DURATION OF CLINICALLY MEANINGFUL ANALGESIC RESPONSE TO INTRA-ARTICULAR MM-II, A NOVEL SUSPENSION OF LARGE, EMPTY, MULTILAMELLAR LIPOSOMES, IN PATIENTS WITH PAINFUL KNEE OSTEOARTHRITIS: ANALYSIS FROM A 26-WEEK PHASE 2B RANDOMISED CONTROLLED TRIAL

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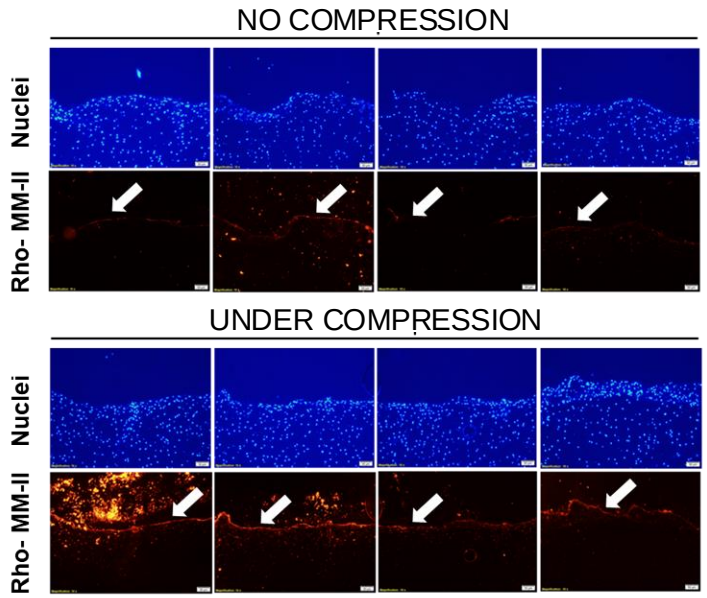
MM-II and its mechanism of action

- Suspension of empty, multilamellar micron-scale liposomes
- Made of phosphatidylcholine-based lipids (DPPC and DMPC)

- DPPC is part of the cartilage's natural lubrication system
- The DPPC:DMPC ratio in MM-II is optimised for cartilage coating and lubrication

In vitro

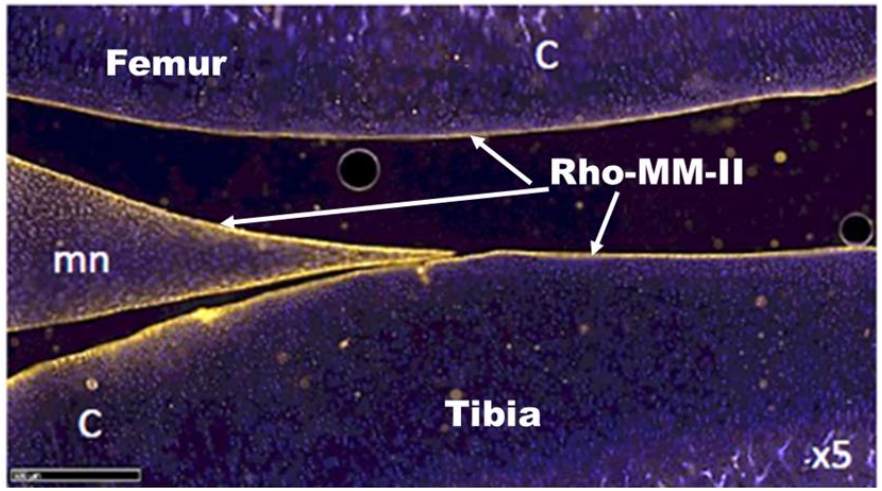
Cartilage binding by rhodamine-MM-II[1]



MM-II coating is enhanced by compression

In vivo

Distribution of rhodamine-MM-II in rabbit knee 1 week post IA injection[2]



