Randomized phase 1 study of the phosphatidylinositol 3-kinase δ inhibitor idelalisib in patients with allergic rhinitis

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Background: Phosphatidylinositol 3-kinase p110δ (PI3K p110δ) activity is essential for mast cell activation, suggesting that inhibition of PI3K p110δ might be useful in treating allergic diseases.

Objective: We sought to determine the effect of the PI3K p110δ–selective inhibitor idelalisib on allergic responses.

Methods: This phase 1 randomized, double-blind, placebo-controlled, 2-period crossover study was conducted with the Vienna Challenge Chamber. Grass pollen–induced allergic symptoms were documented during screening. Eligible subjects received idelalisib (100 mg twice daily) or placebo for 7 days, with allergen challenge on day 7. After a 2-week washout period, subjects received the alternate treatment and repeated allergen challenge.

Results: Forty-one patients with allergic rhinitis received idelalisib/placebo (n = 21) or placebo/idelalisib (n = 20). Idelalisib treatment was well tolerated. Mean total nasal symptom scores were lower during the combined idelalisib treatment periods compared with placebo (treatment difference [idelalisib – placebo], −1.78; 95% CI, −2.53 to −1.03; P < .001). Statistically significant differences were also observed for the combined treatment periods for total symptom scores, nasal airflow, nasal secretion weight, and nasal congestion scores. The percentage of ex vivo–activated basophils (CD63+/CCR3+ cells; after stimulation with grass pollen) was substantially lower for idelalisib-treated compared with placebo-treated subjects. Plasma CCL17 and CCL22 levels were reduced after idelalisib treatment.

Conclusion: Idelalisib treatment was well tolerated in patients with allergic rhinitis and appears to reduce allergic responses clinically and immunologically after an environmental allergic challenge. (J Allergy Clin Immunol 2016;***:****:****:****)

Key words: Phosphatidylinositol 3-kinase, p110δ, grass pollen, allergen challenge chamber, Vienna Challenge Chamber, idelalisib, GS-1101, CCL17, CCL22, allergic rhinitis

The molecular and cellular mechanisms that mediate the allergic inflammatory cascade involve multiple cell types and pathways. The initial response is triggered by inhaled allergen interacting with IgE receptors on mast cells and basophils, resulting in release of preformed inflammatory mediators, primarily histamine, which is important to the early-phase response. Subsequently, synthesis and release of lipid mediators, cytokines, and chemokines occur, which might contribute to the late-phase response and chronic allergic inflammation. Thymus and activation-regulated chemokine (CCL17) and macrophage-derived chemokine (CCL22) bind to their receptor, CCR4, which is prevalently expressed by Th2 lymphocytes, and are responsible for the allergen-induced recruitment of Th2 lymphocytes into sites of allergic inflammation. Plasma CCL17 and CCL22 concentrations have been reported to be increased in patients with allergic rhinitis and other atopic conditions.

Class I phosphatidylinositol 3-kinases (PI3Ks) are a family of intracellular signaling proteins that are essential components of migratory, proliferative, survival, and differentiation pathways in many cell types, including those of hematopoietic origin. The holoenzymes consist of a regulatory subunit (designated p50, p55, p85, or p101) and a catalytic subunit (designated p110α, p110β, and p110γ). In general, activation of PI3K IA isoforms (designated p110α, p110β, and p110δ) is mediated by tyrosine kinases, whereas activation of the PI3K IB isoform (p110γ) is mediated by G protein–coupled receptors. On PI3K activation, p110 generates the key lipid second messenger phosphatidylinositol (3,4,5)-trisphosphate, which acts as a binding site for recruitment and activation of numerous intracellular signaling enzymes that contain pleckstrin homology domains with selectivity for this lipid. The most important of these is the serine/threonine kinase AKT, which mediates a positive pleiotropic effect on cell survival, proliferation, growth, and metabolism. The activity of PI3K is opposed by the lipid phosphatases phosphatase and tensin homolog and SH2-containing-inositol-5′-phosphatase.

