NARRATIVE KNOW-HOW:
AUTOMATING AND STREAMLINING THE
WRITING, QC, AND ASSEMBLY PROCESS
An Education Session for AMWA

November 7, 2019
Kathy Oxberry, Merck
Aldo Ramina, ArborSys
Jennifer Clemens, Merck
Our *Most Epic* Team

Kathy Oxberry  
*Lead Safety Medical Writer*  
Merck

Aldo Ramina  
*Business Analyst*  
ArborSys

Jennifer Clemens  
*Senior Editor*  
Merck
GOALS

• Share what we’ve learned about best practices, automation, and streamlining
• Give you ideas to build a more efficient process to generate patient narratives
• Provide actionable improvement steps, with or without automation
• Hear about your experience
SURF’S UP!
COWABUNGA!

• What is your work environment?
• How many of you write patient narratives?
• Edit narratives?
• Assemble narratives?
• Use automation?
• Create best practices?
• Develop time-saving processes?
The need to deliver a large volume of documents in a short time
The Building Blocks for Writing Patient Narratives

https://www.fda.gov/media/71271/download
MERCK’S TOTALLY RAD NARRATIVE EVOLUTION
What ELSE can we do to help…

Save Time?
Phase 1: A Workable Process

Live Database

Clinical Study Report

Narrative

Bulleted List

Medical Writer

Publisher

Simple Template

Shared Network Drive

Medical Reviewer

MW Peer Review

Medical Writer
Developing a Workable Process

<table>
<thead>
<tr>
<th>PLATFORM</th>
<th>DISPLAYS</th>
<th>DATA</th>
<th>ORGANIZATION AND DELIVERY</th>
</tr>
</thead>
</table>
| • Collaborative workflow?  
• Secure platform?  
• Version control?  
• Metrics? | • Template?  
• Is it standardized?  
• Style guide? | • Data source?  
• Before or after database lock?  
• Does the data change?  
• Standard table format? | • Where do you place your narratives?  
• Patient confidentiality?  
• Consistent organization? |
This worked for us, but with increased workloads we needed to...

Save Time
Phase 2: Improvements

PAIN POINTS

• Writers spending too much time copying and pasting Excel data into the template
• Editors spending too much time QCing
This worked for us, but with increased workloads we needed to…

Save Time
Phase 3: First Automation

SOLVING PAIN POINTS

• Adding the Utility was a big win
• Where else could we improve efficiency?
# Refining the Process

## Platform
- Authoring Repository
- Collaborative environment
- Version control
- Collect metrics
- Secure site

## Displays
- Word Table Template
- Tabular narrative template
- Consistent not prescriptive
- Style guides and process documents

## Data
- Locked Database
- Aligns with SAS data sets from locked database
- Mapped data to tabular template
- Variables aligned with statistical analysis

## Organization and Delivery
- Set the framework for the reviewer
- Define selection criteria
- Moved to appendix

---

*MERCK: INVENTING FOR LIFE*
Phase 4: Developing a Manual Assembly Process

1. Locked Database
   - SDTM XLSX files
2. Secured Document Repository
3. Clinical Study Report
4. Narrative
   - Table
   - Templated Intro
5. Editor QC
6. Medical Reviewer
7. Medical Writer
8. Authoring Repository
9. Utility

Flowchart:
- Locked Database → SDTM XLSX files → Utility → Narrative Shell → Authoring Repository
- Secured Document Repository
- Clinical Study Report
- Narrative
- Editor QC
- Medical Reviewer
- Medical Writer
Things to Consider When Organizing Narratives

NAVIGATION
Ease of review through the use of links and bookmarks
Things to Consider When Organizing Narratives

TOOLS AND PROCESSES
Software, best practices, instruction guides
The Assembly Challenge: Numerous Steps

Pros:
- Workable process
- Polished document

Drawbacks:
- Labor intensive
- Time consuming
This worked for us, but with increased workloads we needed to...

Save Time
Phase 5: Applying Automation — Again

- Locked Database
- Clinical Study Report
- Secured Document Repository
- SDTM XLSX files
- Utility
- Narrative Shell
- Editor #2 Assembly
- Medical Reviewer
- Authoring Repository
- Editor #1 QC
- Medical Writer
- Narrative Shell
- Table Templatized Intro Assembly
Now: We Get to that PDF Much Faster!

