**1 - Search strategy**

*Search terms*

'Sjogren' OR 'systemic sclerosis' OR 'crest' OR 'scleroderma' OR 'lupus' OR 'dermatomyositis' OR 'polymyositis' OR 'myositis' OR 'connective tissue disease' OR ‘undifferentiated connective tissue disease' OR ‘antiphospholipid’

*Filters*

Type of study: interventional.

Phase: phase 2/3 OR phase 3 OR phase 4.

Status: suspended OR terminated OR completed OR withdrawn OR unknown.

First posted: from 01/01/1990 to 01/01/2021.

Starting date: since 01/01/2000 to 31/12/2016

**Supplementary Figure 1.** Flow-chart of study selection. Values are the number of trials.

**Trials identified by ClinicalTrials.gov predefined search, 1191**

**Records excluded, 1016**

* Not on connective tissue diseases, 950
* Non-randomized trials, 56
* Start date before 2000, 10

**Studies checked for publication status, 175**

**Records excluded, 1016**

* Unpublished 82
* Completion date after 1st January 2017 24
* Publication time > 5 years 7

**Trials published in a peer-review journal and included in the study**, **62**

**Table S1**: list of all included published trials in the analysis, with their respective trial registration number, pubmed index and doi if available.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Trial registration number | pubmed | doi | Journal title | title |
| NCT00740948 | 24727841 | 10.7326/M13-1085 | Annals of internal medicine | Treatment of primary Sjogren syndrome with rituximab: a randomized trial. |
| NCT02050360 | 30383134 | 10.7326/M18-0517 | Annals of internal medicine | On-Demand Sildenafil as a Treatment for Raynaud Phenomenon: A Series of n-of-1 Trials. |
| NCT00266669 | 23268365 | 10.1136/annrheumdis-2012-201536 | Annals of the rheumatic diseases | A multi-centre, blinded, randomised, placebo-controlled, laboratory-based study of MQX-503, a novel topical gel formulation of nitroglycerine, in patients with Raynaud phenomenon. |
| NCT00413361 | 23144449 | 10.1136/annrheumdis-2012-202322 | Annals of the rheumatic diseases | Hydroxychloroquine in systemic lupus erythematosus: results of a French multicentre controlled trial (PLUS Study). |
| NCT00624338 | 24951103 | 10.1136/annrheumdis-2013-205067 | Annals of the rheumatic diseases | Efficacy and safety of atacicept for prevention of flares in patients with moderate-to-severe systemic lupus erythematosus (SLE): 52-week data (APRIL-SLE randomised trial). |
| NCT00371319 | 25550339 | 10.1136/annrheumdis-2014-206456 | Annals of the rheumatic diseases | Tacrolimus versus mycophenolate mofetil for induction therapy of lupus nephritis: a randomised controlled trial and long-term follow-up. |
| NCT01295736 | 25995322 | 10.1136/annrheumdis-2014-207001 | Annals of the rheumatic diseases | Efficacy of sildenafil on ischaemic digital ulcer healing in systemic sclerosis: the placebo-controlled SEDUCE study. |
| NCT01196091 | 26338095 | 10.1136/annrheumdis-2015-207653 | Annals of the rheumatic diseases | Efficacy and safety of subcutaneous tabalumab in patients with systemic lupus erythematosus: results from ILLUMINATE-1, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. |
| NCT01205438 | 26293163 | 10.1136/annrheumdis-2015-207654 | Annals of the rheumatic diseases | Efficacy and safety of subcutaneous tabalumab, a monoclonal antibody to B-cell activating factor, in patients with systemic lupus erythematosus: results from ILLUMINATE-2, a 52-week, phase III, multicentre, randomised, double-blind, placebo-controlled study. |
| NCT01112215 | 28450313 | 10.1136/annrheumdis-2016-210882 | Annals of the rheumatic diseases | Enteric-coated mycophenolate sodium versus azathioprine in patients with active systemic lupus erythematosus: a randomised clinical trial. |
