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STUDY PROTOCOL

A Fully Decentralized Randomized Controlled Study of As-Needed Albuterol–Budesonide Fixed-Dose Inhaler in Mild Asthma: The BATURA Study Design

Craig LaForce[1], Frank C Albers[2], Mark Cooper[3], Anna Danilewicz[4], Lynn Dunsire[3], Robert Rees[4], Christy Cappelletti[5]

[1]North Carolina Clinical Research, Chapel Hill, NC, USA; [2]Avillion, Northbrook, IL, USA; [3]BioPharmaceuticals Research and Development, AstraZeneca, Cambridge, UK; [4]Avillion, London, UK; [5]BioPharmaceuticals Research and Development, AstraZeneca, Durham, NC, USA

Correspondence: Mark Cooper, BioPharmaceuticals Reseach and Development, AstraZeneca, Cambridge, UK, Email mark.cooper1@astrazeneca.com

Purpose: Decentralized clinical trials, where trial-related activities occur at locations other than traditional clinical sites (eg participant homes, local healthcare facilities), have the potential to improve trial access for people for whom time and/or distance constraints may impede participation. Albuterol–budesonide 180/160 µg pressurized metered-dose inhaler (pMDI) is FDA approved for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years or older. BATURA (NCT05505734) is a fully decentralized study, investigating as-needed albuterol–budesonide in participants with mild asthma.

Methods: BATURA is a fully decentralized, phase 3b, randomized, double-blind, event-driven exacerbation study conducted in the United States. Participants aged ≥12 years using as-needed short-acting β_2-agonist (SABA), alone or with low-dose inhaled corticosteroid or leukotriene receptor antagonist maintenance, are randomized 1:1 to as-needed albuterol–budesonide 180/160 µg or albuterol 180 µg pMDI for up to 52 weeks (minimum 12 weeks). Participants continue their current maintenance therapy, if applicable. Participants must have used SABA for ≥2 days in the 2 weeks pre-enrollment and have an Asthma Impairment Risk Questionnaire score ≥2 at screening and randomization. All trial-related visits, including screening and consent, are conducted virtually, with study medication shipped directly to each participant's residence. The primary objective is to evaluate the efficacy of as-needed albuterol–budesonide versus albuterol on severe asthma exacerbation risk, measured by time-to-first severe asthma exacerbation (primary endpoint). Secondary endpoints include annualized rate of severe asthma exacerbation and total systemic corticosteroid exposure. Study medication use is captured via a Hailie sensor attached to the study medication pMDI. The intended sample size is 2500 participants.

Conclusion: BATURA evaluates as-needed albuterol–budesonide in participants with mild asthma. The decentralized study model enables the trial to move out of research sites into participant homes, reducing participant burden and improving access.

Keywords: decentralized clinical trials, trial design, albuterol–budesonide, SABA–ICS

Introduction

Clinical trials have traditionally been conducted at specific clinical research sites. However, advances in digital health technologies, including telemedicine, digital healthcare apps, digital imaging, and internet-connected remote sensors, increasingly support accurate, precise, remote data collection.[1–6] These technical innovations, alongside changes in clinical trial implementation strategies necessitated by the COVID-19 pandemic, have catalyzed the adoption of decentralized clinical trial models.[3,6,7] Decentralized trials are those where some (or all) of the activities related to a clinical trial occur at locations other than traditional clinical research sites, including participant homes, local healthcare facilities, or nearby laboratories.[8] Fully decentralized trials, where all trial-related activities occur in non-clinical settings (eg participant homes),[2,5,9] present several potential advantages over research site-based clinical trials, including improved trial access for participants who might not otherwise have the opportunity to participate due to time/distance

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constraints, thus facilitating diversity in the populations recruited.[2,4,10] Furthermore, these trials have the potential to observe near-real-world participant behaviors, clinical events, and responses,[1,3] whilst reducing the burden of participation.[2,11]

Decentralized trial designs are particularly suitable for studying conditions that can be managed using a telemedical approach, especially when endpoint measurements do not require participants to attend a clinical trial site and the therapies being investigated are self-administered and have well-characterized safety profiles.[5] Asthma is usually managed on an outpatient basis, using self-administered therapies,[12,13] therefore making trials investigating this chronic disease suitable for decentralization. As an increasing number of trials are being conducted in a decentralized manner, regulators worldwide, including the United States Food and Drug Administration (FDA) and the European Medicines Agency, have issued recommendations for implementing the decentralization of clinical trials in a participant-centric and risk-proportionate manner.[5,14]

