

Supplementary table S1 | **Broad Spectrum of Diseases Responsive to Anakinra**

<u>Disease Condition</u>	<u>References</u>
Joint, Bone and Muscle Diseases	
rheumatoid arthritis	1-21
psoriatic arthritis	22,23
osteoarthritis	24,25
erosive osteoarthritis of the hand	26
arthrofibrosis/traumatic knee injury	27,28
anterior cruciate knee ligament tear	29
relapsing polychondritis	30-32
recurrent multifocal osteomyelitis	33,34
Majeed Syndrome	35
ankylosing spondylitis	36-38
gout of the lumbar spine	39
antisynthetase syndrome	40
idiopathic inflammatory myopathies ^a	41
articular chondrocalcinosis	42
Hereditary Systemic Autoinflammatory Diseases	
familial Mediterranean fever (FMF)	43-52
CAPS (FCAS, Muckle-Wells Syndrome, NOMID/CINCA)	53-67
Male hypoinfertility in CAPS	68
NLRP12 Autoinflammatory Syndrome	69
TRAPS ^a	70-75
HIDS/ mevalonate kinase deficiency	74,76-82
PAPA	83-87
DIRA	88,89
Blau syndrome/granulomatous arthritis	90
Systemic and Local Inflammatory Diseases	
Schnitzler	91-101
Behçet	52
secondary amyloidosis	48,51,52,61,100,102-106
Henoch-Schonlein purpura	107
recurrent idiopathic pericarditis	61,75,108,109
Systemic-onset Juvenile Idiopathic Arthritis	65,66,104,110-115
Glomerulonephritis in SJIA	116
Adult Onset Still Disease	117-135
Macrophage Activation Syndrome	136-143
Sweet Syndrome/neutrophilic dermatoses	144,145
neutrophilic panniculitis	137,139,146
Erdheim-Chester/histiocytoses	147
Whipple Disease	148
SAPHO	34,149,150
PASH	83
PFAPA	151

Multicentric Castleman Disease	152
Jessner-Kanof Disease	153
Primary Sjogren Syndrome Fatigue	154
Common Diseases	
gout and pyrophosphate crystal arthritis	155-162
post-myocardial infarction cardiac remodeling	163
systolic heart failure	164
smoldering myeloma	165
cerebrovascular accident	166
post-stroke immune suppression	167
hidradenitis suppurativa	83,168,169
type 2 diabetes	170,171
type 1 diabetes	172
metabolic syndrome	173
insulin resistance	174
dry eye syndrome	175
acrodermatitis (form of pustular psoriasis)	176

Footnotes

^aIncludes refractory myositis polymyositis, dermatomyositis and inclusion body myositis.

FMF, Familial Mediterranean Fever; FCAS, Familial Cold Autoinflammatory Syndrome; NLRP12, Nucleotide-binding domain and Leucine-rich Repeat Pyrin containing 12; NOMID, Neonatal Onset Multi-Inflammatory Diseases; TRAPS, TNF Receptor Associated Periodic Syndrome; HIDS, Hyper IgD Syndrome; PAPA, Pyogenic Arthritis, Pyoderma gangrenosum, and Acne; DIRA, Deficiency of IL-1Ra; SAPHO, Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis; PASH, Pyoderma-gangrenosum, Acne, and Suppurativa Hidradenitis; PFAPA, Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis

References

1. Abramson, S.B. & Amin, A. Blocking the effects of IL-1 in rheumatoid arthritis protects bone and cartilage. *Rheumatology (Oxford)* **41**, 972-80 (2002).
2. Bresnihan, B. & Cobby, M. Clinical and radiological effects of anakinra in patients with rheumatoid arthritis. *Rheumatology (Oxford)* **42 Suppl 2**, ii22-8 (2003).
3. Bresnihan, B. et al. Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. *Arthritis Rheum* **41**, 2196-204 (1998).
4. Botsios, C. et al. Anakinra, a recombinant human IL-1 receptor antagonist, in clinical practice. Outcome in 60 patients with severe rheumatoid arthritis. *Reumatismo* **59**, 32-7 (2007).
5. Singh, J.A. et al. Biologics for rheumatoid arthritis: an overview of Cochrane reviews. *Sao Paulo Med J* **128**, 309-10 (2010).
6. Bao, J. et al. Secondary failure to treatment with recombinant human IL-1 receptor antagonist in Chinese patients with rheumatoid arthritis. *Clin Rheumatol* **30**, 697-701 (2011).

