

SUPPLEMENTARY MATERIAL

Quality of life of Japanese dysmenorrhea/heavy menstrual bleeding patients treated with levonorgestrel intrauterine delivery system in a real-world setting

Mikio Momoeda¹, Shigeo Akira², Tasuku Harada³, Jo Kitawaki⁴, Nagamasa Maeda⁵, Ikuko Ota⁶, Keisuke Yoshihara⁷, Noriko Takahashi⁷

¹Department of Integrated Women's Health, St. Luke's International Hospital, Tokyo, Japan

²Meirikai Tokyo Yamato Hospital, Tokyo, Japan

³Department of Obstetrics and Gynecology, Tottori University Faculty of Medicine, Tottori, Japan

⁴Department of Obstetrics and Gynecology, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Kyoto, Japan

⁵Department of Obstetrics and Gynecology, Kochi Medical School, Kochi, Japan

⁶Department of Gynecology, Kurashiki Heisei Hospital, Kurashiki, Japan

⁷Market Access, Bayer Yakuhin, Ltd., Tokyo, Japan

Corresponding authors:

Noriko Takahashi, Ph.D.

Market Access, Bayer Yakuhin, Ltd., 1-6-5 Marunouchi, Chiyoda-ku, Tokyo 100-8265, Japan

Tel: +81 3 6266 7891

Fax: +81 3 6219 9712

Email: noriko.takahashi@bayer.com

Keisuke Yoshihara, Ph.D.

Market Access, Bayer Yakuhin, Ltd., 1-6-5 Marunouchi, Chiyoda-ku, Tokyo 100-8265, Japan

Tel: +81 3 6266 7892

Fax: +81 3 6219 9712

Email: keisuke.yoshihara@bayer.com

Table S1. Overall MDQ total scores and subscores during the premenstrual period and during the menstrual period, and MMAS total scores and subscores during the menstrual period.

