Treatment selection for patients with chronic myeloid leukemia (CML) and the role of quality of life

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per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

GIMEMA International Meeting

New Frontiers in Hematologic Research: Quality of Life and Artificial Intelligence

Disclosures of Name Surname

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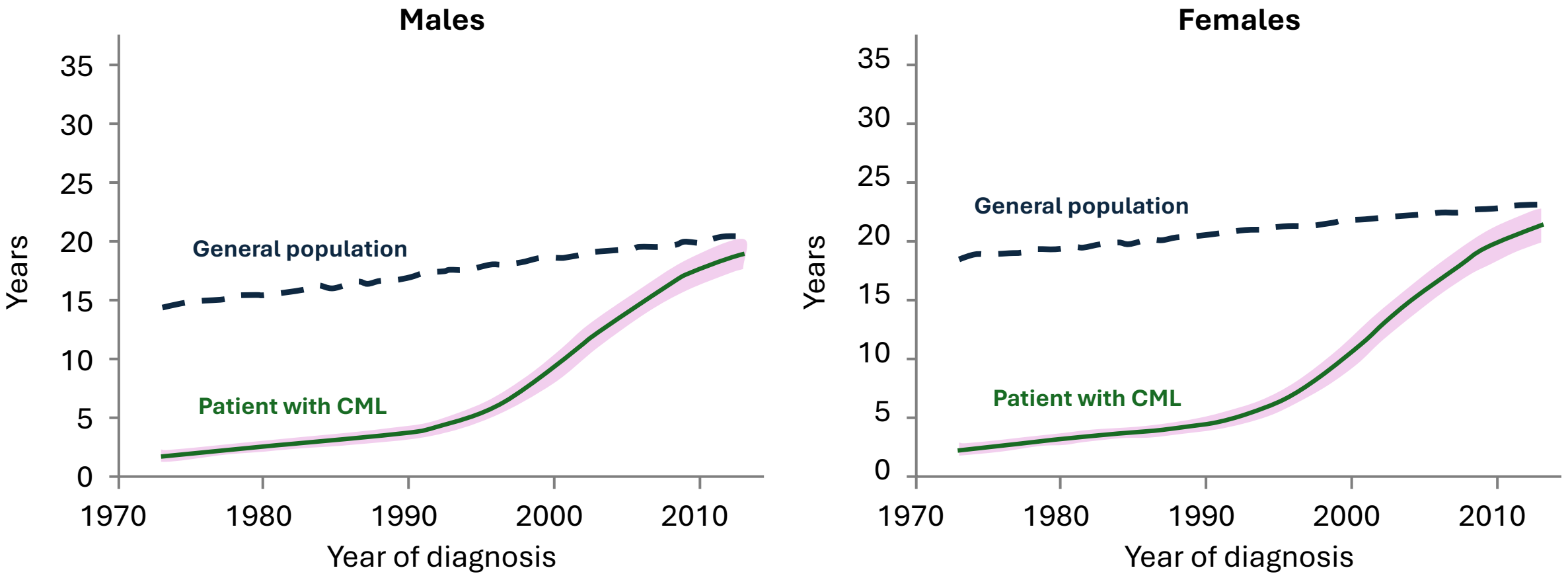
Incyte			x			x	
Pfizer					x		
AOP					x	x	
Abbvie					x	x	
GSK					x	x	
Servier					x	x	
Otsuka					x		

Life Expectancy for Patients with CML is Similar to General Population

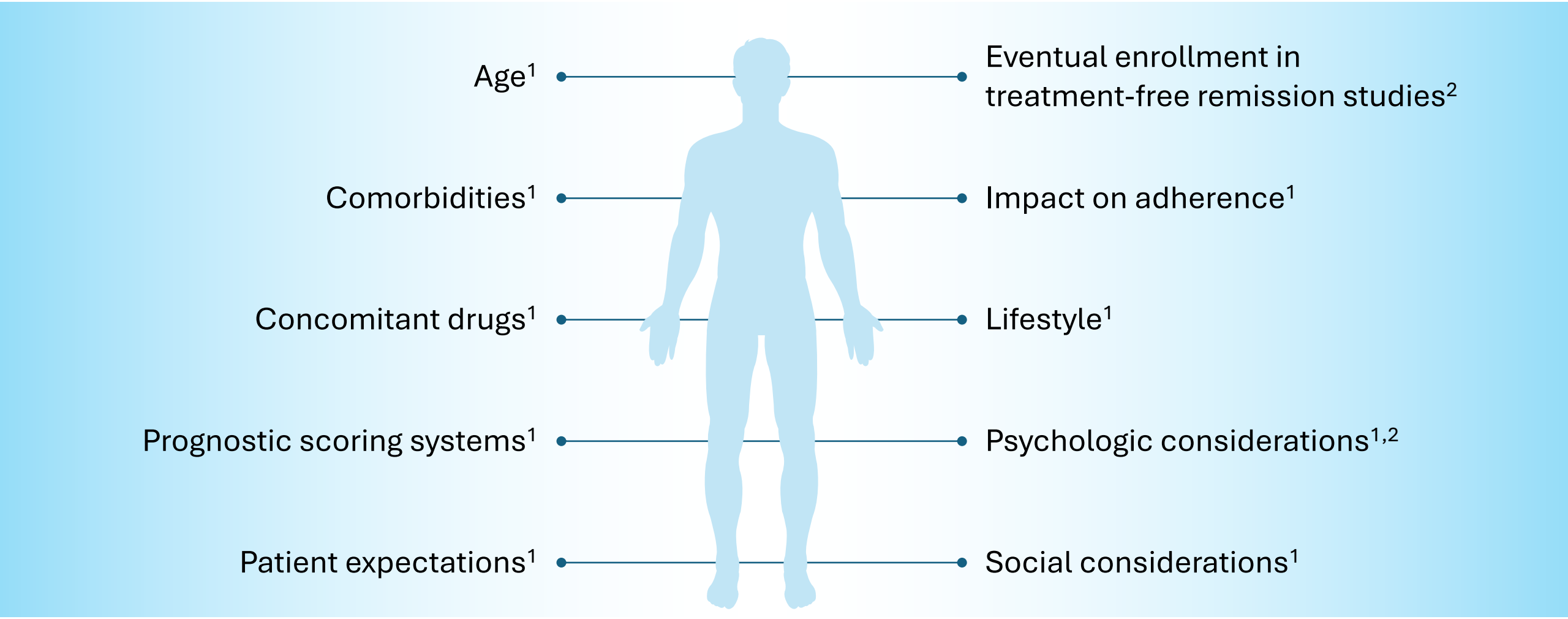
Life Expectancy of an Average 65-year-old Patient



CML=Chronic Myeloid Leukemia.

Bower H, *et al*. *J Clin Oncol* 2016; 34:2851–2857

Patient-Centered Medicine Approach in CML



1. Breccia M & Alimena G. *Expert Rev Hematol* 2015; **8:**5–7; 2. Atallah E & Sweet K. *Curr Hematol Malig Rep* 2021; **16:**433–443

Treatment goals: from QoL preservation to discontinuation (TFR)

Treatment goals are focused on **controlling CML pathology** while **preserving/improving QOL**

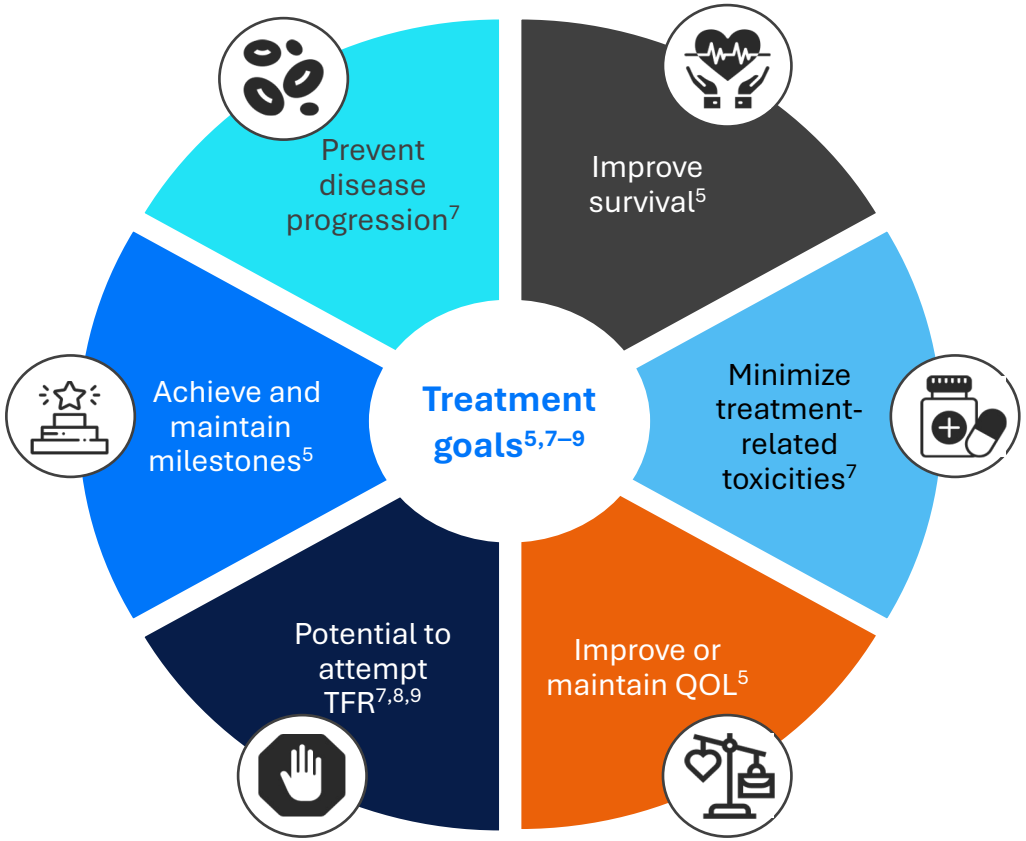
- Specific treatment goals vary by patient, and they may evolve over time and with successive lines of treatment[1]
- Achievement of milestones may be linked to improved outcomes, including reduced progression and prolonged survival[2-4]

Goals in newly diagnosed patients or those with fewer treatments

- TFR and rapid and durable achievement of milestones (EMR, DMR, MMR) [5]

Goals in older patients or those with multiple treatments

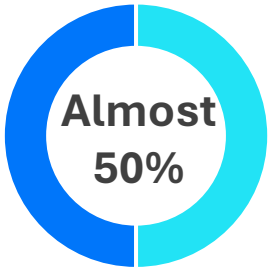
- Maintaining QOL with less-aggressive milestone goals[5,6]



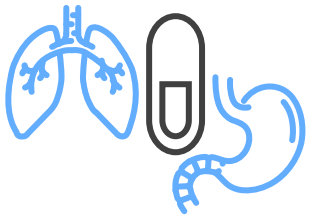
DMR, deep molecular response; EMR, early molecular response; MMR, major molecular response; QOL, quality of life.

1. Saglio G, Jabbour E. Leuk Lymphoma. 2018;59:1523-38. 2. Jabbour E, et al. Blood. 2011;118:4541-6. 3. Hehlmann R, et al. J Clin Oncol. 2011;29:1634-42. 4. Hughes TP, et al. Blood. 2010;116:3758-65. 5. Hochhaus A, et al. Leukemia. 2020;34:966-84. 6. Castagnetti F, et al. Target Oncol. 2021;16:823-38. 7. Cortes J, et al. Am J Hematol. 2019;94:346-57. 8. Hughes TP, Ross DM. Blood. 2016;128:17-23. 9. Hochhaus A, et al. Ann Oncol. 2017;28 (suppl 4):iv41-iv51.

CML treatments that optimize tolerability and efficacy are needed

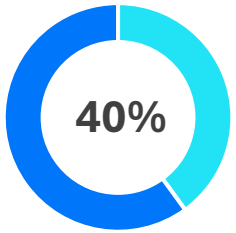


Newly diagnosed patients do not achieve MMR at 12 months with standard TKI therapy[1–3]



Long-term use of 2G TKIs can be associated with AEs (e.g. pleural effusion and GI events[4])

Frontline therapy that allows patients to meet treatment goals, minimize switching, and improve QOL is needed[5]



Patients are dissatisfied with their treatment side-effects[5]

Treatment with TKIs for CML is typically long-term, making medication tolerability a major concern for both patients and HCPs[5]

Many patients skip doses — one-third due to side effects and 25% to feel normal during special occasions[5]

AEs, adverse events; GI, gastrointestinal;
HCPs, healthcare professionals; QOL, quality of life.

1. Cortes JE, et al. J Clin Oncol. 2016;34:2333-40.
2. Hochhaus A, et al. Leukemia. 2016;30:1044-54.
3. Brümmendorf TH, et al. Leukemia. 2022;36:1825-33.
4. Haznedaroglu IC. Mediterr J Hematol Infect Dis. 2015;7:e2015014.
5. Lang F, et al. Poster presented at EHA 2023; poster P668.

