time span: how long was it intended to take to deliver the intervention to each unit?	Yes	ref
		○ Activities to increase compliance or adherence (e.g., incentives)	NA	
Objectives	5	• Specific objectives and hypotheses	Yes	2.2
Outcomes	6	• Clearly defined primary and secondary outcome measures	Yes	2.3
		• Methods used to collect data and any methods used to enhance the quality of measurements	Yes	2.2
		• Information on validated instruments such as psychometric and biometric properties	Yes	ref
Sample Size	7	• How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	Yes	ref
Assignment Method	8	• Unit of assignment (the unit being assigned to study condition, e.g., individual, group, community)	Yes	2.1
		• Method used to assign units to study conditions, including details of any restriction (e.g., blocking, stratification, minimization)	NA	
		• Inclusion of aspects employed to help minimize potential bias induced due to non-randomization (e.g., matching)	NA	

TREND Statement Checklist

Blinding (masking)	9	• Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to study condition assignment; if so, statement regarding how the blinding was accomplished and how it was assessed.	NA	
Unit of Analysis	10	• Description of the smallest unit that is being analyzed to assess intervention effects (e.g., individual, group, or community)	NA	
		• If the unit of analysis differs from the unit of assignment, the analytical method used to account for this (e.g., adjusting the standard error estimates by the design effect or using multilevel analysis)	NA	
Statistical Methods	11	• Statistical methods used to compare study groups for primary methods outcome(s), including complex methods of correlated data	Yes	2.3
		• Statistical methods used for additional analyses, such as a subgroup analyses and adjusted analysis	NA	
		• Methods for imputing missing data, if used	Yes	2.3
		• Statistical software or programs used	Yes	2.3
Results				
Participant flow	12	• Flow of participants through each stage of the study: enrollment, assignment, allocation, and intervention exposure, follow-up, analysis (a diagram is strongly recommended)	Yes (partly)	Fig. 1
		○ Enrollment: the numbers of participants screened for eligibility, found to be eligible or not eligible, declined to be enrolled, and enrolled in the study	NA	
		○ Assignment: the numbers of participants assigned to a study condition	Yes	Fig. 1
		○ Allocation and intervention exposure: the number of participants assigned to each study condition and the number of participants who received each intervention	Yes	Fig. 1
		○ Follow-up: the number of participants who completed the follow-up or did not complete the follow-up (i.e., lost to follow-up), by study condition	Yes	Fig. 1
		○ Analysis: the number of participants included in or excluded from the main analysis, by study condition	Yes	Fig. 1
		• Description of protocol deviations from study as planned, along with reasons	NA	
Recruitment	13	• Dates defining the periods of recruitment and follow-up	Yes	3.
Baseline Data	14	• Baseline demographic and clinical characteristics of participants in each study condition	Yes	Table 1
		• Baseline characteristics for each study condition relevant to specific disease prevention research	NA	
		• Baseline comparisons of those lost to follow-up and those retained, overall and by study condition	NA	
		• Comparison between study population at baseline and target population of interest	Yes (exploratory)	4.1
Baseline equivalence	15	• Data on study group equivalence at baseline and statistical methods used to control for baseline differences	No	

TREND Statement Checklist

Numbers analyzed	16	• Number of participants (denominator) included in each analysis for each study condition, particularly when the denominators change for different outcomes; statement of the results in absolute numbers when feasible	Yes	3.2 & 3.3
		• Indication of whether the analysis strategy was "intention to treat" or, if not, description of how non-compliers were treated in the analyses	Yes	3.
Outcomes and estimation	17	• For each primary and secondary outcome, a summary of results for each estimation study condition, and the estimated effect size and a confidence interval to indicate the precision	Yes	3.1 3.2
		• Inclusion of null and negative findings	NA	
		• Inclusion of results from testing pre-specified causal pathways through which the intervention was intended to operate, if any	NA	
Ancillary analyses	18	• Summary of other analyses performed, including subgroup or restricted analyses, indicating which are pre-specified or exploratory	Yes	3.2
Adverse events	19	• Summary of all important adverse events or unintended effects in each study condition (including summary measures, effect size estimates, and confidence intervals)	NA	
DISCUSSION				
Interpretation	20	• Interpretation of the results, taking into account study hypotheses, sources of potential bias, imprecision of measures, multiplicative analyses, and other limitations or weaknesses of the study	Yes	4.1-5
		• Discussion of results taking into account the mechanism by which the intervention was intended to work (causal pathways) or alternative mechanisms or explanations	Yes	4.5
		• Discussion of the success of and barriers to implementing the intervention, fidelity of implementation	Yes	4.4
		• Discussion of research, programmatic, or policy implications	No	
Generalizability	21	• Generalizability (external validity) of the trial findings, taking into account the study population, the characteristics of the intervention, length of follow-up, incentives, compliance rates, specific sites/settings involved in the study, and other contextual issues	Yes	4.1 & 4.4
Overall Evidence	22	• General interpretation of the results in the context of current evidence and current theory	Yes	4.1,2,3,5

