Effectiveness of Leniolisib in Reducing Infections Among Patients With Activated Phosphoinositide 3-Kinase Delta Syndrome (APDS)

KEY TAKEAWAYS

Overall, adolescent and adult patients with APDS experienced a statistically significant **68% decrease in infection rates** after initiating leniolisib, decreasing from an average of 6 infections per year before initiating leniolisib to 2 infections per year after initiating leniolisib

Patients with APDS with **low baseline infection rates** experienced a statistically significant **38% decrease in infection rates** after initiating leniolisib

Patients with APDS with **high baseline infection rates** experienced a statistically significant **76% decrease in infection rates** after initiating leniolisib

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INTRODUCTION

- APDS is a rare primary immunodeficiency associated with multiple clinical manifestations, including recurrent infections across various organ systems[1-3]
- In a systematic literature review of 351 unique patients with APDS, infections were a major driver of mortality, second only to lymphoma[2]
- In March 2023, leniolisib was approved in the US for the treatment of APDS

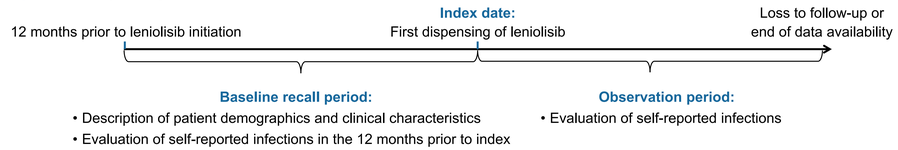
OBJECTIVE

- This study examined the real-world effectiveness of leniolisib by comparing patient-reported infection rates before and after leniolisib initiation

METHODS

- This retrospective, longitudinal analysis of patients initiating leniolisib in the first 20 months post approval (Apr 5, 2023, to Jan 9, 2025) used specialty pharmacy data from PANTHERx Rare Pharmacy's proprietary specialty workflow technology (SWFT) patient engagement platform. Pharmacy-led telephone interviews were used to collect patient-reported infections data, including recall data in the year before leniolisib initiation, and quarterly data collected during leniolisib treatment
- Eligible patients included those with APDS aged ≥12 years who newly initiated leniolisib treatment (index) (**Fig 1**). Patients were excluded if they participated in a clinical trial or expanded access program (EAP) for leniolisib before the index date
- The infection analysis population consisted of patients who had infection assessments during the baseline recall and observation periods
- Patient-reported infection rates were compared after vs before leniolisib initiation among the infection analysis population as well as low (below median baseline infection rate) and high (above median baseline infection rate) infection subgroups using rate ratios, CIs, and *P* values derived from generalized estimating equations Poisson regression models with robust standard errors. Rates of infection, calculated as the number of events divided by the patient-years of observation, were reported per patient-year (PPY)
- This research was reviewed by the WCG institutional review board and was granted an exemption

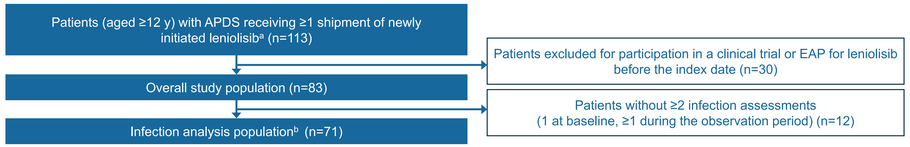
Figure 1 Study Design



RESULTS

- A total of 113 patients were evaluated for inclusion in the study; 30 patients were excluded for participation in a clinical trial or EAP before the index date (**Fig 2**)

Figure 2 Patient Disposition



[a]The first dispensing of leniolisib was the index date. [b]Patients with infection assessments during the baseline and observation periods.
APDS, activated phosphoinositide 3-kinase delta syndrome; EAP, expanded access program.

- The infection analysis population consisted of 71 patients of which 51% were female (**Table 1**); mean (SD) age was 26 (13) years; 80% of patients were prescribed leniolisib by an allergy/immunology specialist; patient characteristics were similar to those in the overall study population
- The mean (SD) length of follow-up among patients in the infection analysis population was 11.1 (4.2) months
- In the infection analysis population, a significant decrease in mean (SD) PPY infections by 68% was observed; 1.87 (2.0) post index vs 5.82 (5.1) at baseline (rate ratio, 0.32; 95% CI, 0.24-0.42; *P*<0.001) (**Fig 3**)
- Patients reported a median (Q1-Q3) of 5 (2-7) infections in the 12-month baseline recall period. Thus, 5 was used to define the low (<5 infections; n=35) and high (≥5 infections; n=36) infection rate subgroups
- Significant reductions were observed in patients with low baseline infection rates (38% reduction, *P*=0.010) and in patients with high baseline infection rates (76% reduction, *P*<0.001) (**Fig 3**)

