Check for updates

Received: 4 January 2023 | Revised: 3 May 2023 | Accepted: 9 May 2023

DOI: 10.1111/pai.13962

LETTER TO THE EDITOR

WILEY

A survey-based study on diagnosis and management of vernal keratoconjunctivitis

To the Editor,

Vernal keratoconjunctivitis (VKC) is a rare, chronic, allergic inflammatory disease affecting the conjunctiva and cornea.[1–8] Primarily observed in children/young adults, VKC has significant detrimental impact on quality of life and potential complications.[1–10] Symptoms include intense ocular itching, redness, mucoid discharge, and photophobia with recurrent flare-ups and seasonal exacerbations.[1–10] The pathogenic mechanisms are believed to comprise a combination of allergic, endocrine, environmental, and/or genetic factors.[1–9] Guidelines and management recommendations are inadequately defined, but treatment typically focuses on topical therapies.[8,9] The aim of the study was to investigate levels of clinical knowledge among Italian ophthalmologists, allergists, and pediatricians on VKC and its therapeutic approaches performing an observational/noninterventional, survey-based study.

Telephone interviews were conducted with clinicians by a company that specialized in multichannel projects in the pharmaceutical field (Merqurio Holding Srl), and current European Union General Data Protection Regulation (GDPR) 2016/679 legislation was followed. Full details of the methodology are available in the Supporting Information along with the three specifically designed questionnaires. Telephone interviews were conducted with 503 ophthalmologists, 276 pediatricians, and 223 allergists (Table S1). Data were analyzed for participants who routinely treated children and had an understanding or knowledge of VKC.

Most ophthalmologists (81%) who routinely treated pediatric patients reported that they had knowledge of VKC and 17% were currently treating VKC patients. The majority of ophthalmologists (57.6%) rated their level of knowledge as high or medium (20.9%). All allergists who routinely treated children had knowledge of VKC, and 89% had treated a case of VKC during their career but typically rated their knowledge of VKC as medium (43.5%) or weak (39.5%). Most pediatricians (84%) had knowledge of VKC, although 77% had not treated any patient affected by the disease. Only 7% of pediatricians were currently treating VKC patients.

Photophobia was the symptom of VKC most commonly reported spontaneously by all three specialist subgroups (19%–23%; Figure 1A). Itching (20%), foreign body sensation (19%), and redness (22%) were also highlighted as frequent symptoms by ophthalmologists, allergists, and pediatricians, respectively. When provided/prompted with a list of potential signs and symptoms of VKC (Figure 1B), photophobia (32%–43%) and itching (25%–42%) were the main options chosen. The differences in spontaneous and suggested signs and symptoms may reflect the relatively poor knowledge of VKC among practitioners. Reporting of other symptoms lacked consistency across the specialists. More than half (52%) of ophthalmologists considered VKC to be an allergic disease. The majority of allergists (66%) did not regard VKC as an allergic disease, even though VKC has been classified as both an IgE- and non-IgE-mediated allergic disease.[7]

Figure 2 provides an overview/summary of key findings from the survey that may help in understanding the VKC patient journey. Most ophthalmologists (78%) would manage VKC themselves, and only 20% would refer the patient to an ocular surface/cornea specialized center. Only 23% of ophthalmologists would request an allergy consultation for their VKC patients, which was lower than expected. Interestingly, ophthalmologists reported that 54% of their VKC patients were self-referred, with parents/caregivers having sought information through the Internet. Because VKC is a relatively rare and not well-known condition, it is not surprising that 53% of ophthalmologists, 72% of pediatricians, and 82% of allergists said that their VKC patients had consulted another clinician/specialist (we presume either an ophthalmologist, allergist, or pediatrician) without receiving a diagnosis. Around one quarter (26%) had previously received advice from a pediatrician. Allergists received visits from VKC patients referred by ophthalmologists in 87% of cases, while 17% were referred by pediatricians. Only 20% of allergists would refer a VKC patient to another center, although 77% required an ophthalmology consultation. Interestingly, according to allergists, 90% of patients were unsuccessfully treated. Fifty-nine percent of allergists reported that patients rarely or never booked a consultation without referral to discuss their disease. As reported by pediatricians (87%), the majority of VKC patients consulted them without looking for information on the disease online. Sixty percent of pediatricians would refer a patient to an ophthalmologist in cases with persistent symptoms despite therapy, but only 3% of pediatricians would refer a VKC patient to an allergist.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.
© 2023 The Authors. *Pediatric Allergy and Immunology* published by European Academy of Allergy and Clinical Immunology and John Wiley & Sons Ltd.

