Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Platelet-Rich Plasma Growth Factor and Cytokine Analysis Methods

PRP samples were treated with a hypotonic 0.5 % Triton-X-100 solution (vol/vol, dilution in distilled water) at a 9 to 1 ratio (PRP to 0.5% Triton-X-100, vol/vol) and incubated for 15 min at room temperature, in order to maximize cell and platelet membrane breakage and growth factor release. PRP was then aliquot and stored at -80°C until quantification (at least overnight). Before the assay, the samples were thawed and vortexed, then centrifuged at maximum speed for 5 minutes at 4°C. The clear lysates were aliquot for each cytokines and growth factor assays.

Cytokines and growth factors, IL-1β, IL-1ra, IL-6, MMP9, TGFβ1 and PDGF-BB were analysed using Luminex multiplex kits purchased from R&D System. Assays were performed according to the protocols provided by the manufacturer. Clear lysates from PRP samples were diluted in the assay process according to manufacturer's recommendation (PDGF-BB and MMP9: 1 in 50 dilutions. IL-1β, IL-1ra and IL-6: 1 in 2 dilutions, TGFβ1: 1 in 14.98 dilutions. All dilutions were performed with assay buffer provided by the assay kits. Luminex assays were performed with Luminex 200 and data analysis with BioPlex manager V6.2. All samples were analysed in duplicate and the results provided as the mean of two data points.

eAppendix 2. Characteristics Included in Imputation Model

- Site
- Radiographic osteoarthritis severity using Kellgren and Lawrence grade
- Medial tibial plateau cross sectional area from baseline MRI
- Age
- Sex
- Body mass index
- Employment status
- Symptom duration,
- Indicator for unilateral symptoms
- Indicator for current medication use
- Treatment expectation,
- Physical activity level from the Physical Activity Scale for the Elderly
- painDETECT category
- Indicator for presence of knee effusion

eTable 1. Checklist of Minimum Reporting Requirements for Clinical Studies of Platelet-Rich Plasma[a]

Section or topic	Item No.	Checklist Item	Response
Study design	1	Study conducted in accordance with CONSORT (RCT), STROBE (cohort, case-control, or cross-sectional), or PRISMA (meta-analysis) guidelines	Y
	2	Relevant institutional and ethical approval	Y
Recipient details	3	Recipient demographics (including age and sex)	Y
	4	Comorbidities (including underlying diabetes, blood dyscrasia, inflammatory conditions, pre-existing joint pathology, and smoking status)	Y
	5	Current anti-inflammatory or antiplatelet medications	Y (excluded)
Injury details	6	Diagnosis (including relevant grading system and chronicity)	Mild-to-moderately severe radiographic tibiofemoral osteoarthritis (KL grade 2-3)
	7	Results of any preoperative imaging	Y
	8	Previous surgical or biologic treatments for current injury	Y (Prior platelet-rich plasma injection or joint replacement were exclusion criteria)
Intervention	9	Intervention described sufficiently to enable replication	Y
	10	Operative findings	Not applicable
Whole blood processing	11	Whole blood storage environment (including concentration and volume of anticoagulant, temperature, and light exposure)	Not stored, blood processed immediately
Whole blood characteristics	12	Whole blood platelet, differential leukocyte, and red cell analysis of all samples	Platelets: 270.98 x 10^9/L Leukocytes: 6.60 x 10^9/L Red blood cells: 4.79 x 10^{12}/L
Platelet-rich plasma processing	13	Platelet-rich plasma processing described sufficiently to enable replication (including commercial kit details and spin protocol)	Regenlab RegenBCT Single spin at 1500 g for 5 mins
	14	Platelet recovery rate of protocol*	80%
	15	Platelet-rich plasma storage temperature and light exposure	Not stored used immediately in temperature-controlled room with room lighting
	16	Time between blood drawing, platelet-rich plasma processing, activation, and delivery	Immediate – within 5 minutes
Platelet-rich plasma characteristics	17	Platelet-rich plasma format (for example: liquid, gel, or membrane)	Liquid
	18	Platelet-rich plasma platelet, differential leukocyte, and red cell analysis of all samples[b]	Platelets: 325 x 10^3/mm^3 (10^9/L) Leukocytes: 1.16 10^3/mm^3 (10^9/L)

Section or topic	Item No.	Checklist Item	Response
			Red blood cells: 0.03 10^6/mm^3 (10^{12}/L)
Activation	19	Activation described sufficiently to enable replication (including volume and concentration of activating agent)	Endogenous activation
Delivery	20	Point of delivery (intraoperative and/or postoperative or serial)	Non-operative Medial patellofemoral approach under ultrasound guidance

Abbreviations: BCT, blood collection tube; KL, Kellgren and Lawrence; RCT, randomized controlled trial; Y, Yes
[a] Checklist taken from Murray et al.[1]
[b] Data obtained from Regenlab RegenBCT[2]

eTable 2. Summary of Platelet-Rich Plasma Characteristics Based on Reporting Recommendations[a]

Category	Platelet-rich plasma characteristics	Response
1. Preparation of platelet-rich plasma		
	Initial blood volume (mL)	20
	Anticoagulant (type)	Sodium citrate
	System (open/closed)	Closed
	Centrifugation (yes/no)	Yes
	Number	1
	Speed (g)	1500
	Other preparation methods	Made using Regenlab RegenBCT
	Final platelet-rich plasma volume (mL)	5
2. Characteristics of platelet-rich plasma		
	Platelet-rich plasma type[b]	23-00-00
	Mean platelet volume (fL)[b]	Platelets: 325 x 10^3/mm^3 (10^9/L) Not assessed in trial platelet-rich plasma samples due to nature of commercial tubes used
	Red Blood Cells (10^6/mm^3)[b]	0.03
	White Blood Cells (10^3/mm^3)[b]	1.16
	Activation	Endogenous
	Platelet-derived growth factor-BB (pg/ml)	4,953 (1,832 – 9,814)
	Interleukin-1 receptor antagonist (pg/ml)	225 (87 – 478)
	Transforming growth factor beta (pg/ml)	64,443 (33,487 – 119,060)
	Interleukin-1 beta (pg/ml)	2 (0 – 10)
	Interleukin-6 (pg/ml)	5 (0 – 20)
	Matrix metallopeptidase-9 (pg/ml)	19,056 (11,969 – 36,567)
3. Application characteristics		
	Formulation type (liquid, gel, scaffold)	Liquid
	Administration route (including image guidance)	Medial patellofemoral approach under ultrasound guidance by an experienced musculoskeletal radiologist
	Dosage (no. of applications and interval)	Total of 3 injections at weekly intervals
	Platelet-rich plasma volume (ml)	5

