

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: Safety and Efficacy of Varicella Zoster Immune Globulin (Human)
(VariZIG™) in Patients At-Risk of Varicella Infection

PROTOCOL NO.: VZ-009

SPONSOR: Cangene Corporation
Winnipeg, Manitoba
Canada

INVESTIGATOR: _____ (Name)
_____ (Address)

United States

SITE(S): _____ (Name)
_____ (Address)

United States

**STUDY-RELATED
PHONE NUMBER(S):** _____ (Investigator)
_____ (Phone)

Maurice Genereux, M.D.
Office 204 275-4368
Cell 204 295-2893

This consent form may contain words that you do not understand. Please read this consent form carefully and do not hesitate to ask the study doctor any questions about this consent form and/or the information provided below. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

In this consent form, “you” always refers to the subject. If you are a legally authorized representative, please remember that “you” refers to the study subject.

APPROVED
AS MODIFIED
Jun 02, 2006

Introduction and Purpose of the Study

You are being asked to participate in a research study of an investigational drug called VariZIG™. Investigational means that VariZIG™ has not been approved by the U.S. Food and Drug Administration (FDA). VariZIG™ is a varicella zoster immune globulin that is manufactured by Cangene Corporation.

Varicella zoster immune globulin™ (VZIG™) is approved for the treatment of people at-risk of developing serious complications after being exposed to someone with chicken pox, but before the development of chicken pox.

Although VariZIG™ is not approved by the FDA, it has already been licensed in Canada. VariZIG™ is currently being studied as a potential alternate to VZIG™ because the company that manufactured VZIG™ in the past is no longer manufacturing it, and treatment with an alternate VZIG is not available.

This research study is being done to make VariZIG™ available to at-risk people who require varicella zoster immune globulin.

The goal of this study is to evaluate the safety and effectiveness of VariZIG™ in subjects at risk of developing serious complications of chicken pox. Alternative treatment may include anti-viral drugs. However, varicella zoster immune globulin is the first choice of treatment after exposure to chicken pox and before development of the disease.

VZIG™ was approved for people at risk of developing serious complications after being exposed to someone with chicken pox. VZIG™ had been shown to either reduce the chance that the person at risk will develop chicken pox, or decrease the seriousness of chicken pox in those at-risk people who develop chicken pox.

Study Description

The study will enroll subjects whose doctor determines they are at-risk of developing severe complications from chicken pox. These subjects include immunocompromised (those with an immune system that does not work properly) adults or children, healthy non-immune adults, babies less than 1 year old, premature babies, pregnant women, and babies whose mothers had chicken pox within 5 days before giving birth or within 2 days after giving birth. You are being asked to participate because you are in one of these at risk categories.

All subjects in this study will receive VariZIG™.

Study Requirements

The study doctor will discuss the requirements to be in the study, and you will be asked to sign this consent form if you agree to participate.

In order to participate in this study, you **MUST NOT:**

- Be sensitive to (like an allergy) blood or blood products.
- Have ever had a severe reaction to other intravenous or intramuscular human immune globulin products.
- Have immunoglobulin A (IgA) deficiency.
- Have evidence of chicken pox already.
- Have Zoster infection (shingles).

Study Length

This study involves 1 injection of VariZIG™, completed in 1 clinic visit. There are also 3 return visits where you will be examined for chicken pox occurrence, have blood tests done, and be checked for a reaction to VariZIG™. Your study participation will be up to 42 days. If you need an additional dose of VariZIG™, you will be asked to repeat the 3 return visits, up to 42 days from when you received the additional dose.

Screening Visit

Your study doctor will determine whether you require VariZIG™. You must meet the study requirements to receive the VariZIG™. If you do, then your doctor will contact Cangene Corporation to order the VariZIG™. On approval of the order, VariZIG™ will be shipped to your study doctor so that you can receive VariZIG™ as soon as possible after your exposure.

Baseline

- **The study doctor will ask about your medical history**, including the use of medications and details of your exposure to chicken pox. Information about recent blood tests will also be collected.

VariZIG™ will be administered by intramuscular (into the muscle) injection.

You will be asked to stay in the clinic for 20 minutes for observation after receiving the injection.

Return Visits

You will be asked to return to your doctor 3 times after VariZIG™ is administered. These return visits will take place as follows:

- Between Day 1 and Day 4 of receiving VariZIG™.
- Between Day 7 and Day 20 (as close as possible to the day the chicken pox rash develops, if it occurs).
- Between Day 28 and Day 42.

At each return visit, information from any blood tests performed by your study doctor will be collected, if it is available. Also, the chicken pox rash will be examined, if it has developed. You will be asked about how you have been feeling since receiving VariZIG™, and about any

medications you may have taken.

End of Study or Early Termination Procedures

If you stop your participation before the end of the study, you will be asked to return for examination of the chicken pox rash (if it has developed), and to see how you have been feeling since receiving VariZIG™. You will also be asked about any medications you may have taken since receiving VariZIG™.