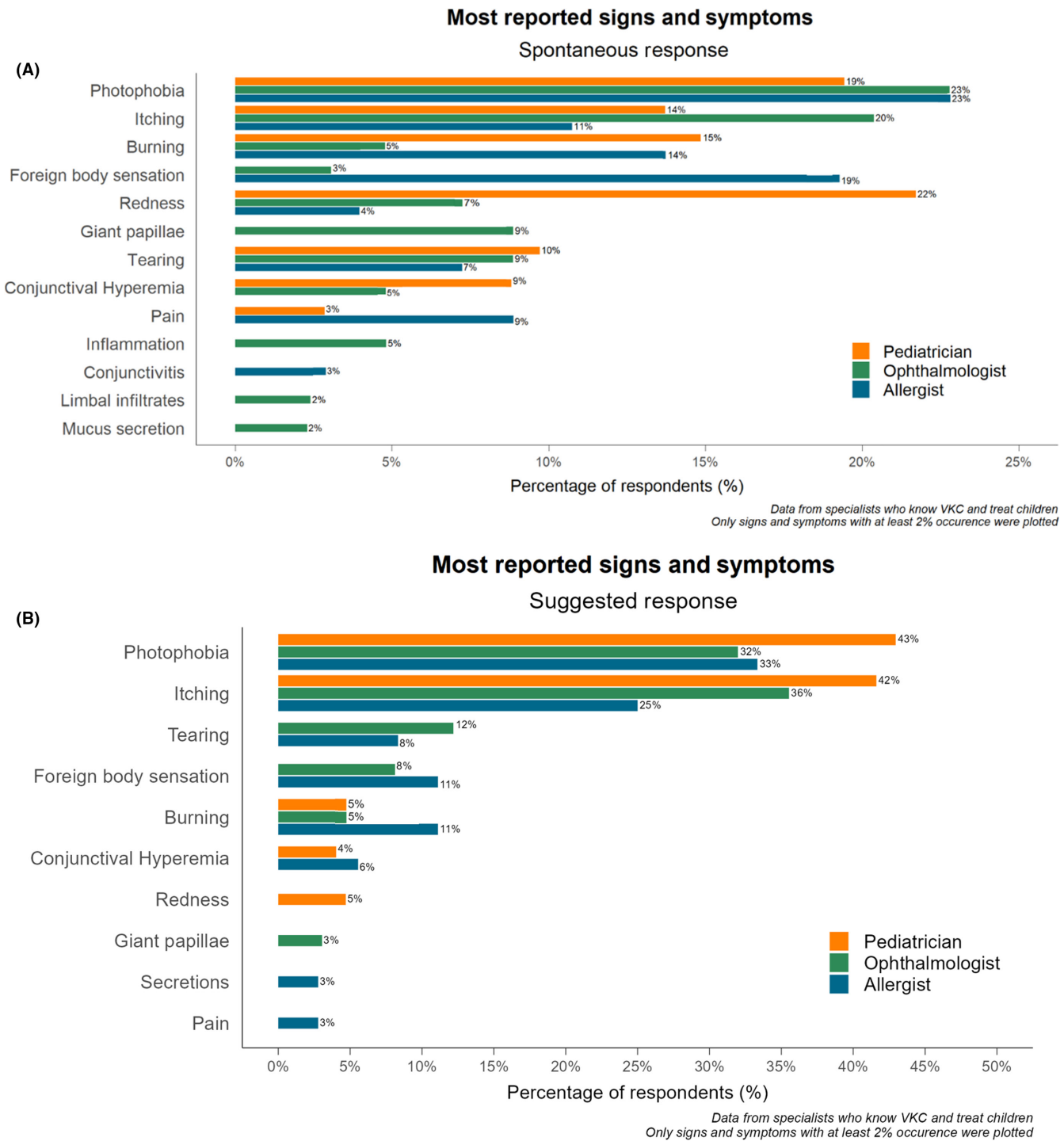

FIGURE 1 Most frequently reported signs and symptoms of vernal keratoconjunctivitis according to clinical specialism (A) spontaneous response (B) suggested response from a provided list. Survey responses to the question: "What are the ocular symptoms and signs that you consider most relevant to suspect vernal keratoconjunctivitis?" VKC, vernal keratoconjunctivitis.

