Pediatric Endocrine Society Annual Meeting; May 15-18, 2025; National Harbor, Maryland, USA

Taking Diazoxide Choline Extended-Release Tablets Long Term Reduced Hyperphagia and Behavioral and Emotional Problems in People With Prader-Willi Syndrome, With and Without a Prior Pause in Treatment (Study C614)

What is Prader-Willi syndrome?

- Prader-Willi syndrome (**PWS**) is a rare disease that is found in about 1 out of every 15,000 babies born in the United States[1]
- PWS is most commonly caused by **genes** on a specific **chromosome** (chromosome 15) that are missing or do not work properly[2]
- PWS affects all races, ethnicities, and sexes equally[4]
- People with PWS have different kinds of signs and symptoms, which change with age[2]
- One of the most challenging parts of having PWS is "**hyperphagia**", which is extreme hunger or an overwhelming urge to eat and having constant thoughts about food even when the body does not need more food[4]
- People with PWS also have other **behavioral and emotional problems** that are not related to food. These can include aggression and depression[5]

Learn more about
genes and chromosomes

What is diazoxide choline?

- Diazoxide choline extended-release tablets (more simply called diazoxide choline) is a medicine approved in the United States for the treatment of hyperphagia in people with PWS who are 4 years of age and older
- Diazoxide choline is a tablet that is taken by mouth once a day

What did this analysis look at?

- This analysis looked at whether taking diazoxide choline for a long time could continue to improve **hyperphagia, as well as behavioral and emotional symptoms** in people with PWS, in people who had a prior interruption in treatment and in people who did not
- During the study, 2 different questionnaires were used:
  - The Hyperphagia Questionnaire for Clinical Trials (HQ-CT) measured participants' hyperphagia-related behaviors and how often they thought about food[6]
  - The Prader-Willi Syndrome Profile (PWSP) measured participants' emotional and behavioral symptoms that were not related to food[7]

✓ HQ-CT Assessment

- The questionnaire included 9 questions about the participants' behavior over the past 2 weeks[6]
- Caregivers answered each question on a scale of 0 to 4, where 0 meant "never" or "none" and 4 meant "very often" or "extremely"[6]
- HQ-CT total scores range from 0 to 36
- Higher scores mean more severe hyperphagia

HQ-CT is licensed to the Foundation for Prader-Willi Research (FPWR). For additional details or questions about the tool, please contact FPWR.

✓ PWSP Questionaire

The PWSP included items grouped into 6 domains:

