



OPEN ACCESS

*CORRESPONDENCE

Kieran Halloran,
✉ kieran.halloran@ualberta.ca

RECEIVED 15 September 2026
REVISED 23 September 2026
ACCEPTED 23 September 2026
PUBLISHED 30 September 2026

CITATION

Halloran K (2026) Guiding light: new European guidelines on CLAD prevention and treatment.
Transpl. Int. 39:17855.
doi: 10.3389/ti.2026.17855

COPYRIGHT

© 2026 Halloran. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](#). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Guiding light: new European guidelines on CLAD prevention and treatment

Kieran Halloran  *

Department of Medicine, University of Alberta, Edmonton, AB, Canada

KEYWORDS

chronic lung allograft dysfunction, clinical practice guideline, clinical trial, lung transplantation, prevention

A Forum discussing

European society for organ transplantation clinical practice guideline on prevention and treatment of chronic lung allograft dysfunction

by Bos S, Hellemons M, Dave K, Engel MFM, Holm A, Morlacchi L, Müller V, Pavanello S, Picard C, Rossi V, Saez-Gimenez B, Gottlieb J and Vos R (2026). *Transpl. Int.* 39:16959. doi: [10.3389/ti.2026.16959](#)

Chronic lung allograft dysfunction (CLAD) is a challenging clinical entity in lung transplantation. It is common, deadly, difficult to prevent, and almost entirely unresponsive to therapy. As the number one killer of lung transplant patients after the first year [1], it also limits lung transplant as a therapy for advanced lung disease both by reducing its cost-effectiveness and requiring stringent selection criteria to minimize its risks. It was described over four decades ago now after the first lung transplants in the 1980s (then referred to collectively as bronchiolitis obliterans syndrome or BOS) [2], but despite significant advances in the time since in understanding its pathology, clinical course, risk factors, outcome associations, physiologic and radiographic subtypes, and finally the development of a consensus definition [3], the lung transplant community has had only limited success in evolving meaningful strategies to address CLAD.

In recent years though, there have been important developments. The first successful multicenter randomized clinical trial (RCT) of CLAD prevention was recently completed by a consortium of Scandinavian countries (ScanCLAD), demonstrating that tacrolimus is superior to cyclosporine in preventing CLAD [4]. Although only a minority of centers were still using cyclosporine as *de novo* immunosuppression after transplant [5], this new evidence can and should change practice there. It also informs clinicians when making decisions about whether to rotate patients from tacrolimus to cyclosporine and for what indications it is worth the trade-off. The successful completion of a multicenter clinical trial studying the role of anti-fibrotic therapy in patients with the BOS subtype of CLAD—specifically, that it showed no benefit—has also helped move the needle on a perennial question in what is understood to be a fibrotic airways process [6]. A single-center RCT in Vienna has also now shown that extracorporeal photopheresis (ECP) may prevent CLAD, in addition to potentially lowering rates of rejection and infection as well [7]. These works build on a previous successful Belgian clinical trial showing that azithromycin prophylaxis can reduce CLAD risk [8].

Despite these advances though, the evidence for CLAD therapeutics remains mixed or entirely lacking, and this can result in heterogeneity in the clinical approach [9, 10]. CLAD is

a universally feared complication, particularly in its rapidly progressive forms, and clinicians faced with an ailing patient and armed with limited evidence do not tend to stand by. The interventions clinicians impose are well-intentioned and may in some cases be beneficial but can set the stage for patient- and system-level harms, such as adverse drug effects, infectious or malignant complications of immunosuppression, and resource utilization without clear benefit. It is these contexts where clinical practice guidelines can make a difference by evaluating the evidence, providing grounded recommendations, and highlighting the important gaps that need to be addressed.