Launch utilities

Final output

AWESOME!
How Much Faster?

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Writing</td>
<td>6.3</td>
<td>2.8</td>
</tr>
<tr>
<td>QC</td>
<td>1.9</td>
<td>1.17</td>
</tr>
</tbody>
</table>

Total time savings ~50%
Some of these improvements were a result of automation... *but not all.*
BEST PRACTICES FOR NARRATIVE WRITING...

- Explore add-ins to reduce tedious tasks and save time
  - Word
  - Excel
- Template, template, template
- Best practices and team collaboration
- Writer’s Guide, style guides
Best Practices

WRITING

1. Align documents and training = write narratives in 1 voice
2. Use active voice and lean text
4. Room for variation (consistency without being prescriptive)
5. Leverage standard template and business rules (ie, standard way of dealing with data)
6. Protect confidentiality: no dates, pronouns, or identifiable info used in text
Best Practices
General Data Protection Regulation (GDPR)

We’ve made sure to communicate to writers and editors that FDA fully supports removal of confidential Personal Health Information (PHI), which is compliant with GDPR and aligns with EMA Policy 0070.

https://eugdpr.org/
Best Practices
General Data Protection Regulation (GDPR)

female
Best Practices
General Data Protection Regulation (GDPR)

- Proactive data minimization and anonymization
  - Day 20 instead of June 20
  - Avoid pronouns
  - Newsworthy, traceable information

- Address in the early stages to **save time**
  - All reviewers
  - Editors/QC
  - Redaction team
What are the fines for violating GDPR?
2% to 5% of annual company revenue or 20M Euros, whichever is greater
Best Practices
Collaboration saves time and money

COLLABORATING
1. Cultivate collaborative feedback loop between writers and QC team
2. Kickoff meetings
3. Editors summarize project findings to Medical Writing team
4. Open dialogue between writers and editors

PROGRAMMING
1. Collect potential enhancements based on user feedback
2. Update narrative utility selectively
3. Proactively address issues in the Word Template
This worked for us, but what have you done to...

Save Time?
Sharing Experiences

• How have you streamlined process steps?
  – Writing
  – Editing
  – Assembly

• What challenges jeopardize the narrative delivery deadline? Solutions?

• What metrics help you identify opportunities for process improvements?

• With the rollout of GDPR in May 2018, how have you changed your approach to managing narratives and confidential data?

• What does the agency want or need?

• Are there alternatives to text-based narratives?

• How can we achieve industry alignment?
Surfs Up Pharmaceuticals

TITLE: A Randomized, Double-Blind, Phase III Study of parsley/sage/rosemary/thyme with or without Reese’s Peanut Butter Cups in Participants with Alopecia. (GOLDILOCKS)