7. Bresnihan, B., Newmark, R.D., Robbins, S., McCabe, D.P. & Genant, H.K. Anakinra reduces the rate of joint destruction after 1 year of treatment in a randomized controlled cohort of patients with rheumatoid arthritis. *Arthritis Rheumat* **43 suppl 9**, S289 (2000).
8. Bresnihan, B., Newmark, R., Robbins, S. & Genant, H.K. Effects of anakinra monotherapy on joint damage in patients with rheumatoid arthritis. Extension of a 24-week randomized, placebo-controlled trial. *J Rheumatol* **31**, 1103-11 (2004).
9. Jiang, Y. et al. A multicenter, double-blind, dose-ranging, randomized, placebo- controlled study of recombinant human interleukin-1 receptor antagonist in patients with rheumatoid arthritis: radiologic progression and correlation of Genant and Larsen scores. *Arthritis Rheum* **43**, 1001-9. (2000).
10. Genant, H.K. et al. Treatment with anakinra reduces the rate of joint destruction and shows accelerated benefit in the secon 6 months of treatment for patients with rheumatoid arthritis. *Ann Rheumat Dis* **40 suppl 1**, 169 (abs) (2001).
11. Cunnane, G., Madigan, A., Murphy, E., FitzGerald, O. & Bresnihan, B. The effects of treatment with interleukin-1 receptor antagonist on the inflamed synovial membrane in rheumatoid arthritis. *Rheumatology (Oxford)* **40**, 62-9. (2001).
12. Devine, E.B., Alfonso-Cristancho, R. & Sullivan, S.D. Effectiveness of biologic therapies for rheumatoid arthritis: an indirect comparisons approach. *Pharmacotherapy* **31**, 39-51 (2011).
13. Wang, S.Y. et al. Circulating Dickkopf-1 is correlated with bone erosion and inflammation in rheumatoid arthritis. *J Rheumatol* **38**, 821-7 (2011).
14. Turkstra, E., Ng, S.K. & Scuffham, P.A. A mixed treatment comparison of the short-term efficacy of biologic disease modifying anti-rheumatic drugs in established rheumatoid arthritis. *Curr Med Res Opin* (2011).
15. Nixon, R., Bansback, N. & Brennan, A. The efficacy of inhibiting tumour necrosis factor alpha and interleukin 1 in patients with rheumatoid arthritis: a meta-analysis and adjusted indirect comparisons. *Rheumatology (Oxford)* **46**, 1140-7 (2007).
16. Cohen, S.B., Strand, V., Aguilar, D. & Ofman, J.J. Patient- versus physician-reported outcomes in rheumatoid arthritis patients treated with recombinant interleukin-1 receptor antagonist (anakinra) therapy. *Rheumatology (Oxford)* **43**, 704-11 (2004).
17. Cohen, S.B. The use of anakinra, an interleukin-1 receptor antagonist, in the treatment of rheumatoid arthritis. *Rheum Dis Clin North Am* **30**, 365-80 (2004).
18. Kavanaugh, A. Anakinra (interleukin-1 receptor antagonist) has positive effects on function and quality of life in patients with rheumatoid arthritis. *Adv Ther* **23**, 208-17 (2006).
19. Cohen, S.B., Woolley, J.M. & Chan, W. Interleukin 1 receptor antagonist anakinra improves functional status in patients with rheumatoid arthritis. *J Rheumatol* **30**, 225-31 (2003).
20. Cohen, S.B. et al. A multicentre, double blind, randomised, placebo controlled trial of anakinra (Kineret), a recombinant interleukin 1 receptor antagonist, in patients with rheumatoid arthritis treated with background methotrexate. *Ann Rheum Dis* **63**, 1062-8 (2004).

21. Fleischmann, R.M. et al. Anakinra, a recombinant human interleukin-1 receptor antagonist (r-metHuIL-1ra), in patients with rheumatoid arthritis: A large, international, multicenter, placebo-controlled trial. *Arthritis Rheum* **48**, 927-34 (2003).
22. Pontifex, E.K. et al. Change in CD3 positive T-cell expression in psoriatic arthritis synovium correlates with change in DAS28 and magnetic resonance imaging synovitis scores following initiation of biologic therapy - a single centre, open-label study. *Arthritis Res Ther* **13**, R7 (2011).
23. Jung, N. et al. An open-label pilot study of the efficacy and safety of anakinra in patients with psoriatic arthritis refractory to or intolerant of methotrexate (MTX). *Clin Rheumatol* **29**, 1169-73 (2011).
24. Chevalier, X. et al. Safety study of intraarticular injection of interleukin 1 receptor antagonist in patients with painful knee osteoarthritis: a multicenter study. *J Rheumatol* **32**, 1317-23 (2005).
25. Chevalier, X. et al. Intraarticular injection of anakinra in osteoarthritis of the knee: a multicenter, randomized, double-blind, placebo-controlled study. *Arthritis Rheum* **61**, 344-52 (2009).
26. Bacconnier, L., Jorgensen, C. & Fabre, S. Erosive osteoarthritis of the hand: clinical experience with anakinra. *Ann Rheum Dis* **68**, 1078-9 (2009).
27. Brown, C., Toth, A. & Magnussen, R. Clinical benefits of intra-articular anakinra for persistent knee effusion. *J Knee Surg* **24**, 61-5 (2011).
28. Brown, C.A., Toth, A.P. & Magnussen, B. Clinical benefits of intra-articular anakinra for arthrofibrosis. *Orthopedics* **33**, 877 (2011).
29. Kraus, V.B. et al. Effects of intraarticular IL1-Ra for acute anterior cruciate ligament knee injury: a randomized controlled pilot trial (NCT00332254). *Osteoarthritis Cartilage* (2012).
30. Chauffier, K., London, J., Beaudouin, C. & Fautrel, B. Indications of anakinra. *Presse Med* **38**, 799-807 (2009).
31. Buonomo, P.S. et al. Relapsing polychondritis: new therapeutic strategies with biological agents. *Rheumatol Int* **30**, 691-3 (2011).
32. Vounotrypidis, P., Sakellariou, G.T., Zisopoulos, D. & Berberidis, C. Refractory relapsing polychondritis: rapid and sustained response in the treatment with an IL-1 receptor antagonist (anakinra). *Rheumatology (Oxford)* **45**, 491-2 (2006).
33. Rech, J. et al. Adult-onset Still's disease and chronic recurrent multifocal osteomyelitis: a hitherto undescribed manifestation of autoinflammation. *Rheumatol Int* (2011).
34. Eleftheriou, D. et al. Biologic therapy in refractory chronic non-bacterial osteomyelitis of childhood. *Rheumatology (Oxford)* **49**, 1505-12 (2011).
35. Herlin, T. et al. Clinical evidence that Majeed syndrome is an IL-1 β mediated autoinflammatory disease. *Ann Rheum Dis* **in press**(2012).
36. Haibel, H., Rudwaleit, M., Listing, J. & Sieper, J. Open label trial of anakinra in active ankylosing spondylitis over 24 weeks. *Ann Rheum Dis* (2005).
37. Bennett, A.N. et al. Sustained response to anakinra in ankylosing spondylitis. *Rheumatology (Oxford)* **47**, 223-4 (2008).
38. Tan, A.L. et al. Efficacy of anakinra in active ankylosing spondylitis: a clinical and magnetic resonance imaging study. *Ann Rheum Dis* **63**, 1041-5 (2004).