Treatment start/switch: choice based on individual comorbidity profile

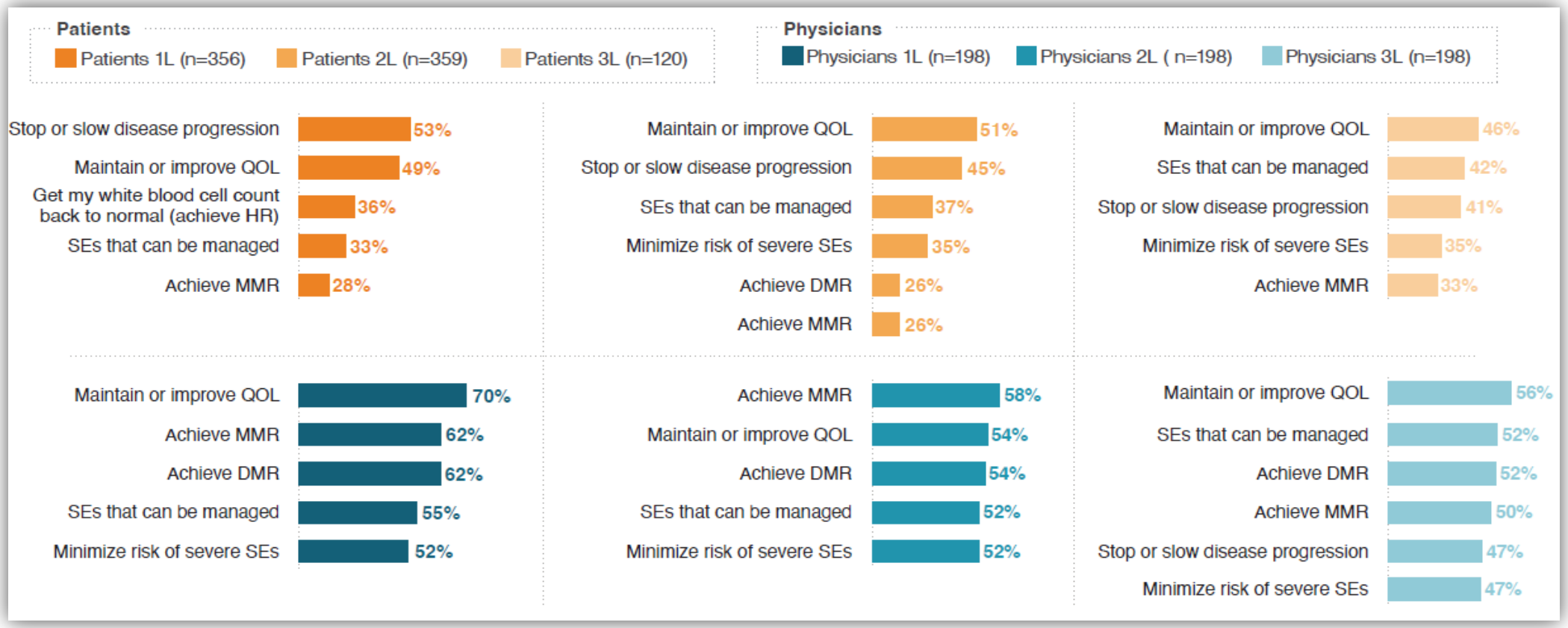
Comorbidities		Imatinib	Nilotinib	Dasatinib	Bosutinib	Ponatinib	Asciminib
Cardiovascular	Hypertension						
	Ischemic heart disease						
	Occlusive peripheral artery disease						
	Congestive heart failure						
	Diabetes						
	QT prolongation						
Pulmonary	Pulmonary disease						
	Pulmonary arterial hypertension						
GI issues							
Pancreatic dysfunction							
Liver dysfunction							
Kidney dysfunction							

Legend	
	Risk of related AEs based on comorbidity
Preferred	Very low
	Low
Less preferred	Intermediate
Avoid, if possible	High

No head-to-head trial data is available. Comparisons should not be drawn

Adapted from Andorsky D, et al. Front Oncol. 2024;14:1369246.

CML SUN: treatment goals by line of therapy

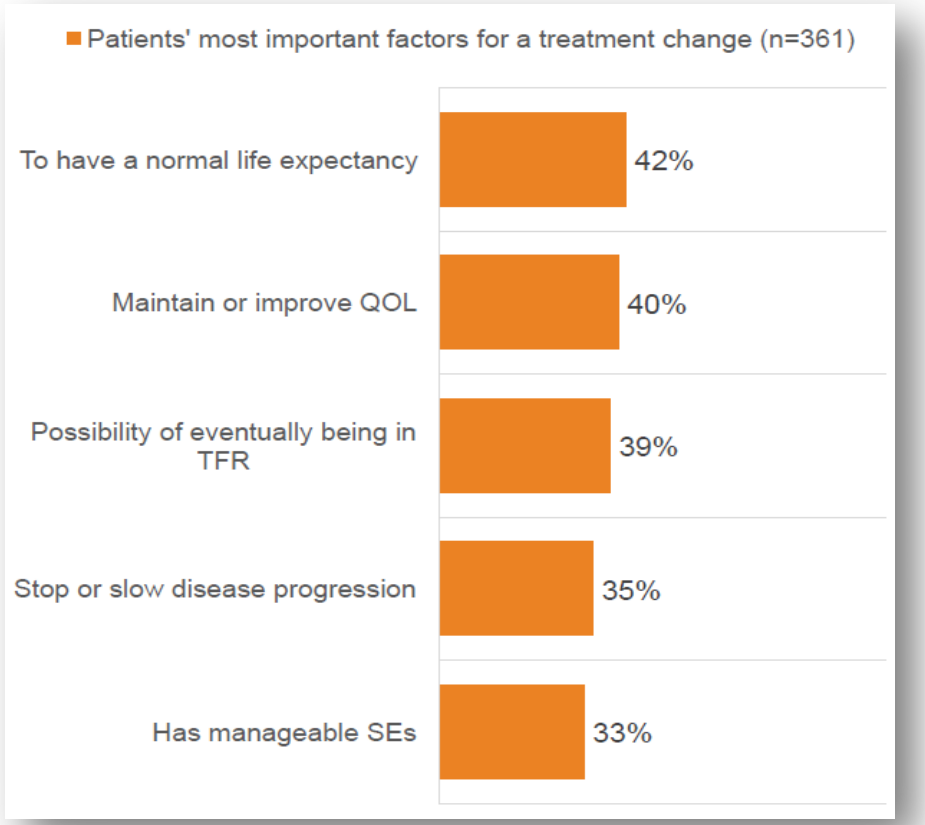


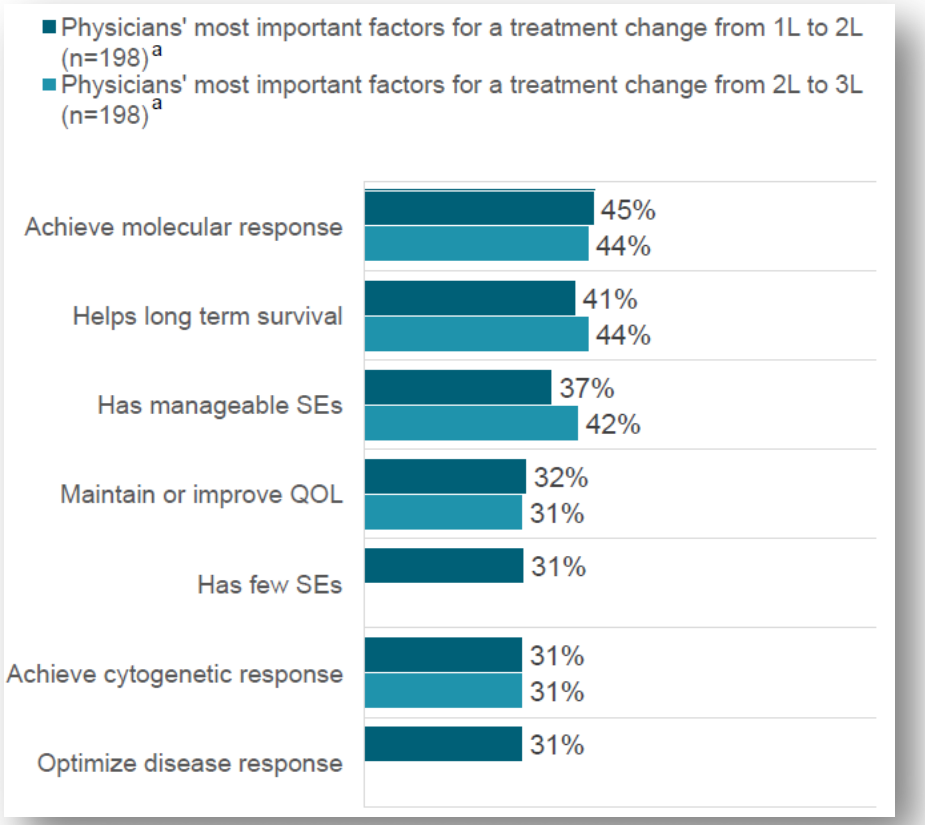
- Patients focused on stopping/slowing disease progression, maintaining/improving QOL, and minimizing/managing SEs as treatment goals, while physicians placed higher emphasis than patients on molecular response goals
- Stopping/slowing disease progression did not rank in the top 5 treatment goals for physicians until 3L, although patients reported this goal across lines of therapy

1L, first line; 2L, second line; 3L, third line; 4L, fourth line; HR, hematologic response; SE, side effect; WBC, white blood cell.

Lang F, et al. Poster presented at EHA 2023; poster #P668.

CML SUN: most important drivers for patients and HCPS when switching therapy



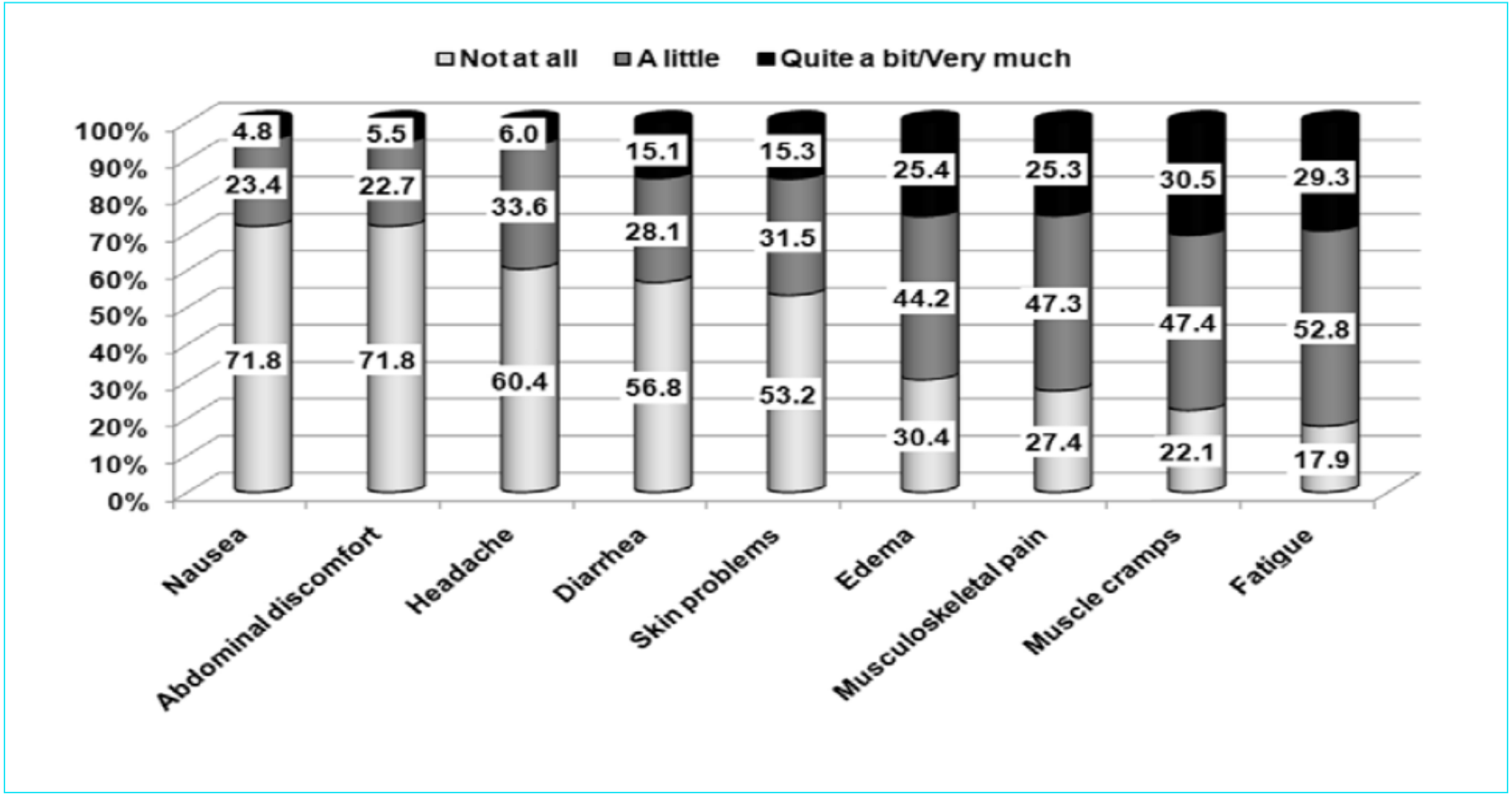


- While both patients and physicians think that maintaining/improving QOL and having manageable SEs are important when switching therapy, patients also consider having a normal life expectancy, the possibility for TFR, and stopping/slowing disease progression, while physicians place more emphasis on achieving molecular and cytogenetic responses than patients