Category	Platelet-rich plasma characteristics	Response
	Dose number of injected platelets ($10^3/mm^3$)[b]	325
	Tissue	Tibiofemoral joint
	Pathology	Mild-to-moderately severe radiographic tibiofemoral osteoarthritis (KL grade 2-3)
4. Other remarkable platelet-rich plasma and study features		
	e.g. further data about preparation, activation, quantification, application, combination with other products (i.e. anesthetics, others.), fresh-frozen.	Fresh platelet-rich plasma, optional prior subcutaneous local anaesthetic injection, and aspiration of effusion if appropriate

Abbreviations: BCT, blood collection tube; KL, Kellgren and Lawrence grade
[a] Kon et al.[3]
[b] Data obtained from Regenlab RegenBCT[2]

eTable 3. Magnetic Resonance Imaging Sequences and Parameters

Sequence	Slices	Slice thickness (mm)	Interslice gap (mm)	Scan time	Resolution	Voxel size	Repetition time (msec)	Echo time (msec)
MELBOURNE SITE (Philips Ingenia 3.0T)								
T1-weighted fat-suppressed 3D Gradient water-selective sequence	200	0.5	-	6:09	220x222	0.5x0.5x0.5	29.5	13.8
Proton density weighted fat-suppressed Sagittal	44	2.5	-	2:20	228x214	0.6x0.6x2.5	3678	35
Proton density weighted fat-suppressed Axial	40	2.5	0.3	2:28	272x249	0.6x0.6x2.5	3234	30
Proton density weighted fat-suppressed Coronal	32	2.5	-	2.30	280x275	0.6x0.6x2.5	2862	20
SYDNEY SITE (SIEMENS Skyra 3.0T)								
T1-weighted 3D Gradient double echo steady state	192	0.6	-	6.32	256x243	0.66x0.63x 0.6	14.1	5.0
Proton density weighted fat-suppressed Sagittal	40	2.4	0.2	2.36	307x384	0.4x0.4x2.2	3500	38
Proton density weighted fat-suppressed Axial	45	2.5	0.3	3.12	384x278	0.4x0.4x2.5	4590	29
Proton density weighted fat-suppressed Coronal	40	2.5	0.3	1.59	307x384	0.4x0.4x2.5	3600	36

eTable 4. Baseline Characteristics of Participants Who Provided Both Primary Outcomes at 12-Months and Those Participants Who Did Not

Characteristic	Incomplete primary outcomes (n=19)	Complete primary outcomes (n=269)	P-value
Age, mean (SD), y	61.8 (5.6)	61.9 (6.5)	0.97
Height, mean (SD), m	1.7 (0.1)	1.7 (0.1)	0.67
Weight, mean (SD), kg	84.2 (12.2)	82.2 (14.1)	0.56
Body mass index, mean (SD)[a]	30.4 (4.0)	29.3 (4.1)	0.25
Knee alignment, mean (SD), degrees[b]	179.7 (4.8) [n=14]	180.7 (3.4) [n=219]	0.28
Symptom duration, median (IQR), y	6.0 (3.0-10.0)	5.0 (2.0-11.0)	0.79
Physical Activity Scale for the Elderly, median (IQR)[c]	199.2 (123.6-264.2)	168.1 (111.2-228.4)	0.53
Medial tibial plateau CSA MRI, mean (SD), cm^2[d]	18.9 (4.1)	18.2 (5.1)	0.57
Overall knee pain, mean (SD)[d]	6.2 (1.5)	5.7 (1.5)	0.12
Medial tibial cartilage volume, mean (SD), mm^3[e]	1256 (469)	1328 (668)	0.53
Knee pain walking, mean (SD)[f]	5.9 (2.3)	5.7 (2.1)	0.66
ICOAP constant pain, mean (SD)[g]	7.4 (3.8)	6.6 (3.9)	0.40
ICOAP intermittent pain, mean (SD)[g]	10.4 (3.9)	10.5 (3.7)	0.91
KOOS pain, mean (SD)[h]	51.3 (12.8)	53.3 (14.5)	0.56
KOOS other symptoms, mean (SD)[h]	59.6 (13.9)	53.2 (16.3)	0.10
KOOS function in daily living, mean (SD)[h]	52.9 (14.7)	59.2 (16.7)	0.11
KOOS function in sport and recreation, mean (SD)[h]	22.6 (18.2)	28.4 (19.2)	0.20
KOOS knee-related quality of life, mean (SD)[h]	33.2 (16.9)	34.1 (16.3)	0.83
Health-related quality of life (AQoL-8D), mean (SD)[i]	0.72 (0.18)	0.72 (0.15)	0.94
Group, No. (%)			
Placebo	13 (68.4)	131 (48.7)	0.10
Platelet-rich plasma	6 (31.6)	138 (51.3)	
Sex, No. (%)			
Male	8 (42.1)	111 (41.3)	0.94
Female	11 (57.9)	158 (58.7)	
KL Grade, No. (%)[j]			
2	7 (36.8)	134 (49.8)	0.27
3	12 (63.2)	135 (50.2)	
Employment status, No. (%)			
Currently employed	11 (57.9)	169 (62.8)	0.67
Not employed	8 (42.1)	100 (37.2)	
Laterality of symptoms, No. (%)			
Unilateral	6 (31.6)	89 (33.1)	0.89
Bilateral	13 (68.4)	180 (66.9)	
Treatment expectation, No. (%)[k]			
No effect	0 (0.0)	5 (1.9)	0.63
Minimal	1 (5.3)	27 (10.0)	
Moderate	10 (52.6)	121 (45.0)	
Large improvement	6 (31.6)	104 (38.7)	
Complete recovery	2 (10.5)	12 (4.5)	
painDETECT category, No. (%)[l]			
Nociceptive knee pain	16 (84.2)	194 (72.0)	0.39
Unclear	3 (15.8)	57 (21.3)	

