Received: 25 April 2024 | Accepted: 5 March 2025

DOI: 10.1111/vde.13340

Veterinary Dermatology

ORIGINAL ARTICLE

A blinded randomised split-body clinical trial evaluating the effect of fluorescent light energy on antimicrobial management of canine interdigital furunculosis

A. Lange[1] | **U. Mayer**[1] | **E. Bensignor**[2] | **L. Cornegliani**[3] | **D. Ferreira**[4] | **I. Matricoti**[5] | **M. Mosca**[6] | **L. Ordeix**[7] | **D. Pin**[6] | **F. Scarampella**[8] | **E. Videmont**[9] | **A. Yu**[10] | **O. Fantini**[11]

[1]Department of Dermatology, AniCura Kleintierspezialisten Augsburg GmbH, Augsburg, Germany

[2]Dermatology Referral Service, Clinique Vétérinaire, Rennes-Cesson, France

[3]Clinica Veterinaria S. Siro – Anicura, Milan, Italy

[4]Dermatologia Veterinaria, Lisbon, Portugal

[5]Servizi Dermatologici Veterinari, Bologna, Italy

[6]VetAgro Sup, Interactions Cells Environment, Université de Lyon, Marcy l'Etoile, France

[7]Fundació Hospital Clínic Veterinari and Departament de Medicina i Cirurgia Animals, Facultat de Veterinària, Universitat Autònoma de Barcelona, Bellaterra, Spain

[8]Studio Dermatologico Veterinario, Milan, Italy

[9]Centre Hospitalier Vétérinaire, Saint-Martin Fillière, France

[10]Guelph Veterinary Specialty Hospital, Guelph, Ontario, Canada

[11]Vetoquinol SA, Paris, France

Correspondence
A. Lange, Department of Dermatology, Anicura Kleintierspezialisten Augsburg GmbH, Augsburg, Germany.
Email: anja.lange@anicura.de

Funding information
Vetoquinol SA

Abstract

Background: Canine interdigital furunculosis (CIF) is a complex, relapsing inflammatory condition, typically complicated by deep bacterial infections requiring prolonged systemic antibiotics.

Hypothesis/Objectives: This split-body study, where dogs acted as their own control, evaluated whether the adjunctive use of fluorescent light energy (FLE) could shorten the time to clinical resolution of CIF and minimise systemic antimicrobial use.

Animals: Thirty-five client-owned dogs with signs of interdigital furunculosis in at least two paws.

Materials and Methods: This prospective, single-blinded, randomised, split-body multicentre clinical trial treated dogs with systemic antibiotics based on bacterial culture and sensitivity. One paw per dog was randomly selected using a coin-toss method for weekly FLE application, while the other paw served as a control. Dogs were scored every 2 weeks over 56 days on two parameters: a global lesion score (including haemorrhagic vesicles, fistulae with draining tracts, crusts and ulcers) and neutrophils engulfing bacteria score (NES, 0–4). Time to clinical resolution and lesion scores were assessed and compared between groups.

Results: At Day (D)28 and D56, the FLE group showed significantly more healed paws (50% and 88%, $p=0.021$) compared to the control (17% and 54%, $p=0.008$). The median time to clinical resolution was shorter for the FLE group (35 days) compared to the control group (56 days, $p=0.017$). No difference in NES score was observed between groups.

Conclusions and Clinical Relevance: This blinded, randomised, split-body clinical trial demonstrated that FLE is an effective adjunctive therapy for CIF. It reduces the time to clinical resolution and increases the resolution rate while minimising the need for antibiotics.

KEYWORDS
dog, fluorescence photobiomodulation, interdigital cysts, interdigital furunculosis, low-level laser therapy, pododermatitis

INTRODUCTION

Canine interdigital furunculosis (CIF) is a chronic inflammatory skin condition affecting the pedal skin.[1–4] The condition is a complex, multifaceted disease often referred to as pedal folliculitis and furunculosis, pododermatitis or interdigital 'cysts' affected tissues may include interdigital spaces, footpads, nail folds or combinations thereof.[4] As the clinical appearance of the lesions on the paw can be identical regardless of the underlying condition,

veterinary surgeons find it frustrating to identify the primary aetiology and institute appropriate therapy.[4] CIF has been associated with hypersensitivities (atopic dermatitis [AD], cutaneous adverse food reaction), demodicosis, endocrine diseases (hypothyroidism, hyperadrenocorticism), foreign bodies and conformational problems with secondary infections as a common sequela.[5] Localised areas of folliculitis can progress to furunculosis, leading to endogenous hair shaft keratin foreign body reactions and the formation of nodules and fistulae with draining tracts.[3,4,6] As a consequence of the persistent foreign material within the skin, resolution of the secondary bacterial infection often requires prolonged courses of antibiotics, and relapse is common, even when the underlying trigger is managed. In addition to recurrent antibiotic therapy, many clinicians use topical or systemic anti-inflammatory drugs, including glucocorticoids and ciclosporin, to manage the inflammation caused by the foreign body reaction. Medical devices, including cold plasma therapy and photobiomodulation using low-level light therapy, have been incorporated into wound and pododermatitis therapeutic regimens.[7–10]

Recent research on fluorescence photobiomodulation has led to a novel approach for CIF through the activation of topical photoconverter substrates containing specialised exogenous chromophores by exposure to blue light (peak wavelength between 440 and 460 nm), resulting in fluorescent light energy (FLE). FLE modulates the inflammatory process in dermatological disorders and has shown promising results in preliminary studies evaluating its use in superficial and deep pyoderma and interdigital furunculosis.[11–13] The aim of this study is to evaluate the effect of FLE in the management of CIF, assessing whether the combination of systemic antibiotics and FLE will accelerate time to healing versus the use of systemic antibiotics alone.

MATERIALS AND METHODS

This was a prospective, multicentre, single-blinded, randomised split-body trial. At each of the 10 facilities, blinding of the study was maintained by the double-investigator technique: the principal investigator was responsible for clinical (using the photographic documentation) and cytological assessment, and a co-investigator was responsible for randomisation, dispensing the product and applying the FLE intervention (Phovia; Vetoquinol SA). The co-investigator was not involved in the outcome assessment. The principal investigator was unaware of the intervention assignment and remained blinded until the last recheck was performed on Day (D)56.

