RESEARCH CONSENT FORM

iKanEat: A randomized-controlled, multicenter trial of megestrol for chronic oral food refusal in children 9 months to 9 years 0 months of age

Sponsor: Eunice Kennedy Shriver National Institute of Child Health & Human Development

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You are being asked to consider a research study for your child. Participating in research is different from getting standard medical care. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you or your child may change your mind at any time. There will be no penalty to you or your child if your child decides not to participate, or if they start the study and decide to stop early. Either way, they can still get medical care and services at the University of Kansas Medical Center (KUMC).

This consent form explains what your child will have to do if they are in the study. It also describes the possible risks and benefits. Please read it carefully and ask as many questions as you or your child need to before deciding about this research.

You or your child can ask questions now or anytime during the study. The researchers will tell you and your child if they receive any new information that might cause you or your child to change your mind about participating.

This research study will take place at the University of Kansas Medical Center (KUMC) with Ann M. Davis, PhD, MPH, ABPP as the researcher. About 6 people will be in the study at KUMC. A total of about 54 people will be in the study at 10 centers across the United States

Why is my child being asked to take part in this study?

Your child is being asked to take part in this study because they are being seen in a clinic for a feeding problem.

Why is this study being done?

Gastrojejunal (G-J) feeding tubes are placed in infants and children who refuse to eat or are unable to eat enough to have normal growth. Although often intended as temporary short-term solutions to medical complications, feeding tubes can become a permanent method for eating.

While tube feeding routinely saves the lives of children who have long-term food refusal, continuation of tube feeding can be hard for patients, caregivers, and families. At the current time, there are few treatments for helping children move from tube to oral

feeding. Some patients may be treated with the help of inpatient programs such as a combination of medical and behavioral techniques to train children to eat orally. These programs typically require hospital stays of 2-4 months.

By doing the current study, we hope to learn if the investigational drug megestrol is helpful in moving children from tube to oral feeding, and to look at whether or not the drug helps with this transition.

What is being tested in this study?

This research study involves a study drug called megestrol. Megestrol is known to increase appetite. Megestrol is a liquid syrup that is given by feeding tube.

Megestrol has not been approved by the United States Food and Drug Administration (FDA) for the treatment of children with feeding problems. Megestrol is an investigational drug that is being studied to find out whether or not the product works for children with feeding problems. Megestrol has been approved by the FDA for the treatment of adults. Though megestrol is not FDA approved to treat children with feeding problems, it is often used for this purpose.

How long will my child be in the study?

If your child is eligible and you decide to allow your child to participate in this study, you/your child's participation will last approximately 24 weeks. This will include 4 in-person visits and at least 12 phone or tele-video calls to see how your child is feeling.

What will my child be asked to do?

You and your child will begin the study by reviewing and signing the consent form. This will happen at a regularly scheduled clinic visit. Once you sign the form, you will be asked to enter your email. You will then receive a link to complete the study surveys in your email. These surveys can be completed during your clinic visit, or at home. You will also receive a phone call from the study team asking you about your child's diet.

Once these surveys are completed, you will attend the 1st study visit (Visit 1). The following is a description of the tests and procedures that will occur in this study.

In this study, your child will be randomly (like flipping a coin) assigned to one of two groups described below:

- Group 1: Megestrol 6 mg/kg split into two equal doses.
- Group 2: Placebo (looks like study drug but has no active ingredients) split into 2 equal doses.

Your child's initial dose will be 6 mg/kg per day split into two doses. The megestrol will be given at the full dose during weeks 10 and 11. At week 12, the dose your child will receive will be reduced by one-third (or 66% of the full dose). At week 13, the dose your child will receive will be reduced by one-third (at 33% of the full dose). Your child will be fully tapered off of the study drug by the end of week 13. You will be given detailed

instructions on how to reduce your child's study drug amount each week during this tapering phase at your week 10 visit. Your child has a 50% chance of being in either group. Neither you nor the investigator will know which group your child has been assigned. The investigator will be able to find out what your child is receiving in the event of a medical emergency. Throughout the rest of this consent form both megestrol and placebo will be referred to as the study drug.