Asthma exacerbations can have a significant impact on the lives of people with asthma, representing a major health burden. Even patients considered to have mild asthma are at risk of acute deteriorations of their asthma symptoms that can lead to severe exacerbations. Indeed, a recent analysis of real-world data (2010–2017) from patients with mild asthma in the United States found that 57% of patients being treated with as-needed short-acting β_2-agonist (SABA) only, and 42% treated with low-dose inhaled corticosteroid (ICS) or leukotriene receptor antagonist (LTRA) maintenance (plus as-needed SABA), experienced ≥1 severe exacerbation requiring systemic corticosteroids annually.[15] As airway inflammation is central to asthma symptoms and exacerbations, current expert international asthma treatment reports and guidelines (including the Global Initiative for Asthma [GINA] report and the National Asthma Education and Prevention Program [NAEPP] guidelines) advocate the concomitant treatment of symptoms and inflammation.[12,13] However, during periods when asthma symptoms worsen, patients typically reach for SABA rescue inhalers, which treat symptoms, but do not address the corresponding increasing inflammation.[16,17]

Albuterol–budesonide 180/160 µg (AIRSUPRA™) is a rescue therapy for asthma that combines a SABA and an ICS in a single pressurized metered-dose rescue inhaler (pMDI).[18,19] The MANDALA study showed that this combination can significantly reduce the risk of a severe exacerbation by 28%, compared with as-needed use of albuterol 180 µg, among people aged ≥18 years.[20] Based on these data, and those from the DENALI study,[19] albuterol–budesonide 180/160 µg pMDI was approved by the FDA in 2023 for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older. Although indicated in the United States across all asthma severities, data for as-needed use of albuterol–budesonide 180/160 µg on the reduction of exacerbation risk are limited to people with moderate-to-severe asthma.[18,19] Furthermore, while adolescents (12–17 years) were included in MANDALA, data in this age group were inconclusive due to low sample size (n=100) and corresponding low event rates.

Here, we report the design of BATURA (NCT05505734), an ongoing, fully decentralized clinical trial evaluating the efficacy and safety of as-needed albuterol–budesonide 180/160 µg pMDI for rescue in participants ≥12 years old with mild asthma. BATURA is the first study of an inhaled asthma therapy to employ a fully decentralized approach and aligns with FDA guidelines for implementing decentralized clinical trials. BATURA will provide data on exacerbation risk and the safety of albuterol–budesonide 180/160 µg, compared with albuterol 180 µg, in participants with mild asthma in a home-based setting.

Study Design and Procedures

Study Overview and Objectives

BATURA is a phase 3b, participant-centric, fully decentralized, randomized, double-blind, parallel-group, event-driven exacerbation study being conducted in the United States. The objective of BATURA is to evaluate the efficacy and safety of albuterol–budesonide 180/160 µg pMDI, compared with albuterol 180 µg pMDI, both used as needed, in participants ≥12 years old with mild asthma (Figure 1). All trial-related activities, including recruitment, enrollment, informed consent, study visits, and data collection (Figure 2) are conducted virtually.