Ethics

This trial was conducted under good general conditions and per local legislation on the use of patients for clinical trials. Before treatments were started, informed consent was obtained by signing a form from all owners whose pets participated in this study; the study protocol, owner responsibilities, all known risks and potential adverse events resulting from the FLE application were clearly explained. The study was conducted after ethical review and validation (no. 2024#08) at Vetoquinol and complied with all animal welfare regulations.

Study population

Inclusion criteria

Client-owned dogs diagnosed with interdigital furunculosis by dermatological specialists at multiple centres in Europe, the United Kingdom and Canada were enrolled. Dogs with CIF on at least two paws were recruited without age, breed, body weight or sex restrictions. CIF lesions included at least one or more of the following lesions: haemorrhagic vesicles/bullae, draining tracts, haemorrhagic crust/papules and ulcers/erosions. Inclusion into the study required a disease severity score of ≥2 and a global lesion score of ≥5 by adding the scores from the different parameters (Table 1) developed by Marchegiani et al.[13] If dogs presented with CIF in more than two paws, the most severe ones were considered for the scope of the study. Dogs with

TABLE 1 Scoring chart for clinical signs of interdigital furunculosis.

Lesion type		Haemorrhagic vesicles/bullae or nodules	Fistula with draining tracts	Haemorrhagic crust/papules	Ulcers/erosions
Score	**Grade**	**Lesion assessment for each paw**			
0	Healed	Absent	Absent	Absent	Absent
1	Mild	Healing lesion	Healing nondraining lesions only	1 small area	Superficial erosions only
2	Moderate	1–2 primary lesions	Single active draining lesion	2 small areas	Single small area of ulceration, no other lesions
3	Severe	3–4 primary lesions	1–2 active draining lesions with other lesions	3–4 more extensive areas	Single more extensive area combined with other lesions or two areas of extensive ulceration without other lesions
4	Very severe	≥5 primary lesions	≥3 active draining lesions with other lesions	≥5 extensive areas	≥2 extensive areas combined with other lesions or ≥3 extensive areas

Note: Small is defined as ≤1 cm in diameter, extensive lesions as >1 cm in diameter.

an underlying allergic skin disease were included provided that their pruritus was adequately controlled only with the use of heartworm, endo- and ectoparasitic preventatives, prescription diets, nonsteroidal anti-inflammatory drugs, vitamin/mineral or essential fatty acid supplements, routine vaccines, allergen-specific immunotherapy (which had been initiated ≥8 months before enrolment), monoclonal antibodies and topical non-antimicrobial shampoos (antiparasitic, conditioner and hypoallergenic properties). Patients were allowed to receive medication to control other underlying medical disorders, including thyroid supplementation (all dogs on thyroid medication were shown to have a normal thyroxine level before starting the trial), diuretics and cardiac drugs.

Exclusion criteria

Dogs were excluded on D0 if they were in poor general health based on a physical examination performed by a veterinarian, had lesions of the paw pads or had evidence of *Malassezia* spp., fungal dermatitis or ectoparasites. Dogs also were excluded if they were treated within the last 30 days with injectable or oral short-acting glucocorticoids; within 90 days with repository glucocorticoids; or with oclacitinib, ciclosporin or other anti-inflammatory or immunosuppressive medication. Dogs with an underlying disease that might affect their ability to respond to antibiotics (e.g. hyperadrenocorticism, diabetes mellitus, leishmaniasis), received concomitant treatment with photosensitising molecules (tetracycline antimicrobial family, clofazimine, dacarbazine, dapsone, griseofulvin, coal tar or topical retinoids) or had a known infection caused by multidrug-resistant (MDR) bacteria were excluded. Withdrawal from the analysis was required following: poor compliance with the study protocol instructions regarding visits and medication; severe adverse effects from any of the products used; the development of any further comorbidities during the study that would have impaired the ability to score study lesions or treatment outcomes; missing one FLE application in the once-a-week regimen or two applications in the twice-a-week regimen; or worsening of pruritus in allergic dogs.

Study timeline

This study was implemented over 8 weeks, with an inclusion visit on D0 and recheck visits every 7 days. All visits had a margin of ±1–2 days for modification if needed. General examination, a detailed examination of the skin and lesions, disease severity and scoring assessment with the global lesion score (GLS) for each study paw, photographic documentation of lesions, assessment and measurement of pruritus intensity (via pruritus visual analogue scale [PVAS] score), a cytological scoring of each body site, neutrophils engulfing bacteria score (NES; Table S1) and the investigator's assessment of the FLE effect at clinical resolution were recorded on D0, D14, D28, D42 and D56. Although the length of the study was 8 weeks, FLE application was stopped at clinical resolution. Treatment was continued for dogs not reaching clinical resolution by D56 (Week 8). Further assessments were conducted during visits on D70 and D84 (Week 12). Dogs that did not reach clinical resolution by Week 12 continued treatment until they did. All dogs achieving clinical resolution at any time up to a maximum of 12 weeks of treatment were enrolled for a further 3-month follow-up period to assess for any recurrence of lesions, defined as the reappearance of one or a combination of lesions in the same previously affected site. Dogs not achieving clinical resolution after 12 weeks were not enrolled in the follow-up study. During the follow-up period, owners were contacted monthly to determine if they had noticed any signs of relapse. All owners were invited for a final clinical examination 3 months after the follow-up period started. A FLE overall satisfaction score was completed by the owners at clinical resolution as very satisfied, satisfied, neutral, dissatisfied or very dissatisfied.

Intervention groups

Every dog was treated with a systemic antibiotic. If only the front paws were affected, one paw received a topical application of FLE until clinical resolution (Group A), while the other remained without intervention (Group B). If all paws were affected, the front and back paws of the same side received a topical application of FLE until clinical resolution (Group A); the other ones were left untreated (Group B). The paw(s) to receive FLE was/were chosen randomly according to a biased coin randomisation. The randomisation was performed on the day of inclusion: left side = heads; right side = tails. Each animal acted as its own control.

Antibiotic intervention

The systemic antibiotic options consisted of cephalexin or amoxicillin and clavulanate at a dosage of 15 mg/kg twice daily and 12.5 mg/kg twice daily, respectively, after verifying the efficacy of this molecule based on antibiotic susceptibility testing; if the isolate was not susceptible to cephalexin or amoxicillin and clavulanate, then another appropriate antibiotic was selected based on the susceptibility results obtained. The choice between cephalexin and amoxicillin/clavulanic acid was determined by several factors. Primarily, the treatment selection was at the discretion of the investigator, taking into account the clinical history of the patients. Additionally, the formulation that best matched the dogs' weight was considered to ensure adherence to the recommended dosage. Antibiotic treatment was stopped upon clinical resolution of lesions on the control paws and was not administered beyond Week 12.

