Website Functionality Panel

Rebecca J. Williams
ClinicalTrials.gov
Alissa Gentile
The Leukemia and Lymphoma Society
Seth A. Morgan
National Multiple Sclerosis Society

Steven Woloshin
The Dartmouth Institute
Stephen J. Rosenfeld
Secretary's Advisory Committee on Human Research Protections (SACHRP)
Website Functionality Session Goals

• Share the responses and top themes from the RFI

• Provide perspectives from panelists on user needs related to website functionality

• Obtain further input from meeting participants on topics related to RFI themes
RFI Topic 2: Website Functionality

NLM sought broad input on the ClinicalTrials.gov website, including its application programming interface (API).

a. Examples of unsupported, **new uses** of the ClinicalTrials.gov website

b. Resources for possible **linking** from ClinicalTrials.gov (e.g., publications, systematic reviews, de-identified individual participant data, general health information)

c. Examples of **current uses** of the ClinicalTrials.gov website

d. Description of whether primary use of ClinicalTrials.gov relies on a **scope** of (1) wide range of studies, or (2) more limited range of studies.
Website Functionality
Facilitate use of information to help public and researchers find studies of interest

ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.

Explore 351,775 research studies in all 50 states and in 209 countries.
ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Visit our disclaimer for details.

Before participating in a study, talk to your healthcare provider and learn about the risks and potential benefits.
API Beta

Key Features

• Supports 3rd party use of site content
• Over 300 search fields available (current API only has 24 key fields)
• Formats:
  • XML, JSON, SVI, tree
• Query and Info URLs
• Documentation available
• Interactive training demos
• https://clinicaltrials.gov/api/gui
Website Functionality: RFI Responses

Number of Comments by Sub-question

1a. New uses: 111
1b. Resources for linking: 73
1c. Current uses: 123
1d. Scope of primary uses: 76
Website Functionality
1a. New Uses

List specific examples of unsupported, new uses of the ClinicalTrials.gov website.
Website Functionality

1c. Current Uses

Provide specific examples of how you currently use ClinicalTrials.gov, including potential improvements.

<table>
<thead>
<tr>
<th>Website Function</th>
<th>Percent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Record</td>
<td>16.9%</td>
<td>51</td>
</tr>
<tr>
<td>Search</td>
<td>11.3%</td>
<td>34</td>
</tr>
<tr>
<td>Search Field</td>
<td>9.3%</td>
<td>28</td>
</tr>
<tr>
<td>Usability</td>
<td>7.6%</td>
<td>23</td>
</tr>
<tr>
<td>General</td>
<td>5.0%</td>
<td>15</td>
</tr>
<tr>
<td>Data Quality</td>
<td>4.7%</td>
<td>14</td>
</tr>
<tr>
<td>Search Results</td>
<td>4.3%</td>
<td>13</td>
</tr>
<tr>
<td>Downloading Content for Analysis</td>
<td>4.3%</td>
<td>13</td>
</tr>
<tr>
<td>Search Filter</td>
<td>4.0%</td>
<td>12</td>
</tr>
<tr>
<td>Others</td>
<td>32.6%</td>
<td>98</td>
</tr>
</tbody>
</table>
Top Response Themes

• Search options and managing search results
• Study record format and content
• Plain language information
Theme: Search Options and Managing Search Results (with selected examples)

Make search more user friendly
- Step-by-step approach to building a search query
- Customize approach for user type (e.g., patients and researchers)
- Simplify

Add more options to search
- Existing structured data elements (e.g., intervention type, study purpose)
- Existing non-structured data elements (e.g., eligibility criteria)
- Other: disease subtype; genetic mutation or biomarker

Improve tools for managing search results
- Sorting and more filtering capabilities
- Formats for downloading search results
- Notifications about updates to saved searches

ClinicalTrials.gov
Most Federal sites have poor search engines. I have been very impressed with the quality of the ClinicalTrials.gov website search engine. It is worth continuing to enhance it … because it enables you to find the study you are interested in reviewing