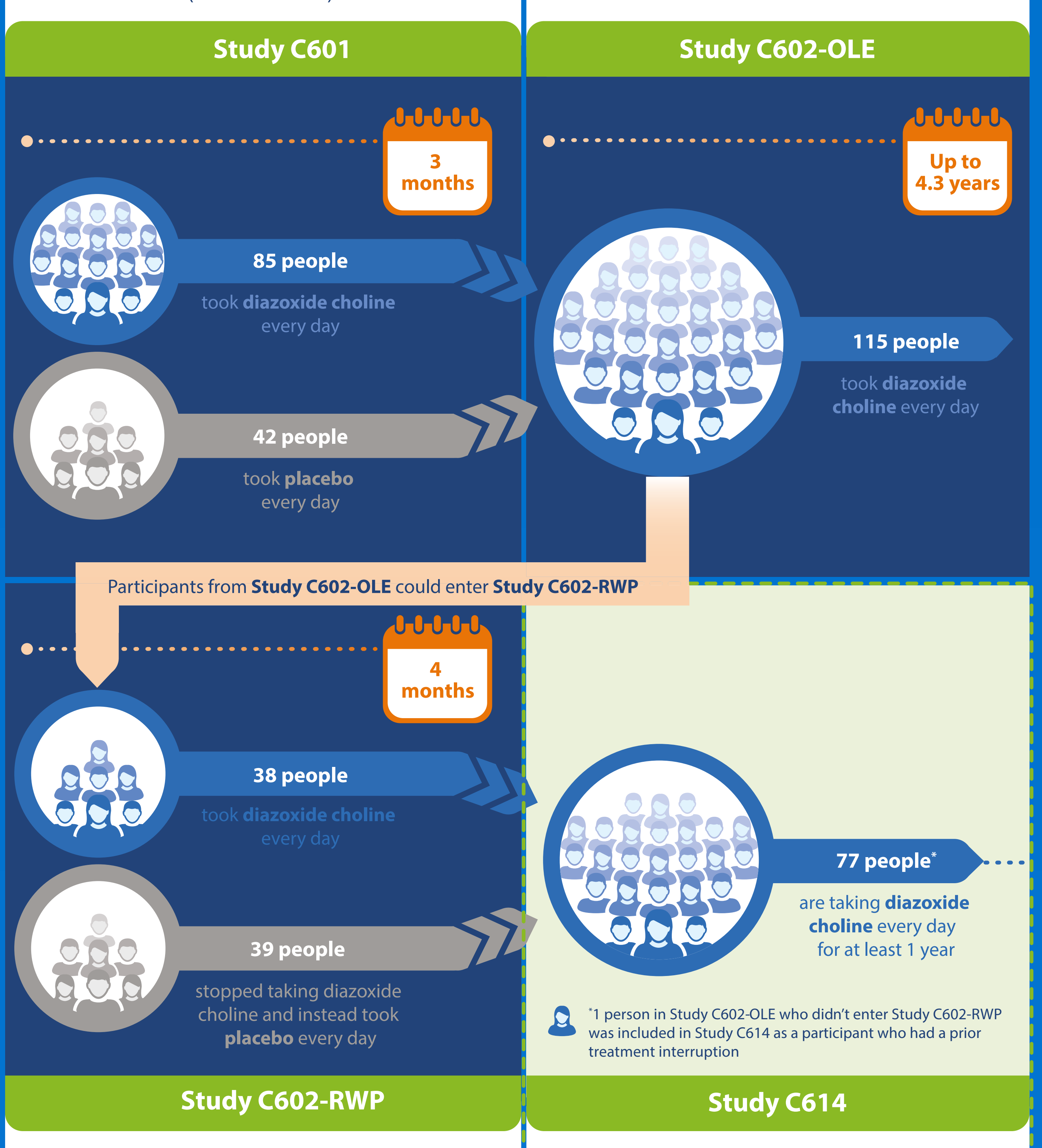
1. **Aggression** (Score of 0-18), or feeling very angry (like hitting or throwing objects)
2. **Anxiety** (Score of 0-22), or feeling extremely worried or nervous about things that might or are happening
3. **Compulsivity** (Score of 0-20), like feeling as if they HAVE to do something, even if they don't want to
4. **Rigidity/Irritability** (Score of 0-20), or feeling stuck, easily annoyed or frustrated
5. **Depression** (Score of 0-10), or feeling extremely sad or hopeless
6. **Disordered thinking** (Score of 0-12), or an inability to 'think straight'

Lower total scores mean fewer or less severe behavioral and emotional symptoms, while higher scores meant more severe behavioral and emotional symptoms

Who participated in these studies?

- In Study C601, people 4 years of age and older who have hyperphagia with PWS took either **diazoxide choline** or a "**placebo**" (a tablet that looked like **diazoxide choline** but contained no medicine)
  - C601 was a randomized, double-blind study, which means that participants took **diazoxide choline** or **placebo** by chance ("randomized"), and neither the participants nor the researchers knew which medicine they took until the study was over ("double-blind")

- At the end of 3 months, people could decide to enter a longer follow-up study called "C602-OLE" where everyone was given **diazoxide choline** for up to 4.3 years
  - "OLE" stands for "open-label extension," which means that both the study participants and the researchers knew that the study participants were taking **diazoxide choline** ("open-label") for a long time



Study C601

3 months

85 people took **diazoxide choline** every day

42 people took **placebo** every day

Study C602-OLE

Up to 4.3 years

115 people took **diazoxide choline** every day

Participants from **Study C602-OLE** could enter **Study C602-RWP**

4 months

38 people took **diazoxide choline** every day

39 people stopped taking diazoxide choline and instead took **placebo** every day

77 people[*] are taking **diazoxide choline** every day for at least 1 year

[*] 1 person in Study C602-OLE who didn't enter Study C602-RWP was included in Study C614 as a participant who had a prior treatment interruption

Study C602-RWP

- Some of the participants in the C602-OLE study agreed to join a second part of Study C602 called "Study C602-RWP"
  - In Study C602-RWP, some participants stopped taking diazoxide choline and were given a **placebo** for 4 months, and others kept taking **diazoxide choline**
  - "RWP" stands for "randomized withdrawal period," which means that study participants were randomly included in either the **placebo** group or the group who continued to take **diazoxide choline** for the 4-month period

Study C614

- After 4 months, participants agreed to join another study called "C614" in which **everyone** was given **diazoxide choline**
  - Study C614 is still active, and participants are continuing to receive **diazoxide choline** long term

Goal of Analysis

This analysis focused on the effects of continuing **diazoxide choline** in participants of Study C614, including those who had stopped taking **diazoxide choline** for 4 months (e.g., participants who had taken **placebo** in Study C602-RWP), and those who continued taking **diazoxide choline** without stopping (e.g., participants who had taken **diazoxide choline** in Study C602-RWP)

Participants included in this analysis

What did this analysis find?