Idelalisib (GS-1101, CAL-101) is a potent and selective small-molecule inhibitor of the δ isoform of the p110 subunit (PI3K p110δ), which was recently approved for the treatment of chronic lymphocytic leukemia and non-Hodgkin lymphoma. It binds reversibly and noncovalently to PI3K p110δ in the ATP-binding site and is competitive with ATP. The PI3K p110δ signaling pathway, as well as its importance in lymphocyte development, differentiation, and activation, has been reviewed in detail. PI3K p110δ catalytic activity is essential for mast cell activation, differentiation, survival, and homeostasis. It is also important
for allergen-specific, IgE–induced early mast cell activation and acute increase in vascular permeability. Furthermore, anti-FceRI–induced basophil degranulation, as assessed based on surface expression of CD63, is potently inhibited by idelalisib. In preclinical models of allergic inflammation, pharmacologic inhibition or genetic inactivation of PI3K p110δ reduces the allergic response. These preclinical studies suggest an important role of PI3K p110δ in patients with allergic diseases, such as allergic rhinitis. In this article we present a proof-of-concept clinical trial to determine the effect of idelalisib on allergic responses in an allergen challenge chamber in subjects with documented grass pollen allergy.

METHODS

Study design

This phase 1, randomized, double-blind, placebo-controlled, 2-period crossover trial was conducted in Austria from January to March 2009 (study identifier: NCT00836914). Screening procedures were performed 21 or fewer days before study drug dosing and followed by an at least 7-day washout period. Eligible subjects were randomized (1:1) to a treatment sequence: 7 days of idelalisib administered twice daily, followed by an at least 14-day washout period and 7 days of placebo twice daily or vice versa (idelalisib after placebo). A follow-up visit occurred at least 7 days after the last study drug treatment. Nasal allergic responses caused by exposure to grass pollen in the Vienna Challenge Chamber (VCC) were measured during screening and at day 7 of each treatment period (idelalisib or placebo); responses were collected during a 4-hour allergen challenge that began 1 hour after study drug dosing. Climatic conditions (temperature, humidity, and CO2 concentration) were kept constant in the VCC during the allergen provocation session. A 5-grass-pollen mix containing Phleum pratense, Dactylis glomerata, Lolium perenne, Anthoxanthum odoratum, and Holcus lanatus was used as the allergen source for this study. The concentration used was about 1500 pollen grains per cubic meter (SD <10%).

The study was conducted according to the protocol; the ethical principles expressed in the World Medical Association’s Declaration of Helsinki, International Conference on Harmonisation Good Clinical Practice guidelines, and applicable national and local laws; and regulations for conducting clinical research and protecting privacy. Approval of the study was obtained from the Austrian national health regulatory authorities and a local ethics committee before it was initiated. Subjects provided written informed consent forms until study’s end. The incidence of treatment-emergent adverse events (TEAEs) was summarized by treatment for all TEAEs, drug-related TEAEs, serious adverse events (SAEs), drug-related SAEs, and discontinuations because of TEAEs. The incidence and number of events were summarized by using the Medical Dictionary for Regulatory Activities (Version 11.0) system organ class, preferred term, and treatment. A physical examination was performed at screening. Vital signs and electrocardiograms were assessed at screening, on the first and last days of each treatment period, and at study’s end (vital signs only). Spirometry was performed at screening and before and hourly during each allergen challenge session.

Allergic response end points consisted of self-reported symptoms collected every 15 minutes; nasal airflow, as measured by means of active anterior rhinomonometer performed every 30 minutes; and nasal secretion weight collected every 30 minutes during the 4-hour allergen challenge. Nasal symptoms (nasal congestion, nasal rhinorrhea, nasal itching, and sneezing attacks) were rated as 0 (no symptoms), 1 (mild), 2 (moderate), or 3 (severe). These scores were summed to produce the TNSS, with a possible range of 0 to 12. Nonnasal symptoms (itching eyes, tearing eyes, eye redness, and itching of the ears and palate) were rated in a similar manner and summed to derive the total nonnasal symptom score (TNNSS; possible range, 0-12).