Table 1 Patient Characteristics

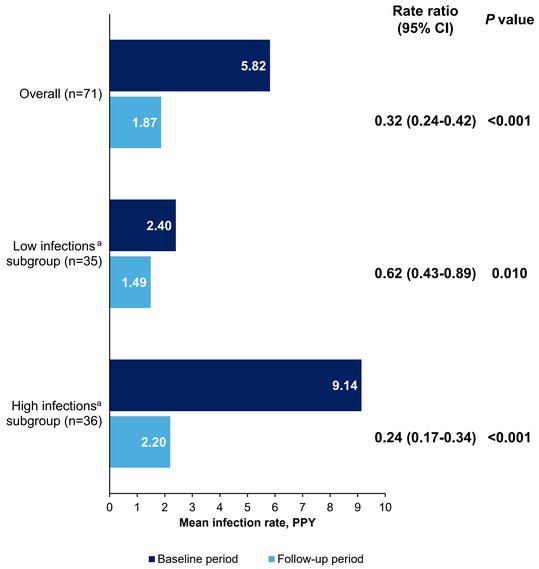
Characteristic	Study population (N=83)	Infection analysis population (n=71)
Age, y, mean ± SD	26.0 ± 13.4	25.8 ± 13.4
Age, y, n (%)		
12-17	35 (42.2)	30 (42.3)
18-29	19 (22.9)	17 (23.9)
30-39	15 (18.1)	12 (16.9)
40-49	9 (10.8)	8 (11.3)
50-59	4 (4.8)	3 (4.2)
60-64	0 (0)	0 (0)
≥65	1 (1.2)	1 (1.4)
Gender, n (%)		
Female	43 (51.8)	36 (50.7)
Male	40 (48.2)	35 (49.3)

Characteristic	Study population (N=83)	Infection analysis population (n=71)
Prescriber specialty/type, n (%)		
Allergy/immunology	68 (81.9)	57 (80.3)
Pediatric	9 (10.8)	9 (12.7)
Specialist	5 (6.0)	5 (7.0)
Primary care	4 (4.8)	4 (5.6)
Hematology/oncology	2 (2.4)	2 (2.8)
Nurse practitioner	2 (2.4)	1 (1.4)
Infectious disease	1 (1.2)	1 (1.4)
Internal medicine	1 (1.2)	1 (1.4)
Insurance plan type, n (%)		
Medicaid	43 (51.8)	39 (54.9)
Commercial	32 (38.6)	27 (38.0)
Medicare	5 (6.0)	4 (5.6)
Unknown	3 (3.6)	1 (1.4)

CONCLUSIONS

- In this US-based retrospective real-world study, treatment with leniolisib was consistently associated with significant 3-fold reductions in overall infection rates
- Significant reductions in infection rates were observed, regardless of patients' infection history
- These real-world results complement those from an open-label extension study of leniolisib in patients ≥12 years of age with APDS, which found a significant reduction in annualized infection rates[4]

Figure 3 Infection Rates at Baseline and After Treatment With Leniolisib



[a]Patients reporting <5 infections in the year prior to index comprised the low infections subgroup, and those with ≥5 infections comprised the high infections subgroup; subgroup classification was based on the median rate of baseline infections in the infection analysis population.
PPY, per patient-year

REFERENCES

1. Jamee M, et al. *Clin Rev Allergy Immunol*. 2020;59(3)323-333. **2.** Büsch K, et al. *Adv Ther*. 2025;42(2):752-771. **3.** Coulter TI, et al. *J Allergy Clin Immunol*. 2017;139(2):597-606.e4. **4.** Rao VK, et al. *J Allergy Clin Immunol*. 2024;153(1):265-274.e9.

DISCLOSURES

NCP is a speaker for Amgen, Pharming Healthcare, Inc., X4 Pharmaceuticals, Inc., ADMA Biologics, Inc., Grifols, and Takeda; performs research for Takeda and ACAAI; and serves on data monitoring committees for Jannsen and Takeda; JK and EB are employees of PANTHERx Rare Pharmacy, which received consulting fees from Pharming Healthcare, Inc.; SM, GG, CS, and FL are employees of Groupe d'analyse SRI, which received consulting fees from Pharming Healthcare, Inc.; MEMY is a speaker/consultant for Pharming Healthcare, Inc., Amgen, and Koru Pharma; JF received consulting fees from Pharming Healthcare, Inc.; AH is an employee of Pharming Healthcare, Inc.

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