A prospective, blinded, randomized, controlled, multicentric clinical trial comparing the efficacy and safety of two treatment protocols of a new otological gel containing AMP2041 (Peptivet® oto gel) in client-owned dogs with acute externa otitis.
Peptivet® otogel

EUDERMIC

The only one with AMP 2041

The new frontier of protection
An animal otitis externa is one of the most frequently seen veterinary conditions and is estimated to affect between 5 and 20% of dogs (1,2). Although not a directly life-threatening condition, otitis diminishes the quality of life of affected patients. Failure to manage otitis externa appropriately often results in recurrent pain, inflammation and infection, eventually progressing to chronic end-stage disease. Successful management of otitis in veterinary patients requires a detailed understanding of the multifactorial pathogenesis of the disorder. Otitis has been classified according to type of exudate as erythematous-ceruminous (ECO) or suppurative (SO) otitis (3). The dominant pathogens (usually as secondary causes) in otitis include Staphylococcus pseudintermedius, Pseudomonas aeruginosa, Proteus mirabilis, Corynebacterium spp., Klebsiella spp. and Escherichia Coli (3,6).

Topical therapy is an important part of the treatment of otitis externa (3,7). Multipurpose products are frequently indicated, particularly as a first-line treatment, because of the mix of micro-organisms and inflammation present in most ears at diagnosis (3); but the increase in bacterial resistance to antibiotics has suggested the need to use, where possible, alternative tools such as disinfectants and antimicrobial peptides (8,9). Synthetic peptides have been formulated to be effective against bacteria. AMP2041 is an antimicrobial peptide in which the in vitro efficacy has already been demonstrated in several studies and on different microorganisms (Gram negative bacteria such as Pseudomonas aeruginosa, Gram-positive bacteria such as Staphylococcus pseudintermedius and yeasts as Malassezia pachydermatis) (10,11).

### SUMMARY

Dogs are often affected by ear infections that affect the external ear canal (otitis externa). In addition to the identification and management of primary and predisposing causes, it is always necessary to have new topical therapies to fight these infections. The aim of this study was to evaluate the antimicrobial activity, in vivo, of an otic gel (Peptivet® oto gel ICF S.r.l., Cremona Italia) containing an ICF patent AMP2041 antimicrobial synthetic peptide plus 0.07% chlorhexidine digluconate (CLX)-Tris-EDTA in 63 dogs affected by acute externa otitis.

### MATERIALS AND METHODS

Dogs with clinical signs of acute or subacute otitis externa were included, bacteria and yeasts were isolated from samples taken at inclusion; other control samples were collected from dogs at day 7, 14 and 28. One group received an ear cleaning Otoact® solution (salicylic acid and squalene) to clean the ear and Peptivet® oto gel (1-3 supplies per affected ear) every 48 hours (PEP48 group) and a second received the products once daily (PEP24 group). Efficacy and tolerability were evaluated on days 7, 14 and 28 to check the relapse’s rate after 2 weeks without therapy.

### RESULTS

The trial demonstrated equivalence of both treatments in terms of efficacy, with a cure rate of 61.2% at day 7 for PEP48 group and 56.7% for PEP24 group; a cure rate of 85.7% at day 14 for PEP48 group and 85.0% for PEP24 group. Both treatment protocols were equally well tolerated by dogs.

### CONCLUSIONS

The demonstration of efficacy of this product antibiotics-free and its use every 48 hours, makes this formulation a useful tool to contrast the development of antibiotic resistance and increase owner’s compliance.
Chlorhexidine in low doses associated with Tris-EDTA has shown similar efficacy especially against Gram negative bacteria (12,13). Topical corticosteroids, such as prednisolone and dexamethasone, are commonly used in the control of the otitis due to their anti-inflammatory, antiproliferative, antipruritic, and anti-exudative effects (19). But in this study, it was used a formulation that contains substances with anti-inflammatory and analgesic action such as Glycophosphoinositol (GPI) lysine salts that are innovative sunflower lecithin derived active ingredients and niacin (Vitamin PP) (14,15, 16). The purpose of the study was to evaluate the clinical efficacy and tolerability, in vivo, of a gel containing antimicrobial peptide AMP2041, chlorhexidine digluconate (0.07%), Tris-EDTA, GPI lysine and niacin (Vitamin PP) in the treatment of acute otitis externa and acute exacerbations of recurrent canine otitis externa comparing two different timing protocols and using a phase III clinical trial protocol.