Blinding

In order to account for differences between study groups, blinding was maintained using a double-investigator technique. The principal investigator was responsible for clinical examinations and cytological analyses, which were performed every 2 weeks, while the co-investigator handled randomisation, product dispensing and the application of FLE. The co-investigator did not participate in outcome assessments. The principal investigator remained blinded to the treatment assignments and was only unblinded after the final recheck at Week 12.

FLE intervention

Dogs were put in a comfortable position, with the lesion accessible for the procedure and the animal's head facing away from the light (or the eyes covered to protect them from the light, for example, with supplied safety goggles). If needed, hair that prevented full contact of the gel with the surface of the lesions was gently clipped.

Sedative and/or immobilising drugs could be employed to manage anxiety, aggression, hyperactivity, discomfort and pain in patients during handling procedures. However, it is noteworthy that in this study, none of the dogs required sedation or immobilisation. The exogenous chromophore was transferred into the jar containing an urea peroxidase-containing gel, and the mixture was stirred until the orange colour was uniform. The jar was covered until the time of application. Wearing gloves, the co-investigator applied a layer of gel approximately 2 mm thick to the surface of the whole lesion with a spatula. Everyone in the room wore safety goggles when the lamp was turned on. The rim of the lamp window was placed as close as possible to the lesion without touching the skin. Lesions were treated once a week with two consecutive 2 min applications; that is, the gel mixture of chromophore and carrier gel was applied, illuminated for 2 min, removed and a new mixture was re-applied after a 1 min rest, illuminated for 2 min and removed again. Once the procedure was completed, the gel was removed from the lesion with saline-soaked gauze.

Statistical analysis

Statistical analysis was performed using SAS v9.1 (SAS Institute Inc.). Clinical resolution rates were compared in two nonindependent samples using the McNemar test for dichotomous variables. Weekly GLS and NES reduction were analysed via a two-factor ANOVA with REML estimation, Kenward–Roger degrees of freedom and specified variance structures. Median resolution times were estimated using the Kaplan–Meier methodology and compared through log-rank testing. The probability of treatment success between the groups at different times was assessed using a binary generalised mixed model with a two-factor analysis. A p-value <0.05 was considered statistically significant.

In our clinical study, we aimed to include 40 dogs, each serving as their own control, to evaluate the effect of the treatment. This number is justified based on the expected clinical resolution rates of 80% in the treatment group and 40% in the control group. To detect this 40% difference with a significance level of 5% (alpha=0.05) and a power of 80% (1–beta=0.80), a sample size calculation indicated that approximately 34–40 dogs would be required. This ensures that the study has adequate power to detect a clinically meaningful difference in outcomes between the treated and untreated paws.

RESULTS

Study population

A total of 38 dogs underwent an initial assessment for inclusion in the study. Three dogs were excluded at enrolment owing to MDR *Staphylococcus* spp. Consequently, 35 dogs were successfully enrolled, consisting of 19 males (17 castrated) and 16 females (15 spayed). These dogs belonged to a diverse range of breeds, with the median age and weight of the cohort being 4 years and 9 months (range 2.1–10 years) and 19.6 kg (range 12.2–43 kg), respectively. Predominant breed representation included French and English bulldogs (10 of 35), mixed-breed dogs (12 of 35), Labrador retrievers and Golden retrievers (5 of 35 each), West Highland white terriers (4 of 35), German shepherd dogs (3 of 35) and Staffordshire bull terriers (3 of 35). Detailed demographic information is presented in Table S2.

Among the 35 dogs, 16 were identified with canine AD. These dogs were included in the study as their condition was adequately controlled with the administration of monoclonal antibodies, prescription diets, essential fatty acids and topical shampoos without antimicrobial therapy. No recurrence of pruritus or flare-ups was observed during the study. No other underlying diseases were identified during the study.

Culture and sensitivity

Microbiological swabs of the lesions yielded *Staphylococcus* spp. (n=35) as the predominant pathogen, encompassing *S. pseudintermedius* and *S. schleiferi* as the isolated species. Several other bacterial strains, including *Streptococcus* spp.,

TABLE 2 Bacteria isolated from canine interdigital lesions.

Bacteria isolated	Number of paws
Staphylococcus pseudintermedius	35
Staphylococcus schleiferi	6
Staphylococcus aureus	3
Streptococcus spp.	6
Enterococcus faecalis	3
Bacillus spp.	5
Proteus spp.	8

Escherichia coli and others, were infrequently detected (Table 2). Notably, five isolates exhibited resistance to amoxicillin and clavulanic acid or cephalexin, prompting the selection of appropriate antibiotics based on susceptibility results (clindamycin, enrofloxacin, marbofloxacin and cefpodoxime).

Eighteen dogs received amoxicillin and clavulanic acid with doses ranging from 12.5 to 18 mg/kg twice daily. The median dose was 13.75 mg/kg with a standard deviation (SD) of approximately 0.88 and a mean duration of 52.2 days. Twelve dogs received cephalexin with doses ranging from 15 to 21 mg/kg twice daily. The median dose was 18.0 mg/kg, with a SD of approximately 1.86 and a mean duration of 56.4 days. One dog received clindamycin at 5.5 mg/kg twice daily for 59 days. One dog received enrofloxacin at 5.4 mg/kg once daily for 51 days; one dog received marbofloxacin at 2.14 mg/kg once daily for 58 days and two dogs received cefpodoxime at 7 mg/kg once daily for 63 days.

Clinical score

All dogs that successfully completed the study presented with various combinations of lesions, including haemorrhagic vesicles/bullae or nodules (n=35), draining tracts (n=8), haemorrhagic crust/papules (n=31) and ulcers/erosions (n=18). At enrolment, no statistically significant difference was observed in global lesion scores between the FLE and control groups (mean GLS 8.50±1.91 for the FLE group and 7.50±1.43 for the control group).