Scale bar = 500 microns

MM-II coats both cartilage and menisci

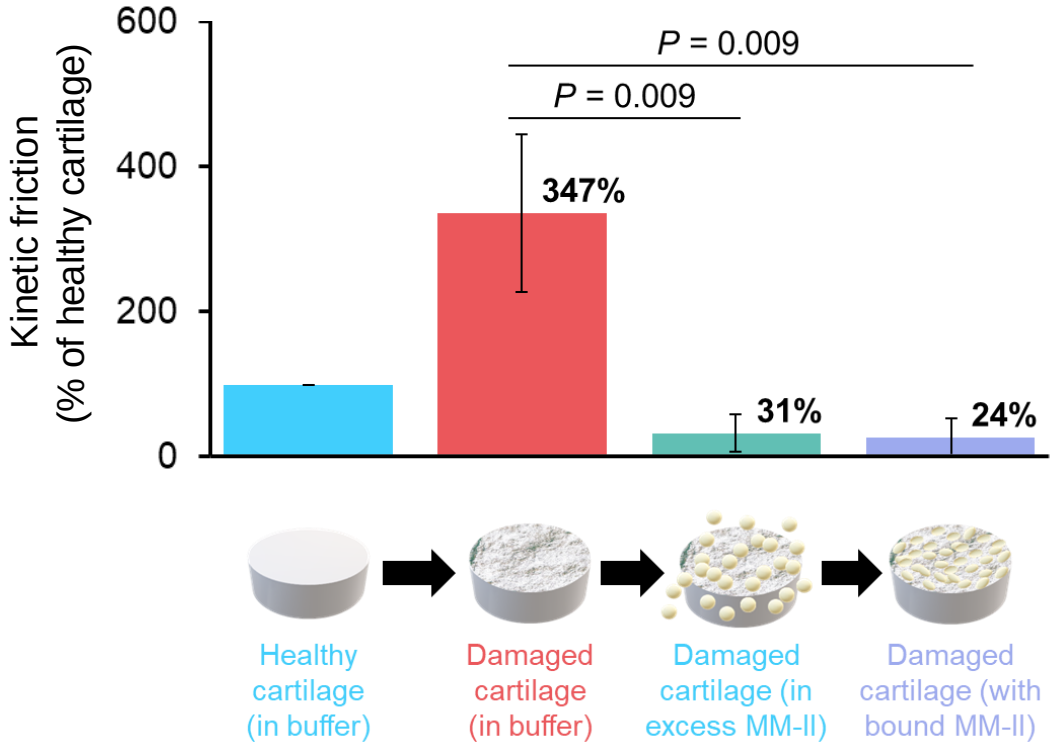
1. Dvir I, et al. *Osteoarthritis and Cartilage.* 2022;30(1):S435.
2. Data on File (confidential). Moebius Medical.

C, cartilage; DMPC, dimyristoylphosphatidylcholine; DPPC, dipalmitoylphosphatidylcholine; IA, intra-articular; mn, meniscus; Rho-MM-II, rhodamine-MM-II.

MM-II and its mechanism of action

In vitro

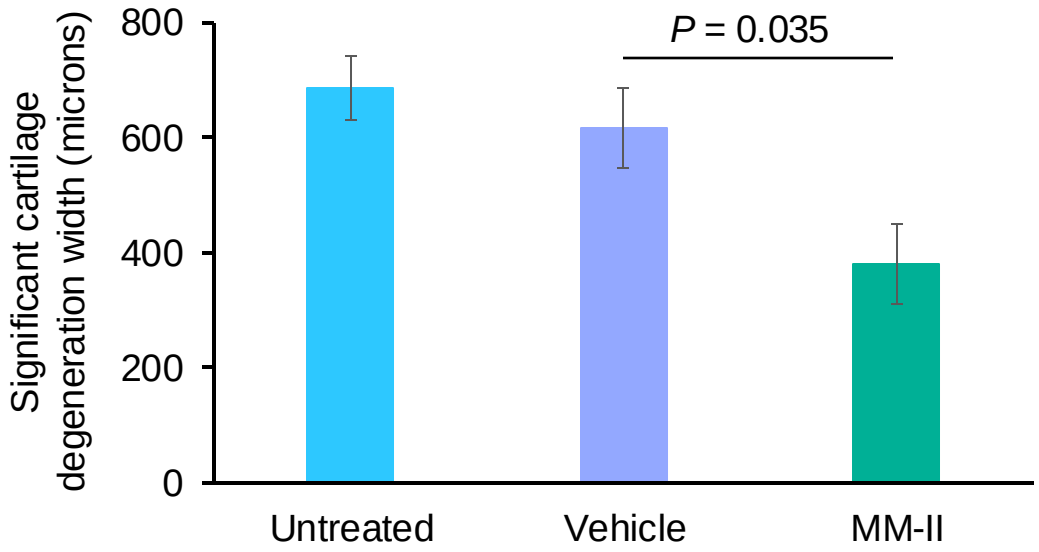
Cartilage-on-glass friction tests[1]



MM-II coating reduces friction

In vivo

28-day rat medial meniscal tear model[2]



Significant cartilage degeneration: cartilage has lost >50% of its thickness[3]

MM-II reduces cartilage degeneration

1. Data on File (confidential). Moebius Medical.
2. Wechsler R. *Osteoarthritis and Cartilage.* 2021;29:S11-12.
3. Gerwin N, et al. *Osteoarthritis and Cartilage.* 2010;18:S24-34.