Materials and methods

A randomized, blinded and controlled study was conducted at 16 referral clinics throughout Italy over a period of 6 months. Dogs of any age, breed and sex presenting with clinical signs compatible with acute otitis externa were enrolled. Eighty-eight dogs presenting with acute or subacute otitis externa (in progress for less than 14 days) were visited. To qualify for inclusion, dogs had to present either with erythematous-ceruminous otitis (ECO) or with suppurative otitis (SO). ECO was defined as the presence of cerumen and erythema (both with scores ≥ 2 on a scale of 0–3) with associated bacterial and yeast observed microscopically. SO was the presence of pus (score ≥ 2 for quantity) with associated microscopically evidence of bacteria.

Dogs were excluded from the trial if they had previously received topical treatment (within 10 days), systemic treatment with an antibiotic, antifungal or nonsteroidal anti-inflammatory (within 10 days), a steroidal anti-inflammatory treatment (within 14 days), or a long acting steroidal anti-inflammatory drug systemically (within 60 days). They were also excluded if concurrent auricular diseases such as ear parasites, foreign bodies, neoplasia or hyperplasia of the ear duct were present, if there was concomitant administration of antibiotics or corticoids during the study, or if they were gestating or suckling female dogs. The study was conducted according to Good Clinical Practice (GCP). Written owner consent was obtained before inclusion and the protocol was approved by the ethical committee of the referral services.

Treatments

All dogs received, just before each treatment, a local ear cleaning with Otoact® (ICF Srl, Cremona, Italy), an ear solution containing only salicylic acid (2 ml x ear). All animals included were divided into 2 groups (randomized) consisting of either the test product, Peptivet® oto gel (ICF Srl, Cremona, Italy) a gel containing antimicrobial peptide AMP2041, chlorhexidine digluconate (CLX), Tris-EDTA; administered every other day, coded PEP48; or the test product administered once daily, coded PEP24 as 2 supplies in dogs up to 30 kg and 3 supplies from those above. Each supply dose is equivalent to 0.5 ml of the product (standard recommended doses). Both products were administered initially in the clinic to demonstrate the correct technique, and thereafter by the dog owners for 14 days (according to the clinical outcome on day 14). The detergent (Otoact®) was applied by massaging the ear canal, leaving it for 5 minutes, then dried with cotton disk. Immediately after application of the gel, the ear was massaged for 1 min to ensure even distribution throughout the entire canal.

Study design

Dogs were assigned to one of the two treatment groups, according to a block randomization procedure (random number generator IBM SPSS Statistics version 21; IBM, Armonk, New York). The products were presented in 40-mL vials for Peptivet® oto gel and 100-mL vials for Otoact® ear solution. Even if the packaging and the products were equal for the two groups, the veterinary investigator delivered a sealed envelope (with a simple progressive number) to each owner so that only the latter knew which group he belonged (PEP48 or PEP24) to ensure blind conditions. A treatment investigator (nurse or veterinarian) was in charge of the treatment regime and demonstrated correct use of the test products, explained treatment and cleaning protocols to owners, and checked compliance with treatment. The owner of each included dog was provided with a copy of the same protocol including a description of the method of ear cleaning. Each investigation block had four numbered treatment boxes according to a randomization list established and kept in the laboratory. At inclusion, a dog was attributed the box with the lowest number by the treatment investigator; this number was used also for its identification during the entire study. When the four cases of the first block were enrolled, the investigator randomly received another block of four treatment boxes to include the next four dogs and so on. And one clinician investigator (compulsorily veterinarian with experience in dermatology) was responsible for all animal examinations and scoring evaluations according to the study protocol requirements.
Ears were also evaluated at baseline and at each examination time by the clinician investigator for leukocytes, bacteria (rod-shaped and cocci), yeast, keratinocytes. Scores were given for each of these parameters on a severity scale of 0–4 (0 = no bacteria ⁄ yeast ⁄ inflammatory cells ⁄ keratinocytes, 1 = present, but slide must be scanned carefully for detection, 2 = present in low numbers, but detectable rapidly without difficulties, 3 = present in larger numbers and detectable rapidly without any difficulties, 3 = massive amounts of bacteria ⁄ yeast ⁄ inflammatory cells ⁄ keratinocytes present and detectable rapidly without difficulties) by using the semiquantitative scale validated by Budach (18). Each investigator was trained to ear cytology and given a sheet with color images of the different ear cells and microorganisms cytological morphology. Swab specimens for cytological examination were obtained on D0 using a long cotton bud stick inserted in the cone of the otoscope all the way down to the junction between the vertical and the horizontal canal and then rolled on a glass slide. After air drying, the slides were fixed and then stained with the Wright's modified method (Hemacolor Stain for Microscopy, Merck, Darmstadt, Germany) and examined under the microscope at 400x and oil immersion magnification (1000x).

