Pharmacokinetics of doxorubicin in conventional transarterial chemoembolization (cTACE) of primary and secondary liver cancer

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COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
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YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

Study Title: Pharmacokinetics of doxorubicin in cTACE of primary and secondary liver cancer.

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Invitation to Participate and Description of Project

You are invited to take part in a research study designed to look at the pharmacokinetics of doxorubicin and doxorubicinol in cTACE of primary liver cancer (cancer that originated in the liver cells) and cancer in the liver that originated elsewhere. TransArterial Chemo Embolization therapy (cTACE) involves administration of chemotherapy directly to the liver tumor via a catheter. With this technique, the chemotherapy targets the tumor while sparing the patient many side effects of traditional chemotherapy that is given to the whole body.

This research is being done to study the pharmacokinetics (what the body does to a drug) of doxorubicin (a chemotherapy drug used in this cTACE procedure) and doxorubicinol (the result after the body processes doxorubicin).

Most of the studies of pharmacokinetics (PK) of doxorubicin used during cTACE were done a few decades ago, when the procedure was new. The cTACE procedure has now matured and is often done in a more focused fashion (lobar or superselectively) than it was in the past. This study will help us to learn if the newer and more focused methods of performing cTACE result in less doxorubicin being present outside of the liver, following cTACE.

You have been asked to take part because you will be undergoing transarterial chemoembolization (TACE) therapy as a standard of care procedure (consent for TACE will be obtained on a separate hospital consent).

About 40 patients will be consented for this study, in order that 30 patients may be enrolled (be treated on the study).

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Guerbet pharmaceutical company is providing funding for this research study.

Description of Procedures

The initial evaluation and screening procedures are standard clinical care and will include the following: physical examination, medical history, blood tests, an imaging study of your abdomen to look at your liver if you have not recently had one.

If you agree to be in this study, we will ask you to do the following things:

You will be having a conventional transarterial chemoembolization (TACE). Part of your routine clinical care will include having a sheath (tube) placed into your femoral artery so that the doctor can have access to perform the cTACE in your liver.

For a part of this research study, we will insert a second sheath. The second sheath will be inserted into your femoral vein, in order to withdraw some blood samples during and immediately after your procedure.

In order to measure the pharmacokinetics of doxorubicin, we will collect about 2 teaspoons of blood from you at these time-points: baseline, 5 minutes, 10, 20, 40, 60, 2 hours, 4 hours, 24 hours, and 3-4 weeks.

Ten (6ml) tubes of blood will be taken from the sheath in your femoral vein, for a total of about 2 1/2 fluid ounces. A follow-up 6 mL blood sample three or four weeks after your procedure will be done by standard insertion of a needle into a vein. An additional 3 mL of blood may be drawn at a time point to prevent contamination or dilution of the research sample. The total volume of blood drawn for this study will be 90 mL (60 mL of blood will be drawn for research, and up to an additional 30 mL of blood may be drawn and discarded as waste) over the course of this study.

You will be in this study for 1 month.

When your specimens and information are stored, we are careful to try to protect your identity from discovery by others. Your samples and information will receive a unique code. Other researchers will only receive coded samples and information, and will not be able to link the code to you. Strict security safeguards are in place to reduce the chance of misuse or unplanned release of information.

Research results will not be returned to you or your doctor. If research results are published, your name and other personal information will not be given.

Risks and Inconveniences

The risks from this research are those involved with the drawing of blood and the placement of the IV catheter (second sheath). They include pain, bruising, swelling and bleeding when the catheter is placed. There is also a risk of infection at the IV site, and very rarely, nerve damage.

Taking blood from a vein with a needle can cause discomfort, bleed or bruising where the needle enters the body. There is also a small risk of infection.

Benefits

There is no direct benefit to you for participation in the study. However, your participation may help the investigators better understand the amount of drug, released from the cTACE materials, that is present outside of the liver. This may help other people with liver cancer in the future.

Economic Considerations

You will not be paid for participation in the study. You will still be responsible for any co-pays and deductibles required by your insurance company for standard treatment. The blood collections to measure the pharmacokinetics of doxorubicin will be done at no cost to you.

Confidentiality and Privacy

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Your blood samples will be coded with a special numbers. Your research chart will be kept in the locked cabinet and /or the locked office. The data that links your identity will be kept on the encrypted and password-protected computer. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and medical record number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI and selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for at least three years after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

The information about your health that will be collected in this study includes:

- Research study records
- Medical, laboratory, imaging records, and other test results of only those services provided in connection with this Study.

Information about you and your health which might identify you may be used by or given to:

- *The U.S. Department of Health and Human Services (DHHS) agencies*
- Representatives from Yale University, the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- Those providers who are participants in the Electronic Medical Record (EMR) system.
- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator Todd Schlachter, MD.
- Funding company (Guerbet)
- Health care providers who provide services to you in connection with this study.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale-New Haven Hospital is required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However to better protect your health information; agreements are in place with these individuals and/or companies that require that they keep your information confidential.

The funding sponsor will see the research information (data) we collect about you. This is Investigator initiated study. For this study the sponsor includes Yale University .Yale researchers will also send the company your health information during the study or at the end of the study. When Yale researchers send information about you to the funding company, they will not send information that directly identifies you such as your name or your address. The sponsor and funding company may also use the information about you for other purposes related to this research or to similar research studies.

This study is financially sponsored by the company Guerbet. Yale researchers will send the company research data during the study or at the end of the study. This data will be de-identified and any information that directly identifies you (such as your name and address) will be removed before being sent. The sponsor and funding company may use this data for other purposes related to research or for similar research studies. Blood specimens will not be sent to Guerbet.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies.

This authorization to use and disclose your health information collected during your participation in this study will never expire.

In Case of Injury

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available.

You do not give up any of your legal rights by signing this form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures (blood draws) as a study participant if you do not allow use of your information as part of this study.

Withdrawing From the Study

If you do become a subject, you are free to stop and withdraw from this study at any time during its course.
To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments.

The researchers may withdraw you from participating in the research if necessary. You may be removed from the study for any of the following reasons:

- At your request (withdrawal of consent)
- You fall out of eligibility criteria
- CTACE procedure cannot be performed as planned
- Usage of illicit drugs or substances that could contribute to toxicity
- You are lost to follow-up contact

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to Todd Schlachter at Yale University, 333 Cedar St, PO Box 208042, New Haven, CT 06520-8042.

If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use [and give out] information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Subject:_____

Signature:_____

Date:_____

_____ _____
Signature of Principal Investigator Date

Or

_____ _____
Signature of Person Obtaining Consent Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/432-5919

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator Todd Schlachter, MD: Phone (203) 785-5885
If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.