		Before insertion of LNG-IUS					3 months after insertion of LNG-IUS					12 months after insertion of LNG-IUS					Comparison of median values before and after insertion ^a	
		N	Mean	SD	Median	Q1 - Q3	N	Mean	SD	Median	Q1 - Q3	N	Mean	SD	Median	Q1 - Q3	vs 3 months <i>p</i> -value	vs 12 months <i>p</i> -value
MDQ	During the premenstrual period																	
	Total score	108	35.8	31.2	25.5	13.0-46.5	95	23.9	22.7	16.0	7.0-32.0	83	18.0	20.4	10.0	4.0-24.0	<0.0001	<0.0001
	Pain	110	8.4	4.9	8.0	4.0-12.0	96	6.1	4.8	5.5	2.0-10.0	85	4.8	4.4	4.0	1.0-8.0	<0.0001	<0.0001
	Concentration	111	4.8	6.3	2.0	0.0-8.0	96	3.4	4.7	1.0	0.0-5.0	85	2.3	4.2	0.0	0.0-2.0	0.0274	<0.0001
	Behavioral effect	112	5.0	4.6	4.0	1.0-8.5	97	3.4	4.1	2.0	0.0-6.0	84	2.5	3.6	1.0	0.0-3.5	<0.0001	<0.0001
	Autonomic response	112	2.4	3.2	1.0	0.0-3.0	97	1.4	2.2	0.0	0.0-2.0	85	0.9	1.6	0.0	0.0-1.0	<0.0001	<0.0001
	Water retention	111	5.1	3.2	5.0	2.0-7.0	95	4.2	3.2	4.0	2.0-6.0	85	3.4	3.0	3.0	1.0-5.0	0.0022	<0.0001
	Negative affect	111	6.2	6.7	4.0	1.0-9.0	96	3.4	4.6	2.0	0.0-5.0	85	2.5	4.2	1.0	0.0-3.0	<0.0001	<0.0001
	Arousal	110	1.6	3.0	0.0	0.0-2.0	96	0.9	1.9	0.0	0.0-1.0	83	0.6	1.3	0.0	0.0-0.0	0.0313	0.0009
	Control	111	2.0	4.0	0.0	0.0-2.0	96	1.4	2.6	0.0	0.0-2.0	85	0.8	1.8	0.0	0.0-0.0	0.1477	<0.0001
	During the menstrual period																	
	Total score	109	41.1	29.3	36.0	19.0-56.0	95	23.7	22.8	16.0	7.0-37.0	82	17.1	18.9	10.0	3.0-24.0	<0.0001	<0.0001
	Pain	111	10.3	4.6	10.0	7.0-14.0	96	6.7	4.7	7.0	2.5-10.0	84	5.0	4.3	4.0	1.0-9.0	<0.0001	<0.0001
	Concentration	111	6.1	6.5	4.0	0.0-10.0	96	3.5	4.7	2.0	0.0-5.5	84	2.4	3.8	0.0	0.0-4.0	<0.0001	<0.0001
	Behavioral effect	113	7.2	4.7	7.0	4.0-11.0	98	3.9	4.1	3.0	0.0-7.0	83	2.6	3.6	1.0	0.0-4.0	<0.0001	<0.0001
	Autonomic response	112	3.1	3.4	2.0	0.0-5.0	97	1.4	2.2	0.0	0.0-2.0	84	0.9	1.6	0.0	0.0-2.0	<0.0001	<0.0001
	Water retention	111	3.9	3.0	4.0	2.0-6.0	95	3.1	3.0	2.0	1.0-5.0	84	2.7	2.7	2.0	1.0-4.0	0.0185	0.0002
	Negative affect	111	6.3	5.9	4.0	2.0-10.0	96	3.1	4.2	1.0	0.0-5.0	84	2.1	3.5	1.0	0.0-2.5	<0.0001	<0.0001
	Arousal	110	1.4	2.6	0.0	0.0-2.0	96	1.0	1.9	0.0	0.0-1.0	82	0.5	1.3	0.0	0.0-0.0	0.3512	0.0051
	Control	111	2.3	3.9	0.0	0.0-3.0	96	1.4	2.9	0.0	0.0-2.0	84	0.7	1.7	0.0	0.0-0.0	0.0043	<0.0001
MMAS	During the menstrual period																	
	Total score	186	50.1	22.8	47.7	37.4-63.0	153	82.7	19.1	89.3	69.3-100.0	135	88.3	14.6	93.9	79.0-100.0	<0.0001	<0.0001
	Practical difficulties	188	4.8	4.7	3.1	0.0-9.4	159	11.2	4.1	14.0	9.4-14.0	149	12.5	3.1	14.0	14.0-14.0	<0.0001	<0.0001
	Effects on social life	186	6.3	2.7	6.7	6.7-6.7	159	9.1	2.0	10.0	10.0-10.0	149	9.6	1.2	10.0	10.0-10.0	<0.0001	<0.0001
	Psychological effects	187	8.0	3.8	8.4	2.9-8.4	159	11.8	3.1	14.0	8.4-14.0	148	12.5	2.8	14.0	14.0-14.0	<0.0001	<0.0001
	Physical health	187	6.4	6.1	4.2	4.2-4.2	159	14.3	7.0	14.9	4.2-21.0	147	15.8	6.5	21.0	14.9-21.0	<0.0001	<0.0001
	Interruption of work	187	9.3	5.3	11.3	4.1-11.3	159	15.7	3.8	18.0	11.3-18.0	146	16.7	2.9	18.0	18.0-18.0	<0.0001	<0.0001
	Family life	187	15.6	6.4	14.0	14.0-23.0	159	20.9	4.1	23.0	23.0-23.0	147	21.7	3.2	23.0	23.0-23.0	<0.0001	<0.0001

^aWilcoxon signed-rank test compared with baseline median value.