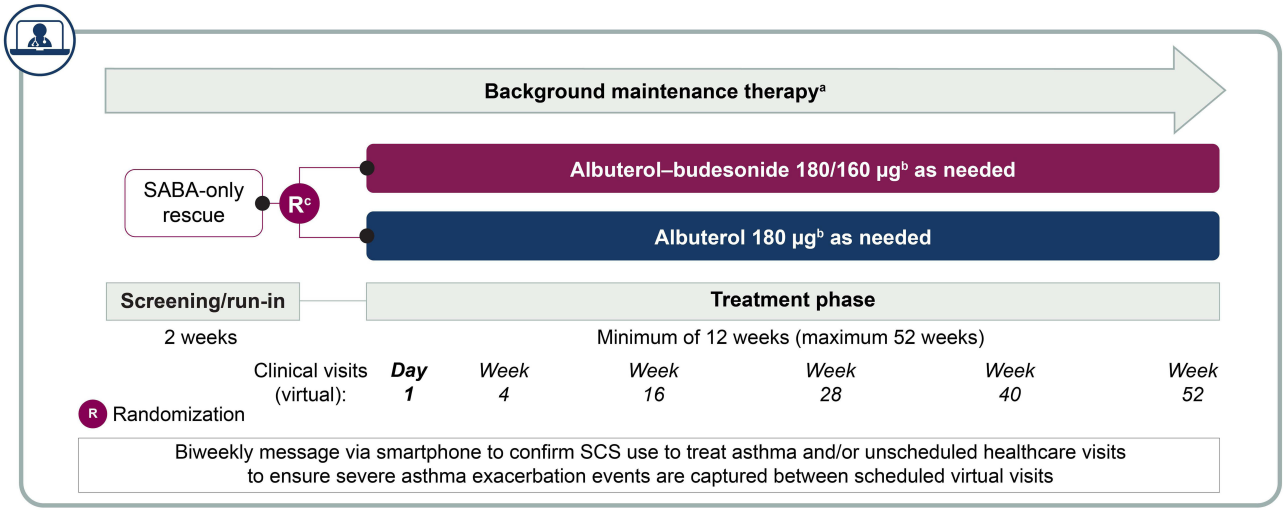

Figure 1 Overview of trial design.
Notes: [a]Participants continue their own maintenance medications throughout the study, if applicable; [b]Study medication is administered via pMDI in two actuations of albuterol–budesonide 90/80 µg or albuterol 90 µg, up to a maximum of 12 inhalations per day; [c]Participants stratified by pre-study asthma medication and number of prior severe exacerbations (0, ≥1) in the 12 months prior to the screening visit.
Abbreviations: ICS, inhaled corticosteroid; LTRA, leukotriene receptor antagonist; R, randomization; SABA, short-acting β_2-agonist; SCS, systemic corticosteroid.

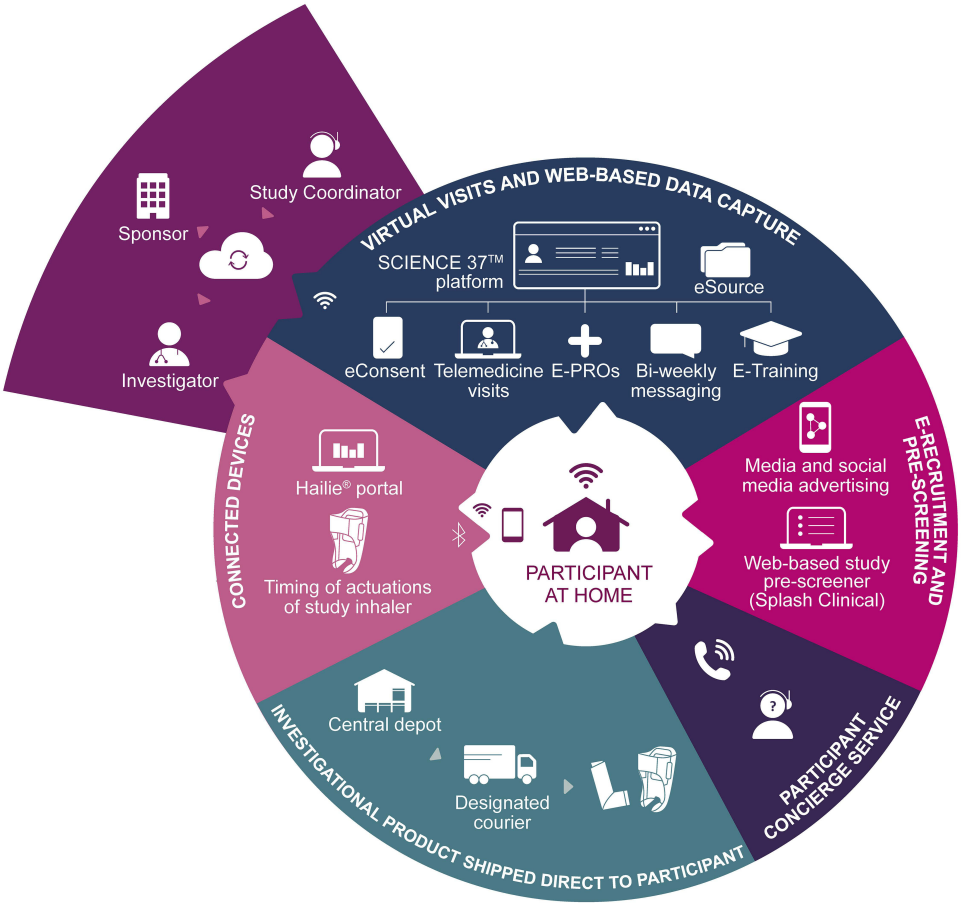

Figure 2 Bringing the study from the research site to the participant's home: decentralized components of BATURA.
Abbreviations: E-PROs, electronic patient reported outcomes; E-Training, electronic training.

