Bridging the Bronchiectasis GAP:

The Latest Emerging Multimodal Treatment Approaches

KEY TAKEAWAYS

Symptoms Indicative of Bronchiectasis[1-3]

Unique features	Overlap with other pulmonary diseases	May be part of other systemic diseases
• Productive cough • Hemoptysis • Recurrent infectious exacerbations & frequent antibiotics • Persistent bacterial infection	• Chronic obstructive pulmonary disease • Asthma	• Genetic and congenital causes • Autoimmune • Immunodeficiency • Gastrointestinal (inflammatory bowel disease, gastroesophageal reflux) • Persistent cough despite treatment

The Role of Neutrophilic Inflammation and the Impact of Pulmonary Exacerbations

- Inflammation in bronchiectasis is typically driven by neutrophils
- Neutrophil numbers and markers of activation correlate with bacterial load
  - Higher neutrophil levels = higher rates of exacerbations
- DPP-1 activates neutrophil serine proteases (NSPs), which activate:
  - Neutrophil elastase (NE)
  - Proteinase 3 (PR3)
  - Cathepsin G (CatG)
- NSPs can:
  - Degrade extracellular matrix components
  - Disrupt epithelial barrier integrity

Provided by The France Foundation

Bridging the Bronchiectasis GAP:

The Latest Emerging Multimodal Treatment Approaches

K E Y T A K E A W A Y S

Implementing a Multimodal Treatment Approach to Improve Outcomes[4-7]

- Airway clearance is key and foundational to every treatment plan

There is no one treatment for bronchiectasis. Instead, we rely on several pharmacologic and non-pharmacologic treatments.

Order of administration:

1st: Short-acting bronchodilators

2nd: Mucolytics

3rd: Airway clearance techniques

4th: Inhaled antibiotics

5th: Inhaled corticosteroids

Bronchodilators

FEV1 ↑ (in BCOS)

Inhaled antibiotics

Bacteria load ↓, QOL ↑, exercise capacity ↑, exacerbation ↓

Mucoactive drugs

- Isotonic saline/humidification – sputum clearance ↑
- Hypertonic saline – QOL ↑, sputum clearance ↑
- Inhaled dry powder mannitol – sputum clearance ↑, antibiotics usage ↓, QOL ↑, time to next exacerbation ↑
- NAC – exacerbation risk ↓

Anti-inflammatory drugs

- ICS – benefits in eosinophilic bronchiectasis
- Brensocatib
- Long-term macrolides: QOL ↑, exacerbation ↓
- Additional therapies in clinical trials

Recently Approved Therapy: Brensocatib[8,9]

- Brensocatib is a small molecule inhibitor of DPP-1
  - Approved in August 2025 to treat non-cystic fibrosis bronchiectasis in patients aged ≥12 years
- Brensocatib reduces neutrophil-driven inflammation, leading to
  - Lower levels of neutrophil elastase and other proteases
  - Lung function improvement (measured by FEV1)
  - Reduced pulmonary exacerbations
  - Improved respiratory symptoms

Provided by The France Foundation

Bridging the Bronchiectasis GAP: The Latest Emerging Multimodal Treatment Approaches

K E Y T A K E A W A Y S

Considerations for Initiating Treatment With Brensocatib[10]

Domain	10 mg	25 mg	Clinical Implication
Exacerbations	Reduced vs placebo	Reduced vs placebo	Similar primary efficacy
FEV1 decline	No significant benefit	Significant benefit	25 mg better for lung-function preservation
Symptoms	Reduced but benefit is not significant	Greater improvement on QOL-B and BEST	25 mg better symptom relief
Safety	Slightly fewer skin AEs	More hyperkeratosis, still usually mild	10 mg may be used if toxicity limits 25 mg

Key Takeaways

1. Early diagnosis is important, and clinicians should consider bronchiectasis in patients with chronic cough and recurrent chest infections
2. Early identification of exacerbations can lead to better patient outcomes
3. Airway clearance is key and foundational
   - Airway clearance comes in many shapes and sizes—consistency is key
   - Needs to be discussed with patients, revisited at each encounter, and possibly logged or tracked for adherence
4. Brensocatib is the first FDA-approved medication for bronchiectasis
   - Reduces neutrophil-driven inflammation by inhibiting DPP-1
5. Additional therapeutics targeting neutrophilic inflammation are in development

Provided by The France Foundation

Bridging the Bronchiectasis GAP: The Latest Emerging Multimodal Treatment Approaches

KEY TAKEAWAYS

References

1. McFarlane L, et al. *Clin Med (Lond).* 2021;21(6):e571-e577.
2. O'Donnell AE. *N Engl J Med.* 2022;387(6):533-545
3. Hill AT, et al. *Thorax.* 2019;74 (suppl 1):1-69.
4. Herrero-Cortina B, et al. *Eur Respir J.* 2023;62(1):2202053.
5. McShane PJ, et al. *Am J Respir Crit Care Med.* 2013; 18:647–656.
6. Choi JY. *Tuberc Respir Dis.* 2023;86(3):183-195.
7. Agent P, et al. *Breathe (Sheff).* 2015;11(2):110-118.
8. Bell SC, Grimwood K. *Engl J Med.* 2025;392(17):1635-1637
9. Chalmers JD, et al. *N Engl J Med.* 2025;392(16):1569-1581.
10. Chalmers JD, Daley CL. *Am J Respir Crit Care Med.* Published online March 30, 2026.

Provided by The France Foundation