| NCT01345253 | 29295825 | 10.1136/annrheumdis-2017-211631 | Annals of the rheumatic diseases | A pivotal phase III, randomised, placebo-controlled study of belimumab in patients with systemic lupus erythematosus located in China, Japan and South Korea. |
| NCT01395745 | 29563108 | 10.1136/annrheumdis-2018-213032 | Annals of the rheumatic diseases | Phase III trial results with blisibimod, a selective inhibitor of B-cell activating factor, in subjects with systemic lupus erythematosus (SLE): results from a randomised, double-blind, placebo-controlled trial. |
| NCT00189124 | 19854713 | 10.1136/ard.2009.117036 | Annals of the rheumatic diseases | Effects of dehydroepiandrosterone on fatigue and well-being in women with quiescent systemic lupus erythematosus: a randomised controlled trial. |
| NCT00543166 | 20191499 | 10.1002/acr.20022 | Arthritis care & research | Dehydroepiandrosterone (DHEA) substitution treatment for severe fatigue in DHEA-deficient patients with primary Sjögren's syndrome. |
| NCT00498615 | 22275160 | 10.1002/acr.21622 | Arthritis care & research | Efficacy of Rho kinase inhibitor fasudil in secondary Raynaud's phenomenon. |
| NCT00371501 | 21309005 | 10.1002/acr.20440 | Arthritis care & research | Effects of rosuvastatin on vascular biomarkers and carotid atherosclerosis in lupus: a randomized, double-blind, placebo-controlled trial. |
| NCT00668330 | 20964867 | 10.1186/ar3170 | Arthritis research & therapy | Ibandronate increases cortical bone density in patients with systemic lupus erythematosus on long-term glucocorticoid. |
| NCT00626197 | 23740801 | 10.1002/art.38037 | Arthritis and rheumatism | Efficacy and safety of ocrelizumab in active proliferative lupus nephritis: results from a randomized, double-blind, phase III study. |
| NCT00410384 | 22127708 | 10.1002/art.30613 | Arthritis and rheumatism | A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. |
| NCT00282347 | 22231479 | 10.1002/art.34359 | Arthritis and rheumatism | Efficacy and safety of rituximab in patients with active proliferative lupus nephritis: the Lupus Nephritis Assessment with Rituximab study. |
| NCT00065806 | 22031171 | 10.1002/art.30645 | Arthritis and rheumatism | Use of atorvastatin in systemic lupus erythematosus in children and adolescents. |
| NCT00070590 | 20506355 | 10.1002/art.27466 | Arthritis and rheumatism | Randomized, prospective, placebo-controlled trial of bosentan in interstitial lung disease secondary to systemic sclerosis. |
| NCT00137969 | 20039413 | 10.1002/art.27233 | Arthritis and rheumatism | Efficacy and safety of rituximab in moderately-to-severely active systemic lupus erythematosus: the randomized, double-blind, phase II/III systemic lupus erythematosus evaluation of rituximab trial. |
| NCT00430677 | 24504810 | 10.1002/art.38260 | Arthritis & rheumatology (Hoboken, N.J.) | Efficacy and safety of abatacept in lupus nephritis: a twelve-month, randomized, double-blind study. |
| NCT01408576 | 27598855 | 10.1002/art.39856 | Arthritis & rheumatology (Hoboken, N.J.) | Efficacy and Safety of Epratuzumab in Moderately to Severely Active Systemic Lupus Erythematosus: Results From Two Phase III Randomized, Double-Blind, Placebo-Controlled Trials. |
| NCT01262365 | 27598855 | 10.1002/art.39856 | Arthritis & rheumatology (Hoboken, N.J.) | Efficacy and Safety of Epratuzumab in Moderately to Severely Active Systemic Lupus Erythematosus: Results From Two Phase III Randomized, Double-Blind, Placebo-Controlled Trials. |
| NCT01261793 | 27598855 | 10.1002/art.39856 | Arthritis & rheumatology (Hoboken, N.J.) | Efficacy and Safety of Epratuzumab in Moderately to Severely Active Systemic Lupus Erythematosus: Results From Two Phase III Randomized, Double-Blind, Placebo-Controlled Trials. |
