

Modeling the Impact of Sotatercept on Morbidity and Mortality in Pulmonary Arterial Hypertension: A Mexican Population Health Perspective

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Introduction

- Pulmonary Arterial Hypertension (PAH) is a rare, progressive disease associated with significant morbidity and high mortality
- In Mexico, PAH management is complicated by delayed diagnosis and limited access to specialized care, often resulting in patients presenting with advanced disease and fewer treatment options¹
- Although current guidelines recommend PAH-targeted therapies such as endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, and prostacyclin pathway agents, many patients continue to experience disease progression and poor long-term outcomes²
- Beyond clinical challenges, PAH is associated with frequent hospitalizations and costly interventions such as lung or heart–lung transplantation, adding pressure to Mexico's healthcare resources
- Sotatercept, a novel activin signaling inhibitor, demonstrated substantial clinical benefits when added to background therapy (BGT) in the phase 3 STELLAR trial³
- The management of PAH involves lifelong treatment, yet clinical evidence for PAH therapies is generally collected in clinical trials with a short duration. Therefore, assessing clinical benefits over a longer period of time can help clinical decision making

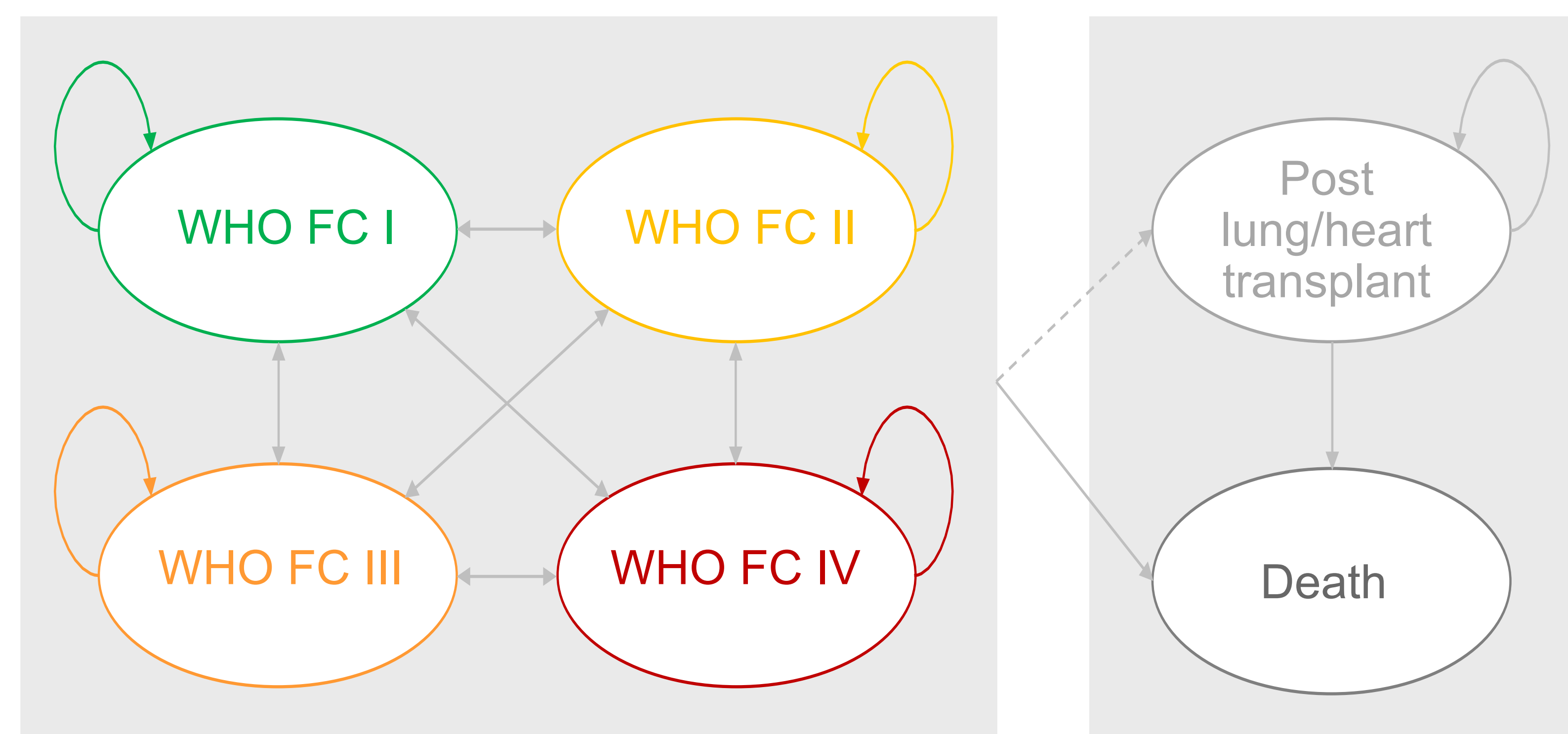
Objective

To model the clinical impact of adding sotatercept to BGT compared with BGT alone in Mexican patients with PAH, reflecting the population enrolled in the STELLAR study—adults with World Health Organization (WHO) functional class (FC) II or III receiving stable background therapy, by estimating improvements in survival and reductions in hospitalizations and lung or heart–lung transplants over a 10-year time horizon.

Model methods