From: Des Jarlais, D. C., Lyles, C., Crepaz, N., & the Trend Group (2004). Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: The TREND statement. *American Journal of Public Health*, 94, 361-366. For more information, visit: http://www.cdc.gov/trendstatement/

ref.: Djodikromo, M. F., Hermens, R. P., Bemt, B. J. V. D., Smit, Y., Govers, T. M., Bekker, C. L., & Blijlevens, N. M. (2023). 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, 23(1), 231. https://doi.org/10.1186/s12885-023-10697-6

Table S2. Characteristics of patients with (expected) loss of MMR

	Expected loss of MMR	Loss of MMR		
Gender	F	F	F	M
Age	58	62	35	56
Median time since diagnosis, years	15.1	5.4	13.8	4.7
TKI used	Imatinib (norm dose)	Imatinib (norm dose)	Imatinib (norm dose)	Dasatinib (low dose (70 mg))
Molecular response of *BCR::ABL1* (IS)	5	4	5	4.5
Time in MMR or DMR, years	11	3.2	9.0	3.8
Dose reduction provided	25%	14%	50%	29%

Abbreviations; MMR: major molecular remission; TKI: tyrosine kinase inhibitor; IS: international scale; DMR: deep molecular remission.

Table S3. Symptom severity per timepoint. b = baseline, t1 = 6 weeks after dose reduction, t2 = 3 months after dose reduction, and t3 = 6 months after dose reduction.

C30	Fatigue				Nausea/vomiting				Pain				Dyspnea				Insomnia				Appetite loss				Constipation				Diarrhea			
Timepoint	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3
Not at all	18%	26%	21%	18%	71%	80%	81%	80%	54%	57%	49%	52%	57%	66%	61%	64%	52%	60%	58%	52%	85%	86%	88%	88%	80%	79%	81%	82%	69%	80%	78%	78%
Mild	72%	66%	74%	74%	25%	20%	18%	18%	35%	35%	43%	42%	34%	25%	32%	26%	27%	26%	32%	32%	8%	12%	8%	10%	14%	16%	16%	14%	21%	18%	18%	20%
Moderate to severe	10%	8%	5%	8%	4%	-	1%	2%	11%	8%	8%	6%	9%	8%	8%	9%	21%	14%	11%	16%	7%	2%	4%	3%	6%	5%	3%	4%	10%	2%	4%	3%
Responses (N)	137	130	131	117	137	130	131	115	137	131	132	119	139	130	133	121	136	130	132	118	137	130	130	115	135	130	129	113	136	128	130	112

CML24	Abdominal pains or cramps				Dry mouth				Skin problems				Headache				Aches or pains in muscles or joints				Hair loss				Excessive sweating				Heartburn			
	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3
	67%	80%	79%	75%	49%	55%	56%	62%	55%	61%	55%	52%	68%	67%	65%	69%	24%	33%	31%	31%	74%	84%	80%	80%	67%	70%	72%	72%	71%	79%	79%	77%
	25%	16%	15%	21%	37%	37%	30%	24%	27%	25%	31%	38%	24%	27%	27%	22%	43%	41%	40%	36%	17%	13%	15%	15%	23%	24%	19%	16%	20%	19%	17%	17%
	8%	4%	6%	5%	14%	8%	14%	14%	18%	14%	14%	10%	7%	5%	8%	9%	33%	26%	28%	33%	9%	4%	5%	5%	10%	6%	9%	13%	10%	2%	4%	6%
	139	132	135	126	138	131	134	125	139	132	135	125	139	132	134	123	138	129	134	122	138	128	133	120	138	127	134	120	136	127	133	118

>>> Table continues on the next page.