Protocol 010

11-7-2019
### TRIAL SUMMARY

<table>
<thead>
<tr>
<th>Abbreviated Title</th>
<th>Phase III study of parsley/sage/rosemary/thyme with or without Reese’s Peanut Butter Cups in Participants with Alopecia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Phase</td>
<td>Phase 3</td>
</tr>
<tr>
<td>Clinical Indication</td>
<td>Alopecia</td>
</tr>
<tr>
<td>Trial Type</td>
<td>Interventional</td>
</tr>
<tr>
<td>Type of Control</td>
<td>Standard of Care (SOC) parsley/sage/rosemary/thyme with Active-Control Reese’s Peanut Butter Cups (RPBC)</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>Oral</td>
</tr>
<tr>
<td>Trial Blinding</td>
<td>Double-blind</td>
</tr>
<tr>
<td>Treatment Groups</td>
<td>There are 2 treatment arms:</td>
</tr>
<tr>
<td></td>
<td>• Reese’s Peanut Butter Cups plus parsley/sage/rosemary/thyme (SOC)</td>
</tr>
<tr>
<td></td>
<td>• parsley/sage/rosemary/thyme (SOC)</td>
</tr>
<tr>
<td>Number of Trial Subjects</td>
<td>Approximately 650 subjects will be enrolled.</td>
</tr>
<tr>
<td>Estimated Duration of Trial</td>
<td>The Sponsor estimates that the trial will require approximately 2 years from the time the first participant signs the Informed Consent Form (ICF) until the last participants’ last study-related phone call or online data entry.</td>
</tr>
<tr>
<td>Duration of Participation</td>
<td>Each participant will be an active surfer who agrees to participate in the trial from the time the ICF is signed through the final contact. There will be a brief enrollment questionnaire, and each Tuesday the participant will receive a text message or e-mail reminder to complete a short weekly survey. Participants will report daily surf activity (location date, and times of water entry and exit) and illness symptoms for the previous 7 days. Participants with alopecia will be assigned to one of two cohorts:</td>
</tr>
<tr>
<td></td>
<td>• Cohort A: Reese’s Peanut Butter Cups plus parsley/sage/rosemary/thyme (SOC)</td>
</tr>
<tr>
<td></td>
<td>• Cohort B: parsley/sage/rosemary/thyme (SOC)</td>
</tr>
<tr>
<td></td>
<td>The study will continue for 2 winters (01-Dec through 01-Apr, 2017-2018 and 2018-2019), documenting surf location in the San Diego/southern California area, recording surf-related illness, unacceptable adverse event(s) (AEs), intercurrent illness that prevents further administration of treatment, investigator’s decision to withdraw the participant or the participant withdraws consent, noncompliance with the trial treatment or procedure requirements, or administrative reasons. Participants will have a post-treatment follow-up to assess alopecia status, with the option to start a topical corticosteroid cream.</td>
</tr>
<tr>
<td>Randomization Ratio</td>
<td>Randomized 1:1 to either receive Reese’s Peanut Butter Cups plus parsley/sage/rosemary/thyme (SOC), or parsley/sage/rosemary/thyme (SOC)</td>
</tr>
</tbody>
</table>
Subject Number: 0100-070210

Treatment Arm: Reese’s Peanut Butter Cups + parsley/sage/rosemary/thyme

Event Category/Preferred Term (Grade)/Day of Onset

Serious Adverse Event (Grade) – Onset Day:

- Compound fracture of femur (Serious) – 04-Jul-2017 (Day 154)

Events of Clinical Interest (Grade) – Onset Day:

- Gastritis (Mild) – 14-Feb-2018 (Day 14)

Participant Characteristics: The surfer, 0100-070210, a 27-year-old, tan white female, was diagnosed with alopecia, Grade III as rated with the NYCAGS, 1 month before the first dose of study medication. The subject was a surfer in La Jolla.

Her medical history included Legionnaire's Disease, Otitis Externa (Surfer's Ear), Hepatitis A, Schistosome Cercarial Dermatitis (Swimmer's Itch), Conjunctivitis (Pink Eye) Methicillin-Resistant Staphylococcus aureus (MRSA), Encephalitis and Meningitis, Gastroenteritis, Leptospirosis, and Dry Eye.

Medications started prior to the administration of study drug included ibuprofen (ADVIL), cyclobenzaprine (FLEXERIL), polyethylene/propylene glycol (SYSTANE), and lorazepam (ATIVAN).

Concomitant medications taken after the administration of study drug included polyethylene/propylene glycol (SYSTANE), lorazepam (ATIVAN), cephalaxin (KEFLEX), influenza virus vaccine (FLULAVAL), azithromycin (Z-PAK), calcium carbonate/citrate plus cholecalciferol (CALCIUM D), acetaminophen (TYLENOL), pantoprazole sodium (PROTONIX), hydrocortisone, sodium chloride, influenza vaccine (FLUZONE), promethazine (PHENERGAN), meclizine (ANTIVERT), alprazolam, and ondansetron (ZOFRAN), aluminum hydroxide and magnesium hydroxide suspension (MAALOX SUSPENSION), aluminum hydroxide, magnesium hydroxide, and simethicone suspension (DI-GEL LIQUID), methamphetamine (METH), kombucha (MIGHTYBOOCH), magnesium hydroxide (PHILLIPS MILK OF MAGNESIA), aluminum hydroxide, magnesium hydroxide, and simethicone suspension (MYLANTA).