VariZIG™ Administration

The amount of VariZIG™ that you will receive depends on your weight. VariZIG™ will be given by injection into a muscle in your shoulder, thigh, or buttock.

Potential Risks/Side Effects

The most frequent treatment related adverse (bad or harmful) events previously seen when VariZIG™ was given include pain at the injection site, headache and rash. Other less frequent adverse reactions were myalgia (muscle aches), rigors (chills), fatigue, nausea and flushing. The most common expected adverse drug reactions that have happened with similar products are chills, fever, headaches, vomiting, allergic reactions, nausea, arthralgia (joint pain) and moderate low back pain.

There is a chance of a serious allergic reaction, which may include face and throat swelling, trouble breathing, seizures and death/(anaphylactoid reaction) in subjects with hypersensitivity (allergy) to blood products.

The administration of similar products occasionally has been associated with the development of allergic reactions.

Common side effects include pain, soreness, redness, swelling, and stiffness in the muscle where it is injected which can last up to 2 days.

VariZIG™ is prepared from human blood. All products made from human blood have some risk of transmitting human disease. The donors of the plasma (blood) used to make VariZIG™ are screened. The process used to make VariZIG™ has also been studied and is designed to kill viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus.

Since VariZIG™ interferes with live vaccines; vaccines such as measles, mumps and rubella (MMR) should not be given until 3 months after VariZIG™.

The risks of having blood drawn include pain, discomfort, and bleeding and/or bruising at the injection site.

There may be risks or side effects, which are unknown at this time.

If you suspect that you have become pregnant, you must notify the study doctor immediately.

New Findings

You will be told about any new information that might change your decision to be in this study.

Are there benefits to taking part in this study?

It is possible that receiving VariZIG™ may prevent you from getting chicken pox. If you do develop chicken pox, your symptoms may be less severe; however this cannot be guaranteed. Information learned in this study may help others in the future.

Cost of Treatment

The cost of VariZIG™ will be billed to you, your physician or a third party provider. Your health insurance company may or may not pay for these charges.

Alternative Treatments

Alternate treatments for at risk people exposed to chicken pox are antiviral drugs or intravenous immune globulin (IVIG) drugs. Antiviral drugs work best if given to an at risk person who has already developed chicken pox, while VariZIG™ is intended to treat these people before any symptoms of chicken pox develop. It is also possible that your doctor may use IVIG to treat you. However, the effectiveness of using IVIG to treat at risk people exposed to chicken pox is not known.

Compensation for Injury

If you are injured or become ill as a result of participation in this study, contact the study doctor immediately. Emergency medical treatment will be provided by the study doctor. Your insurance will be billed for such treatment. The sponsor will pay any charges that your insurance does not cover. No other compensation is routinely available from the study doctor or sponsor.

By signing this consent form, you will not give up any legal rights.

Source of Funding

Funding for this research study will be provided by Cangene Corporation.

Voluntary Participation/Withdrawal

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your study doctor, or the study sponsor (Cangene Corporation), may decide to withdraw you

from the study at any time without your consent if it is in your best interest, if you are unable to meet the requirements of the study, or if the study is cancelled.

Whom can I call if I have questions?

If you have any questions about your treatment or if at any time you feel you have experienced a research-related injury or reaction to the study medication, call: Dr. Robert Gale at 310-442-9010, Dr. Genereux at 204-275-4368 or 204-295-2883 (24-hours), or the study coordinator John A. Hooper, Ph.D. at 816-792-0423 (24-hours) or 816-547-4844 (24-hours).

If you have questions about your rights as a research subject, you may contact:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue, SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: ClientServices@wirb.com.

WIRB is a group of people who perform independent review of research.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will receive a signed and dated copy of this consent form and the Experimental Subject's Bill of Rights for your records.

CONSENT

I have read this consent form (or it has been read to me). The study has been explained to me and I have had all of my questions answered to my satisfaction. I voluntarily consent to participate (allow my child to participate) in this study.

By signing this consent form, I have not given up any of my/my child's legal rights.

Consent and Assent Instructions:

*Consent: Subjects 18 years and older must sign on the subject line below
For subjects under 18, consent is provided by the Legally Authorized Representative*

*Assent: Is not required for subjects 6 years and younger
Is required for subjects ages 7 through 12 years using the separate Assent Form
Is required for subjects ages 13 through 17 years using the Assent Section below*

| | | |
|---|----------------------|--------------------|
| Printed Name of Subject (18 years and older) | Signature of Subject | Date (yyyy/mmm/dd) |
|---|----------------------|--------------------|

| | | |
|--|---|--------------------|
| Printed Name of Legally Authorized Representative (where applicable) | Signature of Legally Authorized Representative (where applicable) | Date (yyyy/mmm/dd) |
|--|---|--------------------|

Authority of Subject's Legally Authorized Representative or Relationship to Subject

| | | |
|---|---|--------------------|
| Printed Name of Person Conducting Informed Consent Discussion | Signature of Person Conducting Informed Consent Discussion | Date (yyyy/mmm/dd) |
|---|---|--------------------|

| | | |
|-------------------------|----------------------|--------------------|
| Printed Name of Witness | Signature of Witness | Date (yyyy/mmm/dd) |
|-------------------------|----------------------|--------------------|

ASSENT SIGNATURES, For Subjects Ages 13 through 17 years:

Assent:

This research study has been explained to me and I agree to be in this study.