Characteristic	Incomplete primary outcomes (n=19)	Complete primary outcomes (n=269)	P-value
Neuropathic-like knee pain	0 (0.0)	18 (6.7)	
Problems in other joints, No. (%)			
Back	12 (63.2)	137 (50.9)	0.30
Hand	6 (31.6)	106 (39.4)	0.50
Foot	6 (31.6)	78 (29.0)	0.81
Neck	5 (26.3)	101 (37.5)	0.33
Shoulder	4 (21.1)	78 (29.0)	0.46
Hip	0 (0.0)	73 (27.1)	0.009
Current pain medication use for knee, No. (%)[m]	16 (84.2)	170 (63.2)	0.06
Acetaminophen alone or in combined formulations	7 (36.8)	98 (36.4)	0.97
Topical anti-inflammatory drugs	3 (15.8)	57 (21.2)	0.58
Non-steroidal anti-inflammatory drugs	6 (31.6)	49 (17.5)	0.15
Oral opioids	0 (0.0)	6 (2.2)	0.51
Oral corticosteroids	2 (10.5)	3 (1.1)	0.002
Presence of knee effusion MRI, No. (%)[n]	13 (68.4)	103 (38.3)	0.01

Abbreviations: AQoL-8D, Assessment of Quality-of-Life instrument-8 dimension; CSA, cross sectional area; ICOAP, Intermittent and Constant Osteoarthritis Pain; IQR, interquartile range; KL, Kellgren and Lawrence; KOOS, Knee Injury and Osteoarthritis Outcome Score; MRI, magnetic resonance imaging.

[a] Calculated as weight in kilograms divided by height in meters squared

[b] Measured as anatomical axis from standing radiograph with 180° indicating neutral alignment, <180°, varus alignment, and >180°, valgus alignment.

[c] 12-item questionnaire that asks about leisure, household and occupational activity over the past week. Scores range from 0 to over 400, with higher scores indicating higher physical activity.

[d] Medial tibial plateau cross-sectional area was measured manually from axial MRI images on the two consecutive images closest to the tibial cartilage by a single rater using OsiriX software. An average of these two areas was used as an estimate of tibial plateau bone area

[e] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume.

[f] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8

[g] ICOAP is an 11-item, two subscale questionnaire for knee/hip osteoarthritis with each item scored 0 (no pain) to 4 (extreme pain). Constant pain subscale range 0-20, intermittent pain subscale range 0-24, higher scores indicate worse pain; MCID=18.5.

[h] KOOS is a knee-specific questionnaire with 42 items covering 5 subscales. Total subscale scores range from 0 to 100 with 0 indicating extreme problems and 100, no problems. MCIDs: pain=15.4, other symptoms=15.1, function in daily living=17.0, function in sport and recreation 11.2, knee-related quality-of-life=16.5

[i] AQoL-8D is an 35 item questionnaire regarding health-related quality-of-life in the past week. Score range -0.04-1.0; higher scores indicate better quality-of-life; MCID=0.06

[j] Grading system of radiographic osteoarthritis disease severity from grade 0 to 4. Grade 2 indicates presence of osteophytes and possible joint space narrowing; Grade 3, multiple osteophytes, definite joint space narrowing, sclerosis, and possible bony deformity.

[k] Treatment expectation was assessed by a 5-point Likert Scale with participants asked “What effect do you think injections of platelet-rich plasma will have on your knee?”

[l] painDETECT is a 13-item screening survey for neuropathic-like pain. Range 0-38. Category ranges: 0-12 indicating nociceptive pain, 13-18 unclear, 19-38 neuropathic-like pain.

[m] Defined as taken at least once per week over the prior month.

[n] Graded from MRI images and scored by a single rater (blind to group) using the MRI Osteoarthritis Knee Score (MOAKS) effusion sub-score, with 0 indicating normal, 1 small, 2 medium and 3 large. Presence of knee effusion was defined as a score of 2 or 3.

eTable 5. Treatment Details, Medications, Co-interventions and Adverse Events for Each Group

Measures	Platelet-rich plasma	Placebo	P value
Number of injections, No. (%)			
0 injections	1/144 (0.7)	0/144 (0)	
1 injection	0/144 (0)	3/144 (2.1)	0.17
2 injections	3/144 (2.1)	1/144 (0.7)	
3 injections	140/144 (97.2)	140/144 (97.2)	
Use of local anaesthetic, No. (%)			
Injection 1	87/143 (60.8)	83/144 (57.6)	0.58
Injection 2	92/143 (64.3)	82/141 (58.2)	0.29
Injection 3	92/140 (65.7)	84/140 (60.0)	0.29
Effusion aspiration prior to injection, No. (%)			
Injection 1	9/143 (6.3)	15/144 (10.4)	0.21
Injection 2	7/143 (4.9)	11/141 (7.8)	0.31
Injection 3	7/140 (5.0)	12/141 (8.6)	0.23
Pain medication use, 2-months, No. (%)[a]	56/140 (40.0)	48/142 (33.8)	0.28
Acetaminophen alone or in combined formulations	46/140 (32.9)	38/142 (26.8)	0.26
Topical anti-inflammatory drugs	18/140 (12.9)	16/142 (11.3)	0.68
Non-steroidal anti-inflammatory drugs	12/140 (8.6)	10/142 (7.0)	0.63
Oral glucocorticoids	2/140 (1.4)	0/142 (0)	0.15
Oral opioids	3/140 (2.1)	1/142 (0.7)	0.31
Pain medication use, 12-months, No. (%)[a]	50/138 (36.2)	56/140 (40.0)	0.52
Acetaminophen alone or in combined formulations	39/138 (28.3)	38/140 (27.1)	0.84
Topical anti-inflammatory drugs	23/138 (16.7)	14/140 (10.0)	0.10
Non-steroidal anti-inflammatory drugs	23/138 (16.7)	25/140 (17.9)	0.79
Oral glucocorticoids	2/138 (1.4)	2/140 (1.4)	0.99
Oral opioids	1/138 (0.7)	3/140 (2.1)	0.32
Cointerventions, 2-months, No. (%)	14/140 (10.0)	10/141 (7.1)	0.38
Physiotherapy	8/140 (5.7)	5/141 (3.5)	0.39
Exercises	11/140 (7.9)	6/141 (4.3)	0.21
Injections	1/140 (0.7)	1/141 (0.7)	0.99
Hydrotherapy	4/140 (2.9)	0/141 (0)	0.04
Cointerventions, 12-months, No. (%)	19/138 (13.8)	10/140 (7.1)	0.07
Physiotherapy	7/138 (5.1)	5/140 (3.6)	0.54
Exercises	15/138 (10.9)	6/140 (4.3)	0.04
Injections	1/138 (0.7)	1/140 (0.7)	0.99
Hydrotherapy	1/138 (0.7)	3/140 (2.1)	0.32
Acupuncture	0/138 (0)	1/140 (0.7)	0.32
Surgery	1/138 (0.7)	3/140 (2.1)	0.32
Adverse events, following injections, No. (%)[b]			
Serious adverse events	0/143 (0)	0/144 (0)	N/A
Knee joint pain	54/143 (37.8)	21/144 (14.6)	<0.001
Knee swelling	13/143 (9.1)	3/144 (2.1)	0.01
Knee stiffness	14/143 (9.8)	2/144 (1.4)	0.002
Nausea/faintness	2/143 (1.4)	1/144 (0.7)	0.56
Injection site pain/bruising	2/143 (1.4)	3/144 (2.1)	0.66

