The Vet Education Live Web-Seminar Series

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“Management of Allergic Dermatitis”

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Management of allergic dermatitis
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These notes will deal predominantly with atopic dermatitis, although many of the treatment modalities mentioned can also be used for the symptomatic control of other allergic dermatoses such as contact dermatitis. Successful management of an allergic dog requires a certain degree of client education. The aim is to allow the owner to be sufficiently informed to allow them make an informed decision about the treatment of their pet.

The biggest cause of unhappiness in owners of an atopic dog is unrealistic expectations. Therefore, before discussing the treatment options, it is important that the owner is made aware of the following four facts:

1. Atopic dermatitis is an incurable disease that requires continuous and lifelong treatment.
2. This will involve some degree of lifelong expense.
3. There is no single treatment for atopic dermatitis that is perfect. All the potential treatments have advantages and disadvantages.
4. It is common for dogs with atopic dermatitis to have flare-ups from time to time. This is likely to involve future visits to the vet or dermatologist.

The treatment options can be divided into five main categories:

1. Allergen specific immunotherapy (specific desensitisation)
2. Anti-itch drugs
3. Skin barrier treatments and shampoos
4. Treatment of secondary infections
5. Environmental treatments and behavioural changes

When deciding on a long term treatment plan, the following three factors need to be taken into account:

1. The effectiveness of the treatments
2. The risk of side effects
3. The cost of the drugs

Successful treatment of an affected dog requires that the above three factors are balanced to the owner’s satisfaction.

1. ALLERGEN-SPECIFIC IMMUNOTHERAPY (SPECIFIC DESENSITIZATION)

Allergen-specific immunotherapy can only be undertaken if the dog has previously had an allergy test. If the owner does not want (or cannot afford) allergy testing, then this form of treatment cannot be used. In such cases, the dogs have to be managed symptomatically.

Allergen specific immunotherapy (hyposensitisation) involves the subcutaneous injection of gradually increasing doses of allergen over a period of time until a maintenance dose is reached. The treatment is thought to work by redressing the imbalance in the animal’s T lymphocyte populations with the net effect that IL-4 secretion is reduced. This reduces IgE synthesis and encourages IgG synthesis, which may be protective.

Selection of the allergens to be included in the vaccine is based on the positive results obtained in either an intradermal skin test or in-vitro IgE blood test.
The vaccine is made by selecting allergens from a positive allergy test. The vaccine is given in gradually increasing doses, starting off with injections every few days and ending up with injections every 3 – 4 weeks. The injections are normally given at home, to increase convenience and decrease costs.

About 25% of dogs can have their skin disease controlled completely with immunotherapy alone. A further 40% show a beneficial response, but may require some additional treatment. The remaining 35% show no response at all. Immunotherapy can take 2 – 9 months before a beneficial effect is seen so it is recommended that dogs receive the vaccine for at least this long before a final decision is reached about its effectiveness.

Immunotherapy is very safe. Adverse effects of allergen immunotherapy are rare but include pruritus at the injection site, generalised pruritus, urticaria and anaphylaxis. However, as a precaution, the dog should be given its injections at a time when veterinary practices are open so that treatment is readily available if necessary.

The vaccine will cost approximately $850 for the first year and $600 per year subsequently, regardless of the size of dog. This works out at about $60 – 70 per month.

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Overall recommendation – Because it has a fairly good success rate, is very cost effective and is very safe for long term use, immunotherapy is often recommended by dermatologists.

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2. ANTI-ITCH DRUGS
Some form of anti-itch medication is usually required to treat atopic dermatitis, especially in the early stages of treatment, or if immunotherapy is not completely successful. Three main options are available, and they vary greatly in their effectiveness, cost and safety profiles.

**Glucocorticoids**
Systemic glucocorticoids are probably the most commonly used drugs in the management of atopic dermatitis. They are very effective and cheap. However, compared to other treatment modalities, they cause the most adverse effects. Systemic glucocorticoids are indicated for the treatment of atopic dermatitis in the following circumstances:

- As a short term treatment for the initial management of severe pruritus or flares (as long as infections have been controlled).
- As a long term treatment in cases in which financial limitations do not permit other forms of treatment, or owners are not prepared to pursue other forms of treatment.
- As an adjunctive treatment in cases that fail to completely respond to other treatment modalities, or do not respond at all.
- In cases of seasonal atopic dermatitis lasting 3 months or less. In these cases, glucocorticoids may be the treatment of choice as long as they are well tolerated by the patient.
- In the early phases of allergen immunotherapy if the pruritus is severe.