At the start of Study C614

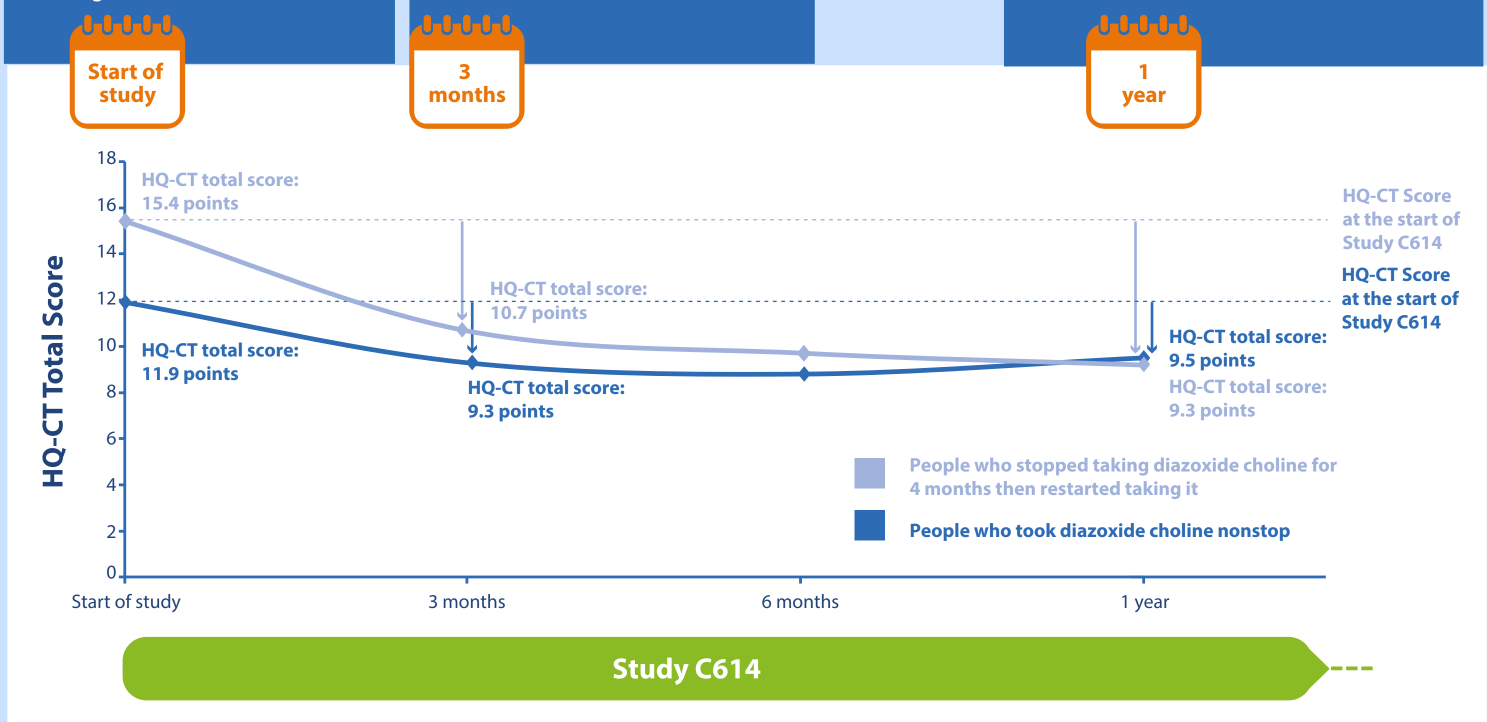
Participants were on average **15.3 years old**	**55.8%** of participants were **female**	The average **HQ-CT total score** was **13.8 points**

Change in Average HQ-CT Total Score Over 1 Year (Study C614)

At the **start of Study C614, hyperphagia was worse** in participants who had previously stopped taking diazoxide choline in Study C602-RWP compared with participants who continued taking diazoxide choline