Topical corticosteroids were favored as first-line treatment by 88% of ophthalmologists, but only 52% of them prescribed conventional antiallergic medications (Figure 3). While most ophthalmologists (84%) were aware that topical cyclosporine A (CsA) is indicated in the treatment of VKC, only 40% reported that they would prescribe CsA or tacrolimus following VKC diagnosis. Most allergists (78%) prescribed steroids as initial therapy for VKC and 9% prescribed topical CsA or tacrolimus but, surprisingly, only 26% prescribed antiallergic drugs. Pediatricians most frequently prescribed corticosteroids (39%), followed by antiallergic medications (28%) and antibiotics (22%). While 57% of pediatricians indicated that CsA would be considered as a treatment option, only 1% said that they prescribed first-line topical CsA therapy for VKC.

13993038, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/pai.13962 by CochraneItalia, Wiley Online Library on [23/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

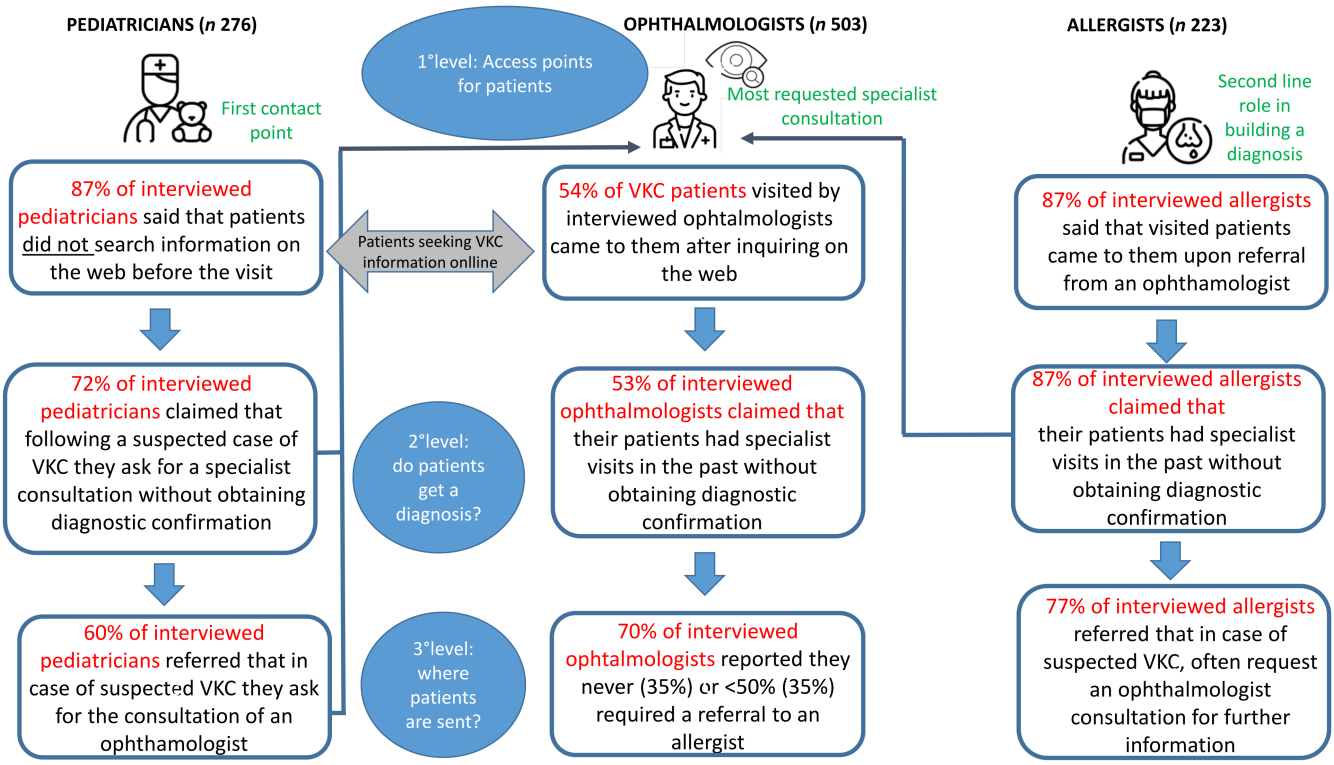

FIGURE 2 Key aspects of the vernal keratoconjunctivitis patient pathway based upon survey responses. Survey data indicated that the VKC patient pathway tended to be complex and lacking in consistency. Pediatricians were typically the first point of contact in the VKC pathway, with allergists usually playing a second-line role. Ophthalmology consultations were the most frequent type of specialist consultation/examination requested by allergists and pediatricians, whereas ophthalmologists generally preferred to manage VKC alone. VKC, vernal keratoconjunctivitis.