Time to clinical resolution

In the primary end-point analysis, the clinical resolution rate per visit (from day 0 to day 56) was assessed, with Figure 1 depicting the results. Statistically significant differences in time to clinical resolution were observed on D28 (Figure 2) and D56, with the FLE group demonstrating a higher success rate. By D28, 50% of paws treated with FLE achieved clinical resolution, compared to 17% in the control group (p=0.021). By D56, 88% of paws treated with FLE achieved clinical resolution, compared to 54% in the control group (p=0.008). The median time to clinical resolution was 35 days in the FLE group, compared to 56 days in the control group (p=0.017).

The probability of achieving clinical resolution of lesions at each time point between the treatment groups is illustrated in Table 3. Notably, on D28, the FLE group exhibited a significantly higher probability of being cured compared to the control group. On D28, in the FLE group, the probability of treatment success was 5.35-fold higher compared to the control group, and this probability increased to 6.01-fold by D56.

Global lesion score and neutrophils engulfing bacteria score

At D28 and D56, a statistically significant improvement in the mean GLS score was observed in the FLE group compared to the control group, as illustrated in Figure 3. Conversely, while NES scores improved in favour of the FLE group at D14, D28 and D56, no statistically significant difference was detected between the two groups (Figure S1).

Adverse effects

Throughout the study duration, no adverse effects were observed.

Pet owner overall satisfaction score

All owners (35, 100%) completed the pet owner overall satisfaction questionnaire, with 2 being very satisfied (7%), 20 being satisfied (57%), 12 being neutral (34%), 1 being dissatisfied (3%) and none being very dissatisfied (0%).

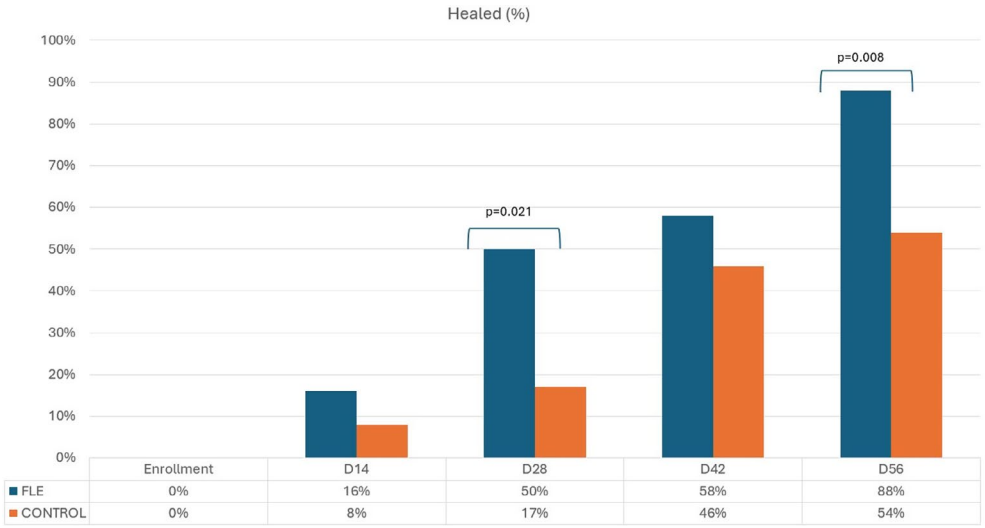

FIGURE 1 Percentage of paws healed by intervention at each time point. D, day; FLE, fluorescent light energy.

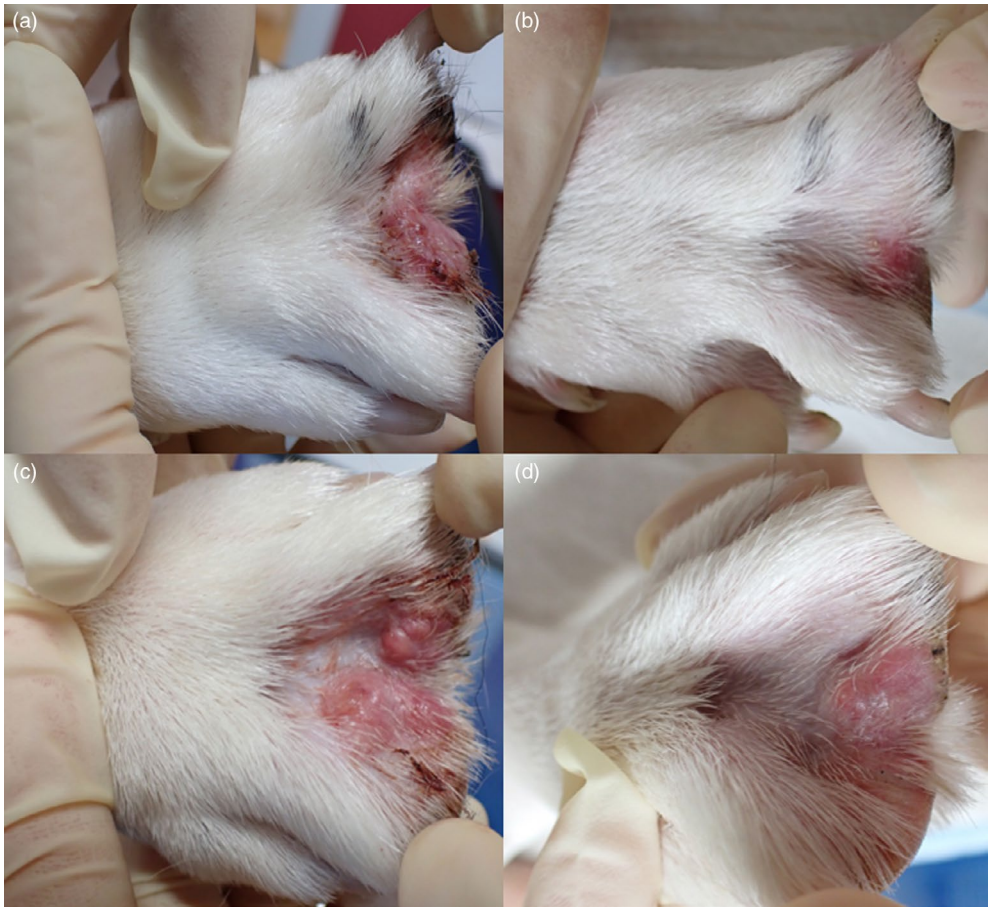

FIGURE 2 Impact of fluorescent light energy (FLE) versus control on canine interdigital furunculosis at different time points. (a, b) FLE Day (D)0 and D28; (c, d) control D0 and D28.

TABLE 3 Probability of cure between intervention groups at each time point (Day [D]).