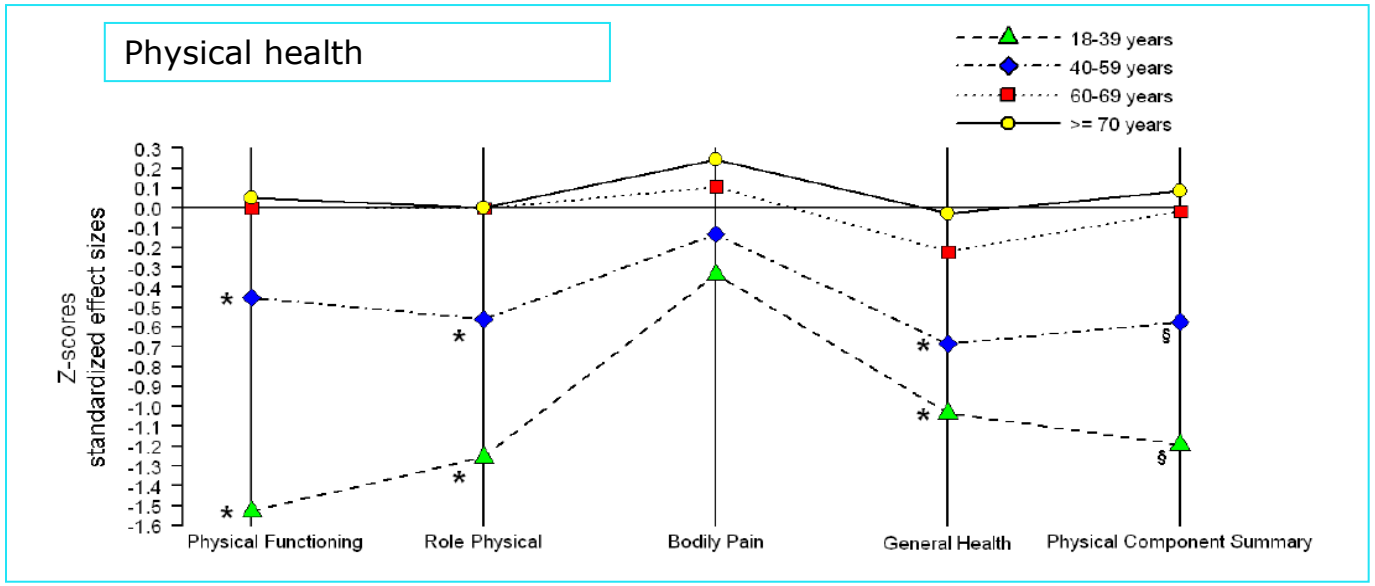
[a] Besides enabling patients to live longer

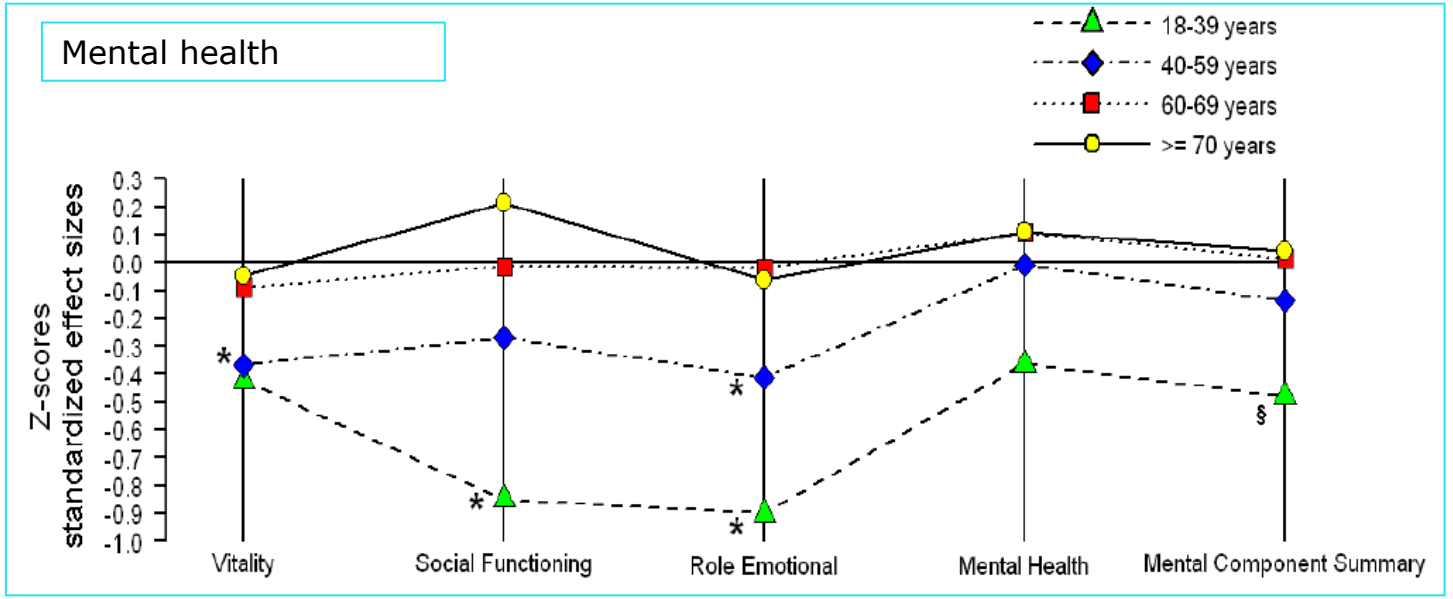
Lang F, et al. Poster presented at EHA 2023; poster #P668.

QoL in patients with CML receiving long-term imatinib therapy

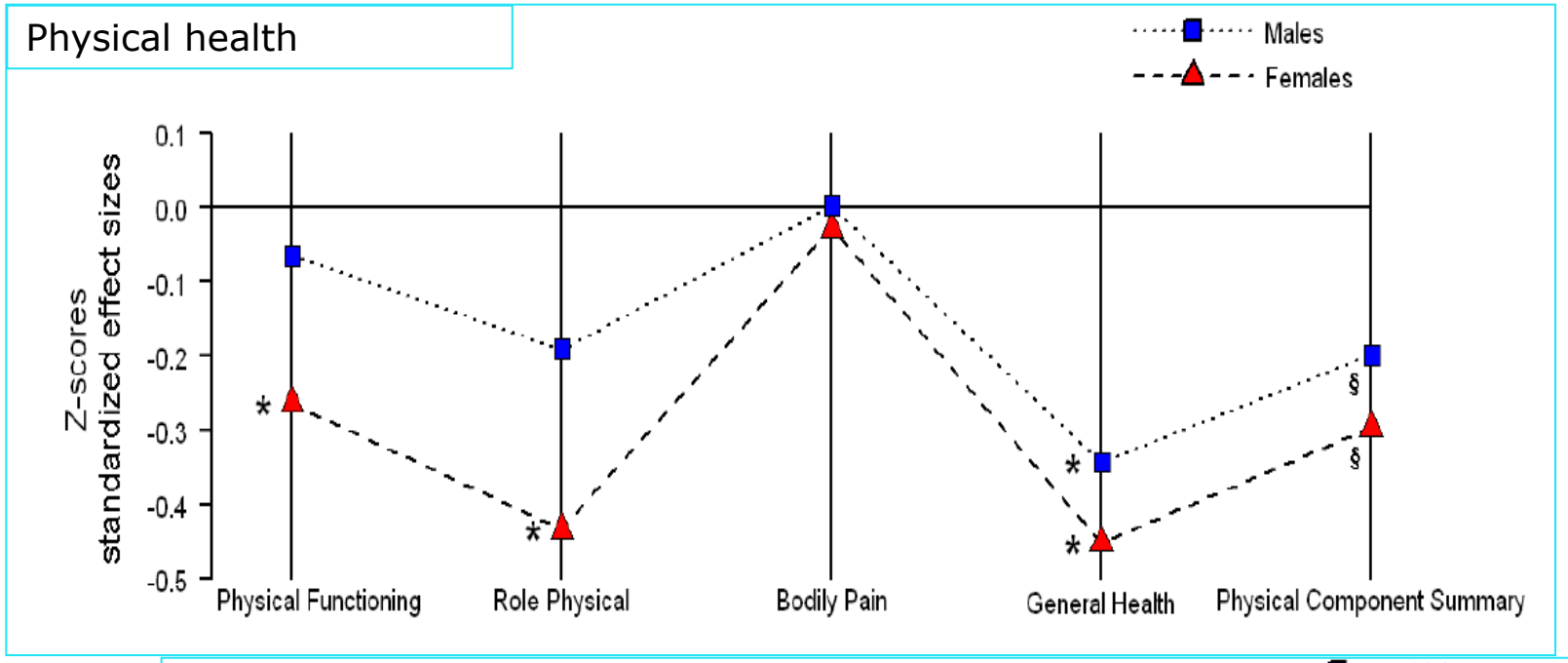


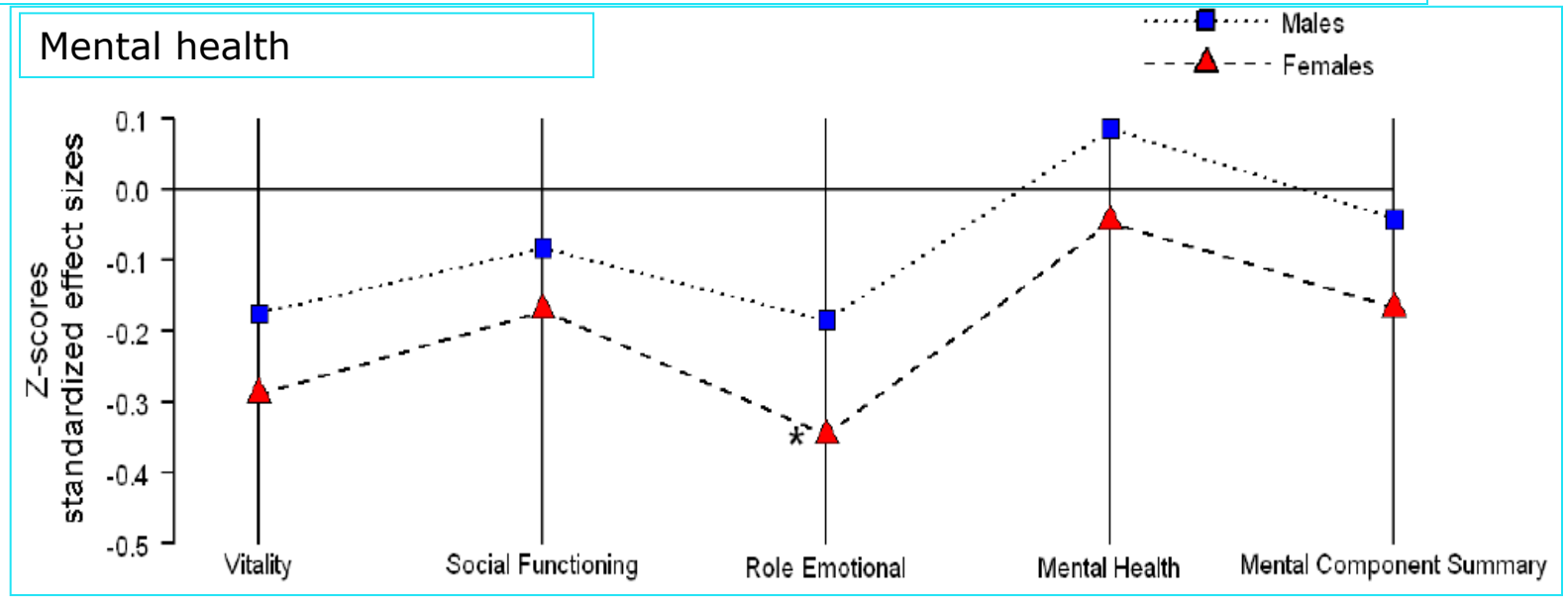
Efficace F, et al. Blood 2010; 118: 4554-4560.