Drowsiness				Oedema				Frequent urination				Eye problems				Muscle cramps				IL 156	Lack of energy				Sore or enlarged nipples or breasts				Feeling dizzy/lightheaded			
b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3		b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3
40%	51%	54%	50%	64%	77%	69%	71%	46%	50%	50%	51%	41%	50%	42%	47%	33%	42%	44%	44%		25%	31%	35%	30%	95%	97%	97%	95%	74%	69%	71%	80%
42%	35%	36%	36%	26%	18%	26%	21%	28%	31%	31%	29%	37%	35%	38%	34%	42%	48%	45%	32%		42%	45%	39%	42%	3%	2%	2%	3%	19%	27%	24%	17%
18%	13%	10%	14%	10%	6%	5%	8%	26%	18%	19%	20%	22%	15%	20%	18%	25%	10%	11%	23%		32%	24%	26%	27%	2%	1%	1%	2%	7%	4%	4%	4%
134	127	131	118	135	125	131	118	134	125	130	116	134	124	128	114	132	123	127	115		118	107	112	102	119	107	112	103	119	107	112	103

Clear thinking problems				Hearing problems				Painful or soreness in mouth				Taste changes				Flatulence problems				Muscle weakness				Coughing problems				Chest pain			
b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3
64%	69%	63%	64%	71%	77%	70%	65%	85%	89%	85%	84%	86%	91%	86%	88%	47%	53%	55%	51%	56%	70%	61%	58%	76%	79%	78%	80%	83%	83%	88%	87%
30%	28%	32%	33%	17%	15%	23%	28%	11%	9%	12%	11%	10%	7%	12%	10%	39%	33%	32%	35%	30%	23%	30%	29%	16%	14%	13%	13%	15%	15%	9%	13%
6%	3%	5%	3%	12%	8%	6%	7%	4%	2%	4%	5%	3%	2%	2%	2%	14%	14%	13%	14%	14%	7%	9%	13%	9%	8%	8%	7%	3%	2%	3%	-
119	107	112	103	117	106	111	101	119	106	110	97	118	105	108	96	118	103	109	92	117	103	107	91	116	103	106	91	115	102	106	90

Fever or chills				Temperature tolerance problems				Hot flushes				Tingling or numbness in hands/feet				Decreased libido				Less sexual enjoyment				Erection difficulty			
b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3	b	t1	t2	t3
85%	86%	81%	86%	62%	64%	65%	62%	83%	86%	86%	81%	54%	70%	55%	52%	57%	66%	57%	57%	60%	73%	63%	70%	52%	58%	52%	67%
14%	11%	12%	10%	28%	31%	26%	25%	9%	10%	9%	11%	32%	24%	32%	36%	16%	15%	14%	21%	15%	16%	19%	17%	20%	19%	28%	20%
1%	3%	7%	4%	10%	5%	9%	13%	8%	4%	5%	8%	13%	7%	13%	13%	27%	20%	29%	22%	25%	11%	19%	13%	28%	24%	21%	13%
114	102	105	90	113	102	103	89	112	102	103	89	112	102	102	87	100	87	86	72	93	82	81	83	60	59	58	46

Table S4. Mean changes and statistical outcomes for all EORTC QLQ-C30, CML24, and IL156 scales at 6 weeks, 3 months, and 6 months.

