

Chapter 234

Immunobiologicals, Cytokines, and Growth Factors in Dermatology

Stephen K. Richardson &

Joel M. Gelfand

REFERENCES

1. Platsoucas CD, et al: Regulation of natural killer cytotoxicity by recombinant alpha interferons. Augmentation by IFN-alpha 7, an interferon similar to IFN-alpha J. *Anticancer Re* **9**(4):849-858, 1989
2. Rook AH, Kuzel TM, Olsen EA: Cytokine therapy of cutaneous T-cell lymphoma: Interferons, interleukin-12, and interleukin-2. *Hematol Oncol Clin North Am* **17**(6):1435-1448, ix, 2003
3. Holman DM, Kalaaji AN: Cytokines in dermatology. *J Drugs Dermatol* **5**(6):520-524, 2006
4. Motzer RJ et al: Phase II trial of branched peginterferon-alpha 2a (40 kDa) for patients with advanced renal cell carcinoma. *Ann Onco* **13**(11):1799-1805, 2002
5. Olsen EA, Bunn PA: Interferon in the treatment of cutaneous T-cell lymphoma. *Hematol Oncol Clin North Am* **9**(5):1089-1107, 1995
6. Richardson S et al: High clinical response rate with multimodality immunomodulatory therapy for Sezary syndrome. *Clin Lymphoma Myeloma* **7**(3):226-232, 2006
7. Watanabe U et al: The risk factor for development of thyroid disease during interferon-alpha therapy for chronic hepatitis C. *Am J Gastroenterol* **89**(3):399-403, 1994
8. Celik G et al: Sarcoidosis caused by interferon therapy. *Respirology* **10**(4):535-540, 2005
9. Raanani P, Ben-Bassat I: Immune-mediated complications during interferon therapy in hematological patients. *Acta Haemato* **107**(3):133-144, 2002
10. Gormley RH et al: Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma. *J Am Acad Dermatol* **62**(2):300-307, 2010
11. Sechler JM et al: Recombinant human interferon-gamma reconstitutes defective phagocyte function in patients with chronic granulomatous disease of childhood. *Proc Natl Acad Sci USA* **85**(13):4874-4878, 1988
12. Errante PR, Frazao JB, Condino-Neto A: The use of interferon-gamma therapy in chronic granulomatous disease. *Recent Pat Antiinfect Drug Discov* **3**(3):225-230, 2008
13. Kaplan EH et al: Phase II study of recombinant human interferon gamma for treatment of cutaneous T-cell lymphoma. *J Natl Cancer Inst* **82**(3):208-212, 1990
14. Vowels BR et al: Aberrant cytokine production by Sezary syndrome patients: Cytokine secretion pattern resembles murine Th2 cells. *J Invest Dermatol* **99**(1):90-94, 1992
15. Kim EJ et al: Immunopathogenesis and therapy of cutaneous T cell lymphoma. *J Clin Invest* **115**(4):798-812, 2005
16. Bolinger AM, Taeubel MA: Recombinant interferon gamma for treatment of chronic granulomatous disease and other disorders. *Clin Pharm* **11**(10):834-850; quiz 892-834, 1992
17. Asadullah K, Sterry W, Trefzer U: Cytokine therapy in dermatology. *Exp Dermatol* **11**(2):97-106, 2002
18. Atkins MB et al: High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: Analysis of 270 patients treated between 1985 and 1993. *J Clin Oncol* **17**(7):2105-2116, 1999
19. Sznol M et al: Review of interleukin-2 alone and interleukin-2/LAK clinical trials in metastatic malignant melanoma. *Cancer Treat Rev* **16**(Suppl. A):29-38, 1989
20. Parkinson DR et al: Interleukin-2 therapy in patients with metastatic malignant melanoma: A phase II study. *J Clin Oncol* **8**(10):1650-1656, 1990
21. Jilaveanu LB, Aziz SA, Kluger HM: Chemotherapy and biologic therapies for melanoma: Do they work? *Clin Dermatol* **27**(6):614-625, 2009
22. Goldbach-Mansky R et al: Neonatal-onset multisystem inflammatory disease responsive to interleukin-1beta inhibition. *N Engl J Med* **355**(6):581-592, 2006