Patient feedback on the study design was sought via interviews with nine individuals with mild or moderate asthma. Patients were enthusiastic about the decentralized study design with potential improvements in trial convenience and accessibility, and provided guidance on participant-friendly terminology to describe visits (eg "virtual" rather than "remote" or "telemedicine"), which was implemented in all participant-facing materials. Areas of potential concern included data privacy, access to study-related information, and replacement of their current inhalers with study medication. These concerns were addressed by providing assurance on data privacy within the informed consent form, an on-demand patient concierge service (with a team of "patient navigators") to support both participants and site staff with any study-related questions, and by clarifying, in participant information, that the study inhaler contains similar medication to their current inhalers (albuterol), or similar medication combined with an additional medication (budesonide).

Participants and Eligibility Criteria

A multi-channel approach to recruitment has been implemented, with a significant emphasis on multimedia, multi-platform outreach, including social media, and employing artificial intelligence (AI) technology to rapidly identify high-probability, eligibility-matched participants. The majority of potential participants identified via multimedia outreach are screened remotely for eligibility via the Splash Clinical website (Figure 2). People aged ≥12 years, with a diagnosis of asthma, using as-needed SABA, either alone or with low-dose ICS or LTRA maintenance, are recruited. To be eligible for participation, they must have used SABA on ≥2 days in the 2 weeks pre-enrollment and have an Asthma Impairment and Risk Questionnaire (AIRQ) score ≥2 at screening and randomization (indicating uncontrolled disease). AIRQ is a validated 10-item tool that assesses both the symptom impairment and exacerbation risk domains of asthma control in patients aged ≥12 years.[21–24] Patients with a score of 0–1 are categorized as well controlled, 2–4 as not well controlled, and 5–10 as very poorly controlled.[21] AIRQ control level has been shown to be highly predictive of exacerbation risk over 12 months and probability of time-to-first exacerbation.[22,25,26]

Participants are also required to have access to a smartphone and an internet connection. Other key inclusion and exclusion criteria are presented in Table 1.

Study Treatment and Allocation

Eligible participants are randomized 1:1 (Figure 1) to receive as-needed albuterol–budesonide 180/160 µg, given as two inhalations of albuterol/budesonide 90/80 µg, or as-needed albuterol 180 µg, given as two inhalations of albuterol 90 µg, all delivered by pMDI. Study-related supplies, including study medication, are shipped from a central depot directly to the residence of each participant via a climate-controlled courier service. Participants must confirm they have received the allocated study medication at the time of delivery. Each participant received a shipment of between four and six study

Table 1 Key Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• ≥12 years of age • Diagnosis of asthma • Current use of SABA alone or SABA plus a background of either lose-dose ICS or LTRA[a] • ≥2 SABA uses for symptoms within 2 weeks prior to enrollment • AIRQ score of ≥2 at V1 and V2 • Negative pregnancy test and use of acceptable birth control • Access to a smartphone and internet connection	• Significant lung disease other than asthma, or any other significant disease • Hospitalization due to asthma in the 3 months prior to enrollment or ICU admission with life-threatening asthma at any time • Daily use of LABA, theophylline, anticholinergics, cromone, or medium-/high-dose ICS as regular maintenance asthma therapy in the 3 months prior to enrollment • Use of SCS for the treatment of asthma or any other condition in the 6 weeks prior to enrollment • Prophylactic use of a SABA to prevent exercise-induced bronchospasm only

Notes: [a]SABA alone: ≥2 filled prescriptions for a SABA inhaler; SABA + low-dose ICS monotherapy: ≥1 filled prescription for a SABA inhaler and ≥1 filled prescription for low-dose ICS; SABA + LTRA: ≥1 filled prescription for a SABA inhaler and ≥1 filled prescription for a LTRA.
Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; ICS, inhaled corticosteroid; ICU, intensive care unit; LABA, long-acting β_2-agonist; LTRA, leukotriene receptor antagonist; SABA, short-acting β_2-agonist; SCS, systemic corticosteroid; V, visit.

