

Supplementary Table 1. **Clinical studies included in the review.** The table provides an overview of the clinical trials identified through a search of ClinicalTrials.gov. Homeopathic interventions, herbal therapies, and studies outside the scope of this review were excluded. Further exclusions, as specified in the table, were applied to studies lacking a corresponding preclinical animal study, studies for which results or data analyses were not publicly available, and studies that compared the efficacy of different drug formulations without including a control or vehicle group.

	NCT ID Study period	Name of the clinical trial	Exclusion reason
NSAID	NCT00092768 2004-03/2005-02	A Study of MK0663 and an Approved Drug in the Treatment of Osteoarthritis (0663-076)	Included
	NCT00092781 2004-03/2005-02	A Study of MK0663 and an Approved Drug in the Treatment of Osteoarthritis (0663-077)	Included
	NCT01461369 2011-10/2012-10	Study of Diclofenac Capsules to Treat Osteoarthritis Pain	Included
	NCT01554163 2012-03/2013-03	Safety and Efficacy of Etoricoxib 30 mg Versus Celecoxib 200 mg in Korean Participants With Osteoarthritis	Included
	NCT01787188 2013-03/2013-10	Study of Meloxicam Capsules to Treat Osteoarthritis Pain	Included
	NCT01980940 2013-12/2014-11	The Single Dose Pharmacokinetics of Two and Proof of Efficacy of One New Etoricoxib Gel Formulation in Participants With Osteoarthritis (MK-0663-168)	Included
	NCT02311881 2015-01/2016-02	A 12-Week Efficacy Study of Paracetamol 1000mg Sustained-release Tablets in Patients With Osteoarthritis	Included
	NCT03209362 2017-10/2018-11	SI-613 Study for Knee Osteoarthritis	Included
	NCT05007808 2021-01/2023-01	Efficacy and Safety of G001 in Patients With Osteoarthritis (OA) of the Knee	Included
	NCT00664560 2008-04/2009-01	Efficacy Study of PN400 (VIMOVO) Twice Daily and Celebrex Once Daily in Patients With Osteoarthritis	No relevant animal study identified

NCT00665431 2008-04/2009-01	Efficacy Study of PN400 (VIMOVO) Twice Daily and Celebrex Once Daily in Patients With Osteoarthritis	No relevant animal study identified
NCT01147458 2010-07/2011-02	A Study Of The Safety And Efficacy Of PF-04191834 In Patients With Osteoarthritis Of The Knee	No relevant animal study identified
NCT01119898 2010-08/2011-02	Exploratory Study of PENNSAID Gel to Treat Symptoms of Knee Osteoarthritis	No relevant animal study identified
NCT01341405 2011-04/2012-01	Study of CG100649 Versus Celecoxib in Osteoarthritis Patients	No relevant animal study identified
NCT01765296 2013-03/2014-04	Phase III Study of CG100649 in Osteoarthritis Patients	No relevant animal study identified
NCT01799213 2013-09/2018-06	Discontinuing NSAIDs in Veterans With Knee Osteoarthritis	No control/placebo comparison
NCT01967550 2013-10/2014-05	Efficacy and Safety of Diclofenac DDEA 2.32 % in Patient Suffering From Knee Osteoarthritis (OA)	No data analysis reported
NCT02067611 2014-02/2016-04	A Study to Evaluate the Efficacy and Safety of X0002 Spray in Subjects With Osteoarthritis	No data analysis reported
NCT02121002 2014-04/2014-12	Study Comparing a Generic Diclofenac Sodium Topical Gel, 1% to Voltaren in the Treatment of Subjects With Osteoarthritis of the Knee	No data analysis reported
NCT02311881 2015-01/2016-02	A 12-Week Efficacy Study of Paracetamol 1000mg Sustained-release Tablets in Patients With Osteoarthritis	No relevant animal study identified
NCT02913521 2015-06/2016-06	Bioequivalence Study With Clinical Endpoint for Diclofenac Sodium Topical Gel 1%	No data analysis reported
NCT02596451 2015-08/2016-03	To Study Generic Diclofenac Sodium Topical Gel 1% in the Treatment of Osteoarthritis of the Knee (Degenerative Joint Disease Presented as Joint Pain, Stiffness, Swelling and Restricted Motion).	No data analysis reported
NCT03172780 2017-05/2017-12	A Bioequivalence Study Using Clinical Endpoint for Diclofenac Sodium Gel 1% in Osteoarthritis Knee*	No data analysis reported
NCT03277066	A 4-week Study to Evaluate the Efficacy and Safety of HP-5000 in Subjects With Knee Osteoarthritis	Comparison between formulations