The results of the survey show that, despite a clear willingness among clinicians to collaborate, seeking advice from each other, diagnostic and treatment pathways remain complex and lengthy in VKC. While knowledge of VKC was generally high among ophthalmologists and pediatricians, most ophthalmologists treat the disease only with corticosteroids while only few pediatricians treat the disease by themselves. In contrast, most allergists had treated VKC during their career but still rated their own knowledge of the disease as medium/low. This suggests that the awareness of VKC and VKC management should be improved among the physicians that may have to deal with these patients. Understanding of key signs/symptoms of VKC was fragmented and inconsistent across clinical specialists, even when prompted and despite the relatively high self-rated knowledge of the disease. Less than 25% spontaneously identified photophobia or itching as key symptoms during the survey and under 10% recognized hyperemia as important VKC signs and symptoms, as reported in the literature.[1,6,8,9] As the first point of contact for patients, pediatricians should pay attention to signs and symptoms such as itching and hyperemia and suggest an ophthalmologic consultation if they persist after treatment. VKC has been included in the classification of ocular allergic diseases, but there appears to be confusion among clinicians regarding the categorization of VKC as either an allergic or nonallergic condition.[7] The survey results reflect the lack of clarity within the literature regarding the pathogenesis of VKC.[1,7,8]

Ophthalmologists preferred to treat VKC alone, but pediatricians and allergists often sought advice from ophthalmology colleagues, emphasizing the considered importance of ophthalmic expertise in disease management. Ophthalmologists were most likely to feel comfortable prescribing topical CsA, which is regarded in the literature to be the main treatment for VKC (with corticosteroids reserved for acute relapses).[8,9] However, the survey revealed that topical corticosteroids were the most commonly prescribed first-line treatment (often in combination with antiallergic medications in pediatric and ophthalmology settings).[9] The frequent use of topical corticosteroids by non-ophthalmologists should be discouraged because of the possible side effects even in VKC children.[6,9] This suggests that clinicians may be unaware of the steroid-sparing effects shown with topical CsA use in VKC.[8,9]

Finally, the frequent use of topical antibiotics (22%) by pediatricians highlights the overuse of these drugs and the lack of knowledge in VKC diagnosis and management. Clinicians routinely working with children would benefit from access to structured training and consistent diagnostic and treatment algorithms to support prompter identification and appropriate management of this debilitating disease. Even though the study obtained responses from a large number of specialists, the identification of the patient journey should have included information from patients/caregivers on the

13993038, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/pai.13962 by CochraneItalia, Wiley Online Library on [23/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

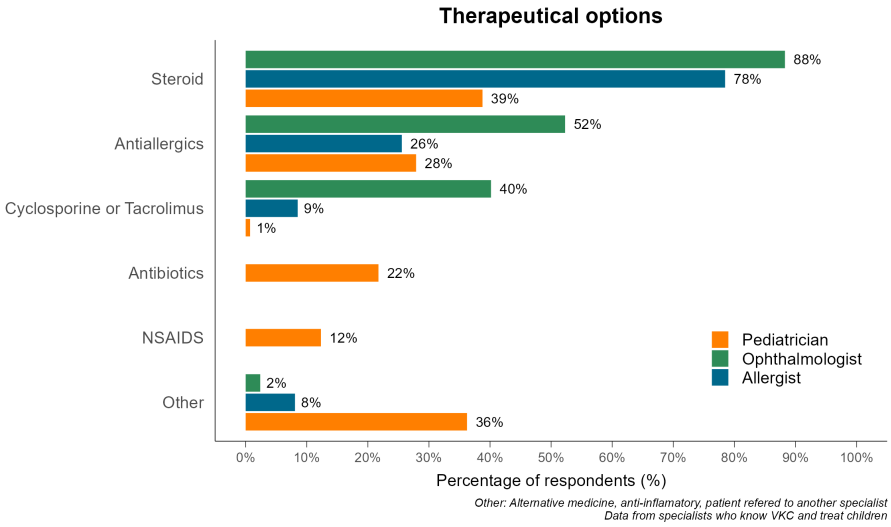

FIGURE 3 Usual first-line therapeutic approach for vernal keratoconjunctivitis used by ophthalmologists, allergists, or pediatricians who treat children. Other: different medicine, artificial tears, anti-inflammatory, patient referred to another specialist. Data from specialists with a knowledge of VKC and treat children. Survey responses to the question: "If you start a therapy which one would you use?" VKC, vernal keratoconjunctivitis.

difficulties they face in obtaining a diagnosis and proper management. It would be interesting to conduct a similar survey online at a European level to increase clinical knowledge and stimulate awareness of VKC in Europe.