At Visit 2, after participating in the study for ten weeks, children in both Groups 1 and 2 will receive the study drug. The dose your child will receive depends on your child's age and weight. The dose of megestrol is 6 mg/kg divided into two equal doses per day. Your child will continue to take the study drug as directed. Five days after beginning the study drug, tube feedings will be reduced by 10% per day over 10 days until the tube feeding is stopped altogether. For example, if your child gets 10 hours of tube feedings per day, you will reduce the tube feeding by 1 hour per day until the child is fully tapered off the tube. You and your physician will discuss which tapering schedule is right for your family. Treatment with the study drug will be stopped after 4 weeks.

Some study visits will take place in the KU Pediatrics clinic and others may take place at the KU Clinical Research Center, Clinical and Translational Science Unit (CTSU), located at 4350 Shawnee Mission Parkway, Fairway KS, 66205. If you have a visit at the CTSU the investigator will inform you of this before you come for your study visit.

Below is a table that lists all the procedures that will happen at each study visit. After table, you will find more details about the study procedures.

			Week																						
Procedures	**Time**	**Pre**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Informed Consent	30 min	X																									
Quality of Life Measures		X											X				X										X
3-Day Diet Recall	30 min	X											X				X										X
Clinic Visit	60 min		X										X				X										X
Blood Draw													X				X										
Stool Sample			X										X				X										X
Tele-Visit*	15-30 min			X		X		X		X		X		X	X	X	X	X		X		X		X		X	
Continuous Tube Feedings				X	X	X	X	X	X	X	X	X															
Tube Taper													X	X													
Megestrol or Placebo													X	X	X	X											

*May have additional tele-visit calls as needed.

Informed consent: If you decide to allow your child to participate in this study, you will be asked to read and sign this consent form before any tests or procedures can be completed and you will be given a copy.

Clinic Visits:

- You will be asked questions about your child's medical history, feeding problems and any medications they are currently taking.
- Your child's vital signs (blood pressure, heart rate, respiratory rate, and temperature) will be measured.
- Your child's height and weight will be measured.

Quality of Life Measures: You will be asked to complete 3 questionnaires about you and your child's quality of life.

3-Day Diet Recall: You will be contacted on 3 different days the week to find out what your child has eaten orally for the past 24 hours. These phone calls will take 5-10 minutes each.

Blood Draw: Approximately 1 teaspoon of blood will be collected from a vein in your child's arm for laboratory tests.

Stool Sample: You will be asked to collect a stool sample from your child prior to each Clinic Visit. This stool sample will tell us how the bacteria in your child's gut changes as your child starts eating more food by mouth. Healthy gut bacteria helps with digestion and immune function. You will be provided with a toilet hat and sterile cup for stool collection, and be asked to collect a stool sample from your child 1 to 7 days before coming to the Clinic Visit. Once collected, you will store the stool in a sterile collection cup in your home freezer and bring it to the Clinic Visit.

Tele-Visits: Study staff will call you once every 2 weeks over the phone or a tele-video call over a software called Zoom (similar to Skype) to see how your child is doing and assess any problems they may be having. These calls will occur weekly during and after the tube feeding taper during weeks 10-15. You may have additional calls with study staff if you and your child need additional support.

Continuous tube feedings: During weeks 1-9 you will remain on a consistent tube feeding schedule. You and the study physician will decide on the best tube feeding regimen.

Tube feeding taper: You will be asked to decrease your child's tube feedings by 10% each day over 10 days until tube feeding is stopped altogether. You and the study physician will decide on the best tube tapering schedule.

Megestrol or Placebo: Your child will be given the study drug (either megestrol or placebo). You will be given instructions on how to give your child this medication. After 4 weeks of treatment your child will stop taking the study drug. At week 12 and 13 you will

decrease your child's study drug to per the physician's instructions. The dose will slowly be decreased over a 2 week period for your child's safety. By the end of week 13, your child will be completely off the study drug.

What are the possible risks or discomforts?

The study drug may cause side effects or other problems. The researchers will be checking your child's medical information during the study to watch for side effects. However, you or your child should tell the research team about anything that is bothering your child or any changes in your child's health since the last visit. The researchers may be able to take steps to reduce side effects. Your child may experience none, some, or all of the side effects listed below. There may be other side effects or risks that are not yet known.