Study design: Main trial

Randomised, double-blind, placebo-controlled, 26-week phase 2b study

- Overall, 397 patients randomised 3:3:3 to 1, 3, and 6 mL MM-II and 1:3:1 to matching placebo
- Full analysis set
  - **3 mL MM-II, N = 83**
    - 80 completed, 3 discontinued
  - **3 mL placebo, N = 78 patients**
    - 71 completed, 7 discontinued

Primary endpoint

- Change in WOMAC pain score at week 12
- **Nominally significant reduction in WOMAC pain for 3 mL MM-II vs 3 mL placebo at week 12 (*P* = 0.047)[1]**

Key secondary endpoints

- WADP scores by VAS at week 12, week 26, and over time
- WOMAC pain scores at week 26 and over time

Key inclusion criteria

- Age ≥40 years
- Radiographic Kellgren-Lawrence grade 2 or 3 in the index knee
- ACR criteria for OA
- WOMAC pain score >2 of 4 within 24 hours of baseline
- Index knee VAS pain score of ≥50 and ≤90 mm for ≥5 of 7 days prior to baseline
- Intolerance or inadequate response to NSAIDs or acetaminophen/paracetamol

Key exclusion criteria

- Moderate to large effusion in the index knee
- Moderate to severe pain in another joint

1. Schnitzer TJ, et al. *Osteoarthritis and Cartilage*. 2023;31(5):688-89.

ACR, American College of Rheumatology; NSAID, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; VAS, visual analog scale; WADP, weekly average of daily pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Objective of this evaluation

To evaluate the durability of pain responses
beyond 12 weeks of treatment
in patients with symptomatic knee OA after a single IA injection of 3 mL of MM-II or placebo

Analyses

Efficacy (full analysis set)

- WOMAC pain score and WADP
  - Change from baseline
  - Percent achieving ≥30% and ≥50% improvement
- Evaluated from baseline to week 26
- *P*-values are nominal

Safety (safety analysis set)

- Incidence of AEs

AE, adverse event; IA, intra-articular; OA, osteoarthritis; WADP, weekly average of daily pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

