

Table S1. CIRS score.

Organ system	Severity
1. Cardiac	0-1-2-3-4
2. Vascular	0-1-2-3-4
3. Haematological	0-1-2-3-4
4. Respiratory	0-1-2-3-4
5. Ophthalmological and ORL	0-1-2-3-4
6. Upper gastrointestinal	0-1-2-3-4
7. Lower gastrointestinal	0-1-2-3-4
8. Hepatic and pancreatic	0-1-2-3-4
9. Renal	0-1-2-3-4
10. Genito-urinary	0-1-2-3-4
11. Musculoskeletal and cutaneous	0-1-2-3-4
12. Neurological	0-1-2-3-4
13. Endocrine, metabolic, mammary	0-1-2-3-4
14. Psychiatric	0-1-2-3-4

Score depending on the severity of the organ/system affected: 0 – Absence of disease, 1 – mild, 2 – moderate, 3 – severe, 4 – very severe

Table S2. QLQ-C30 scores.

Variable	Parameter	Basal (T0)	Intermediate (T1)	Final (T2)	Change from T0 to T1	Change from T0 to T2
QLQ-C30 functional scales						
Physical	N	53	53	20	53	20
	Median (IQR)	93.33 (80.00–100.00)	86.67 (73.33–93.33)	80.00 (66.67–86.67)	0.00 (–6.67 to 6.67)	-6.67 (–20.00 to 0.00)
	<i>p</i> value				0.3625	0.0723
Role	N	53	53	20	53	20
	Median (IQR)	83.33 (66.67–100.00)	83.33 (66.67–100.00)	83.33 (66.67–100.00)	0.00 (–8.33 to 0.00)	0.00 (–29.16 to 0.00)
	<i>p</i> value				0.9786	0.4612
Emotional	N	53	53	20	53	20
	Median (IQR)	83.33 (75.00–91.67)	83.33 (75.00–91.67)	79.17 (66.67–91.67)	0.00 (–8.33 to 12.50)	0.00 (–8.34 to 16.67)
	<i>p</i> value				0.3041	0.8751
Cognitive	N	53	53	20	53	20
	Median (IQR)	100.00 (83.33–100.00)	100.00 (83.33–100.00)	100.00 (79.17–100.00)	0.00 (–8.33 to 0.00)	0.00 (–29.16 to 0.00)
	<i>p</i> value				0.1556	0.0885
Social	N	53	53	20	53	20
	Median (IQR)	100.00 (66.67–100.00)	100.00 (66.67–100.00)	83.33 (66.67–100.00)	0.00 (0.00–0.00)	0.00 (–29.16 to 0.00)
	<i>p</i> value				0.8190	0.4220
QLQ-C30 symptoms						
Fatigue	N	53	53	20	53	20
	Median (IQR)	33.33 (22.22–44.44)	33.33 (11.11–33.33)	33.33 (33.33–36.11)		

	<i>p</i> value				-11.11 (-16.67 to 11.11)	11.11 (-16.66 to 30.55)
					0.2920	0.1920
Nausea and vomiting	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–16.67)	0.00 (0.00–0.00)	0.00 (0.00–16.67)
	<i>p</i> value				0.5084	0.0193
Pain	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–16.67)	0.00 (0.00–16.67)	16.67 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–29.16)
	<i>p</i> value				0.9684	0.1696
Dyspnoea	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–33.33)	0.00 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–33.33)
	<i>p</i> value				0.8387	0.1013
Insomnia	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–33.33)	0.00 (0.00–33.33)	33.33 (0.00–33.33)	0.00 (-33.33 to 0.00)	0.00 (-33.33 to 24.99)
	<i>p</i> value				0.1130	0.6256
Appetite Loss	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–33.33)
	<i>p</i> value				0.6250	0.0339
Constipation	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	16.67 (0.00–66.67)	0.00 (0.00–0.00)	0.00 (0.00–33.33)
	<i>p</i> value				1	0.0101
Diarrhea	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)		
	<i>p</i> value					