Measures	Platelet-rich plasma	Placebo	P value
Adverse events, 2-months, No. (%)			
Serious related adverse events[c]	0/140 (0)	0/141 (0)	N/A
Knee joint pain	33/140 (23.6)	33/141 (23.4)	0.97
Knee swelling	7/140 (5.0)	3/141 (2.1)	0.19
Knee stiffness	3/140 (2.1)	0/141 (0)	0.08
Other lower limb musculoskeletal symptoms	30/140 (21.4)	26/141 (18.4)	0.53
Upper body musculoskeletal symptoms	23/140 (16.4)	18/141 (12.8)	0.38
Medical condition (non-musculoskeletal)	17/140 (12.1)	14/141 (9.9)	0.55
Adverse events, 12-months, No. (%)			
Serious related adverse events[c]	0/138 (0)	0/140 (0)	N/A
Knee joint pain	25/138 (18.1)	21/140 (15.0)	0.48
Knee swelling	3/138 (2.2)	0/140 (0)	0.08
Knee stiffness	5/138 (3.6)	0/140 (0)	0.02
Other lower limb musculoskeletal symptoms	31/138 (22.5)	23/140 (16.4)	0.20
Upper body musculoskeletal symptoms	13/138 (9.4)	18/140 (12.9)	0.36
Medical condition (non-musculoskeletal)	13/138 (9.4)	16/140 (11.4)	0.58

[a] Defined as taken at least once per week over the prior month
[b] Collected from study nurse notes
[c] Serious related adverse events defined as any untoward medical occurrence that resulted in death, was life threatening, required hospitalisation, resulted in significant disability or required medical or surgical intervention.

eTable 6. Platelet-Rich Plasma Growth Factor and Cytokine Concentrations and Comparison With Published Healthy Control Data

Growth factors/ cytokines	Role	N	Study results Median (range)	Published healthy control data Median (IQR/ Range/SE) [4-6]
Platelet-derived growth factor BB (pg/ml)	Regulates cell growth and division, with major role in blood vessel formation. Preferable to be higher in platelet-rich plasma	59	5,258 (2,036 – 10,904)	2,360 (IQR: 1,494 - 3,230)
Interleukin-1 receptor antagonist (pg/ml)	Natural inhibitor of pro-inflammatory effect of interleukin-1 beta. Preferable to be higher in platelet-rich plasma	59	250 (97 – 531)	203 (Range: 112 - 294)
Transforming growth factor beta (pg/ml)	Regulation of inflammatory processes, and plays crucial role in stem cell differentiation and T-cell regulation and differentiation. Preferable to be higher in platelet-rich plasma	59	71,603 (37,208 – 132,289)	5,505 (IQR: 4,679 - 6,480)
Interleukin-1 beta (pg/ml)	Mediator of inflammatory response (ie pro-inflammatory). Preferable to be lower in platelet-rich plasma	44	2 (0 – 11)	79 (Range: 13 - 227)
Interleukin-6 (pg/ml)	Pro-inflammatory cytokine. Preferable to be lower in platelet-rich plasma	58	5 (0 – 22)	72 (Range: 13 - 149)
Matrix metallopeptidase-9 (pg/ml)	Involved in breakdown of extracellular matrix in normal physiological processes. Preferable to be lower in platelet-rich plasma	59	21,174 (13,299 – 40,630)	31,800 (SE: 11,600)

Abbreviations: IQR, interquartile range; SE, standard error

eTable 7. Continuous Outcomes at Baseline and 2-Months by Treatment Group[a,b]

	Platelet-rich plasma (n=144)			Placebo (n=144)			Difference in change between groups	
	Baseline, mean (SD)	2-months, mean (SD)	Change within group, mean (SD)	Baseline, mean (SD)	2-months, mean (SD)	Change within group, mean (SD)	Mean difference (95% CI)	P-value
Primary outcomes								
Overall knee pain[c,d]	5.7 (1.5)	3.5 (2.3)	-2.2 (2.3)	5.7 (1.5)	3.9 (2.4)	-1.8 (2.5)	-0.4 (-1.0, 0.1)	0.14
Secondary outcomes	5.8 (2.1)	3.8 (2.6)	-2.0 (2.6)	5.7 (2.1)	3.9 (2.5)	-1.8 (2.8)	-0.2 (-0.8, 0.4)	0.52
Knee pain walking[c,d]	6.7 (4.1)	3.9 (4.5)	-2.8 (4.5)	6.7 (3.6)	4.0 (3.9)	-2.6 (4.5)	-0.2 (-1.1, 0.7)	0.67
ICOAP, constant pain[d,e]	10.6 (4.1)	7.5 (4.8)	-3.1 (5.3)	10.4 (3.2)	7.6 (4.4)	-2.7 (4.6)	-0.3 (-1.3, 0.7)	0.57
ICOAP, intermittent pain[d,e]	52.9 (15.2)	66.3 (18.2)	13.4 (17.4)	53.5 (13.5)	66.2 (17.2)	12.7 (16.9)	0.5 (-3.3, 4.3)	0.78
KOOS, pain[f,g]	53.9 (15.9)	66.5 (18.2)	12.6 (16.8)	53.3 (16.6)	63.9 (17.6)	10.6 (16.9)	2.3 (-1.4, 6.1)	0.22
KOOS, other symptoms[f,g]	58.7 (16.9)	70.4 (19.7)	11.7 (18.1)	58.8 (16.3)	70.1 (18.0)	11.2 (17.1)	0.5 (-3.3, 4.3)	0.78
KOOS, function in daily living[f,g]	30.1 (19.3)	42.8 (22.8)	12.8 (21.2)	26.0 (18.7)	40.4 (22.4)	14.4 (21.3)	0.1 (-4.8, 5.0)	0.98
KOOS, function in sport and recreation[f,g]	33.8 (15.8)	47.6 (19.1)	13.8 (18.4)	34.2 (16.8)	45.6 (20.3)	11.4 (21.2)	2.3 (-1.9, 6.6)	0.28
KOOS, knee-related quality-of-life[f,g]	0.72 (0.15)	0.74 (0.17)	0.02 (0.12)	0.72 (0.16)	0.75 (0.17)	0.03 (0.11)	-0.01 (-0.03, 0.02)	0.70
Health-related quality-of-life (AQoL-8D)[f,h]	0.72 (0.15)	0.74 (0.17)	0.02 (0.12)	0.72 (0.16)	0.75 (0.17)	0.03 (0.11)	-0.00 (-0.03, 0.03)	0.91

