PALLADIUM

A Phase III study assessing the efficacy and safety of two doses of QMF149 (indacaterol acetate[IND]/mometasone furoate [MF]) delivered via the dose-confirming Breezhaler® device in patients with uncontrolled asthma[1].

PALLADIUM overview

PALLADIUM evaluates the efficacy and safety of IND/MF and is one of the Phase III studies in the PLATINUM clinical development program. This 52-week, multicenter, double-blind, triple dummy, parallel-group study is designed to evaluate the efficacy and safety of two different doses of IND/MF (medium: 150/160 µg and high: 150/320 µg delivered via Breezhaler®) versus two respective MF doses (medium: 400 µg and high: 800 µg delivered via Twisthaler®), and twice-daily salmeterol xinafoate/fluticasone propionate (50/500 µg delivered via Accuhaler®) in patients with uncontrolled asthma[1].

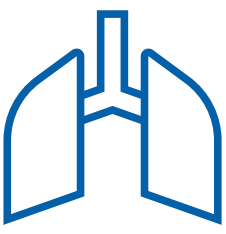
What is QMF149?

QMF149 is the fixed-dose combination of IND and MF and is currently in development for the treatment of patients with uncontrolled asthma. It combines the bronchodilation of the long-acting beta agonist (LABA) IND with the on-target anti-inflammatory effects of MF (an inhaled corticosteroid [ICS]) in a precise once-daily formulation, delivered via the dose-confirming Breezhaler® device.

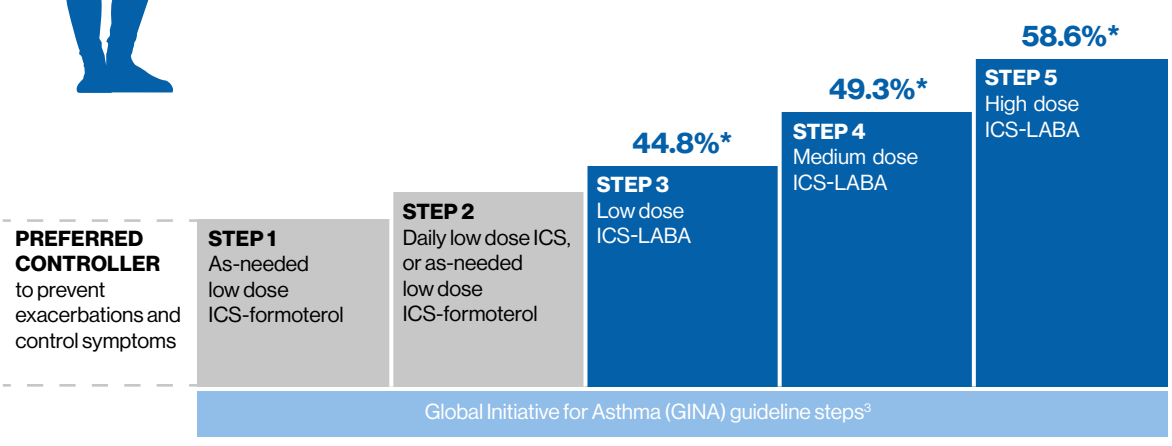
The Breezhaler® is a single-dose dry powder inhalation device and is well established in COPD. Following inhalation, patients are able to see if the transparent capsule is empty and therefore be able to confirm dose delivery[1].

What is asthma?

Asthma affects an estimated **358 million people** worldwide and can cause a significant personal, health and financial burden when uncontrolled[2]. It is a heterogeneous disease characterized by chronic airway inflammation[3] caused by multiple inflammatory pathways[4]. Symptoms of asthma include **coughing, wheezing and breathlessness**[5]. Worsening of these symptoms and lung function is defined as an asthma exacerbation[6]. Patients who have poor symptom control and frequent exacerbations despite current therapy may be considered inadequately controlled or uncontrolled[7].



Despite availability of numerous asthma treatments, over 40% of patients with asthma being treated with maintenance therapy at GINA Step 3, and over 45% at GINA Steps 4 and 5, remain **uncontrolled**[8]. Additionally, nearly 50% of patients with asthma fail to use their device correctly and are considered poorly adherent[9].