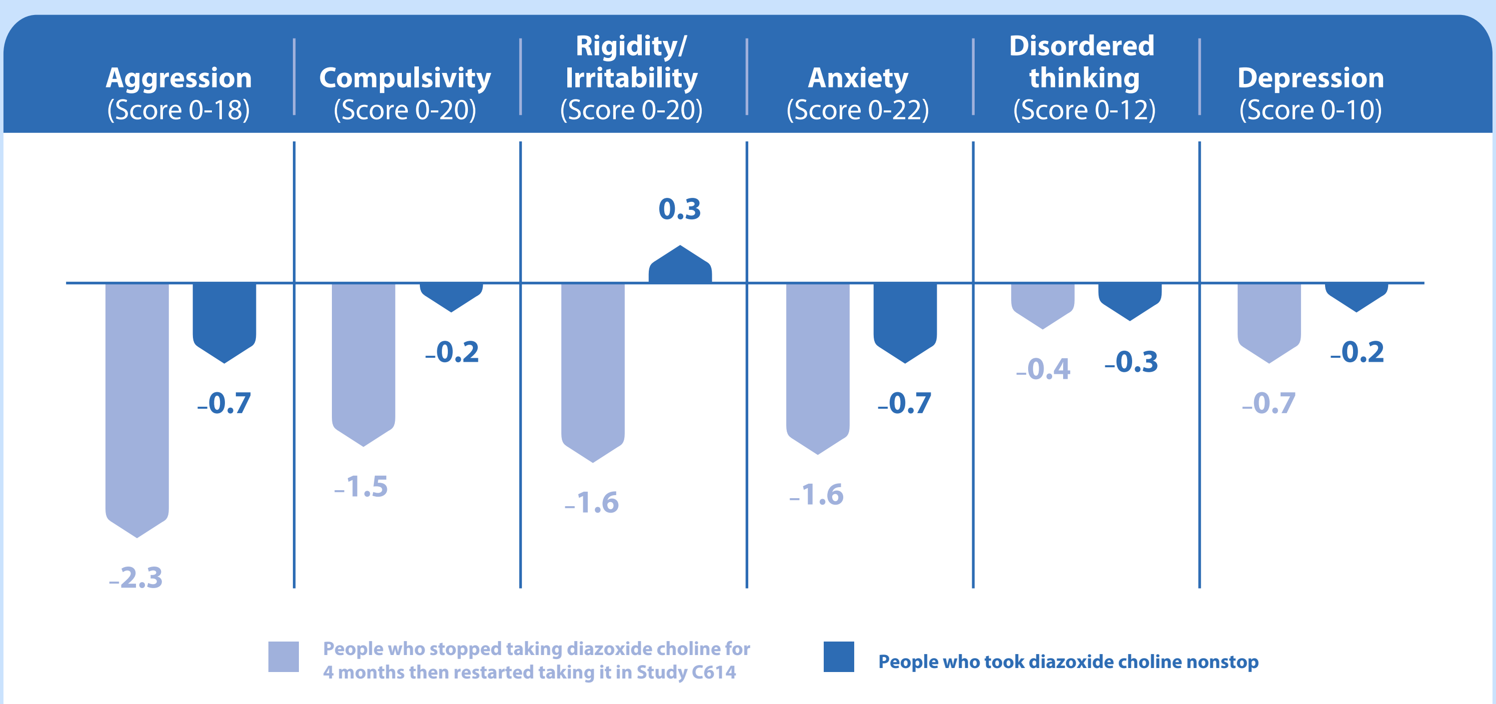
By **3 months, hyperphagia was already improving** in participants who previously stopped taking diazoxide choline in Study C602-RWP, and restarted diazoxide choline in Study C614

After 1 year into Study C614, symptoms continued to improve, with the greatest overall improvement seen in those participants who had previously experienced a treatment interruption before restarting diazoxide choline



Higher HQ-CT scores mean more severe hyperphagia

Change in PWSP Symptom Score After 1 Year in Study C614



One year after participants restarted diazoxide choline, their **behavioral and emotional symptoms were better** than when they first joined Study C614

In the study participants who took diazoxide choline nonstop, symptoms of aggression, compulsion, anxiety, inability to "think straight," and depression got better at 1 year compared with when they first joined Study C614

What are the main conclusions of this analysis?

- In this analysis of Study C614, people with PWS who had a prior treatment interruption showed marked improvements in hyperphagia, as well as behavioral and emotional symptoms, after restarting diazoxide choline
- Continued long-term diazoxide choline treatment for 1 year was also associated with ongoing improvements in these areas, including for those participants who took diazoxide choline without interruption

Who sponsored this study?

- This study was sponsored by Soleno Therapeutics, Inc.
- This summary reports the early results of one study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not just on the results of a single study

Where can I find more information?