- Older pts had similar QoL of general population of equal age

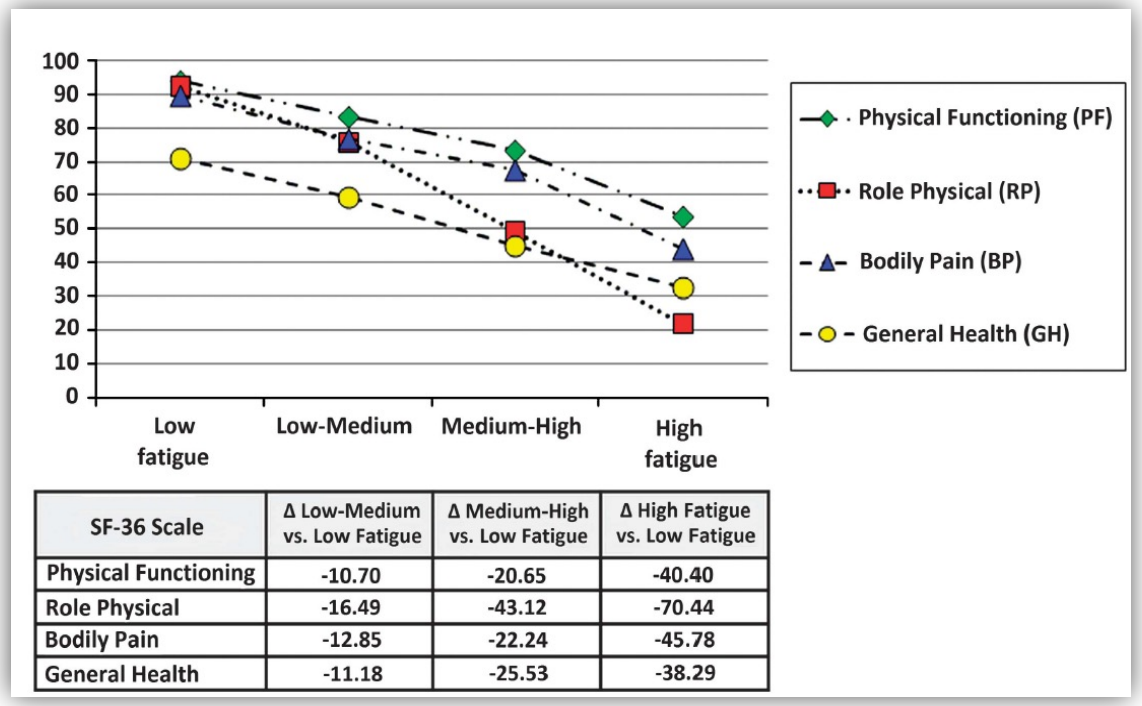




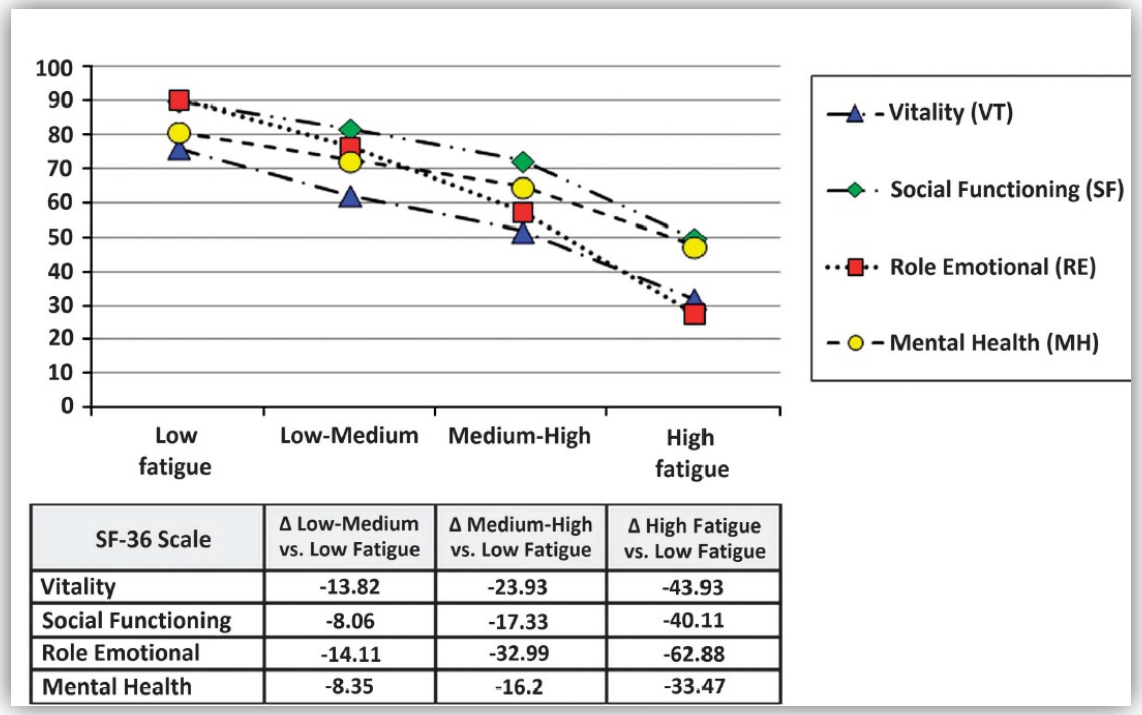
•Women suffered of more Aes: edema (16% vs 39%); fatigue (22%vs 39%); bone pain (18% vs 35%)

Fatigue can reduce QoL in patients with CML

Fatigue significantly limits patients' work and daily activities in time and performance due to physical and emotional health issues



SF-36 Scale	Δ Low-Medium vs. Low Fatigue	Δ Medium-High vs. Low Fatigue	Δ High Fatigue vs. Low Fatigue
Physical Functioning	-10.70	-20.65	-40.40
Role Physical	-16.49	-43.12	-70.44
Bodily Pain	-12.85	-22.24	-45.78
General Health	-11.18	-25.53	-38.29

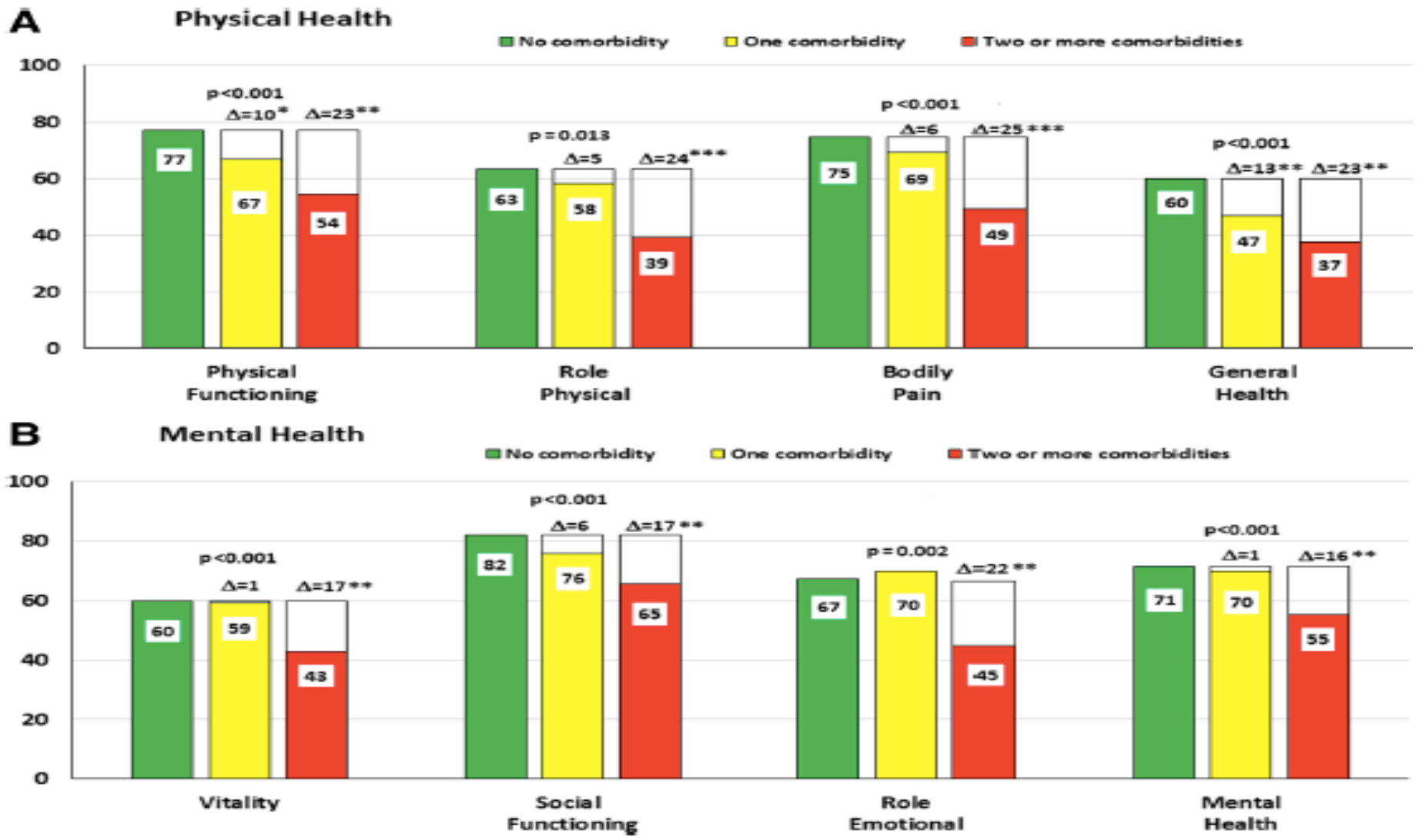


SF-36 Scale	Δ Low-Medium vs. Low Fatigue	Δ Medium-High vs. Low Fatigue	Δ High Fatigue vs. Low Fatigue
Vitality	-13.82	-23.93	-43.93
Social Functioning	-8.06	-17.33	-40.11
Role Emotional	-14.11	-32.99	-62.88
Mental Health	-8.35	-16.2	-33.47

EORTC, European Organisation for Research and Treatment of Cancer; QLQ, Quality of Life Questionnaire; SF, Short Form.

Efficace F, et al. Leukemia. 2013;27:1511-9.

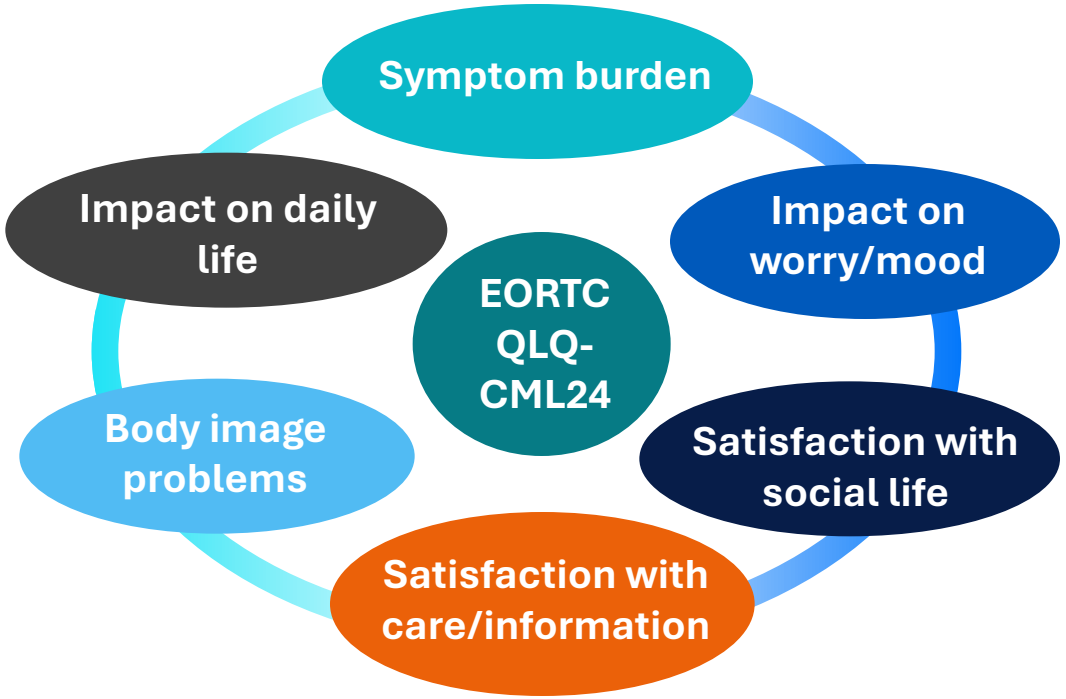
The impact of comorbidity on HR-QoL in elderly patients with chronic myeloid leukemia



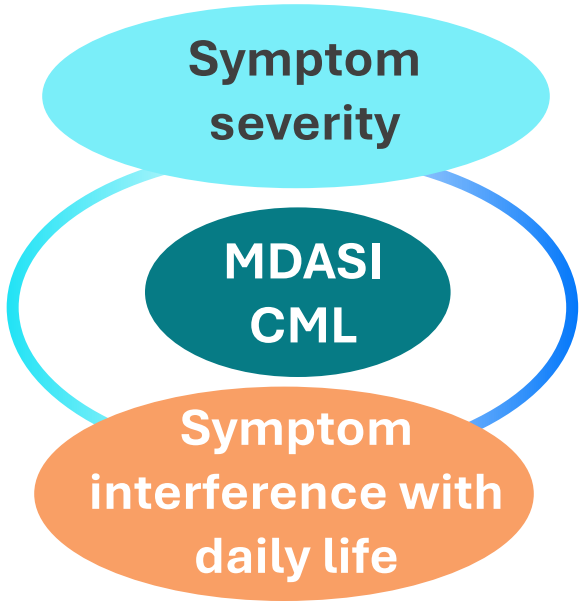
Efficace et al Ann Hematol 2016; 95: 211-219

QOL and symptom burden in CML

QOL
EORTC QLQ-CML24[1]



Symptom burden?
MDASI-CML[2]



EORTC QLQ-CML24, European Organisation for Research and Treatment of Cancer Quality of Life 24-item questionnaire for patients with CML; MDASI, MD Anderson Symptom Inventory.