“The search functions are not user-friendly with respect to finding outcomes for a particular topic. Bringing [search] functionality into the 21st century with search engines and functions like Google, Siri, Alexa is far more likely to serve the general public than the current interface.”
Theme: Study Record Format and Content (with selected examples)

Standardize more content
Examples: interventions, eligibility criteria

More prominently display certain content
Examples: eligibility criteria, funding sources, study status, contact information, updates

Make more content available
Videos to explain specific studies
Study locations displayed on a map
Out-of-pocket costs and payment to participants
Potential risks of study participation

Add features to make using content easier
Sharing study record content with others
Printer-friendly formats
“The biggest issue is the use of different nomenclature and names of indications”

“Using consensus common data elements (CDE) for outcomes would also be helpful, but we recognize that these are largely field specific.”
Theme: Plain Language Information
(with selected examples)

General health information and learning about study participation

Resources for using site features (for patients and researchers)

Study record content, including study descriptions and study results
Plain language information

“The presentation on ClinicalTrials.gov can be made more user-friendly by use of graphics and/or lay language”

“Healthy literacy and plain language need to be applied to all content”
Alissa Gentile, MSN, RN

Director of the CTSC, The Leukemia and Lymphoma Society

The Leukemia and Lymphoma Society Clinical Trial Support Center (CTSC)
Clinical Trial Nurse Navigators increase patients’ opportunities for clinical trial participation by facilitating informed decision-making and minimizing logistical barriers for the patient and family.
Patients/providers access the Clinical Trial Support Center (CTSC)

- Call the Information Resource Center (IRC) 1-800-955-4572
- Patient or caregivers can also fill out the referral form online
  https://www.lls.org/navigation
- American Society of Hematology (ASH) physicians can access the portal at
  https://www.hematology.org/clinicaltrialnavigation/
Process for Supporting Patients
Use of ClinicalTrials.gov Information in the Process

• Search all the fields within CTG
• Brief summary
• Eligibility requirements
• Sites and Site contacts
• NCT number links to CTG
• Study results (links to articles)
Clinical Trial Support Center (CTSC)

• The goal of the CTSC is NOT to enroll every patient into a trial, rather to increase the opportunities for participation by facilitating informed decision-making and minimizing logistical barriers for the patient.

• CTSC nurses work in collaboration with the patient’s healthcare team to decide if a clinical trial is right for them.

• Ultimately, CTSC nurses educate, support, and empower patients to be active participants in, and have control over, their treatment decisions.
The Patient Perspective

Seth A. Morgan, MD
National Multiple Sclerosis Society
“Fear of the future will likely rear its ugly head more often than you’d like…It can be difficult to keep your mind from wandering to a very dark place.” —Debi Wilson

“People are afraid of the dark because they don’t know what’s in it. People are afraid of the unknown.” —Matt Allen G

“More time on the internet caused my fear to spiral out of control.” —Judy Lynn
“How can I save myself from despair? How can I take back control of my body, mind, and spirit?”

—Cathy Chester
Quotes NOT about COVID-19;

Chronic, irreversible, and unpredictable future with Multiple Sclerosis

The Frantic Fear of chronic disease
The Patient Perspective

Denial
Depression
Withdrawal
Grieving
Education about disease
Consideration of research participation
Grasping for anything regardless of scientific validity or risk potential
Access to research options
Gives hope
May present risks of modern day “snake oil salesmen”
Making Sense of Results

Steven Woloshin, MD

Director of the Center for Medicine and the Media, The Dartmouth Institute & Lisa Schwartz Foundation for Truth in Medicine
Disclosures

No industry funding.

Senior Scientific Consultant, NCI, Division of Cancer Control and Population Sciences, and Office of Communications and Public Liaison

Opinions expressed in this presentation are my own and do not reflect the view of the National Institutes of Health, the Department of Health and Human Services, or the United States government.
GOAL
Apple pie

Recipe

Follow recipe

Dessert!

Question
Does this sleeping pill work?