39. Funck-Brentano, T. et al. First observation of the efficacy of IL-1ra to treat tophaceous gout of the lumbar spine. *Rheumatology (Oxford)* **50**, 622-4 (2011).
40. Furlan, A., Botsios, C., Ruffatti, A., Todesco, S. & Punzi, L. Antisynthetase syndrome with refractory polyarthritis and fever successfully treated with the IL-1 receptor antagonist, anakinra: A case report. *Joint Bone Spine* **75**, 366-7 (2008).
41. Dastmalchi, M. et al. Anakinra in patients with refractory idiopathic inflammatory myopathies. *Arthr Rheumat* (2009).
42. Couderc, M., Mathieu, S., Glace, B. & Soubrier, M. Efficacy of anakinra in articular chondrocalcinosis: report of three cases. *Joint Bone Spine* **79**, 330-1 (2012).
43. Alenazi, A., Al Sonbul, A., Al Jumaah, S., Al Mehadib, A. & Al-Mayouf, S.M. A retrospective review of autoinflammatory diseases in Saudi children at a rheumatology clinic. *Ann Saudi Med* **32**, 43-8 (2012).
44. Calligaris, L., Marchetti, F., Tommasini, A. & Ventura, A. The efficacy of anakinra in an adolescent with colchicine-resistant familial Mediterranean fever. *Eur J Pediatr* **167**, 695-6 (2008).
45. Chae, J.J. et al. The B30.2 domain of pyrin, the familial Mediterranean fever protein, interacts directly with caspase-1 to modulate IL-1beta production. *Proc Natl Acad Sci U S A* **103**, 9982-7 (2006).
46. Meinzer, U. et al. Interleukin-1 targeting drugs in familial Mediterranean fever: a case series and a review of the literature. *Semin Arthritis Rheum* **41**, 265-71 (2011).
47. Mitroulis, I., Papadopoulos, V.P., Konstantinidis, T. & Ritis, K. Anakinra suppresses familial Mediterranean fever crises in a colchicine-resistant patient. *Neth J Med* **66**, 489-91 (2008).
48. Moser, C. et al. Successful treatment of familial Mediterranean fever with anakinra and outcome after renal transplantation. *Nephrol Dial Transplant* **24**, 676-8 (2009).
49. Ozen, S., Bilginer, Y., Ayaz, N.A. & Calguneri, M. Anti-interleukin 1 treatment for patients with familial Mediterranean fever resistant to colchicine. *J Rheumatol* (2011).
50. Petropoulou, A.D., Robin, M., Socie, G. & Galicier, L. Transmission of familial Mediterranean fever mutation after bone marrow transplantation and successful treatment with anakinra. *Transplantation* **90**, 102-3 (2011).
51. Stankovic Stojanovic, K. et al. Dramatic beneficial effect of interleukin-1 inhibitor treatment in patients with familial Mediterranean fever complicated with amyloidosis and renal failure. *Nephrol Dial Transplant* (2011).
52. Bilginer, Y., Ayaz, N.A. & Ozen, S. Anti-IL-1 treatment for secondary amyloidosis in an adolescent with FMF and Behcet's disease. *Clin Rheumatol* **29**, 209-10 (2010).
53. Hoffman, H.M. et al. Prevention of cold-associated acute inflammation in familial cold autoinflammatory syndrome by interleukin-1 receptor antagonist prevents. *Lancet* **364**, 1779-1785 (2004).
54. Hedrich, C.M. et al. "Mutation negative" familial cold autoinflammatory syndrome (FCAS) in an 8-year-old boy: clinical course and functional studies. *Rheumatol Int* (2011).