medication kits at the start of the treatment period (depending on when they were enrolled), with each kit including two study medication pMDIs (total of eight-to-twelve pMDIs). The quantity of medication available to each participant is checked during virtual visits; new study medication kits are ordered by investigators and shipped to participants as required. Participants are to use study medication in place of their normal rescue medication, either in response to symptoms or prior to exercise, and should not exceed 12 inhalations/day of study medication. Study medication use is captured via a sensor attachment (Hailie, Adherium Limited) on the participant's pMDI, which records each inhaler actuation, but is not built to recognize inhalation technique. Participants are trained, remotely, in the administration, handling, and cleaning of their study medication. All participants prescribed permitted background maintenance therapies (see Table 1) continue these medications as instructed by their healthcare provider. Participants are not permitted to use a spacer with study medication pMDIs, but may with their usual maintenance inhalers.

Randomization is assigned using a central randomization and trial supply management system, stratified by each participant's background therapy and number of severe exacerbations in the 12 months prior to screening. BATURA will continue until either 1) 345 first severe asthma exacerbations have been observed and all patients have completed 12 weeks of study, 2) all participants have completed 52 weeks of treatment, or 3) an unblinded interim analysis (planned to occur once 172 first severe exacerbations have been observed) has determined that the study may be stopped early for demonstrated efficacy.

Digital Health Technologies to Support Decentralization

The SCIENCE37 mobile software application and associated websites are being used to provide digital support to participants and investigators from screening through to study completion (Figure 2). This platform supports electronic informed consent, electronic patient-reported outcome (PRO) questionnaire completion, telemedicine visits, participant education, and eSource documentation. SCIENCE37 also hosts instructional videos and other information helpful to trial participants and investigators, and enables participants to request additional study medication in a blinded fashion. Additionally, the system prompts participants, via bi-weekly notifications, to inform investigators of worsening asthma symptoms (Figure 2) which will then stimulate unscheduled virtual visits to gather further information regarding the potential for a severe asthma exacerbation.

Alongside study medication, each participant receives two Hailie sensors, which automatically log pMDI actuations in real time once attached to an inhaler and paired (via Bluetooth) with the Hailie app on the participant's smartphone. This allows detailed measurement of the inhaled dose received by each participant, thereby facilitating identification of potential overdose and estimation of ICS exposure resulting from use of study medication. Participants are instructed on how to mount Hailie sensors to their study medication pMDIs and pair with an appropriate device. While the sensors initially provided are expected to have sufficient battery life for the study period and follow-up, additional sensors can be ordered in case of damage or loss. In case of technical difficulties and/or related questions, a telephone-based patient concierge service (Patient Navigator) has been established.

Assessments and Endpoints

Study endpoints are detailed in Figure 3; all endpoints were chosen to be safely evaluated without the need for participants to attend a clinical trial site.

The primary endpoint is time-to-first severe exacerbation, where an exacerbation is defined as a worsening of asthma signs and/or symptoms and increased use of as-needed rescue medication. Exacerbations are considered severe if they resulted in at least one of the following: a temporary bolus/burst of systemic corticosteroid (SCS) for ≥3 consecutive days (or a single depo-injectable dose of corticosteroids) to treat symptoms of asthma worsening; an emergency room or urgent care visit due to asthma that required SCS (as per the above); inpatient hospitalization due to asthma; or death. The primary analysis is based on an estimand "while-on-treatment" strategy (see Statistical Analysis).

Secondary endpoints include time-to-first severe exacerbation (based on an estimand using an intention-to-treat analysis), annualized rate of severe asthma exacerbations, total SCS exposure (mg/year) per participant, and total days of SCS exposure. Tertiary and exploratory endpoints include healthcare resource use (HCRU), working days lost to asthma-related illness, and PROs measured using the AIRQ and EuroQol-5 Dimension-5 Level (EQ-5D-5L) instrument. Safety endpoints include the number, frequency, severity, type, and outcome of adverse events and serious adverse events.