Protocol
Design, subjects, Intervention(s)
Analysis plan

Implement protocol

Results
Research

**GOAL**
Apple pie

**Recipe**

**Follow recipe**

**Dessert!**

**Question**
Does this sleeping pill work?

**Protocol**
Design, subjects, Intervention(s), Analysis plan

**Implement protocol**

**Results**

Clinic trial...
A Phase III Study of Eszopiclone in Patients With Insomnia (Study SEP 190-150)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Sponsor:
Eisai Co., Ltd.

Information provided by (Responsible Party):
Eisai Inc. (Eisai Co., Ltd.)

ClinicalTrials.gov Identifier: NCT00770692

Recruitment Status: Completed
First Posted: October 10, 2006
Results First Posted: November 22, 2012
Last Update Posted: November 22, 2012
Brief Summary:
The purpose of this study is to evaluate the long-term safety of eszopiclone (2, 3 mg) in non-elderly patients with insomnia and eszopiclone (1, 2 mg) in elderly patients with insomnia.

Detailed Description:
This is a multicenter, randomized, double-blinded study to evaluate the long-term safety of SEP-190 (2, 3 mg) in non-elderly patients with insomnia and SEP-190 (1, 2 mg) in elderly patients with insomnia.

Study Design:
- Study Type: Interventional
- Actual Enrollment: 369 participants
- Allocation: Randomized
- Intervention Model: Parallel Assignment
- Masking: Double (Participant, Investigator)
- Primary Purpose: Treatment
- Official Title: A Phase III Study of SEP-190 (Eszopiclone) in Patients With Insomnia
- Study Start Date: October 2008
- Actual Primary Completion Date: May 2010
- Actual Study Completion Date: May 2010

Links to glossary would be nice!
### Participant Flow

**Recruitment Details**

161 non-elderly & 194 elderly participants were enrolled in the screening period 1 week prior to the first dose. Among these, 20 non-elderly & 24 elderly participants discontinued during the screening period. 161 non-elderly and 194 elderly participants enrolled. 1 elderly participant enrolled for treatment did not receive treatment.

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Eszopiclone 1 mg - Elderly</th>
<th>Eszopiclone 2 mg - Elderly</th>
<th>Eszopiclone 2 mg - Non-elderly</th>
<th>Eszopiclone 3 mg - Non-elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm/Group Description</td>
<td>Elderly participants: Eszopiclone 1 mg tablet and 1 tablet of placebo 2 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg tablet additionally until the end of study treatment.</td>
<td>Elderly participants: Eszopiclone 2 mg tablet and 1 tablet placebo 1 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg tablet additionally until the end of study treatment.</td>
<td>Non-elderly participants: Eszopiclone 2 mg tablet and 1 tablet of placebo 3 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg tablet additionally until the end of study treatment.</td>
<td>Non-elderly participants: Eszopiclone 3 mg tablet and 1 tablet of placebo 2 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg tablet additionally until the end of study treatment.</td>
</tr>
</tbody>
</table>

### Period Title: Overall Study

<table>
<thead>
<tr>
<th>Status</th>
<th>1 mg Elderly</th>
<th>2 mg Elderly</th>
<th>2 mg Non-elderly</th>
<th>3 mg Non-elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Started</td>
<td>81</td>
<td>83</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td>Completed</td>
<td>69</td>
<td>74</td>
<td>70</td>
<td>66</td>
</tr>
<tr>
<td>Not Completed</td>
<td>12</td>
<td>9</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Reason Not Completed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Withdrawal by Subject</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Adverse Event</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Investigator Judgment</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

1 participant whose compliance was unknown, was regarded as a "treatment compliance unknown".
### Outcome Measures

1. **Primary Outcome**
   - **Title**: Incidence of Adverse Events
   - **Description**: Incidence of adverse events
   - **Time Frame**: Up to 25 weeks (24 weeks treatment period & 1 week follow-up)

2. **Secondary Outcome**
   - **Title**: Mean Change From Baseline In Sleep Latency
     - **Description**: Based on subjective symptoms, the participants recorded their sleep latency
     - **Time Frame**: Baseline (screening period) and 4 weeks of treatment