AUTHOR CONTRIBUTIONS

Andrea Leonardi: Conceptualization; methodology; writing – review and editing. **Francesca Mori:** Conceptualization; methodology; writing – review and editing. **Daniele Giovanni Ghiglioni:** Conceptualization; methodology; writing – review and editing.

ACKNOWLEDGMENTS

The survey and subsequent analysis were conducted by Merqurio Holding s.r.l., Naples, Italy. Medical writing services were provided on behalf of the authors by Rebecca Down at Copperfox Communications Limited.

FUNDING INFORMATION

The VKC patient journey survey and subsequent data analysis was funded by Santen Italy s.r.l. Medical writing fees and open access publishing fees were also kindly provided by Santen Italy s.r.l.

CONFLICT OF INTEREST STATEMENT

Andrea Leonardi has received consultancy or speaker fees from Santen, Alcon, Thea, Faez Pharma, and Ursa Pharma. Francesca Mori and Daniele Giovanni Ghiglioni have no relevant declarations or conflicts of interest.

ETHICS STATEMENT

The survey was conducted in line with current legislation and the principles of the European Union General Data Protection Regulation (GDPR) 2016/679 for the collection of privacy consent. At the beginning of each interview, clinicians were informed that the questionnaire was anonymous and that the data collected would be treated in an aggregate manner in accordance with Italian privacy law.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/pai.13962.

Andrea Leonardi[1]
Francesca Mori[2]
Daniele Giovanni Ghiglioni[3]

[1]*Department of Neuroscience, Ophthalmology Unit, University of Padua, Padova, Italy*
[2]*Allergy Unit, Meyer Children's Hospital, Florence, Italy*
[3]*Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano – SC Pediatria Pneumoinfettivologia – Ambulatorio Allergologia Pediatrica, Milan, Italy*

Correspondence
Andrea Leonardi, Department of Neuroscience, Ophthalmology Unit, University of Padua, Padova, Italy.
Email: andrea.leonardi@unipd.it

Editor: Carmen Riggioni

ORCID

Andrea Leonardi https://orcid.org/0000-0002-7246-8580
Francesca Mori https://orcid.org/0000-0001-7483-0128

REFERENCES

1. Leonardi A. Vernal keratoconjunctivitis: pathogenesis and treatment. *Prog Retin Eye Res*. 2002;21(3):319-339.
2. Sacchetti M, Plateroti R, Bruscolini A, Giustolisi R, Marenco M. Understanding vernal keratoconjunctivitis: beyond allergic mechanisms. *Life*. 2021;11(10):1012.
3. Vichyanond P, Pacharn P, Pleyer U, Leonardi A. Vernal keratoconjunctivitis: a severe allergic eye disease with remodeling changes. *Pediatr Allergy Immunol*. 2014;25(4):314-322.
4. Pattnaik L, Acharya L. A comprehensive review on vernal keratoconjunctivitis with emphasis on proteomics. *Life Sci*. 2015;128:47-54.

13993038, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/pai.13962 by CochraneItalia, Wiley Online Library on [23/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

5. Leonardi A, Busca F, Motterle L, et al. Case series of 406 vernal keratoconjunctivitis patients: a demographic and epidemiological study. *Acta Ophthalmol Scand*. 2006;84(3):406-410.
6. Dahlmann-Noor A, Bonini S, Bremond-Gignac D, et al. Novel insights in the management of vernal keratoconjunctivitis (VKC): European expert consensus using a modified nominal group technique. *Ophthalmol Ther*. 2023;12(2):1207-1222.
7. Leonardi A, Bogacka E, Fauquert JL. Ocular allergy: recognizing and diagnosing hypersensitivity disorders of the ocular surface. *Allergy*. 2012;67(11):1327-1337.
8. Brindisi G, Cinicola B, Anania C, et al. Vernal keratoconjunctivitis: state of art and update on treatment. *Acta Biomed*. 2021;92(S7):e2021517.
9. Leonardi A. Management of vernal keratoconjunctivitis. *Ophthalmol Ther*. 2013;2(2):73-88.
10. Ghauri AJ, Fisher K, Kenworthy A. Understanding the journey of patients with vernal keratoconjunctivitis: a qualitative study of the impact on children and families. *J Pediatr Ophthalmol Strabismus*. 2021;58(5):298-303.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

13993038, 2023, 5, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/pai.13962 by CochraneItalia, Wiley Online Library on [23/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License