Description of Adverse Event(s): On 01-Feb-2017 (Day 1) the surfer girl was randomly assigned to the Reese’s Peanut Butter Cups (RPBC) + parsley/sage/rosemary/thyme (SOC) cohort and started treatment for alopecia. RPBC was given Q3W per month and parsley/sage/rosemary/thyme QID during the 4 months of winter surfing season for as long as she was in the study.

On 15-Feb-2017 (Day 15) she experienced burning indigestion in the stomach with abdominal pain, bloating, nausea, vomiting, and a 5-pound weight loss. She went to the ED and was diagnosed with gastritis (mild). A breath test was negative for Helicobacter pylori. HGB and Vitamin B12 laboratory test results were WNL. She was treated with IV fluids, Maalox suspension, and discharged to home the same day with instructions to continue Maalox suspension (Table).

On 04-Jul-2017 (Day 154) our very tan surfer girl was celebrating at Robb Field Skate Park, with an ample dose of crystal meth (recreational user) and kamikaze shots with beer chasers, when she attempted to do a backside bigspin (a 360 backside pop shove-it with a 180 body varial [pop shove-it] going the same direction). Something went terribly wrong and our surfer landed on the railing precipitating a compound fracture of the right femur. She was taken by ambulance to Sharp Memorial Hospital and admitted with a compound fracture of the right femur (serious). The same day urine drug toxicology results were positive for methamphetamine and alcohol. Our surfer girl was treated for short-term meth withdrawal, with supportive measures of IV fluids, and observed for fatigue,
depression, and increased appetite. She was discharged on 14-Jul-17 (Day 164) with arrangements for in-home physical therapy and analgesics.

No action was taken with study medication as a result of this event. There was no treatment delay.


The last dose of study drug was administered on 25-Mar-2018 (Day 418) when she completed the study.

The investigator considered compound fracture of the femur (serious) was not related to RPBC, and gastritis (mild) was related to RPBC but not related to SOC.

### Table. Relevant Antacid Use During the Study

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Antacids</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 99 to Day 140</td>
<td>Aluminum hydroxide and magnesium hydroxide suspension (Maalox Suspension)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 141 to Day 168</td>
<td>Aluminum hydroxide, magnesium hydroxide, and simethicone suspension (Di-Gel liquid)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 169 to Day 505</td>
<td>Magnesium hydroxide (Phillips Milk of Magnesia)</td>
<td>2-4 tablets PO Q4</td>
</tr>
<tr>
<td>Day 309 and continuing</td>
<td>Aluminum hydroxide, magnesium hydroxide, and simethicone suspension (Mylanta)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
</tbody>
</table>

PO = by mouth; HS = hour of sleep; PC = after meals; QID = four times per day; Q4 = every 4 hours.

https://www.timeanddate.com/date/durationresult.html

Tick box: yes or no
Yes = 1 day is added
Subject Number: 0100-070210

Treatment Arm: Reese’s Peanut Butter Cups + parsley/sage/rosemary/thyme

Event Category/Preferred Term (Grade)/Day of Onset

Serious Adverse Event (Grade) – Onset Day:

• Compound fracture of femur (Serious) Day 154

Events of Clinical Interest (Grade) – Onset Day:

• Gastritis (Mild) Day 14

Participant Characteristics: The participant, 0100-070210, was diagnosed with alopecia, Grade [I, II, III or IV] as rated with the NYCAGS. The participant's history included Legionnaire's Disease, Otitis Externa (Surfer's Ear), Hepatitis A, Schistosome Cercarial Dermatitis (Swimmer's Itch), Conjunctivitis (Pink Eye), Methicillin-Resistant Staphylococcus aureus (MRSA), Encephalitis and Meningitis, Gastroenteritis, Leptospirosis, and Dry Eye.

Medications started prior to the administration of study drug included ibuprofen (ADVIL), cyclobenzaprine (FLEXERIL), polyethylene/propylene glycol (SYSTANE), and lorazepam (ATIVAN).