3. **Secondary Outcome**
   - **Title**: Mean Change From Baseline In Wake Time After Sleep Onset (WASO)
     - **Description**: Based on subjective symptoms, the participants recorded their WASO definition
     - **Time Frame**: Baseline (screening period) and 4 weeks of treatment

4. **Secondary Outcome**
   - **Title**: Mean Change From Baseline In Total Sleep Time
     - **Description**: Based on subjective symptoms, the participants recorded their total sleep time
     - **Time Frame**: Baseline (screening period) and 4 weeks of treatment

5. **Secondary Outcome**
   - **Title**: Mean Change From Baseline In Total Number ofAwakenings
     - **Description**: Based on subjective symptoms, the participants recorded their number of awakenings
     - **Time Frame**: Baseline (screening period) and 4 weeks of treatment
### Arm/Group Description

- **Elderly participants:** Excupetine 2 mg tablet and 1 tablet of placebo 2 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg tablet additionally until the end of study treatment.
- **Non-elderly participants:** Excupetine 3 mg tablet and 1 tablet of placebo 2 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg placebo tablet additionally to maintain blind until the end of study treatment.

### Overall Number of Baseline Participants

<table>
<thead>
<tr>
<th>Group</th>
<th>80</th>
<th>83</th>
<th>84</th>
<th>77</th>
<th>324</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline Analysis Population Description</strong></td>
<td>[Not Specified]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Age Continuous Mean (Standard Deviation) Unit of measure: Years

<table>
<thead>
<tr>
<th>Group</th>
<th>Number Analyzed</th>
<th>80 participants</th>
<th>83 participants</th>
<th>84 participants</th>
<th>77 participants</th>
<th>324 participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>70.4 (6.5)</td>
<td>70.7 (6.7)</td>
<td>40.1 (10.8)</td>
<td>41.9 (11.3)</td>
<td>55.6 (17.1)</td>
</tr>
</tbody>
</table>

### Sex: Female, Male

<table>
<thead>
<tr>
<th>Group</th>
<th>Number Analyzed</th>
<th>80 participants</th>
<th>83 participants</th>
<th>84 participants</th>
<th>77 participants</th>
<th>324 participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td>35</td>
<td>40</td>
<td>29</td>
<td>41</td>
<td>139</td>
</tr>
</tbody>
</table>

### Outcome Measures

#### 1. Primary Outcome

- **Title**: Incidence of Adverse Events

  Incidence of adverse events was defined as: (number of participants with adverse events/ number of participants analyzed in the safety analysis) × 100.

  An adverse event was defined as any unwanted or untoward disease or its symptom, sign, or abnormality in laboratory parameters in a subject who receives a study drug. An adverse event does not necessarily have a causal relationship with the study drug. The investigators or subinvestigators evaluated adverse events and recorded the results in the case report form.
### 1. Primary Outcome

**Title**<br>Incidence of Adverse Events

**Description**<br>Incidence of adverse events was defined as: (number of participants with adverse events/number of participants analyzed in the safety analysis set)*100.

An adverse event was defined as any unwanted or untoward disease or its symptom, sign, or abnormality in laboratory parameters in a subject who receives a study drug. An adverse event does not necessarily have a causal relationship with the study drug. The investigator or sub-investigator evaluated adverse events and recorded the results in the case report form (CRF). The investigator or sub-investigator recorded all adverse events occurring after the start of study treatment in the CRF, irrespective of the causal relationship with the study drug or the study procedures. All data collected from the follow-up was recorded in CRF.

**Time Frame**<br>Up to 25 weeks (24 weeks treatment period & 1 week follow-up)

### Outcome Measure Data

### Analysis Population Description

Safety analysis set: All 161 non-elderly participants who were enrolled in the treatment period were included. All 154 elderly patients who were enrolled in the treatment period were included. The participant who was excluded from the efficacy analysis set was included in the safety analysis set because the participant had evaluable safety data.