Read more
about the C614 study

NCT05701774
(Study C614)

For more information
about general clinical studies

www.ClinicalTrials.gov

The full title of this presentation
Resuming Diazoxide Choline Extended-Release (DCCR) after 16-week Randomized Withdrawal is Associated with Significant Improvements in Hyperphagia and Behavioral Symptoms in PWS (Study C614)

Researchers
Kathryn Obrynba, Jack Yanovski, Eric Felner, Ashley Shoemaker, Nicola Bridges, Julie Perry, Jing Gong, Neil Cowen, Evelien Gevers, Jennifer Miller

References
1. Driscoll DJ et al. *Mol Genet Genomic Med.* 2019;7(3):e514.
2. Cassidy SB et al. *Genet Med.* 2017;14(1):19-26.
3. Centers for Disease Control and Prevention. Genetics basics. May 14, 2024. https://www.cdc.gov/genomics-and-health/about/index.html.
4. Bohonowych J et al. *Genes.* 2019;10(9):713.
5. Schwartz L et al. *J Neurodev Disord.* 2021;13:25.
6. Matesevac L et al. *Sci Rep.* 2023;13(1):20573.
7. Dykens EM et al. *Orphanet J Rare Dis.* 2024;19(1):83.

Acknowledgements
Soleno Therapeutics, Inc., would like to thank all the people who took part in this study.
Editorial/medical writing support under the guidance of the authors was provided by Megan K. Elder, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Soleno Therapeutics, Inc., Redwood City, CA, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (*Ann Intern Med.* 2022;175:1298-1304. doi: 10.7326/M22-1460).

SOLENO THERAPEUTICS

To access a copy of this PLS and the associated poster presentation, please click here

Pediatric Endocrine Society Annual Meeting; May 15-18, 2025; National Harbor, Maryland, USA

Taking Diazoxide Choline Extended-Release Tablets Long Term Reduced Hyperphagia and Behavioral and Emotional Problems in People With Prader-Willi Syndrome, With and Without a Prior Pause in Treatment (Study C614)

Learn more about genes and chromosomes X

Chromosomes are packages of DNA inside human cells[3]
Each human cell (except for sperm and egg cells) has 23 pairs of chromosomes[3]

DNA within chromosomes is made up of sections called genes[3]
Genes carry the instructions needed for the body to function[3]

- PWS affects all races, ethnicities, and sexes equally[4]
- People with PWS have different kinds of signs and symptoms, which change with age[2]
- One of the most challenging parts of having PWS is "**hyperphagia**", which is extreme hunger or an overwhelming urge to eat and having constant thoughts about food even when the body does not need more food[4]
- People with PWS also have other **behavioral and emotional problems** that are not related to food. These can include aggression and depression[5]

What is diazoxide choline?

- Diazoxide choline extended-release tablets (more simply called diazoxide choline) is a medicine approved in the United States for the treatment of hyperphagia in people with PWS who are 4 years of age and older
- Diazoxide choline is a tablet that is taken by mouth once a day

What did this analysis look at?

- This analysis looked at whether taking diazoxide choline for a long time could continue to improve **hyperphagia, as well as behavioral and emotional symptoms** in people with PWS, in people who had a prior interruption in treatment and in people who did not
- During the study, 2 different questionnaires were used:
  - The Hyperphagia Questionnaire for Clinical Trials (HQ-CT) measured participants' hyperphagia-related behaviors and how often they thought about food[6]
  - The Prader-Willi Syndrome Profile (PWSP) measured participants' emotional and behavioral symptoms that were not related to food[7]

✓ HQ-CT Assessment

- The questionnaire included 9 questions about the participants' behavior over the past 2 weeks[6]
- Caregivers answered each question on a scale of 0 to 4, where 0 meant "never" or "none" and 4 meant "very often" or "extremely"[6]
- HQ-CT total scores range from 0 to 36
- Higher scores mean more severe hyperphagia

HQ-CT is licensed to the Foundation for Prader-Willi Research (FPWR). For additional details or questions about the tool, please contact FPWR.