Enter the European Society for Organ Transplantation (ESOT) CLAD guidelines, reported in this issue of *Transplant International* [11]. A panel of noted European lung transplant experts spanning 8 countries has produced a document that at least in part fills this role. The group conducted a comprehensive literature search resulting in 8 recommendations addressing various CLAD prevention and treatment subjects, including macrolide therapy, maintenance immunosuppressive choices, extracorporeal photopheresis, and anti-rejection therapies, among others. The choice of what topics to address is strategic, as these reflect some of the most widely used and widely available therapies for CLAD, some of which have significant risk such as anti-thymocyte globulin and alemtuzumab. It should be noted that this is not the first guideline on CLAD management. A 2014 joint statement of the International Society for Heart and Lung Transplantation (ISHLT), European Respiratory Society, and American Thoracic Society summarized potential treatment strategies for CLAD (then BOS), in addition to diagnostic recommendations, though there was limited focus on prevention. This document also predated the 2019 definition consensus statement and particularly given the evolution of the evidence-base in the interim, a new guideline statement 12 years later is logical and much needed.

Due to limitations imposed by the ESOT guideline format, which restricts these documents to 8 PICO questions and associated recommendations, the authors acknowledge that they could not delve comprehensively into other important topics which are relevant to CLAD prevention and treatment. These include the role of induction therapy, palliative care strategies, retransplantation, anti-reflux surgery, corticosteroid therapy, and others. While understandable, these are regrettable omissions which render the document non-definitive and mean the community must await either a new iteration of this document or another guideline from another organization. Induction therapy and retransplantation in particular are important aspects of transplant care on which guidance is needed, particularly given practice is heterogeneous [12]. There have been several clinical trials on induction therapy in lung transplantation, but none have demonstrated an effect, and these drugs can have risks for patients with frequent

infections [13, 14]. Meanwhile retransplantation is a critical therapeutic resource for advanced CLAD in an otherwise well patient but one which is difficult to balance against first-time transplants in donor resource-constrained settings. While it is addressed by the ISHLT candidate selection guidelines, this document would seem an ideal place to formally comment on its use.

Considered on its own merits though, this author group has produced a meaningful evidence-based document with measured clinical guidance that will be helpful for smaller/newer lung transplant programs, in training lung transplant clinicians, and in helping existing programs re-evaluate their current approaches. Most importantly, it sheds light on the area most in need of study: CLAD therapeutics. It is this author's hope that with the evolution of the evidence base in recent years, armed with a standard definition and consensus endpoints [15], and with the current trials underway, we are entering an era in which the next iteration of a CLAD management document contains evidence for therapies which are not only effective in preventing CLAD, but in treating patients already affected by it.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

KH wrote the editorial.

Funding

The author(s) declared that financial support was not received for this work and/or its publication.

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Abbreviations: CLAD, chronic lung allograft dysfunction; BOS, bronchiolitis obliterans syndrome; RCT, randomized clinical trial; ECP, extracorporeal photopheresis; ESOT, European Society for Organ Transplantation; ISHLT, International Society for Heart and Lung Transplantation.

