PROLASTIN®
alpha$_1$-proteinase inhibitor (human)
Continuous Commitment.

- The only alpha$_1$-proteinase inhibitor with more than 17 years of continuous commitment
- Elevates AAT levels[12]
- Shown to improve survival rate and slow FEV_1 decline[13,14]*
- Well tolerated
- Easy to dose
- Free Talecris AlphaKit available for AAT testing

The most commonly reported side effect with Prolastin is flu-like symptoms, resolving spontaneously over 24 hours.[15]

*Nonrandomized/uncontrolled trials.

Before prescribing, please see full Prescribing Information inside back pocket.

For clinical and technical questions on Prolastin, call Talecris Clinical Communications at 1-800-520-2807.

For information on Talecris Direct, call 1-800-305-7881.

To order free Talecris AlphaKits, call 1-800-562-7222.

Patient Notification System
for the plasma-derived and recombinant analog industry
www.patientnotificationsystem.org

Talecris Biotherapeutics funds and supports the Patient Notification System—fast, confidential notification of plasma product withdrawals and recalls. 1-888-UPDATE-U

QSEAL

The Plasma Protein Therapeutics Association (PPTA) recognized Talecris Biotherapeutics as an industry leader that voluntarily goes beyond regulatory requirements to enhance the safety and quality of life-saving plasma therapies through the QSEAL (Quality Standards of Excellence, Assurance and Leadership) certification. PPTA (Tel) 202-789-3100 www.plasmatherapeutics.org

Talecris BIOTHERAPEUTICS

 Printed in USA September 2005 01015N

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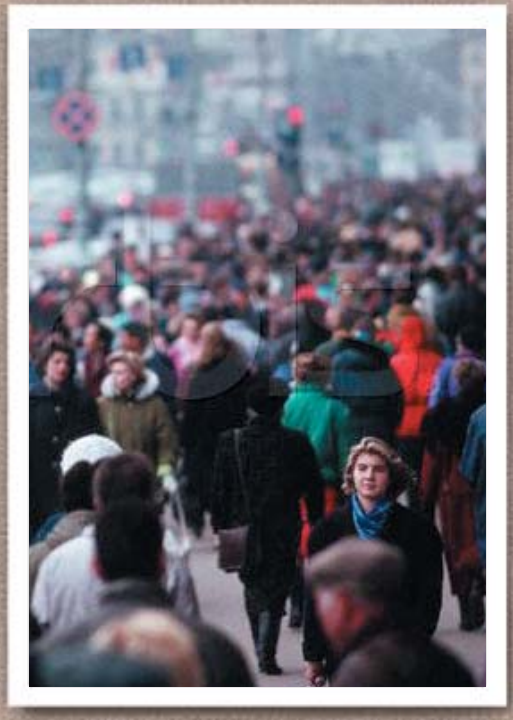
Alpha$_1$-antitrypsin Deficiency

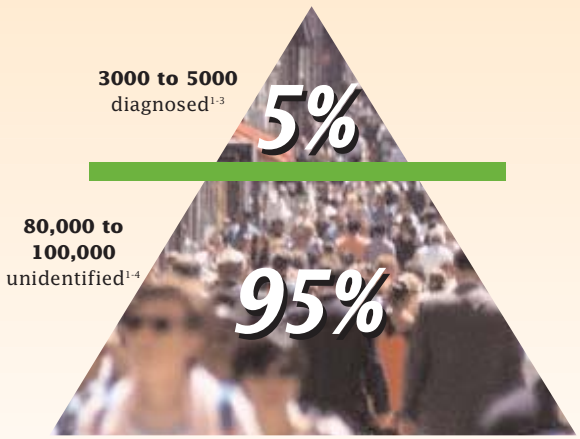
5000 Americans diagnosed with AAT deficiency are just...