A six-state Markov model (Figure 1) was developed to project clinical outcomes for Mexican patients with PAH over 10 years, comparing sotatercept + BGT with BGT alone. Health states were based on WHO FC I–IV and included post–lung/heart–lung transplant, and death. Transition probabilities were sourced from STELLAR, and mortality rates—adjusted for WHO FC—were derived from the COMPERA registry and related published literature. Hospitalization and transplant rates were informed by published Mexican literature. All parameter values and sources are presented in Table 1. A 5% annual discount rate was applied to all clinical outcomes.⁴

Figure 1. Model structure



FC, functional class; WHO, World Health Organization.

Table 1. Model inputs and data sources

Inputs	Details	Source
Baseline patient characteristics	Mean age: 47.9 years; Female: 79.3%; Male: 20.7%	STELLAR ³
Baseline patient distribution*	WHO FC I: 0.0%; WHO FC II: 63.9%; WHO FC III: 36.1%; WHO FC IV: 0.0%	Jerjes-Sánchez C, et al. 2024 ¹
HR of all-cause mortality (sotatercept + BGT vs BGT alone)	0.25	McLaughlin, et al. 2024 ⁵
Probability of lung/heart–lung transplant per 12-week cycle**	WHO FC I: 0.9%; WHO FC II: 1.9%; WHO FC III: 3.0%; WHO FC IV: 4.1%	Diez, et al. 2023 ⁶
Probability of post-transplant mortality per 12-week cycle	2.8%	Bernstein, et al. 2018 ⁷
Probability of PAH hospitalization per 12-week cycle	WHO FC I: 4.5%; WHO FC II: 6.7%; WHO FC III: 12.9%; WHO FC IV: 20.5%	Klok, et al. 2024 ⁸
Lung/heart–lung transplant hospitalization assumption	4.5%	Assumption based on clinical expert opinion
HR of PAH hospitalization (sotatercept + BGT vs BGT alone)	0.08	STELLAR; MSD data on file, 2023
RR for WHO FC improvement (sotatercept vs placebo)	2.02	
RR for WHO FC worsening (sotatercept vs placebo)	0.34	

*Based on the Mexican registry, the proportion of patients in Functional Class (FC) I, II, III, and IV is 10.8%, 55.7%, 31.4%, and 2.0%, respectively. Since the model begins with patients in FC II and FC III, the percentages were normalized to 63.9% (55.7 / [55.7 + 34.1]) for FC II and 36.1% (34.1 / [55.7 + 34.1]) for FC III.

**Due to the lack of information, we assume that data by functional class are similar to those by risk status. The formula used converts a yearly rate into a 12-week probability using a compounding method: $1 - (1 - \text{yearly probability})^{1/5}$ (weeks per month). Values for FC III and FC IV are linearly extrapolated based on those for FC I and FC II.