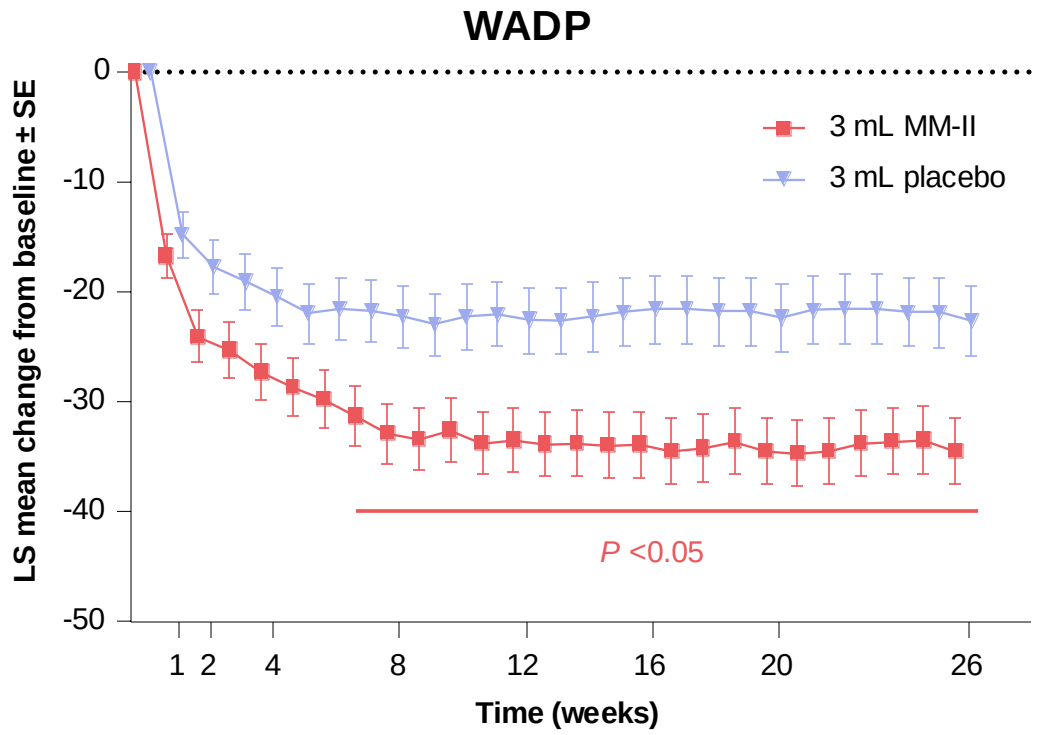
Patient baseline characteristics

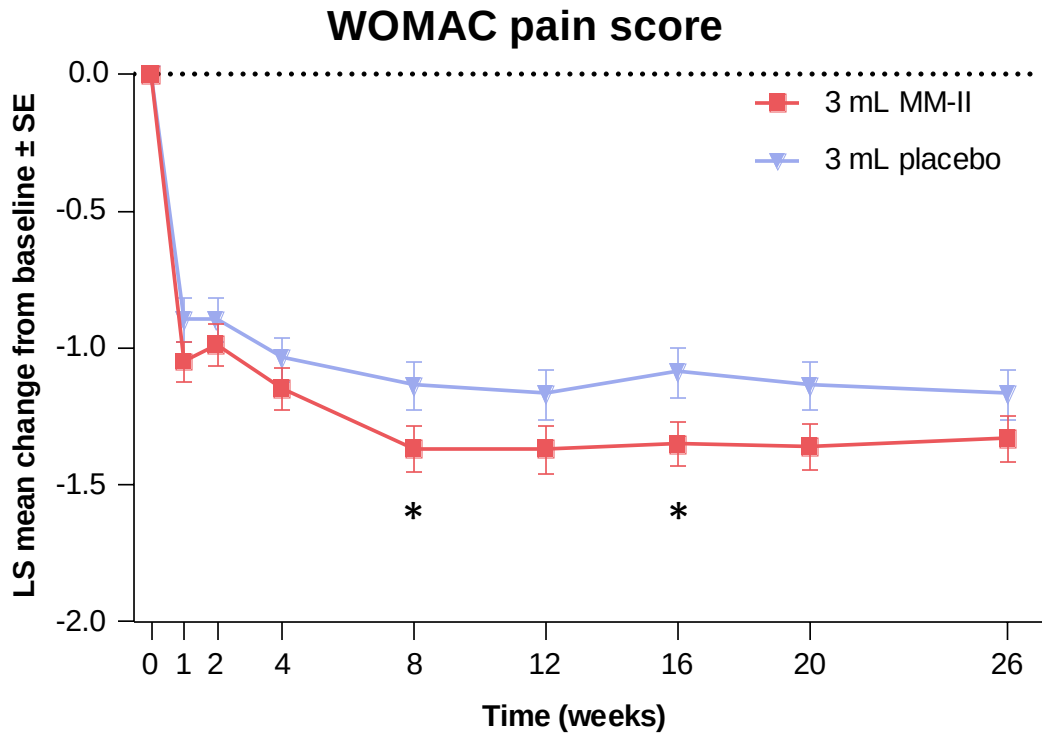
Full analysis set

Parameter	3 mL MM-II (N = 83)	3 mL placebo (N = 78)
Age, years	64.4 (8.36)	62.3 (7.90)
Race, n (%)		
Asian	19 (22.9%)	21 (26.9%)
Black or African American	10 (12.0%)	3 (3.8%)
White	54 (65.1%)	54 (69.2%)
BMI, kg/m²	30.53 (5.97)	30.74 (6.37)
WOMAC pain score	2.43 (0.33)	2.34 (0.35)
WOMAC stiffness score	2.24 (0.66)	2.31 (0.73)
WOMAC function score	2.19 (0.58)	2.21 (0.51)
VAS index knee pain group, n (%)		
≤74	56 (67.5%)	53 (67.9%)
≥75	27 (32.5%)	25 (32.1%)

Data are presented as mean (SD) unless otherwise noted.
Percentages are based on the number of participants with nonmissing data. Percentages for parameters dependent on previous responses are based on the number of participants with nonmissing data that met the specified criteria.
BMI, body mass index; SD, standard deviation; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