Comparison	Time	Difference odds-ratio estimate	95% odds-ratio confidence interval	*p*-value (significance)
FLE versus control	D14	2.284	[0.316;16.514]	0.411 (NS)
	D28	5.352	[1.221;23.465]	0.026 (S)
	D42	1.642	[0.446;6.039]	0.453 (NS)
	D56	6.013	[1.120;32.290]	0.037 (S)

Abbreviations: FLE, fluorescent light energy; NS, not significant; S, significant.

Results obtained during the 3-month follow-up observation period

By D70, 92% of paws treated with FLE achieved clinical resolution, compared to 75% in the control group (p=0.250). By D84, 96% of paws treated with FLE achieved clinical resolution, compared to 86% in the control group (p=0.500). Thirty-three dogs were enrolled in the follow-up assessment period. Seven experienced a relapse during the 3-month observation period. Among these seven dogs, five had lesions on both the FLE-treated and control paws, while two had lesions only on the control paw. The GLS was two for the FLE-treated area and five for the control area (p=0.048). During the follow-up period, the use of any drugs necessary to treat underlying conditions or any new conditions that arose was permitted.

DISCUSSION

Canine interdigital furunculosis is a challenging, multifactorial condition that often leads to recurrent secondary infections. In this study, *Staphylococcus* species were the primary pathogens, consistent with previous research on CIF and interdigital pyoderma.[4,13,14] Notably, 3 of 38 dogs were withdrawn owing to MDR organisms, highlighting the need for pre-treatment culture and sensitivity testing to guide antibiotic selection, as recommended by prior studies on CIF management.[12] Fluoroquinolones are known to modulate the immune system[15] yet it is unlikely that these effects had an impact on the outcome of the results, as only two dogs were treated with fluoroquinolones for a similar duration of antibiotic treatment compared to the other dogs in this study.

Our results demonstrated that FLE combined with systemic antibiotics significantly reduced the time to clinical resolution compared to antibiotics alone. By Week 4, 50% of paws in the FLE group achieved clinical resolution, compared to 17% in the control group and by Week 8, 88% of paws in the FLE group had healed, compared to 54% in the control group. This is

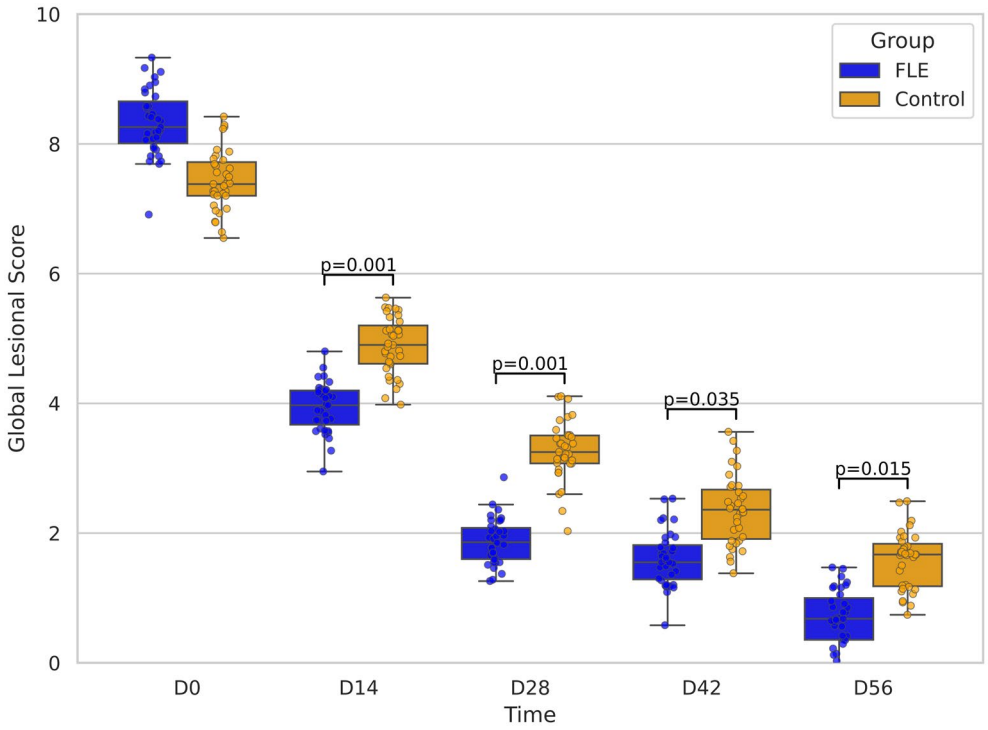

FIGURE 3 Comparison of global lesional score between intervention groups at each time point. D, day; FLE, fluorescent light energy.

consistent with previous findings in CIF, where adjunctive therapies such as FLE showed similar efficacy in reducing lesion severity and accelerating recovery.[11,13] Marchegiani et al.[13] (2022) reported comparable resolution rates when FLE was used once or twice weekly, although their study involved a smaller sample size of 12 dogs. Our study, with a larger population, confirms and strengthens the hypothesis that FLE can significantly enhance the treatment of CIF.

No significant differences were observed in NES between the two groups, yet the GLS was consistently lower in the FLE group, with statistical significance at D28 and D56. Similar results were observed in studies on canine pyoderma and interdigital pyoderma, where adjunctive FLE led to faster lesion resolution and improved healing outcomes.[13,14,16,17] The mechanism of action is hypothesised to involve the upregulation of epidermal growth factor and matrix metalloproteinase-1, which accelerate re-epithelialisation and modulate inflammatory responses. This mechanistic pathway has been documented in other FLE studies, showing its potential to promote wound healing and reduce inflammatory cytokines such as interleukin-6.[11,18]

Potential adverse effects associated with using the FLE system include hair colour change, erythema that regresses within 6–12 h, skin hyperpigmentation and transient pain at the wound site. As shown in previous studies[16,17] no adverse events were observed during the entire trial.

The investigation herein is similar to the research by Marchegiani et al.[13] in 2019 yet, the use of the split-body design in this study enhances the validity of the results and allows for a more direct comparison between FLE-treated and control paws within the same subject. The split-body design, where each dog serves as its own control, provides a robust method to minimise interindividual variability and reduce sample size while maintaining statistical power.[19] However, limitations such as the exclusion of resistant infections and topical antimicrobial agents should be addressed in future studies to assess the full potential of FLE in real-world clinical settings.