55. Metyas, S.K. & Hoffman, H.M. Anakinra prevents symptoms of familial cold autoinflammatory syndrome and Raynaud's disease. *J Rheumatol* **33**, 2085-7 (2006).
56. Hawkins, P.N., Lachmann, H.J., Aganna, E. & McDermott, M.F. Spectrum of clinical features in Muckle-Wells syndrome and response to anakinra. *Arthr Rheumat* **50**, 607-612 (2004).
57. Hawkins, P.N., Lachmann, H.J. & McDermott, M.F. Interleukin-1 receptor antagonist in the Muckle-Wells syndrome. *N Engl J Med* **348**, 2583-2584 (2003).
58. Klein, A.K. & Horneff, G. Improvement of sensoneurinal hearing loss in a patient with Muckle-Wells syndrome treated with anakinra. *Klin Padiatr* **222**, 266-8 (2011).
59. Gattorno, M. et al. Pattern of interleukin-1beta secretion in response to lipopolysaccharide and ATP before and after interleukin-1 blockade in patients with CIAS1 mutations. *Arthritis Rheum* **56**, 3138-48 (2007).
60. Rynne, M., Maclean, C., Bybee, A., McDermott, M.F. & Emery, P. Hearing improvement in a patient with variant Muckle-Wells syndrome in response to interleukin 1 receptor antagonism. *Ann Rheum Dis* **65**, 533-4 (2006).
61. Kuemmerle-Deschner, J.B. et al. NLRP3 E311K mutation in a large family with Muckle-Wells syndrome - description of a heterogeneous phenotype and response to treatment. *Arthritis Res Ther* **13**, R196 (2011).
62. Goldbach-Mansky, R. et al. Neonatal-onset multisystem inflammatory disease responsive to interleukin-1beta inhibition. *N Engl J Med* **355**, 581-92 (2006).
63. Lovell, D.J., Bowyer, S.L. & Solinger, A.M. Interleukin-1 blockade by anakinra improves clinical symptoms in patients with neonatal-onset multisystem inflammatory disease. *Arthritis Rheum* **52**, 1283-6 (2005).
64. Lepore, L. et al. Follow-up and quality of life of patients with cryopyrin-associated periodic syndromes treated with Anakinra. *J Pediatr* **157**, 310-315 e1 (2011).
65. Goldbach-Mansky, R. Current status of understanding the pathogenesis and management of patients with NOMID/CINCA. *Curr Rheumatol Rep* **13**, 123-31 (2011).
66. Miyamae, T. et al. Effect of anakinra on arthropathy in CINCA/NOMID syndrome. *Pediatr Rheumatol Online J* **8**, 9 (2011).
67. Sibley, C.H. et al. Sustained response and prevention of damage progression in patients with neonatal-onset multisystem inflammatory disease (NOMID) treated with anakinra. *Arthritis Rheum* (2012).
68. Tran, T.A. et al. Muckle-Wells Syndrome and Male Hypofertility: A Case Series. *Semin Arthritis Rheum* (2012).
69. Jeru, I. Role of Interleukin-1 in NLRP12-Associated Autoinflammatory Disorders and Resistance to Anti-Interleukin-1 Therapy. (2011).
70. Sacre, K. et al. Dramatic improvement following interleukin 1beta blockade in tumor necrosis factor receptor-1-associated syndrome (TRAPS) resistant to anti-TNF-alpha therapy. *J Rheumatol* **35**, 357-8 (2008).
71. Simon, A. et al. Beneficial response to interleukin-1 receptor antagonist in TRAPS. *Am J Med* **117**, 208-210 (2004).
72. Gattorno, M. et al. Persistent efficacy of anakinra in patients with tumor necrosis factor receptor-associated periodic syndrome. *Arthritis Rheum* **58**, 1516-20 (2008).