Oral prednisolone (or prednisone) is the glucocortioid of choice for the treatment of atopic dermatitis. In the vast majority of cases, there is no indication for using any other drug. In cases in which severe polydipsia and polyuria are a problem, oral methyl
Prednisolone can be used as an alternative. Other oral steroids such as triamcinolone, betamethasone and dexamethasone are less suitable for the treatment of atopic dermatitis because their long duration of action does not allow successful alternate day therapy. However, these drugs can be beneficial in some severe cases that have failed to respond adequately to prednisolone. Injectable steroids should be avoided because they do not allow precise dosage control. They should only be contemplated in cases in which the owner is totally unable to administer tablets to their animal.

There are two main objectives when using long-term glucocorticoids for the management of canine atopic dermatitis:
1. To achieve the minimal effective dose (MED) and
2. To achieve alternate day therapy (ADT).
For prednisolone, induction doses should be 0.5 – 1.0 mg/kg/day. For methylprednisolone, induction doses should be 0.4 – 0.8 mg/kg/day. For both drugs, after a beneficial response is seen (5 – 7 days), the total dose can be given every 48 hours. For long-term use, the alternate day therapy should be gradually reduced to the lowest dose that is capable of controlling the pruritus. For cats, these doses may need to be doubled.

The major drawback to the use of systemic glucocorticoids in dogs is the large number of adverse effects that will invariably occur. Short term use of systemic glucocorticoids can lead to polydipsia, polyuria, polyphagia, panting, aggression and diarrhoea. Methylprednisolone has fewer mineralocorticoid effects than prednisolone and can reduce the severity of polydipsia and polyuria. Prolonged use of glucocorticoids can lead to signs of iatrogenic hyperglucocorticism (muscle wastage, pot belly, hepatomegaly, fat redistribution, osteoporosis, calcinosis cutis, alopecia, poor wound healing, recurrent pyoderma, generalised demodicosis, comedones, silent urinary tract infections, pyelonephritis, cataracts, insulin resistant diabetes mellitus). Despite requiring higher doses of glucocorticoids, these adverse effects are rare in cats. Glucocorticoids have caused gastro-intestinal ulceration, especially in patients receiving non-steroidal anti-inflammatory drugs. Glucocorticoids may also predispose to pancreatitis. Sudden withdrawal of glucocorticoids after prolonged therapy can lead to an Addisonian crisis (adrenal insufficiency). Glucocorticoids should be avoided in animals with pre-existing renal disease and diabetes mellitus. Glucocorticoids should not be given to pregnant animals as they can cause foetal abnormalities and abortion.

If systemic glucocorticoids are going to be used for long term management, it is important that the patient is regularly monitored. The following represents the type of monitoring undertaken by the author.

6 monthly check up
General (water intake, urine output, appetite, activity level)
Body weight
Measurement of abdominal circumference (using tape measure)
Skin and coat
   Coat thinning
   Alopecia
   Skin infections (staphylococcal or Malassezia)
   Cutaneous atrophy (especially on ventral abdomen)
   Comedones (especially on ventral abdomen)
   If comedones or alopecia present, check for demodicosis
Calcinosis cutis (especially back of neck, dorsum and ventral abdomen)
Musculature (especially of head and abdominal wall)
Spinal alignment (check for ventral bowing)
Liver palpation
Angle of penis carriage (check for ventral deviation from horizontal)
Cataracts

12 monthly check up
All of the above, plus:
Haematology profile
Biochemistry profile
Urine analysis (ideally including culture from cystocentesis sample if possible to check for silent urinary tract infection)

**Topical Glucocorticoids**
Topical glucocorticoids can be very useful for the treatment of localised areas of atopic dermatitis. These might include the medial pinnae, the perineum or a focal patch of dermatitis. Topical glucocorticoids vary in potency. Betamethasone, Dexamethasone and Mometasone are the most potent, followed by triamcinolone, followed by hydrocortisone. Clinicians should decide on the level of potency required and apply the creams or sprays once or twice daily to the affected area. If prolonged treatment is used, the lowest potency cream should be used at the lowest frequency possible. Long term use must be monitored very carefully because skin thinning may occur.