CONCLUSIONS

In summary, our findings indicate that FLE, as an adjunct management option alongside systemic antibiotics, is safe to use and has the potential to expedite clinical resolution in the treatment of CIF, thus decreasing the reliance on prolonged antibiotic treatment regimens.

ACKNOWLEDGEMENTS

This study was funded by Vetoquinol which made this study possible. We are also grateful to the owners and their patients who participated in this research and made this work possible.

AUTHOR CONTRIBUTIONS

A. Lange: Investigation; writing – original draft; writing – review and editing. **U. Mayer:** Investigation; writing – review and editing. **E. Bensignor:** Investigation; writing – original draft. **L. Cornegliani:** Investigation; writing – original draft. **D. Ferreira:** Investigation; writing – original draft. **I. Matricoti:** Investigation; writing – original draft. **M. Mosca:** Investigation; writing – original draft. **L. Ordeix:** Investigation; writing – original draft. **D. Pin:** Investigation; writing – original draft. **F. Scarampella:** Investigation; writing – original draft. **E. Vidémont:** Investigation; writing – original draft. **A. Yu:** Investigation; writing – original draft; writing – review and editing. **O. Fantini:** Conceptualization; investigation; funding

acquisition; writing – original draft; methodology; visualization; validation; writing – review and editing; formal analysis; project administration; supervision; data curation; resources.

FUNDING INFORMATION
The study was initiated and funded by Vetoquinol SA.

CONFLICT OF INTEREST STATEMENT
A.L. has not declared any conflicts of interest. All other authors have received a lecture honorarium from Vetoquinol. O.F. is a Vetoquinol employee.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID
A. Lange https://orcid.org/0009-0000-7785-9372
E. Bensignor https://orcid.org/0000-0002-0404-3185
L. Cornegliani https://orcid.org/0000-0001-5291-4080
D. Ferreira https://orcid.org/0000-0003-2500-8298
M. Mosca https://orcid.org/0000-0002-7682-2452
F. Scarampella https://orcid.org/0000-0002-4581-7263

REFERENCES
1. Bloom P. Idiopathic pododermatitis in the dog: an uncommon but frustrating disease. Vet J. 2008;176(2):123–4.
2. Breathnach RM, Fanning S, Mulcahy G, Bassett HF, Jones BR. Canine pododermatitis and idiopathic disease. Vet J. 2008;176(2):146–57.
3. Duclos D. Canine pododermatitis. Vet Clin North Am Small Anim Pract. 2013;43(1):57–87.
4. Bajwa J. Canine pododermatitis. Can Vet J. 2016;57(9):991–3.
5. Miller WH, Griffin CE, Campbell KL. Muller and Kirk's small animal dermatology. St. Louis, MO: Elsevier Mosby; 2013. p. 201–2.
6. Duclos DD, Hargis AM, Hanley PW. Pathogenesis of canine interdigital palmar and plantar comedones and follicular cysts, and their response to laser surgery. Vet Dermatol. 2008;19(3):134–41.
7. Hasse S, Duong Tran T, Hahn O, Kindler S, Metelmann HR, von Woedtke T, et al. Induction of proliferation of basal epidermal keratinocytes by cold atmospheric-pressure plasma. Clin Exp Dermatol. 2016;41(2):202–9. https://doi.org/10.1111/ced.12735
8. Schmidt A, Bekeschus S, Wende K, Vollmar B, von Woedtke T. A cold plasma jet accelerates wound healing in a murine model of full-thickness skin wounds. Exp Dermatol. 2017;26(2):156–62.
9. Hoisang S, Kampa N, Seesupa S, Jitpean S. Assessment of wound area reduction on chronic wounds in dogs with photobiomodulation therapy: a randomized controlled clinical trial. Vet World. 2021;14(8):2251–9.
10. Perego R, Mazzeo M, Spada E, Proverbio D. Critically appraised topic on low-level laser therapy (LLLT) in dogs: an advisable treatment for skin diseases? Vet Sci. 2022;9(9):505. https://doi.org/10.3390/vetsci9090505
11. Marchegiani A. Klox fluorescence biomodulation system proceedings 61st BSAVA congress. 2018. p. 442.
12. Marchegiani A. Abstracts of the 29th annual congress of the ECVD-ESVD, 7-9th September 2017, Lausanne, Switzerland. Vet Dermatol. 2017;28(6):533–53.
13. Marchegiani A, Spaterna A, Cerquetella M, Tambella AM, Fruganti A, Paterson S. Fluorescence biomodulation in the management of canine interdigital pyoderma cases: a prospective, single-blinded, randomized and controlled clinical study. Vet Dermatol. 2019;30(5):371 –e109.
14. Marchegiani A, Fruganti A, Gavazza A, Spaterna A, Cerquetella M. Fluorescence biomodulation for canine interdigital furunculosis: updates for once-weekly schedule. Front Vet Sci. 2022;9:880349.
15. Assar S, Nosratabadi R, Khorramdel Azad H, Masoumi J, Mohamadi M, Hassanshahi G. A review of immunomodulatory effects of fluoroquinolones. Immunol Investig. 2021;50(8):1007–26.
16. Marchegiani A, Fruganti A, Spaterna A, Cerquetella M, Tambella AM, Paterson S. The effectiveness of fluorescent light energy as adjunct therapy in canine deep pyoderma: a randomized clinical trial. Vet Med Int. 2021;2021:6643416.
17. Marchegiani A, Fruganti A, Bazzano M, Cerquetella M, Dini F, Spaterna A. Fluorescent light energy in the management of multi drug resistant canine pyoderma: a prospective exploratory study. Pathogens. 2022;11(10):1197. https://doi.org/10.3390/pathogens11101197
18. Scapagnini G, Marchegiani A, Rossi G, Zago M, Jowarska J, Wael M. Management of all three phases of wound healing through the induction of fluorescence biomodulation using fluorescence light energy. In: Proc. SPIE 10863, photonic diagnosis and treatment of infections and inflammatory diseases II, 108630W. 2019. https://doi.org/10.1117/12.2508066
19. Leducq S, Caille A, Le Cleach L, Samimi M, Tavernier E, Maruani A, et al. Research techniques made simple: randomized controlled trials for topical drugs in dermatology: when and how should we use a within-person design? J Invest Dermatol. 2020;140(5):931–8. e1.

