A Randomized, Double-Blind Placebo-Controlled Phase III Study of the Efficacy and Safety of DPI-386 Nasal Gel Compared to Current Standard of Care for Prevention of Motion Sickness

Barry Feinberg, MD & David Helton

Background:

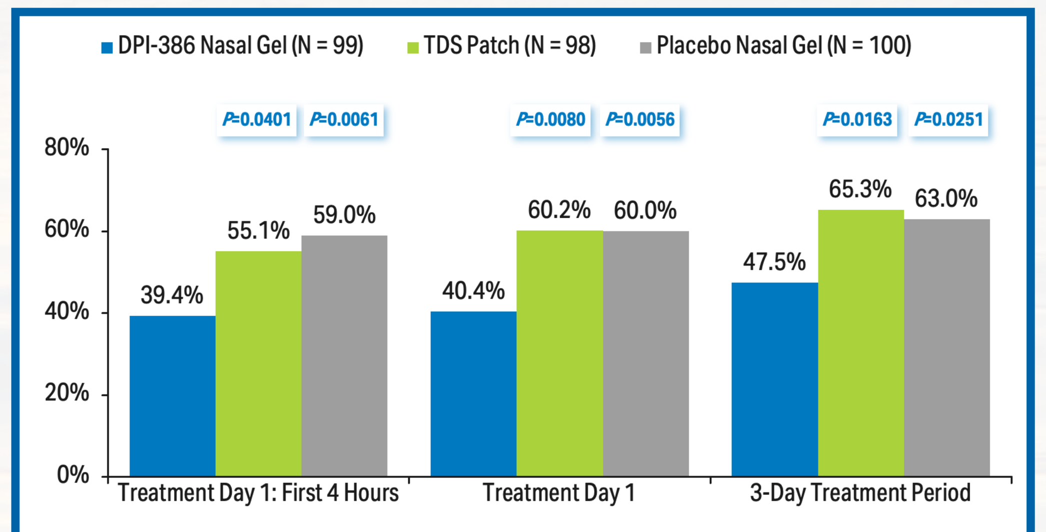
Motion sickness (MS) remains a problem for the military across the Services. The anticholinergic scopolamine is one of the more efficacious anti-motion sickness medications. However currently available oral and transdermal scopolamine medications have drawbacks compromising utility, including delayed onset of action and dose-related side effects which are significant issues for Warfighters in operational use. The current standard of care is the scopolamine patch (Transderm Scop, TDS Patch) which is indicated for the prevention of nausea and vomiting associated with MS.

MS is a condition characterized by a feeling of unwellness brought on by certain kinds of movement. The usual symptoms may include dizziness, irritability, inability to concentrate, fatigue, pale skin (pallor), cold sweating, headache, restlessness, and drowsiness which can be followed by nausea and vomiting. DPI-386 is a low dose nasal scopolamine gel which was developed in collaboration with the US Navy and NASA. In clinical studies, DPI-386 has demonstrated a rapid onset of action (PK) with limited to no side effects as compared to the TDS patch. The data presented here focus on the ability of DPI-386 or TDS patch to prevent the onset symptoms of MS excluding nausea and vomiting.

Approach and Solution:

Defender has recently completed a Phase 3 clinical trial in 300 subjects (100 subjects per arm) comparing the efficacy and safety (including cognitive and attentional processing) of DPI- 386 nasal gel to the TDS patch and placebo in the prevention of the symptoms of MS. Subjects self-administered six doses of DPI-386 or placebo nasal gel over three days at sea with a minimum of six hours between doses. The TDS patch was placed behind the ear on day one and remained on through day three. Incidence of MS was significantly lower for DPI-386 Nasal Gel compared to TDS patch within 4 hours on Day 1 ($p = 0.0307$), through the end of Day 1 ($p = 0.0032$), and during the 3-day treatment period ($p = 0.0046$). With respect to placebo, incidence of MS was significantly lower for DPI-386 Nasal Gel within 4 hours on Day 1 ($p = 0.0163$), through the end of Day 1 ($p = 0.0063$), and during the 3-day treatment period ($p = 0.0072$). Outcomes from cognitive and attentional tests will be presented. No unexpected adverse events occurred. In conclusion, DPI-386 significantly prevented motion sickness symptoms relative to the TDS patch or placebo.

DPI-386-MS-21: Subject Incidence of Nausea Using MedDRA Preferred Term (ITT Population)



Note: Subject incidence of nausea is derived as any subject who reports an AE with coded MedDRA preferred term of "Nausea" or "Motion Sickness" and onset after the first dose of study treatment on Treatment Day 1.