Topical glucocorticoids are potent anti-inflammatory drugs and they can be very effective at treating focal areas of atopic dermatitis. However, some topical glucocorticoids can suppress the pituitary adrenal axis and lead to elevated liver enzymes. This is much less of a problem with Mometasone (Elocon) and Hydrocortisone aceponate (Cortavance) because systemic absorption is very low. However, prolonged use can cause thinning of the skin, scaling, comedones, alopecia and secondary pyoderma. Owners should wear gloves when applying these products.

Systemic glucocorticoids are the cheapest drugs available to treat atopic dermatitis, costing about $15 - $30 per month. Topical treatments are often more expensive than this.

<table>
<thead>
<tr>
<th>Overall recommendation – Because of the risk of side effects when used for long periods, dermatologists prefer to recommend cortisone for short term use, unless financial limitations preclude other forms of treatment. Whenever cortisone has to be used for longer periods, the aim should be to use the lowest dose possible, preferably given every other day. Cortisone creams and sprays can be used safely if monitored carefully and can be very useful for stubborn areas of dermatitis.</th>
</tr>
</thead>
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**Cyclosporine (Atopica)**
Cyclosporine is licensed for the treatment of canine atopic dermatitis in many countries. It is expensive, but the cost varies depending on the size of dog, the mark-up applied by the practice and the frequency of administration.
Cyclosporine should be given at a dose of 5mg/kg, once daily. If the capsule sizes don’t allow this precise dose to be achieved, increase, rather than decrease, the dose. The tablet must be given on an empty stomach. However, this often makes dogs vomit, especially initially. This is not a reason for stopping medication altogether. It is worth persisting and trying the following strategies:

- Give the capsules with food until the vomiting ceases. Then gradually increase the interval between the meal and the dosing. Once you have got to a couple of hours, the capsules can then usually be given on a completely empty stomach.
- If that doesn’t work, an anti-emetic can be given before the cyclosporine capsules. Metoclopramide or maropitant (Cerenia, Pfizer) are potential options.
- Try giving the capsules last thing at night. The dog is usually asleep when it would otherwise be feeling nauseous.

If these guidelines are followed, the vast majority of dogs will tolerate long term administration of cyclosporine without vomiting, even if they vomit initially. After a week of dosing modifications, the problem usually resolves.

Many studies have shown that the efficacy of cyclosporine can approach that seen with prednisolone. However, in the author’s experience, the responses seen with cyclosporine are different to those seen with prednisolone. The following table summarises those differences:

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Prednisolone</th>
<th>Cyclosporine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of dogs that respond well</td>
<td>&gt;95%</td>
<td>≈ 80%</td>
</tr>
<tr>
<td>Time taken to reach maximum response</td>
<td>Few days</td>
<td>4-6 weeks</td>
</tr>
<tr>
<td>Side effects noticed by owner during induction</td>
<td>PU/PD</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Side effects noticed by owner during long term</td>
<td>Many</td>
<td>None</td>
</tr>
<tr>
<td>Long term pruritus control</td>
<td>Partial</td>
<td>Complete</td>
</tr>
</tbody>
</table>

The drug should always be given once daily initially. Unlike with glucocorticoids, it may take 4 – 6 weeks before maximum efficacy is reached. A reduction in dosing frequency should only be considered if a substantial improvement has been observed. If that is the case, the full dose can be given on alternate days for a trial period. If the pruritus worsens, the dog should be put back on daily treatment and continued on that indefinitely. If the dog continues to do well on alternate day dosing, twice weekly dosing can be attempted. In the author’s experience, about 70% of dogs will require daily dosing, 25% can be maintained on alternate day dosing and only about 5% can manage on twice weekly dosing.

Reducing the daily dose below 5mg/kg is not normally recommended as this can reduce blood concentrations to below therapeutic levels. However, it can be done successfully in some dogs.