Supplementary table 1

	2017-09/2019-09		
	NCT03691844 2018-10/2019-07	AMZ001 for the Treatment of Knee Osteoarthritis Symptoms	No relevant animal study identified
Corticosteroid	NCT02116972 2014-04/2015-11	Study of FX006 vs Normal Saline in Patients With Osteoarthritis of the Knee	Included
	NCT02357459 2015-01/2016-01	Study of FX006 for the Treatment of Pain in Patients With Osteoarthritis of the Knee	Included
	NCT00521989 2007-08/2009-07	CRx-102 Osteoarthritis Multicenter Evaluation Trial	No relevant animal study identified
	NCT01487161 2012-06/2013-04	Study of FX006 in Patients With Osteoarthritis of the Knee	No control/placebo comparison
	NCT02468583 2015-02/2016-07	Proof of Concept Study Comparing FX006 to Kenalog®-40 in Patients With Post-Traumatic Osteoarthritis of the Knee	No control/placebo comparison
	NCT02688400 2016-05/2018-06	Effect of Diacerein vs Celecoxib on Symptoms and Structural Changes in Symptomatic Knee Osteoarthritis	No control/placebo comparison
	NCT03005873 2017-03/2018-07	Phase IIa, Randomized, Double Blinded, Placebo Controlled, Dose Finding Study for TLC599 in OA Patients	No relevant animal study identified
	NCT03191903 2017-05/2018-04	Study of Cingala™ for the Relief of Knee Osteoarthritis Compared to Triamcinolone Hexacetamide	No relevant animal study identified
	NCT03390036 2017-12/2018-07	Study of Cingal for the Relief of Knee Osteoarthritis Compared to Triamcinolone Hexacetamide at 39 Weeks Follow up	No relevant animal study identified
	NCT03793010 2018-12/2019-08	Study to Evaluate the Efficacy and Safety of FX006 in Patients With Hip Osteoarthritis	No data analysis reported
	NCT04160091 2019-11/2020-06	Study to Evaluate the Efficacy and Safety of FX006 in Patients With Glenohumeral Osteoarthritis or Shoulder Adhesive Capsulitis	No data analysis reported
	NCT04123561 2019-11/2022-02	Extended and Controlled Release Liposomal Formulated Dexamethasone for Chronic Knee OA Pain	No relevant animal study identified

Supplementary table 1

	NCT04231318 2020-09/2022-05	Study of Cingal® and Triamcinolone Hexacetamide for the Relief of Knee Osteoarthritis Pain	No relevant animal study identified
	NCT04120402 2021-09/2023-06	Study to Evaluate the Efficacy and Safety of EP-104IAR in Patients With Osteoarthritis of the Knee	No relevant animal study identified
Opioid	NCT00950651 2002-03/2002-11	A Comparison of the Analgesic Efficacy and Safety of Once Daily Tramadol HCl / ContramidA® Tablets to Twice Daily Tramadol HCl (SR) for the Treatment of Osteoarthritis of the Knee	Included
	NCT00832416 2003-01/2003-08	A Four-Arm Study Comparing the Analgesic Efficacy and Safety of Tramadol Once a Day 100, 200 and 300 mg Versus Placebo for the Treatment of Pain Due to Osteoarthritis of the Knee	Included
	NCT00852917 2003-01/2003-08	A Four-Arm Study Comparing the Analgesic Efficacy and Safety of Tramadol Once a Day 100, 200 and 300 mg Versus Placebo for the Treatment of Pain Due to Osteoarthritis of the Knee (With 7-Day Follow-up)	Included
	NCT00833794 2004-10/2006-01	A Two-Arm Study Comparing the Analgesic Efficacy and Safety of Tramadol HCl Once-a-Day Versus Placebo for the Treatment of Pain Due to Osteoarthritis	Included
	NCT00421928 2007-01/2008-12	Tapentadol (CG5503)	Included
	NCT00486811 2007-06/2008-07	A Study to Evaluate the Efficacy and Safety of CG5503 Prolonged Release (PR) in Subjects With Moderate to Severe Chronic Pain Due to Osteoarthritis of the Knee	Included
	NCT00487435 2007-06/2009-06	An Open-label Extension Study With Flexible Dosing of Extended-release (ER) Tapentadol (CG5503) to Treat Patients With Moderate to Severe Chronic Pain	Included
	NCT00531427 2007-09/2009-04	Buprenorphine Transdermal System (BTDS) in Subjects w/Mod-sev Osteoarthritis (OA) Chronic Pain of Knee	Included
	NCT00983073 2009-09/2010-09	Evaluation of Effectiveness and Tolerability of Tapentadol Hydrochloride in Subjects With Severe Pain Due to Osteoarthritis Taking Either WHO Step I or Step II Analgesics or no Regular Analgesic	Included
	NCT01124604 2010-04/2010-12	An Efficacy and Safety Study for Tapentadol Extended Release (JNS024ER) in Chronic Pain Participants	Included
	NCT01755546 2012-12/2014-11	Long-term Open-Label Safety Study to Evaluate EN3409	Included