	Baseline vs 6 weeks				Baseline vs 3 months				Baseline vs 6 months			
QLQ C30	Δ	*P*	CI		Δ	*P*	CI		Δ	*P*	CI	
Global health status/QoL	3.92	0.111	-0.92	8.75	1.43	0.470	-2.49	5.35	4.69	0.057	-0.14	9.53
Functioning scales												
Physical functioning	4.60	0.026*	0.56	8.63	2.37	0.125	-0.67	5.40	2.60	0.173	-1.15	6.35
Role functioning	7.14	0.025*	0.90	13.39	4.23	0.159	-1.68	10.14	5.51	0.097	-1.01	12.03
Emotional functioning	5.02	0.023*	0.70	9.35	4.72	0.012*	1.05	8.39	3.75	0.115	-0.93	8.42
Cognitive functioning	7.36	0.006**	2.11	12.61	4.47	0.034*	0.35	8.59	4.05	0.156	-1.57	9.66
Social functioning	4.03	0.214	-2.35	10.41	5.15	0.022*	0.75	9.54	8.25	0.014*	1.72	14.78
Symptom scales												
Fatigue	-5.92	0.057	-12.01	0.17	-6.84	0.005**	-11.54	-2.15	-6.22	0.044*	-12.28	-0.17
Nausea/vomiting	-5.33	0.003*	-8.83	-1.82	-4.67	0.008**	-8.11	-1.22	-5.50	0.007**	-9.48	-1.52
Pain	-1.76	0.573	-7.94	4.41	-1.06	0.674	-6.03	3.91	-3.79	0.198	-9.59	2.01
Dyspnea	-4.30	0.131	-9.90	1.30	-2.60	0.329	-7.86	2.65	-2.92	0.319	-8.72	2.87
Insomnia	-4.13	0.245	-11.13	2.86	-6.40	0.015*	-11.52	-1.28	-3.09	0.379	-10.02	3.84
Appetite loss	-3.01	0.193	-7.55	1.54	-2.69	0.183	-6.66	1.28	-4.72	0.031*	-9.01	-0.43
Constipation	0.28	0.905	-4.31	4.87	-3.03	0.101	-6.66	0.60	-2.61	0.250	-7.10	1.87
Diarrhea	-7.28	0.005**	-12.34	-2.23	-5.42	0.013*	-9.69	-1.15	-7.52	0.006**	-12.80	-2.23
Financial difficulties	-3.42	0.158	-8.19	1.35	-2.80	0.114	-6.29	0.68	-4.71	0.094	-10.25	0.82
QLQ CML24												
Symptom burden	-5.82	0.000***	-8.94	-2.70	-3.45	0.006**	-5.88	-1.03	-3.65	0.024*	-6.80	-0.49
Impact on worry/mood	-4.17	0.046*	-8.26	-0.07	-4.30	0.018*	-7.85	-0.75	-0.78	0.743	-5.50	3.94
Impact on daily life	-6.45	0.015*	-11.62	-1.28	-6.03	0.001**	-9.69	-2.36	-6.15	0.018*	-11.23	-1.08
Body image problems	-8.33	0.026*	-15.66	-1.00	-7.47	0.017*	-13.58	-1.36	-6.73	0.041*	-13.17	-0.29
Satisfaction with care/info	-1.83	0.679	-10.61	6.94	-0.58	0.879	-8.17	7.00	-2.08	0.620	-10.39	6.22
Satisfaction with social life	-3.33	0.343	-10.27	3.60	-3.79	0.221	-9.89	2.32	-5.38	0.074	-11.28	0.53
QLQ IL156												

Lack of energy	-4.17	0.302	-12.14	3.81	-5.56	0.097	-12.14	1.03	-7.41	0.077	-15.63	0.82
Sore or enlarged nipples or breasts	-2.06	0.259	-5.67	1.54	-0.65	0.672	-3.67	2.38	-0.36	0.870	-4.76	4.04
Feeling dizzy/lightheaded	0.34	0.913	-5.90	6.59	-1.62	0.495	-6.30	3.07	-5.43	0.067	-11.25	0.38
Clear thinking problems	-2.06	0.488	-7.95	3.82	0.97	0.693	-3.90	5.84	-1.81	0.525	-7.45	3.83
Hearing problems	-3.51	0.294	-10.11	3.10	-3.33	0.158	-7.99	1.32	0.74	0.831	-6.12	7.60
Pain or soreness in mouth	-2.78	0.279	-7.84	2.28	-0.66	0.685	-3.88	2.56	1.16	0.664	-4.15	6.47
Taste changes	-1.42	0.468	-5.29	2.45	-1.68	0.253	-4.59	1.22	-1.59	0.567	-7.08	3.90
Flatulence problems	-1.45	0.703	-8.96	6.07	-4.00	0.202	-10.18	2.18	-2.92	0.471	-10.94	5.11
Muscle weakness	-6.23	0.084	-13.32	0.86	-2.41	0.471	-9.00	4.19	-0.43	0.919	-8.77	7.92
Coughing problems	0.00	1.000	-5.92	5.92	1.39	0.589	-3.70	6.47	-3.90	0.191	-9.78	1.99
Chest pain	1.52	0.453	-2.48	5.51	-1.40	0.436	-4.96	2.16	-2.22	0.300	-6.47	2.02
Fever or chills	1.52	0.468	-2.62	5.65	3.16	0.106	-0.69	7.00	1.33	0.581	-3.46	6.12
Temperature tolerance problems	-1.53	0.649	-8.20	5.14	-3.26	0.235	-8.68	2.16	0.00	1.000	-8.95	8.95
Hot flushes	-2.33	0.495	-9.06	4.41	-1.47	0.508	-5.84	2.91	-0.91	0.823	-9.01	7.18
Tingling or numbness in hands/feet	-6.51	0.084	-13.93	0.90	-2.59	0.428	-9.06	3.88	2.82	0.464	-4.81	10.45
Decreased libido	-0.50	0.927	-11.23	10.23	-1.45	0.725	-9.62	6.73	-1.92	0.705	-12.06	8.21
Less sexual enjoyment	-6.01	0.272	-16.87	4.84	-6.15	0.116	-13.87	1.56	-5.43	0.368	-17.47	6.61
Erection difficulty	0.00	1.000	-15.14	15.14	-5.26	0.262	-14.63	4.11	-13.33	0.070	-27.80	1.14