References

1. Dellgren G, Cherikh WS, Singh TP, Kim KH, Lewis A, Keller BC, et al. The international thoracic organ transplant registry of the international society for heart and lung transplantation: 2026 annual report of heart and lung transplantation. *J Heart Lung Transpl* (2026). doi: 10.1016/j.healun.2026.04.001
2. Burke CM, Theodore J, Dawkins KD, Yousem SA, Blank N, Billingham ME, et al. Post-transplant obliterative bronchiolitis and other late lung sequelae in human heart-lung transplantation. *Chest* (1984) 86(6):824–9. doi: 10.1378/chest.86.6.824
3. Verleden GM, Gnanville AR, Lease ED, Fisher AJ, Calabrese F, Corris PA, et al. Chronic lung allograft dysfunction: definition, diagnostic criteria and approaches to treatment. A consensus report from the pulmonary council of the ISHLT. *J Heart Lung Transpl* (2019) 38:1–44. doi: 10.1016/j.healun.2019.03.009
4. Dellgren G, Lund TK, Raivio P, Leuckfeld I, Svahn J, Holmberg EC, et al. Effect of once-per-day tacrolimus versus twice-per-day ciclosporin on 3-year incidence of chronic lung allograft dysfunction after lung transplantation in scandinavia (ScanCLAD): a multicentre randomised controlled trial. *Lancet Respir Med* (2023) 12:34–44. doi: 10.1016/s2213-2600(23)00293-x
5. Combs MP, Walter K, Hixson H, Belloli EA, Najor MS, Chan KM, et al. Impact of tacrolimus vs cyclosporine on chronic lung allograft dysfunction incidence and allograft survival in the international society of heart and lung transplantation registry. *J Heart Lung Transpl* (2025) 44(3):307–17. doi: 10.1016/j.healun.2024.10.013
6. Perch M, Corris P, Lordan J, Bessa V, Magnusson J, Verleden GM, et al. A European multi-center, randomized controlled trial of pirfenidone in bronchiolitis obliterans syndrome after bilateral lung transplantation. *Eur Respir J* (2025) 67:2402154. doi: 10.1183/13993003.02154-2024
7. Benazzo A, Cho A, Auner S, Schwarz S, Kovacs Z, Ramazanova D, et al. Extracorporeal photopheresis for the prevention of rejection after lung transplantation: a prospective randomised controlled trial. *Eur Respir J* (2025) 65(2):2400733. doi: 10.1183/13993003.00733-2024
8. Vos R, Vanaudenaerde BM, Verleden SE, De Vleeschauwer SI, Willems-Widyastuti A, Van Raemdonck DE, et al. A randomised controlled trial of azithromycin to prevent chronic rejection after lung transplantation. *Eur Respir J* (2010) 37(1):164–72. doi: 10.1183/09031936.00068310
9. Kapnadak SG, Milinic T, Morrell ED, Brandon W, Mayer M, Knapp S, et al. Approach to prevention and management of chronic lung allograft dysfunction in North American lung transplant centers. *J Heart Lung Transpl* (2026) 45:1470–3. doi: 10.1016/j.healun.2026.06.004
10. Michaels M, Kaur K, Weatherald J, Nagendran J, Aversa M, Nador R, et al. Variability in lung transplant clinical practices in Canada: results of a national survey. *Transpl Direct* (2026) 12(2):e1897. doi: 10.1097/txd.0000000000001897
11. Bos S, Hellemons M, Dave K, Engel MFM, Holm A, Morlacchi L, et al. European society for organ transplantation clinical practice guideline on prevention and treatment of chronic lung allograft dysfunction. *Transpl Int* (2026) 39:16959. doi: 10.3389/ti.2026.16959
12. Shagabayeva L, Osho AA, Moonsamy P, Mohan N, Wolfe S, Langer NB, et al. Induction therapy in lung transplantation: a contemporary analysis of trends and outcomes. *Clin Transpl* (2022) 36(11):e14782. doi: 10.1111/ctr.14782
13. Snell GI, Westall GP, Levvey BJ, Jaksch P, Keshavjee S, Hoopes CW, et al. A randomized, double-blind, Placebo-controlled, multicenter study of rabbit ATG in the prophylaxis of acute rejection in lung transplantation. *Am J Transpl* (2014) 14(5):1191–8. doi: 10.1111/ajt.12663
14. Jaksch P, Ankersmit J, Scheed A, Kocher A, Muraközy G, Klepetko W, et al. Alemtuzumab in lung transplantation: an open-label, randomized, prospective single center study. *Am J Transpl* (2014) 14(8):1839–45. doi: 10.1111/ajt.12824
15. Greenland JR, Perch M, Halloran K, Levine DJ, Morrell ED, Reed A, et al. Considerations for endpoints in lung transplant clinical trials: an ISHLT consensus statement. *J Heart Lung Transpl* (2025) 45:e104–e128. doi: 10.1016/j.healun.2025.09.017