	Median (IQR)				0.00 (0.00–0.00)	0.00 (0.00–0.00)
	<i>p</i> value				0.4004	0.6105
Financial Difficulties	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	<i>p</i> value				0.4560	0.5247
QLQ-C30 Global Health Status	N	53	53	20	53	20
	Median (IQR)	133.33 (116.67–150.00)	133.33 (133.33–166.67)	133.33 (100.00–166.67)	0.00 (0.00–16.67)	0.00 (–16.67 to 12.50)
	<i>p</i> value				0.1888	0.6085
QLQ-C30 Final scoring	N	53	53	20	53	20
	Median (IQR)	88.80 (81.24–94.87)	89.74 (82.31–94.36)	80.77 (73.33–86.64)	1.28 (–3.03 to 4.42)	–11.28 (–19.69 to –0.85)
	<i>p</i> value				0.8944	0.0089

The number of non missing observations and the median value (IQR) of each variable distribution are reported at each time point. Change distributions have been estimated using data from patients characterized by non missing observations for the two time points and are described by sample size, median value (IQR). *p*-values derive from the the Wilcoxon test for paired samples.

Table S3. BR23 scores.

Variable	Parameter	Basal (T0)	Intermediate (T1)	Final (T2)	Change from T0 to T1	Change from T0 to T2
BR23 Symptoms scales						
Systemic therapy side effects	N	51	53	20	51	20
	Median (IQR)	4.76 (0.00–19.05)	14.29 (9.52–19.05)	16.67 (9.52–25.00)	4.76 (0.00–9.52)	7.14 (1.19–19.05)
	<i>p</i> value				0.0138	0.0018
Upset by hair loss	N	53	52	20	52	20
	Median (IQR)	0.00 (0.00–0.00)	0.00 (0.00–33.33)	0.00 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	<i>p</i> value				0.5166	0.2278
Arm symptoms	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–11.11)	0.00 (0.00–11.11)	16.67 (0.00–22.22)	0.00 (0.00–5.55)	0.00 (0.00–19.44)
	<i>p</i> value				0.1912	0.014
Breast symptoms	N	53	53	20	53	20
	Median (IQR)	0.00 (0.00–8.33)	0.00 (0.00–8.33)	4.17 (0.00–8.33)	0.00 (0.00–0.00)	0.00 (0.00–8.33)
	<i>p</i> value				0.8709	0.1648
BR23 Functional scales						
Body image	N	52	53	20	52	20
	Median (IQR)	100.00 (66.67–100.00)	91.67 (75.00–100.00)	79.17 (58.34–100.00)	0.00 (0.00–8.33)	0.00 (–22.91 to 14.58)
	<i>p</i> value				1	0.1240
Future perspective	N	53	52	19	52	19
	Median (IQR)	66.67 (33.33–66.67)	66.67 (33.33–75.00)	66.67 (33.33–66.67)	0.00 (–33.33 to 33.33)	0.00 (–33.33 to 33.33)

	<i>p</i> value				0.9681	0.4813
Sexual functioning	N	53	53	18	53	18
	Median (IQR)	0.00 (0.00–33.33)	0.00 (0.00–16.67)	0.00 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	<i>p</i> value				0.2227	0.8986
Sexual enjoyment	N	53	53	18	53	18
	Median (IQR)	0.00 (0.00–33.33)	0.00 (0.00–0.00)	0.00 (0.00–25.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	<i>p</i> value				0.1445	0.7358

The number of non missing observations and the median value (IQR) of each variable distribution are reported at each time point. Change distributions have been estimated using data from patients characterized by non missing observations for the two time points and are described by sample size, median value (IQR). *p*-values derive from the the Wilcoxon test for paired samples.

Table S4. Frequency of important differences between basal (T0) and intermediate (T1) in QLQ-C30 scores by comorbidity and polypharmacy conditions.