Asterisks indicate levels of statistical significance: $p \leq 0.05$ (*), $p \leq 0.01$ (**), and $p \leq 0.001$ (***). CI: confidence interval.

Table S5. EORTC QLQ-C30, CML24 and IL156 summary scores.

	baseline		6 weeks		3 months		6 months	
	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)
QLQ C30								
Global health status/QoL	67 (17)	58 (20)	67 (17)	61 (17)	67 (17)	60 (19)	67 (17)	60 (17)
Functioning scales								
Physical functioning	87 (27)	83 (18)	93 (20)	87 (15)	87 (20)	86 (16)	93 (20)	86 (14)
Role functioning	83 (33)	78 (27)	100 (33)	84 (22)	100 (33)	82 (25)	100 (33)	83 (23)
Emotional functioning	92 (25)	83 (20)	92 (17)	88 (16)	92 (17)	88 (16)	92 (27)	84 (20)
Cognitive functioning	83 (33)	81 (23)	100 (17)	88 (17)	100 (17)	87 (18)	83 (17)	84 (21)
Social functioning	100 (33)	82 (26)	100 (21)	86 (21)	100 (17)	86 (23)	100 (17)	88 (22)
Symptom scales								
Fatigue	33 (33)	33 (24)	22 (33)	26 (23)	22 (22)	26 (20)	22 (33)	29 (22)
Nausea/vomiting	0 (17)	9 (18)	0 (0)	4 (9)	0 (0)	5 (13)	0 (0)	6 (14)
Pain	0 (33)	19 (25)	0 (33)	16 (22)	17 (33)	18 (22)	0 (33)	18 (21)
Dyspnea	0 (33)	18 (25)	0 (33)	15 (24)	0 (33)	16 (23)	0 (33)	15 (23)
Insomnia	0 (33)	25 (30)	0 (33)	19 (26)	0 (33)	18 (25)	0 (33)	22 (25)
Appetite loss	0 (0)	8 (21)	0 (0)	5 (13)	0 (0)	6 (18)	0 (0)	5 (16)
Constipation	0 (0)	9 (20)	0 (0)	9 (19)	0 (0)	8 (18)	0 (0)	8 (19)
Diarrhea	0 (33)	14 (24)	0 (0)	8 (16)	0 (0)	9 (17)	0 (0)	8 (16)
Financial difficulties	0 (0)	7 (22)	0 (0)	3 (12)	0 (0)	5 (17)	0 (0)	3 (13)
QLQ-CML24								
Symptom burden	21 (15)	22 (13)	15 (13)	17 (12)	15 (18)	18 (12)	17 (18)	19 (13)
Impact on worry/mood	8 (25)	15 (17)	8 (17)	11 (13)	8 (17)	11 (14)	8 (25)	15 (18)
Impact on daily life	11 (22)	19 (20)	11 (22)	13 (16)	11 (22)	12 (16)	11 (22)	13 (18)
Body image problems	0 (33)	22 (29)	0 (33)	15 (23)	0 (33)	15 (23)	0 (33)	14 (22)
Satisfaction with care/info	100 (33)	86 (24)	100 (33)	81 (25)	100 (33)	81 (26)	100 (33)	83 (24)
Satisfaction with social life	67 (33)	71 (31)	67 (33)	67 (30)	67 (33)	68 (32)	67 (33)	71 (29)
IL156								