✓ PWSP Questionaire

The PWSP included items grouped into 6 domains:

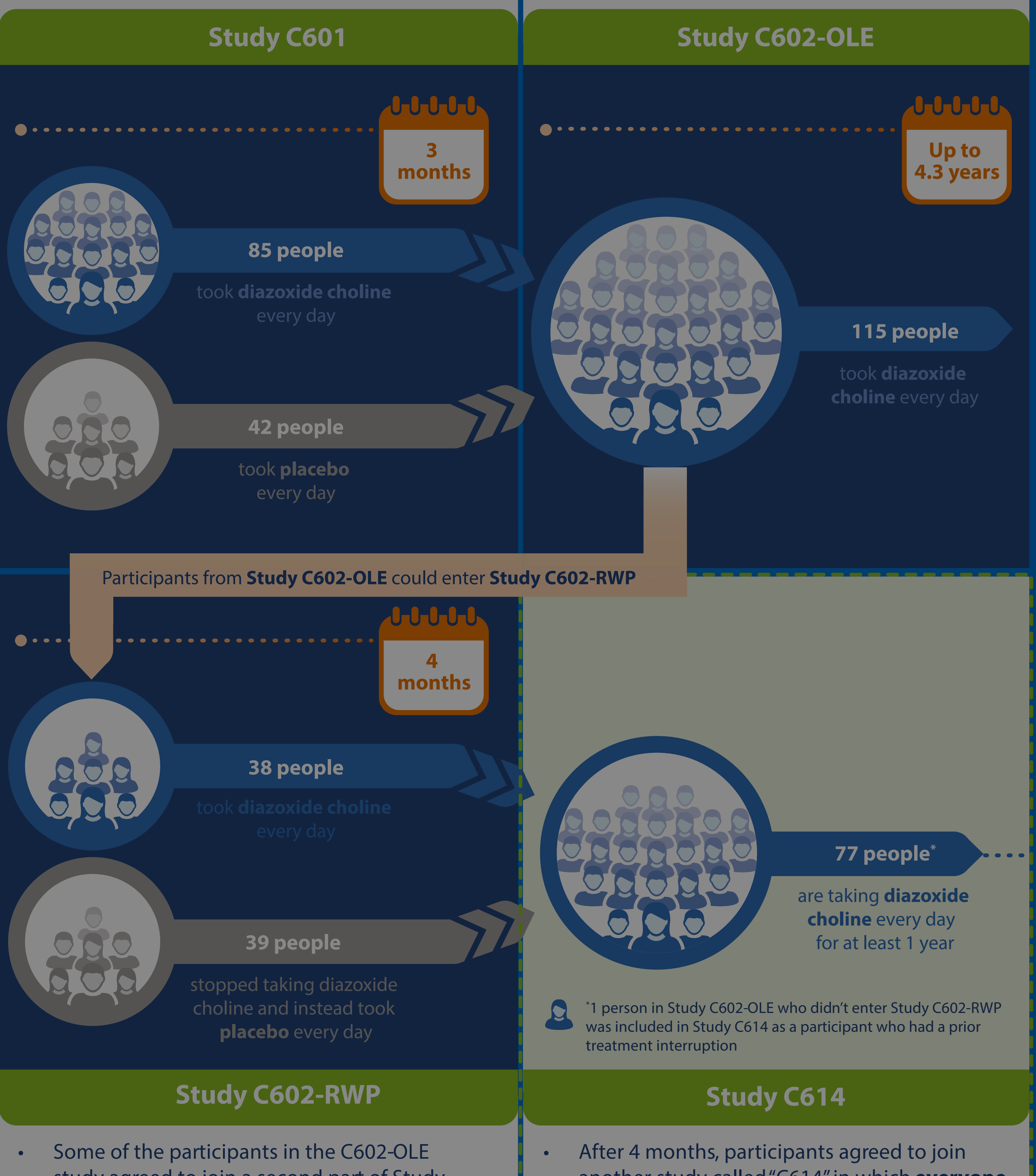
1. **Aggression** (Score of 0-18), or feeling very angry (like hitting or throwing objects)
2. **Anxiety** (Score of 0-22), or feeling extremely worried or nervous about things that might or are happening
3. **Compulsivity** (Score of 0-20), like feeling as if they HAVE to do something, even if they don't want to
4. **Rigidity/Irritability** (Score of 0-20), or feeling stuck, easily annoyed or frustrated
5. **Depression** (Score of 0-10), or feeling extremely sad or hopeless
6. **Disordered thinking** (Score of 0-12), or an inability to 'think straight'

Lower total scores mean fewer or less severe behavioral and emotional symptoms, while higher scores meant more severe behavioral and emotional symptoms

Who participated in these studies?