23. 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**(1):258-267, 2010
24. Szabolcs P et al: Dendritic cells and macrophages can mature independently from a human bone marrow-derived, post-colony-forming unit intermediate. *Blood* **87**(11):4520-4530, 1996
25. Kaplan G: Recent advances in cytokine therapy in leprosy. *J Infect Dis* **167** (Suppl. 1):S18-S22, 1993
26. Braunstein S et al: GM-CSF activates regenerative epidermal growth and stimulates keratinocyte proliferation in human skin in vivo. *J Invest Dermatol* **103**(4):601-604, 1994
27. Vaquerano JE et al: Regression of in-transit melanoma of the scalp with intralesional recombinant human granulocyte-macrophage colony-stimulating factor. *Arch Dermatol* **135**(10):1276-1277, 1999
28. Hoeller C et al: Perilesional injection of r-GM-CSF in patients with cutaneous melanoma metastases. *J Invest Dermatol* **117**(2):371-374, 2001
29. Spittler LE et al: Adjuvant therapy of stage III and IV malignant melanoma using granulocyte-macrophage colony-stimulating factor. *J Clin Oncol* **18**(8):1614-1621, 2000
30. O'Day SJ et al: Maintenance biotherapy for metastatic melanoma with interleukin-2 and granulocyte macrophage-colony stimulating factor improves survival for patients responding to induction concurrent biochemotherapy. *Clin Cancer Res* **8**(9):2775-2781, 2002
31. Spittler LE et al: Recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF, sargramostim) administered for 3 years as adjuvant therapy of stages II(T4), III, and IV melanoma. *J Immunother* **32**(6):632-637, 2009
32. Chaperot L et al: Differentiation of antigen-presenting cells (dendritic cells and macrophages) for therapeutic application in patients with lymphoma. *Leukemia*. **14**(9):1667-1677, 2000
33. Bouwhuis SA et al: Extracorporeal photopheresis and adjuvant aerosolized granulocyte-macrophage colony-stimulating factor for Sezary syndrome. *Mayo Clin Proc* **77**(2):197-200, 2002
34. Wieman TJ, Smiell JM, Su Y: Efficacy and safety of a topical gel formulation of recombinant human platelet-derived growth factor-BB (becaplermin) in patients with chronic neuropathic diabetic ulcers. A phase III randomized placebo-controlled double-blind study. *Diabetes Care* **21**(5):822-827, 1998
35. Steed DL: Clinical evaluation of recombinant human platelet-derived growth factor for the treatment of lower extremity ulcers. *Plast Reconstr Surg* **117**(Suppl. 7):143S-149S; discussion 150S-151S, 2006
36. Smiell JM: Clinical safety of becaplermin (rhPDGF-BB) gel. Becaplermin Studies Group. *Am J Surg* **176**(Suppl. 2A):68S-73S, 1998
37. LaDuca JR, Gaspari AA: Targeting tumor necrosis factor alpha. New drugs used to modulate inflammatory diseases. *Dermatol Clin* **19**(4):617-635, 2001
38. Springer TA: Adhesion receptors of the immune system. *Nature* **346**(6283):425-434, 1990
39. Gottlieb AB et al: Pharmacodynamic and pharmacokinetic response to anti-tumor necrosis factor-alpha monoclonal antibody (infliximab) treatment of moderate to severe psoriasis vulgaris. *J Am Acad Dermatol* **48**(1):68-75, 2003
40. Hancock GE, Kaplan G, Cohn ZA: Keratinocyte growth regulation by the products of immune cells. *J Exp Med* **168**(4):1395-1402, 1988
41. Gelfand JM et al: Prevalence and treatment of psoriasis in the United Kingdom: A population-based study. *Arch Dermatol* **141**(12):1537-1541, 2005
42. Ettehadi P: Elevated tumour necrosis factor-alpha (TNF-alpha) biological activity in psoriatic skin lesions. *Clin Exp Immunol* **96**(1):146-151, 1994
43. Boyman O: Spontaneous development of psoriasis in a new animal model shows an essential role for resident T cells and tumor necrosis factor-alpha. *J Exp Med* **199**(5):731-736, 2004
44. Bonifati C et al: Correlated increases of tumour necrosis factor-alpha, interleukin-6 and granulocyte monocyte-colony stimulating factor levels in suction blister fluids and sera of psoriatic patients—Relationships with disease severity. *Clin Exp Dermatol* **19**(5):383-387, 1994
45. Mussi A et al: Serum TNF-alpha levels correlate with disease severity and are reduced by effective therapy in plaque-type psoriasis. *J Biol Regul Homeost Agents* **11**(3):115-118, 1997
46. Sieper J, Van Den Brande J: Diverse effects of infliximab and etanercept on T lymphocytes. *Semin Arthritis Rheum*. **34**(5 Suppl. 1):23-27, 2005
47. Wallis RS, Ehlers S: Tumor necrosis factor and granuloma biology: Explaining the differential infection risk of etanercept and infliximab. *Semin Arthritis Rheum* **34**(5 Suppl. 1):34-38, 2005
48. Nestorov I: Clinical pharmacokinetics of TNF antagonists: How do they differ? *Semin Arthritis Rheum* **34**(5 Suppl. 1):12-18, 2005