MM-II provided sustained pain relief to week 26



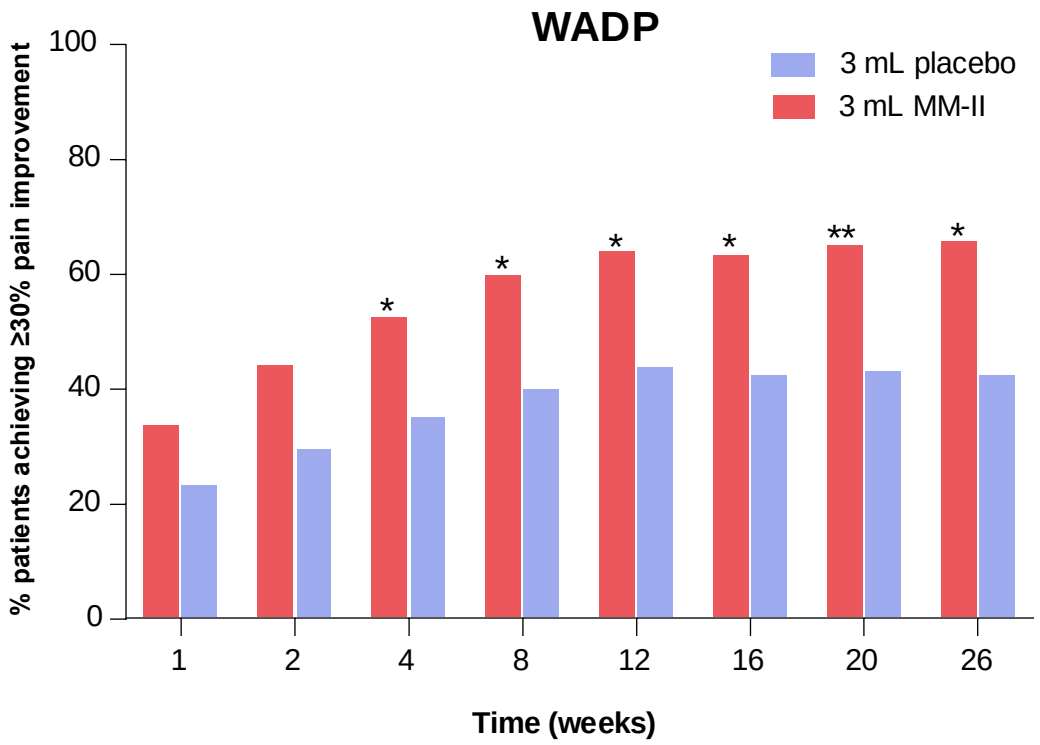


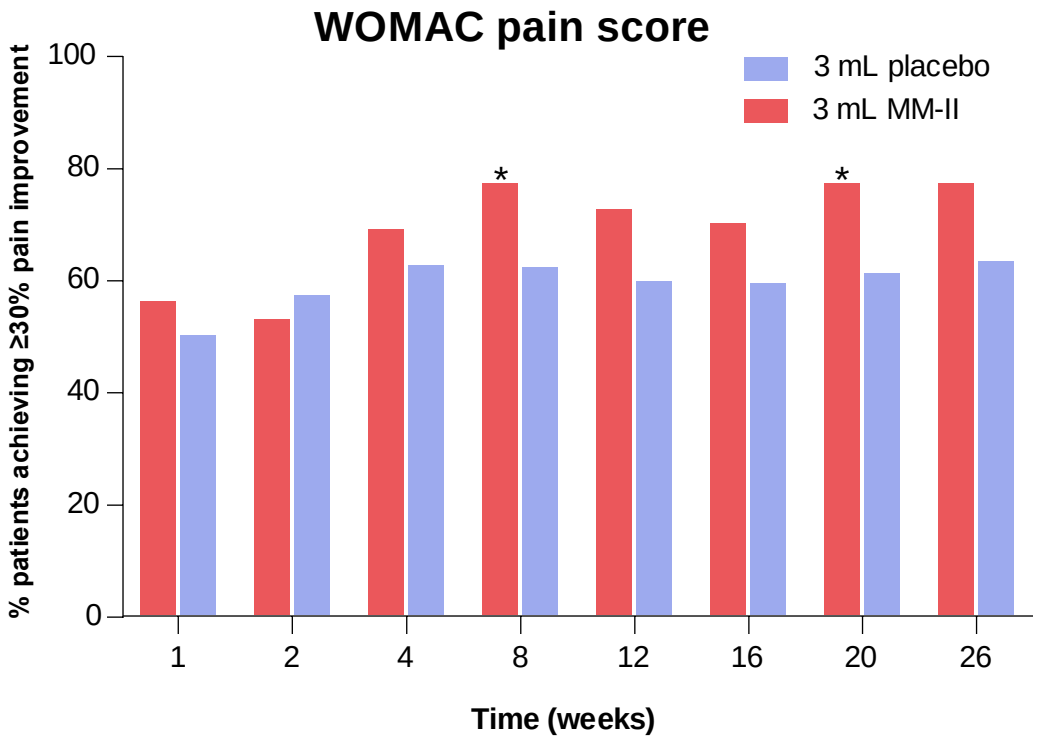
3 mL MM-II, n =	57	56	56	54	56	54	57	53
3 mL placebo, n =	60	60	58	57	55	55	56	50