Supplementary table 1

	NCT00312221 2004-04/2005-08	Safety and Efficacy of Buprenorphine Transdermal System (BTDS) in Subjects With Moderate to Severe Osteoarthritis Pain	No control/placebo comparison
	NCT00420992 2006-12/2007-11	A Study of Embeda (Kadian NT, ALO-01) in Subjects With Pain Due to Osteoarthritis of the Hip or Knee	No relevant animal study identified
	NCT00631319 2008-02/2009-06	A Double-blind Study of Controlled Release OROS Hydromorphone Compared to Placebo in Patients With Chronic Osteoarthritis (OA) Pain	No data analysis reported
	NCT00736853 2008-06-2009-01	An Efficacy and Safety Study of Acetaminophen Plus Tramadol Hydrochloride (JNS013) in Participants With Chronic Pain	No relevant animal study identified
	NCT01008618 2009-01/2010-02	A Confirmatory Study of Fentanyl in Participants With Osteoarthritis or Low Back Pain	No relevant animal study identified
	NCT00979953 2009-10/2010-06	Efficacy and Safety Study Evaluating ADL5859 and ADL5747 in Participants With Pain Due to Osteoarthritis of the Knee	No data analysis reported
	NCT01240863 2010-11/2011-08	Study to Evaluate the Efficacy and Safety of Hydrocodone Bitartrate Extended-Release Tablets (CEP-33237) for Relief of Moderate to Severe Pain in Patients With Osteoarthritis or Low Back Pain Who Require Opioid Treatment for an Extended Period of Time	No relevant animal study identified
	NCT01298765 2011-03/2012-08	Longterm Safety Study of BEMA Buprenorphine in Subjects With Chronic Pain	No data analysis reported
	NCT01451385 2011-09/2012-06	Study of COV795 in Subjects With Osteoarthritis or Chronic Low Back Pain	No data analysis reported
	NCT01619839 2012-06/2013-09	A Phase 2 Study To Assess The Efficacy, Tolerability, And Safety OF NKTR-181 In Subjects With Chronic OA Knee Pain	No data analysis reported
	NCT02944448 2016-09/2017-05	A Study Evaluating Pain Relief and Safety of Orally Administered CR845 in Patients With Osteoarthritis of Hip or Knee	No data analysis reported
	NCT03008590 2018-05/2019-12	Low Dose Naltrexone for Chronic Pain From Arthritis	No relevant animal study identified
Anti con	NCT00408421 2006-11/2007-10	Duloxetine Versus Placebo for Osteoarthritis Knee Pain	Included

Supplementary table 1

	NCT00433290 2007-02/2008-05	Duloxetine vs. Placebo in the Treatment of Osteoarthritis Knee Pain	Included
	NCT00485472 2007-03/2008-01	Trial to Assess Efficacy and Safety of Lacosamide in Subjects With Osteoarthritis of the Knee	Included
	NCT00945945 2009-07/2010-05	A Study of Duloxetine in Patients With Osteoarthritis Knee Pain	Included
	NCT01931475 2013-09/2015-06	A Study of Duloxetine in Participants With Chronic Pain Due to Osteoarthritis in China	Included
	NCT02248480 2014-10/2015-06	A Study of Duloxetine (LY248686) in Participants With Chronic Osteoarthritis and Knee Pain in Japan	Included
	NCT02335346 2015-01/2016-03	An Extension Study of Duloxetine in Osteoarthritis and Knee Pain (Extension of F1J-JE-HMGX, NCT02248480)	Included
TRPV1 modulator	NCT03429049 2018-01/2019-11	A Phase 3 Efficacy and Safety Study of Intra-articular CNTX-4975-05 (Capsaicin) vs Placebo in Subjects With OA Knee Pain	Included
	NCT03528369 2018-05/2018-12	A Phase 2 Clinical Trial Examining the Effects on Osteoarthritic Knee Pain of CGS-200-1, CGS-200-5 and Vehicle Control	Included
	NCT03660943 2018-09/2020-06	A Clinical Study to Test Efficacy and Safety of Repeat Doses of CNTX-4975-05 in Patients With Osteoarthritis Knee Pain	Included
	NCT00878501 2009-03/2009-07	Study to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of AZD1386 in Patients With Osteoarthritis (OA) of the Knee	No data analysis reported
Biological therapies	NCT00399490 2006-09/2008-02	Open-label Extension Study Of RN624	Included
	NCT00669409 2008-06/2009-12	A Phase 1/2A, Single Dose Study Of PF-04383119 In Japanese Patients With Moderate To Severe Pain From Osteoarthritis Of The Knee	Included
	NCT00733902 2008-09/2010-01	Tanezumab in Osteoarthritis of the Knee	Included
	NCT00744471	Tanezumab in Osteoarthritis Of The Hip	Included