- In Study C601, people 4 years of age and older who have hyperphagia with PWS took either **diazoxide choline** or a "**placebo**" (a tablet that looked like **diazoxide choline** but contained no medicine)
  - C601 was a randomized, double-blind study, which means that participants took **diazoxide choline** or **placebo** by chance ("randomized"), and neither the participants nor the researchers knew which medicine they took until the study was over ("double-blind")

- At the end of 3 months, people could decide to enter a longer follow-up study called "C602-OLE" where everyone was given **diazoxide choline** for up to 4.3 years
  - "OLE" stands for "open-label extension," which means that both the study participants and the researchers knew that the study participants were taking **diazoxide choline** ("open-label") for a long time



Study C601

3 months

85 people took **diazoxide choline** every day

42 people took **placebo** every day

Study C602-OLE

Up to 4.3 years

115 people took **diazoxide choline** every day

Participants from **Study C602-OLE** could enter **Study C602-RWP**

4 months

38 people took **diazoxide choline** every day

39 people stopped taking diazoxide choline and instead took **placebo** every day

77 people* are taking **diazoxide choline** every day for at least 1 year

*1 person in Study C602-OLE who didn't enter Study C602-RWP was included in Study C614 as a participant who had a prior treatment interruption

Study C602-RWP

- Some of the participants in the C602-OLE study agreed to join a second part of Study C602 called "Study C602-RWP"
  - In Study C602-RWP, some participants stopped taking diazoxide choline and were given a **placebo** for 4 months, and others kept taking **diazoxide choline**
  - "RWP" stands for "randomized withdrawal period," which means that study participants were randomly included in either the **placebo** group or the group who continued to take **diazoxide choline** for the 4-month period

Study C614

- After 4 months, participants agreed to join another study called "C614" in which **everyone** was given **diazoxide choline**
  - Study C614 is still active, and participants are continuing to receive **diazoxide choline** long term

Goal of Analysis

This analysis focused on the effects of continuing **diazoxide choline** in participants of Study C614, including those who had stopped taking **diazoxide choline** for 4 months (e.g., participants who had taken **placebo** in Study C602-RWP), and those who continued taking **diazoxide choline** without stopping (e.g., participants who had taken **diazoxide choline** in Study C602-RWP)

Participants included in this analysis

What did this analysis find?

At the start of Study C614

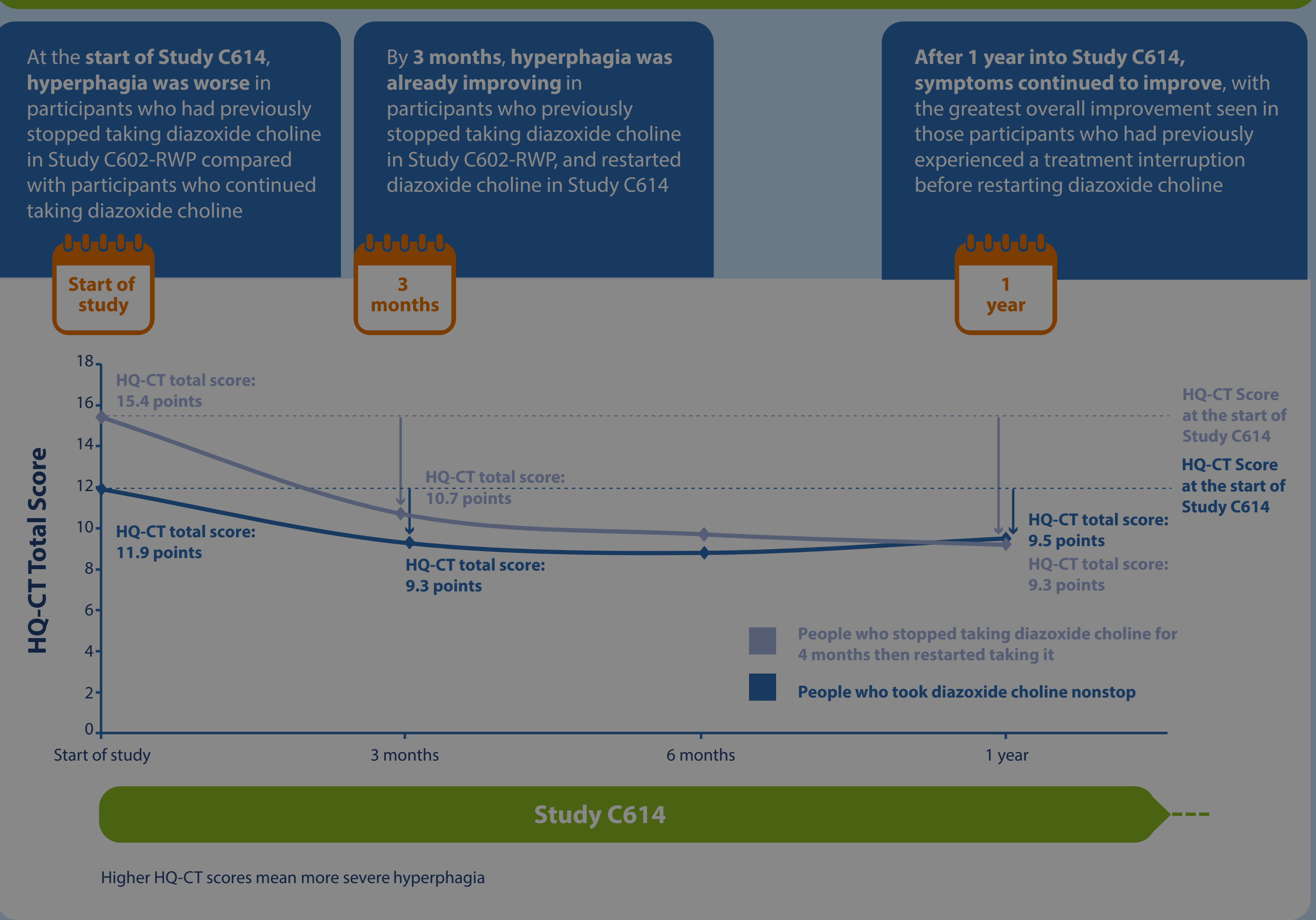
Participants were on average **15.3 years old**	**55.8%** of participants were **female**	The average **HQ-CT total score** was **13.8 points**