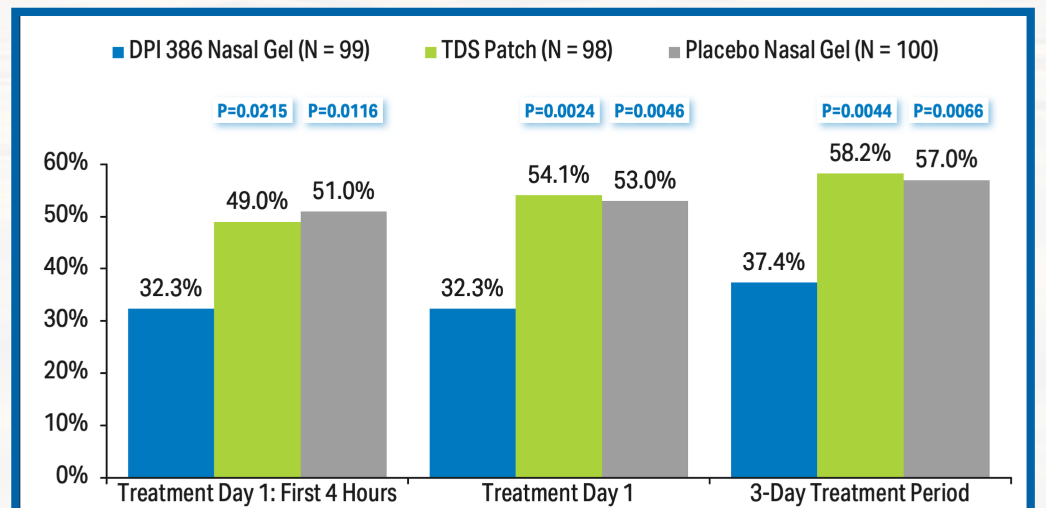
ANAM CORE+CPT: DPI-386 Studies 22 and 24

There was no difference between DPI-386 and Placebo in AMAM CORE + CPT Testing

This battery consists of the ANAM CORE battery plus the Running Memory Continuous Performance Test (CPT). This battery has the following tests:

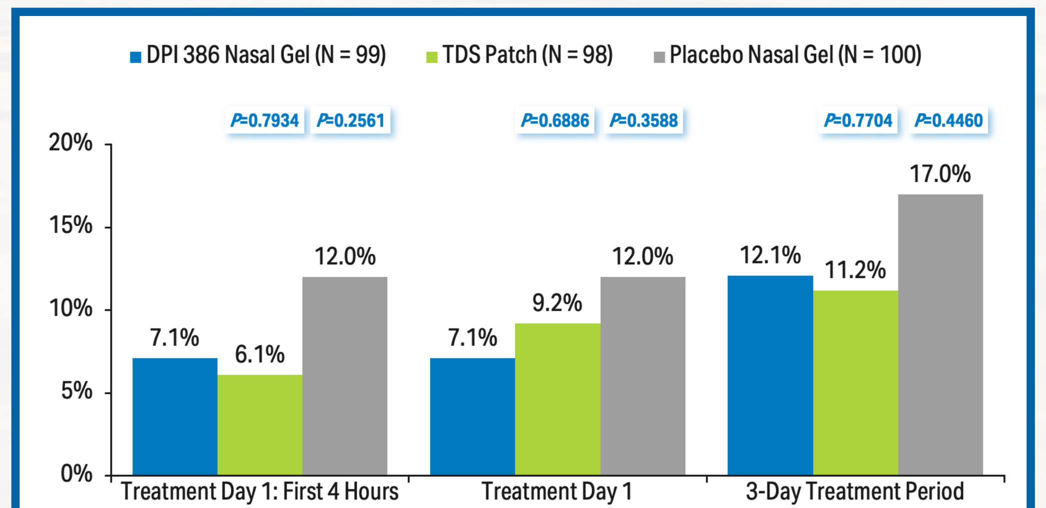
- Sleepiness Scale
- Symptoms Checklist
- Mood Scale
- Simple Reaction Time
- Code Substitution – Learning (CPS)
- Procedural Reaction Time
- Mathematical Processing
- Matching to Sample (M2S)
- Code Substitution – Delayed (CDD)
- Simple Reaction time (repeated)
- Go/No-Go
- Running Memory Continuous Performance Test (CPT)

DPI-MS-386-21: Subject Incidence of Motion Sickness Using Verbatim AE Term (ITT Population)



Note: Point estimates and 95% CI under the column "TDS Patch" represents the difference between DPI-386 Nasal Gel and TDS Patch. Similarly, point estimate and 95% CI under the column "Placebo Nasal Gel" represents the difference between DPI-386 Nasal Gel and Placebo Nasal Gel.

DPI-386-MS-21: Subject-Reported Incidence of Nausea Based on Adverse Event Verbatim Term ITT Population



Note: Subject incidence of nausea is derived as any subject who reports an AE verbatim term that includes the text string "Nausea," "Nauseous," "Queasiness," or "Queasy" with onset after the first dose of study treatment on Treatment Day 1.

Examine

Current routes of administration for the anti-motion sickness agent scopolamine.

Identify

The difference between motion sickness symptoms and nausea and vomiting.

Understand

The efficacy and side effects profile of scopolamine administered in a novel dosage form at a lower than conventional dose for prevention of motion symptoms.