Supplementary table 1

2008-11/2010-08		
NCT00830063 2009-05/2010-08	Tanezumab In Osteoarthritis Of The Knee	Included
NCT00863304 2009-06/2010-08	Tanezumab in Osteoarthritis of the Hip or Knee	Included
NCT00985621 2009-10/2011-02	Tanezumab In Osteoarthritis Of The Hip Or Knee	Included
NCT02192190 2014-07/2015-06	A Study of LY2951742 in Participants With Mild to Moderate Osteoarthritis Knee Pain	Included
NCT02447276 2015-05/2016-11	Study of REGN475 in Patients With Pain Due to Osteoarthritis of the Knee or Hip	Included
NCT02528188 2015-07/2019-02	Long Term Safety and Efficacy Study of Tanezumab in Subjects With Osteoarthritis of the Hip or Knee	Included
NCT02683239 2016-02/2021-06	Long-Term Safety and Efficacy Study of Fasinuramab in Patients With Pain Due to Osteoarthritis (OA) of the Knee or Hip	Included
NCT02709486 2016-03/2018-11	Study of the Analgesic Efficacy and Safety of Subcutaneous Tanezumab in Subjects With Osteoarthritis of the Hip or Knee.	Included
NCT03161093 2017-08/2021-08	A Study to Determine the Safety and the Efficacy of Fasinuramab Compared to Placebo and Naproxen for Treatment of Adults With Pain From Osteoarthritis of the Knee or Hip	Included
NCT03285646 2017-10/2019-05	Evaluate the Efficacy and Safety of Fasinuramab in Patients With Moderate-to-Severe Chronic Low Back Pain and Osteoarthritis of the Hip or Knee	Included
NCT03304379 2017-10/2020-11	Study to Determine the Safety and the Efficacy of Fasunumab Compared to Placebo and Nonsteroidal Anti-inflammatory Drugs (NSAIDs) for Treatment of Adults With Pain From Osteoarthritis of the Knee or Hip	Included
NCT03956550 2019-05/2020-10	A Study to Examine the Efficacy and Safety of REGN5069 in Patients With Pain Due to Osteoarthritis of the Knee	Included
NCT00809354 2009-02/2011-01	Long-Term Analgesic Efficacy And Safety Of Tanezumab Alone Or In Combination With Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Versus NSAIDs Alone In Patients With Osteoarthritis Of The Knee Or Hip	No control/placebo comparison

Supplementary table 1

	NCT00864097 2009-08/2010-11	Analgesic Efficacy And Safety of Tanezumab Added On To Diclofenac SR In Patients With Osteoarthritis Of The Knee Or Hip	No control/placebo comparison
	NCT00994890 2009-11/2011-03	A Long Term Study of the Safety of Tanezumab When Administered By Subcutaneous Injections	No control/placebo comparison
	NCT02683785 2016-03/2017-11	A Study to Investigate the Efficacy and Safety of GSK3196165 in Inflammatory Hand Osteoarthritis	No relevant animal study identified
	NCT02674386 2016-08/2019-07	Long-term Observational Study of Subjects From Tanezumab Studies Who Undergo a Total Knee, Hip or Shoulder Replacement	No relevant animal study identified
	NCT03245008 2017-09/2021-03	Efficacy and Safety of MT-5547 in Patients With Osteoarthritis Accompanied by Moderate to Severe Pain	No relevant animal study identified
	NCT04456686 2020-07/2021-08	Chronic Pain Master Protocol (CPMP): A Study of LY3016859 in Participants With Osteoarthritis	No relevant animal study identified
	NCT04675034 2020-12/2023-08	A Study of the Efficacy and Safety of MEDI7352 in Participants With Painful Osteoarthritis of the Knee	No relevant animal study identified
Other small molecules	NCT00589979 2007-03/2008-10	Efficacy and Safety of the Lidoderm Patch Applied to Patients With Osteoarthritis of the Knee	Included
	NCT00589979 2008-06/2008-10	Efficacy and Safety of the Lidoderm Patch Applied to Patients With Osteoarthritis of the Knee	Included
	NCT01091116 2010-03/2011-03	A Locally Injected Bradykinin Antagonist for Treatment of Osteoarthritis	Included
	NCT02205814 2014-04/2015-01	Fasitibant Intra-articular Injection in Patients With Symptomatic Osteoarthritis of the Knee	Included
	NCT02536833 2015-09/2017-04	A Study Evaluating the Safety, Tolerability, and Efficacy of SM04690 Injected in the Target Knee Joint of Moderately to Severely Symptomatic Osteoarthritis Subjects	Included
	NCT02951026 2016-09	Evaluation of Safety and Efficacy of a Single Lorecivivint Injection in Patients with Knee Osteoarthritis: A Multicenter, Observational Extension Trial	Included
	NCT03122860	A Study Evaluating the Safety and Efficacy of SM04690 for the Treatment of Moderately to Severely Symptomatic Knee Osteoarthritis	Included