3 mL MM-II, n =	83	82	81	80	79	77	77	79	79
3 mL placebo, n =	78	78	75	75	74	72	71	72	71

*P <0.05.
Full analysis set.
P-values for WADP are from a mixed model repeated measures with fixed effects for treatment (MM-II 3 mL and placebo 3 mL), visit, and treatment-by-visit interaction; random effect for subject; and covariates site, baseline Weekly Average Daily VAS Global Pain Score, baseline BMI group, and baseline VAS group. P-values for WOMAC pain score are from separate analysis of covariance models at each time point with main effect treatment (MM-II 3 mL and placebo 3 mL) and covariates site, baseline WOMAC pain score, baseline BMI group, and baseline VAS group. P-values are unadjusted for multiplicity.
BMI, body mass index; LS, least square; SE, standard error; OA, osteoarthritis; VAS, visual analog scale; WADP, weekly average of daily pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Knee pain responders ≥30% for MM-II sustained to week 26



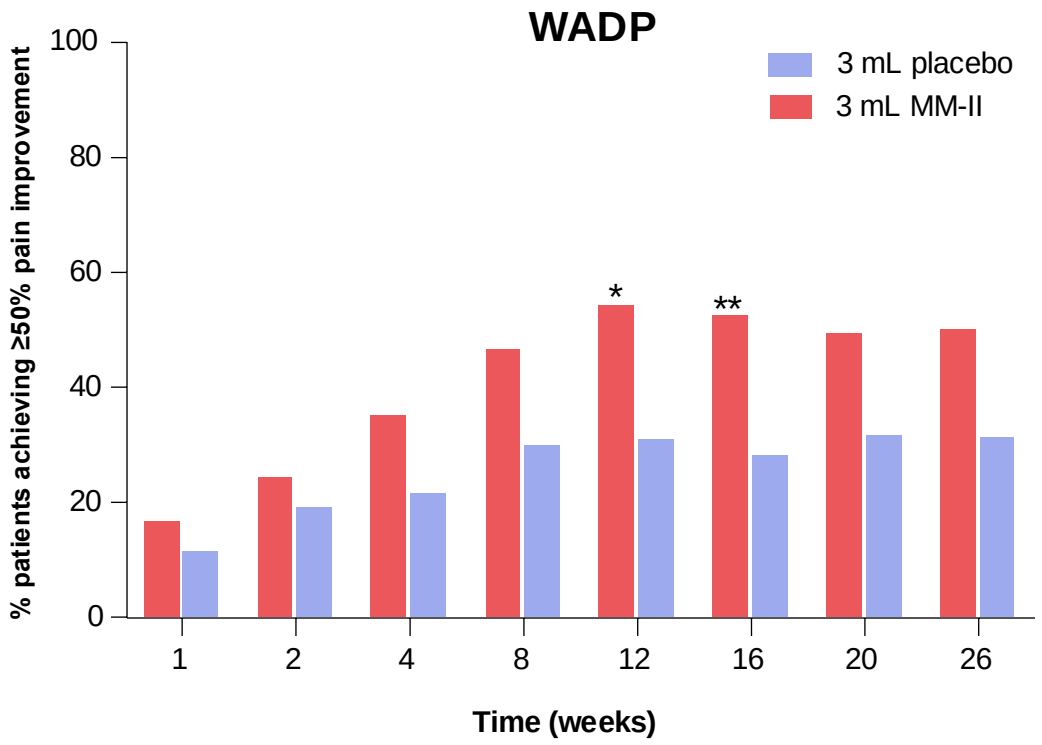


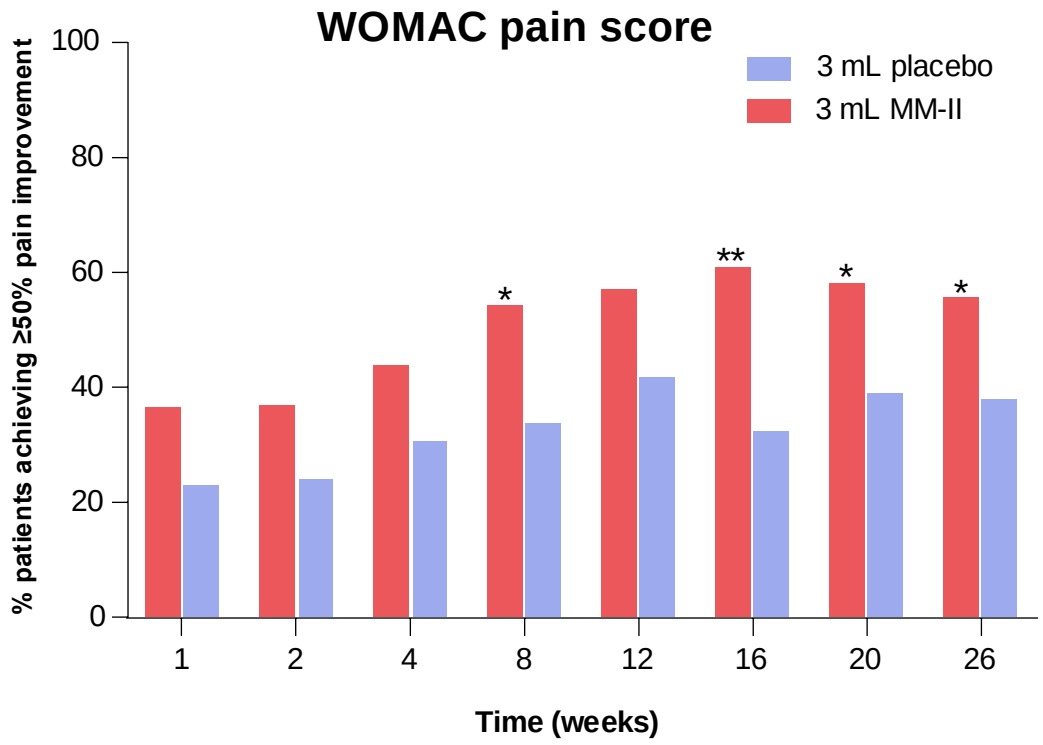
3 mL MM-II, n =	83	82	80	77	77	76	77	70
3 mL placebo, n =	78	78	74	73	71	71	72	64

3 mL MM-II, n =	82	81	80	79	77	77	79	79
3 mL placebo, n =	78	75	75	74	72	71	72	71

* *P* <0.05.
** *P* <0.01.
Full analysis set.
P-values for WADP are from individual CMH tests against 3 mL placebo stratified by region and baseline BMI group. *P*-values for WOMAC pain score are from individual CMH tests against 3 mL placebo stratified by region, baseline BMI group, and baseline VAS group.
P-values are unadjusted for multiplicity.
BMI, body mass index; CMH, Cochran–Mantel–Haenszel; OA, osteoarthritis; VAS, visual analog scale; WADP, weekly average of daily pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Knee pain responders ≥50% for MM-II sustained to week 26



