Sponsor Biocodex
Clinical Protocol No: STICLO

A Double-Blind, Multi-Center, Randomized Study Evaluating the Efficacy and Safety of Stiripentol in Patients with Sever Myoclonic Epilepsy in Infancy (SMEI)

INTRODUCTION

Your child is being invited to participate in a research study to examine the effectiveness and safety of an experimental drug called Diacomit when taken with valproate and clobazam (which are authorised drugs for epilepsy). This consent form explains why we are performing this research study and what his/her role would be. This form also describes the possible risks involved in participating in this study. After carefully reading and reviewing this information with your childs' study doctor, you should know enough about this study to be able to make an informed decision on whether or not you would like your child to participate.

If you decide to allow your child to participate in this study, please sign and date the last page of this form in the presence of the person who explained the study to you. You will be given a copy of this information and the signed form to keep for your records.

DESCRIPTION OF RESEARCH

What is Diacomit?

Diacomit is an experimental oral (taken by mouth) drug. Diacomit is an inhibitor of cytochrome P450 and member of a class of drugs referred to as α-ethylene alcohols; these drugs have shown to have activity in the central nervous system.

This study will involve the following drugs: Diacomit, valproate (an inhibitor of the neurotransmitter GABA), and clobazam (an anticonvulsant).

Your child has a chance of receiving either active Diacomit or placebo. A placebo ("dummy drug") looks like the active drug, but contains inactive substances which are not expected to have an effect on your disease. The active and dummy capsules are identical in appearance; no identifying information is on the capsules. Additional information about study drugs is provided in the next pages of the consent form.

Why is your child being asked to participate?

Your child has been diagnosed as severe myoclonic epilepsy in infants (SMEI). Unfortunately, current treatments are unable to completely control the disease.

What is the purpose of this study?

The purpose of this study is to determine whether patients receiving Diacomit with valproate and clobazam treatment experience a decrease in the number of seizures compared to those patients who receive placebo with valproate and clobazam treatment. The study will also examine the safety of the combination treatment of Diacomit treatment.

It is planned that a total of 100 patients will participate in France. Approximately 15 centres in will participate in the study. The study is being sponsored by Biocodex, a pharmaceutical company based in France.

DESCRIPTION OF STUDY

What are the treatment groups?

This study is randomised, which means your child will be randomly assigned (similar to a flip of a coin) to one of the two treatment groups. One group will receive Diacomit in combination with valproate and clobazam. This will be referred to as the Active Group. The second group will

receive placebo (dummy capsules) in combination with valproate and clobazam; this will be referred to as the Placebo Group. If randomised to the Active Group, your child will receive Diacomit; if your child is in the Placebo Group, he/she will receive dummy Diacomit.

Neither you, the site staff, nor your child's study doctor will know which group he/she is in, **but your doctor can find out if necessary.**

What may your child be asked to do while on this study?

After you sign this informed consent and before your child is enrolled into the study, certain tests and procedures will be performed to ensure that he/she meet the study entry criteria.

Before treatment starts, he/she will have a complete physical examination and undergo blood sampling. The doctor will explain these procedures, including any possible risks.

If he/she meets certain requirements, the doctor will enrol your child into the study. He/she will have another physical examination and a sample of blood will be taken (approximately 10 mL or 2 teaspoons) for a safety test.

During treatment, he/she will also have a periodic complete physical exam. The schedule of the various tests will be explained in more detail.

Once he/she has been discontinued from treatment, he/she will be asked to return to the study doctor. He/she will have a complete physical exam, weight will be measured and safety tests, including blood test, will be performed.

What are the treatment schedules and how might they be altered?

If your child is randomly chosen to receive treatment in the Active Group, he/she will take Diacomit capsules by mouth twice a day for 2 months, according to instructions provided by the doctor. Depending on his/her tolerance to the treatment, the amount of Diacomit he/she is receiving may be increased or decreased.