Variable	Parameter	TOTAL	CIRS			DRUGS		
			≥ 5	< 5	p value	≥ 2	< 2	p value
QLQ-C30 functional scales								
Physical functioning	Improved ($x \geq +5$)	16 (30.18%)	9 (33.33%)	7 (26.92%)	0.7664	10 (37.04%)	6 (23.07%)	0.3718
	Stable ($-5 < x < +5$)	14 (26.42%)	4 (14.82%)	10 (38.46%)	n.t.	5 (18.52%)	9 (34.62%)	n.t.
	Worsened ($x \leq -5$)	23 (43.40%)	14 (51.85%)	9 (34.62%)	0.2709	12 (44.44%)	11 (42.31%)	1
Role functioning	Improved ($x \geq +5$)	12 (22.64%)	7 (25.93%)	5 (19.23%)	0.7445	6 (22.22%)	6 (23.07%)	1
	Stable ($-5 < x < +5$)	28 (52.83%)	12 (44.44%)	16 (61.54%)	n.t.	12 (44.44%)	16 (61.54%)	n.t.
	Worsened ($x \leq -5$)	13 (24.53%)	8 (29.63%)	5 (19.23%)	0.5256	9 (33.34%)	4 (15.39%)	0.1212
Emotional functioning	Improved ($x \geq +5$)	26 (49.06%)	14 (51.85%)	12 (46.15%)	0.7857	14 (51.85%)	12 (46.15%)	0.7857
	Stable ($-5 < x < +5$)	12 (22.64%)	6 (22.32%)	6 (23.08%)	n.t.	7 (25.93%)	5 (19.23%)	n.t.
	Worsened ($x \leq -5$)	15 (28.30%)	7 (25.93%)	8 (30.77%)	0.7664	6 (22.22%)	9 (34.62%)	0.3718
Cognitive functioning	Improved ($x \geq +5$)	3 (5.66%)	2 (7.41%)	1 (3.85%)	1	2 (7.41%)	1 (3.85%)	1
	Stable ($-5 < x < +5$)	37 (69.81%)	18 (66.66%)	19 (73.07%)	n.t.	16 (59.26%)	21 (80.77%)	n.t.
	Worsened ($x \leq -5$)	13 (24.53%)	7 (25.93%)	6 (23.08%)	1	9 (33.33%)	4 (15.38%)	0.2021
Social functioning	Improved ($x \geq +5$)	12 (22.64%)	9 (33.33%)	3 (11.54%)	0.0993	7 (25.93%)	5 (19.23%)	0.7445
	Stable ($-5 < x < +5$)	31 (58.49%)	12 (44.44%)	19 (73.07%)	n.t.	15 (55.55%)	16 (61.54%)	n.t.
	Worsened ($x \leq -5$)	10 (18.87%)	6 (22.23%)	4 (15.39%)	0.7277	5 (18.52%)	5 (19.23%)	1
QLQ-C30 symptoms								
Fatigue	Worsened ($x \geq +5$)	16 (30.19%)	8 (29.63%)	8 (30.77%)	1	9 (33.33%)	7 (26.92%)	0.7664
	Stable ($-5 < x < +5$)	10 (18.87%)	5 (18.52%)	5 (19.23%)	n.t.	5 (18.52%)	5 (19.23%)	n.t.
	Improved ($x \leq -5$)	27 (50.94%)	14 (51.85%)	13 (50%)	1	13 (48.15%)	14 (53.85%)	0.7857

