

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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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
<i>BCR::ABL1</i> (%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?	
			✓	section
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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Description of the smallest unit that is being analyzed to assess intervention effects (e.g., individual, group, or community) 	NA	
		<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Statistical methods used to compare study groups for primary methods outcome(s), including complex methods of correlated data 	Yes	2.3
		<ul style="list-style-type: none"> Statistical methods used for additional analyses, such as a subgroup analyses and adjusted analysis 	NA	
		<ul style="list-style-type: none"> Methods for imputing missing data, if used 	Yes	2.3
		<ul style="list-style-type: none"> Statistical software or programs used 	Yes	2.3
Results				
Participant flow	12	<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> 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	
		<ul style="list-style-type: none"> Assignment: the numbers of participants assigned to a study condition 	Yes	Fig. 1
		<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> Analysis: the number of participants included in or excluded from the main analysis, by study condition 	Yes	Fig. 1
		<ul style="list-style-type: none"> Description of protocol deviations from study as planned, along with reasons 	NA	
Recruitment	13	<ul style="list-style-type: none"> Dates defining the periods of recruitment and follow-up 	Yes	3.
Baseline Data	14	<ul style="list-style-type: none"> Baseline demographic and clinical characteristics of participants in each study condition 	Yes	Table 1
		<ul style="list-style-type: none"> Baseline characteristics for each study condition relevant to specific disease prevention research 	NA	
		<ul style="list-style-type: none"> Baseline comparisons of those lost to follow-up and those retained, overall and by study condition 	NA	
		<ul style="list-style-type: none"> Comparison between study population at baseline and target population of interest 	Yes (exploratory)	4.1
Baseline equivalence	15	<ul style="list-style-type: none"> Data on study group equivalence at baseline and statistical methods used to control for baseline differences 	No	

TREND Statement Checklist

Numbers analyzed	16	<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> Inclusion of null and negative findings 	NA	
		<ul style="list-style-type: none"> Inclusion of results from testing pre-specified causal pathways through which the intervention was intended to operate, if any 	NA	
Ancillary analyses	18	<ul style="list-style-type: none"> Summary of other analyses performed, including subgroup or restricted analyses, indicating which are pre-specified or exploratory 	Yes	3.2
Adverse events	19	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> 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
		<ul style="list-style-type: none"> Discussion of the success of and barriers to implementing the intervention, fidelity of implementation 	Yes	4.4
		<ul style="list-style-type: none"> Discussion of research, programmatic, or policy implications 	No	
Generalizability	21	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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		Loss of MMR	
	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 <i>BCR::ABL1</i> (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	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	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.

QLQ C30	Baseline vs 6 weeks				Baseline vs 3 months				Baseline vs 6 months			
	Δ	<i>P</i>	CI		Δ	<i>P</i>	CI		Δ	<i>P</i>	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
<i>Functioning scales</i>												
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
<i>Symptom scales</i>												
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)						
QLQ C30								
Global health status/QoL	67 (17)	58 (20)	67 (17)	61 (17)	67 (17)	60 (19)	67 (17)	60 (17)
<i>Functioning scales</i>								
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)
<i>Symptom scales</i>								
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.

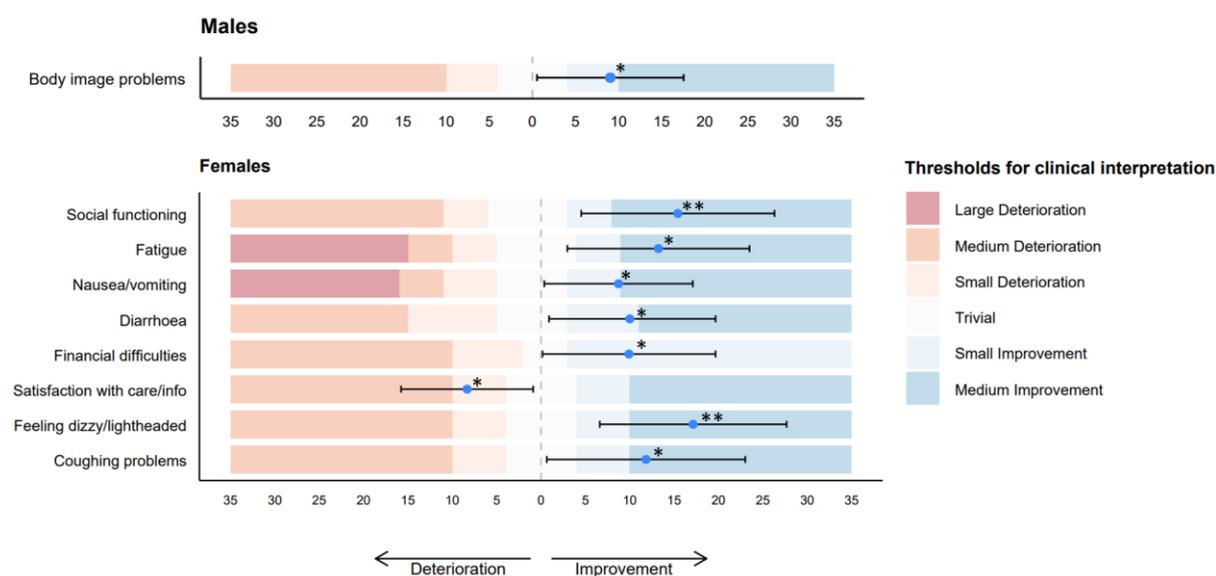
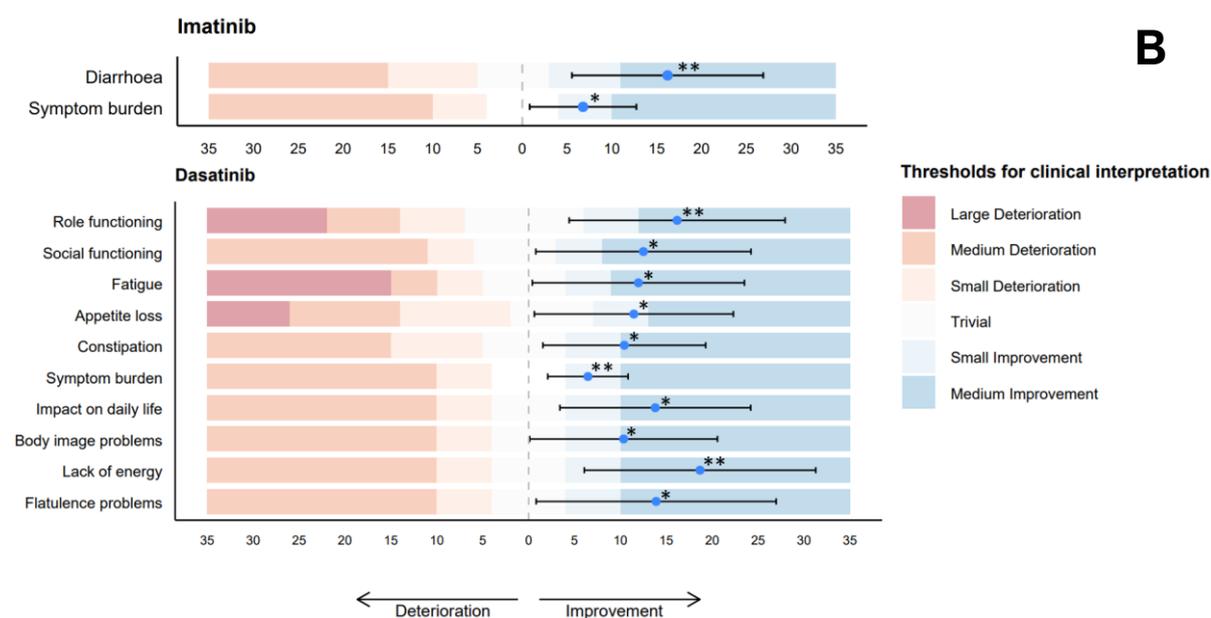
A**B**