Subject's Signature for Assent

Date

Age (years)

I confirm that I have explained the study to the extent compatible with the subject's understanding, and that the subject has agreed to be in the study.

Signature of Person Conducting Assent Discussion

Date

----- **Use the following only if applicable** -----

If this consent form is read to the subject because the subject (or legally authorized representative) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject (or the subject's legally authorized representative). The subject (or the subject's legally authorized representative) freely consented to be in the research study.

Printed Name of Impartial
Witness

Signature of Impartial Witness

Date (yyyy/mmm/dd)

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.

Confidentiality and Authorization to Use and Disclose Protected Health Information

During your participation in this research study, the study doctor and study staff will collect or record personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study forms. The study doctor will keep this personal health information in your study-related medical records (that we will refer to as “your records”). In addition, the study doctor may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition, such as medical records from your primary care physician.

Your records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called “Protected Health Information” (which we will refer to as “PHI”).

Examples of PHI that may be used or disclosed include: past and present health information; demographic information such as name, address, date of birth; results of physical exams, and laboratory/diagnostic tests; any information that can be traced back to you such as Social Security Number, medical record numbers, telephone number, etc.; responses to study drug such as side effects; pregnancy test results and information regarding pregnancy outcomes.

Under federal law (the “Privacy Rule”), your PHI that is created or obtained during this research study cannot be “used” to conduct the research or “disclosed” (given to anyone) for research purposes without your permission. This permission is called an “Authorization.” Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this consent form. By signing, you are agreeing to allow the study doctor and study staff to use your PHI to conduct this study; to make decisions about your medical care, to monitor your health status in order to assess the safety of administration of VariZIG™ to people in high risk groups.

Your PHI may also be used to review records on the information collected in this study; to review study procedures; possibly to develop new tests, procedures and commercial products; to prepare reports or publications; or for other uses permitted by law.

By signing this authorization, you also are agreeing to allow the study doctor to

disclose PHI as described below:

Your PHI may be disclosed to the sponsor of this study and any agents, representatives or consultants working on behalf of the sponsor to conduct this study (referred to as “the sponsor”). The sponsor will analyze and evaluate the PHI and may disclose it to FFF Enterprises, Inc., an agent for the sponsor, the United States Food and Drug Administration (FDA) or similar regulatory agencies in the United States and/or foreign countries, and the Western Institutional Review Board[®] (WIRB[®]). WIRB is a group of people who perform independent review of research.

The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor; however, the sponsor may look at your complete study records, which would identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.

Others who may see your PHI include: FFF Enterprises, Inc., insurance companies; study doctor’s staff; United States Department of Health and Human Services; United States Centers for Disease Control and Prevention (CDC); Government agencies that require reporting of reportable diseases; Government agencies in other countries; persons or companies that monitor the quality of research practice.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes. Due to the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at meetings or in publications, however, your identity will not be disclosed. Your permission for review of confidential information is granted by signing this consent form. You acknowledge that your medical information may be held and processed on a computer.

Your identity will remain private and except for the disclosures described above, will not be shared with others unless such disclosure is required by law. If your PHI is given to the parties listed above and/or to others who are not required to follow the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see and make copies of your PHI. You are agreeing, however, by signing this consent form, not to see or copy your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records.

This permission will be good until December 31, 2050. You have a right to revoke it at any time. If you revoke the authorization, your PHI will no longer be used for this study, except to extent the parties to the research have already taken action based upon your authorization or need the information to complete analysis and reports for this research.

To revoke your Authorization, you must send a written notice to the study doctor's office, stating that you are revoking your Authorization to use or Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue your participation in this study. The research team can continue to share any of the PHI that they already have. Your PHI may still be shared if you have a bad reaction from the study drug or experience any research-related injuries.

Once your PHI has been shared by the researcher with someone outside of this study, it may no longer be protected. There is a chance that your PHI will be shared with others in ways that are not listed here and released without your permission.

Authorization:

I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

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| _____ Printed Name of Subject (18 years and older) | _____ Signature of Subject | _____ Date (yyyy/mmm/dd) |
|--|-------------------------------|-----------------------------|

| | | |
|---|--|-----------------------------|
| _____ Printed Name of Legally Authorized Representative (where applicable) | _____ Signature of Legally Authorized Representative (where applicable) | _____ Date (yyyy/mmm/dd) |
|---|--|-----------------------------|

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or other procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of a signed and dated written consent form when one is required.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Signature of Subject

Date

Signature of Witness

Date