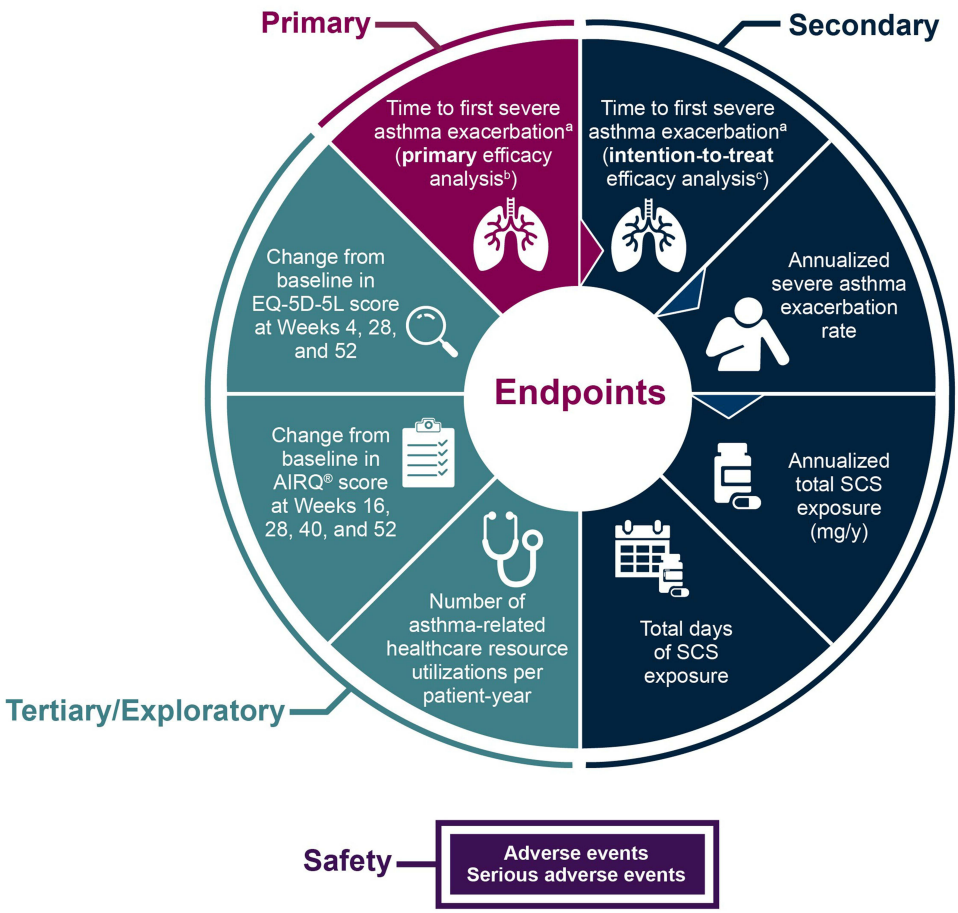

Figure 3 Study endpoints.

Notes: [a]Exacerbations are defined as worsening of asthma signs/symptoms and the increased use of as-needed rescue medication. An exacerbation is considered severe if it results in ≥1 of the following: a temporary bolus/burst of SCS for ≥3 consecutive days (or a single depo-injectable dose of corticosteroids) to treat symptoms of asthma worsening; an emergency room or urgent care visit due to asthma that requires SCS (as per the above); inpatient hospitalization due to asthma; or death; [b]The primary efficacy analysis (while-on-treatment estimand) is limited to data collected during the on-treatment period before treatment discontinuation or a change in maintenance therapy; [c]The intention-to-treat analysis includes all observed data obtained during the study, regardless of participant randomization status, treatment discontinuation, or a change in maintenance therapy.

Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; EQ-5D-5L, EuroQol-5 Dimension-5 Level; SCS, systemic corticosteroid.

Statistical Analysis

BATURA is a superiority trial; the primary analysis of time-to-first severe asthma exacerbation will use data collected during the on-treatment period, before treatment discontinuation or a change in maintenance therapy (while-on-treatment strategy). A secondary intention-to-treat analysis will also be conducted for time-to-first severe asthma exacerbation, including all observed data obtained during the study, regardless of participant randomization status, treatment discontinuation, or change in maintenance therapy (treatment policy).

Time-to-first severe asthma exacerbation will be analyzed using a Cox proportional hazards regression model, including factors for treatment, pre-study asthma therapy (SABA only, low-dose ICS + SABA, or LTRA + SABA), and the number of severe exacerbations (0, ≥1) in the 12 months prior to screening. A two-sided test will evaluate the null hypothesis that the adjusted hazard ratio for the primary treatment comparison is equal to 1, versus the alternative hypothesis that it is not equal to 1. Annualized rate of severe asthma exacerbations will be analyzed using a negative binomial generalized linear model, including the same factors as the primary analysis model, with time at risk on the logarithm scale as an offset variable; the annualized rate ratio and 95% confidence interval will be estimated for the treatment comparison. The treatment comparison for annualized SCS exposure will be made using a Wilcoxon rank-sum test, and descriptive statistics will be calculated for adverse event data. The above tests will be type I error controlled via

a hierarchical testing procedure, using the following endpoint testing order: time-to-first exacerbation (primary efficacy analysis), time-to-first exacerbation (intention-to-treat efficacy analysis), annualized severe exacerbation rate, and annualized total SCS exposure (Figure 3).