73. Kimberley, F.C., Lobito, A.A., Siegel, R.M. & Sreaton, G.R. Falling into TRAPS--receptor misfolding in the TNF receptor 1-associated periodic fever syndrome. *Arthritis Res Ther* **9**, 217 (2007).
74. Rigante, D. et al. Treatment with anakinra in the hyperimmunoglobulinemia D/periodic fever syndrome. *Rheumatol Int* **27**, 97-100 (2006).
75. Cantarini, L., Lucherini, O.M., Cimaz, R. & Galeazzi, M. Recurrent pericarditis caused by a rare mutation in the TNFRSF1A gene and with excellent response to anakinra treatment. *Clin Exp Rheumatol* **28**, 802 (2010).
76. Ruiz Gomez, A. et al. Clinical, genetic, and therapeutic diversity in 2 patients with severe mevalonate kinase deficiency. *Pediatrics* **129**, e535-9 (2012).
77. Bodar, E.J., van der Hilst, J.C., Drenth, J.P., van der Meer, J.W. & Simon, A. Effect of etanercept and anakinra on inflammatory attacks in the hyper-IgD syndrome: introducing a vaccination provocation model. *Neth J Med* **63**, 260-4 (2005).
78. Cailliez, M. et al. Anakinra is safe and effective in controlling hyperimmunoglobulinaemia D syndrome-associated febrile crisis. *J Inherit Metab Dis* **29**, 763 (2006).
79. Stoffels, M. & Simon, A. Hyper-IgD syndrome or mevalonate kinase deficiency. *Curr Opin Rheumatol* **23**, 419-23 (2011).
80. Simon, A. & van der Meer, J.W. Pathogenesis of familial periodic fever syndromes or hereditary autoinflammatory syndromes. *Am J Physiol Regul Integr Comp Physiol* **292**, R86-98 (2007).
81. Bodar, E.J. et al. On-demand anakinra treatment is effective in mevalonate kinase deficiency. *Ann Rheum Dis* **70**, 2155-8 (2011).
82. Shendi, H.M., Walsh, D. & Edgar, J.D. Etanercept and anakinra can prolong febrile episodes in patients with hyperimmunoglobulin D and periodic fever syndrome. *Rheumatol Int* **32**, 249-51 (2012).
83. Braun-Falco, M., Kovnerystyy, O., Lohse, P. & Ruzicka, T. Pyoderma gangrenosum, acne, and suppurative hidradenitis (PASH)-a new autoinflammatory syndrome distinct from PAPA syndrome. *J Am Acad Dermatol* (2011).
84. Brenner, M., Ruzicka, T., Plewig, G., Thomas, P. & Herzer, P. Targeted treatment of pyoderma gangrenosum in PAPA (pyogenic arthritis, pyoderma gangrenosum and acne) syndrome with the recombinant human interleukin-1 receptor antagonist anakinra. *Br J Dermatol* **161**, 1199-201 (2009).
85. Dierselhuis, M.P., Frenkel, J., Wulffraat, N.M. & Boelens, J.J. Anakinra for flares of pyogenic arthritis in PAPA syndrome. *Rheumatology* **44**, 406-408 (2005).
86. Schellevis, M.A. et al. Variable expression and treatment of PAPA syndrome. *Ann Rheum Dis* **70**, 1168-70 (2011).
87. Shoham, N.G. et al. Pyrin binds the PSTPIP1/CD2BP1 protein, defining familial Mediterranean fever and PAPA syndrome as disorders in the same pathway. *Proc Natl Acad Sci U S A* **100**, 13501-6 (2003).
88. Reddy, S. et al. An autoinflammatory disease due to homozygous deletion of the IL1RN locus. *N Engl J Med* **360**, 2438-44 (2009).
89. Aksentjevich, I. et al. An autoinflammatory disease with deficiency of the interleukin-1-receptor antagonist. *N Engl J Med* **360**, 2426-37 (2009).
90. Arostegui, J.I. et al. NOD2 gene-associated pediatric granulomatous arthritis: clinical diversity, novel and recurrent mutations, and evidence of clinical

- improvement with interleukin-1 blockade in a Spanish cohort. *Arthritis Rheum* **56**, 3805-13 (2007).
91. Adam, Z. et al. Schnitzler syndrome--report on a fourteen-year course of the disease and an overview of information on the disease. *Vnitr Lek* **54**, 1140-53 (2008).
 92. Cascavilla, N., Bisceglia, M. & D'Arena, G. Successful treatment of Schnitzler's syndrome with anakinra after failure of rituximab trial. *Int J Immunopathol Pharmacol* **23**, 633-6 (2010).
 93. De Koning, H.D. et al. Beneficial reponse to anakinra and thalidomide in Schnitzler's syndrome. *Ann Rheum Dis*, J. C. H. (2005).
 94. Eiling, E., Moller, M., Kreiselmaier, I., Brasch, J. & Schwarz, T. Schnitzler syndrome: treatment failure to rituximab but response to anakinra. *J Am Acad Dermatol* **57**, 361-4 (2007).
 95. Gran, J.T., Midtvedt, O., Haug, S. & Aukrust, P. Treatment of Schnitzler's syndrome with anakinra: report of three cases and review of the literature. *Scand J Rheumatol* **40**, 74-9 (2011).
 96. Larocca, C.A. et al. Schnitzler's syndrome associated with pancreatitis: a disease of IL-1 dysregulation. *Clin Rheumatol* **31**, 169-74 (2012).
 97. Lipsker, D. The Schnitzler syndrome. *Orphanet J Rare Dis* **5**, 38 (2010).
 98. Martinez-Taboada, V.M., Fontalba, A., Blanco, R. & Fernandez-Luna, J.L. Successful treatment of refractory Schnitzler syndrome with anakinra: comment on the article by Hawkins et al. *Arthritis Rheum* **52**, 2226-7 (2005).
 99. Schuster, C. et al. Schnitzler syndrome: response to anakinra in two cases and a review of the literature. *Int J Dermatol* **48**, 1190-4 (2009).
 100. Szturz, P. et al. Schnitzler syndrome: diagnostics and treatment. *Klin Onkol* **24**, 271-7 (2011).
 101. Volz, T. et al. Dermal Interleukin-1 Expression and Effective and Long-lasting Therapy with Interleukin-1 Receptor Antagonist Anakinra in Schnitzler Syndrome. *Acta Derm Venereol* **in press**(2012).
 102. Kuemmerle-Deschner, J.B. et al. Efficacy and safety of anakinra therapy in pediatric and adult patients with the autoinflammatory Muckle-Wells syndrome. *Arthritis Rheum* **63**, 840-9 (2011).
 103. Leslie, K.S. et al. Phenotype, genotype, and sustained response to anakinra in 22 patients with autoinflammatory disease associated with CIAS-1/NALP3 mutations. *Arch Dermatol* **142**, 1591-7 (2006).
 104. Neven, B. et al. Long-term efficacy of the interleukin-1 receptor antagonist anakinra in ten patients with neonatal-onset multisystem inflammatory disease/chronic infantile neurologic, cutaneous, articular syndrome. *Arthritis Rheum* **62**, 258-67 (2011).
 105. Thornton, B.D., Hoffman, H.M., Bhat, A. & Don, B.R. Successful treatment of renal amyloidosis due to familial cold autoinflammatory syndrome using an interleukin 1 receptor antagonist. *Am J Kidney Dis* **49**, 477-81 (2007).
 106. Ait-Abdesselam, T. et al. Anakinra efficacy in a Caucasian patient with renal AA amyloidosis secondary to cryopyrin-associated periodic syndrome. *Joint Bone Spine* **77**, 616-7 (2011).
 107. Boyer, E.M., Turman, M. & O'Neil, K.M. Partial response to anakinra in life-threatening Henoch-Schonlein purpura: case report. *Pediatr Rheumatol Online J* **9**, 21 (2011).

