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

**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
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 oxidase
2. Limit dimorphic fungus survival in macrophages through zinc sequestration and ROS generation
3. Increase expression of pattern-recognition receptor Dectin-1 in macrophages
4. Increase expression of myeloperoxidase in neutrophil extracellular traps
5. Increase chitotriosidase expression (cleaves Candidal chitin)

Proof of Mechanism: murine Aspergillus model

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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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