Talecris BIOTHERAPEUTICS

...the tip of the iceberg

Alpha$_1$-antitrypsin (AAT) deficiency: The fatal pulmonary disease undetected in 95% of cases



- North American/European prevalence: 1 in 2000 to 7000, comparable to cystic fibrosis[3]
- Occurs in up to 3% of patients with chronic obstructive lung disease[3]
- Caused by genetic mutation found primarily in patients of northern European descent[5]
- Deficiency of AAT exposes lung tissue to erosion by AAT-neutralized enzyme[1,6]

AAT deficiency: Often misdiagnosed as asthma or chronic obstructive pulmonary disease (COPD)[7]

	Signs and symptoms	Response: inhaled ß agonists/ steroids	Age of onset	Chest x-ray
AAT deficiency	Dyspnea, wheeze, cough, weight loss, cor pulmonale, pneumonia	Poor	20–40	Bibasal bullous changes and avascularity, flattened diaphragm, pulmonary hypertension
Asthma	Dyspnea, wheeze, cough, flares, night symptoms	Good	2–20 and 40–50	Typically normal, no pulmonary hypertension
COPD	Same as for AAT deficiency	Variable	60–70	Upper-lobe bullous changes and avascularity, flattened diaphragm, pulmonary hypertension

Adapted from Pina and Horan.[7]

- Diagnosis, if it occurs, takes an average of 7.2 years after symptom onset[4]
- Lung function spirals down year after year, leading to early disability and mortality[4,7,8]
- Missed or late diagnosis deprives patient of proper care[1,9]
- Only a specific blood test can diagnose AAT deficiency

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ATS/ERS recommendations for AAT deficiency testing[10]:

- COPD (all subjects)
- Early-onset pulmonary emphysema (regardless of smoking history)
- Family members of known AAT-deficient patients
- Dyspnea and cough occurring in multiple family members (same or different generations)
- Liver disease of unknown cause
- Adults with bronchiectasis without evident etiology
- Patients with asthma whose spirometry fails to return to normal with therapy
- Unexplained panniculitis and antiproteinase-3 vasculitis

Talecris Biotherapeutics: Committed to the identification and treatment of AAT deficiency

Test with our FREE Talecris AlphaKit

The Talecris AlphaKit contains: data form, special filter paper for sampling, device for obtaining blood sample from a fingerstick, full instructions, and return envelope for sending sample by regular mail

- Validated, simple testing method[2,11]
- Measures AAT levels and, if needed, genetic phenotype
- Results in 10 working days
- All costs paid by Talecris Biotherapeutics

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Treat with Prolastin, alpha$_1$-proteinase inhibitor (human)

- The only alpha$_1$-proteinase inhibitor with more than 17 years of continuous commitment
- Produced sustained elevation of AAT levels in the lower respiratory tract[12]
- Slowed decline in forced expiratory volume in 1 second (FEV_1)*[13,14]
- Improved survival versus no-replacement therapy*[13]
- Easy to administer, usually reimbursable

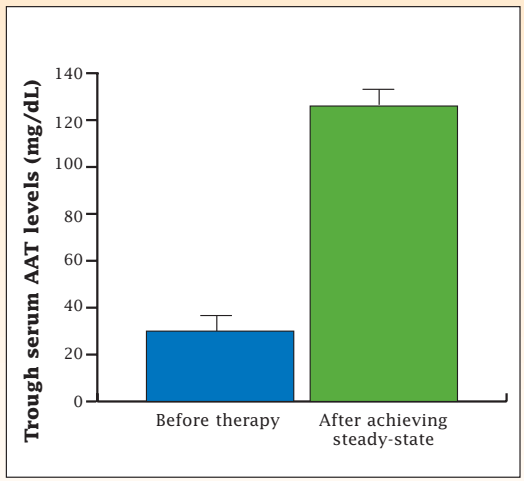
Prolastin—alpha$_1$-proteinase inhibitor (human)—is contraindicated in individuals with selective immunoglobulin A (IgA) deficiencies who have known antibody against IgA (anti-IgA antibody), since these patients may experience severe reactions, including anaphylaxis, to IgA that may be present.

*Clinical trials simultaneously meeting all 4 criteria—prospective, long-term, controlled, and randomized—have not been performed to evaluate the effect of chronic replacement therapy with Prolastin on the regression or progression of emphysema in AAT deficiency. Prolastin does not correct any underlying lung damage induced by AAT deficiency, but may retard the progression of lung damage.