Lack of energy	33 (58)	39 (31)	33 (33)	33 (28)	33 (67)	32 (30)	33 (67)	34 (11)
Sore or enlarged nipples or breasts	0 (0)	3 (14)	0 (0)	1 (8)	0 (0)	1 (10)	0 (0)	3 (13)
Feeling dizzy/lightheaded	0 (33)	12 (23)	0 (33)	12 (20)	0 (33)	11 (20)	0 (0)	8 (17)
Clear thinking problems	0 (33)	15 (22)	0 (33)	12 (19)	0 (33)	15 (22)	0 (33)	13 (19)
Hearing problems	0 (33)	14 (25)	0 (0)	10 (21)	0 (33)	12 (21)	0 (33)	14 (22)
Pain or soreness in mouth	0 (0)	7 (19)	0 (0)	4 (13)	0 (0)	7 (19)	0 (0)	7 (17)
Taste changes	0 (0)	6 (18)	0 (0)	3 (12)	0 (0)	6 (15)	0 (0)	5 (16)
Flatulence problems	33 (33)	23 (26)	0 (33)	21 (27)	0 (33)	20 (27)	0 (33)	22 (27)
Muscle weakness	0 (33)	20 (26)	0 (33)	13 (21)	0 (33)	17 (25)	0 (33)	16 (25)
Coughing problems	0 (0)	11 (21)	0 (0)	10 (20)	0 (0)	12 (26)	0 (0)	9 (21)
Chest pain	0 (0)	7 (17)	0 (0)	6 (15)	0 (0)	5 (14)	0 (0)	4 (11)
Fever or chills	0 (0)	5 (13)	0 (0)	6 (15)	0 (0)	9 (20)	0 (0)	7 (18)
Temperature tolerance problems	0 (33)	17 (24)	0 (33)	14 (21)	0 (33)	16 (25)	0 (33)	19 (28)
Hot flushes	0 (0)	9 (22)	0 (0)	7 (19)	0 (0)	6 (17)	0 (0)	9 (21)
Tingling or numbness in hands/feet	0 (33)	21 (27)	0 (33)	13 (24)	0 (33)	21 (27)	0 (33)	21 (25)
Decreased libido	0 (67)	27 (35)	0 (33)	20 (31)	0 (67)	27 (35)	0 (33)	23 (30)
Less sexual enjoyment	0 (33)	25 (35)	0 (33)	14 (26)	0 (33)	21 (32)	0 (33)	16 (28)
Erection difficulty	0 (67)	30 (37)	0 (33)	23 (30)	0 (33)	25 (30)	0 (33)	16 (26)

Abbreviations; IQR: interquartile range; SD: standard deviation.