Abbreviations: AQoL-8D, Assessment of Quality-of-Life instrument-8 dimension; CI, confidence intervals; ICOAP, Intermittent and Constant Osteoarthritis Pain; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference; SD, standard deviation

[a] Adjusted for baseline value of outcome, stratifying variables (site and Kellgren and Lawrence grade), and clustering of 2- and 12-month outcomes within participants

[b] Missing outcomes were imputed. 20 datasets were imputed separately by group using predictive mean matching with 5 nearest neighbours, with results combined using Rubin's rules

[c] Measured on an 11-point numeric rating scale, range 0-10; higher scores indicate worse pain; MCID=1.8

[d] For change within groups, negative change indicates improvement. For difference in change between groups, negative difference favors platelet-rich plasma group.

[e] ICOAP is an 11-item, two subscale questionnaire for knee/hip osteoarthritis with each item scored 0 (no pain) to 4 (extreme pain). Constant pain subscale range 0-20, intermittent pain subscale range 0-24, higher scores indicate worse pain; MCID=18.5.

[f] For change within groups, positive change indicates improvement. For difference in change between groups, positive difference favors platelet-rich plasma group.

[g] KOOS is a knee-specific questionnaire with 42 items covering 5 subscales. Total subscale scores range from 0 to 100 with 0 indicating extreme problems and 100, no problems. MCIDs: pain=15.4, other symptoms=15.1, function in daily living=17.0, function in sport and recreation 11.2, knee-related quality-of-life=16.5

[h] AQoL-8D is a 35 item questionnaire regarding health-related quality-of-life in the past week. Score range -0.04-1.0; higher scores indicate better quality-of-life; MCID=0.06

eTable 8. Continuous Outcomes at Baseline and 2-Months by Treatment Group for Complete Case Data[a]

	Platelet-rich plasma			Placebo			Difference in change between groups	
	Baseline, mean (SD) (n=144)	2-months, mean (SD) (n=141)	Change within group, mean (SD)	Baseline, mean (SD) (n=144)	2-months, mean (SD) (n=142)	Change within group, mean (SD)	Mean difference (95% CI) (n=283)	P-value
Primary outcomes								
Overall knee pain[b,c]	5.7 (1.5)	3.5 (2.3)	-2.2 (2.3)	5.7 (1.5)	3.9 (2.4)	-1.8 (2.5)	-0.4 (-1.0, 0.1)	0.14
Secondary outcomes	5.8 (2.1)	3.8 (2.6)	-2.0 (2.6)	5.7 (2.1)	3.9 (2.5)	-1.8 (2.8)	-0.2 (-0.8, 0.4)	0.52
Knee pain walking[b,c]	6.7 (4.1)	3.9 (4.5)	-2.8 (4.5)	6.7 (3.6)	4.0 (3.9)	-2.6 (4.5)	-0.2 (-1.1, 0.7)	0.67
ICOAP, constant pain[b,e]	10.6 (4.1)	7.5 (4.8) [n=140]	-3.1 (5.3)	10.4 (3.2)	7.6 (4.4) [n=141]	-2.7 (4.6)	-0.3 (-1.3, 0.7) [n=281]	0.57
ICOAP, intermittent pain[b,e]	52.9 (15.2)	66.3 (18.2) [n=140]	13.4 (17.4)	53.5 (13.5)	66.2 (17.2) [n=141]	12.7 (16.9)	0.5 (-3.3, 4.3) [n=281]	0.78
KOOS, pain[d,f]	53.9 (15.9)	66.5 (18.2)	12.6 (16.8)	53.3 (16.6)	63.9 (17.6)	10.6 (16.9)	2.3 (-1.4, 6.1)	0.22
KOOS, other symptoms[d,f]	58.7 (16.9)	70.4 (19.7)	11.7 (18.1)	58.8 (16.3)	70.1 (18.0)	11.2 (17.1)	0.5 (-3.3, 4.3)	0.78
KOOS, function in daily living[d,f]	30.1 (19.3)	42.8 (22.8)	12.8 (21.2)	26.0 (18.7)	40.4 (22.4)	14.4 (21.3)	0.1 (-4.8, 5.0)	0.98
KOOS, function in sport and recreation[d,f]	33.8 (15.8)	47.6 (19.1)	13.8 (18.4)	34.2 (16.8)	45.6 (20.3)	11.4 (21.2)	2.3 (-1.9, 6.6)	0.28
KOOS, knee-related quality-of-life[d,f]	0.72 (0.15)	0.74 (0.17)	0.02 (0.12)	0.72 (0.16)	0.75 (0.17)	0.03 (0.11)	-0.01 (-0.03, 0.02)	0.70
Health-related quality-of-life (AQoL-8D)[d,g]	0.72 (0.15)	0.74 (0.17) [n=140]	0.02 (0.12)	0.72 (0.16)	0.75 (0.17)	0.03 (0.11)	-0.00 (-0.03, 0.03) [n=282]	0.91

Abbreviations: AQoL-8D, Assessment of Quality-of-Life instrument-8 dimension; CI, confidence intervals; ICOAP, Intermittent and Constant Osteoarthritis Pain; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference; SD, standard deviation

[a] Adjusted for baseline value of outcome, stratifying variables (site and Kellgren and Lawrence grade), and clustering of 2- and 12-month outcomes within participants

[b] For change within groups, negative change indicates improvement. For difference in change between groups, negative difference favors platelet-rich plasma group.

[c] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8.

[d] For change within groups, positive change indicates improvement. For difference in change between groups, positive difference favors platelet-rich plasma group.

[e] ICOAP is an 11-item, two subscale questionnaire for knee/hip osteoarthritis with each item scored 0 (no pain) to 4 (extreme pain). Constant pain subscale range 0-20, intermittent pain subscale range 0-24, higher scores indicate worse pain; MCID=18.5.