Abbreviations: LNG-IUS, levonorgestrel-releasing intrauterine system; MDQ, Menstrual Distress Questionnaire; MMAS, Menorrhagia Multi-Attribute Scale; Q, quartile; SD, standard deviation.

Table S2. MDQ scores during the premenstrual period by patient background (missing data imputed).

MDQ (Premenstrual)		Before insertion of LNG-IUS			3 months after insertion of LNG-IUS			12 months after insertion of LNG-IUS			Comparison of median values before and after insertion ^a		Interaction ^b
		N	Median	Q1 - Q3	N	Median	Q1 - Q3	N	Median	Q1 - Q3	vs 3 months <i>p</i> -value	vs 12 months <i>p</i> -value	<i>p</i> -value
Age, years	<40	40	33.5	16.0 -58.0	39	15.0	7.0 -43.0	36	9.5	5.0 -20.5	<0.0001	<0.0001	0.3595
	≥40	68	22.5	12.0 -41.0	63	16.0	7.0 -32.0	55	16.0	4.0 -28.0	0.0014	<0.0001	
BMI, kg/m ²	<25	76	29.0	16.0 -56.0	74	19.5	8.0 -43.0	64	11.0	5.5 -25.0	<0.0001	<0.0001	0.5495
	≥25	12	30.0	10.5 -78.0	9	14.0	1.0 -32.0	10	13.5	2.0 -32.0	-	-	
History of drug therapy	Yes	44	22.0	10.0 -36.0	43	15.0	7.0 -28.0	39	11.0	6.0 -23.0	0.0068	<0.0001	0.6500
	No	64	31.0	15.5 -55.5	59	18.0	7.0 -40.0	52	8.5	3.0 -27.0	<0.0001	<0.0001	
History of childbirth	Yes	78	29.0	13.0 -44.0	74	14.0	6.0 -28.0	69	9.0	3.0 -21.0	<0.0001	<0.0001	0.6493
	No	29	22.0	10.0 -49.0	27	20.0	12.0 -56.0	21	16.0	10.0 -41.0	0.5767	0.0332	
History of surgery	Yes	36	22.0	13.5 -39.5	28	14.5	9.0 -22.0	27	16.0	7.0 -20.0	0.0116	0.0311	0.8358
	No	72	29.0	13.0 -52.0	74	17.0	7.0 -45.0	64	9.0	3.0 -27.0	<0.0001	<0.0001	
Complications from primary disease (excluding duplicate cases)													
	Primary	27	23.0	13.0 -54.0	28	18.5	7.5 -27.5	26	8.5	2.0 -21.0	0.0297	0.0001	0.9409
	Secondary	81	27.0	13.0 -44.0	74	15.5	7.0 -40.0	65	11.0	5.0 -26.0	<0.0001	<0.0001	
	Uterine fibroid	17	17.0	12.0 -40.0	14	10.5	6.0 -35.0	14	8.0	4.0 -11.0	0.1660	0.0005	0.9088
	Adenomyosis	32	27.0	12.5 -36.0	30	15.0	7.0 -23.0	24	13.5	4.0 -25.0	<0.0001	0.0003	
	Endometriosis	16	31.5	20.5 -64.5	16	25.5	11.5 -45.0	14	20.0	6.0 -44.0	0.0598	0.0383	
Baseline VAS score	0—<30	23	9.0	4.0 -23.0	21	8.0	2.0 -25.0	21	6.0	2.0 -18.0	0.7451	0.2527	0.0872
	30—<70	33	33.0	20.0 -57.0	29	15.0	7.0 -28.0	24	8.5	3.5 -18.5	0.0001	<0.0001	
	70—100	26	27.5	15.0 -60.0	23	22.0	12.0 -61.0	22	16.5	6.0 -26.0	0.0040	<0.0001	

^aWilcoxon signed-rank test compared with baseline median value.

^bTwo-way analysis of variance with repeated measures.