If your child is randomly chosen to receive treatment in the Placebo Group, he/she will take dummy capsules by mouth twice a day for 2 months, according to instructions provided to the by your doctor.

Your child will also take tablets of valproate twice (one in the morning and one in the evening) a day and clobazam once a day while on study.

Both active and dummy drug are packaged in blister cards or sachets. Please do not remove the drugs from their original containers prior to the scheduled dose. Unused drug must be returned to the study doctor during your next follow-up visit.

During the study, your child may not take any other investigational drugs or any additional treatments.

Diacomit, placebo, valproate and clobazam will be provided free of charge. Your child's participation in this study will typically last as long as 2 months or more, provided that he/she does not experience a worsening of their disease or are unable to tolerate the study drugs. If he/she is unable to tolerate Diacomit, he/she will be permitted to continue on valproate and clobazam alone.

If your child has stopped taking all of the study medications because he/she has experienced a worsening of his/her disease, he/she will still be followed to assess his/her disease.

Any additional tests done for purposes of providing information to the study protocol during this time period will be conducted with no cost to you.

RISKS, SIDE EFFECTS AND DISCOMFORTS TO PARTICIPANTS

What are the potential side effects of the medications your child will be taking?

Your child may experience one or more of the following from Diacomit or placebo:

- Nausea, vomiting, diarrhoea, constipation, indigestion, abdominal pain
- Headache
- Loss of appetite
- Insomnia
- Drowsiness
- Ataxia (inability to coordinate muscle movements)
- Hypotonia (low muscle strength)
- Dystonia (muscle disorders)

If you have any questions, the study doctor will be able to explain more about possible side effects from the drugs in this study. There may be other side effects that we are unaware of and we will monitor your child carefully to identify any that arise, and deal with them accordingly.

Are there any additional potential risks?

This clinical research study may involve additional unforeseeable risks to your child. Your child's doctor will inform you if new information that may influence your child's' participation in this study becomes available. At that time, you will be asked to give your consent again for continued participation.

POTENTIAL BENEFITS

What are the potential benefits of participating in this study?

It is possible, but not guaranteed, that your child may experience a longer period of time in which his/her disease stays stable. Conversely, this treatment may not benefit your child at all. Future patients may benefit from what is learned from this research study.

FINANCIAL RISKS

Will you be responsible for any costs?

You will not have to pay for hospital visits, tests, study-related medications, hospitalisations, emergency hospital visits or any special care that are only done for the research purpose of this study or are directly related or are a direct consequence of this study.

You, or your medical insurer, will be responsible for those costs that are not an immediate part of this study. Hospital visits, tests, medications, hospitalisations or care not related to this study will not be paid by Biocodex.

TREATMENT AND COMPENSATION FOR INJURY

What happens if your child is injured as a result of participating in this study?

We do not expect your child to suffer any harm or injury because of his/her participation in this study. If, however, your child's health does suffer as a result of his/her being in the study then he/she will be compensated, in accordance with the guidelines set forth by *your national Association of Pharmaceutical Industries*. In such a situation, he/she will not have to prove that the harm or injury, which affects him/her, is anyone's fault. If he/she is injured as a result of being in this study, treatment will be made available to him/her.

If your child is injured as a result of the study treatment, Biocodex will provide reimbursement for the reasonable costs of medical treatment for his/her injury. There will be no monetary compensation.

If you are not happy with any proposed compensation, you may pursue your claim through legal action.

ALTERNATIVES

Are there any alternative treatments available if you decide not to allow your child to participate?

Unfortunately, current treatments are unable to completely control the disease.

If you choose not to allow your child to participate in this research study, you have the following options:

- You may choose for your child not to receive treatment at all, in which case, your doctor will determine the best supportive care for him/her.

Will there be any compensation for participating?

The study drugs will be provided free of charge and you will not have to pay for any study visits or tests required specifically by the clinical research study. You will not be reimbursed for participating in this study.