Change in Average HQ-CT Total Score Over 1 Year (Study C614)

At the **start of Study C614**, **hyperphagia was worse** in participants who had previously stopped taking diazoxide choline in Study C602-RWP compared with participants who continued taking diazoxide choline

By **3 months, hyperphagia was already improving** in participants who previously stopped taking diazoxide choline in Study C602-RWP, and restarted diazoxide choline in Study C614

After 1 year into Study C614, symptoms continued to improve, with the greatest overall improvement seen in those participants who had previously experienced a treatment interruption before restarting diazoxide choline



Higher HQ-CT scores mean more severe hyperphagia

Change in PWSP Symptom Score After 1 Year in Study C614

One year after participants restarted diazoxide choline, their **behavioral and emotional symptoms were better** than when they first joined Study C614

In the study participants who took diazoxide choline nonstop, symptoms of aggression, compulsion, anxiety, inability to "think straight," and depression got better at 1 year compared with when they first joined Study C614

What are the main conclusions of this analysis?

- In this analysis of Study C614, people with PWS who had a prior treatment interruption showed marked improvements in hyperphagia, as well as behavioral and emotional symptoms, after restarting diazoxide choline
- Continued long-term diazoxide choline treatment for 1 year was also associated with ongoing improvements in these areas, including for those participants who took diazoxide choline without interruption

Who sponsored this study?

- This study was sponsored by Soleno Therapeutics, Inc.
- This summary reports the early results of one study. The results of this study may differ from those of other studies. Health professionals should make treatment decisions based on all available evidence, not just on the results of a single study

Where can I find more information?

Read more about the C614 study

NCT05701774 (Study C614)

For more information about general clinical studies

www.ClinicalTrials.gov

The full title of this presentation
Resuming Diazoxide Choline Extended-Release (DCCR) after 16-week Randomized Withdrawal is Associated with Significant Improvements in Hyperphagia and Behavioral Symptoms in PWS (Study C614)

Researchers
Kathryn Obrynba, Jack Yanovski, Eric Felner, Ashley Shoemaker, Nicola Bridges, Julie Perry, Jing Gong, Neil Cowen, Evelien Gevers, Jennifer Miller

References
1. Driscoll DJ et al. *Mol Genet Genomic Med.* 2019;7(3):e514.
2. Cassidy SB et al. *Genet Med.* 2017;14(1):19-26.
3. Centers for Disease Control and Prevention. Genetics basics. May 14, 2024. https://www.cdc.gov/genomics-and-health/about/index.html.
4. Bohonowych J et al. *Genes.* 2019;10(9):713.
5. Schwartz L et al. *J Neurodev Disord.* 2021;13:25.
6. Matesevac L et al. *Sci Rep.* 2023;13(1):20573.
7. Dykens EM et al. *Orphanet J Rare Dis.* 2024;19(1):83.

Acknowledgements
Soleno Therapeutics, Inc., would like to thank all the people who took part in this study.
Editorial/medical writing support under the guidance of the authors was provided by Megan K. Elder, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Soleno Therapeutics, Inc., Redwood City, CA, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (*Ann Intern Med.* 2022;175:1298-1304. doi: 10.7326/M22-1460).

To access a copy of this PLS and the associated poster presentation, please click here