Supplementary table 1

2017-04/2018-04		
NCT03928184 2019-05/2021-08	Patient-Reported and Radiographic Outcomes in Evaluating Lorecivint (SM04690) for the Treatment of Knee Osteoarthritis (STRIDES-Xray)	Included
NCT04129944 2019-10/2020-08	A Study to Assess the Safety and Efficacy of a Single Dose of UBX0101 in Patients With Osteoarthritis of the Knee	Included
NCT04385303 2020-05/2021-09	Patient-Reported Outcomes in Evaluating Lorecivint (SM04690) for Moderate to Severe Knee Osteoarthritis (STRIDES-1)	Included
NCT00041756 2002-07/2004-02	Efficacy and Safety of PG-530742 in the Treatment of Mild to Moderate Knee Osteoarthritis	No relevant animal study identified
NCT00486434 2007-05/2010-09	Efficacy and Safety of Oral Salmon Calcitonin in Patients With Knee Osteoarthritis	No relevant animal study identified
NCT00704847 2008-06/2011-06	Efficacy and Safety of Oral Salmon Calcitonin in Patients With Knee Osteoarthritis (OA 2 Study)	No relevant animal study identified
NCT00790790 2008-11/2010-01	A Study in the Treatment of Osteoarthritis Knee Pain	No relevant animal study identified
NCT01319929 2011-03/2011-09	A Study of LY2828360 in Patients With Osteoarthritic Knee Pain	No relevant animal study identified
NCT01554579 2012-03/2013-11	A Four-Week Multicenter Study Evaluating the Safety and Efficacy of Gefapixant (AF-219/MK-7264) in Subjects With Osteoarthritis of the Knee	No data analysis reported
NCT01654302 2013-09/2015-02	Efficacy and Safety of Synera in Osteoarthritis Pain	No data analysis reported
NCT02068599 2014-04/2015-05	A Study to Evaluate the Safety and Efficacy of Topically Applied TV-45070 (Ointment) in Participants With Primary Osteoarthritis (OA) Affecting a Single Knee	No relevant animal study identified
NCT02705625 2016-01/2017-05	A Study to Evaluate the Efficacy, Safety and Tolerability of MIV-711 in Osteoarthritis Patients	No relevant animal study identified
NCT03028870 2017-03/2017-11	A Study to Evaluate the Analgesic Efficacy and Safety of V120083 in Subjects With Osteoarthritis (OA) of the Knee	No data analysis reported

Supplementary table 1

	NCT04627038 2020-11/2021-10	Chronic Pain Master Protocol (CPMP): A Study of LY3556050 in Participants With Osteoarthritis	No relevant animal study identified
	NCT04506463 2020-12/2022-08	Efficacy and Safety of MM-II for Treatment of Knee Pain in Subjects With Symptomatic Knee Osteoarthritis	No relevant animal study identified
	NCT05008835 2021-07/2022-11	Evaluate the Efficacy and Safety of ACP-044 in Subjects With Pain Associated With Osteoarthritis of the Knee	No data analysis reported
	NCT05080660 2021-10/2022-06	Chronic Pain Master Protocol (CPMP): A Study of LY3526318 in Participants With Osteoarthritis	No relevant animal study identified
	NCT05139030 2022-01/2022-07	Phase 3 Adductor Canal Block With EXPAREL in Subjects Undergoing Primary Unilateral Total Knee Arthroplasty	No control/placebo comparison
	NCT05620563 2022-11/2023-06	A Chronic Pain Master Protocol (CPMP): A Study of LY3857210 In Participants With Osteoarthritis Pain	No relevant animal study identified

Supplementary Table 2. **Participant characteristics in the selected clinical trials.** Data include the ClinicalTrials.gov identifier (NCT number), number of participants, age, percentage of female participants, body mass index (BMI), baseline pain level, and duration of pain symptoms. BMI and pain measures were extracted from study reports or inclusion criteria when available. *NA* indicates information not available. Abbreviations: VAS, Visual Analog Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; ACR, American College of Rheumatology; NRS, Numeric Rating Scale; BPI, Brief Pain Inventory; PGADS, Patient Global Assessment of Disease Status.

