Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Glycopyrronium (Bromide) in Children (6 to Less Than 12 Years) With Asthma

Last Update: Dec 31, 2024

A Phase II, Double-blind, Randomized, Multiple Dose, Cross Over, Three-treatment, Three-period, Six Sequence Placebo Controlled Trial to Evaluate Efficacy, Pharmacokinetics (PK), Pharmacodynamics (PD) and Safety and Tolerability of Glycopyrronium (Bromide) in Children From 6 to Less Than 12 Years of Age With Asthma.

ClinicalTrials.gov Identifier:
NCT05222529

Novartis Reference Number:CQVM149C2201

See if you Pre-qualify

All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The purpose of this study is to characterize the bronchodilator effect, systemic exposure and safety/tolerability of two different doses of inhaled glycopyrronium, when compared to placebo. Outcome of this study will be used to determine the dose of inhaled glycopyrronium for the development of fixed dose combination indacaterol/mometasone/glycopyrronium (QVM149) for children aged 6 to less than 12 years old with moderate to severe asthma. The study design is a double-blind, placebo controlled, randomized sequence, three-treatment, three-period, six-sequence, cross-over multiple-dose study to evaluate efficacy, pharmacokinetics, pharmacodynamics, and safety and tolerability of glycopyrronium bromide (bromide) in children from 6 to less than 12 years of age with asthma with forced expiratory volume in one second (FEV1) ≥60% and ≤ 90% of the predicted normal value for the participant.

This study will consist of 4 phases: Screening, Run-in, Treatment and Follow-up.

After the screening phase, participants will enter the Run-in Phase to further assess eligibility and those participants that meet all eligibility criteria will be randomized. Study treatment will be administered in addition to background asthma LABA+ICS controller therapy (salmeterol xinafoate 50µg/fluticasone propionate 100µg) from entering the run-in period, through to the end of the treatment phase, including the 2 wash-out periods. Participants will be randomized to one of 6 different sequences with an equal (1:1:1:1:1:1) randomization ratio. The Treatment Phase will last 10 weeks, and every sequence is divided in three treatment periods: Glycopyrronium bromide 12.5 µg, Glycopyrronium bromide 25µg or matching placebo dry powder in capsules for inhalation, via Breezhaler. Each treatment period lasts 2 weeks and 2 consecutive treatment periods are separated by a 2-week wash-out period. Participants who discontinue their study treatment prematurely will be required to return to the clinic for an Early Termination Visit. 30 days after last treatment date, a final telephone contact must be conducted for safety follow-up.

The total duration of the trial for a participant (from screening to follow up) is approximately 20 weeks including safety follow-up.

Condition
Asthma
Phase
Phase2
Overall Status
Recruiting
Number of Participants
42
Start Date
Aug 29, 2022
Completion Date
Jun 19, 2025
Gender
All
Age(s)
6 Years - 11 Years (Child)

Interventions

Drug

Glycopyrronium bromide 12.5ug

12.5ug Glycopyrronium bromide capsules for oral inhalation via Breezhaler
Drug

Glycopyrronium bromide 25ug

25µg Glycopyrronium bromide capsules for oral inhalation via Breezhaler
Drug

Placebo

Placebo to Glycopyrronium bromide capsules for oral inhalation via Breezhaler

Eligibility Criteria

Inclusion Criteria:

* Confirmed diagnosis of asthma for at least 6 months
* Signed informed consent by parent(s)/legal guardian(s) and assent by the pediatric participant (depending on local requirements)
* Participant on stable dose of inhaled low-to-medium dose ICS with one additional controller for at least 4 weeks prior to run-in
* Pre-Bronchodilator FEV1 ≥60% to ≤90% of predicted normal at beginning of Run-in and randomization. If FEV1 eligibility criteria are not met at -45min pre-dose of the End of Run-in (Visit 30), the visit can be

rescheduled once within 5 days from the previous attempt.
* FEV1 reversibility, done using up to 4 puffs of SABA (up to 400µg salbutamol or 360µg albuterol) at Run-in visit (Visit 20): increase \> and/or = 12% (performed according to American Thoracic Society (ATS)/European Respiratory Society (ERS) 2019 guidelines). All participants must perform a reversibility test at start of Run-in. If reversibility is not demonstrated at Run-in, it may be attempted at up to two ad hoc, unscheduled separate visits within 5 days from previous attempt. If reversibility is still not demonstrated after repeated assessment participants must be screen failed
* Demonstrated acceptable inhaler use technique for Diskus/Accuhaler (prior to run-in) and Breezhaler (prior to randomization) and able to complete spirometry procedures prior to randomization.
* A parent/legal guardian must be designated to complete all e-Diary entries and attend all clinic visits with the participant.
* Parents/legal guardian must be willing and able to assist the child with the procedures outlined in the protocol, e.g. compliance with study medication, completion of electronic participant diary
* Female participants of child-bearing potential, who might become sexually active, must be informed of the need to prevent pregnancy during the study using effective contraceptive methods. The decision on the contraceptive method should be reviewed at least every 3 months to evaluate the individual need and compatibility of the method chosen.

Exclusion Criteria:

* Systemic corticosteroid use for any reason within 3 months of Run-in
* Participants on low to medium mono ICS alone
* Participants requiring six or more puffs of rescue medication per day on more than two consecutive days in the four weeks prior to Screening (Visit 1) and/or in the four weeks prior to the Run-in visit
* Participants who have had an asthma attack/exacerbation requiring a) systemic corticosteroids (SCS) or b) hospitalization or c) emergency room visit, within 3 months prior to Screening (Visit 1), or more than 3 separate exacerbations in the 12 months preceding the Screening visit
* Participants with a known narrow-angle glaucoma, bladder dysfunction, bladder outlet obstruction or any other conditions where anticholinergic treatment is contraindicated prior to Screening (Visit 1)
* Participants with a history of long QT syndrome or whose corrected QT interval (QTc) measured at start of Run-in and confirmed at Baseline (prior to randomization) (Fridericia method) is prolonged (\> 450 msec for boys and girls) and confirmed by a central assessor (these patients should not be rescreened)
* Suspected or documented active infections (bacterial, viral, fungal, mycobacterial or other, including active SARS-CoV-2, tuberculosis or atypical mycobacterial disease) of the upper or lower respiratory tract, sinus or middle ear that is not resolved within 6 weeks of Screening (Visit 1)
* History of Type I diabetes or uncontrolled Type II diabetes
* Participants who are sexually active at screening
* Hemoglobin levels outside normal ranges at Run-in (Visit 20)
* Female patients of childbearing potential (e.g., are menstruating) who do not agree to abstinence or, if they become sexually active during study participation, do not agree to the use of contraception as defined in the inclusion criteria.

Additional protocol-defined inclusion / exclusion criteria may apply.

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