Supporting Information

Two-year follow-up of tirabrutinib monotherapy in Waldenström's macroglobulinemia

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TABLE S1 Treatment-related adverse events of interest

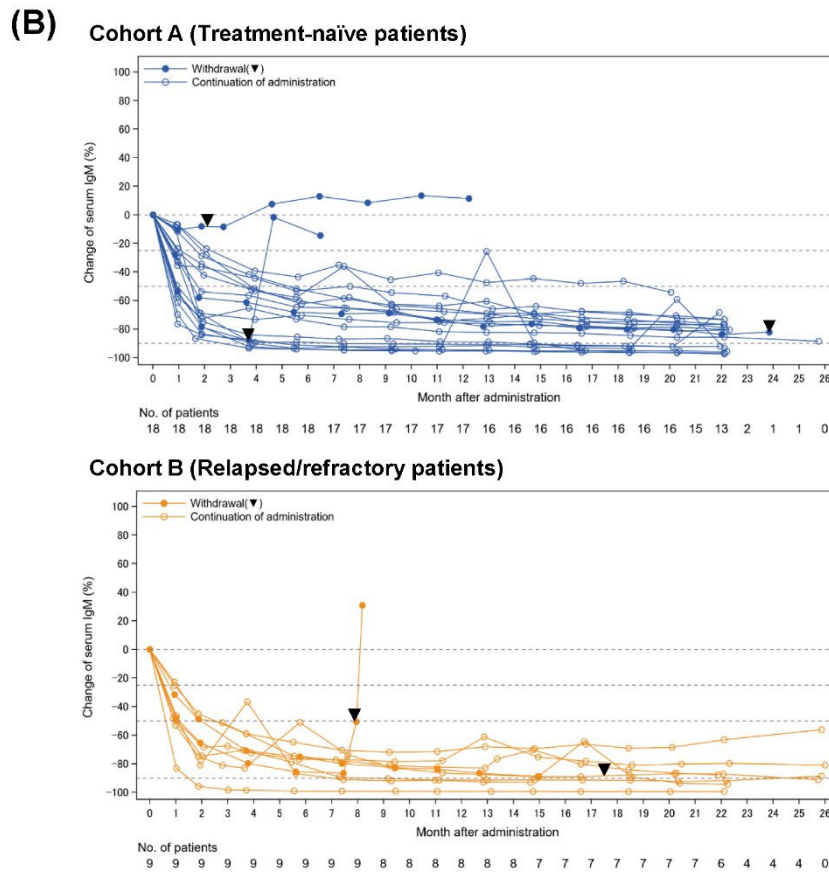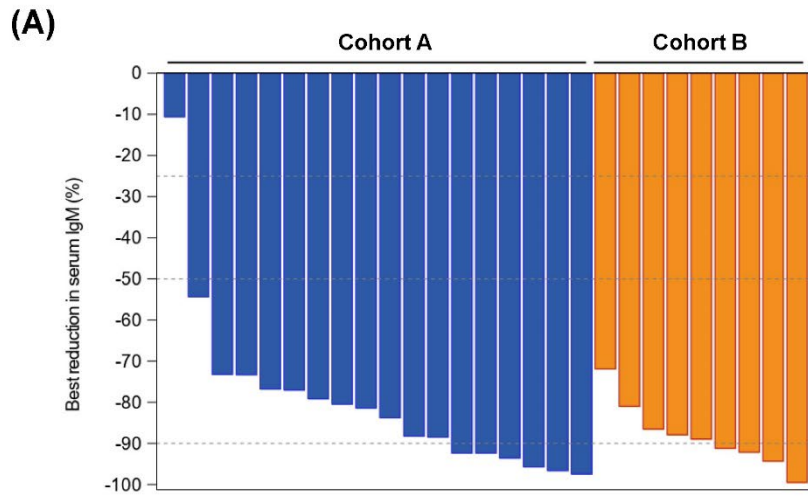|	Cohort A Treatment-naïve N = 18		Cohort B Relapsed/refractory N = 9		All N = 27	
	Any grade	Grade 3-4	Any grade	Grade 3-4	Any grade	Grade 3-4
Skin	13 (72)	2 (11)	1 (11)	0	14 (52)	2 (7)
Rash	9 (50)	0	1 (11)	0	10 (37)	0
