



Cytopoint: Experiences and Questions Roundtable

(originally published in the May 2017 edition of Derm Dialogue)

Moderator: Kimberly Coyner

Secretary: Emily Rothstein

Attendees: 19

Private dermatology specialty practice=13

Private practice: 4

University=0

Other= 2 veterinary dermatologists from Zoetis

This round table was designed to discuss multiple specific questions (which were emailed to participants prior to the meeting) about our collective Cytopoint experiences in clinical practice.

1. Number of dogs you have treated with Cytopoint/CADI?

- Kim Coyner : between 10/2015-12/31/16: 244 dogs/847 injections; 3-4 /week average
- Mary Schick: >234 dogs
- Karen Kuhl: 400, 3-4/week
- Others were similar to lower numbers

Further comments included a discussion of the need for Zoetis and dermatologists to educate private practitioners on this new drug, mechanism of action, indications and contraindications (such as administration to cats), and that the roll out of this drug has not seemed to have had as much fanfare as Apoquel did in the past. Some private practitioners were unaware of the drug or its appropriate use, or were cautious to use it after having issues with Apoquel supply in the past; Andy Hillier (Zoetis) stated that Zoetis has been disseminating information about Cytopoint at lectures and meetings, as well as online resources for veterinarians (<https://www.zoetisus.com/products/dogs/cytopoint/>) and pet owners (<http://www.cytopoint4dogs.com/>).

2. % patients which were treatment successes? (injection was helpful for at least 4 weeks)

- Kim Coyner: 151 dogs (62%) were itch free at least 4 weeks, 67 dogs (27%) were not itch free for at least 4 weeks, and 26 dogs (11%) had no follow up to determine efficacy. Of the 151 dogs considered treatment successes: 64% dogs had pruritus control for 4 weeks, 9% for 6 weeks, 10% for 8 weeks, and 17% > 8 weeks (usually seasonal itch flares or dogs that responded to hypoallergenic diets).
- Sarah Columbini: 70% of her patients are itch free for 3 weeks-3 months post Cytopoint injection.
- Emily Rothstein: Has 3 German shepherd patients which are itch free for several months after Cytopoint.

Further comments included that most owners noted some itch 2-3 days just before the 4 week point, stimulating the question of whether Cytopoint can be used more frequently, ie. every 3 weeks? Andy Hillier stated that there is no data to suggest problems with 3 weeks administration frequency but also no data to document long term safety of this administration, though prior safety studies in laboratory dogs demonstrated safety of Cytopoint at 5X the label dose.

3. The question was then **asked how many participants were administering Cytopoint more frequently than every 4 weeks?**
- A few participants were comfortable using it q 3 weeks.
 - Others used it as labelled q 4 weeks and instructed owners to administer Apoquel if needed to control itch until the next Cytopoint injection could be given.
 - Two Canadian attendees administer Cytopoint at the 4 week label frequency as the drug is still under conditional licensure in Canada.

The question was then raised about **if Cytopoint becomes more effective with subsequent dosing?**

- Andy Hillier stated that there have been reports that Cytopoint is more effective in some patients after the second or third injection.
- Mary Schick concurred she had seen this occur.
- Most participants did not have that experience.

4. **% of cases which Cytopoint injections initially were very helpful then stopped working or caused side effects and had to be discontinued?**

- Kim Coyner: 5 dogs (2%) were initially helped for the first 1-2 Cytopoint injections then subsequent injections did not help and 2 dogs (0.8%) had side effects such as lethargy and GI upset severe enough to cause discontinuation.
- Karen Kuhl: 5-10% (10 of 400) worked less and less each shot given until failed altogether (no time given).
- Two other participants experienced decreased efficacy after 2nd or 3rd injection.
- Andy Hillier discussed reasons for Cytopoint treatment failure including other flare factors (infections, parasites; all agreed this was a common reason for pruritus flares in atopic dogs but that as dermatologists we are capable of identifying these flare factors, so unlikely to be the case in our patients), and anti-drug-antibodies (occurred in 2.5% of dogs in one Cytopoint clinical trial), but the latter should not be a slow but abrupt decline in efficacy.

