



SARGRAMOSTIM IN THE MANAGEMENT OF FUNGAL INFECTIONS

SEPTEMBER 25, 2020

Sargramostim - Ready for Investigational Use Today



- FDA approved in 6 disease indications →
 - > 500,000 recipients
 - **Safe in pediatrics and adults**
- Leukine® 250 mcg/single-dose vials
 - Given by **nebulizer for investigational use**



Leukine®
sargramostim

250 mcg/single-dose vial
Refrigerate, 2-8°C (36-46°F)
Do not freeze or shake
Protect from light

NDC 71837-5843-1
Rx only Dosage: See insert
Mfd. by: Partner Therapeutics, Inc.
Lexington, MA 02421



(01)00371837584316

RL10152

U.S. Lic. No. 2087 AW001-00

Labeled indications:

- 1) Shorten time to neutrophil recovery and reduce incidence of severe life-threatening, and fatal infections in adults over 55 years old after induction chemotherapy for acute myeloid leukemia
- 2) Mobilization of hematopoietic progenitor cells for autologous transplantation in adults
- 3) Acceleration of myeloid reconstitution after autologous stem cell transplantation
- 4) Acceleration of myeloid reconstitution after allogeneic stem cell transplantation
- 5) Treatment of delayed neutrophil recovery or graft failure after bone marrow transplantation in adults or children at least 2 years of age
- 6) To increase survival after acute exposure to myelosuppressive doses of radiation

Inhalation Safety Data Supports Investigational Use

Existing Product, Delivered with Standard Nebulizers



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled GM-CSF for Pulmonary Alveolar Proteinosis

R. Tazawa, T. Ueda, M. Abe, K. Tatsumi, R. Eda, S. Kondoh, K. Morimoto, Takeshi Tanaka, E. Yamaguchi, A. Takahashi, M. Oda, H. Ishii, S. Izumi, H. Sugiyama, A. Nakagawa, K. Tomii, M. Suzuki, S. Konno, S. Ohkouchi, N. Tode, T. Handa, T. Hirai, Y. Inoue, T. Arai, K. Asakawa, T. Sakagami, A. Hashimoto, Takahiro Tanaka, T. Takada, A. Mikami, N. Kitamura, and K. Nakata

CHEST

Original Research

DIFFUSE LUNG DISEASE

Duration of Benefit in Patients With Autoimmune Pulmonary Alveolar Proteinosis After Inhaled Granulocyte-Macrophage Colony-Stimulating Factor Therapy

Ryushi Tazawa, MD; Yoshikazu Inoue, MD; Toru Arai, MD; Toshihori Takada, MD; Yiamnori Kasahara, MD, FCCP; Masayuki Hojo, MD; Shinya Ohkouchi, MD; Yoshiko Tsuchihashi, MD; Masanori Yokokura, MD; Ryosuke Eda, MD; Hideaki Nakayama, MD; Hayayuki Ishii, MD; Takanobu Nei, MD; Konosuke Morimoto, MD; Yasuyuki Nasuhara, MD, FCCP; Masahiro Ebina, MD; Masanori Akira, MD; Toshiro Ichinose, MD; Koichiro Tatsumi, MD, FCCP; Etsuro Yamaguchi, MD; and Koh Nakata, MD

Clin Drug Investig (2014) 34:553–564
DOI 10.1007/s40261-014-0208-z

ORIGINAL RESEARCH ARTICLE

Long-Term Inhaled Granulocyte Macrophage–Colony-Stimulating Factor in Autoimmune Pulmonary Alveolar Proteinosis: Effectiveness, Safety, and Lowest Effective Dose

Spyros A. Papiris • Panagiotis Tsirigotis • Likurgos Kolilekas • Georgia Papadaki • Andriana I. Papaiannou • Christina Triantafyllidou • Anastasis Papaporfiriou • Anna Karakatsani • Konstantinos Kageouridis • Matthias Gries • Effrosyni D. Manali

Sheng et al. Respiratory Research
<https://doi.org/10.1186/s12931-018-0862-4>

Respiratory Research

RESEARCH

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Better approach for autoimmune pulmonary alveolar proteinosis treatment: inhaled or subcutaneous granulocyte-macrophage colony-stimulating factor: a meta-analyses

Gaohong Sheng¹*, Peng Chen^{2,3†}, Yanqiu Wei¹, Jiaoqiao Chu¹, Xiaolei Cao⁴ and Hui-Lan Zhang^{1,5} 

The Aerogen® Ultra

High-Performance Aerosol Drug Delivery



Chronic investigational nebulized therapy – feasible and tolerable

Anti-infectious, including antifungal, mechanisms of GM-CSF



- Increase proliferation of myeloid-derived cell, including neutrophils
- Activate and differentiate myeloid cells, including macrophages and dendritic cells

1. Enhance neutrophil **oxidative burst** and antifungal activity via NADPH oxidase¹
2. Limit dimorphic fungus survival in macrophages through **zinc sequestration** and ROS generation²
3. Increase expression of pattern-recognition receptor **Dectin-1** in macrophages³
4. Increase expression of **myeloperoxidase** in neutrophil extracellular traps⁴
5. Increase **chitotriosidase** expression (cleaves *Candida* chitin)⁵

Proof of Mechanism: murine *Aspergillus* model⁶

Summary – Sargramostim for Fungal Infections



1. Nebulized and systemic sargramostim **available now** for investigational use
2. Inhalational safety data support **combination testing** with antifungal agents
3. Nonredundant mechanisms demonstrate *in vivo* proof of mechanism

We Seek To Partner To Advance Antifungal Therapy

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