49. Wallis RS: Granulomatous infectious diseases associated with tumor necrosis factor antagonists. *Clin Infect Dis* **38**(9):1261-1265, 2004
50. Alexis AF, Strober BE: Off-label dermatologic uses of anti-TNF- α therapies. *J Cutan Med Surg* **9**(6):296-302, 2005
51. Grant A et al: Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: A randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol* **62**(2):205-217, 2010
52. BTS recommendations for assessing risk and for managing Mycobacterium tuberculosis infection and disease in patients due to start anti-TNF- α treatment. *Thorax* **60**(10):800-805, 2005
53. Roux CH et al: Safety of anti-TNF- α therapy in rheumatoid arthritis and spondylarthropathies with concurrent B or C chronic hepatitis. *Rheumatology (Oxford)*, **45**(10):1294-1297 2006
54. Parke FA, Reveille JD: Anti-tumor necrosis factor agents for rheumatoid arthritis in the setting of chronic hepatitis C infection. *Arthritis Rheum* **51**(5):800-804, 2004
55. Zein NN: Etanercept as an adjuvant to interferon and ribavirin in treatment-naive patients with chronic hepatitis C virus infection: A phase 2 randomized, double-blind, placebo-controlled study. *J Hepatol* **42**(3):315-322, 2005
56. Boetticher NC et al: A randomized, double-blinded, placebo-controlled multicenter trial of etanercept in the treatment of alcoholic hepatitis. *Gastroenterology* **135**(6):1953-1960, 2008
57. Bongartz T et al: Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: Systematic review and meta-analysis of rare harmful effects in randomized controlled trials. *JAMA* **295**(19):2275-2285, 2006
58. Strangfeld A et al: Risk of herpes zoster in patients with rheumatoid arthritis treated with anti-TNF- α agents. *JAMA* **301**(7):737-744, 2009
59. Leombruno JP et al: The safety of antitumor necrosis factor treatments in rheumatoid arthritis: Meta and exposure-adjusted pooled analyses of serious adverse events. *Ann Rheum Dis* **68**(7):1136-1145, 2009
60. Adams AE et al: Aggressive cutaneous T-cell lymphomas after TNF α blockade. *J Am Acad Dermatol* **51**(4):660-662, 2004
61. Dommasch E, Gelfand JM: Is there truly a risk of lymphoma from biologic therapies? *Dermatol Ther* **22**(5):418-430, 2009
62. Bongartz T: Etanercept therapy in rheumatoid arthritis and the risk of malignancies: A systematic review and individual patient data meta-analysis of randomised controlled trials. *Ann Rheum Dis* **68**(7):1177-1183, 2009
63. Mariette X et al: Lymphoma in patients treated with anti-TNF: Results of the 3-year prospective French RATIO registry. *Ann Rheum Dis* **69**(2):400-408, 2010
64. Gelfand JM et al: The Risk of lymphoma in patients with psoriasis. *J Invest Dermatol* **126**(10):2194-2201, 2006
65. Ubriani R, Van Voorhees AS: Onset of psoriasis during treatment with TNF- α antagonists: A report of 3 cases. *Arch Dermatol* **143**(2):270-272, 2007
66. Kary S et al: New onset or exacerbation of psoriatic skin lesions in patients with definite rheumatoid arthritis receiving tumour necrosis factor alpha antagonists. *Ann Rheum Dis* **65**(3):405-407, 2006
67. Reich K et al: Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: A phase III, multicentre, double-blind trial. *Lancet* **366**(9494):1367-1374, 2005
68. Baert F et al: Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. *N Engl J Med* **348**(7):601-608, 2003
69. Wagner CL et al: Consequences of immunogenicity to the therapeutic monoclonal antibodies ReoPro and Remicade. *Dev Biol (Basel)* **112**:37-53, 2003
70. Lipsky PE et al: Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. *N Engl J Med* **343**(22):1594-1602, 2000
71. Kruger-Krasagakis S et al: Programmed cell death of keratinocytes in infliximab-treated plaque-type psoriasis. *Br J Dermatol* **154**(3):460-466, 2006
72. Adams DR, Buckel T, Sceppe JA: Infliximab associated new-onset psoriasis. *J Drugs Dermatol* **5**(2):178-179, 2006
73. Menter A et al: Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. *J Am Acad Dermatol* **58**(1):106-115, 2010
74. Batchelor JM, Ingram JR, Williams H: Adalimumab vs methotrexate for the treatment of chronic plaque psoriasis. *Arch Dermatol* **145**(6):704-706; discussion 706, 2009