5. **Participants were then asked if they were using Cytopoint for symptomatic relief when infection was present causing severe pruritus/while infection was treated?**

- Reaction was mixed.
- Some participants used Cytopoint regardless of infection and felt it worked well.
- Others waited until infection was controlled (and used a short course of steroids or Apoquel if needed, stopping well before antibiotics were finished) prior using Cytopoint for the concern that if it did not work due to infection clients would be reluctant to try it again in the future.

The question was raised of how many patients are referred specifically for Cytopoint injections, not many had this experience. The discussion then expanded to the need for a definitive diagnosis of atopy prior to use of Cytopoint- Andy Hillier said Zoetis has a 4 pronged algorithm discussing the diagnostic and therapeutic approach to a pruritic dog. This algorithm is a Cytopoint iDetailer is used by Zoetis reps when they talk to veterinarians and is not approved for external use or general distribution.

6. **What side effects have you seen?**

- Kim Coyner: pain on injection 1 dog, vomiting 7 dogs, diarrhea 2, (total GI upset: 9 dogs/3.7%); anorexia, lethargy 4 dogs/1.6%, increased itch 4 dogs/1.6%.

- Sarah Columbini: has seen GI side effects including vomiting or diarrhea occurring 1 day to 3 weeks post injection and had one patient with consistently repeatable lethargy and nasal congestion 2-3 d after injection.
- Vincent Defalque: requires patients to wait 15 min in office after each injection but has seen no adverse reactions. (Andy Hillier commented that patients were required to wait 30 min in the Cytopoint clinical trial and no allergic reactions occurred).
- One participant from Canada had one patient with diarrhea post Cytopoint which is controllable with Tylosin and another patient which developed angioedema after the first Cytopoint injection, the first time immediately and the second injection angioedema developed the following morning.
- Karen Kuhl: had 2 patients that developed hives 8-10 days after receiving Cytopoint, and had no prior history of hives, however other allergenic causes were possible since the episodes occurred in the spring; 1 of these dogs had a good response/control of pruritus, the other patient (a veterinary technician's dog) developed subsequent hairloss and the injection helped for only 2 weeks and so was not repeated.
- Mary Schick: had a few patients who were lethargic for 2-3 hours after Cytopoint injections, but may have just been exhausted from itching and finally able to rest; she felt the lethargic dogs were often the best Cytopoint responders.
- Three other participants had patients with pain on injection, often in small dogs, but one participant had 2 large dogs in one day with pain on injection that had not occurred on prior injections, this was reported to Zoetis in case of a drug lot issue.

This then led to a discussion of the difficulty some US participants had in reporting possible adverse events to Zoetis, that in some cases the Zoetis representative seemed to minimize or deny the possibility of a relationship between the drug and suspected adverse event, or list the adverse events noted in the clinical trials (which is unnecessary to relate to diplomates who have already read these studies or have been the participants in the clinical trials); the statement was made that it would solve the issue if dermatologists could have a dedicated report line. Round table participants from Canada related that they never experienced these issues when calling Zoetis and could even report events online.

The discussion then shifted to the question about **possible side effects of long term IL-31 inhibition?**

- Andy Hillier related that in safety studies of Cytopoint given at 10mg/kg for 7 treatments, no adverse effects occurred, and that redundant cytokines could be expected to take over any maintenance functions.
- Additionally IL-31 is known to have a role in other inflammatory diseases (increased IL 31 has been found in asthma and IBD), but has not been found to have an essential role in normal immune function.
- (Moderator note: IL-31 receptors are found on canine keratinocytes, monocytes, and dorsal root ganglia where cell bodies of sensory neurons reside; in human and mouse studies IL-31 receptors have also been found on eosinophils, mast cells, bronchial epithelia, colonic subepithelial myofibroblasts, spleen, bone marrow, ovary, and testes).

7. Have you had cases in which Apoquel was not helpful but Cytopoint was?

- Kim Coyner: 6 dogs (2.5%)
- Kinga Gortel : had a few dogs.
- One participant noted that Cytopoint was helpful in half of her Apoquel failures.
- Patrick Mckeever :noted he has had several severe pododermatitis cases which did not respond to either Apoquel or Cytopoint.