Rash maculopapular	3 (17)	0	0	0	3 (11)	0
Erythema multiforme	1 (6)	1 (6)	0	0	1 (4)	1 (4)
Rash erythematous	1 (6)	1 (6)	0	0	1 (4)	1 (4)
Bleeding	3 (17)	0	1 (11)	0	4 (15)	0
Epistaxis	1 (6)	0	1 (11)	0	2 (7)	0
Mouth hemorrhage	1 (6)	0	0	0	1 (4)	0
Purpura	1 (6)	0	0	0	1 (4)	0
Cytopenia	7 (39)	4 (22)	6 (67)	4 (44)	13 (48)	8 (30)
Neutropenia	3 (17)	2 (11)	5 (56)	3 (33)	8 (30)	5 (19)
Leukopenia	2 (11)	0	3 (33)	0	5 (19)	0
Lymphopenia	2 (11)	2 (11)	2 (22)	2 (22)	4 (15)	4 (15)
Thrombocytopenia	3 (17)	0	0	0	3 (11)	0
Infection	6 (33)	1 (6)	3 (33)	0	9 (33)	1 (4)
Pneumonia	3 (17)	0	0	0	3 (11)	0
Urinary tract infection	2 (11)	0	0	0	2 (7)	0
Atypical mycobacterial infection	1 (6)	1 (6)	0	0	1 (4)	1 (4)
Cystitis	1 (6)	0	0	0	1 (4)	0
Oral herpes	1 (6)	0	0	0	1 (4)	0
Paronychia	1 (6)	0	0	0	1 (4)	0
Upper respiratory tract infection	1 (6)	0	0	0	1 (4)	0
Corneal infection	0	0	1 (11)	0	1 (4)	0
Herpes Zoster	0	0	1 (11)	0	1 (4)	0
Oral fungal infection	0	0	1 (11)	0	1 (4)	0

Number (%) of patients is shown.