1. Schedule
All dogs were examined by the clinician investigator on days 0 (D0), 7 (D7), 14 (D14) and 28 (D28). In cases of bilateral otitis, each ear was considered and studied as a single case.
The affected ear(s) were cleaned with Otoact® before all applications of the test product (1): by the treatment investigator on D0 (2); by the owner every other day in the PEP48 group and every day in the PEP24 group; (3) at each visit until the end of treatment by the treatment investigator.

2. Evaluation
Ears were evaluated at baseline and at each examination time by the clinician investigator for skin erythema, oedema, pruritus, pain, ulceration, state of tympanum, quantity of cerumen and pus. Scores were given for each of these parameters on a severity scale of 0–3 (0 = none, 1 = slight, 2 = moderate, and 3 = severe), except for state of tympanum (intact/no intact), according to the OTI3 scale recently validated by Nuttall (9). Owner evaluation of the pruritus and pain, using the visual analogue scale (VAS) validated by Hill, on days 0, 7, 14 and 28 (17). Response to therapy, ease of administration and to local and general tolerance was assessed (excellent, good, average or bad) by the clinician investigator, still under blind conditions and the owner at the end of the treatment (D14) and after two weeks (D28).
3. Efficacy criteria

For both treatment groups, signalment, history (length of symptoms, previous episodes of, and treatments for otitis) and the clinical and cytological data were compared on D0 to ensure homogeneity before further comparison. The primary assessment criterion was the clinical cure rate (on D7 and on D14 according to the length of treatment).

A cure was defined as a return to normal of all parameters (score = 0), except for cerumen quantity in ECO for which the score could be 1. Several secondary criteria were also analyzed, namely the time to cure, relapse rate, and response rate (defined as cases cured or showing clear improvement). The development of clinical parameters was described, and the frequency of reactions and general adverse effects attributable to the auricular treatment were calculated for each group.

4. Statistical analysis

To assess whether there was a difference in efficacy between the two groups (percentage of clinical and cytological cure) means were compared for each control using the equivalence approach. The 95% confidence interval of the odds ratio was calculated. The null hypothesis H0 equivalence was rejected with p <0.05.

• to assess microorganism’s comparison of means between the groups (coccici and rods bacteria and malasetiae) a contingency table 2 × 2 (Fisher’s exact test) were used.

• to assess comparison of means of the parameters in a group in the different clinical controls and comparison of means between groups the t-test (Student t test) was used. The statistical results were calculated using IBM SPSS Statistics version 21 software; IBM. Armonk, New York.

Results

Only 63 (71.6%) of the 88 dogs presenting with otic problems were eventually studied, mainly because of failure to meet the inclusion criteria (20 cases, 22.7%) and serious deviations in visit times (3 cases, 3.4%). Others were excluded for reasons of no randomization (two cases), prior local treatment (one case) and cessation of treatment too early (D7 instead of D14).

The statistical analyses were performed on the data obtained from these 63 dogs (31 dogs were included in PEP48 group and 32 in PEP24 group). Breeds represented included Pugs and French bulldog, West Highland white terriers, Labrador retrievers and mixed breeds. Median age was 4.8 years and 5.6 years, and average body size was 19.5 and 20.3 kg for the PEP48 and PEP24 group, respectively. About half of the animals (55.4% PEP48; 54.2% PEP24) had previously suffered episodes of inflammation of the external ear canal (in which allergic dermatitis was made), but only 14.4% in the PEP48 group and 12.3% in PEP24 group had been treated previously. Unilateral and bilateral otitis occurred almost equally (bilateral otitis in 71.0% of dogs in PEP48 group and 87.5% in the PEP24 group). Symptoms lasted on average from 2 to 4 weeks (49.2% PEP48 and 42.9% PEP24). Cases of ECO were more common (53.1% PEP48; 61.7% PEP24) than SO (46.9% PEP48; 38.3% PEP24). 49 ears were treated in PEP48 and 60 ears in PEP24 group.

