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"TARGETING INFLAMMATION IN NCFBE: PHARMACOKINETIC AND PHARMACODYNAMIC INSIGHTS ON BRENSOCATIB"

SOWMIYA S. Pharm D (PB) V Year.

Under the guidance of Dr. M. Dheenadhayalan

School Of Pharmaceutical Sciences, VISTAS, Tamil Nadu, India- 600117

Email ID- sakthivelopd@gmail.com

ABSTRACT:

Background:
Non-cystic fibrosis bronchiectasis (NCFBE) is marked by chronic airway inflammation where neutrophil serine proteases play a central role. Brensocatib, an oral dipeptidyl peptidase-1 inhibitor, prevents activation of these enzymes and may reduce disease burden.

Objective:
To characterize the pharmacokinetics of brensocatib, assess exposure–response relationships for efficacy and safety, and inform dose selection.

Methods:
Data from phase I (healthy adults) and phase II (NCFBE patients) studies were pooled to develop a population PK model. Covariates affecting drug disposition were examined, and pharmacokinetic/pharmacodynamic (PK/PD) associations with sputum neutrophil elastase, pulmonary exacerbations, and adverse events were explored.

Results:
A two-compartment model with linear clearance best described the data. Age influenced distribution volume, and renal function affected clearance, though changes were not clinically significant. Higher exposures correlated with suppression of neutrophil elastase and fewer exacerbations, while safety outcomes showed no exposure-related trends.

Conclusions:
Brensocatib demonstrated predictable PK and meaningful PD effects in NCFBE. Once-daily doses of 10 mg and 25 mg achieved target engagement and favourable safety, supporting their use in phase III clinical development.

Keywords:

Brensocatib, Dipeptidyl peptidase-1 (DPP-1) inhibitor, non-cystic fibrosis bronchiectasis (NCFBE).