Concomitant medications taken after the administration of study drug included polyethylene/propylene glycol (SYSTANE), lorazepam (ATIVAN), cephalexin (KEFLEX), influenza virus vaccine (FLULAVAL), azithromycin (Z-PAK), calcium carbonate/citrate plus cholecalciferol (CALCIUM D), acetaminophen (TYLENOL), pantoprazole sodium (PROTONIX), hydrocortisone, sodium chloride, influenza vaccine (FLUZONE), promethazine (PHENERGAN), meclizine (ANTIVERT), alprazolam, and ondansetron (ZOFRAN), aluminum hydroxide and magnesium hydroxide suspension (MAALOX SUSPENSION), aluminum hydroxide, magnesium hydroxide, and simethicone suspension (DI-GEL LIQUID), methamphetamine (METH), kombucha (MIGHTYBOOCH), magnesium hydroxide (PHILLIPS MILK OF MAGNESIA), aluminum hydroxide, magnesium hydroxide, and simethicone suspension (MYLANTA).

Description of Adverse Event(s): On Day 1 the surfer girl was randomly assigned to the Reese’s Peanut Butter Cups (RPBC) + parsley/sage/rosemary/thyme (SOC) cohort and started treatment for alopecia. RPBC was given Q3W per month and parsley/sage/rosemary/thyme QID during the 4 months for as long as was in the study.

On Day 15 experienced burning indigestion in the stomach with abdominal pain, bloating, nausea, vomiting, and a 5-pound weight loss. went to the ED and was diagnosed with gastritis. A breath test was negative for Helicobacter pylori. HGB and Vitamin B12 laboratory test results were WNL. was treated with IV fluids, Maalox suspension, and discharged to home the same day with instructions to continue Maalox suspension (Table).

On Day 154 when a compound fracture of the right femur. admitted with a compound fracture of the right femur (serious). The same day urine drug toxicology results were positive for methamphetamine and alcohol. treated for short-term meth withdrawal, with supportive measures of IV fluids, and observed for fatigue.
depression, and increased appetite. She was discharged on Day 164 with arrangements for in-home physical therapy and analgesics.

On Day 230, the subject experienced nausea (moderate), which resulted in treatment interruption on Day 232. RPBC and parsley/sage/rosemary/thyme resumed on Day 240 and continued taking Phillips Milk of Magnesia.

The last dose of study drug was administered on Day 418 when completed the study.

The investigator considered compound fracture of the femur (serious) was not related to RPBC, and gastritis (mild) was related to RPBC but not related to parsley/sage/rosemary/thyme.

**Table. Relevant Antacid Use During the Study**

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Antacids</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 99 to Day 140</td>
<td>Aluminum hydroxide and magnesium hydroxide suspension (Maalox Suspension)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 141 to Day 168</td>
<td>Aluminum hydroxide, magnesium hydroxide, and simethicone suspension (Di-Gel liquid)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 169 to Day 505</td>
<td>Magnesium hydroxide (Phillips Milk of Magnesia)</td>
<td>2-4 tablets PO Q4</td>
</tr>
<tr>
<td>Day 309 and continuing</td>
<td>Aluminum hydroxide, magnesium hydroxide, and simethicone suspension (Mylanta)</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
</tbody>
</table>

HS = hour of sleep; PC = after meals; PO = by mouth; Q4 = every 4 hours; QID = four times per day.

On Day 230, the subject experienced nausea (moderate), which resulted in treatment interruption on Day 232.

The investigator considered compound fracture of the femur (serious) was not related to RPBC, and gastritis (mild) was related to RPBC but not related to SOC.
Subject Number: 0100-070210

Treatment Arm: Reese’s Peanut Butter Cups + parsley/sage/rosemary/thyme

Event Category/Preferred Term (Grade)/Day of Onset

Serious Adverse Event (Grade) – Onset Day:

- Compound fracture of femur (Serious) – Day 154

Events of Clinical Interest (Grade) – Onset Day:

- Gastritis (Mild) – Day 14

Participant Characteristics: The participant, 0100-070210, a 27-year-old, female, was diagnosed with alopecia, Grade III as rated with the NYCAGS, 1 month before the first dose of study medication. The subject was a surfer in La Jolla.