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						
4	11 (19)	13 (14)	8 (12)	5 (14)	8 (25)	6 (15)
4.5	6 (11)	17 (18)	9 (13)	5 (14)	8 (25)	6 (15)
5	14 (25)	21 (23)	15 (22)	9 (25)	6 (19)	11 (28)
	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	<ul style="list-style-type: none">• SDM conversation already took place• Everything already known by patient
Logistical reasons	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Physician assumed patient couldn't complete PDA due to old age and being unfamiliar with digital tools
Patient refusal	<ul style="list-style-type: none">• Patient did not want to use the PDA• No need for PDA according to patient

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

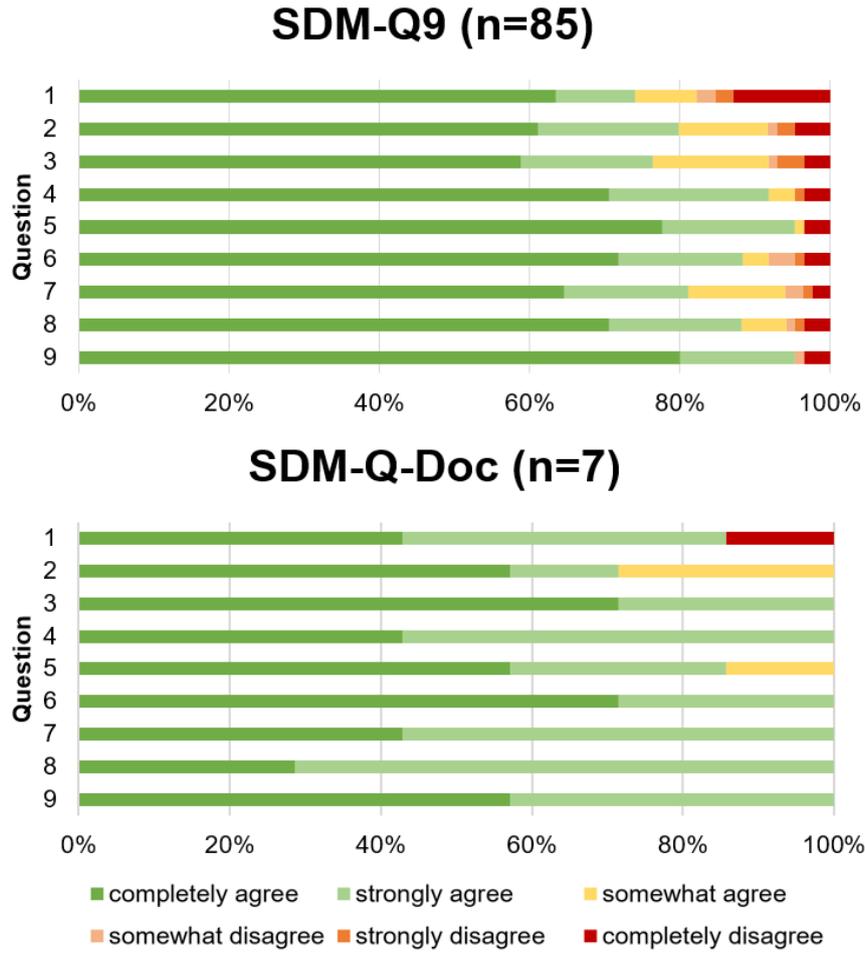


Figure S2. Distribution of Participant Responses for Each Item on the SDM-Q-9 and SDM-Q-Doc Scales

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.