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Eszopiclone 1 mg - Elderly</th>
<th>Eszopiclone 2 mg - Elderly</th>
<th>Eszopiclone 2 mg - Non-elderly</th>
<th>Eszopiclone 3 mg - Non-elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arm/Group Description:</strong></td>
<td>Elderly participants: Eszopiclone 1 mg tablet and 1 tablet of placebo 2 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg placebo tablet additionally until the end of study treatment.</td>
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<td>Non-elderly participants: Eszopiclone 2 mg tablet and 1 tablet of placebo 3 mg daily by mouth at bedtime for 24 weeks. Dose escalation occurred after 4 weeks of treatment. Participants received 1 mg placebo tablet additionally until the end of study treatment.</td>
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</tr>
<tr>
<td><strong>Overall Number of Participants Analyzed</strong></td>
<td>81</td>
<td>83</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td><strong>Measure</strong></td>
<td>Percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type:</strong></td>
<td>Number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Unit of Measure:</strong></td>
<td>Percentage of Participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Percentage of Participants</strong></td>
<td>81.5</td>
<td>78.5</td>
<td>82.1</td>
<td>87.3</td>
</tr>
</tbody>
</table>

### 2. Secondary Outcome

**Title**<br>Mean Change From Baseline In Sleep Latency

**Description**<br>Based on subjective symptoms, the participants recorded their sleep latency (the amount of time measured in minutes it takes to fall asleep) in a sleep diary questionnaire for the week preceding the start of the study treatment (the day on which the patient was enrolled in the treatment period), as well as between the day on which the study treatment started and the Week 4 visit. For pre-treatment (screening period), the representative value was calculated from the data of the 7 days preceding the day on which the participant was enrolled in the treatment period. For the change in sleep latency, the mean change from baseline to the last observation (LO) was calculated using the last observation carried forward method.
### Outcome Measure Data

#### Analysis Population Description

Efficacy analysis set: all of the 161 non-elderly participants who were enrolled in the treatment period. Among the 184 elderly participants who were enrolled in the treatment period, 183 (80 in the 1 mg group and 83 in the 2 mg group) were included in the efficacy set, excluding 1 participant in the 1 mg group who had no evaluable efficacy data.

<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Eosiphozone 1 mg - Elderly</th>
<th>Eosiphozone 2 mg - Elderly</th>
<th>Eosiphozone 2 mg - Non-elderly</th>
<th>Eosiphozone 3 mg - Non-elderly</th>
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</tr>
<tr>
<td>Overall Number of Participants Analyzed</td>
<td>80</td>
<td>83</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td>Mean (Standard Deviation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit of Measure: minutes</td>
<td>minutes</td>
<td>minutes</td>
<td>minutes</td>
<td>minutes</td>
</tr>
<tr>
<td>Baseline</td>
<td>65.5 (40.5)</td>
<td>70.7 (47.1)</td>
<td>71.8 (53.0)</td>
<td>64.0 (42.2)</td>
</tr>
<tr>
<td>Overall Period (Change From Baseline)</td>
<td>-32.1 (35.0)</td>
<td>-37.0 (42.7)</td>
<td>-36.7 (51.8)</td>
<td>-32.8 (55.4)</td>
</tr>
</tbody>
</table>

#### Secondary Outcome

**Title**: Mean Change From Baseline in Wake Time After Sleep Onset (WASO)

**Description**: Based on subjective symptoms, the participants recorded their WASO defined as total awakening time from falling asleep to first awakening in a sleep diary questionnaire for the week preceding the start of the study treatment (the day on which the patient was enrolled in the treatment period), as well as between the day on which the study treatment started and the Week 4 visit. For pre-treatment (screening period), the representative value was calculated from the data of the 7 days preceding enrollment in the treatment period. A median of all the data between the day of enrollment in the treatment period and the day before dose escalation judgment was presented as the data of the overall period. The change was calculated as the WASO of the overall period assessment - WASO at baseline (screening period).