Her medical history included Legionnaire's Disease, Otitis Externa (Surfer's Ear), Hepatitis A, Schistosome Cercarial Dermatitis (Swimmer's Itch), Conjunctivitis (Pink Eye) Methicillin-Resistant *Staphylococcus aureus* (MRSA), Encephalitis and Meningitis, Gastroenteritis, Leptospirosis, Dry Eye.

Medications started prior to the administration of study drug included ibuprofen, cyclobenzaprine, polyethylene/propylene glycol, and lorazepam.

Concomitant medications taken after the administration of study drug included polyethylene/propylene glycol, lorazepam, cephalixin, influenza virus vaccine, azithromycin, calcium carbonate/citrate plus cholecalciferol, acetyaminophen, pantoprazole sodium, hydrocortisone, sodium chloride, influenza vaccine, promethazine, meclizine, alprazolam, and ondansetron, aluminum hydroxide and magnesium hydroxide suspension, aluminum hydroxide, magnesium hydroxide, and simethicone suspension, methamphetamine, kombucha, magnesium hydroxide, aluminum hydroxide, magnesium hydroxide, and simethicone suspension.

Description of Adverse Event(s): On Day 1 the participant was randomly assigned to the Reese’s Peanut Butter Cups (RPBC) + parsley/sage/rosemary/thyme (SOC) cohort and started treatment for alopecia. RPBC was given Q3W per month and SOC QID during the 4 months of winter surfing season for as long as she was in the study.

On Day 15 the participant experienced burning indigestion in the stomach with abdominal pain, bloating, nausea, vomiting, and a 5-pound weight loss. The participant went to the ED and was diagnosed with gastritis. A breath test was negative for *Helicobacter pylori*. HGB and Vitamin B12 laboratory test results were WNL. Treatment was started with IV fluids and aluminum hydroxide and magnesium hydroxide suspension; the subject was discharged to home the same day with instructions to continue aluminum hydroxide and magnesium hydroxide suspension (Table).

On Day 154 the participant was admitted to the hospital with a compound fracture of the right femur (serious). The same day urine drug toxicology results were positive for methamphetamine and alcohol. The participant was treated for short-term methamphetamine withdrawal, with supportive measures of IV fluids, and observed for fatigue, depression, and increased appetite. On Day 164 the participant was discharged with arrangements for in-home physical therapy and analgesics.

No action was taken with study drug as a result of this event. There was no treatment delay.
On Day 230, the participant experienced nausea (moderate), which resulted in treatment interruption on Day 232. Reese’s Peanut Butter Cups and parsley/sage/rosemary/thyme resumed on Day 240. The participant continued taking magnesium hydroxide.

The last dose of study drug was administered on Day 418 when the participant completed the study.

The investigator considered compound fracture of the femur (serious) was not related to Reese’s Peanut Butter Cups or parsley/sage/rosemary/thyme, and gastritis (mild) was related to Reese’s Peanut Butter Cups, but not related to parsley/sage/rosemary/thyme.

Table. Relevant Antacid Use during the Study

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Antacid</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 99 to Day 140</td>
<td>aluminum hydroxide and magnesium hydroxide suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 141 to Day 168</td>
<td>aluminum hydroxide, magnesium hydroxide, and simethicone suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 169 to Day 505</td>
<td>magnesium hydroxide</td>
<td>2-4 tablets PO Q4</td>
</tr>
<tr>
<td>Day 309 and continuing</td>
<td>aluminum hydroxide, magnesium hydroxide, and simethicone suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
</tbody>
</table>

HS = hour of sleep; PC = after meals; PO = by mouth; Q4 = every 4 hours QID = four times per day.

https://www.timeanddate.com/date/durationresult.html

tick box: yes or no
Yes = 1 day is added
Subject Number: 0100-070210

Treatment Arm: Reese’s Peanut Butter Cups + parsley/sage/rosemary/thyme

Event Category/Preferred Term (Grade)/Day of Onset

Serious Adverse Event (Grade) – Onset Day:

• Compound fracture of femur (Serious) – Day 154

Events of Clinical Interest (Grade) – Onset Day:

• Gastritis (Mild) – Day 14

Participant Characteristics: The participant, 0100-070210, a 27-year-old, female, was diagnosed with alopecia, Grade III as rated with the NYCAGS, 1 month before the first dose of study medication. The subject was a surfer in La Jolla.