[f] KOOS is a knee-specific questionnaire with 42 items covering 5 subscales. Total subscale scores range from 0 to 100 with 0 indicating extreme problems and 100, no problems. MCIDs: pain=15.4, other symptoms=15.1, function in daily living=17.0, function in sport and recreation 11.2, knee-related quality-of-life=16.5.

[g] AQoL-8D is a 35 item questionnaire regarding health-related quality-of-life in the past week. Score range -0.04-1.0; higher scores indicate better quality-of-life; MCID=0.06.

eTable 9. Continuous Outcomes at Baseline and 12-Months by Treatment Group for Complete Case Data[a]

	Platelet-rich plasma			Placebo			Difference in change between groups	
	Baseline, mean (SD) (n=144)	12 months, mean (SD) (n=138)	Change within group, mean (SD)	Baseline, mean (SD) (n=144)	12 months, mean (SD) (n=140)	Change within group, mean (SD)	Mean difference (95% CI) (n=278)	P-value
Primary outcomes								
Overall knee pain[b,c]	5.7 (1.5)	3.5 (2.6)	-2.1 (2.7)	5.7 (1.5)	3.9 (2.6)	-1.8 (2.5)	-0.4 (-0.9, 0.2)	0.19
Annual percent change in medial tibial cartilage volume[d,e,f]	-	-1.4 (7.2) [n=140]	-1.4 (7.2)	-	-1.2 (6.8) [n=132]	-1.2 (6.8)	-0.2 (-1.9, 1.5) [n=272]	0.81
Secondary outcomes								
Average knee pain walking[b,c]	5.8 (2.1)	3.8 (2.7)	-2.0 (2.6)	5.7 (2.1)	4.1 (2.8)	-1.6 (2.8)	-0.3 (-0.9, 0.2)	0.25
ICOAP, constant pain[b,g]	6.7 (4.1)	3.8 (4.1)	-2.9 (4.8)	6.7 (3.6)	3.9 (4.5)	-2.6 (4.5)	-0.1 (-1.1, 0.8)	0.77
ICOAP, intermittent pain[b,g]	10.6 (4.1)	7.4 (4.6)	-3.2 (5.3)	10.4 (3.2)	7.4 (5.2)	-2.8 (4.8)	-0.2 (-1.3, 0.9)	0.71
KOOS, pain[d,h]	52.9 (15.2)	67.9 (18.4)	14.9 (19.0)	53.5 (13.6)	65.6 (20.1)	12.0 (17.8)	2.6 (-1.2, 6.5)	0.18
KOOS, other symptoms[d,h]	53.9 (15.9)	67.3 (19.1)	13.6 (19.0)	53.3 (16.6)	63.6 (20.2)	10.4 (17.1)	3.4 (-0.3, 7.2)	0.07
KOOS, function in daily living[d,h]	58.7 (17.0)	72.7 (18.5)	13.7 (19.1)	58.8 (16.3)	71.7 (19.8)	12.6 (17.8)	1.0 (-2.9, 4.8)	0.62
KOOS, function in sport and recreation[d,h]	30.1 (19.4)	45.1 (25.4)	14.8 (24.9)	26.0 (18.8)	41.2 (25.1)	15.1 (21.5)	1.3 (-3.7, 6.2)	0.62
KOOS, knee-related quality-of-life[d,h]	33.8 (15.8)	50.9 (20.2)	17.1 (20.5)	34.2 (16.9)	48.5 (22.1)	14.5 (19.7)	2.7 (-1.6, 7.0)	0.22
Health-related quality-of-life (AQoL-8D)[d,i]	0.72 (0.15)	0.77 (0.17)	0.04 (0.13)	0.72 (0.16)	0.75 (0.17)	0.04 (0.12)	0.00 (-0.03, 0.03)	0.92

Abbreviations: AQoL-8D, Assessment of Quality-of-Life instrument-8 dimension; CI, confidence intervals; ICOAP, Intermittent and Constant Osteoarthritis Pain; KOOS, Knee Injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference; SD, standard deviation

[a] Adjusted for baseline value of outcome, stratifying variables, and clustering of 2- and 12-month outcomes within participants (except for annual percentage change in medial tibial cartilage volume given no 2-month data)

[b] For change within groups, negative change indicates improvement. For difference in change between groups, negative difference favors platelet-rich plasma group.

[c] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8.

[d] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume. Annual percent change in cartilage volume was calculated as (follow-up cartilage volume - baseline cartilage volume)/(baseline cartilage volume x time between MRI scans) x 100

[e] For change within groups, positive change indicates improvement. For difference in change between groups, positive difference favors platelet-rich plasma group.

[f] As the primary outcome is annual percentage change, baseline values cannot be presented.

[g] ICOAP is an 11-item, two subscale questionnaire for knee/hip osteoarthritis with each item scored 0 (no pain) to 4 (extreme pain). Constant pain subscale range 0-20, intermittent pain subscale range 0-24, higher scores indicate worse pain; MCID=18.5.

[h] KOOS is a knee-specific questionnaire with 42 items covering 5 subscales. Total subscale scores range from 0 to 100 with 0 indicating extreme problems and 100, no problems. MCIDs: pain=15.4, other symptoms=15.1, function in daily living=17.0, function in sport and recreation 11.2, knee-related quality-of-life=16.5.

[i] AQoL-8D is a 35 item questionnaire regarding health-related quality-of-life in the past week. Score range -0.04-1.0; higher scores indicate better quality-of-life; MCID=0.06.

eTable 10. Global Improvement and Other Joint Structural Outcomes Using Complete Case Data

