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ENaC inhibition in cystic fibrosis: potential role in the new era of CFTR modulator therapies

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ENaC inhibition with BI 1265162 is a promising strategy to optimise outcomes in patients with CF either eligible, or ineligible, for CFTR modulator therapy. Phase II clinical trials of BI 1265162 must now show this translates into clinical benefit. https://bit.ly/2OQ1IUI

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Small-molecule cystic fibrosis transmembrane conductance regulator (CFTR) modulator drugs for cystic fibrosis are the first therapies since the disease was initially described by Fanconi *et al.* [1] in 1936 to target and partially restore the function of the CFTR Cl^- channel. CFTR modulator therapy is expected to have significant clinical benefits for many, but it does not result in a cure and is not appropriate or available for all patients with cystic fibrosis [2, 3]. In this review, evidence is described suggesting that inhibiting the epithelial Na^+ channel (ENaC) responsible for the Na^+/fluid absorption that contributes to airway surface dehydration and impaired mucociliary clearance (MCC) observed in cystic fibrosis airways may significantly improve clinical outcomes irrespective of the CFTR genotype, and may synergise with currently approved CFTR modulators to further improve clinical outcomes.