Nausea and vomiting	Worsened ($x \geq +5$)	6 (11.32%)	3 (11.11%)	3 (11.54%)	1	5 (18.52%)	1 (3.85%)	0.1917
	Stable ($-5 < x < +5$)	44 (83.02%)	22 (81.48%)	22 (84.61%)	n.t.	20 (74.07%)	24 (92.30%)	n.t.
	Improved ($x \leq -5$)	3 (5.66%)	2 (7.41%)	1 (3.85%)	1	2 (7.41%)	1 (3.85%)	1
Pain	Worsened ($x \geq +5$)	11 (20.75%)	8 (29.63%)	3 (11.54%)	0.1751	4 (14.81%)	7 (26.92%)	0.3265
	Stable ($-5 < x < +5$)	32 (60.38%)	16 (59.26%)	16 (61.54%)	n.t.	16 (59.26%)	16 (61.54%)	n.t.
	Improved ($x \leq -5$)	10 (18.87%)	3 (11.11%)	7 (26.92%)	0.1751	7 (25.93%)	3 (11.54%)	0.2935
Dyspnea	Worsened ($x \geq +5$)	6 (11.32%)	4 (14.82%)	2 (7.69%)	0.6687	4 (14.81%)	2 (7.69%)	0.6687
	Stable ($-5 < x < +5$)	43 (81.13%)	21 (77.77%)	22 (84.62%)	n.t.	20 (74.08%)	23 (88.46%)	n.t.
	Improved ($x \leq -5$)	4 (7.55%)	2 (7.41%)	2 (7.69%)	1	3 (11.11%)	1 (3.85%)	0.6104
Insomnia	Worsened ($x \geq +5$)	8 (15.09%)	6 (22.23%)	2 (7.69%)	0.2501	5 (18.52%)	3 (11.54%)	0.7040
	Stable ($-5 < x < +5$)	28 (52.83%)	11 (40.73%)	17 (65.38%)	n.t.	10 (37.04%)	18 (69.23%)	n.t.
	Improved ($x \leq -5$)	17 (32.08%)	10 (37.04%)	7 (26.92%)	0.5587	12 (44.44%)	5 (19.23%)	0.0772
Appetite Loss	Worsened ($x \geq +5$)	7 (13.21%)	3 (11.11%)	4 (15.38%)	0.7040	4 (14.81%)	3 (11.54%)	1
	Stable ($-5 < x < +5$)	41 (77.36%)	19 (70.37%)	22 (84.62%)	n.t.	18 (66.67%)	23 (88.46%)	n.t.
	Improved ($x \leq -5$)	5 (9.43%)	5 (18.52%)	0 (0%)	0.0510	5 (18.52%)	0 (0%)	0.0510
Constipation	Worsened ($x \geq +5$)	9 (16.98%)	4 (14.82%)	5 (19.23%)	0.7277	5 (18.52%)	4 (15.38%)	1
	Stable ($-5 < x < +5$)	34 (64.15%)	15 (55.55%)	19 (73.08%)	n.t.	13 (48.15%)	21 (80.77%)	n.t.
	Improved ($x \leq -5$)	10 (18.87%)	8 (29.63%)	2 (7.69%)	0.0777	9 (33.33%)	1 (3.85%)	0.0113
Diarrhea	Worsened ($x \geq +5$)	6 (11.32%)	3 (11.11%)	3 (11.54%)	1	4 (14.81%)	2 (7.69%)	0.6687
	Stable ($-5 < x < +5$)	44 (83.02%)	23 (85.19%)	21 (80.77%)	n.t.	22 (81.49%)	22 (84.62%)	n.t.
	Improved ($x \leq -5$)	3 (5.66%)	1 (3.70%)	2 (7.69%)	0.6104	1 (3.70%)	2 (7.69%)	0.6104

Financial Difficulties	Worsened ($x \geq +5$)	4 (7.55%)	1 (3.70%)	3 (11.54%)	0.3507	2 (7.41%)	2 (7.69%)	1
	Stable ($-5 < x < +5$)	47 (88.68%)	24 (88.89%)	23 (88.46%)	n.t.	23 (85.18%)	24 (92.31%)	n.t.
	Improved ($x \leq -5$)	2 (3.77%)	2 (7.41%)	0 (0%)	0.4906	2 (7.41%)	0 (0%)	0.4906
QLQ-C30 Global Health Status	Improved ($x \geq +5$)	24 (45.29%)	13 (48.14%)	11 (42.31%)	0.7846	15 (55.55%)	9 (34.62%)	0.1704
	Stable ($-5 < x < +5$)	21 (39.62%)	10 (37.04%)	11 (42.31%)	n.t.	7 (25.93%)	14 (53.84%)	n.t.
	Worsened ($x \leq -5$)	8 (15.09%)	4 (14.82%)	4 (15.38%)	1	5 (18.52%)	3 (11.54%)	0.7040
QLQ-C30 Final scoring	Improved ($x \geq +5$)	12 (22.64%)	9 (33.33%)	3 (11.54%)	0.0993	8 (29.63%)	4 (15.38%)	0.3265
	Stable ($-5 < x < +5$)	32 (60.38%)	12 (44.44%)	20 (76.92%)	n.t.	14 (51.85%)	18 (69.22%)	n.t.
	Worsened ($x \leq -5$)	9 (16.98%)	6 (22.23%)	3 (11.54%)	0.4672	5 (18.52%)	4 (15.38%)	1

Patients' conditions were labelled as "improved", "stable" or "worsened" based on their individual change (x) from baseline to intermediate times.

n.t. = not tested

Table S5. Frequency of important differences between basal (T0) and intermediate (T1) in BR23 scores by comorbidity and polypharmacy conditions.