75. Lecluse LL et al: Extent and clinical consequences of antibody formation against adalimumab in patients with plaque psoriasis. *Arch Dermatol* **146**(2):127-132, 2010
76. Torti DC, Feldman SR: Interleukin-12, interleukin-23, and psoriasis: Current prospects. *J Am Acad Dermatol* **57**(6):1059-1068, 2007
77. Papp KA et al: Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet* **371**(9625):1675-1684, 2008
78. Griffiths CE et al: Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. *N Engl J Med* **362**(2):118-128, 2010
79. Novelli F, Casanova JL: The role of IL-12, IL-23 and IFN-gamma in immunity to viruses. *Cytokine Growth Factor Rev.* **15**(5):367-377, 2004
80. MacLennan C et al: Interleukin (IL)-12 and IL-23 are key cytokines for immunity against *Salmonella* in humans. *J Infect Dis* **190**(10):1755-1757, 2004
81. Van de Vosse E et al: Human genetics of intracellular infectious diseases: Molecular and cellular immunity against mycobacteria and salmonellae. *Lancet Infect Dis* **4**(12):739-749, 2004
82. Dorner T, Burmester GR: The role of B cells in rheumatoid arthritis: Mechanisms and therapeutic targets. *Curr Opin Rheumatol* **15**(3):246-252, 2003
83. Edwards JC, Cambridge G: Sustained improvement in rheumatoid arthritis following a protocol designed to deplete B lymphocytes. *Rheumatology (Oxford)* **40**(2):205-211, 2001
84. Cerny T et al: Mechanism of action of rituximab. *Anticancer Drug* **13**(Suppl. 2):S3-S10, 2002
85. FDA warns of safety concern regarding rituxan in new patient population, www.fda.gov/News-Events/Newsroom/PressAnnouncements/2006/ucm108810.htm.
86. Marcelin AG et al: Rituximab therapy for HIV-associated Castleman disease. *Blood* **102**(8):2786-2788, 2003
87. Clifford KS, Demierre MF: Progression of classic Kaposi's sarcoma with rituximab. *J Am Acad Dermatol* **53**(1):155-157, 2005
88. Schmidt E et al: Rituximab in autoimmune bullous diseases: Mixed responses and adverse effects. *Br J Dermatol* **156**(2):352-356, 2007
89. Ahmed AR et al: Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. *N Engl J Med* **355**(17):1772-1779, 2006
90. Kerl K et al: Intralesional and intravenous treatment of cutaneous B-cell lymphomas with the monoclonal anti-CD20 antibody rituximab: report and follow-up of eight cases. *Br J Dermatol* **155**(6):1197-1200, 2006
91. Lafyatis R et al: B cell depletion with rituximab in patients with diffuse cutaneous systemic sclerosis. *Arthritis Rheum* **60**(2):578-583, 2009
92. Administration FaD: FDA warns of safety concern regarding Rituxan in new patient population [online]. <http://www.fda.gov/bbs/topics/NEWS/2006/NEW01532.html>, accessed Dec 18, 2006
93. Ellis CN, Krueger GG: Treatment of chronic plaque psoriasis by selective targeting of memory effector T lymphocytes. *N Engl J Med* **345**(4):248-255, 2001
94. Cooper JC et al: Alefacept selectively promotes NK cell-mediated deletion of CD45RO+ human T cells. *Eur J Immunol* **33**(3):666-675, 2003
95. Lebwohl M et al: An international, randomized, double-blind, placebo-controlled phase 3 trial of intramuscular alefacept in patients with chronic plaque psoriasis. *Arch Dermatol* **139**(6):719-727, 2003
96. Fivenson DP, Mathes B: Treatment of generalized lichen planus with alefacept. *Arch Dermatol* **142**(2):151-152, 2006
97. Heffernan MP et al: Alefacept for alopecia areata. *Arch Dermatol* **141**(12):1513-1516, 2005
98. Strober BE et al: Alefacept for severe alopecia areata: A randomized, double-blind, placebo-controlled study. *Arch Dermatol* **145**(11):1262-1266, 2009
99. Kraan MC et al: Alefacept treatment in psoriatic arthritis: reduction of the effector T cell population in peripheral blood and synovial tissue is associated with improvement of clinical signs of arthritis. *Arthritis Rheum* **46**(10):2776-2784, 2002
100. Mease PJ, Gladman DD, Keystone EC: Alefacept in combination with methotrexate for the treatment of psoriatic arthritis: Results of a randomized, double-blind, placebo-controlled study. *Arthritis Rheum* **54**(5):1638-1645, 2006
101. Gribetz CH et al: An extended 16-week course of alefacept in the treatment of chronic plaque psoriasis. *J Am Acad Dermatol* **53**(1):73-75, 2005
102. Menter A et al: The efficacy of multiple courses of alefacept in patients with moderate to severe chronic plaque psoriasis. *J Am Acad Dermatol* **54**(1):61-63, 2006