108. Picco, P. et al. Successful treatment of idiopathic recurrent pericarditis in children with interleukin-1beta receptor antagonist (anakinra): an unrecognized autoinflammatory disease? *Arthritis Rheum* **60**, 264-8 (2009).
109. Scott, I.C., Vijay Hajela, V., Hawkins, P.N. & Lachmann, H.J. A case series and systematic literature review of anakinra and immunosuppression in idiopathic recurrent pericarditis. *J Cardiology Cases* **4**, e93—e97 (2011).
110. Paul, S.M. et al. Functional outcomes of treatment of neonatal onset multisystem inflammatory disease (NOMID) with anakina. *Arthr Rheumat* **52 (suppl)**, S536 (2005).
111. Pascual, V., Allantaz, F., Arce, E., Punaro, M. & Banchereau, J. Role of interleukin-1 (IL-1) in the pathogenesis of systemic onset juvenile idiopathic arthritis and clinical response to IL-1 blockade. *J Exp Med* **201**, 1479-86 (2005).
112. Quartier, P. et al. A multicentre, randomised, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). *Ann Rheum Dis* (2011).
113. Gattorno, M. et al. The pattern of response to anti-interleukin-1 treatment distinguishes two subsets of patients with systemic-onset juvenile idiopathic arthritis. *Arthritis Rheum* **58**, 1505-15 (2008).
114. Nigrovic, P.A. et al. Anakinra as first-line disease-modifying therapy in systemic juvenile idiopathic arthritis: report of forty-six patients from an international multicenter series. *Arthritis Rheum* **63**, 545-55 (2011).
115. Dewitt, E.M. et al. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. *Arthritis Care Res* (2012).
116. Belot, A. et al. ANCA-associated glomerulonephritis in systemic-onset juvenile idiopathic arthritis. *Am J Kidney Dis* **59**, 439-43 (2012).
117. Aelion, J.A. & Odhav, S.K. Prompt response to treatment with anakinra in adult onset Still's disease. *Ann Rheum Dis* **63 (suppl 1)**, 265 (abs) (2004).
118. Fitzgerald, A.A., Leclercq, S.A., Yan, A., Homik, J.E. & Dinarello, C.A. Rapid responses to anakinra in patients with refractory adult-onset Still's disease. *Arthritis Rheum* **52**, 1794-1803 (2005).
119. Haraoui, B., Bourrelle, D. & Kaminska, E. Anakinra in the treatment of adult onset Still's disease. *Ann Rheum Dis* **63 (suppl 1)**, 263 (abs) (2004).
120. Kalliolias, G.D., Georgiou, P.E., Antonopoulos, I.A., Andonopoulos, A.P. & Liossis, S.N. Anakinra treatment in patients with adult-onset Still's disease is fast, effective, safe and steroid sparing: experience from an uncontrolled trial. *Ann Rheum Dis* **66**, 842-3 (2007).
121. Kotter, I. et al. Anakinra in patients with treatment-resistant adult-onset Still's disease: four case reports with serial cytokine measurements and a review of the literature. *Semin Arthritis Rheum* **37**, 189-97 (2007).
122. Lahiri, M. & Teng, G.G. A case of refractory adult-onset Still's disease treated with anakinra. *Int J Rheum Dis* **13**, e36-41 (2010).
123. Laskari, K., Tzioufas, A.G. & Moutsopoulos, H.M. Efficacy and long-term follow-up of IL-1R inhibitor anakinra in adults with Still's disease: a case-series study. *Arthritis Res Ther* **13**, R91 (2011).
124. Lequerre, T. et al. Interleukin-1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still disease: preliminary experience in France. *Ann Rheum Dis* **67**, 302-8 (2008).

