SUPPLEMENTARY MATERIALS

Safety and Efficacy of Hybrid Cooperative Complexes of Sodium Hyaluronate and Sodium Chondroitin for the Treatment of Patients with Symptomatic Knee Osteoarthritis

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Supplementary Material

Table S1. Patient reported outcomes (median [IQR] WOMAC scores) for patients who needed two injections at the 30-day follow-up visit.

Table S2. Patient reported outcomes (median [IQR] VAS and PtGA scores) for patients who needed two injections at the 30-day follow-up visit.

Table S3. Safety findings and number of patients who needed rescue medication for patients who needed two injections at the 30-day follow-up visit.

Table S1. Patient reported outcomes (median [IQR] WOMAC scores) for patients who needed two injections at the 30-day follow-up visit

	Median (IQR)							
	Baseline	After the first injection		After the second injection on Day 30			Change from baseline to Day 180	Friedman test p-value
		7-day f/u[a]	14-day f/u[a]	30-day f/u[a]	90-day f/u[a]	180-day f/u[a]		
N	15	15	15	15	15	15		
Pain	7 (7,9)	5 (4, 7)	4 (3, 6)	5 (4, 7)	5 (2, 6)	4 (2, 6)	3	**<0.0002[b]**
Stiffness	4 (2, 5)	2 (1, 3)	3 (0, 3)	3 (1, 4)	2 (0, 3)	2 (1, 4)	2	0.0694
Physical function	26 (19, 35)	17 (11, 25)	14 (11, 23)	22 (13, 29)	22 (10, 23)	16 (8, 22)	10	**0.0005[b]**
Total score	40 (29, 58)	26 (17, 32)	21 (18, 29)	26 (21, 37)	25 (14, 33)	20 (15, 35)	20	**0.0002[b]**

A lower WOMAC score indicates lower symptom intensity. Descriptive statistics were used to establish median (IQR) values for patients who had the second injection at the 30-day follow-up visit (N=15). [a]Follow-up period since first injection [b]Statistically significant p-values (<0.05). F/u, follow-up; IQR, interquartile range; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table S2. Patient reported outcomes (median [IQR] VAS and PtGA scores) for patients who needed two injections at the 30-day follow-up visit

	Median (IQR)							
	Baseline	After the first injection		After the second injection on Day 30			Change from baseline to Day 180	Friedman test p-value
		7-day f/u†	14-day f/u†	30-day f/u[a]	90-day f/u[a]	180-day f/u[a]		
N	15	15	15	15	15	15		
VAS pain score	6 (5, 7)	6 (4, 6)	5 (3, 6)	6 (4, 7)	5 (4, 7)	5 (3, 7)	1	0.2799
PtGA score,[b]	N/A	3 (2, 3)	3 (2, 3)	2 (2, 3)	2 (2, 4)	2 (2, 3)	N/A	0.3480

Descriptive statistics were used to establish median (IQR) values for patients who had the second injection at the 30-day follow-up visit (N=15). One patient with missing VAS and PtGA scores for the 180-day f/u visit (due to dropping out of the study) was excluded from the Friedman's test as this statistical test cannot compute missing values. [a]Follow-up period since first injection. [b]PtGA scores: 4 = much improved, 3 = slightly improved, 2 = no change, 1 = slightly worsened, 0 = much worse. F/u, follow-up; IQR, interquartile range; N/A, not applicable; PtGA, patient global assessment of disease activity; VAS, visual analogue scale.

Table S3. Safety findings and number of patients who needed rescue medication for patients who needed two injections at the 30-day follow-up visit

	After the first injection		After the second injection on Day 30		
	7-day f/u[a]	**14-day f/u[a]**	**30-day f/u[a]**	**90-day f/u[a]**	**180-day f/u[a]**
N	15	15	15	15	15
DR-AEs,[b] n (%)	7 (46.7)[c]	0	0	0	0
Other AEs unrelated to use of the device, n (%)	0	0	0	0	0
DR-AE duration from the day of injection, days					
Mean (SD)	1.0 (1.4)	N/A	N/A	N/A	N/A
Median (range)	0 (0, 4)	N/A	N/A	N/A	N/A
Patients who required rescue therapy, n (%)	7 (46.7)	1 (6.7)	9 (60.0)	5 (33.3)	6 (40.0)

[a]Follow-up period since first injection. [b]DR-AE related to the use of an investigational medical device. [c]Five patients had swelling, three patients had rigidity, one patient had a burning sensation, and one patient had pain; median duration of adverse device event symptoms was 0 (IQR, 0, 2) days. Individual patients could have more than one adverse device event. AE, adverse event; DR-AE, device-related adverse events; F/u, follow-up; IQR, interquartile range; n, number of patients; N/A, not applicable; SD standard deviation.