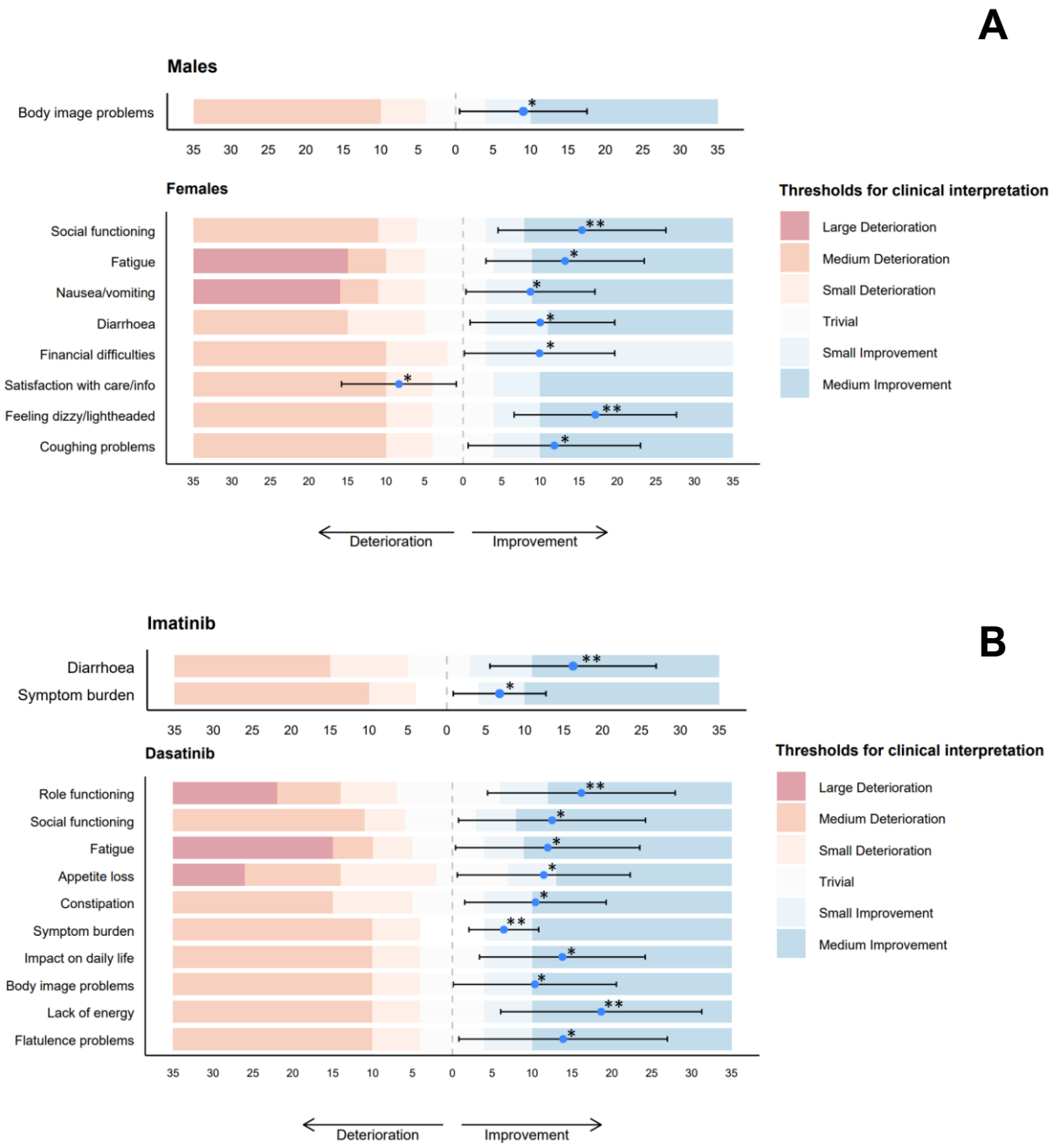


Figure S1. Statistically significant mean changes in EORTC QLQ-C30, CML24, and IL156, after six months of dose reduction. (A) Differences by sex (male (n=93) and female (n=53)); (B) Differences by TKI subgroup (imatinib (n=67) and dasatinib (n=36)). Dots with 95% confidence intervals represent the observed mean changes in EORTC scores. Asterisks indicate levels of statistical significance: $p \leq 0.05$ (*) and $p \leq 0.01$ (**). Colored bars indicate evidence-based thresholds for meaningful differences on the EORTC scales, based on the criteria established by Cocks et al.[2].

Table S6. Participant characteristics analyzed subgroups (N).

	Females (53)	Males (93)	Imatinib (67)	Dasatinib (36)	Nilotinib (32)	70+ (40)
Mean age (SD)	60 (13.8)	59 (13.7)	58 (14.8)	59 (13.6)	63 (12.1)	75 (3.4)
Sex, male, N (%)			46 (69)	21 (58)	19 (59)	27 (68)
TKI used, N (%)						
Imatinib	21 (37)	46 (49)				18 (45)
Dasatinib	15 (26)	21 (23)				12 (30)
Bosutinib	4 (7)	5 (5)				1 (3)
Nilotinib	13 (23)	19 (20)				9 (23)
Ponatinib	-	2 (2)				-
Median time since diagnosis, years (IQR)	7.5 (4.3 – 13.0)	8.4 (5.1 – 14.1)	9.8 (5.0 – 13.8)	6.1 (3.6 – 11.8)	11.6 (6.7 – 14.8)	6.1 (4.0 – 10.8)
Molecular response of BCR::ABL1 (%IS), N (%)						
3	11 (19)	13 (14)	8 (12)	5 (14)	8 (25)	6 (15)
4	6 (11)	17 (18)	9 (13)	5 (14)	8 (25)	6 (15)
4.5	14 (25)	21 (23)	15 (22)	9 (25)	6 (19)	11 (28)
5	22 (39)	42 (45)	35 (52)	17 (47)	10 (31)	17 (43)
Median time in MMR or DMR, years (IQR)	3.2 (1.9 – 6.3)	4.4 (2.2 – 8.1)	5.3 (2.2 – 9.4)	3.1 (1.7 – 4.9)	4.5 (2.1 – 7.1)	3.5 (1.9 – 6.3)

Abbreviations; SD: standard deviation; TKI: tyrosine kinase inhibitor; IQR: Interquartile range; IS: international scale; MMR: major molecular remission; DMR: deep molecular remission.