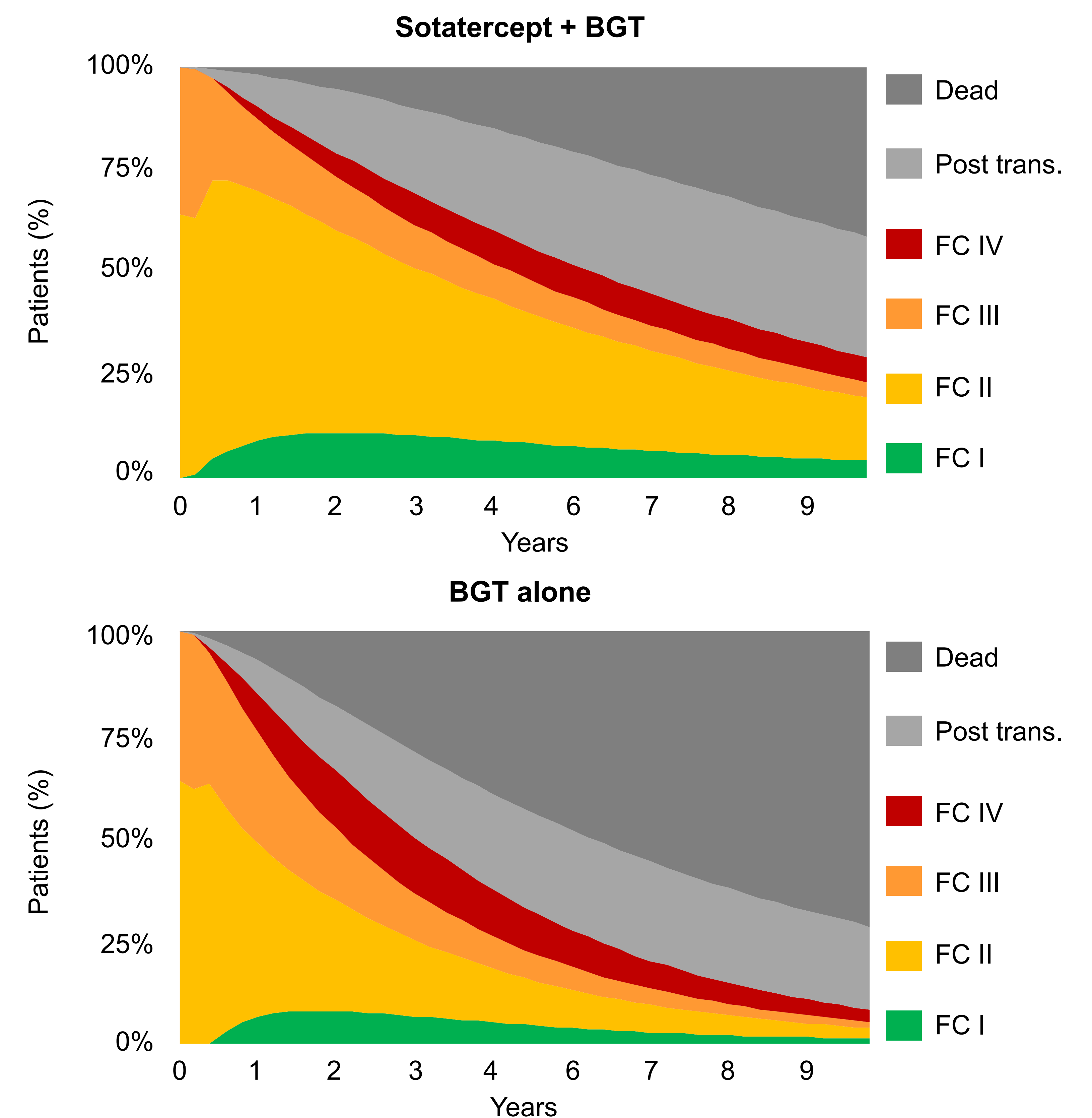
Model results

- Sotatercept + BGT was expected to maintain a greater proportion of patients in lower WHO functional classes (FC I–II) for a longer duration, while slowing progression to FC III/IV and reducing mortality compared with BGT alone (Figure 2)
- Over a 10-year period, sotatercept + BGT increased average life expectancy to 6.47 years, compared with 4.85 years for BGT alone, representing a survival gain of 1.62 life years
- For every 1,000 patients, sotatercept + BGT was projected to reduce PAH-related hospitalizations by ≈90% (1,714 fewer hospitalizations) and prevent 5.39 lung or heart–lung transplants
- Applied to Mexico's estimated 4,694 adult PAH patients in 2025, these benefits translate to approximately 8,045 hospitalizations avoided and 25 transplants prevented compared with BGT alone

References

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Figure 2. Patient distribution (without half cycle correction)



FC, functional class; WHO, World Health Organization.

Discussions and Conclusions

- The inclusion of sotatercept alongside BGT marks a notable step forward in PAH treatment in Mexico, offering enhanced outcomes compared to BGT alone
- Model projections suggest that the introduction of sotatercept will reduce disease burden by improving survival, lowering hospitalization rates, and maintaining patients in less severe WHO functional classes for longer
- These projected benefits are particularly relevant in Mexico, where access to complex interventions like lung transplantation is scarce and PAH care is largely centralized in a few expert centers
- By helping stabilize patients earlier and reducing dependence on intensive medical resources, sotatercept aligns with Mexico's national efforts to improve chronic disease care and broaden access to specialized therapies
- Overall, these findings highlight sotatercept's potential to significantly improve clinical outcomes and optimize resource use for PAH patients in Mexico



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