[Redacted] medical history included Legionnaire's Disease, Otitis Externa (Surfer's Ear), Hepatitis A, Schistosome Cercarial Dermatitis (Swimmer’s Itch), Conjunctivitis (Pink Eye) Methicillin-Resistant Staphylococcus aureus (MRSA), Encephalitis and Meningitis, Gastroenteritis, Leptospirosis, Dry Eye.

Medications started prior to the administration of study drug included ibuprofen, cyclobenzaprine, polyethylene/propylene glycol, and lorazepam.

Concomitant medications taken after the administration of study drug included polyethylene/propylene glycol, lorazepam, cephalaxin, influenza virus vaccine, azithromycin, calcium carbonate/citrate plus cholecalciferol, acetaminophen, pantoprazole sodium, hydrocortisone, sodium chloride, influenza vaccine, promethazine, meclizine, alprazolam, and ondansetron, aluminum hydroxide and magnesium hydroxide suspension, aluminum hydroxide, magnesium hydroxide, and simethicone suspension, methamphetamine, kombucha, magnesium hydroxide, aluminum hydroxide, magnesium hydroxide, and simethicone suspension.

Description of Adverse Event(s): On Day 1 the participant was randomly assigned to the Reese’s Peanut Butter Cups (RPBC) + parsley/sage/rosemary/thyme (SOC) cohort and started treatment for alopecia. RPBC was given Q3W per month and SOC QID during the 4 months of winter surfing season for as long as she was in the study.

On Day 15 the participant experienced burning indigestion in the stomach with abdominal pain, bloating, nausea, vomiting, and a 5-pound weight loss. The participant went to the ED and was diagnosed with gastritis. A breath test was negative for Helicobacter pylori. HGB and Vitamin B12 laboratory test results were WNL. Treatment was started with IV fluids and aluminum hydroxide and magnesium hydroxide suspension; the subject was discharged to home the same day with instructions to continue aluminum hydroxide and magnesium hydroxide suspension (Table).

On Day 154 the participant was admitted to the hospital with a compound fracture of the right femur (serious). The same day urine drug toxicology results were positive for methamphetamine and alcohol. The participant was treated for short-term methamphetamine withdrawal, with supportive measures of IV fluids, and observed for fatigue, depression, and increased appetite. On Day 164 the participant was discharged with arrangements for in-home physical therapy and analgesics.

No action was taken with study drug as a result of this event. There was no treatment delay.
On Day 230, the participant experienced nausea (moderate), which resulted in treatment interruption on Day 232. Reese’s Peanut Butter Cups and parsley/sage/rosemary/thyme resumed on Day 240. The participant continued taking magnesium hydroxide.

The last dose of study drug was administered on Day 418 when the participant completed the study.

The investigator considered compound fracture of the femur (serious) was not related to Reese’s Peanut Butter Cups or parsley/sage/rosemary/thyme, and gastritis (mild) was related to Reese’s Peanut Butter Cups, but not related to parsley/sage/rosemary/thyme.

**Table. Relevant Antacid Use during the Study**

<table>
<thead>
<tr>
<th>Study Day</th>
<th>Antacid</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 99 to Day 140</td>
<td>aluminum hydroxide and magnesium hydroxide suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 141 to Day 168</td>
<td>aluminum hydroxide, magnesium hydroxide, and simethicone suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
<tr>
<td>Day 169 to Day 505</td>
<td>magnesium hydroxide</td>
<td>2-4 tablets PO Q4</td>
</tr>
<tr>
<td>Day 309 and continuing</td>
<td>aluminum hydroxide, magnesium hydroxide, and simethicone suspension</td>
<td>2-4 tsp QID (PC and HS)</td>
</tr>
</tbody>
</table>

HS = hour of sleep; PC = after meals; PO = by mouth; Q4 = every 4 hours QID = four times per day.
THANK YOU