A sample size of 955 participants per treatment group, and a total of 345 first severe asthma exacerbation events, was initially calculated to provide 90.8% power to detect a 30% reduction in the risk of a severe asthma exacerbation for participants using albuterol–budesonide versus albuterol, with a two-sided hypothesis test and overall type I error rate of 5%. This reduction is supported by results from the MANDALA study, in which the risk of a severe exacerbation was reduced by 27% with albuterol–budesonide 180/160 µg, versus albuterol, in participants ≥12 years old with moderate-to-severe asthma.[18] This assumed a first severe exacerbation event probability of 0.21 with the as-needed use of albuterol, based on assessment of real-world studies in participants with mild asthma and an assumed 10% drop-out rate. After a blinded sample size re-estimation, following lower than expected rates of first severe exacerbation, a total trial population of 2500 is being enrolled. An independent data monitoring committee will perform an unblinded interim analysis for efficacy when 172 first severe exacerbation events have been observed, based on analysis of the primary and first secondary endpoints.

Discussion

Populations with mild asthma are at substantial risk of exacerbations. A recent United States-based healthcare claims study found that 57% of patients with asthma treated according to GINA step 1, and 42% treated according to GINA step 2, had experienced a severe exacerbation in the previous 12 months.[15] In people with asthma, airway inflammation and bronchoconstriction contribute to airway narrowing and airflow limitation, leading to asthma symptoms and exacerbations.[27–29] Both inflammation and symptoms vary over time and in intensity, and can lead to unpredictable exacerbations.[12,13,28,29] People with asthma often reach for rescue therapies, prioritizing quick relief when symptoms occur. However, treatment with SABA-only rescue does not address the corresponding rise in inflammation. Combination rescue therapy with an ICS and a fast-acting bronchodilator can address this issue, since symptoms and inflammation are treated concomitantly when most needed, reducing the risk of an exacerbation. As such, both global and local recommendations on the management of asthma, including the GINA report, recommend combination anti-inflammatory-rescue therapies (containing ICS and either SABA or formoterol) for use across multiple asthma severities. While MANDALA provided evidence of the efficacy of as-needed SABA-ICS on the reduction of exacerbation risk in patients with moderate-to-severe asthma, evidence in mild asthma is limited, and BATURA will fill this data gap.

Consistent with MANDALA, time-to-first severe asthma exacerbation was chosen as the primary endpoint for BATURA, with annualized rate of severe asthma exacerbation and annualized SCS exposure included as secondary endpoints. BATURA also included, as exploratory endpoints, PROs of EQ-5D-5L,[30] to assess participant quality of life, and AIRQ, to assess asthma control. AIRQ is a validated 10-item, low literacy-demand tool that assesses both the symptom impairment and exacerbation risk domains of asthma control in patients aged ≥12 years.[21–24] It comprises seven symptom-based questions with a 2-week recall period and three exacerbation history questions with a 12-month recall period.[21] A longitudinal study of the AIRQ in over 1100 patients with asthma found that worsening baseline control, as indicated by the AIRQ control level, was predictive of increasing exacerbation risk over the subsequent 12 months.[22] This longitudinal study also found that AIRQ rated fewer patients as having well-controlled asthma who had current symptom impairment or previous- and subsequent-year exacerbations compared with the Asthma Control Test, the GINA symptom control tool, or expert specialist opinion.[22,26]

BATURA is the first fully decentralized trial for asthma, and has been designed to align with the FDA guidance document on Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Table 2).[5] The participant group enrolled is at low risk of harm as they are currently managed in an outpatient setting using self-administered therapies with well-characterized safety profiles.[12,13] In addition, no complex medical assessments are required to evaluate the endpoints selected. Furthermore, the fully decentralized design of the BATURA trial allows participants to fit trial activities around their everyday lives, thus lessening participant burden. Data are collected in the home environment, using familiar devices and an automated sensor.[1,3] This approach also reduces the burden of travel which, as well as being more convenient to participants, may reduce per-trial carbon footprint.[31,32] It is hoped decentralization will