**Time Frame**: Baseline screening period and 4 weeks of treatment

#### Analysis Population Description

Efficacy analysis set: all of the 161 non-elderly participants who were enrolled in the treatment period. Among the 184 elderly participants who were enrolled in the treatment period, 183 (80 in the 1 mg group and 83 in the 2 mg group) were included in the efficacy set, excluding 1 participant in the 1 mg group who had no evaluable efficacy data.
<table>
<thead>
<tr>
<th>Arm/Group Title</th>
<th>Eszopicline 1 mg- Elderly</th>
<th>Eszopicline 2 mg- Elderly</th>
<th>Eszopicline 2 mg- Non-elderly</th>
<th>Eszopicline 3 mg- Non-elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Number of Participants Analyzed</td>
<td>80</td>
<td>83</td>
<td>84</td>
<td>77</td>
</tr>
<tr>
<td>Mean (Standard Deviation)</td>
<td>Unit of Measure</td>
<td>Baseline</td>
<td>Overall Period (Change From Baseline)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>minutes</td>
<td>314.2 (73.2)</td>
<td>63.6 (64.1)</td>
<td>307.9 (60.0)</td>
</tr>
</tbody>
</table>
Outcome: Do you sleep longer if you take pill?

What if you didn’t take the drug at all?
What is this in hours?
Pain in neck to look at other outcomes

**including harms**
Lunesta
(compared to sugar pill) to reduce current symptoms for adults with insomnia

What this drug is for:
To make it easier to fall or to stay asleep

Who might consider taking it:
Adults age 18 and older with insomnia for at least 1 month

Recommended monitoring:
No blood tests, watch out for abnormal behavior

Other things to consider:
Reduce caffeine intake (especially at night), increase exercise, establish a regular bedtime, avoid daytime naps

How long has the drug been in use?
Lunesta was approved by FDA in 2005. As with all new drugs, we simply don't know how its safety record will hold up long-term.

Did Lunesta make a difference?

<table>
<thead>
<tr>
<th>People given a sugar pill</th>
<th>People given LUNESTA (3 mg each night)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNESTA users slept longer (37 minutes longer due to drug)</td>
<td>5 hours 45 minutes</td>
</tr>
</tbody>
</table>

Did Lunesta have side effects?

<table>
<thead>
<tr>
<th>Side effect</th>
<th>None observed</th>
<th>None observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>No difference between LUNESTA and a sugar pill</td>
<td>6%</td>
<td>26%</td>
</tr>
<tr>
<td>More had unpleasant taste in their mouth (additional 20% due to drug)</td>
<td>3%</td>
<td>10%</td>
</tr>
<tr>
<td>More had dizziness (additional 7% due to drug)</td>
<td>3%</td>
<td>9%</td>
</tr>
<tr>
<td>More had dry mouth (additional 9% due to drug)</td>
<td>2%</td>
<td>7%</td>
</tr>
<tr>
<td>More had nausea (additional 1% due to drug)</td>
<td>6%</td>
<td>11%</td>
</tr>
</tbody>
</table>
WARNING! Lots can go wrong

GOAL Apple pie

Recipe

Follow recipe

Dessert!

Just because you see results doesn’t mean you should believe them!

GOAL Sleeping pill

Protocol Design, subjects, Intervention(s) Analysis plan

Implement protocol

Results
Results

What is the question?
Good design?
Outcomes you care about?
Standards and Website Functionality

Stephen J. Rosenfeld, MD, MBA
Chair, Secretary’s Advisory Committee on Human Research Protections (SACHRP)
my (personal) perspective
uninformative trials and the role of the IRB

scientific validity

v.