There was also a significant sex difference between groups (PEP48 group 83.9% females; PEP24 group 62.5%). Apart from this parameter, both groups were considered to be equally balanced.
1. Cytological parameters

A reduction in the total score of the parameters of the 37.7% at D7 and of the 60.5% and D14 in PEP48 group while 37.3% at D7 and of the 62.1% at D14 in PEP24 group was seen. Cytological results during the study of PEP48 and PEP24 groups detected that means comparison of cytological parameters between D0-D7, D0-D14, D0-D28 of the respective groups, shows statistically significant difference with $p < 0.01$ (mean comparison test paired data) (Fig. 1 and Fig. 2).
Table 1 Comparison of cytological and clinical results in different groups and otitis

<table>
<thead>
<tr>
<th>Number (%)</th>
<th>Cure</th>
<th>Clear improvement</th>
<th>Improvement</th>
<th>Failure</th>
<th>Relapse</th>
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<td>D7</td>
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<tr>
<td>D7</td>
<td>2 (8.3)</td>
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<td>14 (56.0)</td>
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<tr>
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<td>4 (16.0)</td>
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<tr>
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<td>5 (19.2)</td>
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<td>2 (7.7)</td>
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<td>2 (7.7)</td>
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<tr>
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<td>10 (39.4)</td>
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<td>12 (46.5)</td>
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<tr>
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<td><strong>SO</strong></td>
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<tr>
<td>D7</td>
<td>8 (34.8)</td>
<td>3 (13.0)</td>
<td>8 (34.8)</td>
<td>4 (17.4)</td>
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<tr>
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<td>10 (43.5)</td>
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<tr>
<td>D7</td>
<td>4 (17.4)</td>
<td>8 (34.8)</td>
<td>0 (0)</td>
<td>11 (47.4)</td>
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<tr>
<td>D14</td>
<td>14 (60.9)</td>
<td>8 (34.8)</td>
<td>0 (0)</td>
<td>1 (4.3)</td>
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*EOD, every other day. °SID, solum in die.

73.1% and 64.7% of the ECO were cure or clear improvement at D7 in PEP48 group and in PEP24 group respectively. 88.5% and 88.2% at D14, 47.8% and 52.2% of the SO were cure or clear improvement at D7 in PEP48 group and in PEP24 group respectively and 82.6% and 87.0% at D14 (Table 1). 58.3% and 50.0% of bacterial cocci-shape otitis were cure or clear improvement at D7 in PEP48 group and in PEP24 group respectively and 83.3% and 64.3% at D14. 66.7% and 41.7 % of bacterial rod-shape otitis were cure or clear improvement at D7 in PEP48 group and in PEP24 group respectively and 77.8% and 75.0% at D14 (Table 2). Cytological results between the two groups detected that means comparison of parameters at D7 and D14 shows equivalence retain the null hypothesis with p > 0.05: D7 (Student t test p=0.93) and D14 (Student t test p=0.53) (Fig. 3).
Cytological results between the two groups detected that means comparison of cocci-shaped bacteria at D7 shows statistically significant difference with $p < 0.05$: Fisher exact test statistic value is 0.009 (a greater reduction in PEP 24 group); while at D14 Fisher exact test statistic value is 0.19. The result is not significant at $p < 0.05$.

The same at D28 (Fisher exact test statistic value is 0.31) (Fig. 4). The means comparison of rod-shaped bacteria shows a result not significant at $p > 0.05$: Fisher exact test statistic value is 1 and 0.66 respectively at D7 and D14. Statistically significant difference with $p < 0.05$: Fisher exact test statistic value is 0.040 (a greater reduction in PEP 48 group); at D28 (Fig.5).
Finally, the cytological results between the two groups detected that means comparison of yeasts is never statistically significant difference with $p < 0.05$; Fisher exact test statistic value is 0.77 (D7); 0.56 (D14) and 0.22 (D28) (Fig. 6).