Variable	Variable change ID	TOTAL	CIRS			DRUGS		
			≥ 5	< 5	p value	≥ 2	< 2	p value
BR23 Symptoms scales								
Systemic therapy side effects	Worsened ($x \geq +5$)	21 (39.62%)	12 (44.44%)	9 (34.62%)	1	10 (37.04%)	11 (42.31%)	0.7822
	Stable ($-5 < x < +5$)	25 (47.17%)	10 (37.04%)	15 (57.69%)	n.t.	13 (48.15%)	12 (46.15%)	n.t.
	Improved ($x \leq -5$)	7 (13.21%)	5 (18.52%)	2 (7.69%)	0.4203	4 (14.81%)	3 (11.54%)	1
Upset by hair loss	Worsened ($x \geq +5$)	6 (11.32%)	4 (14.82%)	2 (7.69%)	0.6687	3 (11.11%)	3 (11.54%)	1
	Stable ($-5 < x < +5$)	45 (84.91%)	21 (77.77%)	24 (92.31%)	n.t.	23 (85.19%)	22 (84.61%)	n.t.
	Improved ($x \leq -5$)	2 (3.77%)	2 (7.41%)	0 (0%)	0.4906	1 (3.70%)	1 (3.85%)	1
Arm symptoms	Worsened ($x \geq +5$)	13 (24.53%)	7 (25.93%)	6 (23.08%)	1	7 (25.93%)	6 (23.08%)	1
	Stable ($-5 < x < +5$)	33 (62.26%)	18 (66.66%)	15 (57.69%)	n.t.	16 (59.26%)	17 (65.38%)	n.t.
	Improved ($x \leq -5$)	7 (13.21%)	2 (7.41%)	5 (19.23%)	0.2501	4 (14.81%)	3 (11.54%)	1
Breast symptoms	Worsened ($x \geq +5$)	6 (11.32%)	2 (7.41%)	4 (15.38%)	0.6695	3 (11.11%)	3 (11.54%)	1
	Stable ($-5 < x < +5$)	39 (73.58%)	23 (85.18%)	16 (61.54%)	n.t.	21 (77.78%)	18 (69.23%)	n.t.
	Improved ($x \leq -5$)	8 (15.09%)	2 (7.41%)	6 (23.08%)	0.1415	3 (11.11%)	5 (19.23%)	0.4672
BR23 Functional scales								
Body image	Improved ($x \geq +5$)	14 (26.42%)	9 (33.33%)	5 (19.23%)	0.3520	8 (29.63%)	6 (23.08%)	0.7570
	Stable ($-5 < x < +5$)	27 (50.94%)	13 (48.15%)	14 (53.85%)	n.t.	12 (44.44%)	15 (57.69%)	n.t.
	Worsened ($x \leq -5$)	12 (22.64%)	5 (18.52%)	7 (26.92%)	0.7432	7 (25.93%)	5 (19.23%)	0.7445
Future perspective	Improved ($x \geq +5$)	17 (32.08%)	9 (33.33%)	8 (30.77%)	1	7 (25.93%)	10 (38.46%)	0.3869

	Stable (-5 < x < +5)	20 (37.74%)	10 (37.04%)	10 (38.46%)	n.t.	12 (44.44%)	8 (30.77%)	n.t.
	Worsened (x ≤ -5)	16 (30.19%)	8 (29.63%)	8 (30.77%)	1	8 (29.63%)	8 (30.77%)	1
Sexual functioning	Improved (x ≥ +5)	3 (5.66%)	1 (3.70%)	2 (7.69%)	0.6104	2 (7.41%)	1 (3.85%)	1
	Stable (-5 < x < +5)	39 (73.58%)	20 (74.07%)	19 (73.08%)	n.t.	19 (70.37%)	20 (76.92%)	n.t.
	Worsened (x ≤ -5)	11 (20.76%)	6 (22.23%)	5 (19.23%)	1	6 (22.22%)	5 (19.23%)	1
Sexual enjoyment	Improved (x ≥ +5)	2 (3.77%)	0 (0%)	2 (7.69%)	0.2358	0 (0%)	2 (7.69%)	0.2358
	Stable (-5 < x < +5)	43 (81.12%)	22 (81.48%)	21 (80.77%)	n.t.	23 (85.19%)	20 (76.92%)	n.t.
	Worsened (x ≤ -5)	8 (15.09%)	5 (18.52%)	3 (11.54%)	0.7040	4 (14.81%)	4 (15.39%)	1

Patients' conditions were labelled as 'improved', 'stable' or 'worsened' based on their individual change (x) from baseline to intermediate times.

n.t. = not tested