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

How to cite this article: Lange A, Mayer U, Bensignor E, Cornegliani L, Ferreira D, Matricoti I, et al. A blinded randomised split-body clinical trial evaluating the effect of fluorescent light energy on antimicrobial management of canine interdigital furunculosis. Vet Dermatol. 2025;36:291–301. https://doi.org/10.1111/vde.13340

Zusammenfassung
Hintergrund: Die interdigitale Furunkulose (CIF) des Hundes ist eine komplexe, wiederkehrende entzündliche Erkrankung, die typischerweise durch tiefe bakterielle Infektionen verkompliziert wird und dadurch den verlängerten Einsatz von systemischen Antibiotika bedingt.
Hypothese/Ziele: Diese Split-Body Studie, wo Hunde als ihre eigene Kontrolle dienten, evaluierte, ob der zusätzliche Einsatz von fluoreszierender Lichtenergie (FLE) die Zeitdauer bis zur klinischen Abheilung der CIF verkürzen und den Einsatz systemischer Antibiotika minimieren könnte.
Tiere: Fünfunddreißig Hunde in Privatbesitz mit Zeichen von interdigitaler Furunkulose an mindestens zwei Pfoten.
Materialien und Methoden: Diese prospektive einfachblinde, randomisierte, Split-Body Multicenter klinische Studie behandelte Hunde basierend auf einer bakteriellen Kultur und Sensibilität mit systemischen Antibiotika. Eine Pfote pro Hund wurde zufällig mittels Münzwurfmethode zur wöchentlichen FLE-Anwendung ausgewählt, während die andere Pfote als Kontrolle diente. Die Hunde wurden 56 Tage lang alle 2 Wochen in Bezug auf zwei Parameter bewertet: ein globaler Läsionswert (inklusive hämorrhagische Bläschen, Fisteln mit Fistelgängen, Krusten und Ulzera) und ein Wert, welcher das Ausmaß der Bakterien verschlingender Neutrophiler bestimmte (NES, 0-4). Die Zeit bis zur klinischen Heilung und die Läsionswerte wurden erfasst und zwischen den Gruppen verglichen.
Ergebnisse: Am Tag (D)28 und D56 zeigte die FLE-Gruppe signifikant häufiger geheilte Pfoten (50% und 88%, p=0,021) im Vergleich zur Kontrolle (17% und 54%, p=0,008). Der Medianwert der Zeit bis zur klinischen Abheilung war in der FLE-Gruppe kürzer (35 Tage) im Vergleich zur Kontrollgruppe (56 Tage, p=0,017). Es wurde kein Unterschied zwischen den Gruppen in Bezug auf den NES-Wert festgestellt.
Schlussfolgerungen und klinische Bedeutung: Diese blinde, randomisierte, Split-Body Studie zeigte, dass FLE eine wirksame Zusatzbehandlung für CIF darstellt. Es reduziert die Zeit bis zur klinischen Heilung und erhöht die Heilungsrate während es den Antibiotikaeinsatz minimiert.

摘要
背景: 犬趾间疖病 (CIF) 是一种复杂的复发性炎症疾病 , 通常因深部细菌感染而变得复杂 , 需要长期全身抗生素治疗。
假设/目标: 这项分体研究以犬作为自身对照 , 评估辅助使用荧光能量 (FLE) 是否可以缩短 CIF 的临床缓解时间并最大限度地减少全身抗菌药物的使用。
动物: 三十五只客户拥有的犬 , 至少两只爪子有趾间疖病的迹象。
材料和方法: 这项前瞻性、单盲、随机、分体多中心临床试验根据细菌培养和敏感性对犬进行全身抗生素治疗。使用掷硬币法随机选择每只犬的一只爪子进行每周 FLE 应用 , 而另一只爪子作为对照。在 56 天内 , 每 2 周对犬进行一次评分 , 评分依据两个参数:整体病变评分(包括血疱、带引流道的瘘管、结痂和溃疡)和中性粒细胞吞噬细菌评分(NES , 0-4)。评估并比较各组之间的临床缓解时间和病变评分。
结果: 在第 28 天和第 56 天 , FLE 组的爪子愈合率明显高于对照组(分别为 17% 和 54% , p = 0.008)(分别为 50% 和 88% , p = 0.021)。与对照组(56 天 , p = 0.017)相比 , FLE 组的临床缓解中位时间(35 天)较短。各组之间的 NES 评分无差异。
结论和临床意义: 这项盲法、随机、分体临床试验表明 , FLE 是 CIF 的有效辅助疗法。它缩短了临床缓解时间并提高了缓解率 , 同时最大限度地减少了对抗生素的需求。

Résumé
Contexte: La furonculose interdigitale canine (FID) est une affection inflammatoire complexe et récidivante, généralement compliquée par des infections bactériennes profondes nécessitant une antibiothérapie systémique prolongée.
Hypothèse/Objectifs: Cette étude à corps séparés, où les chiens ont agi comme leur propre contrôle, a évalué si l'utilisation complémentaire de l'énergie lumineuse fluorescente (ELF) pouvait raccourcir le délai de résolution clinique de la FIC et minimiser l'utilisation d'antimicrobiens systémiques.
Animaux: trente-cinq chiens appartenant à des clients et présentant des signes de furonculose interdigitale sur au moins deux pattes.
Matériels et méthodes: Cet essai clinique multicentrique prospectif, en simple aveugle, randomisé et à corps séparé a traité les chiens avec des antibiotiques systémiques sur la base de la culture et de la sensibilité bactériennes. Une patte par chien a été choisie au hasard à l'aide d'une méthode de pile ou face pour une application hebdomadaire de FLE, tandis que l'autre patte a servi de contrôle. Les chiens ont été évalués toutes les 2 semaines pendant 56 jours sur la base de deux paramètres : un score lésionnel global (comprenant des vésicules hémorragiques, des fistules avec des voies de drainage, des croûtes et des ulcères) et un score d'engloutissement des bactéries par les neutrophiles (NES, 0-4). Le délai de résolution clinique et les scores des lésions ont été évalués et comparés entre les groupes.
Résultats: Au jour (J)28 et J56, le groupe FLE présentait significativement plus de pattes guéries (50 % et 88 %, p=0,021) que le groupe témoin (17 % et 54 %, p=0,008). Le délai médian de résolution clinique était plus court dans le groupe FLE (35 jours) que dans le groupe témoin (56 jours, p=0,017). Aucune différence de score NES n'a été observée entre les groupes.