Table S7. Reasons not to use PDA during decision-making

Category	Reason
No need for PDA	• SDM conversation already took place • Everything already known by patient
Logistical reasons	• PDA was not sent due to time constraints • Preference to proceed immediately with decision-making once eligibility was confirmed • Not sent by study team (4x) • Not received by patient (2x)
Physician's assessment	• Physician assumed patient couldn't complete PDA due to old age and being unfamiliar with digital tools
Patient refusal	• Patient did not want to use the PDA • No need for PDA according to patient

Abbreviations; PDA: patient decision aid; SDM: shard decision making.

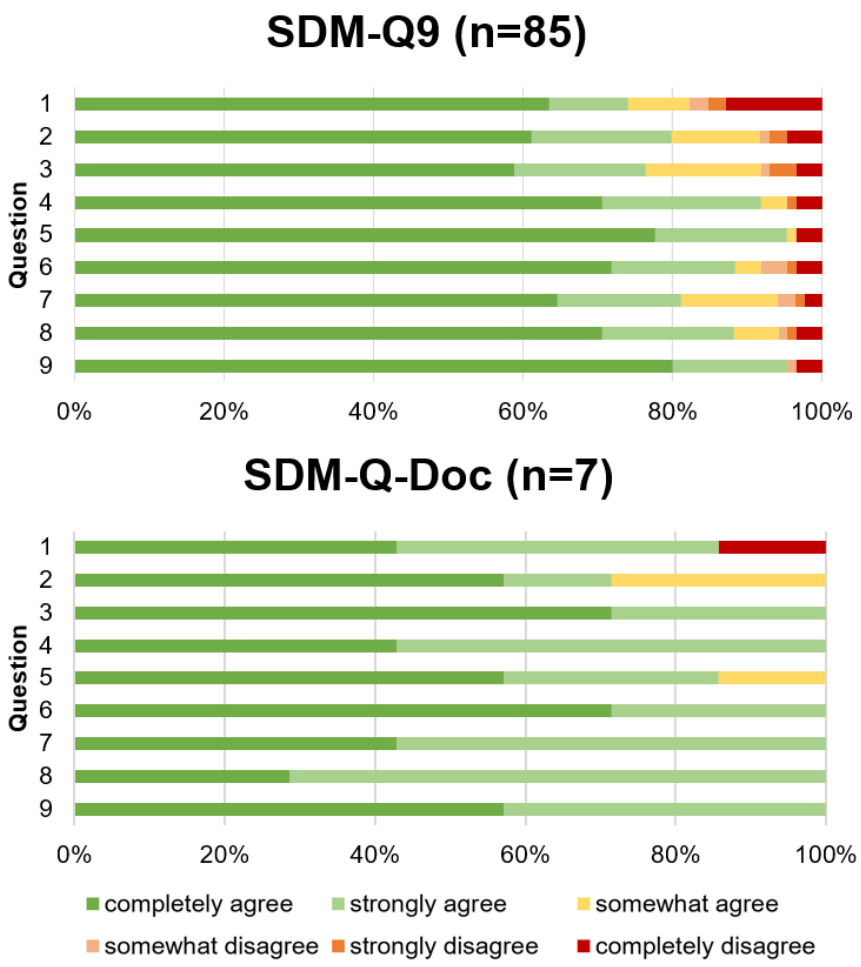


Figure S2. Distribution of Participant Responses for Each Item on the SDM-Q-9 and SDM-Q-Doc Scales

Table S8 – DCS median subscores and total score.

Subscores (N)	Median score (IQR)
Uncertainty (101)	8.3 (25)
Informed (107)	16.7 (25)
Values clarity (104)	16.7 (25)
Support (102)	8.3 (25)
Effective decision (101)	6.3 (25)
Total (101)	**12.5 (25)**

IQR: interquartile range

References Part 2: Supplementary Tables and Figures

1. 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.

2. 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.