	NCT ID / Number of participants	Age (mean±SD)	Female (%)	BMI (mean±SD)	Pain at baseline	Pain duration
NSAID	NCT00092768 417	62±10	66	NA	WOMAC pain: 67±16	>6 months
	NCT00092781 419	62±9	65	NA	WOMAC pain: 67±16	>6 months
	NCT01461369 305	62±9	67	31.2±5.16	WOMAC: 72±16	NA
	NCT01554163 239	62±9	90	NA	[VAS pain score >800 mm (range: 0-100 mm)]	>6 months
	NCT01787188 402	61±9	66	30.9±5.01	WOMAC (range: 0-96): 69±16	NA
	NCT01980940 70	61±8	69	NA	NA	>6 months
	NCT02311881 770	61±8	63	NA	Moderate to moderately-severe self-reported pain	>3 months

	NCT03209362 80	60±8	51	30.63±4.44	NA	NA
	NCT05007808 210	65±8	60	NA	NRS (range: 0-10) : 7.6±1.35	>6 months
	NCT00664560 614	62±8	64	NA	[ACR functional class rating of I, II or III]	>6 months
	NCT00665431 610	62±8	64	NA	[ACR functional class rating of I, II or III]	>6 months
	NCT01147458 190	60±8	58	[≤39 kg/m ²]	WOMAC Pain (range:0-20): 11.17 ± 2.67	NA
	NCT01119898 259	61±8	67	NA	Pain intensity when walking on a flat surface Moderate-sever pain	NA
	NCT01341405 125	61±8	90	NA	[WOMAC pain (range: 0-10): 4-8]	>3 months
	NCT01765296 362	62±8	85	NA	[WOMAC pain (range: 0-10): 4-8]	>3 months
	NCT01799213 490	58±11	11	NA	WOMAC pain (range: 0-20): 5.6±3.8	>3 months
	NCT01967550 304	65±7	65	NA	NA	>6 months
	NCT02067611	NA	NA	[18.5-39.9 kg/m ²]	[VAS (range: 0-100 mm): 40-90 mm]	>6 months

	216					
	NCT02121002 1175	NA	64	NA	[VAS (range: 0-100 mm)≥ 20 mm]	NA
	NCT02311881 770	61±8	63	NA	[Moderate to moderately-severe self-reported pain]	>3 months
	NCT02913521 786	57±11	74	NA	[WOMAC pain (range: 0-20): 9]	>6 months
	NCT02596451 1143	56±11	64	NA	[WOMAC pain (range: 0-20): 9]	>6 months
	NCT03172780 1220	53±10	69	NA	WOMAC pain (range: 0-20): 12.4±2.12	NA
	NCT03277066 283	58±9	26	[≤40 kg/m ²]	NA	>6 months
	NCT03691844 44	NA	67	[≤45 kg/m ²]	NRS (range: 0-50) : 27.5 ±5.41	>3 weeks
Corticosteroid	NCT02116972 310	59±8	57	[≤40 kg/m ²]	NA	>6 months
	NCT02357459 486	62±10	61	[≤40 kg/m ²]	NA	>6 months
	NCT00521989 279	59±9	63	NA	[WOMAC pain (range: 0-100): 30-80 mm]	>6 months

	NCT01487161 228	62	53	[≤40 kg/m ²]	[NRS (range: 0-10): 5-9]	NA
	NCT02468583 6	42	20	NA	NA	NA
	NCT02688400 380	64±7	75	NA	[VAS while walking on a flat surface (range: 0-100 mm) ≥ 40 mm]	NA
	NCT03005873 75	64±9	50	NA	VAS (range: 0-10): 6.62 ± 1.14	>6 months
	NCT03191903 57	58±9	68	[≤40 kg/m ²]	WOMAC pain (range: 0-100 mm): 63.4±11.2	>6 months
	NCT03390036 52	58±9	69	NA	WOMAC pain (range: 0-100 mm): 63.7 +/- 11.2	NA
	NCT03793010 68	61±9	60	30.91±5.70	[WOMAC pain (range:0-10)]	>3 months
	NCT04160091 10	61±11	20	29.45±2.80	[NRS (range: 0-10)≥3]	>1 month
	NCT04123561 50	61±9	59	31.35±4.83	[NRS (range: 0-10)≥4]	NA
	NCT04231318 23	59±9	61	[≤40 kg/m ²]	[WOMAC pain (range: 0-100 mm): 50-90 mm]	>6 months