Abbreviations: BMI, body mass index; LNG-IUS, levonorgestrel-releasing intrauterine system; MDQ, Menstrual Distress Questionnaire; MMAS, Menorrhagia Multi-Attribute Scale; Q, quartile; VAS, visual analog scale.

Table S3. MDQ scores during the menstrual period by patient background (missing data imputed)

MDQ (During menstruation)		Before insertion of LNG-IUS			3 months after insertion of LNG-IUS			12 months after insertion of LNG-IUS			Comparison of median values before and after insertion ^a		Interaction ^b
		N	Median	Q1 - Q3	N	Median	Q1 - Q3	N	Median	Q1 - Q3	vs 3 months <i>p</i> -value	vs 12 months <i>p</i> -value	<i>p</i> -value
Age, years	<40	40	42.5	30.5 -70.5	39	18.0	7.0 -37.0	36	10.0	4.5 -23.5	< 0.0001	< 0.0001	0.0363
	≥40	69	30.0	16.0 -48.0	63	16.0	6.0 -41.0	54	11.5	2.0 -24.0	< 0.0001	< 0.0001	
BMI, kg/m ²	<25	76	37.0	20.0 -63.0	74	18.5	9.0 -41.0	64	11.5	4.0 -24.5	< 0.0001	< 0.0001	0.6759
	≥25	12	49.5	14.5 -70.0	9	10.0	2.0 -31.0	10	13.0	2.0 -36.0	-	-	
History of drug therapy	Yes	44	28.0	12.0 -44.0	43	16.0	7.0 -37.0	38	11.5	5.0 -22.0	< 0.0001	< 0.0001	0.1984
	No	65	41.0	21.0 -67.0	59	19.0	6.0 -41.0	52	10.0	3.0 -25.0	< 0.0001	< 0.0001	
History of childbirth	Yes	78	37.0	20.0 -55.0	74	15.0	6.0 -35.0	68	9.5	3.0 -20.5	< 0.0001	< 0.0001	0.4684
	No	30	33.0	16.0 -59.0	27	19.0	12.0 -51.0	21	16.0	10.0 -46.0	0.0914	0.0068	
History of surgery	Yes	37	33.0	16.0 -56.0	28	16.5	9.0 -31.0	26	15.5	9.0 -22.0	< 0.0001	0.0008	0.7024
	No	72	37.0	20.0 -60.0	74	16.0	6.0 -44.0	64	9.5	2.5 -25.0	< 0.0001	< 0.0001	
Complications from primary disease (excluding duplicate cases)													
	Primary	27	38.0	20.0 -67.0	28	14.0	5.5 -36.5	26	8.5	2.0 -20.0	< 0.0001	< 0.0001	0.4188
	Secondary	82	35.5	18.0 -53.0	74	17.5	7.0 -37.0	64	12.0	4.0 -24.5	< 0.0001	< 0.0001	
	Uterine fibroid	17	32.0	11.0 -41.0	14	11.0	6.0 -31.0	14	7.0	2.0 -15.0	0.0527	0.0015	0.9735
	Adenomyosis	32	35.0	19.5 -55.0	30	16.0	9.0 -37.0	24	13.0	8.0 -24.0	< 0.0001	< 0.0001	
	Endometriosis	16	40.0	26.0 -55.5	16	19.0	6.0 -38.5	14	15.0	4.0 -29.0	0.1484	0.0281	
Baseline VAS score	0—<30	23	16.0	8.0 -36.0	21	7.0	2.0 -16.0	21	6.0	1.0 -15.0	0.0005	0.0010	0.1923
	30—<70	34	35.0	21.0 -65.0	29	16.0	11.0 -22.0	24	9.5	4.0 -20.0	< 0.0001	< 0.0001	
	70—100	26	41.5	27.0 -53.0	23	35.0	16.0 -51.0	21	19.0	9.0 -29.0	0.0016	< 0.0001	

^aWilcoxon signed-rank test compared with baseline median value.

^bTwo-way analysis of variance with repeated measures.