2. Clinical parameters
Clinical results during the study of PEP48 and PEP24 groups detected that means comparison of clinical parameters between D0-D7, D0-D14, D0-D28 of the respective groups, shows statistically significant difference with $p < 0.01$ (Fig. 7 and Fig. 8).
• 46 on 49 dogs (93.9%) treated with Peptivet® oto gel every other day and 56 on 60 dogs (93.3%) treated with Peptivet® oto gel every day responded satisfactorily (i.e. cured or clearly improved) at D7;
• 48 on 49 dogs (98.0%) in PEP 48 group and 58 on 60 dogs (96.7%) in PEP 24 group responded satisfactorily at D14.

Statistically no significant difference between groups (test t Student p = 0.70 at D7 and p=0.31 at D14) was detected (Fig. 9). PEP 48 group was more effective than PEP 24 group treatment against ECO showing a difference of 8.4% at D7 and of 10.3% at D14. While, on the contrary, PEP 24 group was more effective than PEP 48 group treatment against SO showing a difference of 4.4% both at D7 and at D14.

Analysis of three weight classes (< 10 kg, 10–25 kg, > 25 kg) did not reveal any influence of size on the efficacy of either product. All clinical parameters gradually improved from D0 to D14 with both groups. Improvements in erythema and pus were particularly rapid. An amazing improvement was obtained in the pain and itching. Relapse, after 14 days without therapy, occurred in 12.2% of dogs treated with PEP48 protocol compared with 10.0% of dogs treated with PEP 24h protocol, although this difference was not statistically significant (Fisher’s exact test, p = 0.76).

3. Tolerability of treatment

Of the 63 cases assessed for local tolerance, two dogs treated every day exhibited local discomfort (erythema and pruritus) just after administration of the Otoact® solution in the first days. No local side effects were reported in the PEP48 group.

Discussion

Topical treatment is the method of choice in otitis externa because antimicrobial concentrations of the agents come into direct contact with the pathogens. It is very important to use topical products after ear cleaning to avoid the reduction of effectiveness of the active ingredients (for example some antibiotics such as bacitracin and polymyxin B are inactivated by pus) (20).

The results show that both protocols with Peptivet® oto gel are effective and well tolerated in the medical management of acute otitis externa in dogs.

The results compare favorably with those of another in vitro study that we published recently (19); a satisfactory response, as antimicrobial activity, was achieved and the product had a rapid and long-lasting in vitro activity against clinical canine otitis isolates of Pseudomonas aeruginosa. In our clinical study, the 7-day treatment was successful in 13 and 16 cases treated with PEP48 and PEP24 respectively.
However, it now seems that as 25 and 27 dogs, respectively, required 14 days of treatment to cure, over 1 week of treatment with these products may be necessary. In particular, according to the cytological D7 data between the two groups, in the presence of bacterial (cocci) otitis is recommended to set the first week at one administration per day. The results of this study demonstrate that Peptivet® oto gel has comparable efficacy to topical ear product-containing antibiotics, steroids and antifungals (20, 21).

So Peptivet® oto gel can be used for canine infectious otitis (ECO, SO) as a first line therapy, right with the aim to be curative and reduce the use of antibiotics, local selection pressure, and finally reducing the incidence of bacterial resistant strains. Both groups proved to be significantly equivalent in efficacy, regardless of the classification chosen (ECO/5O). The active principles act on the otitis mechanisms whatever the origin of the disease, even when this origin is a mix infection. They bring about a complete recovery in the various cases, which is correlated with very low rates of failure and relapse. Satisfactory owner’s response was achieved in 98.0% and 96.7% of dogs treated with PEP48 and PEP24 protocol, respectively. The volume of product (as per label doses) was used considering the body size. However, analysis of three weight classes revealed no difference in efficacy results. Thus, as mean weight was similar between both tested groups, any differences in efficacy between treatments could probably be attributed more to the different number of microorganisms and bacterial strains than to a bias in dog size.