103. Goffe B et al: An integrated analysis of thirteen trials summarizing the long-term safety of alefacept in psoriasis patients who have received up to nine courses of therapy. *Clin The* 27(12):1912-1921, 2005
104. Gottlieb AB et al: CD4+ T-cell-directed antibody responses are maintained in patients with psoriasis receiving alefacept: Results of a randomized study. *J Am Acad Dermatol* 49(5):816-825, 2003
105. Leonardi CL et al: Etanercept as monotherapy in patients with psoriasis. *N Engl J Med*. 349(21):2014-2022, 20, 2003
106. Paller AS et al: Etanercept treatment for children and adolescents with plaque psoriasis. *N Engl J Med*. 358(3):241-251, 2008
107. Gottlieb AB et al: Etanercept can safely be withdrawn from patients with psoriasis and re-establishes disease control on retreatment. Presented at: *Summer Academy 2004 of the American Academy of Dermatology* New York, July 28–August 1, 2004, New York, Poster p. 89
108. Turk MJ et al: Concomitant tumor immunity to a poorly immunogenic melanoma is prevented by regulatory T cells. *J Exp Med* 200(6):771-782, 2004
109. Jones E et al: Depletion of CD25+ regulatory cells results in suppression of melanoma growth and induction of autoreactivity in mice. *Cancer Immun* 2:1, 2002
110. Attia P et al: Inability of a fusion protein of IL-2 and diphtheria toxin (Denileukin Diftitox, DAB389IL-2, ONTAK) to eliminate regulatory T lymphocytes in patients with melanoma. *J Immunother* 28(6):582-592, 2005
111. Zou W: Regulatory T cells, tumour immunity and immunotherapy. *Nat Rev Immunol* 6(4):295-307, 2006
112. Olsen E et al: Pivotal phase III trial of two dose levels of denileukin diftixox for the treatment of cutaneous T-cell lymphoma. *J Clin Oncol* 19(2):376-388, 2001
113. Talpur R et al: CD25 expression is correlated with histological grade and response to denileukin diftixox in cutaneous T-cell lymphoma. *J Invest Dermatol* 126(3):575-583, 2006
114. Bagel J et al: Administration of DAB389IL-2 to patients with recalcitrant psoriasis: A double-blind, phase II multicenter trial. *J Am Acad Dermatol* 38(6 Pt 1):938-944, 1998
115. Gottlieb AB et al: Use of interleukin-2 fusion protein, DAB389-IL-2, for the treatment of psoriasis. *Dermatol Ther* 5:48-63, 1998