The major side effects are vomiting and diarrhoea. These signs are usually transient and can be overcome by following the guidelines outlined above. Less common adverse effects include gingival hyperplasia, hypertrichosis, papillomatosis, and lymphoplasmacytoid dermatitis. To date, no clinically relevant effects have been seen on the kidney although some authors have seen rises in renal parameters. Many
dermatologists used to monitor basic biochemical parameters whilst dogs were on cyclosporine therapy to check for the development of any abnormalities, but this does not seem to be essential. Cats appear to be more tolerant and usually only suffer from diarrhoea. However, there is a danger of developing toxoplasmosis in cats and pre-treatment evaluation of toxoplasma titers are recommended. Naive cats are at most risk. Periodic reinspections are also important to check for the development of other cutaneous problems. The long term risks are currently unknown. Extrapolation from the human literature might suggest that an increased risk of malignancy could be seen in dogs receiving cyclosporine for many years, but this risk has not yet been determined.

Overall recommendation – Cyclosporine is a very useful drug and is prescribed quite commonly by dermatologists if finances allow. It can be used as an alternative to immunotherapy, or if immunotherapy is not successful.

**Antihistamines**

Antihistamines can be effective in up to 20% of cases, but they are normally only recommended in mild cases, or as steroid sparing agents. In Australia, chlorpheniramine would be the most commonly used agent.

Overall recommendation – Although they are not particularly effective on their own, dermatologists may recommend trying these drugs in mild cases, or to help reduce the amount of other drugs that need to be given.

### 3. SKIN BARRIER TREATMENTS AND SHAMPOOS

Helping to repair the skin barrier and keeping the skin surface in good condition is an important part of the management of atopic skin. Barrier treatments can improve the skin’s ability to prevent allergens from penetrating the skin. Barrier function can be improved by both nutritional supplements and topical treatments.

**Skin Support diet (made by Royal Canin)**

This diet has been shown to improve the appearance of atopic skin and to reduce the level of itching. It is specially formulated to provide ingredients that improve barrier function and skin integrity.

**Essential fatty acid supplements (omega 6 and omega 3)**

Essential fatty acids are usually derived from evening primrose oil, borage oil and marine fish oil. The rationale for the use of essential fatty acids in the treatment of atopic dermatitis is based on their ability to modify and reduce the production of pro-inflammatory prostaglandins in the skin. They may also have beneficial effects on barrier function. At best, essential fatty acids are only likely to be beneficial in about 10 - 20% of cases. When combined with antihistamines, there can be a synergistic effect. Even if there is no effect on the level of pruritus, essential fatty acid supplementation often leads to a noticeable improvement in skin and coat quality.

Essential fatty acids can occasionally cause diarrhoea. Rarely, essential fatty acids have precipitated pancreatitis. These can be used as an alternative to the skin support
diet and added to the normal diet as nutritional supplements (such as Megaderm) or applied to the skin surface (Essential 6).

**Alpha Keri oil**
This can be diluted in water and applied directly to the dog’s coat once a day. To start with, about a capful should be added to a bucket of water which is then poured over the coat and worked into the skin. If the coat appears greasy, the concentration can be reduced.

**Medicated shampoos**
Shampoos are beneficial because:
- They can be used to manage secondary bacterial or yeast infections
- They remove sweat, sebum and other cutaneous debris
- They can be used primarily for anti-pruritic effects
- They can remove allergens from the skin surface

**Overall recommendation** – Feeding skin support diet or giving essential fatty acids, regular bathing and applying Alpha Keri oil provides a beneficial baseline alongside the other treatments that will be prescribed.

**4. TREATMENT OF SECONDARY INFECTIONS**
Antimicrobial drugs or shampoos are frequently required in dogs with atopic dermatitis because they are prone to secondary bacterial and yeast infections. If severe, the infections will need to be treated systemically. Milder infections can be treated with shampoos.