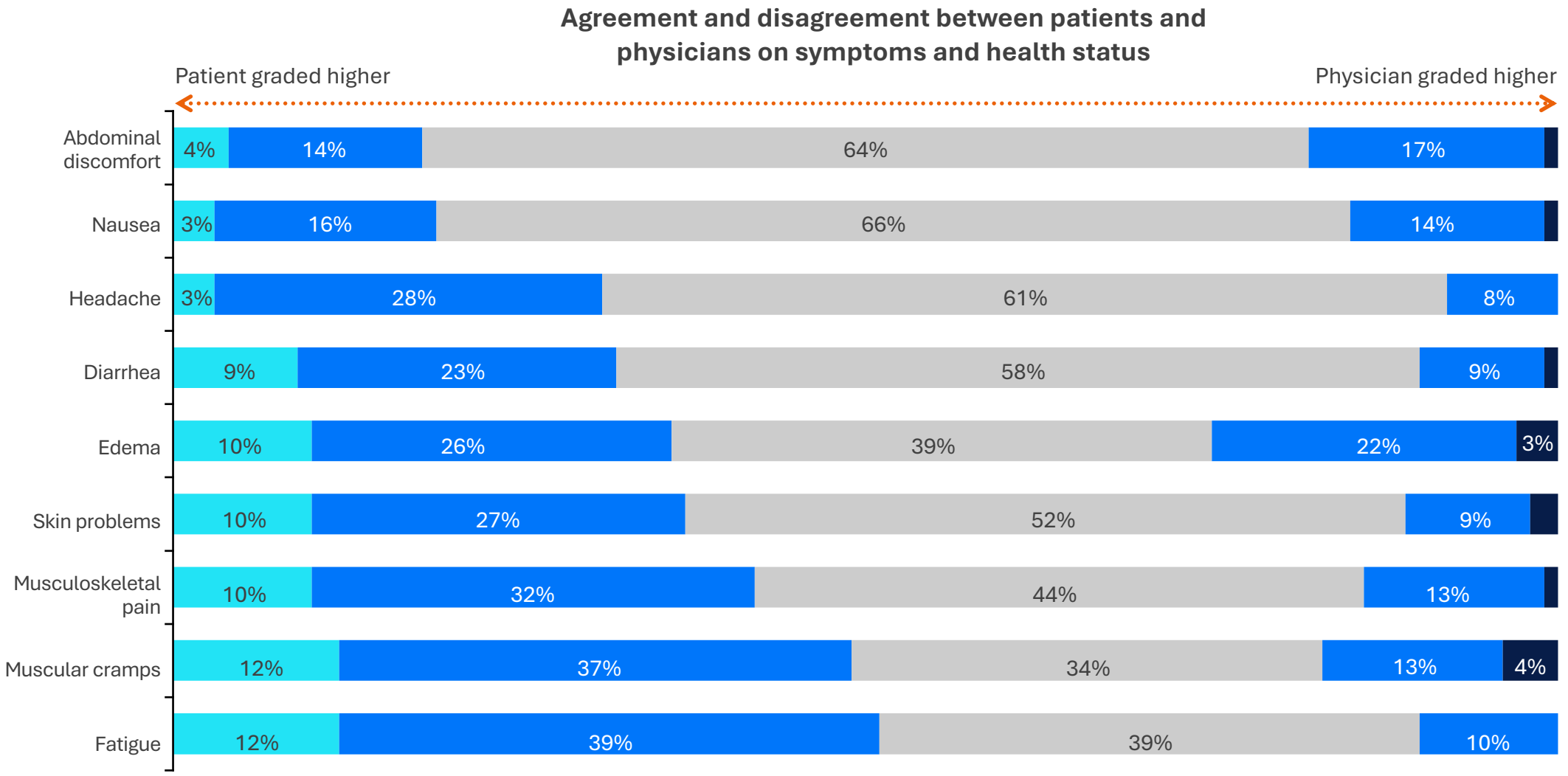
1. Efficace F, et al. Leuk Lymphoma. 2021;62:669-78.
2. Williams LA, et al. Blood. 2013;122:641-7.

Development of EORTC tool to measure QoL in patients with CML

Items included in the EORTC QLQ-CML24 (each item is rated on a four-point scale: *not at all, a little, quite a bit* and *very much*).
31) Have you had abdominal pains or cramps?
32) Have you had a dry mouth?
33) Have you been concerned about changes in your weight?
34) Have you had skin problems (e.g. color changes, itchy, dry or flaking skin)?
35) Have you had headaches?
36) Have you had aches or pains in your muscles or joints?
37) Have you had hair loss?
38) Have you sweated excessively?
39) Have you had acid indigestion or heartburn?
40) Have you felt drowsy?
41) Have you experienced any swelling in certain parts of your body (e.g. ankles, legs or around your eyes)?
42) Have you had to urinate frequently?
43) Have you had problems with your eyes (e.g. burning, watery, irritated or dry)?
44) Have you had muscle cramps?
45) Have you had emotional ups and downs?
46) Have you worried about your future health?
47) Have you had any difficulties carrying on with your usual activities because of getting tired easily?
48) Have you worried about getting an infection?
49) Have you felt dissatisfied with your body as result of the disease or treatment?
50) How much has your treatment been a burden to you?
51) Have you needed social support (e.g. family, friends or relatives) to undergo therapy or to cope with the disease?
52) Have you felt satisfied with the care you have received?
53) Have you felt satisfied with the information you have received (e.g. about the disease and its treatment)?
54) Have you felt satisfied with the quality of your social life (including family and/or friends)?

Efficace F, et al. Qual Life Res.2014;23:825-36.

Intolerance can also be related to different perceptions of the physician and patient

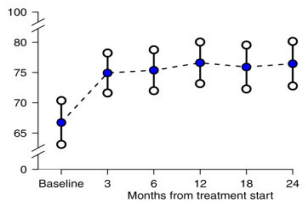


Adapted from Efficace F, et al. Haematologica. 2014;99:788-93.

HR-QoL in CML patients treated with 1st line nilotinib

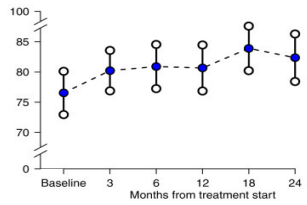
EORTC QLQ–C30

Global Health Status/QOL



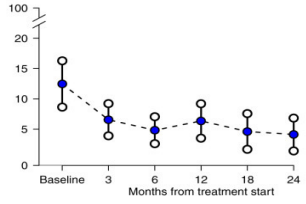
HRQOL assessment	Mean (95% CI)
Baseline	66.7 (63.1-70.4)
3 months	74.9 (71.6-78.2)
6 months	75.4 (72.0-78.8)
12 months	76.6 (73.2-80.0)
18 months	75.9 (72.3-79.5)
24 months	76.5 (72.8-80.1)
Time effect: $P < .001$	

Emotional Functioning



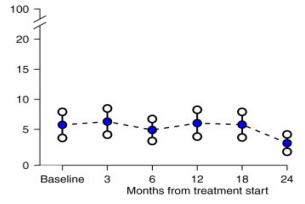
HRQOL assessment	Mean (95% CI)
Baseline	76.5 (73.0-80.1)
3 months	80.2 (76.9-83.6)
6 months	80.9 (77.3-84.5)
12 months	80.6 (76.8-84.4)
18 months	83.9 (80.2-87.6)
24 months	82.3 (78.4-86.3)
Time effect: $P = .004$	

Appetite Loss



HRQOL assessment	Mean (95% CI)
Baseline	12.5 (8.6-16.3)
3 months	6.5 (3.9-9.2)
6 months	4.8 (2.6-7.0)
12 months	6.3 (3.5-9.2)
18 months	4.6 (1.7-7.6)
24 months	4.1 (1.4-6.8)
Time effect: $P = .003$	

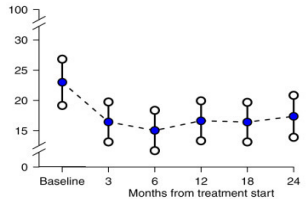
Nausea/Vomiting



HRQOL assessment	Mean (95% CI)
Baseline	5.7 (3.5-7.9)
3 months	6.3 (4.1-8.5)
6 months	4.9 (3.0-6.7)
12 months	6.0 (3.8-8.2)
18 months	5.8 (3.6-7.9)
24 months	2.7 (1.3-4.1)
Time effect: $P = .003$	

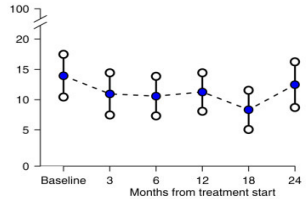
EORTC QLQ–FA12

Physical Fatigue



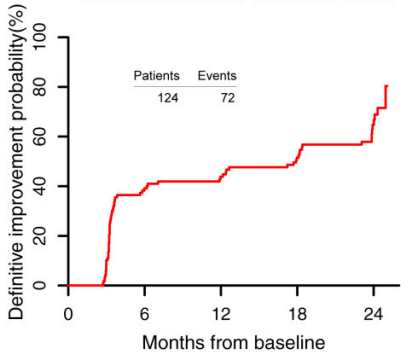
HRQOL assessment	Mean (95% CI)
Baseline	23.0 (19.2-26.8)
3 months	16.5 (13.2-19.8)
6 months	15.0 (11.7-18.4)
12 months	16.6 (13.3-19.9)
18 months	16.4 (13.1-19.7)
24 months	17.4 (13.9-20.8)
Time effect: $P < .001$	

Cognitive Fatigue

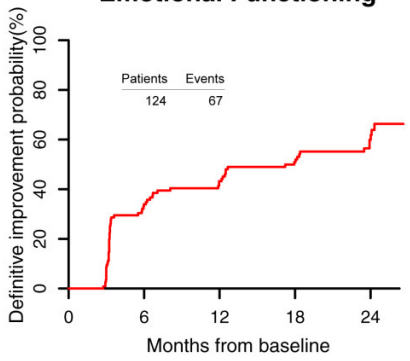


HRQOL assessment	Mean (95% CI)
Baseline	13.9 (10.4-17.5)
3 months	10.9 (7.5-14.4)
6 months	10.6 (7.3-13.8)
12 months	11.3 (8.1-14.4)
18 months	8.3 (5.1-11.6)
24 months	12.5 (8.7-16.2)
Time effect: $P = .014$	