Supplementary table 2

	NCT04120402 318	64±9	58	[≤40 kg/m ²]	NA	>6 months
Opioid	NCT00950651 860	61±9	83	[≤35 kg/m ²]	[WOMAC pain subscale (range: 0-500)≥ 150 mm]	>3 months
	NCT00832416 565	60±9	60	[≤38 kg/m ²]	[WOMAC pain subscale (range: 0-500)≥ 150 mm]	NA
	NCT00852917 552	61±9	62	[≤38 kg/m ²]	[WOMAC pain subscale (range: 0-500)≥ 150 mm]	NA
	NCT00833794 646	62±9	63	[≤37 kg/m ²]	[NRS (range: 0-10)≥4]	NA
	NCT00421928 1023	58±10	60	NA	[Pain intensity the last 3 days (range: 0-11) ≥ 5]	>3 months
	NCT00486811 987	62±9	72	NA	[Pain intensity the last 3 days (range: 0-11) ≥ 5]	>3 months
	NCT00487435 1154	54±11	58	NA	NA	NA
	NCT00531427 567	59±10	63	NA	NA	>12 months
	NCT00983073 224	67±11	68	NA	NA	>3 months

	NCT01124604 91	65±15	68	NA	[Pain intensity the last 3 days (range: 0-11) ≥ 5]	>3 months
	NCT01755546 224	52±12	56	32.10±7.20	Moderate to severe pain	>3 months
	NCT00313846 326	61±10	57	NA	Moderate to severe pain	>12 months
	NCT00312221 418	58±10	74	NA	NA	>12 months
	NCT00420992 547	54±12	58	NA	NA	>3 months
	NCT00980798 288	65±10	72	NA	[BPI (range: 0-10) ≥ 5]	>3 months
	NCT00631319 343	56±10	54	NA	NA	>6 months
	NCT00736853 321	57±18	61	NA	NA	>3 months
	NCT01008618 218	67±13	67	NA	[VAS≥50 mm]	>3 months
	NCT00982280 63	65±10	59	NA	[NRS (range: 0-10)≥ 5]	>3 months

	NCT00979953 408	57±8	59	NA	[NRS (range: 0-10)≥ 4]	>6 months
	NCT01240863 294	53±11	60	32.90±7.74	[NRS (range: 0-10)≥ 5]	>3 months
	NCT01298765 302	56±13	61	32.23±6.85	NRS (range: 0-10): 3.3 ±1.94	>3 months
	NCT01451385 376	52±14	59	NA	NRS (range: 0-10): 6.7±1.64	>3 months
	NCT01619839 213	60±10	60	[18-39 kg/m ²]	NA	NA
	NCT02944448 761	61±10	63	[≤40 kg/m ²]	[NRS(range: 0-10)≥ 5]	NA
	NCT03008590 23	63±10	17	34±7.3	BPI (range:0-10): 5.9±1.2	NA
Anticonvulsants and antidepressants	NCT00408421 231	62±9	65	[≤40 kg/m ²]	BPI (range:0-10): 6.20±1.56	Pain onset: 9.17±8.47 years
	NCT00433290 256	63±9	77	29.55±4.58	BPI (range:0-10): 6.11±1.33	Pain onset: 7.44±7.15 years
	NCT00485472 149	62±7	75	NA	NA	>6 months
	NCT00945945	64±10	68	[≤40 kg/m ²]	[BPI (range: 0-10) ≥ 4]	>3 months

	424					
	NCT01931475 407	61±8	76	[≤40 kg/m ²]	[BPI (range: 0-10) ≥ 4]	>3 months
	NCT02248480 353	66±8	78	NA	[BPI (range: 0-10) ≥ 4]	>3 months
	NCT02335346 93	66±8	72	NA	[BPI (range: 0-10) ≥ 4]	>3 months
	NCT01018680 524	61±9	57	[≤40 kg/m ²]	BPI (range: 0-10): 6.16±1.54	>3 months Pain onset: 9.49±8.90 years
TRPV1 modulator	NCT03429049 325	62±9	63	31.77±5.73	WOMAC pain (range: 0-50): 31.45±7.79	>6 months
	NCT03528369 122	60	63	NA	WOMAC pain (range: 0-500): 351.5 (254 to 490)	>3 months
	NCT03660943 324	63±9	61	32.38±5.62	WOMAC (range: 0-96): 31.5±7.28	>6 months
	NCT00878501 241	62	69	NA	NA	NA
Biological therapies	NCT00399490 287	59±8	61	NA	NA	NA
	NCT00669409 83	NA	69	NA	NA	NA