Table 2 BATURA Study Design Aligns with FDA Guidelines for Use of a Decentralized Approach

Study Characteristics Suitable for a Decentralized Design[5]	BATURA
Therapies are simple to administer or use	Study drug is self-administered via pMDI, the most commonly prescribed medical device worldwide
Therapies have well-characterized safety profiles	Albuterol–budesonide: • Albuterol has been an approved treatment for asthma since 1981[33] • Budesonide was initially approved for the treatment of asthma in the United States in 1997[34]
Study does not require complex medical assessments	Exacerbations as a primary endpoint are well defined
Telehealth visits, where in-person interaction is required	All visits are virtual, including screening and consent
Digital health technologies can be used to transmit data remotely from trial participants	Study medication use is captured electronically
Study-related supplies can be distributed directly to participants at their locations	Study drug and related supplies are shipped directly to participants

Abbreviations: FDA, United States Food and Drug Administration; pMDI, pressurized- metered dose inhaler.

encourage a more diverse range of people to be enrolled, therefore improving the representation of groups which have been under-represented in clinical trial populations.

Trial decentralization can present a number of challenges to implementation, including the need to maintain participant and trial site engagement with remote study procedures and documentation requirements, and the need to remotely ensure compliance with these procedures and documentation requirements.[5,9,35] Decentralization may improve access to clinical trials by removing geographical barriers to participation, but can create digital barriers for some participants, both in recruitment and with use of digital health technologies during the study (ie ability to install and use sensors and digital platforms without the hands-on assistance of investigators and site staff). To address this concern, participants in BATURA were allowed to use their own Smartphone device and every effort was made to ensure that the study software applications (SCIENCE37 and Hailie portal) were easy to use, with a patient concierge service established to provide technical assistance as necessary. Another challenge of fully decentralized trials is that, by moving the study out of the research site and into the participant's home, much of the face-to-face interaction involved in site-based clinical trials is removed, which can result in participants having a more distant relationship with both study staff and the study itself, potentially creating challenges to participant engagement and retention. Despite these concerns, the majority of literature concerning patient retention in clinical trials has found that decentralized clinical trials typically have superior rates of retention to those seen in site-based clinical trials.[11,36] A decentralized design may also necessitate the exclusion of certain tests and procedures that may have been considered in a site-based study. For example, in BATURA the decision was made to reduce participant burden by not including eDiaries, and lung function assessment was considered to be unfeasible due to the challenges of performing spirometry in a home setting. In general, both technologies and social attitudes are evolving quickly to support studies of this nature; as trial decentralization and digitization become more common, it is likely that improved applications and increased participant and investigator experience will address many such concerns.

The BATURA study, using an innovative decentralized approach, is investigating the efficacy of as-needed albuterol–budesonide 180/160 µg to reduce the risk of severe exacerbations in people with mild asthma, building on what has already been shown in the MANDALA study in patients with moderate-to-severe asthma.[18,20]

Conclusion

BATURA employs a novel, decentralized study design to evaluate the efficacy and safety of as-needed albuterol–budesonide 180/160 µg in participants ≥12 years of age with mild asthma. This decentralized design enables the study to move out of the clinical research site and into participant homes, thus reducing participant burden, potentially reaching people for whom time

and/or distance constraints may impede clinical trial participation, therefore expanding clinical trial access to a broader population.

Abbreviations

AI, artificial intelligence; AIRQ, Asthma Impairment and Risk Questionnaire; eICF, electronic informed consent form; EQ-5D-5L, EuroQol-5 Dimension-5 Level; FDA, United States Food and Drug Administration; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; ICU, intensive care unit; LABA, long-acting β_2-agonist; LTRA, leukotriene receptor antagonist; pMDI, pressurized metered-dose inhaler; R, randomization; SABA, short-acting β_2-agonist; SCS, systemic corticosteroid.

Data Sharing Statement

The datasets used and analyzed during the study described in this manuscript may be obtained in accordance with the data sharing policy of Avillion's co-development partner AstraZeneca, as described at https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

Ethics Approval and Consent to Participate

BATURA is being performed in accordance with the Declaration of Helsinki and is consistent with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use and Good Clinical Practice (ICH/GCP) and applicable regulatory requirements. All portions of the protocol, electronic informed consent form (eICFs), and other relevant documents have been approved by an institutional review board (ADVARRA, Maryland, US).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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