FIGURE S1 Serum IgM. (A) Best reduction in serum IgM. (B) Change of serum IgM after the study drug administration.
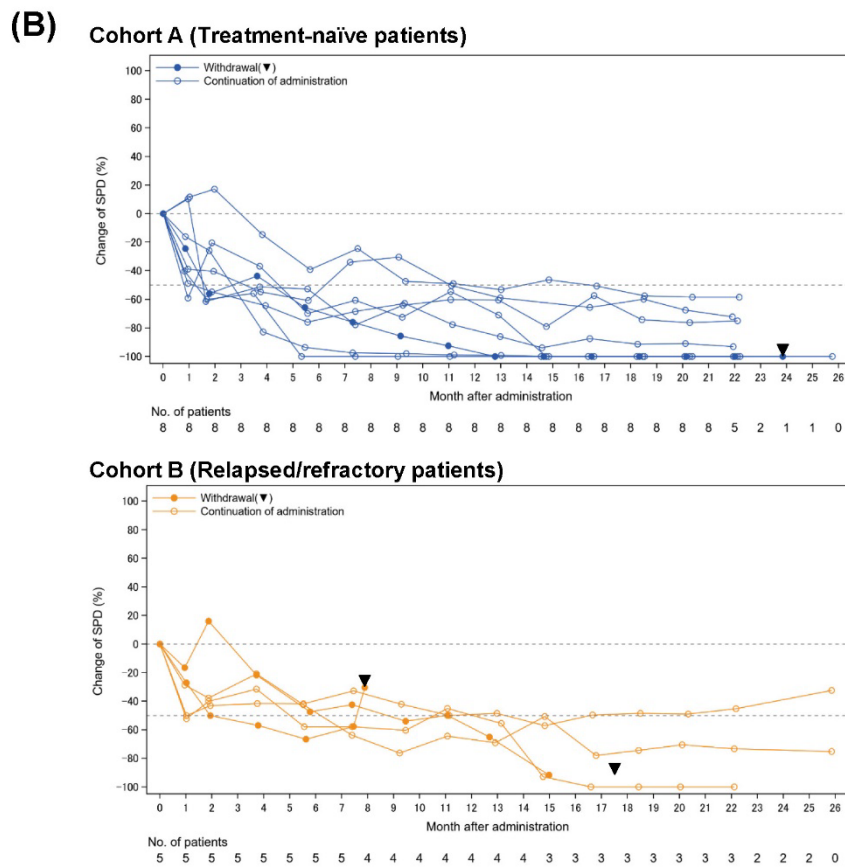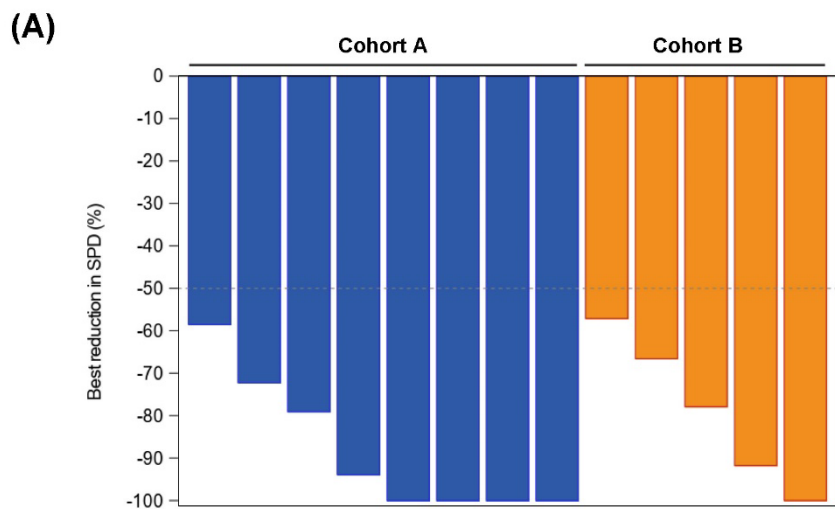
FIGURE S2 Sum of the products of the greatest diameters (SPD). (A) Best reduction in SPD. (B) Change of SPD after the study drug administration.
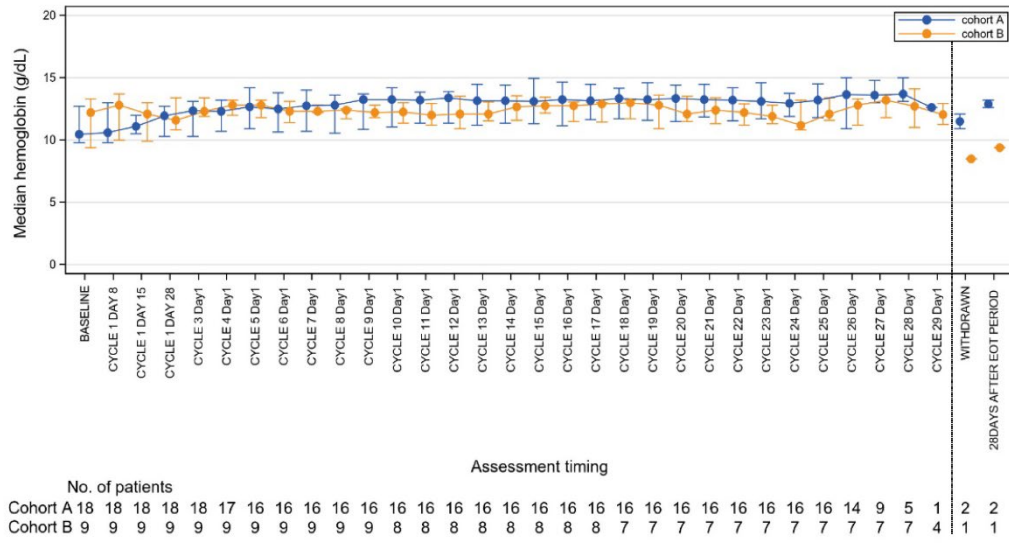
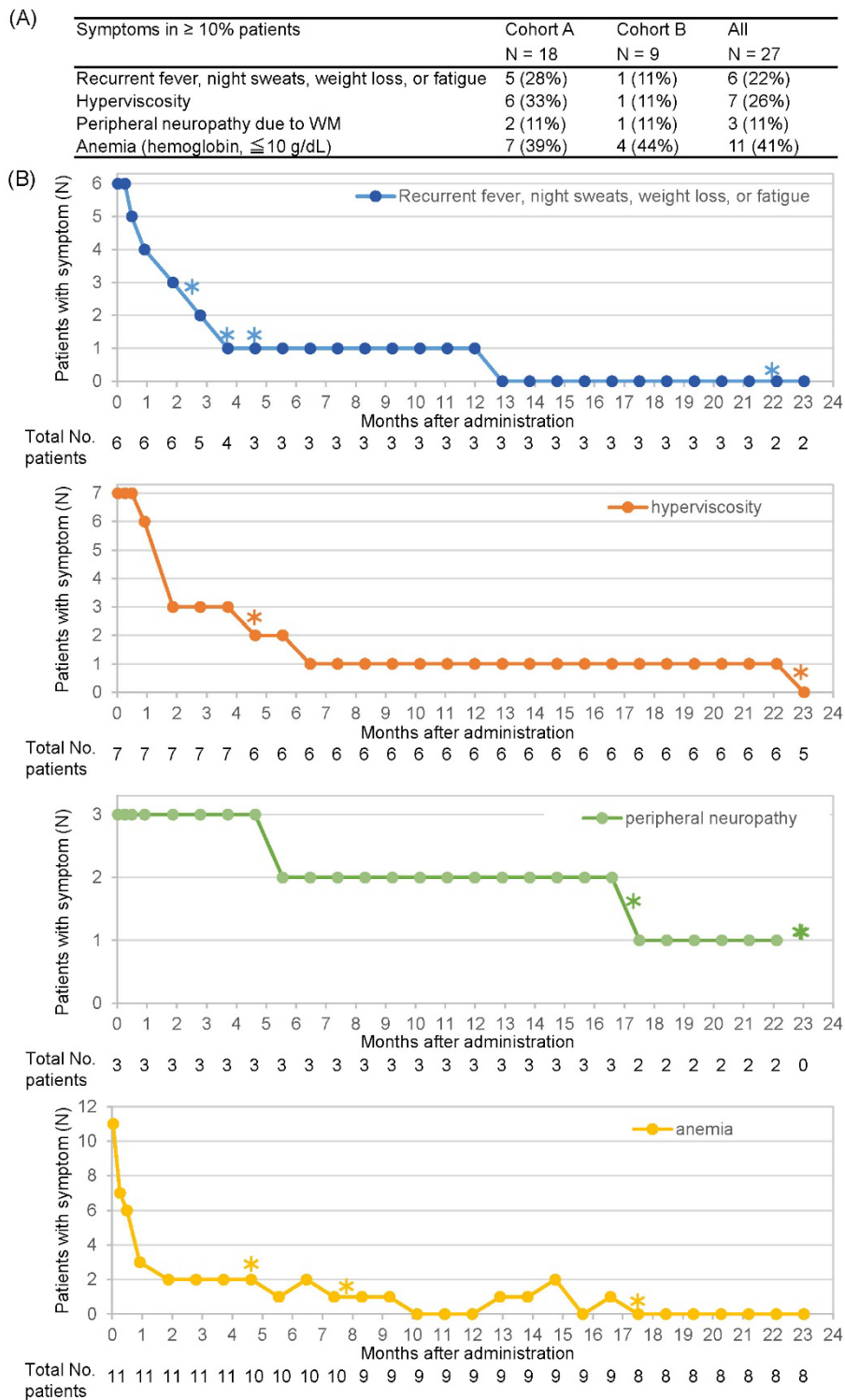FIGURE S3 Hemoglobin. Median hemoglobin at each assessment timing is shown.