The primary efficacy end point was mean change from baseline in average TNSS. TNSSs from 2 to 4 hours of allergen challenge were averaged for each subject (time-weighted average; area under the curve from 2 to 4 hours). Selected secondary efficacy end points included the effect of treatment on TNNSSs, total symptom score (TSSs [sum of the TNSS and TNNSS]; possible range, 0-24), nasal airflow (determined by using active anterior rhinomonometer at a pressure difference of 150 Pa across nasal passages; right and left nostril values were summed), and nasal secretion weight (determined by using preweighed tissues). Pharmacokinetic samples were obtained on the first and last days of each treatment period. Idelalisib concentrations in plasma samples were analyzed with a validated liquid chromatography–tandem mass spectrometry method with a lower limit of quantitation of 1 ng/mL. Pharmacodynamic effects were assessed with the FlowCytometry Assay (Bühlmann Laboratories AG, Schönenucht, Switzerland) by using samples collected before dosing and 1.5 and 3 hours (±15 minutes) after dosing on the first day of each treatment period. Basophils in whole blood samples were stimulated ex vivo with grass pollen allergens, and activated basophils were detected by using flow cytometry. The percentage of activated basophils (CD63+/CCR3+ cells) from samples collected before dosing was used as baseline.
change from baseline values for samples collected after dosing was expressed as a relative percentage of the baseline value. Subjects with baseline values of less than 20% CD63<sup>−</sup>/CCR3<sup>−</sup> cells after grass pollen stimulation were considered nonresponders and excluded from the analysis.

Plasma samples were collected on day 1 (baseline 1), day 21 (baseline 2), and 7 days after idelalisib (day 7 and day 28) or placebo (day 7 and day 28) treatment before allergen challenge and stored after deep freezing at about −80°C until analysis. For assessment of concentrations of CCL17, CCL22, and IFN-γ, frozen plasma samples were thawed and analyzed by using multiplexed bead suspension arrays (MBAs; Millipore, Billerica, Mass). MBAs were analyzed with a Luminex 200 machine, and data were organized and analyzed with 3.1 xPONENT software (Luminex, Austin, Tex).

**Statistics**
A sample size of 36 subjects was considered sufficient to provide 80% power to detect a treatment effect of 1.0 for change from baseline TNSS (assuming and SD of 2.1) with a 2-sided α value of .05.<sup>1</sup> Enrollment of 45 subjects was planned to allow for nonevaluable subjects. All subjects and study site personnel, including those assessing outcomes, were blinded. Investigators enrolled and assigned subjects to interventions according to a blinded randomization schedule. Randomization was done by a contracted vendor using a random number generator to assign treatments to sequential subject identifiers; the randomization scheme was provided to the drug supply vendor, which labeled the appropriate drug supply bottles (placebo or active) with the subject identifiers. The site then enrolled subjects and assigned them to the next sequential identifier.

Analyses were performed by treatment sequence group (idelalisib/placebo vs placebo/idelalisib) and/or by combined treatment periods (idelalisib vs placebo). The analysis of treatment sequence effects was exploratory; all other efficacy, safety, and pharmacokinetic analyses were prespecified. During the 4-hour exposure to grass pollen in the VCC, TNSSs were measured every 15 minutes. A time-weighted average (area under the curve from 2 to 4 hours) for the period 2 to 4 hours after exposure was calculated for each subject as follows:

\[ \frac{\sum_{i=1}^{n}(t_{i+1} - t_i) \times (Score_{t_i} + Score_{t_{i+1}})}{2 \times T_{2-4h}} \]

where \( t_i \) was the actual time of assessment, \( Score \) was the value at time point \( t \), and \( T_{2-4h} \) was the actual length of the 2- to 4-hour time interval. For the combined treatment periods, change from baseline average TNSS was assessed with a linear ANOVA model with terms for sequence, treatment, subject, and period; baseline assessments were performed at the beginning of each antigen exposure. Secondary efficacy end points were assessed with similar ANOVA models. When the assumptions of normal distribution of the error terms were not met in the ANOVA models, nonparametric analyses similar to the methods presented by Koch<sup>2</sup> were applied by using the Wilcoxon rank test to assess treatment and carryover effects.

Statistical analyses were performed with SAS software, version 8.0 (SAS Institute, Cary NC), and nQuery, version 6.01 (for sample size calculations; Statistical Solutions, Saugus, Mass).

**RESULTS**

**Disposition**
Forty-one of 47 screened subjects were randomized, 21 to the idelalisib/placebo treatment sequence and 20 to the
placebo/idelalisib sequence (Fig 1 and Table 1). All 41 randomized subjects received treatment (safety analysis set), and 39 completed the study (efficacy analysis set). Two subjects discontinued early from the study: 1 had scheduling problems after 6 days of treatment with placebo in period 1 and withdrew, and the second had increased hepatic enzyme levels after treatment with placebo in period 1 and was discontinued per protocol. All other subjects completed the study according to the protocol.