| NCT01551069 | 27992698 | 10.1002/art.40018 | Arthritis & rheumatology (Hoboken, N.J.) | Effects of Hydroxychloroquine in Patients With Cutaneous Lupus Erythematosus: A Multicenter, Double-Blind, Randomized, Parallel-Group Trial. |
| NCT01484496 | 28118533 | 10.1002/art.40049 | Arthritis & rheumatology (Hoboken, N.J.) | Efficacy and Safety of Subcutaneous Belimumab in Systemic Lupus Erythematosus: A Fifty-Two-Week Randomized, Double-Blind, Placebo-Controlled Study. |
| NCT02165111 | 28426903 | 10.1002/art.40123 | Arthritis & rheumatology (Hoboken, N.J.) | The Therapeutic Efficacy of Botulinum Toxin in Treating Scleroderma-Associated Raynaud's Phenomenon: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. |
| NCT02257957 | 29970389 | 10.1136/bjophthalmol-2018-312072 | The British journal of ophthalmology | Randomised, prospective clinical trial of platelet-rich plasma injection in the management of severe dry eye. |
| NCT01347008 | 28281457 |  | Clinical and experimental rheumatology | Evaluation of the effect of sildenafil on the microvascular blood flow in patients with systemic sclerosis: a randomised, double-blind, placebo-controlled study. |
| NCT00348296 | 23910617 |  | Clinical and experimental rheumatology | A randomized, double-blind, placebo-controlled trial: intravenous immunoglobulin treatment in patients with diffuse cutaneous systemic sclerosis. |
| NCT01850979 | 25956572 | 10.1016/j.clae.2015.04.004 | Contact lens & anterior eye : the journal of the British Contact Lens Association | Treatment of Sjögren's syndrome dry eye using 0.03% tacrolimus eye drop: Prospective double-blind randomized study. |
| NCT00080457 | 16697324 | 10.1016/j.jacc.2006.01.057 | Journal of the American College of Cardiology | Treatment of pulmonary arterial hypertension with the selective endothelin-A receptor antagonist sitaxsentan. |
| NCT01601028 | 27366013 | 10.3346/jkms.2016.31.7.1127 | Journal of Korean medical science | Effect of Hydroxychloroquine Treatment on Dry Eyes in Subjects with Primary SjÃƒÂ¶gren's Syndrome: a Double-Blind Randomized Control Study. |
| NCT00632866 | 25027140 | 10.1001/jama.2014.7682 | JAMA | Effects of hydroxychloroquine on symptomatic improvement in primary SjÃƒÂ¶gren syndrome: the JOQUER randomized clinical trial. |
| NCT01474122 | 27163986 | 10.1001/jama.2016.5258 | JAMA | Effect of Macitentan on the Development of New Ischemic Digital Ulcers in Patients With Systemic Sclerosis: DUAL-1 and DUAL-2 Randomized Clinical Trials. |
| NCT01474109 | 27163986 | 10.1001/jama.2016.5258 | JAMA | Effect of Macitentan on the Development of New Ischemic Digital Ulcers in Patients With Systemic Sclerosis: DUAL-1 and DUAL-2 Randomized Clinical Trials. |
| NCT00424476 | 21296403 | 10.1016/S0140-6736(10)61354-2 | Lancet (London, England) | Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. |
| NCT01532869 | 27156934 | 10.1016/S0140-6736(16)00232-4 | Lancet (London, England) | Safety and efficacy of subcutaneous tocilizumab in adults with systemic sclerosis (faSScinate): a phase 2, randomised, controlled trial. |
| NCT00323960 | 26645190 | 10.1016/S0140-6736(15)01021-1 | Lancet (London, England) | Prednisone versus prednisone plus ciclosporin versus prednisone plus methotrexate in new-onset juvenile dermatomyositis: a randomised trial. |
| NCT01925209 | 31397289 | 10.1016/S1474-4422(19)30200-5 | The Lancet. Neurology | Safety and efficacy of intravenous bimagrumab in inclusion body myositis (RESILIENT): a randomised, double-blind, placebo-controlled phase 2b trial. |
| NCT00573157 | 20511279 |  | Lupus | Abstracts of the 9th International Congress on SLE. June 24-27 2010. Vancouver, Canada. |
| NCT01322308 | 21993383 | 10.1177/0961203311422096 | Lupus | Pioglitazone improves the cardiovascular profile in patients with uncomplicated systemic lupus erythematosus: a double-blind randomized clinical trial. |