125. Moulis, G., Sailer, L., Astudillo, L., Pugno, G. & Arlet, P. May anakinra be used earlier in adult onset Still disease? *Clin Rheumatol* **29**, 1199-200 (2010).
126. Mylona, E. et al. Acute hepatitis in adult Still's disease during corticosteroid treatment successfully treated with anakinra. *Clin Rheumatol* **27**, 659-61 (2008).
127. Naumann, L. et al. IL1-receptor antagonist anakinra provides long-lasting efficacy in the treatment of refractory adult-onset Still's disease. *Ann Rheum Dis* **69**, 466-7 (2010).
128. Raffener, B. et al. Adult-onset Still's disease with myocarditis successfully treated with the interleukin-1 receptor antagonist anakinra. *Joint Bone Spine* **78**, 100-1 (2011).
129. Rudinskaya, A. & Trock, D.H. Successful treatment of a patient with refractory adult-onset Still's disease with anakinra. *J Clin Rheumatol* **9**, 330-332 (2003).
130. Tamaki, H. et al. Marked effect and steroid-sparing ability of anakinra on a patient with refractory adult-onset Still's disease. *Mod Rheumatol* **20**, 200-4 (2010).
131. Vasques Godinho, F.M., Parreira Santos, M.J. & Canas da Silva, J. Refractory adult onset Still's disease successfully treated with anakinra. *Ann Rheum Dis* **64**, 647-8 (2005).
132. Vordenbaumen, S., Ostendorf, B., Sander, O., Richter, J. & Schneider, M. Continuation of anakinra despite the development of a pruritic rash in an otherwise refractory case of adult-onset Still's disease. *Ann Rheum Dis* **68**, 450-1 (2009).
133. Youssef, J., Lazaro, E., Blanco, P. & Viallard, J.F. Blockade of interleukin 1 receptor in Still's disease affects activation of peripheral T-lymphocytes. *J Rheumatol* **35**, 2453-6 (2008).
134. Woo, P. Anakinra treatment for systemic juvenile idiopathic arthritis and adult onset Still disease. *Ann Rheum Dis* **67**, 281-2 (2008).
135. Teran, A. et al. Adult-onset Still's disease with liver failure requiring liver transplantation. *Gastroenterol Hepatol* **32**, 681-6 (2009).
136. Durand, M., Troyanov, Y., Laflamme, P. & Gregoire, G. Macrophage activation syndrome treated with anakinra. *J Rheumatol* **37**, 879-80 (2011).
137. Behrens, E.M., Kreiger, P.A., Cherian, S. & Cron, R.Q. Interleukin 1 receptor antagonist to treat cytophagic histiocytic panniculitis with secondary hemophagocytic lymphohistiocytosis. *J Rheumatol* **33**, 2081-4 (2006).
138. Bruck, N. et al. Rapid and sustained remission of systemic juvenile idiopathic arthritis-associated macrophage activation syndrome through treatment with anakinra and corticosteroids. *J Clin Rheumatol* **17**, 23-7 (2011).
139. Aronson, I.K. & Worobec, S.M. Cytophagic histiocytic panniculitis and hemophagocytic lymphohistiocytosis: an overview. *Dermatol Ther* **23**, 389-402 (2010).
140. Chou, R.C., Dinarello, C.A., Ferry, J.A. & Dal Cin, P. A 36-year-old woman with recurrent high-grade fevers, hypotension, and hypertriglyceridemia. *Arthritis Care Res* **62**, 137-140 (2010).
141. Ravelli, A., Grom, A.A., Behrens, E.M. & Cron, R.Q. Macrophage activation syndrome as part of systemic juvenile idiopathic arthritis: diagnosis, genetics, pathophysiology and treatment. *Genes Immun* **13**, 289-98 (2012).
142. Miettunen, P.M., Narendran, A., Jayanthan, A., Behrens, E.M. & Cron, R.Q. Successful treatment of severe paediatric rheumatic disease-associated

- macrophage activation syndrome with interleukin-1 inhibition following conventional immunosuppressive therapy: case series with 12 patients. *Rheumatology (Oxford)* **50**, 417-9 (2012).
143. Record, J.L., Beukelman, T. & Cron, R.Q. Combination therapy of abatacept and anakinra in children with refractory systemic juvenile idiopathic arthritis: a retrospective case series. *J Rheumatol* **38**, 180-1 (2011).
 144. Delluc, A. et al. Efficacy of anakinra, an IL1 receptor antagonist, in refractory Sweet syndrome. *Ann Rheum Dis* **67**, 278-9 (2008).
 145. Kluger, N., Gil-Bistes, D., Guillot, B. & Bessis, D. Efficacy of anti-interleukin-1 receptor antagonist anakinra (Kineret(R)) in a case of refractory Sweet's syndrome. *Dermatology* **222**, 123-7 (2011).
 146. Lipsker, D., Perrigouard, C., Foubert, A. & Cribier, B. Anakinra for difficult-to-treat neutrophilic panniculitis: IL-1 blockade as a promising treatment option for neutrophil-mediated inflammatory skin disease. *Dermatology* **220**, 264-7 (2010).
 147. Aouba, A. et al. Rationale and efficacy of interleukin-1 targeting in Erdheim-Chester disease. *Blood* **116**, 4070-6 (2010).
 148. Zaidan, M., Bercot, B., Petit, A., Bardin, T. & Richette, P. Whipple disease mimicking adult-onset Still's disease and treated by anakinra: diagnosis using PCR. *Scand J Rheumatol* (2012).
 149. Colina, M. et al. Dysregulation of P2X7 receptor-inflammasome axis in SAPHO syndrome: successful treatment with anakinra. *Rheumatology (Oxford)* **49**, 1416-8 (2010).
 150. Wendling, D., Prati, C. & Aubin, F. Anakinra treatment of SAPHO syndrome: short-term results of an open study. *Ann Rheum Dis* (2012).
 151. Stojanov, S. et al. Periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) is a disorder of innate immunity and Th1 activation responsive to IL-1 blockade. *Proc Natl Acad Sci U S A* **108**, 7148-53 (2011).
 152. Galeotti, C. et al. IL-1RA agonist (anakinra) in the treatment of multifocal Castleman disease. *J Pediatr Hematol Oncol* **30**, 920-924 (2008).
 153. Sparsa, L. et al. Jessner-Kanof disease induced by leflunomide: a dermal variant of cutaneous lupus? *Rheumatol Int* **31**, 255-8 (2012).
 154. Norheim, K.B., Harboe, E., Goransson, L.G. & Omdal, R. Interleukin-1 inhibition and fatigue in primary Sjogren's syndrome - a double blind, randomised clinical trial. *PLoS One* **7**, e30123 (2012).
 155. McGonagle, D., Tan, A.L., Madden, J., Emery, P. & McDermott, M.F. Successful treatment of resistant pseudogout with anakinra. *Arthritis Rheum* **58**, 631-3 (2008).
 156. McGonagle, D. et al. Management of treatment resistant inflammation of acute on chronic tophaceous gout with anakinra. *Ann Rheum Dis* **66**, 1683-4 (2007).
 157. So, A., De Smedt, T., Revaz, S. & Tschopp, J. A pilot study of IL-1 inhibition by anakinra in acute gout. *Arthritis Res Ther* **9**, R28 (2007).
 158. So, A. Epidemiology: Gout--bad for the heart as well as the joint. *Nat Rev Rheumatol* **6**, 386-7 (2010).
 159. Singh, D. & Huston, K.K. IL-1 inhibition with anakinra in a patient with refractory gout. *J Clin Rheumatol* **15**, 366 (2009).
 160. Gratton, S.B., Scalapino, K.J. & Fye, K.H. Case of anakinra as a steroid-sparing agent for gout inflammation. *Arthritis Rheum* **61**, 1268-70 (2009).