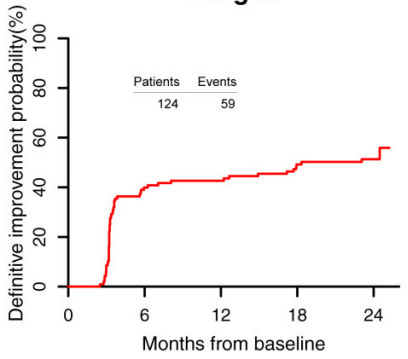
Global Health Status/QOL



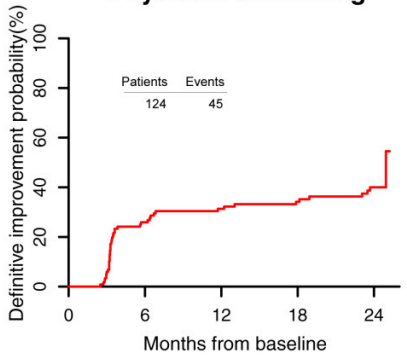
Emotional Functioning



Fatigue



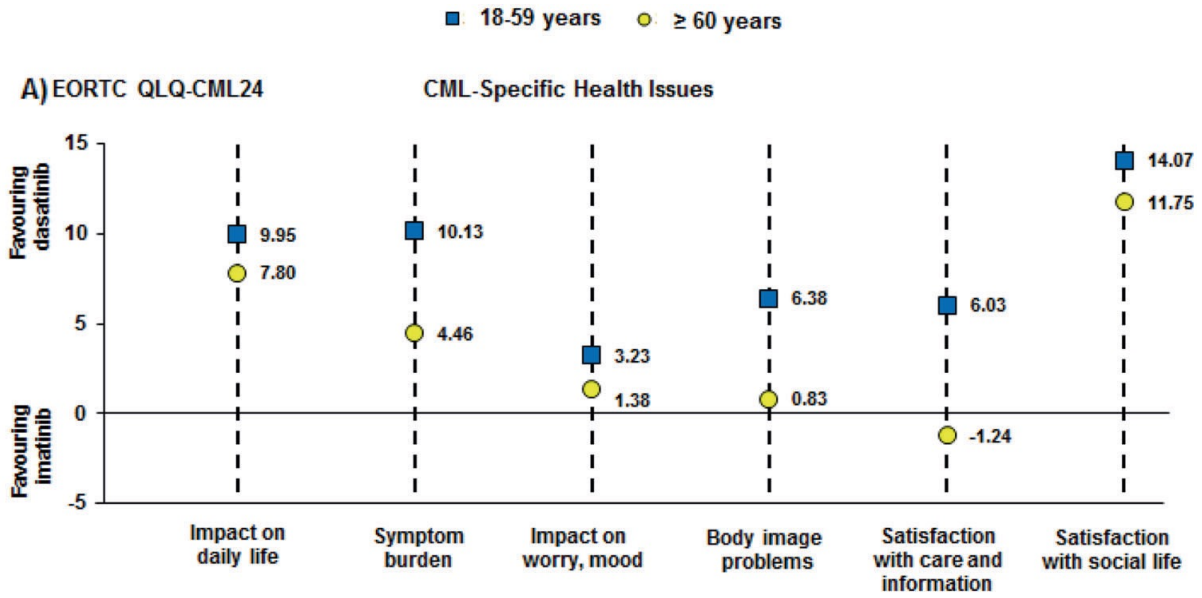
Physical Functioning

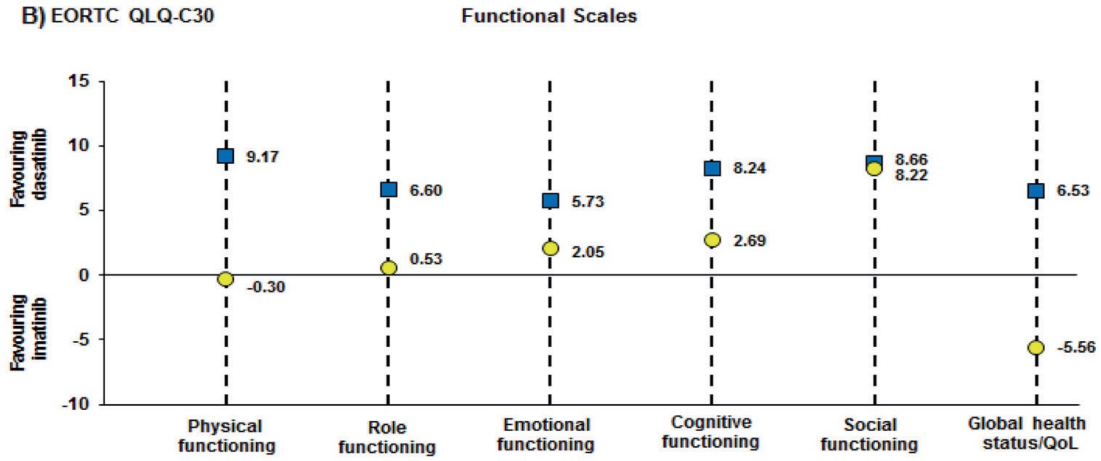


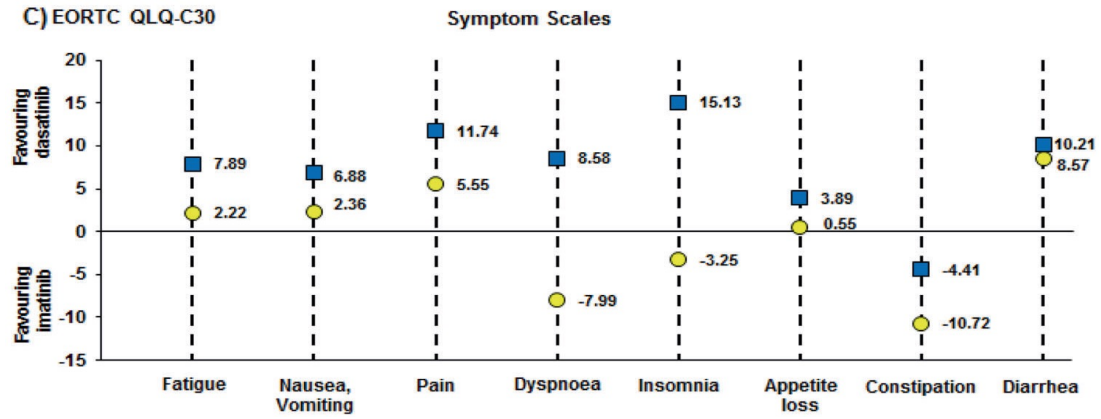
- 130 patients treated with nilotinib
- Among the 4 prespecified primary HRQOL endpoints, statistically significant improvements over time were found for Physical Functioning (P = .013), Role Functioning (P = .004), and Fatigue (P < .001). Clinically meaningful improvements were found already 3 months after the treatment start. The baseline patient self-reported fatigue severity was an independent predictive factor for the achievement of a major molecular response with an odds ratio of 0.960

Efficace et al Cancer 2018; 124: 2228-37

HR-QoL in CML patients treated with 1st line dasatinib



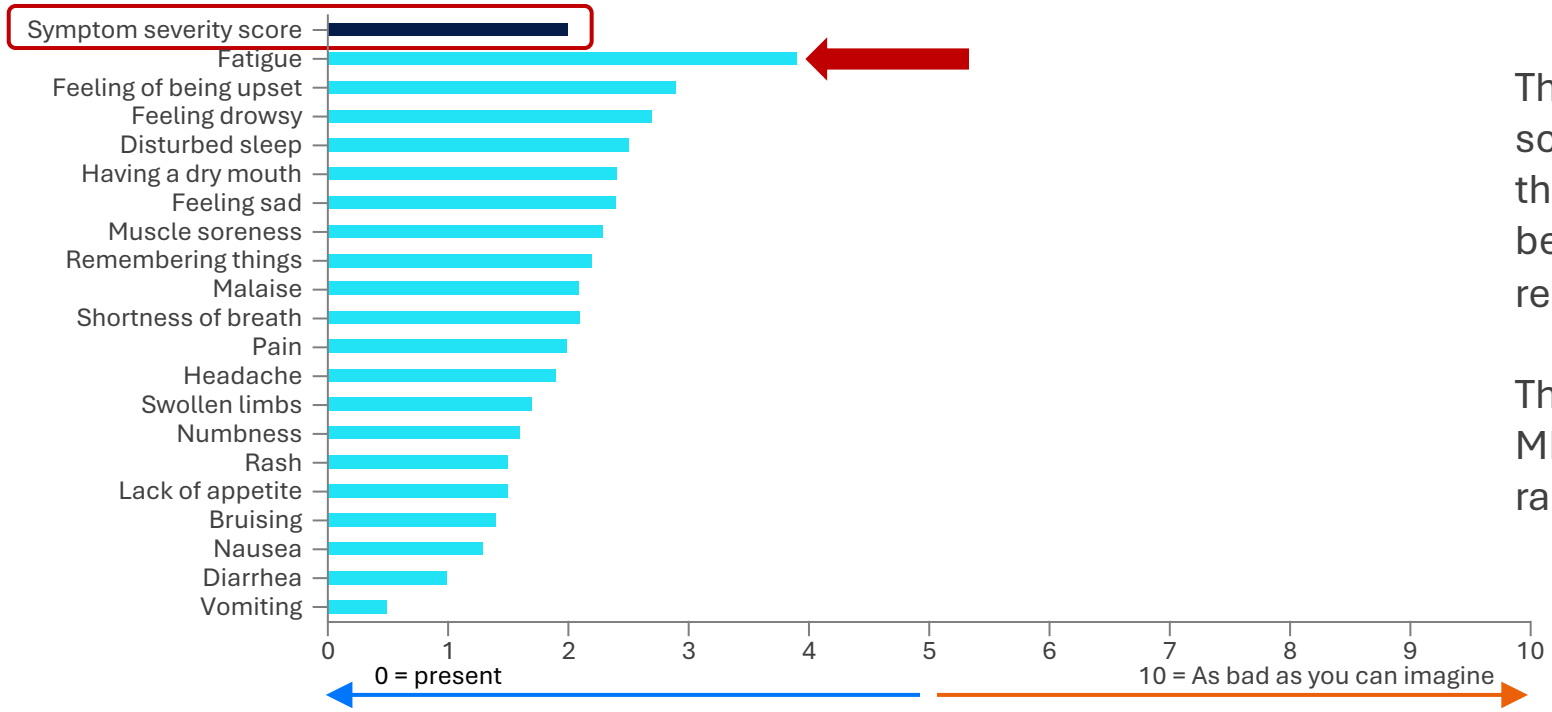




- 323 patients treated with imatinib (223) or with dasatinib (100)
- Patients treated with dasatinib reported better disease-specific HRQOL outcomes in impact on daily life (Δ = 8.72, 95% confidence interval [CI]: 3.17–14.27, p = 0.002), satisfaction with social life (Δ = 13.45, 95% CI: 5.82–21.08, p = 0.001), and symptom burden (Δ = 7.69, 95% CI: 3.42–11.96, p = 0.001). Analysis by age groups showed that, in patients aged 60 years and over, differences favoring dasatinib were negligible across several cancer generic an disease-specific HRQOL domains.

Efficace et al Leukemia 2020; 34: 488-498

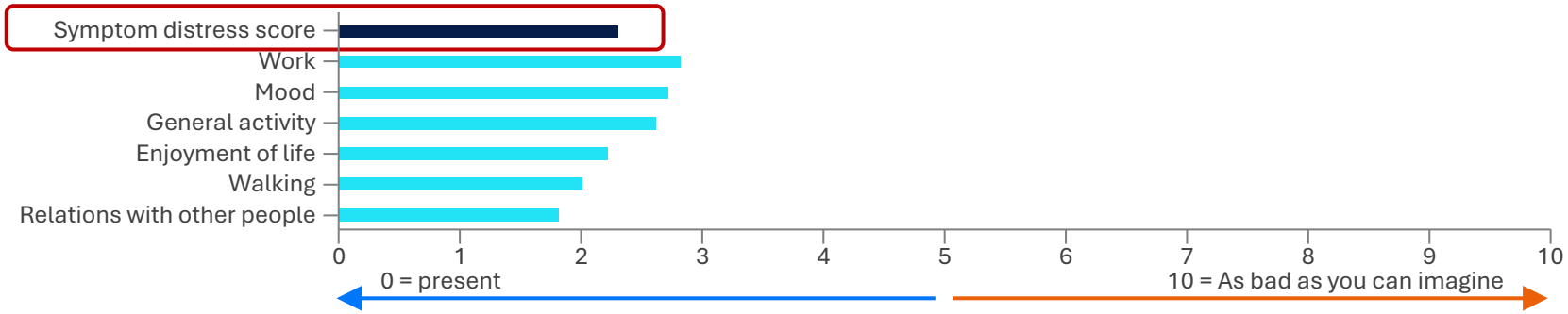
Asciminib: symptom severity score in the ASCEMBL trial



The **mean MDASI-CML** symptom severity score at **baseline** was **2.0 points**, indicating that overall symptoms reported by patients before the start of treatment were of a relatively low severity

There were no meaningful differences in MDASI-CML baseline scores between randomized treatment arms

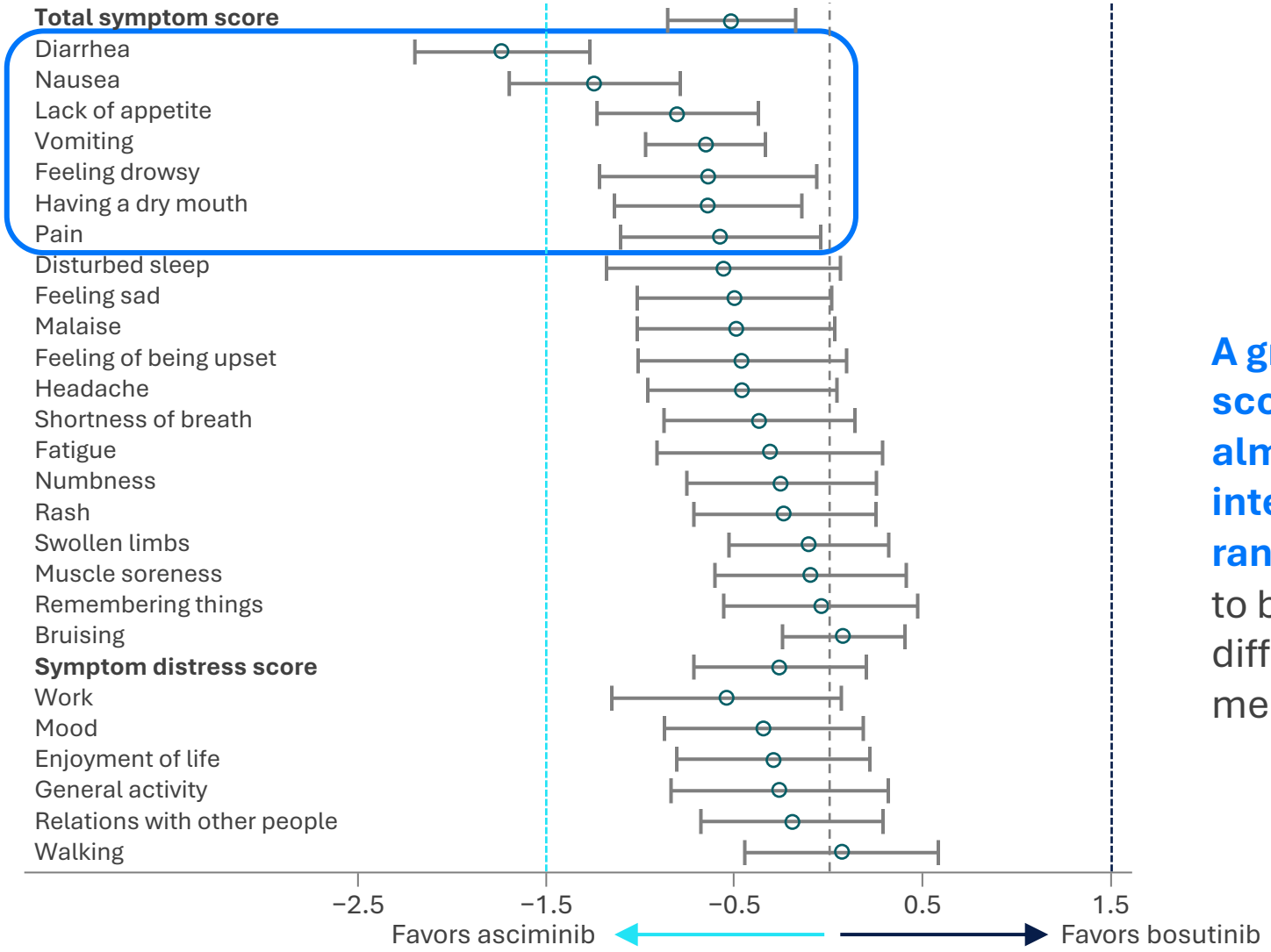
Patients reported that CML interfered with their daily life slightly; the mean symptom distress score was 2.3 points



MDASI-CML, MD Anderson Symptom Inventory for CML.