Side effects of megestrol affect up to 5% of adults and older children. Those side effects include:

- Diarrhea
- Rash
- Gas
- High blood pressure
- Weakness
- Trouble sleeping
- Nausea
- Low levels of oxygen in the blood causing pall skin color and sleepiness
- Adrenal insufficiency (pale skin color, cold to the touch, weight loss, thirsty, dizzy or disoriented)
- Fever
- Stomach pain and discomfort
- Heartburn
- High levels of sugar in the blood, which can cause tiredness, blurry vision, increased thirst and hunger, and passing urine often.
- Headache
- Pain
- Vomiting
- Pneumonia
- Urinary Frequency

Are there other risks or discomforts?

You may become tired due to the number of questionnaires there are in the study. You may stop and rest at any time.

Drawing blood from a vein may cause momentary discomfort at the site of the blood draw, possible bruising, redness, and swelling around the site, bleeding at the site, feeling of lightheadedness when the blood is drawn, and rarely, an infection at the site of the blood draw.

Are there benefits to being in this study?

Your child may or may not benefit from this study. You may benefit if the treatment is effective, which could lead to improvements in your child's quality of life. Researchers hope that the information from this research study may be useful in the treatment of other patients with feeding problems.

Will it cost anything to be in the study?

You will not be charged for your child's participation in the study.

Will my child get paid to participate in the study?

You will receive $100.00 for each completed clinic visit/measures collection (weeks 0, 10, 14, 24). If you complete the entire study, payment may be up to $400.00. If your participation in this study ends early, you will be paid only for the visits you have completed. Below is a table of the study payment timeline:

	Visit 1 (Week 0)	Visit 2 (Week 10)	Visit 3 (Week 14)	Visit 4 (Week 24)	**Total for Study Completion**
Online Surveys	*$25*	*$25*	*$25*	*$25*	
Diet Recalls	*$25*	*$25*	*$25*	*$25*	
Stool Sample	*$25*	*$25*	*$25*	*$25*	
Clinic Visit	*$25*	*$25*	*$25*	*$25*	
Total	**$100**	**$100**	**$100**	**$100**	**$400**

You will be given a ClinCard, which works like a debit card. After a study visit, payment will added onto your card by computer. The money will be available within 1 business day. You can use the ClinCard at an ATM or at a store. No one at KUMC will know where you spent the money. You will be given one card during the study. If your card is lost or stolen, please call (866) 952-3795.

The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to set you up in the ClinCard system. Study payments are taxable income. A Form 1099 will be sent to you and the Internal Revenue Service if your payments are $600 or more in a calendar year.

Your personal information will be kept on a secure computer. It will be removed from the computer after the study is over and the money on the card has been used. Your information will not be shared with other businesses. It will be kept completely confidential.

Will the researchers get paid for doing the study?

The research team and the institution (KUMC Research Institute, Inc.) will receive payments from the sponsor, National Institute of Child Health (NICH), for conducting this study. Payments will be used for research purposes only.

What happens if my child gets hurt or sick during the study?

If your child has a serious side effect or other problem during this study, you should immediately contact Dr. Ann Davis at 913-588-6323 If it is after 5:00 p.m., a holiday or a weekend, you should call 913-588-6300 and ask for the attending pediatrician on call. Please tell the physician that you are in this research study. A member of the research team will decide what type of treatment, if any, is best for you at that time.. You may call your child's primary care physician if it is not a doctor at KUMC. Once your child has received all necessary care please call Dr. Ann M. Davis to inform her of your child's serious side effect or other problem at 913-588-6323.

If your child has a bodily injury as a result of participating in this study, treatment will be provided for your child at the usual charge. Treatment may include first aid, emergency care and follow-up care as needed. Claims will be submitted to your health insurance policy, your government program, or other third party, but you will be billed for the costs that are not covered by the insurance. You and your child do not give up any legal rights by signing this form.

If you think your child have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow payment to persons who are injured in research at KUMC.

Does my child have to be in the study?

Being in research is voluntary. You or your child can choose whether or not to participate. Even if you or your child decides not to join the study, you or your child can still come to KUMC for services and treatment.

What other choices does my child have?

You or your child can choose not to be in the study. Instead of being in this study, your child can receive treatment that is already available, such as visiting the KUMC feeding team or other multidisciplinary feeding teams or pediatric gastroenterologists.

How will my child's privacy be protected?