In practice, ototoxicity is rare in small animals and the risk is probably somewhat overstated (22). No studies were made in dogs regarding AMP2041 in middle ear. On the contrary, some peptides have been found useful in reducing ototoxicity of neomycin in humans (23). The systemic absorption of this molecule is minimal after topical application and therefore adverse effects should not be observed in dogs receiving Peptivet® oto gel. In addition, other components of the product, chlorhexidine digluconate and Tris-EDTA, are known to be safe for use in the middle ear at these percentages (24, 25, 26). However the use of the product in the middle ear needs clinical trials in healthy and suffering from otitis media dogs to the assessment of any ototoxicity. The use of topical corticosteroids is motivated by the fact that they reduce the pain, and this makes the dog more available to be manipulated to topical therapies (increased compliance). In Peptivet® oto gel we obtained an incredible reduction in pain without the use of steroids; this may be due to the fact that some molecules have anti-inflammatory and pain-relieving properties such as GPI and Vitamin PP.
As recommended by Griffin and Nuttall (27, 28), affected ears were gently flushed with a cleaning solution to remove ear wax and purulent material, because topical ear products are much less effective in productive otitis. It is, however, not known exactly how the ears were cleaned by the owners, even though identical information was supplied to all participants. Nevertheless, owner compliance with the cleaning protocol and its methodology was verified at each examination time by the treatment investigator, and there is no reason to doubt the overall efficacy of this procedure. However, a complete evaluation of the contribution, if any, of ear cleaning to the efficacy results was not possible because the two treatment groups were not compared with a third group with solely an ear cleaning protocol. It may, however, be supposed that any contribution of this cleaning protocol to efficacy is insignificant as antimicrobial solution but it could have had cerumenolytic activity due the squalene's presence. Nonetheless, bias resulting from the cleaning protocol cannot be completely ruled out, and may be the reason why the treatment failed in some cases.

In this study, efficacy criteria were linked to the clinical symptoms of canine otitis externa as the main aim was to demonstrate a clinical efficacy and because microbiological results were considered to be less revealing of the pathology (concentration of topical antimicrobial molecules are at least 1000 times the MIC90) (28). Microbiological tests were not carried out because the goal of this study was to evaluate the clinical efficacy of the product in the external otitis. In addition, there are several factors that can affect the reliability of bacterial and fungal cultures: the ability of the operator in properly collecting samples, the anatomical site choice (studies show the presence of different pathogenic bacteria between the vertical and horizontal ear duct) (28), the culture medium for transportation, time and temperature by sampling on arrival to the laboratory. Cytology was used only to distinguish ECO (identification of bacteria and yeast) from SO (bacteria only), and to exclude animals with parasitic otitis. This examination was performed by each veterinarian. Although the collection and preparation technique has been explained to all investigators, it remains a potential bias in the different abilities and cytological reading skills of each individual veterinarian. However, it was considered sufficiently objective to develop analysis groups and otitis type comparison. However next studies involving a single cytological operator.

**Results**

Only 63 (71.6%) of the 88 dogs presenting with otic problems were eventually studied, mainly because of failure to meet the inclusion criteria (20 cases, 22.7%) and serious deviations in visit times (3 cases, 3.4%). Others were excluded for reasons of no randomization (two cases), prior local treatment (one case) and cessation of treatment too early (D7 instead of D14).

The statistical analyses were performed on the data obtained from these 63 dogs (31 dogs were included in PEP48 group and 32 in PEP24 group). Breeds represented included Pugs and French bulldog, West Highland white terriers, Labrador retrievers and mixed breeds. Median age was 4.8 years and 5.6 years, and average body size was 19.5 and 20.3 kg for the PEP48 and PEP24 group, respectively. About half of the animals (55.4% PEP48; 54.2% PEP24) had previously suffered episodes of inflammation of the external ear canal (in which allergic dermatitis was made), but only 14.4% in the PEP48 group and 12.3% in PEP24 group had been treated previously. Unilateral and bilateral otitis occurred almost equally (bilateral otitis in 71.0% of dogs in PEP48 group and 87.5% in the PEP24 group). Symptoms lasted on average from 2 to 4 weeks (49.2% in PEP48 and 42.9% in PEP24). Cases of ECO were more common (53.1% in PEP48; 61.7% PEP24) than SO (46.9% in PEP48; 38.3% in PEP24). 49 ears were treated in PEP48 and 60 ears in PEP24 group.

There was also a significant sex difference between groups (PEP48 group 83.9% females; PEP24 group 62.5%). Apart from this parameter, both groups were considered to be equally balanced.

**Bibliography**


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“In vitro antimicrobial activity of a gel containing antimicrobial peptide AMP2041, chlorhexidine digluconate and Tris-EDTA on clinical isolates of Pseudomonas aeruginosa from canine otitis”

Giovanni Ghibaudo, Davide Santospirito, Andrea Sala, Sara Flisi, Simone Taddei, Sandro Cavirani, Clotilde Silvia Cabassi

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