	Platelet-rich plasma	Placebo	Absolute difference (95% CI)[a]	Risk Ratio (95% CI)[a]	P-value
Global change at 2-months[b,c]					
Improved overall	68/141 (48.2)	51/141 (36.2)	14.28 (3.13, 25.43)	1.41 (1.07, 1.85)	0.02
Improved pain	66/141 (46.8)	53/141 (37.6)	10.71 (-0.57, 21.99)	1.29 (0.98, 1.70)	0.07
Improved function	53/141 (37.6)	46/141 (32.6)	6.24 (-4.74, 17.23)	1.19 (0.87, 1.64)	0.27
Global change at 12-months[b,c]					
Improved overall	64/138 (46.4)	52/140 (37.1)	9.18 (-2.08, 20.45)	1.25 (0.95, 1.64)	0.11
Improved pain	64/138 (46.4)	50/140 (35.7)	10.96 (-0.34, 22.26)	1.31 (0.99, 1.73)	0.06
Improved function	59/138 (42.8)	45/140 (32.1)	10.65 (-0.46, 21.75)	1.33 (0.98, 1.81)	0.06
MOAKS subscores at 12-months[d,e]					
Worse meniscus morphology[f]	37/140 (26.43)	37/133 (27.82)	-1.10 (-11.61, 9.42)	0.96 (0.65, 1.42)	0.84
Worse inter-condylar synovosis[g]	12/140 (8.57)	17/133 (12.78)	-3.39 (-10.56, 3.78)	0.73 (0.36, 1.44)	0.36
Number of areas of cartilage thinning[h]					
0	72/140 (51.4)	71/133 (53.4)		Reference	
1	27/140 (19.3)	37/133 (27.8)		0.75 (0.41, 1.37)	0.35
2	17/140 (12.1)	16/133 (12.0)		1.16 (0.53, 2.52)	0.71
3+	24/140 (17.1)	9/133 (6.8)		2.88 (1.22, 6.80)	0.02
Change in whole knee effusion[i]					
Improved	31/140 (22.1)	32/133 (24.1)		0.90 (0.50, 1.62)	0.73
No change	84/140 (60.0)	76/133 (57.1)		Reference	
Worsened	25/140 (17.9)	25/133 (18.8)		0.93 (0.49, 1.78)	0.84
Other MRI measures at 12-months[e]					
Bone marrow lesion progression[j]	34/140 (24.3)	25/132 (18.9)	5.11 (-4.44, 14.66)	1.27 (0.81, 1.99)	0.30
Cartilage defects progression[k]	25/140 (17.9)	15/132 (11.4)	6.23 (-2.08, 14.54)	1.54 (0.85, 2.79)	0.15

Abbreviations: CI, confidence intervals; MOAKS, MRI osteoarthritis knee score; MRI, magnetic resonance imaging

[a] Absolute differences > 0 and risk ratios >1 indicate that the risk of the outcome is greater in platelet-rich plasma group

[b] Rated using 7-point Likert scales with terminal descriptors of 'much worse' to 'much better'. Participants were asked to indicate their overall change in their study knee, change in their knee pain, and change in function compared to baseline, with those indicating 'moderately better' or 'much better' classified as improved.

[c] Adjusted for stratifying variables, and clustering of 2- and 12-month outcomes within participants

[d] MOAKS is a semi-quantitative MRI scoring tool for knee osteoarthritis. It was assessed by a single rater (blind to group) grading baseline and 12-month MRI images.

[e] Adjusted for stratifying variables

[f] Three regions scored 0-9 for morphological features for each meniscus. Defined as worse if any region of either the medial or lateral meniscus was scored higher at 12-months compared to baseline.

[g] Incorporating synovitis and effusion and scored 0-3, with Grade 0 being normal, 1 mild, 2 moderate and 3 severe. Defined as worse if the score was higher at 12-months compared to baseline.
[h] Fourteen regions each scored 0-3 with Grade 0 indicating no area with cartilage loss, 1 indicating <10% of cartilage surface area with loss, 2 indicating 10-75% of cartilage surface area with loss and Grade 3 indicating > 75% of cartilage surface area with loss. Number of regions where the score was higher at 12-months compared to baseline.
[i] Scored 0-3, with Grade 0 being normal, 1 small, 2 medium and 3 large. Improved was defined as a lower score at 12-months compared to baseline, no change was defined as the same score and worsened was defined as a higher score.
[j] Assessed by a single rater (blind to group and timepoint) grading baseline and 12-month MRI images. Bone marrow lesions were scored in the medial distal femur and medial proximal tibia as 0-3 (Grade 0, absent; Grade 1, occupies <1/3 of the region; Grade 2, occupies 1/3 to 2/3 of the region; Grade 3, occupies >2/3 of the region). Progression was defined as an increase in bone marrow lesion grade of ≥1 in either the medial distal femur or medial proximal tibia from baseline to 12-months.
[k] Assessed by a single rater (blind to group and timepoint) grading baseline and 12-month MRI images. Cartilage defects were scored in the medial tibia and medial femur as 0-4 (Grade 0, normal cartilage; Grade 1, focal blistering and intracartilaginous low-signal intensity area with an intact surface and bottom; Grade 2, irregularities on the surface or bottom and loss of thickness of less than 50%; Grade 3, deep ulceration with loss of thickness of more than 50%; Grade 4, full-thickness chondral wear with exposure of subchondral bone). Progression was defined as a score increase ≥ 1 from baseline to 12-months in either the medial tibia or medial femur.

eTable 11. Continuous Primary Outcomes by Treatment Group for Complete Case Data Excluding Participants Due to Different Centrifuge Speed[a]

Primary outcomes	Mean (SD) change within groups Month 2 minus baseline		Difference in change between groups Month 2 minus baseline		Mean (SD) change within groups Month 12 minus baseline		Difference in change between groups Month 12 minus baseline	
	Platelet-rich plasma	Placebo	Mean difference (95% CI)	P-value	Platelet-rich plasma	Placebo	Mean difference (95% CI)	P-value
Overall knee pain[b,c]	-2.2 (2.3) [n=124]	-1.9 (2.5) [n=129]	-0.4 (-1.0, 0.2)	0.22	-2.1 (2.8) [n=121]	-1.7 (2.5) [n=127]	-0.5 (-1.1, 0.1)[d]	0.10
Annual percent change in medial tibial cartilage volume[e,f]			-	-	-1.5 (7.3), [n=123]	-1.2 (6.6) [n=120]	-0.3 (-2.1, 1.4)[g]	0.71

Abbreviations: CI, confidence intervals; MCID, minimal clinically important difference; SD, standard deviation

[a] 30 participants recruited prior to December 7, 2017 were excluded due to use of a different centrifuge speed

[b] For change within groups, negative change indicates improvement. For difference in change between groups, negative difference favors platelet-rich plasma group.

[c] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8

[d] Adjusted for baseline value of outcome, stratifying variables, and clustering of 2- and 12-month outcomes within participants

[e] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume. Annual percent change in cartilage volume was calculated as (follow-up cartilage volume - baseline cartilage volume)/(baseline cartilage volume x time between MRI scans) x 100.

[f] For change within groups, positive changes indicate improvement. For difference in change between groups, positive difference favor platelet-rich plasma group.