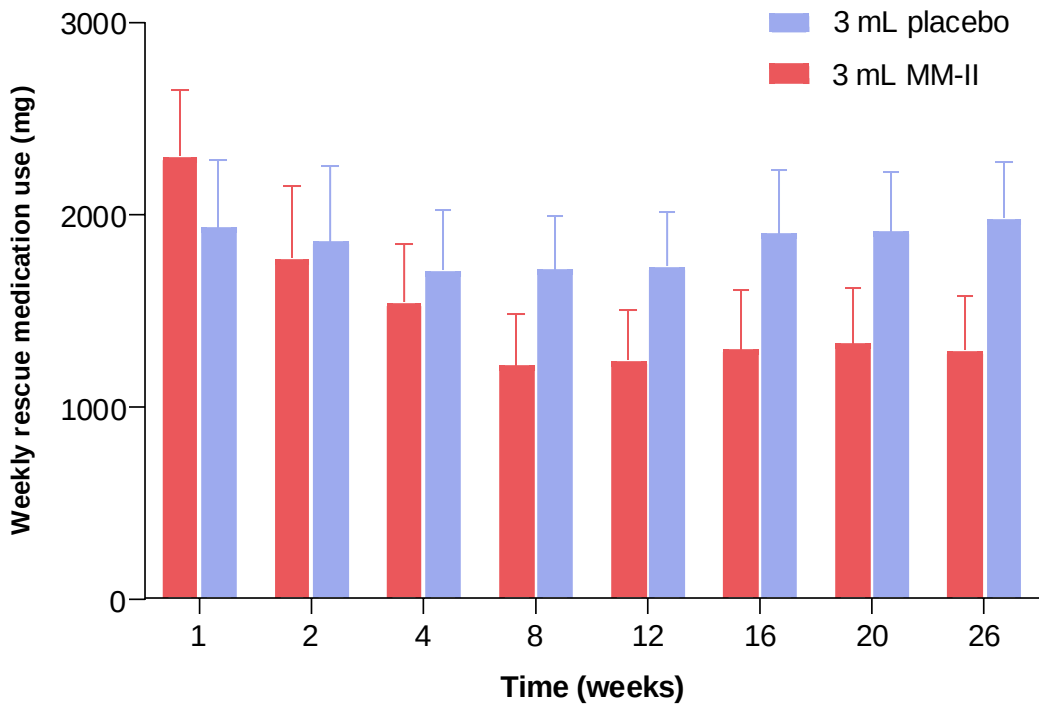


3 mL MM-II, n =	83	82	80	77	77	76	77	70
3 mL placebo, n =	78	78	74	73	71	71	72	64

3 mL MM-II, n =	82	81	80	79	77	77	79	79
3 mL placebo, n =	78	75	75	74	72	71	72	71

* *P* <0.05.
** *P* <0.01.
Full analysis set.
P-values for WADP are from individual CMH tests against 3 mL placebo stratified by region and baseline BMI group. *P*-values for WOMAC pain score are from individual CMH tests against 3 mL placebo stratified by region, baseline BMI group, and baseline VAS group.
P-values are unadjusted for multiplicity.
BMI, body mass index; CMH, Cochran–Mantel–Haenszel; OA, osteoarthritis; VAS, visual analog scale; WADP, weekly average of daily pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Lower rescue medication use maintained through 26 weeks with MM-II



3 mL MM-II, n =	82	81	80	79	77	76	78	76
3 mL placebo, n =	78	74	74	72	71	71	71	71

Full analysis set.
Rescue medication was acetaminophen/paracetamol.

MM-II had an acceptable tolerability profile, and no serious or severe AEs were reported in patients treated with 3 mL of MM-II

Safety analysis set

Parameter, n (%)	3 mL MM-II N = 86		3 mL placebo N = 78	
	Weeks 0–26	Weeks 12–26	Weeks 0–26	Weeks 12–26
AEs	49 (57.0)	33 (38.4)	46 (59.0)	28 (35.9)
SAEs	0	0	3 (3.8)	3 (3.8)
Treatment-related AEs*	2 (2.3)	0	1 (1.3)	0
Procedure-related AEs‡	6 (7.0)	0	1 (1.3)	0
Severe AEs	0	0	2 (2.6)	2 (2.6)
Injection-site AEs†	3 (3.5)	0	2 (2.6)	2 (2.6)
AEs leading to discontinuation#	0	0	1 (1.3)	1 (1.3)

*Includes AEs possibly, probably, and certainly related to the study treatment.
‡Includes AEs possibly, probably, and certainly related to study procedure.
†A total of 5 AEs from the same study site were reported inaccurately as injection-site AEs and excluded.
#As reported on the study completion/early discontinuation page of the electronic case report form.
AE, adverse event, SAE; serious adverse event.

Conclusions

- MM-II dosed at 3 mL provided a durable response in patients with knee OA
  - Responses were clinically meaningful and appeared relatively rapidly
  - Pain relief lasted for up to 26 weeks after a single IA injection

- MM-II was well tolerated
  - No severe AEs were reported in the 3 mL MM-II group
  - Overall safety profiles were consistent between MM-II and placebo

AE, adverse event; IA, intra-articular; OA, osteoarthritis.

Impact on clinical practice

- There is an urgent need for effective and safe treatments for OA
  - Currently available therapies are limited in efficacy and duration of response
- MM-II may address these limitations by offering durable and meaningful pain relief with good tolerability
- A CE marking application is in the process of being filed for the European Union and a phase 3 clinical program in the United States is planned

CE, Conformite Europeenne; OA, osteoarthritis.