Abbreviations: BMI, body mass index; LNG-IUS, levonorgestrel-releasing intrauterine system; MDQ, Menstrual Distress Questionnaire; Q, quartile; VAS, visual analog scale.

Table S4. MMAS scores during the menstrual period by patient background (missing data imputed).

MMAS (During menstruation)		Before insertion of LNG-IUS			3 months after insertion of LNG-IUS			12 months after insertion of LNG-IUS			Comparison of median values before and after insertion ^a		Interaction ^b
		N	Median	Q1 - Q3	N	Median	Q1 - Q3	N	Median	Q1 - Q3	vs 3 months <i>p</i> -value	vs 12 months <i>p</i> -value	<i>p</i> -value
Age, years	<40	46	47.7	37.4 -63.0	36	88.5	68.7 -100.0	33	93.9	72.6 -100.0	<0.0001	<0.0001	0.7335
	≥40	140	48.1	36.7 -62.3	123	89.3	69.3 -100.0	113	95.4	83.2 -100.0	<0.0001	<0.0001	
BMI, kg/m ²	<25	126	47.7	33.2 -61.9	106	88.3	66.3 -100.0	97	93.9	76.5 -100.0	<0.0001	<0.0001	0.9524
	≥25	27	55.3	39.1 -73.0	24	92.7	84.4 -100.0	20	97.7	81.0 -100.0	<0.0001	<0.0001	
History of drug therapy	Yes	74	48.5	36.5 -63.0	67	89.8	74.7 -100.0	62	100.0	77.6 -100.0	<0.0001	<0.0001	0.9120
	No	112	47.7	37.4 -62.3	92	88.3	68.0 -100.0	84	93.9	81.0 -100.0	<0.0001	<0.0001	
History of childbirth	Yes	147	47.7	37.4 -62.3	131	89.3	71.9 -100.0	121	94.4	83.2 -100.0	<0.0001	<0.0001	0.4783
	No	38	49.8	33.1 -63.0	27	88.3	63.0 -100.0	24	87.8	66.9 -100.0	<0.0001	<0.0001	
History of surgery	Yes	61	47.7	33.4 -57.3	51	89.3	71.9 -100.0	45	93.9	82.6 -100.0	<0.0001	<0.0001	0.5805
	No	125	48.5	37.4 -63.0	108	89.3	68.7 -100.0	101	95.4	79.3 -100.0	<0.0001	<0.0001	
Complications from primary disease (excluding duplicate cases)	Primary	45	49.5	39.1 -64.3	42	95.4	73.7 -100.0	36	94.2	82.4 -100.0	<0.0001	<0.0001	0.7120
	Secondary	141	47.7	36.9 -62.3	117	88.3	68.0 -100.0	110	93.9	79.3 -100.0	<0.0001	<0.0001	
	Uterine Fibroid	48	46.6	31.9 -56.7	40	89.3	69.3 -100.0	33	95.4	82.6 -100.0	<0.0001	<0.0001	0.3862
	Adenomyosis	45	48.5	36.9 -58.1	37	88.3	69.3 -94.4	39	93.9	83.2 -100.0	<0.0001	<0.0001	
	Endometriosis	7	52.1	37.4 -95.4	4	91.6	70.3 -100.0	4	87.1	68.1 -100.0	-	-	
Baseline PBAC score	<75	9	74.7	54.0 -89.3	8	97.7	80.1 -100.0	9	100.0	93.9 -100.0	-	-	0.0698
	≥75	28	47.7	42.9 -62.6	24	91.3	75.1 -100.0	20	97.0	87.1 -100.0	<0.0001	<0.0001	

^aWilcoxon signed-rank test compared with baseline median value.

^bTwo-way analysis of variance with repeated measures.

Abbreviations: BMI, body mass index; LNG-IUS, levonorgestrel-releasing intrauterine system; MMAS, Menorrhagia Multi-Attribute Scale; PBAC, pictorial blood loss assessment chart; Q, quartile.