Subjects’ characteristics

Demographic and baseline characteristics were well balanced between treatment sequence groups (Table 1). Median age was 27.6 years (range, 20-49 years), and all subjects were male. For the 39 subjects who completed the study, median time since the diagnosis of allergic rhinitis was 17 years, 1 subject (placebo/idelalisib) had a diagnosis of atopic dermatitis 15 years before screening, and none of the subjects had active asthma at screening. Use of concomitant medications was not reported by any subjects at screening, and none of the subjects had any nasal symptoms before challenge with grass pollen in the VCC (TNSS = 0). The mean TNSS after 2 hours of environmental allergen challenge in the VCC was 6.0 for both treatment sequences. The median TNSS was 6.0 in each treatment sequence, with a range of 6.0 to 8.0 in the idelalisib/placebo group and 6.0 to 9.0 in the placebo/idelalisib group.

Safety

As summarized in Table II, idelalisib was well tolerated during oral administration twice daily over 7 days. The frequency of TEAEs was higher after administration of placebo than it was after administration of idelalisib. No subjects experienced an SAE or discontinued prematurely because of TEAEs. During treatment with idelalisib, 2 (5.1%) of 39 subjects had a total of 4 TEAEs, which included nasopharyngitis (2 events), oral herpes, and myalgia. All TEAEs were considered to be of mild intensity and not related to study medication. During treatment with placebo, 4 (9.8%) of 41 subjects had a total of 14 TEAEs, which included fatigue, laryngitis, increased hepatic enzyme levels, headache, cough, nasal discomfort, and throat irritation. One subject had 4 occurrences of headache. All other TEAEs were single occurrences. All TEAEs were considered to be of mild intensity and not related to study medication.

Efficacy

Mean TNSSs over time were lower during the combined idelalisib treatment periods than during the combined placebo treatment periods (Fig 2, A). The treatment difference (idelalisib − placebo) for the combined treatment periods was −1.78 (95% CI, −2.53 to −1.03; P < .001; Table III). Statistically significant treatment differences (P < .05) were also observed for the combined treatment periods for TSSs, nasal airflow, nasal secretion weight, and nasal congestion scores (Fig 2 and 3).
Table III), but statistically significant differences were not observed for TNSSs (Table III).

Treatment differences for TNSSs were also examined separately for each treatment period. The treatment difference for TNSSs in period 1 (idelalisib) versus period 2 (placebo) was not statistically significant for the idelalisib/placebo treatment sequence (treatment difference, $-0.56; 95\% CI, -1.87$ to $0.75; P = 0.395$). In contrast, the treatment difference (idelalisib − placebo) was significant for the placebo/idelalisib treatment sequence (treatment difference, $-3.00; 95\% CI, -4.60$ to $-1.40; P = 0.001$). Paired comparison of idelalisib and placebo was also done at each time point for TNSSs, and the values with significant differences ($P < 0.05$) are marked in Fig 2, A.

Comparable patterns were observed for the other secondary efficacy end points. The average nasal airflow before allergen challenge (baseline) and the average nasal airflow after allergen exposure in the VCC are shown in Fig 2, B. For the combined treatment periods, the mean (SD) change from baseline in average nasal airflow (2-4 hours) was $93.4 \text{ cm}^3/\text{s} (116.7 \text{ cm}^3/\text{s})$ for idelalisib and $-162.1 \text{ cm}^3/\text{s} (141.1 \text{ cm}^3/\text{s})$ for placebo. The difference between treatments was $72.27 (95\% CI, 15.53$ to $129.0)$. The treatment effect was statistically significant ($P < 0.014$).

Fig 2, C, shows the average nasal congestion score for the combined treatment periods. The mean (SD) change from baseline in nasal congestion was $1.6 (0.7)$ for idelalisib and $2.0 (0.6)$ for placebo. The difference between treatments was $-4.2 (95\% CI, -0.65$ to $-0.19)$. The treatment effect ($P = 0.001$) and period effect ($P = 0.002$) were statistically significant.

### Pharmacokinetics and pharmacodynamics

Mean (SD) plasma idelalisib concentrations were 1087 ng/mL (643.8 ng/mL) 1.5 hours after the first dose (day 1) of idelalisib and 792.7 ng/mL (315.8 ng/mL) 3 hours after the first dose. Mean (SD) plasma idelalisib concentrations were 474.1 ng/mL (316.1 ng/mL) before the last dose (day 7) of idelalisib and 843.6 ng/mL (440.4 ng/mL) 4 to 5 hours after the last dose.