Adapted from Réa D, et al. Leukemia. 2023;37:1060-7.

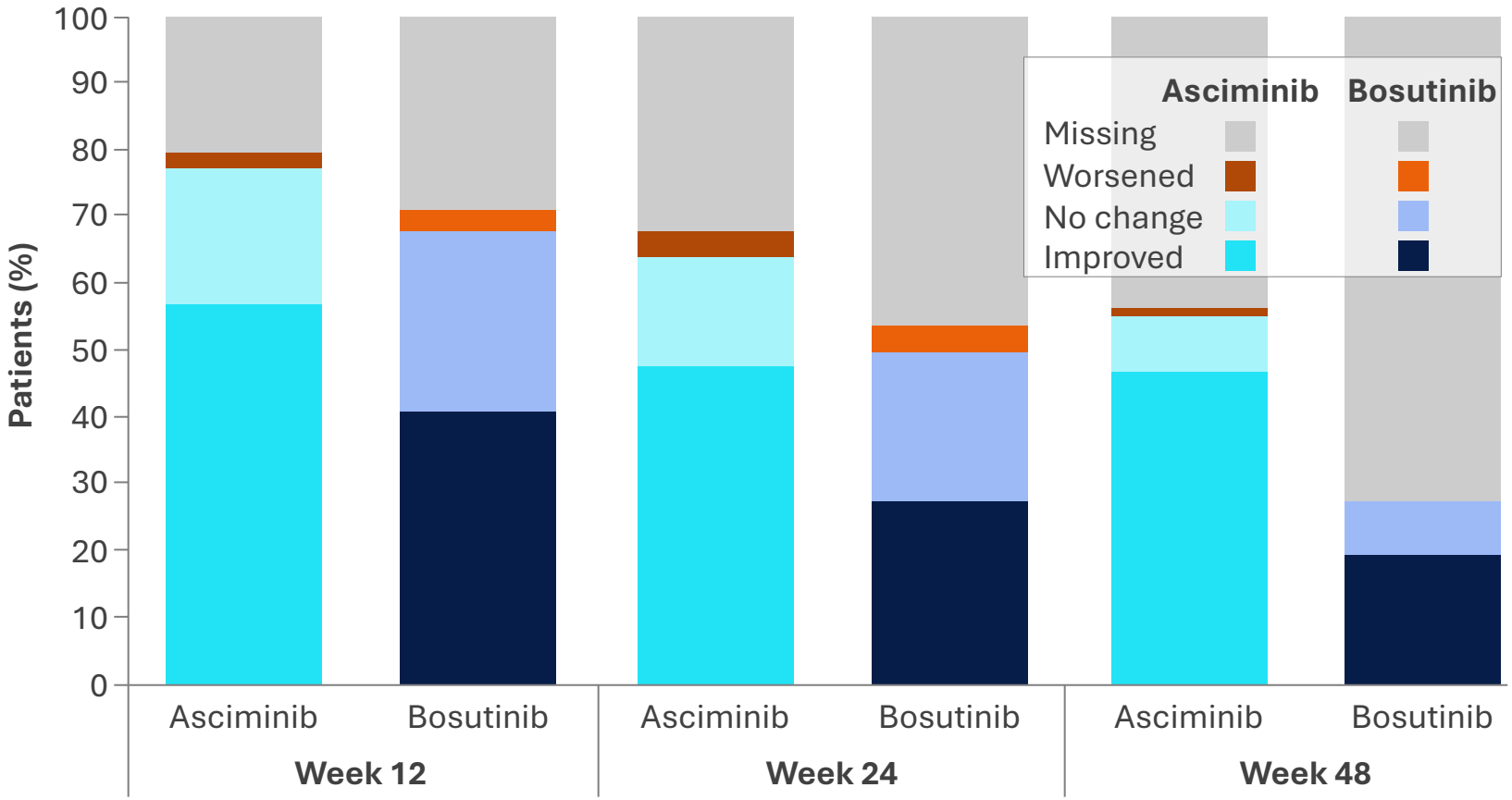
MDASI-CML symptom and interference items: the difference between treatment arms in change from baseline scores



A greater decrease in the symptom severity score, symptom distress score, and in almost all individual symptom and interference items was noted for patients randomized to asciminib treatment compared to bosutinib treatment. Although, most differences in scores did not reach a clinically meaningful difference

Adapted from Réa D, et al. Leukemia. 2023;37:1060-7.

PGIC-CML item response by timepoint for asciminib and bosutinib



By Week 48, 47% of patients in the asciminib arm reported that their CML symptoms had improved since starting treatment vs 20% in the bosutinib arm

Of note, very few patients in either treatment arm (n ≤ 6, < 4%) reported any worsening of their CML symptoms at any timepoint

Response groupings were based on a 7-point scale from 1 (very much improved) to 7 (very much worse). Improved: responses 1, 2, or 3; stable: response 4; worsened: responses 5, 6, or 7.

Adapted from Réa D, et al. Leukemia. 2023;37:1060-7.

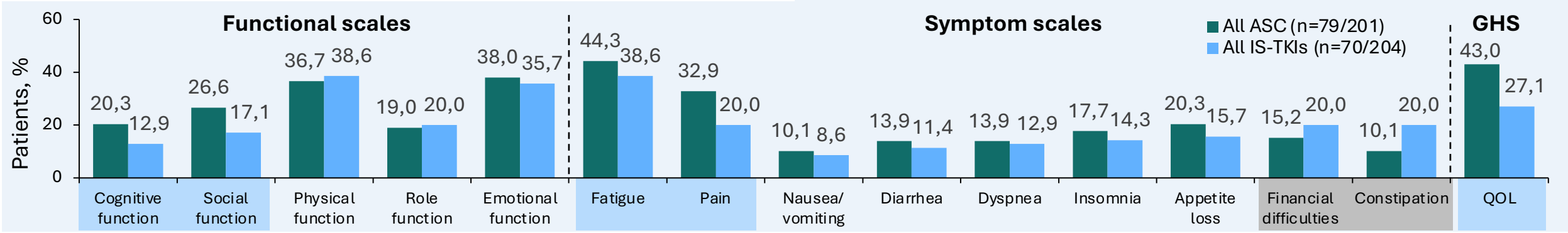
ASC4FIRST: Week 48 PROs in ND CP-CML

Methods

- ≥1 PRO assessment: ASC (n=194), IS-TKIs (n=195)
- Completion rates in pts (with PRO assessments at baseline and ≥1 post baseline) receiving ASC vs IS-TKI were balanced for QLQ-C30 and QLQ-CML24

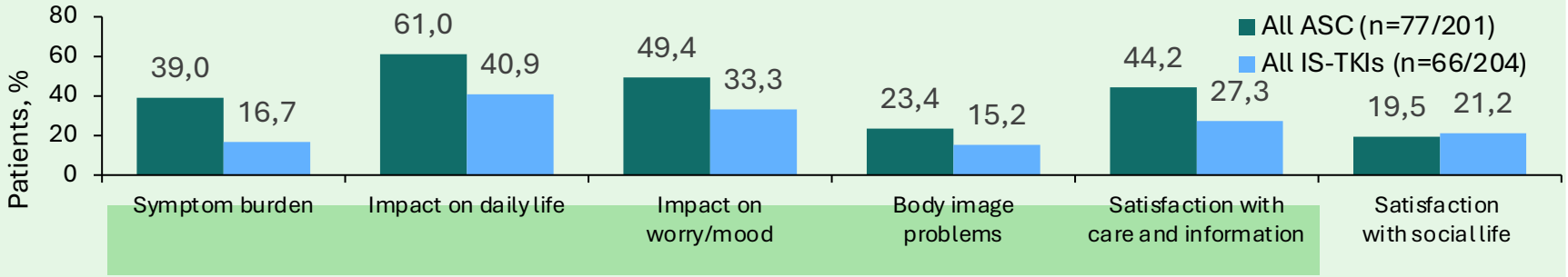
EORTC QLQ-C30*

- **More patients receiving ASC** vs IS-TKIs had improvements in:
  - **Fatigue, pain, HRQOL, and cognitive and social functioning**
- **Fewer patients receiving ASC** vs IS-TKIs had improvements in:
  - **Financial difficulties and constipation**



EORTC QLQ-CML24*

- **More patients receiving ASC** vs IS-TKIs had improvements in:
  - **Symptom burden, impact on daily life, worry/mood, body image, and satisfaction with care and information**



*Improvements[a] in EORTC QLQ-C30 and EORTC QLQ-CML24
scores from baseline to wk 48 in pts with both baseline and wk 48 assessments in ASC4FIRST. a Improvements were defined as an increase in functional scales and GHS/QOL and decrease for symptom scales.
AE=Adverse Event. ASC=Asciminib. EORTC=European Organization for Research and Treatment of Cancer. GHS=Global Health Status. GI=Gastrointestinal.
IS-TKI=Investigator-Selected Tyrosine Kinase Inhibitor. PRO=Patient Reported Outcomes. QLQ-C30=Quality of Life Questionnaire.
Hochhaus et al, Poster #PS1588. 2025 EHA Congress. June 12–15, 2025, Milan, Italy.

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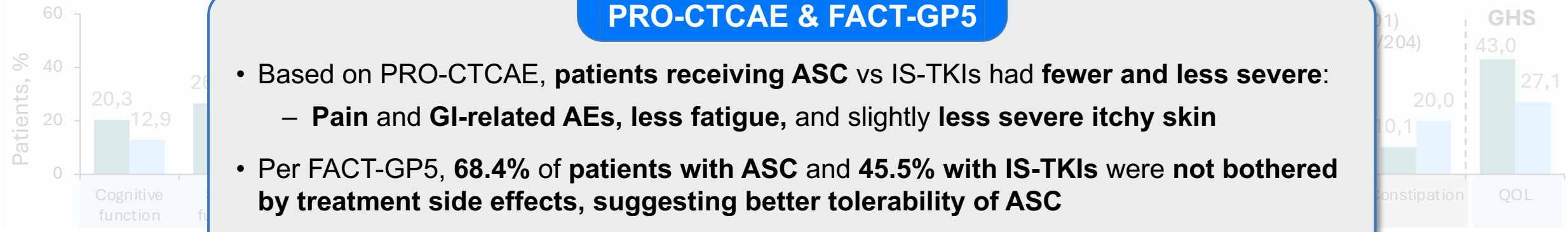
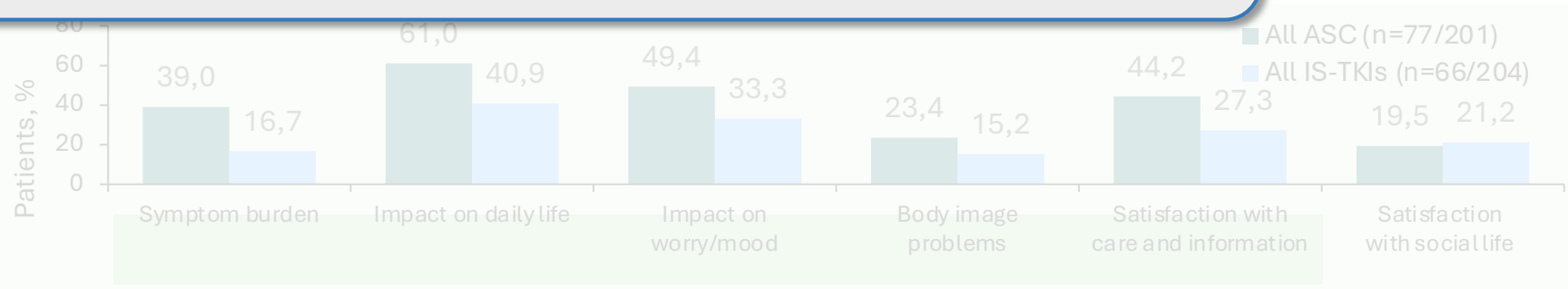


PRO-CTCAE & FACT-GP5

- Based on PRO-CTCAE, **patients receiving ASC** vs IS-TKIs had **fewer and less severe**:
  - **Pain** and **GI-related AEs, less fatigue,** and slightly **less severe itchy skin**
- Per FACT-GP5, **68.4%** of **patients with ASC** and **45.5% with IS-TKIs** were **not bothered by treatment side effects, suggesting better tolerability of ASC**

EORTC QLQ-CML24*

- **More patients receiving ASC** vs IS-TKIs had improvements in:
  - **Symptom burden, impact on daily life, worry/mood, body image, and satisfaction with care and information**



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Cancer

ORIGINAL ARTICLE | Full Access

Patient-reported symptom monitoring and adherence to therapy in patients with newly diagnosed chronic myeloid leukemia

Fabio Efficace PhD, Francesco Cottone PhD, Betina Yanez PhD, Vamsi Kota MD, Fausto Castagnetti MD, Giovanni Caocci MD, Massimiliano Bonifacio MD, Andrea Patriarca MD, Isabella Capodanno MD, Maria Cristina Miggiano MD, Mario Tiribelli MD, Massimo Breccia MD, Luigia Luciano MD, Valentina Giai MD, Alessandra Iurlo MD, Elisabetta Abruzzese MD, Carmen Fava MD, Shira Dinner MD, Jessica K. Altman MD, Gianantonio Rosti MD, Jorge Cortes MD, Marco Vignetti MD, David Cella PhD ... See fewer authors

Pilot Trial

Grant 1R21CA230367-01A1
National Cancer Institute (NCI)

Efficace F, et. al, Cancer. 2024 Jan;130(2):287-299.