	NCT00733902 690	62±10	61	[≤39 kg/m ²]	NA	NA
	NCT00744471 621	NA	62	[≤39 kg/m ²]	NA	NA
	NCT00830063 828	61±10	60	[≤39 kg/m ²]	NA	NA
	NCT00863304 849	NA	64	NA	NA	NA
	NCT00985621 614	57±10	63	[≤39 kg/m ²]	NA	NA
	NCT02192190 268	58±9	62	NA	NA	NA
	NCT02447276 342	61±8	65	31.12±4.9	[WOMAC pain >4]	NA
	NCT02528188 3021	61±9	65	NA	[WOMAC pain (range: 0-20): ≥5]	NA
	NCT02683239 5331	64±9	73	NA	[WOMAC pain (range: 0-20): ≥4]	>3 months
	NCT02709486 849	65±8	69	NA	[WOMAC pain (range: 0-20): ≥5]	NA
	NCT03161093	62.9 (8.85)	5	NA	[Moderate to severe pain]	>3 months

	3307					
	NCT03285646 63	59±10	62	NA	NRS (range: 0-10): 6.73±1.40	NA
	NCT03304379 1650	62±9	70	NA	WOMAC pain (range: 0-20): 6.42±1.34	>3 months
	NCT03956550 259	64±9	80	[≤39 kg/m ²]	WOMAC pain (range: 0-20): 6.36±1.18	NA
	NCT00809354 2700	NA	71	[≤39 kg/m ²]	NA	NA
	NCT00864097 607	NA	78	[≤39 kg/m ²]	NA	NA
	NCT00994890 679	NA	69	[≤39 kg/m ²]	NA	NA
	NCT02683785 44	59±7	91	NA	[NRS (range: 0-10)≥ 5]	NA
	NCT02674386 150	65±8	59	NA	NA	NA
	NCT03245008 62	67±9	79	26.8±4.3	WOMAC pain (range: 0-20): 6.02 ± 1.35	NA
	NCT04456686 117	63±9	77	[≤39 kg/m ²]	NRS (range: 0-10): 5.61 ±1.52	>3 months

	NCT04675034 345	64±9	67	NA	NA	NA
Other small molecules	NCT00589979 93	61±10	65	[≤40 kg/m ²]	NA	NA
	NCT01091116 423	66±9	60	NA	WOMAC pain (range: 0-500 mm): 286±74	6 months Pain onset: 8 years
	NCT02205814 431	64±8	61	26.9±2.50	WOMAC pain (range: 0-500 mm): 280.8±39.61	NA
	NCT02536833 455	60±9	59	[≤40 kg/m ²]	[VAS (range: 0-100 mm): 30-80 mm]	>6 months
	NCT02951026 703	61±9	61	29.05±4.3	[WOMAC pain (range: 0-100) ≥ 60]	>6 months
	NCT03122860 694	59±9	58	28.97±4.01	NA	>6 months
	NCT03928184 501	60±8	66	[≤40 kg/m ²]	[NRS (range: 0-10)≥4] [WOMAC pain (range: 0-50 mm): 20-40]	
	NCT04129944 183	64	36	[≤40 kg/m ²]	[NRS (range: 0-10): 4-9]	NA
	NCT04385303 470	61±8	60	[≤35 kg/m ²]	NA	>6 months
	NCT00041756	63±0.4	71	NA	NA	NA

	395					
	NCT00486434 1176	64±7	68	NA	NA	NA
	NCT00704847 1030	64±7	61	NA	NA	NA
	NCT00790790 147	59±7	69	[≤40 kg/m ²]	[Pain score (range: 0-10): 4-8]	>3 months
	NCT01319929 39	63±7	36	[19-35 kg/m ²]	[Pain score (range: 0-10): 4-8]	>3 months
	NCT01554579 171	NA	64	NA	[NRS (range: 0-10): 5-9]	NA
	NCT01654302 38	58±8	61	NA	Knee pain after exercise intervention (range: 1-10): 6.08±1.33	>1 months
	NCT02068599 38	60±9	59	28.17±3.11	NA	NA
	NCT02705625 240	62±7	77	NA	[NRS (range: 0-10): ≥4]	NA
	NCT03028870 291	60±9	63	NA	[NRS (range: 0-10): 4-9]	>6 months
	NCT04627038 202	63±9	57	[≤40 kg/m ²]	[VAS (range: 0-100 mm): 40-95 mm]	>3 months

	NCT04506463 369	NA	65	NA	NA	>6 months
	NCT05008835 61	57±5	67	[≤39 kg/m ²]	NRS (range: 0-10): 5.7±1.55	NA
	NCT05080660 160	64±9	63	[≤40 kg/m ²]	NRS (range: 0-10): 5.65±1.50	>3 months
	NCT05139030 166	62±8	49	32.07±4.90	NRS (range: 0-10): 5.2±2.27	NA
	NCT05620563 147	63±9	87	[≤40 kg/m ²]	NRS (range: 0-10): 5.57±1.64	>3 months