**5. ENVIRONMENTAL TREATMENTS AND BEHAVIOUR MODIFICATION**
Allergen avoidance means trying to prevent a dog from coming into contact with things it is allergic to. The following are some suggestions:

<table>
<thead>
<tr>
<th>Type of allergy</th>
<th>Suggestions for avoidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dust and dust mites</td>
<td>Use HEPA filtered vacuum cleaner</td>
</tr>
<tr>
<td></td>
<td>Use hypoallergenic mattress and pillow covers</td>
</tr>
<tr>
<td></td>
<td>Avoid stuffed toys - or place them in the deep freezer for 24 hours once a month</td>
</tr>
<tr>
<td></td>
<td>Wash bedding in hot water (&gt; 70°C)</td>
</tr>
<tr>
<td></td>
<td>Use anti-dust mite sprays (available from pharmacy)</td>
</tr>
<tr>
<td></td>
<td>Keep dog out of bedroom</td>
</tr>
<tr>
<td>Grass, plant and pollen allergies</td>
<td>Find out the plants and trees that are present in the dog’s location.</td>
</tr>
<tr>
<td></td>
<td>Try to avoid contact with the areas that are known to provoke symptoms</td>
</tr>
<tr>
<td></td>
<td>Keep lawns mowed short</td>
</tr>
<tr>
<td></td>
<td>Rinse dog off after walking through grass and wooded areas</td>
</tr>
</tbody>
</table>
As most allergens are very common in the environment of dogs, it is usually impossible to achieve complete allergen avoidance. Although it might be helpful, it rarely reduces the itching dramatically, unless a particular plant can be avoided.

**Overall recommendation –** Because it can do no harm, attempts at allergen avoidance can always be tried, but they are unlikely to yield significant results when carried out alone.

**INDIVIDUALISED MANAGEMENT PROGRAMME**

The management programme for an atopic dog needs to be tailored for each case. The three main factors that need to be considered, and discussed with the client are:

1. Efficacy
2. Adverse effects
3. Cost

The client needs to be fully aware of these factors for each of the treatment modalities mentioned above. The client must be informed that there isn’t a treatment that is excellent in all three of the above categories. They must therefore make a decision on which two factors are most important to them, and their pet. The following list summarises the treatment options:

- Very effective / few adverse effects / high cost: Cyclosporine
- Very effective / many adverse effects / low cost: Glucocorticoids
- Moderately effective / moderate cost / few adverse effects: Immunotherapy
- Low efficacy / moderate cost / few adverse effects: Antihistamines
- Low efficacy / moderate cost / few adverse effects: EFAs

When treating cases of atopic dermatitis, any of the above treatment options can be used as a sole therapy but whether or not they work will depend on the severity and idiosyncrasies of the case. A few, very mild cases may be manageable with antihistamines, essential fatty acids or topical therapy alone. In more typical cases, such treatment would be unlikely to be effective and more potent therapeutic options would need to be considered. Immunotherapy, cyclosporine or glucocorticoids are usually the starting options and which is chosen will very much depend on input received from the client. If cost is the major issue, glucocorticoids might be the most appropriate option. If allergy testing had been performed, and the owners were not averse to the idea of regular injections, immunotherapy would be the favoured option. If the owners wanted a single, daily oral treatment and financial considerations were not relevant, cyclosporine might surface as the best option. Alongside these treatments, it is advisable to introduce some form of treatment that will enhance barrier function. Once the baseline treatment has been established, it may be beneficial to bring in adjunctive therapies in an attempt to increase efficacy, reduce adverse effects or decrease costs. In many cases, regardless of the other therapies being used, glucocorticoids might be needed in the beginning until the other treatments have had time to take effect. Antihistamines and/or essential fatty acids are also often used as adjunctive treatments but clinicians should bear in mind that this increases the complexity of the treatment regime and in some circumstances might reduce compliance. Throughout treatment, allergen avoidance and topical therapy could also be used as background treatments, helping to some degree with pruritus control but also to control flares and secondary infections. Regular ear
cleaning and occasional use of medicated ear drops, along with periodic courses of antibiotics may also be required for those dogs that are prone to secondary skin or ear infections. Hence, in a typical case of atopic dermatitis, a dog may require between 1 and 3 of the treatments described above at the same time, with more severe cases sometimes requiring 4 to 5 concurrent treatments to achieve satisfactory control.