Objectives (selected for the purpose of the presentation):

- **To evaluate adherence to therapy (pill counts and self-reported measure)**
- **To evaluate molecular responses at 3 and at 6 months (ELN 2020 Criteria)**

Patient characteristics= 93 newly diagnosed CML (median age=57 years)

Imatinib (43%)

2nd gen TKIs (47%)

-Follow-up= 6 months

EMPATHY trial: Adherence to TKI Therapy

Pill Count Adherence (PCA)

Outcome definition: We determined that the intervention achieved «optimal adherence» if ≥82% of patients took ≥90% of the prescribed TKI therapy (number of pills) over 6 months period.

➡ **The intervention achieved an "optimal adherence"** rate as 92.5% of patients took at least 90% of the prescribed drugs.

Validated self-reported measure (ARMS-7)

TABLE 2 Self-reported adherence at 3 and 6 months according to the Adherence to Refills and Medications Scale-7 questionnaire by type of initial tyrosine kinase inhibitor.

	Imatinib	Second-generation TKI[a]	Total	*p*
3 months				
Mean ± SD	7.84 ± 1.69	7.63 ± 1.00	7.72	.653
Median	7.00	7.00	7.00	
Range	7.00–15.00	7.00–11.00	7.00–15.00	
No.	37	46	83	
Missing	2	5	7	
6 months				
Mean ± SD	7.76 ± 1.13	7.84 ± 1.46	7.81	.753
Median	7.00	7.00	7.00	
Range	7.00–11.00	7.00–13.00	7.00–13.00	
No.	38	45	83	
Missing	1	5	6	

ARMS-7 scores

Lower scores indicate **higher adherence**

Efficace F, et. al, Cancer. 2024 Jan;130(2):287-299.

EMPATHY trial: molecular responses at 3 and 6 months

TABLE 6 Molecular response according to the European LeukemiaNet criteria at 3 and 6 months by type of tyrosine kinase inhibitor.

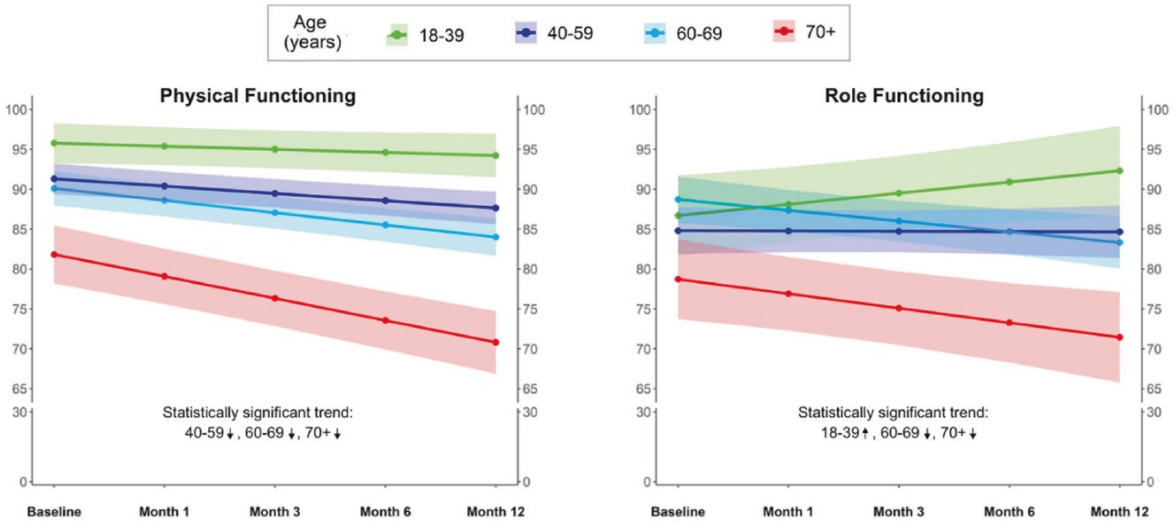
ELN response	Category	Imatinib (%)	2nd gen TKIs (%)[a]	Total No. (%)
3 months, *n* = 79				
Optimal	BCR::ABL1^{IS} ≤ 10%	28 (80.00)	41 (93.18)	69 **(87.34)**
Warning	BCR::ABL1^{IS} > 10%	7 (20.00)	3 (6.82)	10 (12.66)
6 months, *n* = 81				
Optimal	BCR::ABL1^{IS} ≤ 1%	25 (65.79)	36 (83.72)	61 (75.31)
Warning	BCR::ABL1^{IS} > 1%–10%	8 (21.05)	5 (11.63)	13 (16.05)
Failure	BCR::ABL1^{IS} > 10%	5 (13.16)	2 (4.65)	7 (8.64)

NEXT STEP:

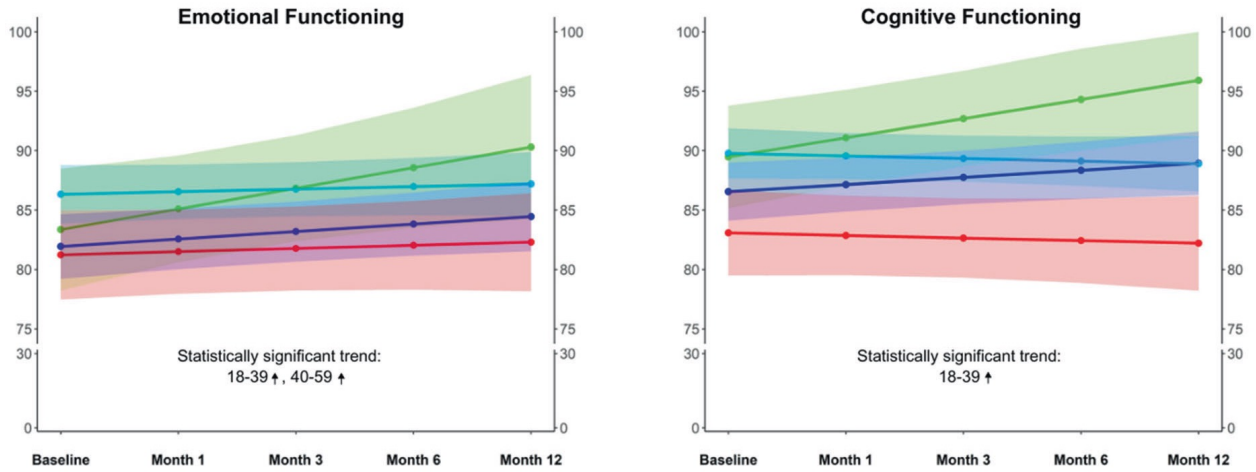
Systematic ePRO symptom monitoring ← **RCT** → **Standard CML monitoring care**

Efficace F, et al, Cancer. 2024 Jan;130(2):287-299.

QoL in TFR: EURO-SKI trial

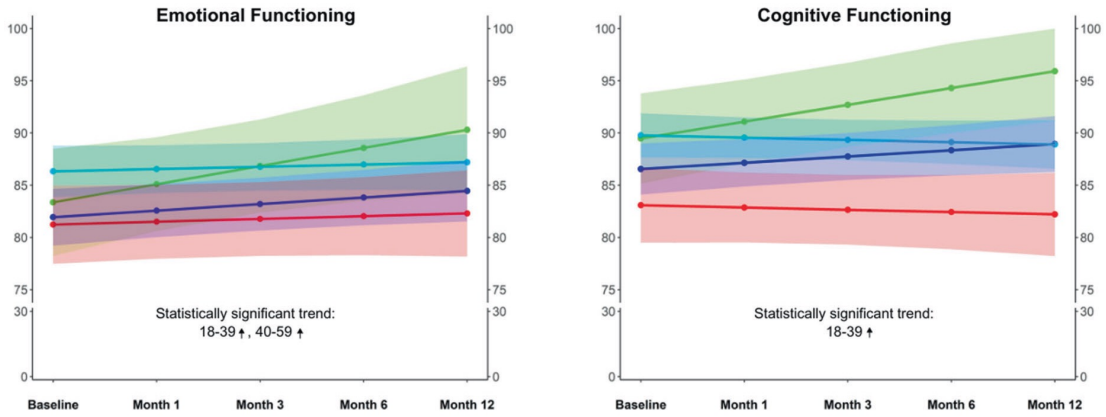


- 686/728 (94%) patients completed QoL assessment
- QoL evaluation depends on specific age groups
- Younger pts benefiting the most

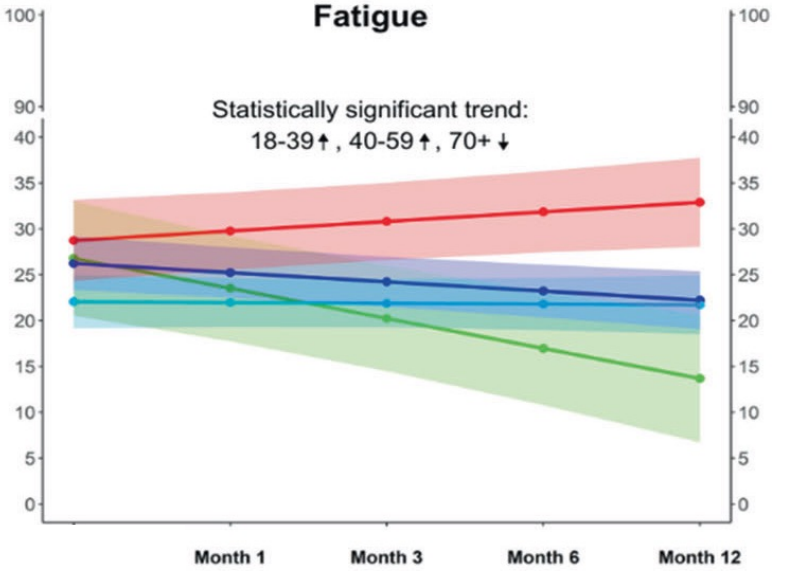


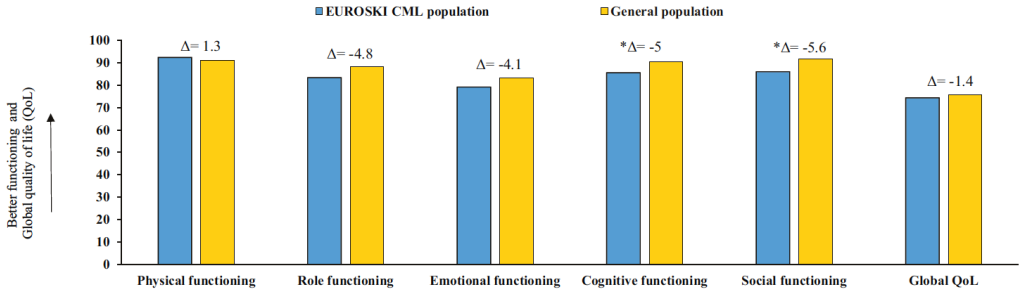
Efficace F, et al. Leukemia 2024;38: 1722-30.

QoL in TFR: EURO-SKI trial (II)

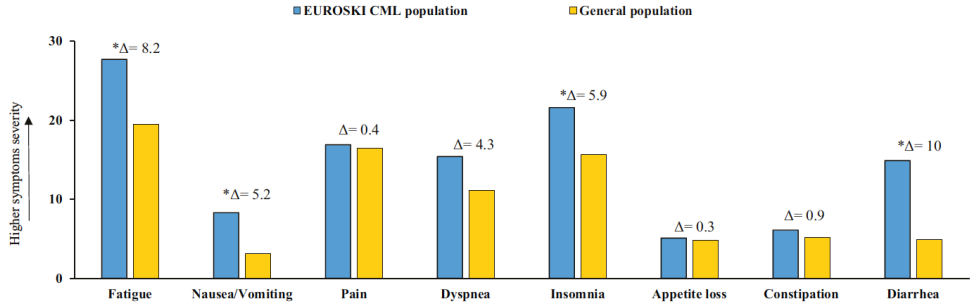


a





b



Efficace F, et al. Leukemia 2024;38: 1722-30.

Conclusions

- We move towards patient-centered decision-making in CML: in this light, the existence of PRO instruments specific for CML patients facilitate individualized approach

- Main evidences are that imatinib provides clear advantage in terms of HRQoL when compared to IFN but only few reports on HRQoL with second-generation TKIs in clinical practice were reported

- Documenting HRQoL and side effects of CML treatments from patients' perspective is needed to evaluate overall treatment effectiveness and net clinical benefit of newer therapeutic strategies