Conclusions et pertinence clinique: Cet essai clinique en aveugle, randomisé et à corps séparés a démontré que le FLE est un traitement d'appoint efficace pour la FIC. Il réduit le délai de résolution clinique et augmente le taux de résolution tout en minimisant le besoin d'antibiotiques.

要約
背景: 犬の趾間癰腫症(CIF)は複雑な再発性の炎症性疾患であり、通常、抗生物質の長期投与を必要とする深在性細菌感染を合併する。
仮説/目的: このスプリットボディ研究では、犬自身が対照群となり、蛍光灯エネルギー(FLE)の補助的使用がCIFの臨床的治癒までの時間を短縮し、全身性抗菌薬の使用を最小限に抑えられるかどうかを評価した。
供試動物: 少なくとも2肢に趾間癰腫症の徴候がある35頭のオーナー所有犬。
材料と方法: この前向き、単盲検、無作為化、スプリットボディ多施設臨床試験では、細菌培養検査および薬剤感受性試験に基づき、全身性抗菌薬による治療を行った。犬1頭につき片方の前足をコイントス法で無作為に選択し、毎週FLEを投与し、もう片方の前足を対照とした。犬は2週間ごとに56日間にわたり、2つのパラメータについて採点された。すなわちグローバル病変スコア(出血性小水疱、排膿路を伴う瘻孔、痂皮、潰瘍を含む)および好中球貪食細菌スコア(NES、0~4)である。臨床的治癒までの期間および病変スコアを評価し、群間で比較した。
結果: Day(D)28およびD56において、FLE群はコントロール群(17%と54%、p=0.008)と比較して、治癒した前足が有意に多かった(50%と88%、p=0.021)。臨床的治癒までの期間の中央値は、FLE群(35日)は対照群(56日、p=0.017)に比べて短かった。NESスコアに群間差はみられなかった。
結論と臨床的意義: この盲検無作為化分割体臨床試験により、FLEはCIFに対する有効な補助療法であることが実証された。FLEは臨床的治癒までの期間を短縮し、抗生物質の必要性を最小限に抑えながら治癒率を高める。

Resumo
Contexto: A furunculose interdigital canina (FIC) é uma condição inflamatória complexa e recorrente, tipicamente complicada por infecções bacterianas profundas que requerem antibióticos sistêmicos prolongados.
Hipótese/Objetivos: Este estudo de corpo dividido, onde os cães atuaram como seu próprio controle, avaliou se o uso adjuvante de energia de luz fluorescente (FLE) poderia encurtar o tempo para resolução clínica da FIC e minimizar o uso de antimicrobianos sistêmicos.
Animais: trinta e cinco cães de propriedade de clientes com sinais de furunculose interdigital em pelo menos duas patas.
Materiais e métodos: Este ensaio clínico prospectivo, simples-cego, randomizado e multicêntrico de corpo dividido tratou cães com antibióticos sistêmicos com base na cultura bacteriana e sensibilidade. Uma pata por cão foi selecionada aleatoriamente utilizando um método de cara ou coroa para aplicação semanal de FLE, enquanto a outra pata serviu como controle. Os cães foram pontuados a cada 2 semanas ao longo de 56 dias em dois parâmetros: uma escore global da lesão (incluindo vesículas hemorrágicas, fístulas com tratos drenantes, crostas e úlceras) e escore de neutrófilos fagocitando bactérias (NES, 0–4). O tempo para resolução clínica e os escores das lesões foram avaliados e comparados entre os grupos.
Resultados: No Dia (D)28 e D56, o grupo FLE apresentou significativamente mais patas curadas (50% e 88%, *p*=0,021) em comparação com o controle (17% e 54%, *p*=0,008). O tempo médio para resolução clínica foi menor para o grupo FLE (35 dias) em comparação com o grupo controle (56 dias, *p*=0,017). Nenhuma diferença na pontuação NES foi observada entre os grupos.
Conclusões e relevância clínica: Este ensaio clínico cego, randomizado e de corpo dividido demonstrou que o FLE é uma terapia adjuvante eficaz para FIC. Reduz o tempo de resolução clínica e aumenta a taxa de resolução, minimizando a necessidade de antibióticos.

RESUMEN
Introducción: la forúnculos interdigital canina (CIF, por sus siglas en inglés) es una afección inflamatoria compleja y recurrente, típicamente complicada por infecciones bacterianas profundas que requieren antibióticos sistémicos en uso prolongado.
Hipótesis/Objetivos: Este estudio de cuerpo dividido, en el que los perros actuaron como su propio control, evaluó si el uso de energía de luz fluorescente (FLE) adjunta a otra terapia, podría acortar el tiempo de resolución clínica de la CIF y minimizar el uso de antimicrobianos sistémicos.
Animales: Treinta y cinco perros de propietarios particulares con signos de furunculosis interdigital en al menos dos patas.
Materiales y métodos: Este ensayo clínico multicéntrico, prospectivo, simple ciego, al azar y de cuerpo dividido trató a perros con antibióticos sistémicos según el cultivo bacteriano y la sensibilidad. Se seleccionó aleatoriamente una pata por perro mediante el método de lanzamiento de moneda para la aplicación semanal de FLE, mientras que la otra pata sirvió como control. Se evaluó a los perros cada 2 semanas durante 56 días según dos parámetros: una puntuación global de la lesión (incluyendo vesículas hemorrágicas, fístulas con tractos de drenaje, costras y úlceras) y una puntuación de neutrófilos con bacterias fagocitadas (NES, 0-4). Se evaluaron el tiempo hasta la resolución clínica y las puntuaciones de la lesión, y se compararon entre los grupos.

Resultados: En los días 28 y 56, el grupo FLE mostró significativamente más patas cicatrizadas (50 % y 88 %, p=0,021) en comparación con el grupo control (17 % y 54 %, p=0,008). La mediana del tiempo hasta la resolución clínica fue menor en el grupo FLE (35 días) en comparación con el grupo control (56 días, p=0,017). No se observaron diferencias en la puntuación NES entre los grupos.
Conclusiones y relevancia clínica: Este ensayo clínico ciego, al azar y de cuerpo dividido demostró que la FLE es una terapia adyuvante eficaz para la CIF. Reduce el tiempo de resolución clínica y aumenta la tasa de resolución minimizando la necesidad de antibióticos.