In summary, the treatment of atopic dermatitis possibly involves more options than for any other condition. This requires a great deal of therapeutic decision making and there is often a degree of trial and error in arriving at the most satisfactory regime. Clinicians who do not wish to explore dermatological management in such depth would be well advised to refer these cases to a dermatologist for initial diagnosis and treatment recommendations.
SUMMARY OF TREATMENT OPTIONS

How effective are the treatments?
Steroid tablets - effective in nearly 100% of cases
Cyclosporine - effective in approximately 80% of cases
Desensitisation - beneficial in approximately 65% of cases
Antihistamines - beneficial in approximately 20% of cases
Essential fatty acids - beneficial in approximately 20% of cases
Antimicrobials - effective when infection present
Barrier treatments - helpful to restore skin function
Shampoos - helpful to treat and prevent infection and soothe the skin

What are the risks of side effects?
Steroid tablets - Can cause major side effects when used for a long time
Cyclosporine - Rarely causes long term side effects
Desensitisation - Rarely causes side effects
Antihistamines - Rarely cause side effects
Essential fatty acids - Rarely cause side effects
Antimicrobials - May cause stomach upsets. Major side effects are rare
Shampoos - May occasionally irritate the skin
Barrier treatments - No major side effects

What do the treatments cost? (depends on size of dog)
Cyclosporine - approximately $175 - $700 per month
Antimicrobials - approximately $50 – $100 for a course
Desensitisation - approximately $60 - $70 per month
Antihistamines - approximately $40 - $150 per month
Shampoos - approximately $25 - $50 per month
Essential fatty acids - approximately $20 - $50 per month
Steroid tablets - approximately $15 - $30 per month
Barrier treatments - approximately $10 - $15 per month

Putting all this information together, the following treatment strategies are those that are typically recommended:
• Lowest cost option – Cortisone tablets, Alpha keri oil ($200 - $400 per year)
• Moderate cost option – Desensitisation, Cortisone creams, Skin support diet/EFA’s, ($800 – $1200 per year)
• High cost option – Cyclosporine, Skin support diet/EFA’s ($2500 - $7000 per year)

Even if a dog starts on one treatment strategy, it may be necessary to change it to another one if there is not a good response. However, with appropriate treatment, most dogs with atopic dermatitis can be given a normal quality of life and spared the misery of constant scratching.
CLINICAL TRIAL OF A NEW DRUG FOR THE TREATMENT OF CANINE ATOPIC DERMATITIS
Specialist dermatologists around Australia are conducting a clinical trial on behalf of Pfizer Animal Health to investigate the efficacy of a new drug for the treatment of canine atopic dermatitis.

What’s in it for you?
You will be contributing to a trial that will improve knowledge on the management of atopic dermatitis and should lead to the marketing of an effective new drug for treating atopic dogs. That’s got to be a good thing.

What’s in it for the dog?
The dog will be treated with either the new drug or a positive control drug approved for the treatment of atopic dermatitis. Both are likely to be helpful in giving the dog some relief from its itching. The trial is blinded so the investigators are not aware which treatment the dog is receiving.

What’s in it for the owner?
5 free consultations, free drugs, free haematology and biochemistry profile at each visit, and a financial incentive on completion of the trial.

How long does the trial last?
The trial for each dog will last up to 12 weeks. Recruitment of cases will continue throughout 2012.

What are the main inclusion criteria?
1. Dogs must be at least 12 months of age.
2. They must have moderate to severe itching and dermatitis that has been present/treated for at least 10 months.
3. They should be strongly suspected of having atopic dermatitis based on typical history, clinical signs and exclusion of other diagnoses (flea allergy dermatitis, mange, food allergy, bacterial or fungal dermatitis, otitis)
4. If intradermal testing or serologic testing for IgE has previously been conducted, please supply the results at the time of referral (neither test is essential for recruitment onto the trial, but if they are deemed necessary, the cost is not covered by the trial).

What if the dog is already on drugs?
If you have a potential case, please one of the investigators and they will advise you about drug withdrawal times.

What happens at the end of the trial?
The dog will either go back onto the management that it was on before, or other options could be explored with the owner (for example skin testing and immunotherapy).

If you have any cases that might be suitable for recruitment onto this trial, please contact your nearest specialist dermatologist