(A)

Symptoms in ≥ 10% patients	Cohort A N = 18	Cohort B N = 9	All N = 27
Recurrent fever, night sweats, weight loss, or fatigue	5 (28%)	1 (11%)	6 (22%)
Hyperviscosity	6 (33%)	1 (11%)	7 (26%)
Peripheral neuropathy due to WM	2 (11%)	1 (11%)	3 (11%)
Anemia (hemoglobin, ≦10 g/dL)	7 (39%)	4 (44%)	11 (41%)

(B)

FIGURE S4 Patients with each major symptom. (A) Symptoms observed in ≥10% patients are shown. (B) The number of patients is plotted over time. Total number of patients who had each symptom at baseline and continued to be followed up at Day 1 of each cycle is shown. Asterisks represent censored regardless of whether patients already resolved symptoms.
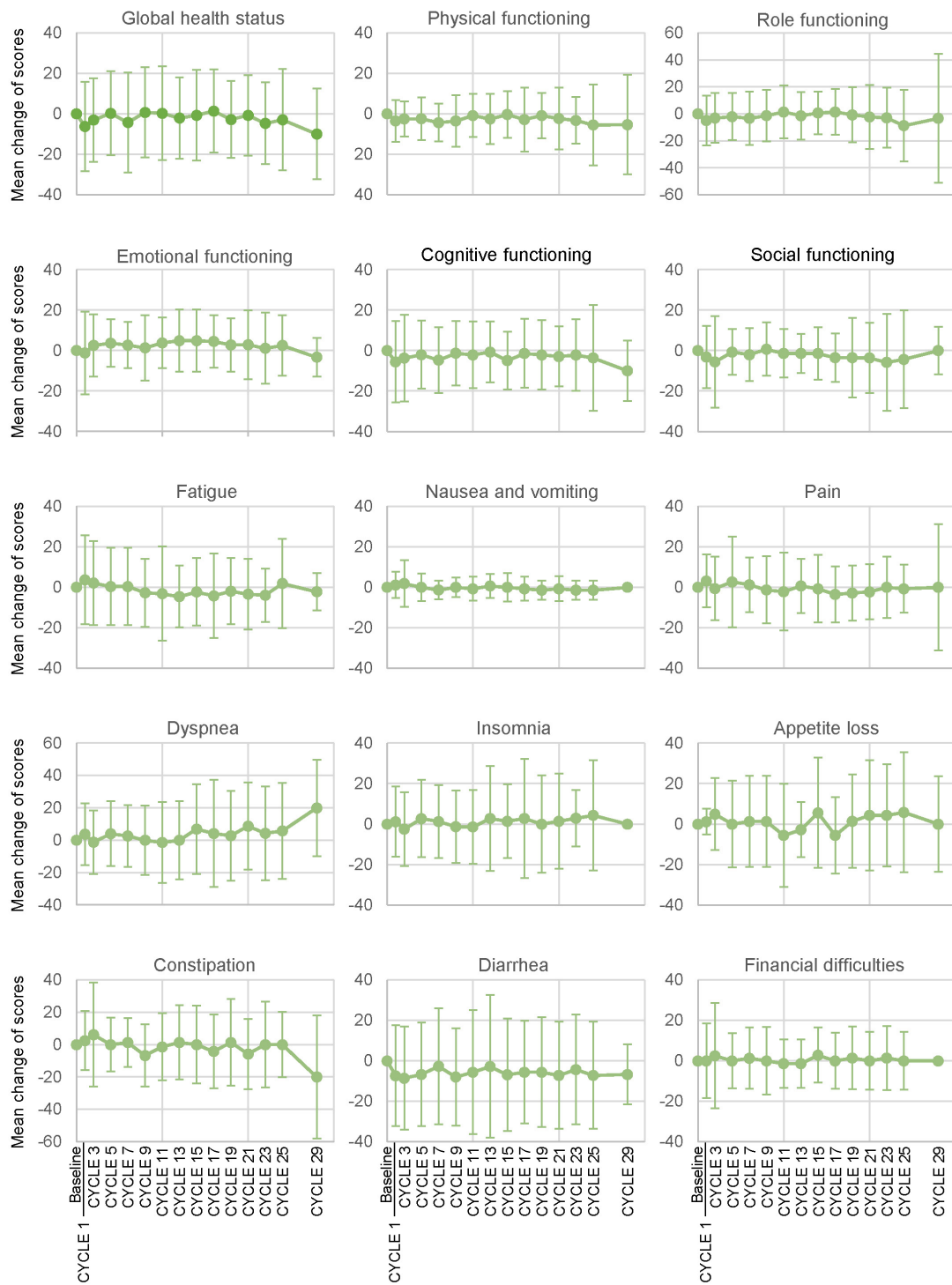
FIGURE S5 QLQ-C30. The mean change of scores of each question is shown. Survey was performed at enrollment, Day 28 of Cycle 1, and Day 1 of the other cycles.