The hospital is being reimbursed by Biocodex for all study-related tests and procedures which are done in addition to those considered the normal treatment for patients with your child's disease.

Who should I contact?

You are encouraged to ask questions at any time during the clinical research study. If you have any further questions regarding this treatment or you experience a research-related injury, you should contact Dr. …… at ……...

Your child's participation is voluntary. He/she may withdraw at any time without any penalty or loss of benefits. His/her participation may be ended at any time with or without your consent if it is considered to be in his/her best interests. In addition, the sponsor may stop the study at any time without your consent.

CONFIDENTIALITY

As a patient in this study, his/her individual medical information will be used only for purposes of this study. The handling, storage and destruction of data will comply with the 1998 Data Protection Act (DPA). **The EU DPA has strict guidelines for data derived from individuals in the European Union. The study sponsor has committed to complying with these guidelines.**

No individual identities will be used in any reports or publications resulting from this study. Information from this study will be sent to the study sponsor. Information from this study will be submitted to governmental agencies in other countries where the study drug treatment may be considered for approval. Authorised persons within this study site, governmental agencies in other countries, the sponsor, Biocodex, or its representatives, and the IRB (Institutional Review Board) /Ethics Committee who approved this study will be allowed to see your child's records to check on the study. Information that identifies your child will be kept confidential based on applicable laws and regulations.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

This study is designed to provide useful information that will help determine if further research with a larger group of patients is warranted. It is customary that the results of this study – whether positive or negative – will be published in a medical journal. Frequently, researchers present their findings at medical meetings. In some cases, if the results lead to a different way of prescription of the drugs, and the manufacturer may use the data generated from this study to support their submissions to regulatory authorities. As stated

previously, no individual identities will be used in any reports or publications resulting from this study.

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INFORMED CONSENT STATEMENT AND AUTHORIZATION:

A Double-Blind, Multi-Centre, Randomized Study Evaluating the Efficacy and Safety of Stiripentol in Patients with Sever Myoclonic Epilepsy in Infancy (SMEI)

I______(name of subject's parent or legal guardian)**, HAVE READ AND I UNDERSTAND ALL THE INFORMATION IN THIS INFORMATION AND CONSENT FORM. I HAVE BEEN GIVEN THE CHANCE TO DISCUSS IT AND ASK QUESTIONS. THE INFORMATION IN THIS FORM HAS ALSO BEEN EXPLAINED TO MY CHILD. ALL MY QUESTIONS AND MY CHILD'S QUESTIONS HAVE BEEN ANSWERED TO MY SATISFACTION. I VOLUNTARILY CONSENT TO ALLOW MY CHILD TO TAKE PART IN THIS STUDY. I UNDERSTAND I WILL RECEIVE A COPY OF THIS INFORMATION AND CONSENT FORM.**

BY SIGNING THIS INFORMATION AND CONSENT FORM, I AM REQUESTING THAT I BE GIVEN THE STUDY DRUG TO ADMINISTER TO MY CHILD THAT I UNDERSTAND IS NOT IN CHILD-RESISTANT PACKAGING.

BY SIGNING THIS INFORMATION AND CONSENT FORM, I HAVE NOT GIVEN UP ANY OF THE LEGAL RIGHTS, WHICH MY CHILD OTHERWISE WOULD HAVE AS A SUBJECT IN A RESEARCH STUDY.

I AUTHORIZE THE COLLECTION, USE AND DISCLOSURE OF MY CHILD'S MEDICAL INFORMATION IN ACCORDANCE WITH THIS FORM.

_____ _____

Signature of Parent/Legal Guardian (Circle One) **Date of Signature**

_____ _____

Printed name of Parent/Legal Guardian **Printed Name of Child**

_____ _____

Signature of Person Administering this Consent **Date of Signature**

_____

Printed Name of Person Administering this Consent