8. Have you had cases in which Cytopoint was not helpful but Apoquel was?

- Kim Coyner: 19 dogs (8%).
- Several other participants had cases as well.

The discussion of the different mechanisms of action of Cytopoint vs/ Apoquel (IL-31 sole inhibition vs. JAK enzyme inhibition) followed to explain the different effects in some dogs. Michele Rosenbaum (Zoetis) stated that in some dogs

there may be polymorphisms in the JAK enzymes such that Apoquel cannot bind to and inactivate these enzymes, or some dogs may use other signaling pathways besides the JAK enzyme pathway to activate the cell after cytokine (IL-31, etc) binding.

9. Are you checking labwork (which labs/why/how frequently?)

- No one was checking labwork.

10. In what situations are you using Cytopoint? (ie. itch control during initial allergy workup, alternative to Apoquel, alternative to IDAT/desensitization, complementary to desensitization for itch control while desensitization has time for effect, seasonal flares, neuropathic itch, other diseases?)

- Most participants were using it in typical atopic dogs as an alternative to steroids and Apoquel .
- It was considered especially helpful in cases in which owners were worried about perceived side effects from other drugs often promulgated by online research.
- Andy Hillier cautioned against the use of Cytopoint during hypoallergenic diet trials due to the variability of duration of effect of the drug making response to a diet trial harder to interpret.
- One participant found Cytopoint was helpful to control pruritus associated with sarcoptic mange (under treatment) in 3 cases.
- Others stated it was a useful non-immunosuppressive option to control pruritus in dogs which developed neoplasia.
- Other uses mentioned included adjunctive use as pruritus control for pemphigus foliaceus (2 participants, 3 cases), erythema multiforme (1 dog), epitheliotropic lymphoma (2 participants) and calcinosis cutis (1 participant).

11. How many clients have elected to stop allergy immunotherapy and switch to Cytopoint injections as sole treatment for their atopic dogs?

- Few participants had seen this.

12. How are you pricing Cytopoint ?

- Most were using MSRP and had no issues with setting up Cytopoint in practice software.
- Kim Coyner had to set up a dual pricing structure in Impromed to acct for cost difference in small vs large dogs to match the MRSP and this made it not possible to track inventory accurately.
- Andy Hillier stated that Zoetis has designed pricing strategies for most veterinary software programs and instructions on how this can be accomplished be can obtained through your local Zoetis rep.

13. Have you administered Cytopoint to any atopic dogs with pre-existing or a history of prior immune mediated disease (ie. vasculitis, DLE, pemphigus, drug eruption, ITP, AIHA etc.) and have there been any side effects or flare of immune mediated disease noted?

- Kim Coyner has used in in 2 pemphigus foliaceus dog and one erythema multiforme dog with good control of pruritus and no exacerbation of immune mediated disease.
- One participant had used Cytopoint on one dog with immune mediated thrombocytopenia with no issues.
- Andy Hillier stated that immune mediated issues were unlikely due to the specificity of Cytopoint to IL-31 only.
- One participant asked if yearly booster vaccinations could be given at the same time as Cytopoint and Andy Hillier stated yes, but the suggestion was made to use a different injection site.
- One participant mentioned that immunologic adverse effects have been seen with multiple mAbs in humans (Moderator note: This is correct, however there is not a direct comparison as are no IL-31 mAbs currently approved for use in humans. A helpful summary article for human mAbs: Hansel T et al. The Safety and Side Effects of Monoclonal Antibodies. *Nature Reviews Drug Discovery* 2010; 9: 325-338).

The following questions were not discussed due to lack of time:

14. After the first 1-2 doses, are you having a technician administer the Cytopoint injections/no doctor exam?
15. Do some clients have difficulty bringing in the pets consistently to avoid flare if an injection is late? Do some clients elect to change to a different antipruritic medication (Apoquel/steroid/Atopica) for that reason? How often have you seen these issues occur? Are you allowing owners experienced in giving injections to purchase a Cytopoint vial and administer it to their pets at home?