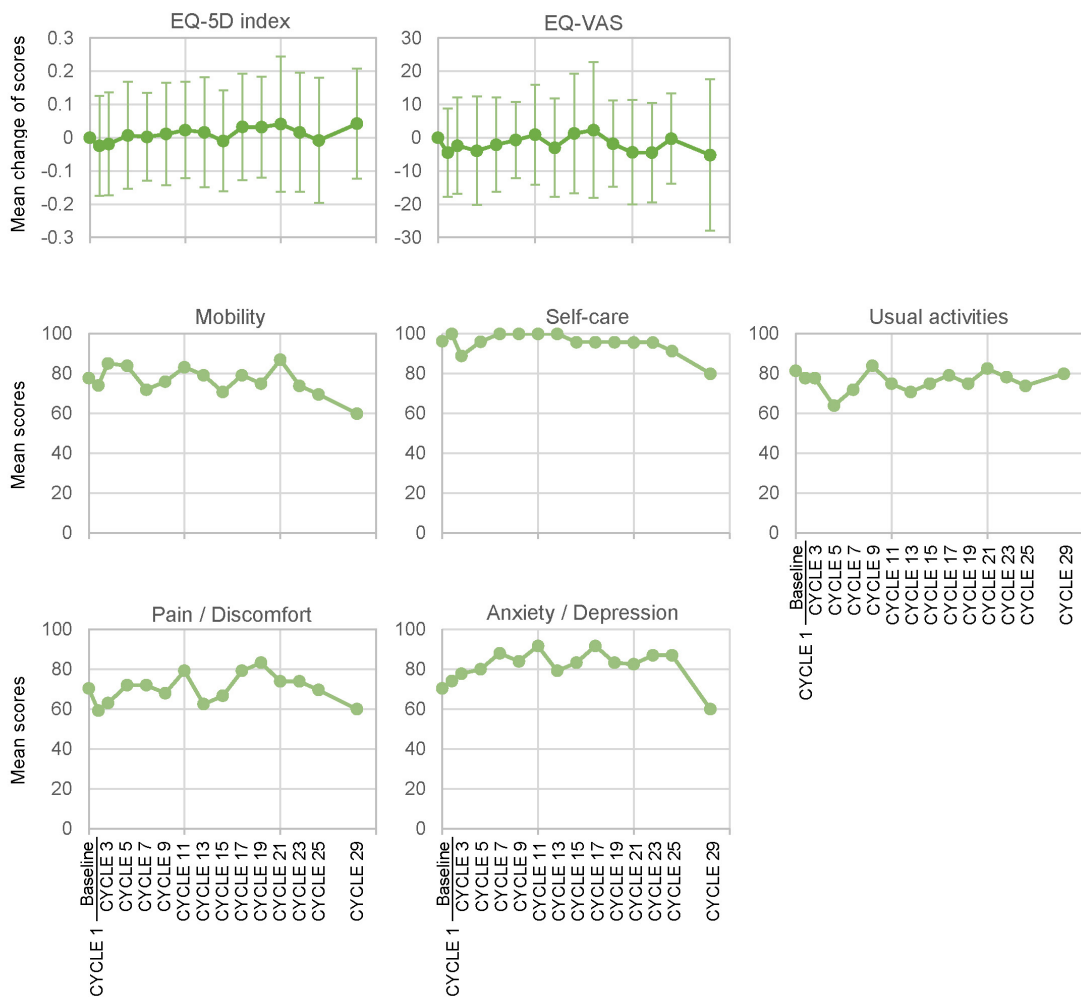
FIGURE S6 EQ-5D. The mean change of scores in the EQ-5D index and the visual analog scale (EQ-VAS) is shown. The mean scores of each question are also shown. Survey was performed at enrollment, Day 28 of Cycle 1, and Day 1 of the other cycles.
