

Drug Description

PRO 542 is a recombinant fusion protein comprising human IgG2 in which the Fv portions of both the heavy and light chains have been replaced by the D1D2 domains of human CD4. [1]

HIV/AIDS-Related Uses

PRO 542 has broad and potent activity against HIV -1 in vitro[2] and has demonstrated encouraging antiviral activity in humans.[3]

PRO 542 has been studied in Phase I trials in HIV infected adults and children. It is currently being investigated for the treatment of HIV in Phase II clinical studies.[4]

Pharmacology

CD4 is a high affinity receptor for HIV. PRO 542 incorporates the gp120 binding region of CD4 and therefore has the potential to bind and neutralize all strains of HIV. CD4-based molecules neutralize HIV by several mechanisms, including competitive inhibition of attachment, dissociation of the exterior envelope glycoprotein (gp120), and inhibition of cell-to-cell transmission of the virus. The incorporation of a human IgG2 heavy chain increases the half-life and minimizes the potential for immunogenicity of the protein.[5]

In a Phase I study of HIV infected adults, evidence of antiviral activity was observed as a reduction in plasma HIV RNA levels. Area under the concentration-time curve (AUC) and peak serum concentrations (C_{max}) increased linearly with dose. The observed terminal serum half-life was 3 to 4 days. No patient developed antibodies to PRO 542.[6]

PRO 542 has also been studied in HIV infected children in a Phase I/II study. Dose proportionality was also observed in children. Acute decreases in HIV RNA concentration of greater than 0.7 log₁₀ copies/ml were observed in four of six children treated with four weekly 10mg/kg doses. Reductions on HIV RNA levels were sustained for 14 days after treatment in three children.[7]

Adverse Events/Toxicity

In early clinical trials, PRO 542 has been well tolerated and no safety concerns have been raised.[8] [9] [10]

Drug and Food Interactions

In vitro, PRO 542 and enfuvirtide (Fuzeon) are potentially synergistic in blocking virus-cell and cell-cell fusion. Synergistic inhibition of virus-cell and cell-cell fusion has been observed for phenotypically diverse viruses over a broad range of drug concentrations.[11]

Clinical Trials

For information on clinical trials that involve PRO 542, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: PRO 542 AND HIV Infections.

Dosing Information

Mode of Delivery: Intravenous.[12]

Dosage Form: PRO 542 is prepared as a liquid in Phosphate Buffered Saline at a concentration of 5 mg/ml. Vials containing 5 mg, 20 mg, or 100 mg are available for clinical trials.[13]

Storage: PRO 542 should be stored at or below -70 C.[14]

Chemistry

CAS Number: 383198-58-1[15]

Other Names

PRO-542[16]

CD4-IgG2[17]

Further Reading

Ketas TJ, Frank I, Klasse PJ, Sullivan BM, Gardner JP, Spenlehauer C, Nesis M, Olson WC, Moore JP,

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Further Reading (cont.)

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Nagashima KA, Thompson DA, Rosenfield SI, Maddon PJ, Dragic T, Olson WC. Human immunodeficiency virus type 1 entry inhibitors PRO 542 and T-20 are potently synergistic in blocking virus-cell and cell-cell fusion. *J Infect Dis.* 2001 Apr 1;183(7):1121-5.

Shearer WT, Israel RJ, Starr S, Fletcher CV, Wara D, Rathore M, Church J, DeVille J, Fenton T, Graham B, Samson P, Staprans S, McNamara J, Moyer J, Maddon PJ, Olson WC. Recombinant CD4-IgG2 in human immunodeficiency virus type 1-infected children: phase 1/2 study. The Pediatric AIDS Clinical Trials Group Protocol 351 Study Team. *J Infect Dis.* 2000 Dec;182(6):1774-9.

Jacobson JM, Lowy I, Fletcher CV, O'Neill TJ, Tran DN, Ketas TJ, Trkola A, Klotman ME, Maddon PJ, Olson WC, Israel RJ. Single-dose safety, pharmacology, and antiviral activity of the human immunodeficiency virus (HIV) type 1 entry inhibitor PRO 542 in HIV-infected adults. *J Infect Dis.* 2000 Jul;182(1):326-9.

Manufacturer Information

PRO 542
Progenics Pharmaceuticals, Inc.
777 Old Saw Mill Road
Tarrytown, NY 10591

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help
Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

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3. J Infect Dis - 2000 Dec;182(6):1774-9.
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