The researchers will protect your child's information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your child's study records. Your child's health information is protected by a federal privacy law called HIPAA. By signing this consent form, you and your child are giving permission for KUMC to use and share your child's health information. If you decide not to sign the form, your child cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study. Your child may be identified by information such as name, address, phone, date of birth, social security number, or

other identifiers. Your child's health information will be used at KUMC by Dr. Ann M. Davis, members of the research team, The University of Kansas Hospital Medical Record Department, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

By signing this form, you are giving Dr. Davis and the research team permission to share information about your child with persons or groups outside KUMC. Your child's information will be shared with representatives of National Institutes of Health (the sponsor of the study), the monitoring company that inspects study data, other business partners of the sponsor who help with the study, the study's Data and Safety Monitoring Board, the U.S. Food and Drug Administration (FDA) and U.S. agencies that oversee human research (if a study audit is performed). These groups or agencies may make copies of study records for audit purposes. The purpose for using and sharing your child's information is to make sure the study is done properly and to evaluate the safety and effectiveness of the study drug.

The HIPAA privacy law may not apply to everyone who receives your child's health information. Your child's information might not be protected by HIPAA if persons outside KUMC disclose it. In some cases, there may be other laws that protect your child's information from improper use.

Your child's blood sample will be sent to a 3rd party for processing (such as Quest Labs). Your child's sample will be identified by name and date of birth.

Your child's stool sample will be split in half. One half of the sample will be sent to a 3rd party called Novogene for processing. The other half will be stored in the research lab until the Novogene processing is complete. Once the processing is complete, both samples will be destroyed. Your child's sample will be identified by subject ID.
Some of your information will be shared with representatives of Zoom, which is the tele-visit software developed outside of KUMC. Zoom may record the mobile meetings and store them on their secure server. These groups or agencies may store this information for auditing purposes

Your permission to use and share your child's health information will not expire unless you cancel it. Any research information that is placed in your child's medical record will be kept indefinitely.

While your child is participating in this study, you may see and copy any study information that is placed in your child's KUMC medical record. However, some study information is kept only by the researcher. The records kept only by the researcher may not be available to you or your child until the end of the study.

The researchers may publish the results of the study. If they do, they will only discuss group results. Your child's name will not be used in any publication or presentation about the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Certificate of Confidentiality
This research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). This protects the researchers from being forced to give out personal information about you in response to a court order. This does not stop you from voluntarily releasing information about yourself or your participation in this research.

One exception to the Certificate is if you agree that we can give out research information with your name on it. This includes any purposes described in this consent form.

Other exceptions are information we must report if we learn about child abuse or neglect or if we think you might harm yourself or others.

Can my child stop being in the study?

Your child may stop being in the study at any time. You or your child's decision to stop will not prevent your child from getting treatment or services at KUMC. If your child would be harmed by stopping the study drug suddenly, the researchers may ask your child to gradually reduce the dose. Your child might be asked to come back for a final study visit.

You or your child have the right to cancel your child's permission for researchers to use your child's health information. If you want to cancel your child's permission, please write to Dr. Ann M. Davis. The mailing address is Dr. Ann M. Davis, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel permission to use your child's health information, your child will be withdrawn from the study. The researchers will stop collecting any additional information about your child unless they need information about a side effect of the study drug. They may use and share information that was gathered before they received your cancellation.

Could my child's participation be stopped early?

This study might be stopped, without your or your child's consent, by the investigator or the sponsor of the study. Your child's participation also might be stopped by the investigator or by the sponsor if it is in your child's best interest or if you or your child do not follow the study requirements.

Neither the sponsor, nor the investigator, nor the University of Kansas Medical Center will be obligated to provide your child with any study drug or treatment if the study is stopped early. Your child's physician will decide about future treatment, if it is needed.

Who can I or my child talk to about the study?

Before you sign this form, Dr. Davis or other members of the study team should answer all your or your child's questions. You or your child can talk to the researchers if you have any more questions, suggestions, concerns or complaints after signing this form. If you or your child have any questions about your child's rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160.

CONSENT

Dr. Davis or the research team has given you and your child information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that your child may experience during this study.

By signing this form, you say that your child is freely and voluntarily consenting to participate in this research study. You have read the information and had your questions answered.

You will be given a signed copy of the consent form to keep for your records.

Date ___/___/___

Child's Name: _____

Child's Age: _____

Parent's Name: _____
(please print)

Parent's Signature: _____

Name of Person Obtaining Consent: _____
(please print)

Signature of Person Obtaining Consent: _____