161. Announ, N., Palmer, G., Guerne, P.A. & Gabay, C. Anakinra is a possible alternative in the treatment and prevention of acute attacks of pseudogout in end-stage renal failure. *Joint Bone Spine* **76**, 424-6 (2009).
162. Molto, A., Ea, H.K., Richette, P., Bardin, T. & Liote, F. Efficacy of anakinra for refractory acute calcium pyrophosphate crystal arthritis. *Joint Bone Spine* (2012).
163. Abbate, A. et al. Interleukin-1 blockade with anakinra to prevent adverse cardiac remodeling after acute myocardial infarction. *Am J Cardiol* **105**, 1371-1377 (2010).
164. Van Tassell, B.W. et al. Enhanced interleukin-1 activity contributes to exercise intolerance in patients with systolic heart failure. *PLOS One* **in press**(2012).
165. Lust, J.A. et al. Induction of a chronic disease state in patients with smoldering or indolent multiple myeloma by targeting interleukin 1{beta}-induced interleukin 6 production and the myeloma proliferative component. *Mayo Clin Proc* **84**, 114-22 (2009).
166. Emsley, H.C. et al. A randomised phase II study of interleukin-1 receptor antagonist in acute stroke patients. *J Neurol Neurosurg Psychiatry* **76**, 1366-72 (2005).
167. Smith, C.J. et al. Interleukin-1 receptor antagonist reverses stroke-associated peripheral immune suppression. *Cytokine* **58**, 384-9 (2012).
168. Hsiao, J.L. et al. Hidradenitis suppurativa and concomitant pyoderma gangrenosum: a case series and literature review. *Arch Dermatol* **146**, 1265-70 (2011).
169. Netea, M.G. et al. Overproduction of interleukin-17 in a family with hidradenitis suppurativa: response to anakinra therapy. *J. Invest. Dermatol* **in press**(2011).
170. Larsen, C.M. et al. Sustained effects of interleukin-1 receptor antagonist treatment in type 2 diabetes. *Diabetes Care* **32**, 1663-8 (2009).
171. Larsen, C.M. et al. Interleukin-1-receptor antagonist in type 2 diabetes mellitus. *N Engl J Med* **356**, 1517-26 (2007).
172. Sumpter, K.M., Adhikari, S., Grishman, E.K. & White, P.C. Preliminary studies related to anti-interleukin-1beta therapy in children with newly diagnosed type 1 diabetes. *Pediatr Diabetes* (2011).
173. van Asseldonk, E.J. et al. Treatment with anakinra improves disposition index but not insulin sensitivity in nondiabetic subjects with the metabolic syndrome: a randomized, double-blind, placebo-controlled study. *J Clin Endocrinol Metab* **96**, 2119-26 (2011).
174. van Asseldonk, E.J.P. et al. One week of treatment with the IL-1 receptor antagonist anakinra improves insulin sensitivity in patients with type 1 diabetes mellitus: results from a clinical trial *Diabetologia* **in press**(2012).
175. Dana, R. et al. Randomized phase II trial of safety and efficacy of topical interleukin-1 receptor antagonist (IL-1Ra) for treatment of meibomian gland dysfunction (MGD) – associated ocular surface disease. *Fed Clin Immunol Soc Abstract* **107**(2012).
176. Lutz, V. & Lipsker, D. Acitretin- and tumor necrosis factor inhibitor-resistant acrodermatitis continua of hallopeau responsive to the interleukin 1 receptor antagonist anakinra. *Arch Dermatol* **148**, 297-9 (2012).