Prolastin

Raises AAT levels without compromising safety

Markedly increased patients' levels of AAT[12]



Trial of 21 patients with AAT deficiency, evaluated before treatment and weekly for up to 6 months during therapy with an alpha$_1$-proteinase inhibitor (Cutter Biological). An additional 9 normal subjects served as controls, with an average serum AAT level of 220 mg/dL.

- Over a 1-month period, treated patients averaged AAT levels within normal range (163 ± 4 mg/dL)[12]
- AAT levels in the epithelial-lining fluid of the lungs was significantly increased from baseline after 6 days of treatment ($P<0.0001$)

This product is prepared from pooled human plasma, which may contain the causative agents of hepatitis and other viral diseases. While collection and manufacturing procedures are designed to minimize risk of virus transmission, this risk cannot be completely eliminated.

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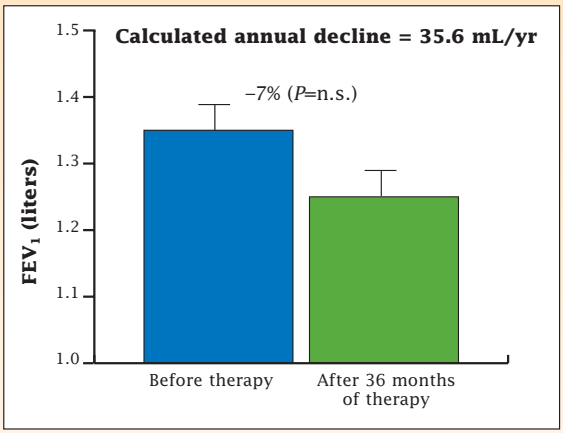
Slower-than-expected long-term decline in FEV_1



Uncontrolled, prospective study of 20 patients with severe AAT deficiency followed during 36 months with $alpha_1$-proteinase inhibitor. Expected decline in FEV_1 in patients with nonaugmented AAT deficiency may range from 40 mL/y to 316 mL/y (120 mL/36 mo to 948 mL/36 mo).[14]

- Prolastin, $alpha_1$-proteinase inhibitor (human), significantly delayed the decline in FEV_1 among patients with baseline FEV_1 35% to 49% predicted (P=0.03)[13]

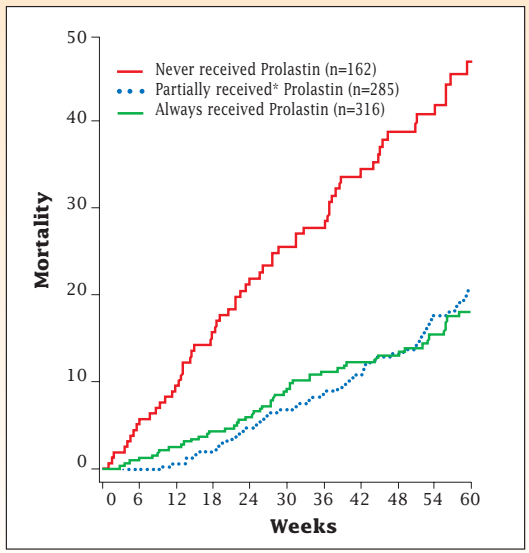
The most commonly reported side effect with Prolastin is flu-like symptoms, resolving spontaneously over 24 hours.[15]

Prolastin

Delays the progression of AAT deficiency

Significantly higher survival rates with Prolastin[13]

In patients with baseline FEV_1 <50% predicted



Nonrandomized multicenter study evaluating AAT augmentation with Prolastin in a database of 1129 patients enrolled in the $Alpha_1$-Antitrypsin Deficiency Registry of the National Heart, Lung, and Blood Institute (NHLBI). Adapted from $Alpha_1$-Antitrypsin Deficiency Registry Study Group.[9,13]

*Patients partially receiving therapy either started therapy >3 months after study enrollment, permanently discontinued therapy, or temporarily stopped then restarted therapy.

- Overall mortality risk significantly lower for Prolastin recipients than for nonrecipients —Risk ratio = 0.64:1, recipients versus nonrecipients, P=0.02.

- Mortality risk especially reduced among patients with baseline FEV_1 35% to 49% predicted —Risk ratio = 0.21:1, recipients versus nonrecipients, P<0.001.