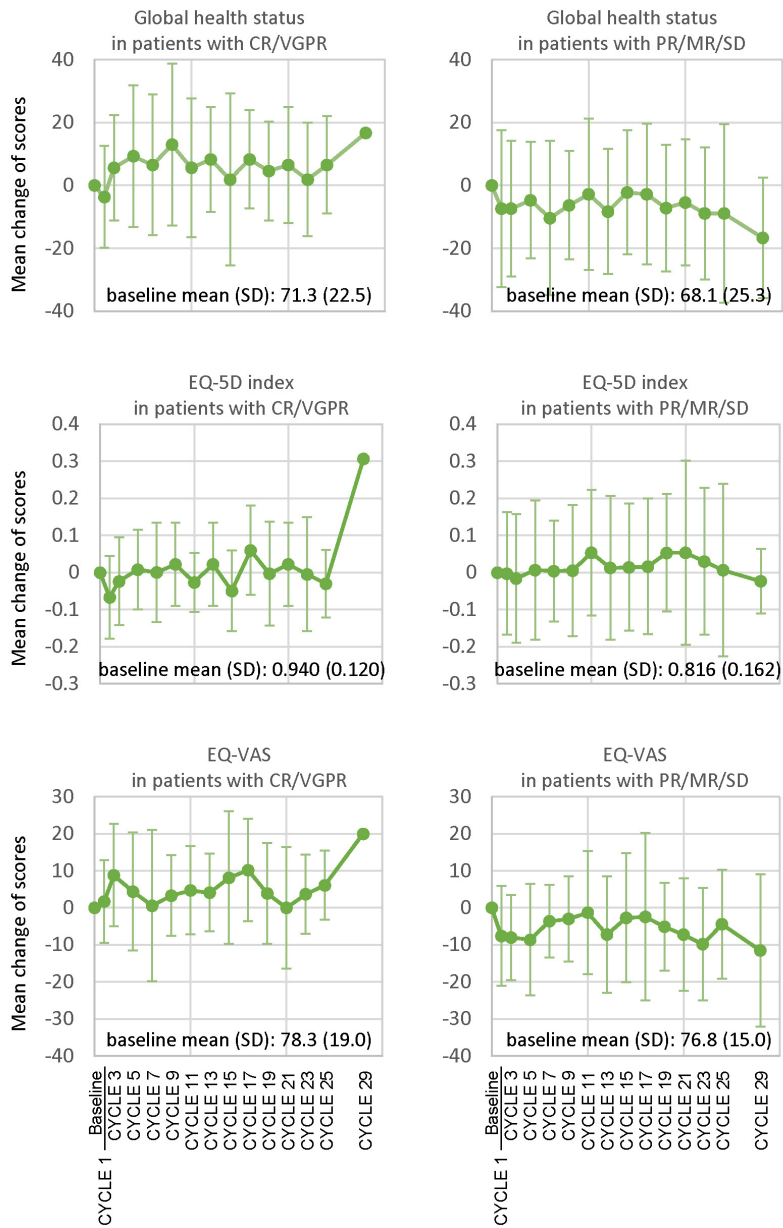
FIGURE S7 Subgroup analysis of QOL in patients with CR/VGPR and with PR/MR/SD. The mean change with standard deviation (SD) of scores in the QLQ-C30 question "global health status", the EQ-5D index, and the EQ-5D visual analog scale (EQ-VAS) is shown. Survey was performed at enrollment, Day 28 of Cycle 1, and Day 1 of the other cycles.