The percentage of activated basophils (CD63$^+$/CCR3$^+$ cells; after stimulation ex vivo with grass pollen) was substantially lower for idelalisib-treated subjects than for placebo-treated subjects (Fig 2, D, and Table IV) and did not differ substantially for subjects in the 2 treatment sequences (idelalisib/placebo and placebo/idelalisib; Table V). The mean change from baseline in the relative percentage of CD63$^+$/CCR3$^+$ cells 1.5 and 3 hours after the day 1 morning dose was $-76.3\%$ and $-65.5\%$, respectively, for idelalisib and $-9.9\%$ and $-5.7\%$, respectively, for placebo. These results indicate that idelalisib inhibited ex vivo basophil activation.

Evaluation of plasma samples obtained before treatment and after 7 days of daily treatment with idelalisib resulted in reductions in concentrations of circulating CCL17 and CCL22 (Fig 3). Mean ± SEM values were reduced from $13.9 \pm 1.57$ to $8.2 \pm 0.88$ pg/mL for CCL17 and from $1214 \pm 99.2$ to $887 \pm 72.9$ pg/mL for CCL22; all of these changes were statistically significant ($P < 0.0001$, paired t test). In contrast, placebo treatment did not significantly alter CCL17 and CCL22 concentrations. The IFN-γ concentration was not significantly altered by either idelalisib or placebo treatments. Additionally, total IgE levels in serum, both before and after treatment, were...
DISCUSSION

Idelalisib is an orally bioavailable new chemical entity that potently and selectively blocks PI3K p110δ activity. Idelalisib was initially evaluated in healthy subjects during clinical development and was found to be well tolerated as a single dose and with repeat dosing for 7 days. The results in healthy subjects during short-term administration supported evaluation of idelalisib as a clinical tool to test the concept of targeting PI3K p110δ in pathogenesis of the allergic response.

The current phase 1 proof-of-concept study demonstrated that idelalisib is well tolerated when administered at a dose of 100 mg twice daily over 7 days in subjects with allergic rhinitis. No SAEs or discontinuations caused by TEAEs occurred during the study. TEAEs were mild, and the incidence was higher after administration of placebo than it was after administration of idelalisib. All TEAEs were considered unrelated to study medication.

Idelalisib is currently marketed for the treatment of certain patients with the B-cell malignancies follicular lymphoma, small lymphocytic lymphoma, and chronic lymphocytic leukemia. The marketed drug carries a boxed warning for fatal and serious toxicities involving hepatotoxicity, severe diarrhea, colitis, pneumonitis, and intestinal perforation. The tolerability of idelalisib in
the current study is probably related to the short treatment period
used compared with that in patients with cancer, who typically
received idelalisib for substantially longer durations.

Idelalisib effectively reduced the symptoms of allergic rhinitis
during a 4-hour environmental allergen challenge in the VCC and
was significantly superior to placebo for the primary efficacy end
point of change from baseline TNSS and for some secondary
efficacy end points, including TSSs and average nasal airflow.
Allergy medications (eg, corticosteroids, antihistamines, and
anticholinergic) were prohibited during the study, but it could
not be verified whether subjects were compliant with these
conditions.

The study was conducted from the beginning of February to
mid-March 2009. During this period, grass pollen was not
significantly present in or around Vienna because the grass pollen
season extends from mid-May to July. The birch allergen season
started in the beginning of April. Hazel and alder tree allergens,
which are the most common early allergens, started in March but
were not noticeable in 2009. Regarding molds, of 41 subjects in
this study, 4 were allergic to *Alternaria* species with a positive
SPT response and 3 with *Cladosporium* species with a positive
SPT response, but allergic symptoms were not present during
the trial.

Period effects were observed in several analyses ($P < .05$
for TNSSs, TNNSSs, and TSSs). Although idelalisib was
numerically superior to placebo in each treatment sequence, the
differences between idelalisib and placebo were larger and
generally statistically significant for subjects in the placebo/
idelalisib sequence and were generally smaller and not
statistically significant for subjects in the idelalisib/placebo
sequence. There is no obvious explanation for this pattern of
results. It is possible that the apparent period effect was simply
due to chance and was not reflective of a true biological effect.