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Well tolerated in clinical studies at 60 mg/kg weekly[15]

Flu-like symptoms the most common adverse reaction	
Adverse effect	% of patients
Delayed fever (self-limiting within 24 h)	0.77%
Light-headedness	0.19%
Dizziness	0.19%

- In clinical trials, only 6 reactions, none severe, were observed in 517 infusions of Prolastin, alpha$_1$-proteinase inhibitor (human)
- Mild transient leukocytosis and dilutional anemia also reported several hours after infusion
- Since market entry, occasional reports of other flu-like symptoms, allergic-like reactions, chills, dyspnea, rash, tachycardia, and, rarely, hypotension have been received[15]

Prolastin

Easy to dose

- 60 mg/kg intravenously once weekly
- 30-minute infusion at home, in the hospital, or in the physician's office

Backed by Talecris Biotherapeutics

- Ongoing support to the Alpha-1 community through grants, programs, educational materials, and sponsorship of Team Alpha-1

Free Talecris AlphaKit

- Talecris Biotherapeutics pays all costs for AAT testing
- To order Talecris AlphaKits, call 1-800-562-7222

References:

1. Mullins CD, Blatt L, Wang J. Societal implications of the pharmacoeconomics of α_1-antitrypsin deficiency. *Expert Rev Pharmacoeconomic Outcomes Res.* 2002;2:243-249. **2**. Campbell EJ. Alpha1-antitrypsin deficiency: incidence and detection program. *Respir Med.* 2000;94 Suppl C:S18-S21. **3**. World Health Organization. Alpha$_1$-Antitrypsin Deficiency. Memorandum from a meeting, 1997. Available at: www.alpha1.org.uk,. Accessed July 22, 2002. **4**. Stoller JK, Smith P, Yang P, Spray J. Physical and social impact of alpha 1-antitrypsin deficiency: results of a survey. *Cleve Clin J Med.* 1994;61:461-467. **5**. Miravitlles M. Alpha$_1$-antitrypsin deficiency: epidemiology and prevalence. *Respir Med.* 2000;94 Suppl C:S12-S15. **6**. Lomas DA. Loop-sheet polymerization: the mechanism of alpha$_1$-antitrypsin deficiency. *Respir Med.* 2000;94 Suppl C: S3-S6. **7**. Pina JS, Horan MP. Alpha$_1$-antitrypsin deficiency and asthma. The continuing search for the relationship. *Postgrad Med.* 1997;101:153-156, 159-162, 167-168. **8**. Buist AS. Alpha1-Antitrypsin deficiency—diagnosis, treatment, and control: identification of patients. *Lung.* 1990;168 Suppl:543-551. **9**. McElvaney NG, Stoller JK, Buist AS, et al. Baseline characteristics of enrollees in the National Heart, Lung, and Blood Institute Registry of Alpha1-antitrypsin deficiency. *Chest.* 1997;111:394-403. **10**. American Thoracic Society/European Respiratory Society Statement: Standards for the Diagnosis and Management of Individuals with Alpha-1 Antitrypsin Deficiency. *Am J Respir Crit Care Med.* 2003;168:818-900. **11**. Wencker M. Screening for alpha1-Pi deficiency in patients with lung diseases. *Respir Med.* 2000;94 Suppl C:S16-S17. **12**. Wewers MD, Casolaro MA, Sellers SE, et al. Replacement therapy for alpha1-antitrypsin deficiency associated with emphysema. *N Engl J Med.* 1987;316:1055-1062. **13**. Survival and FEV$_1$ decline in individuals with severe deficiency of alpha1-antitrypsin. The Alpha-1-Antitrypsin Deficiency Registry Study Group. *Am J Respir Crit Care Med.* 1998;158:49-59. **14**. Schwaiblmair M, Vogelmeier C, Fruhmann G. Long-term augmentation therapy in twenty patients with severe alpha-1-antitrypsin deficiency—three-year follow-up. *Respiration.* 1997;64:10-15. **15**. Prolastin® full Prescribing Information. Research Triangle Park, NC: Talecris Biotherapeutics, Inc; 2005.

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