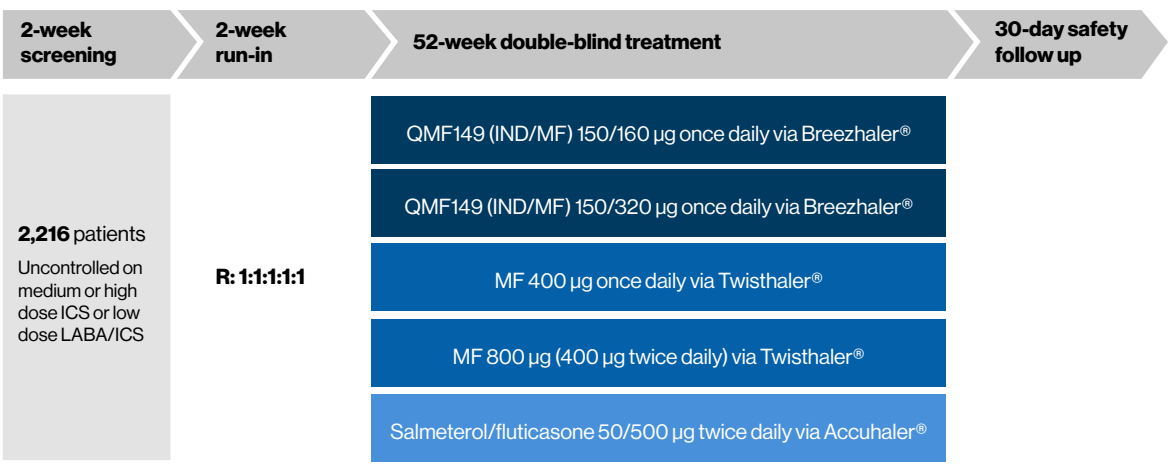
*of patients remain uncontrolled[8]

Adapted from GINA 2019

Trial design

PALLADIUM is a multicenter, parallel-group, Phase III, double-blind, triple-dummy study[1,10]

- The total patient population for the study included 2,216 patients, all of whom were symptomatic despite treatment with mid or high stable dose of ICS and/or low dose combinations of ICS with LABA
- Patients were randomized (1:1:1:1:1) to receive IND/MF (150/160 µg or 150/320 µg), MF (400 µg or 800 µg) or salmeterol/fluticasone (50/500 µg)
- The study included a 2-week screening period, a run-in period of 2 weeks, a 52-week treatment period and a 30-day follow-up period after the last dose of study drug



Primary objective[1,10]

The primary objective was to demonstrate the superiority of either IND/MF dose, delivered via Breezhaler®, to the respective MF dose, delivered via Twisthaler®, in terms of trough FEV_1 after 26 weeks of treatment in patients with uncontrolled asthma. Forced Expiratory Volume in 1 second (FEV_1) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing.

Key secondary objective[1,10]

The key secondary objective was to demonstrate the superiority of IND/MF (combined doses) to MF (combined doses) in terms of ACQ-7 (an asthma control questionnaire validated to evaluate different levels of asthma conrol) after 26 weeks of treatment in patients with uncontrolled asthma.

Other secondary objectives[1]

IND/MF via Breezhaler® in comparison to MF via Twisthaler®:

- Trough FEV_1 at week 52
- Pre-dose FEV_1 at week 4 and week 12
- FEV_1 over 52 weeks
- PEF (peak expiratory flow) over 26 and 52 weeks
- ACQ-7 scores at week 4, 12, and 56
- % patients with MID (minimal important difference) of ACQ≥0.5 at week 26 and 52
- Daily e-diary over 52 weeks – (% of asthma symptoms free days no day-time symptoms, % night with no awakenings, % morning with no symptoms)
- Rescue medication use over 26 and 52 weeks (a day with no rescue medication use is defined from the diary data as any day where the patient recorded no rescue medicine use during the previous 12 hours)
- Asthma exacerbations over 52 weeks
- % rescue medication free days over 26 and 52 weeks
- Quality of life assessed by Asthma Quality of Life Questionnaire (AQLQ)
- Incidence of composite endpoint of serious asthma outcomes (asthma related hospitalization, asthma related intubation, asthma related death)
- Adverse events, vital signs, ECG and laboratory analysis
- FVC (forced vital capacity - the total amount of air exhaled during the FEV test) over 52 weeks
- FEF (forced expiratory flow) over 52 weeks

IND/MF via Breezhaler® in comparison to salmeterol/fluticasone via Accuhaler®:

- Trough FEV_1 at 26 weeks
- ACQ-7 scores at 26 weeks

1 Clinicaltrial.gov: https://clinicaltrials.gov/ct2/show/NCT02554786. Last accessed November 2019.
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Zinc job code: GLRESP/QVM149/0063