A carryover effect of idelalisib treatment seems an unlikely
explanation because it would have led to a greater treatment
effect during the idelalisib/placebo sequence than during the

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<th>TABLE V. <em>Ex vivo</em> basophil activation after stimulation with grass pollen by treatment period</th>
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**Samples were obtained at 1.5 hours (±15 minutes) and 3 hours (±15 minutes) after treatment with idelalisib/placebo.
†Percentage of CD63+/CCR3+ cells without grass pollen stimulation was approximately 5%.

FIG 3. Changes in plasma concentrations of CCL17, CCL22, and IFN-γ during idelalisib therapy. Geometric
means with 95% confidence limits are shown. $P$ values were computed by using paired $t$ tests. BL-I, Baseline
for idelalisib treatment; BL-P, baseline for placebo treatment; NS, not significant.
placebo/idelalisib sequence, the opposite of what was observed. It is possible that there was a residual effect from the prior environmental chamber allergen challenge that might have led to a differential treatment effect for the 2 treatment periods; specifically, the washout period from the screening chamber challenge to the period 1 chamber challenge was 1 week, whereas the washout period between periods 1 and 2 was 2 weeks. The apparent period effect was statistically significant (P < .05) for subjective measures (TNSSs, TNNSSs, and TSSs) but not for objective measures (nasal airflow and nasal secretion weight). No period effect was evident for pharmacodynamic measures because idelalisib inhibited ex vivo basophil activation in response to allergen stimulation and decreased plasma levels of CD63 /CCR3 basophils, regardless of sequence. The magnitude of the decrease in TNSSs for idelalisib versus placebo (1.78) is similar to results previously obtained in the VCC with antihistamines but is not as large as effects reported with nasal glucocorticosteroids.25,26

Attenuation of the allergic response with idelalisib treatment could be due to its inhibition of allergen-induced activation of mast cells and basophils. Mast cells and basophils express FcεRI on their surfaces, which makes them primary effectors in allergic responses. Antigen-induced aggregation of FcεRI-bound IgE activates a series of intracellular signaling events, including PI3K p110δ, culminating in secretory granule exocytosis and the release of proinflammatory mediators that promote the allergic cascade. Idelalisib-treated subjects had substantially lower numbers of activated basophils in an ex vivo antigen-induced basophil activation assay. These results are consistent with the role of PI3K p110δ in the control of mast cell and basophil activation established by using pharmacologic inhibitors and gene targeting in mice.9,12

Another interesting aspect of this work is the evaluation of CCL17 and CCL22 because these chemokines bind to their receptor, CCR4, and promote allergen-induced recruitment of Tö2 lymphocytes into sites of allergic inflammation.3,5 Inhibition of CCL17 and CCL22 concentrations by idelalisib treatment might reflect its activity beyond mast cell and basophil cell activation. PI3K p110δ also plays an important role in T-cell receptor–induced T-cell activation,33,34 and pharmacologic inhibitors reduce T-cell receptor–induced cytokine production by both naive and memory human T cells in vitro.35 Further studies are necessary to better understand the mechanism of this treatment. Although results from the current study support the concept of PI3K p110δ inhibition in the allergic rhinitis response, it should not be taken as supporting the use of idelalisib in patients with allergic rhinitis for a number of reasons. First, the effects of idelalisib in the clinical allergic rhinitis setting have not been assessed. Second, the current study was limited in treatment duration, and the effects of longer treatment in patients with allergic rhinitis are unknown. Lastly, the potential risks of chronic treatment with idelalisib in patients with allergic rhinitis might outweigh potential benefits.

In conclusion, idelalisib was well tolerated when administered orally at a dose of 100 mg twice daily over 7 days. Idelalisib reduced the allergic response after an environmental allergen challenge, with significant improvements noted in nasal symptoms, nasal airflow, and nasal secretion weight compared with placebo. An unexpected period effect was observed in some analyses, which might represent a limitation of the crossover study design. The positive results from this proof-of-concept study support further investigation of targeting PI3K p110δ in patients with allergic rhinitis and other mast cell–mediated disorders.

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Clinical implications: This phase 1 clinical trial demonstrated that inhibition of the p110δ isoform of PI3K by idelalisib (100 mg twice daily) appears to reduce allergic responses after an environmental allergen challenge.

REFERENCES


