Tasipimidine, a novel orally dosed alpha-2 adrenoceptor agonist, alleviates canine acute anxiety and fear associated with travel – a pilot study

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Affiliations and conflict of interest

• The study was sponsored by Orion Corporation Orion Pharma.
• MK, MH and PP are employees of Orion Corporation.
• BC and CM, are paid consultants of Orion Corporation
Study outline

- **Objective**: to evaluate the efficacy and clinical safety of tasipimidine oral solution against placebo for alleviation of acute anxiety related to car travel in dogs
- **Design**: randomized, double-blind, placebo-controlled, cross-over, exploratory pilot clinical field trial.
- **Investigational product**: Tasipimidine 0.3 mg/ml oral solution at the dose 30 mcg/kg,
- **Dosing regimen**: orally, 1h before car drive
- **Sample size**: 19 dogs with history of travel anxiety
- **Safety**: Functional alertness, Adverse events
Study design

- Screening period
  - Pre-screening
  - Owner training

- Baseline
  - Car ride and Health check-up at veterinary clinic
  - Baseline contact video and health check review

- Treatment period
  - Treatment 1: 8 ± 2 days
  - Treatment 2: 8 ± 2 days
  - End-of-study contact

Randomisation
**Study dogs**

**Screening status:**
- Advertisement seen 1114
- Pre-screening started 186
- Passed pre-screening web-questionnaire 45
- Enrolled for baseline (BL) 22
- Excluded after BL 3
- Randomised after BL 19

**Recruited study dogs (n=19):**
- Median age 4.9 years (range 2-12)
- Median weight 11.6 kg (range 5-34)
- 11 females and 8 males
# Efficacy variables

## External observer’s assessment of signs of anxiety and fear

- ✔️ Assessed from video recordings based on the ethogram during the first evaluable 10 minutes of each car ride

## Owners’ assessment of treatment effect

- ✔️ Effect of the product based on the dog’s behaviour during car travel during the first 10 minutes
- ✔️ Scores: “excellent effect”, “good effect”, “some effect”, “no effect” or “negative effect”.

<table>
<thead>
<tr>
<th>Sign</th>
<th>Duration</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restlessness</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Hypersalivation</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Panting</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Barking</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Whining</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Trembling</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Lip/Nose licking</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Yawning</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Swallowing</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Autogrooming</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Changes of the posture</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Low Tails</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Ears Backwards</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Crouching</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Destructive activity</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Other, specify</td>
<td></td>
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</tr>
</tbody>
</table>
Results

External observer assessment

• Statistically significant treatment effect in favor of tasipimidine for both signs based on duration (p<0.0001) and based on frequency (p=0.013)
• Treatment sequence was statistically significant for the signs based on duration (p=0.0085)
• From individual signs tasipimidine significantly reduced panting (p<0.0001) and lip/nose licking (p=0.001)
• Tasipimidine treated dogs showed also numerically less frequently following anxiety behaviours: Ears backwards, low tail, restlessness, trembling and whining, changes of the posture, yawning

Owner assessment

• Favorable treatment effect for tasipimidine compared to placebo (OR 23.3; 95% CI 4.58-118.2; p = 0.0001)
• Treatment sequence effect significant (p=0.01)

<table>
<thead>
<tr>
<th>Response</th>
<th>Placebo</th>
<th>Tasipimidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent effect</td>
<td>1 (5.3 %)</td>
<td>3 (15.8 %)</td>
</tr>
<tr>
<td>Good effect</td>
<td>1 (5.3 %)</td>
<td>9 (47.4 %)</td>
</tr>
<tr>
<td>Some effect</td>
<td>1 (5.3 %)</td>
<td>3 (15.8 %)</td>
</tr>
<tr>
<td>No effect</td>
<td>15 (78.9%)</td>
<td>4 (21.1 %)</td>
</tr>
<tr>
<td>Negative effect</td>
<td>1 (5.3 %)</td>
<td>0 (0.0 %)</td>
</tr>
</tbody>
</table>
Results and limitations

• Limitation of a cross-over study: owners expect that if the treatment effect was not seen in the first period that the second treatment must be the active treatment

  • This was seen also in this study where the treatment effect with tasipimidine was better in dogs when administered prior to the second car ride

• When the results only for the first car ride were taken into account for assessing the treatment effect, the active study medication was more efficacious than placebo.
Functional alertness assessment revealed three dogs that were scored “not as alert as usual” and one dog scoring “reluctant to stand up and uncoordinated when walking.”

Adverse events:
- No serious adverse events were reported
- Three cases of mild ataxia reported for tasipimidine
- Lethargy was reported for 2 dogs in the tasipimidine treatment and for one dog in the placebo treatment
Conclusion

• Tasipimidine treatment reduced signs of travel anxiety significantly in dogs in the objective video assessment.

• Treatment effect was also visible in the Owner overall assessment.

• There were no safety concerns, but for some dogs a dose reduction for subsequent car rides could be warranted.
Thank you!

For further questions, please contact:

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