scientific value
<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Clinical Trials</th>
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<tbody>
<tr>
<td>Recurrent Acute Myeloid Leukemia</td>
<td>NCT0306240, NCT0245862, NCT0373663, NCT03813147</td>
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<tr>
<td>Acute Myeloid Leukemia</td>
<td>NCT0306240, NCT03813147</td>
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<td>Advanced Solid Tumors, Neoplasms, Advanced Solid</td>
<td>NCT02957368</td>
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<td>Previously Untreated Acute Myeloid Leukemia</td>
<td>NCT0013908</td>
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<tr>
<td>Myelodysplastic Syndromes</td>
<td>NCT0281077, NCT03238248, NCT03184006</td>
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<tr>
<td>Leukemia, Myelomonocytic, Chronic</td>
<td>NCT0281077, NCT03266654, NCT03814005</td>
</tr>
<tr>
<td>Leukemia, Myeloid, Acute</td>
<td>NCT0281077, NCT03266654, NCT03814005</td>
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<tr>
<td>Advanced Solid Tumors</td>
<td>NCT0212770</td>
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<tr>
<td>Solid Tumors</td>
<td>NCT01862228</td>
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<tr>
<td>Lymphoma, Diffuse Large-Cell B-cell</td>
<td>NCT01415765</td>
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<tr>
<td>Lymphoma, Diffuse Large-Cell</td>
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<tr>
<td>Large-Cell Lymphoma, Diffuse</td>
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<tr>
<td>Diffuse, Large B-cell Lymphoma</td>
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<td>Metastatic Melanoma</td>
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<td>Myelodysplastic Syndrome</td>
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<td>Lymphoma</td>
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<td>Hodgkin Lymphoma</td>
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<td>Hematologic Malignancies</td>
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<td>Advanced Nonhematologic Malignancies</td>
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</tbody>
</table>

NIH National Library of Medicine
some (exploratory) data
“If I have seen further it is by standing on the shoulders of Giants.”
—Isaac Newton

“‘Normal science’ means research firmly based upon one or more past scientific achievements, achievements that some particular scientific community acknowledges for a time as supplying the foundation for its further practice.”
—Thomas Kuhn
Summary and Next Steps

Rebecca J. Williams, PharmD, MPH
Acting Director of ClinicalTrials.gov
ClinicalTrials.gov Modernization Overview

Current year: Engagement
- Engage with stakeholders to determine and validate approach and specifications
  - Request for Information (RFI) and Public Meeting
- Develop modernization roadmap
- Enhance internal business processes

Future (years 2 – 5): Implementation
- Implement modernization roadmap
  - User testing/evaluation and continue engagement
  - Improvements to support compatibility across clinical trial lifecycle (seamless end-to-end process)
  - Upgrade system infrastructure components
ClinicalTrials.gov Modernization Goals

- Establish a modern infrastructure to support long-term sustainability
- Make information easy to find and use to maximize its value
- Simplify submission process to improve user experience and enhance data quality
- Enhance quality control review process efficiency to accommodate growth
Modernization External Activities FY2020

NLM Board of Regents Public Service Working Group

Transparent, bi-directional forum to communicate and receive input about modernization and support validation of ClinicalTrials.gov modernization roadmap

Dec 13 Kick-off Webinar

Dec 20 Webinar

Feb 3 Meeting

May 1 Meeting

Sept 14 or 15 Meeting


July 30 Request for Information (RFI) Comments Start

Mar 14 Request for Information (RFI) Comments End

Apr 30 Public Meeting

Host meeting with stakeholders to share high-level summary from RFI and obtain further input

NIH Institutes and Centers (IC) Engagement

Met with 20+ NIH ICs (including Directors) to learn IC needs

RFI External Engagement

Organization-hosted web meetings to engage key stakeholders directly

External Engagement Continued

Participate in conferences and other stakeholder meetings; further share and validate roadmap

NIH/NLM Activities

NIH IC Engagement: Continue engaging NIH points of contact monthly
Thank you again for joining us today!

Please visit the ClinicalTrials.gov Modernization webpage for the latest updates on the modernization effort.

- **Public Comments Received in Response to Request for Information (RFI):** [ClinicalTrials.gov Modernization](#) and [ClinicalTrials.gov Summary of Responses to the RFI](#) are currently available.

- The meeting recording and presentation slides will be available within 30 days.

- You can also subscribe to receive Hot Off the PRS! email updates.

- Additional questions/comments? Email register@clinicaltrials.gov.