[g] Adjusted for baseline value of outcome and stratifying variables

eTable 12. Continuous Primary Outcomes by Treatment Group for Complete Case Data Adjusting for Differences in Use of Effusion Aspiration

Primary outcomes	Mean (SD) change within groups Month 2 minus baseline		Difference in change between groups Month 2 minus baseline		Mean (SD) change within groups Month 12 minus baseline		Difference in change between groups Month 12 minus baseline	
	Platelet-rich plasma	Placebo	Mean difference (95% CI)	P-value	Platelet-rich plasma	Placebo	Mean difference (95% CI)	P-value
Overall knee pain[a,b,c]	-2.2 (2.3) [n=140]	-1.8 (2.5) [n=142]	-0.4 (-1.0, 0.1) [n=282]	0.14	-2.1 (2.7) [n=137]	-1.8 (2.5) [n=140]	-0.4 (-0.9, 0.2) [n=277]	0.19
Annual percent change in medial tibial cartilage volume[d,e,f]	-	-	-	-	-1.4 (7.2) [n=139]	-1.2 (6.8) [n=132]	-0.3 (-2.0, 1.4) [n=271]	0.76

Abbreviations: CI, confidence intervals; MCID, minimal clinically important difference; SD, standard deviation

[a] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8

[b] For change within groups, negative change indicates improvement. For difference in change between groups, negative difference favors platelet-rich plasma group.

[c] Adjusted for baseline value of outcome, stratifying variables, and clustering of 2- and 12-month outcomes within participants and effusion aspiration prior to injection

[d] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume. Annual percent change in cartilage volume was calculated as (follow-up cartilage volume - baseline cartilage volume)/(baseline cartilage volume x time between MRI scans) x 100.

[e] For change within groups, positive change indicates improvement. For difference in change between groups, positive difference favors platelet-rich plasma group.

[f] Adjusted for baseline value of outcome, stratifying variables and effusion aspiration prior to injection

eTable 13. Binary Moderators for the Primary Outcomes at 12-Months

Outcome	Moderator	Platelet-rich plasma	Placebo	Platelet-rich plasma minus Placebo (95%CI)	Interaction p-value
Overall knee pain[a]	KL Grade[b]				0.52
	2	-2.48 (2.66) [n=66]	-1.77 (2.31) [n=71]	-0.57 (-1.41, 0.26) [n=137]	
	3	-1.75 (2.76) [n=72]	-1.74 (2.65) [n=69]	-0.19 (-1.01, 0.64) [n=141]	
	Presence of knee effusion[c]				0.35
	No	-1.94 (2.61) [n=80]	-1.90 (2.58) [n=88]	-0.15 (-0.90, 0.61) [n=168]	
	Yes	-2.33 (2.89) [n=58]	-1.52 (2.31) [n=52]	-0.72 (-1.65, 0.21) [n=110]	
Annual percent change in medial tibial cartilage volume[d]	KL Grade[b]				0.90
	2	-1.71 (6.79) [n=68]	-1.38 (5.81) [n=68]	-0.32 (-2.71, 2.06) [n=136]	
	3	-1.16 (7.66) [n=72]	-1.06 (7.75) [n=64]	-0.10 (-2.48, 2.28) [n=136]	
	Presence of knee effusion[c]				0.52
	No	-2.17 (7.15) [n=81]	-1.45 (6.53) [n=87]	-0.75 (-2.89, 1.39) [n=168]	
	Yes	-0.41 (7.27) [n=59]	-0.80 (7.35) [n=45]	0.41 (-2.35, 3.17) [n=104]	

Abbreviations: CI, confidence intervals; KL, Kellgren and Lawrence; MRI, magnetic resonance imaging; SD, standard deviation

[a] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8

[b] Grading system of radiographic osteoarthritis disease severity from grade 0 to 4. Grade 2 indicates presence of osteophytes and possible joint space narrowing; Grade 3, multiple osteophytes, definite joint space narrowing, sclerosis, and possible bony deformity.

[c] Graded from MRI images and scored by a single rater (blind to group) using the MRI Osteoarthritis Knee Score (MOAKS) effusion sub-score, with 0 indicating normal, 1 small, 2 medium and 3 large. Presence of knee effusion was defined as a score of 2 or 3.

[d] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume. Annual percent change in cartilage volume was calculated as (follow-up cartilage volume - baseline cartilage volume)/(baseline cartilage volume x time between MRI scans) x 100.

eTable 14. Continuous Moderators for the Primary Outcomes at 12-Months

Outcome (change from baseline)	Moderator	Moderator coefficient for Platelet-rich plasma Coefficient (95% CI)	p-value	Moderator coefficient for Placebo Coefficient (95% CI)	p-value	Interaction between moderator and group Difference Platelet-rich plasma minus Placebo (Interaction term estimate) (95% CI)	p-value
Overall knee pain[a]	Knee alignment (degrees)	0.05 (-0.10, 0.20)	0.55	-0.05 (-0.19, 0.08)	0.46	0.10 (-0.09, 0.28)	0.31
Annual percent change in medial tibial cartilage volume[b]	Knee alignment (degrees)	-0.60 (-1.03, -0.18)	0.005	-0.18 (-0.58, 0.22)	0.38	-0.42 (-0.97, 0.12)	0.13
Overall knee pain[a]	BMI (kg/m^2)	0.01 (-0.10, 0.13)	0.82	0.05 (-0.04, 0.14)	0.27	-0.04 (-0.19, 0.11)	0.61
Annual percent change in medial tibial cartilage volume[b]	BMI (kg/m^2)	0.03 (-0.29, 0.36)	0.84	0.18 (-0.09, 0.45)	0.19	-0.15 (-0.57, 0.28)	0.50

Abbreviations: BMI, body mass index; CI, confidence intervals.

[a] Measured on an 11-point numeric rating scale for average knee pain in past week, score range 0 (no pain) to 10 (worst pain possible); higher scores indicate worse pain; MCID=1.8.

[b] A single rater (blind to group and timepoint) measured medial tibial cartilage volume from sagittal MRI images by manually drawing disarticulation contours around the cartilage boundaries on each section using OsiriX software. These data were re-sampled by bilinear and cubic interpolation for the final 3-dimensional rendering. The cartilage plate volume was determined by summing the pertinent voxels within the resultant binary volume. Annual percent change in cartilage volume was calculated as (follow-up cartilage volume - baseline cartilage volume)/(baseline cartilage volume x time between MRI scans) x 100.

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