| NCT01597492 | 28467293 | 10.1177/0961203317703495 | Lupus | A randomized, open-label study to investigate the effect of belimumab on pneumococcal vaccination in patients with active, autoantibody-positive systemic lupus erythematosus. |
| NCT01015456 | 26835147 | 10.1136/lupus-2015-000120 | Lupus science & medicine | A multicentre, randomised controlled study of enteric-coated mycophenolate sodium for the treatment of relapsed or resistant proliferative lupus nephritis: an Asian experience. |
| NCT00429377 | 19688181 | 10.1007/s10165-009-0218-5 | Modern rheumatology | Efficacy and safety of tacrolimus for lupus nephritis: a placebo-controlled double-blind multicenter study. |
| NCT00335985 | 21971943 | 10.1007/s10165-011-0534-4 | Modern rheumatology | Effects of intravenous immunoglobulin therapy in Japanese patients with polymyositis and dermatomyositis resistant to corticosteroids: a randomized double-blind placebo-controlled trial. |
| NCT00377637 | 22087680 | 10.1056/NEJMoa1014460 | The New England journal of medicine | Mycophenolate versus azathioprine as maintenance therapy for lupus nephritis. |
| NCT00138983 | 16914703 | 10.1056/NEJMoa053569 | The New England journal of medicine | Alendronate or alfacalcidol in glucocorticoid-induced osteoporosis. |
| NCT00082511 | 16914703 | 10.1056/NEJMoa053569 | The New England journal of medicine | Alendronate or alfacalcidol in glucocorticoid-induced osteoporosis. |
| NCT00114530 | 29298160 | 10.1056/nejmoa1703327 | The New England journal of medicine | Myeloablative Autologous Stem-Cell Transplantation for Severe Scleroderma. |
| NCT00404794 | 22295934 | 10.1111/j.1440-1797.2012.01574.x | Nephrology (Carlton, Vic.) | Pilot 24 month study to compare mycophenolate mofetil and tacrolimus in the treatment of membranous lupus nephritis with nephrotic syndrome. |
| NCT02049112 | 25617119 | 10.1016/j.oooo.2014.12.005 | Oral surgery, oral medicine, oral pathology and oral radiology | Efficacy and safety of a new oral saliva equivalent in the management of xerostomia: a national, multicenter, randomized study. |
| NCT00740285 | 21299861 | 10.1186/1750-1172-6-5 | Orphanet journal of rare diseases | Lidocaine for systemic sclerosis: a double-blind randomized clinical trial. |
| NCT00828178 | 23817872 | 10.1007/s00296-013-2811-3 | Rheumatology international | Omega-3 in SLE: a double-blind, placebo-controlled randomized clinical trial of endothelial dysfunction and disease activity in systemic lupus erythematosus. |
| NCT02645565 | 29450636 | 10.1007/s00296-018-3995-3 | Rheumatology international | Comparing the efficacy of low-dose vs high-dose cyclophosphamide regimen as induction therapy in the treatment of proliferative lupus nephritis: a single center study. |
| NCT00626665 | 20837499 | 10.1093/rheumatology/keq291 | Rheumatology (Oxford, England) | Efficacy of tadalafil in secondary Raynaud's phenomenon resistant to vasodilator therapy: a double-blind randomized cross-over trial. |
| NCT01878526 | 27179107 | 10.1093/rheumatology/kew216 | Rheumatology (Oxford, England) | Effectiveness of add-on therapy with domperidone vs alginic acid in proton pump inhibitor partial response gastro-oesophageal reflux disease in systemic sclerosis: randomized placebo-controlled trial. |
| NCT02302352 | 31056685 | 10.1093/rheumatology/kez160 | Rheumatology (Oxford, England) | Effect of probiotics on gastrointestinal symptoms and immune parameters in systemic sclerosis: a randomized placebo-controlled trial. |
| NCT00611663 | 28784280 | 10.1016/j.vaccine.2017.07.094 | Vaccine | Pneumococcal vaccination in patients with systemic lupus erythematosus: A multicenter placebo-controlled randomized double-blind study. |