etop
Information | Research

EMPHASIS-lung
ETOP 3-12

1) This template Patient Information Sheet and Informed Consent has been written according to International Conference on Harmonization (ICH) guidelines which state the Informed Consent Form (ICF) should adhere to Good Clinical Practices (GCP) and to the ethical principles that have origin in the Declaration of Helsinki.

2) This template can be edited to incorporate information specific to your institution. Please forward the edited version to the ETOP Coordinating Office for approval prior to submission to Ethics Committee(EC)/IRB. The final version should receive the Local EC/IRB approval in advance of use.

3) Following the ICH-GCP guidelines, the ICF should contain information about the following items:

a) The trial involves research

b) Purpose of the trial

c) Trial treatment(s) and the probability of random assignment

d) The subject's responsibilities

e) The aspects of the trial that are experimental

f) Risks

g) Benefits

h) Alternative treatments available

i) Compensation/expenses

j) Subject's participation is voluntary/right to withdraw

k) Confidentiality

l) Information about course of the trial

m) Circumstance under which trial may be terminated

n) Contact persons for further information or in case of injury

o) The approximate number of subjects involved in the trial

p) Duration of subject's participation in the trial

4) This template has been designed to cover the above items. If the Local EC/IRB requires modifications, none of the above items should be completely excluded, nor should the meaning of the highlighted areas be modified. Such modifications must be submitted to ETOP for approval.

5) In order to assist in the preparation of your customized version, an electronic file in MS Word will be distributed via e-mail to all Principal Investigators and ETOP members may download it from the ETOP web site (www.etop-eu.org).

PATIENT INFORMATION SHEET AND INFORMED CONSENT APPENDIX I

ETOP PATIENT INFORMATION SHEET FOR CLINICAL RESEARCH

Dear Patient

You are being asked to participate in a clinical research study. The doctors at different centers of the European Thoracic Oncology Platform (ETOP) and in other cooperative groups or centers throughout the world study the nature of lung cancer and attempt to develop improved methods of diagnosis and treatment. This is called clinical research. In order to decide whether or not you should agree to be part of this clinical research study you should understand enough about its risks and benefits to make an informed judgment. Your participation in this research study is entirely voluntary and you will be given sufficient time to decide whether you wish to participate. This process is known as Informed Consent.

This Patient Information Sheet gives detailed information about the research study, which your doctor will discuss with you. Once you understand the study, if you wish to participate, you will be asked to sign the Patient Informed Consent Form. You will have a copy of this document and of the signed Patient Informed Consent Form to keep as a record.

The clinical research study being proposed to you is:

EMPHASIS-lung
ETOP 3-12
A randomized phase III trial of erlotinib versus docetaxel in patients with advanced squamous cell non-small cell lung cancer who failed first line platinum based doublet chemotherapy stratified by VeriStrat Good vs VeriStrat Poor

Erlotinib **M**aldi TOF **Pha**se III **Si**gnature in **S**quamous cell non-small cell lung cancer

PURPOSE OF THE RESEARCH STUDY

You have been diagnosed with a type of lung cancer that is called “non small cell lung cancer (NSCLC)”. Your lung cancer has recently recurred despite previous treatment with chemotherapy. Your doctor has decided that further treatment of your cancer is necessary.

In previous clinical studies of NSCLC, treatment with Taxotere® (Docetaxel) showed a survival advantage in patient with advanced, relapsed NSCLC. Relapsed means that despite treatment, the cancer is growing. Similar results have been reported the treatment with Tarceva® (Erlotinib).

The aim of the current study is to compare the efficacy (how well the treatment works) and tolerability (how severe the side effects are) of these two treatments in patients with advanced NSCLC. Also, the aim is to explore how well the VeriStrat®

test is able to predict the response of NSCLC to one of the two drugs, Docetaxel and Erlotinib.

VeriStrat is a test that will look for certain proteins in your blood that are related to your cancer, prior to receiving treatment with drugs such as Erlotinib. The results of the test have been shown to correlate with how well a tumour responds to treatments such as Erlotinib. VeriStrat is currently marketed in the USA as a test for patients with advanced NSCLC whose tumour has grown after previous treatment.

Docetaxel and Tarceva are both approved by the Health Authorities in Europe and Switzerland for the treatment of NSCLC.

EMPHASIS is an international clinical research study. A total of 500 patients from centers throughout Europe and Switzerland are expected to be enrolled in this study over a period of 18 months. In *country* it is planned that *xx* patients will take part. The study will take approximately 42 months to be completed.

This clinical trial is conducted according to all applicable national laws and international guidelines. The trial has been approved by the independent Ethics Committee concerned *insert name of the Ethics Committee*.

VOLUNTARY PARTICIPATION/RIGHT TO REFUSE OR WITHDRAW

Your participation in this clinical research study is entirely voluntary. If you decide not to participate in the study, this will not affect your medical care in any way. If you begin the study, you will have the right to withdraw at any time without giving any reason. This will not affect your future medical care. You will be asked to have a final examination before you withdraw and you will be advised for other available care which suits your needs and medical condition. If you should withdraw, data already collected until then will be used for analysis.

If you participate in the study, you should follow the instructions of your treating physician, follow the schedule of treatment visits, inform your physician of any new signs and symptoms you have, and about any non-study medication or supplement you take.

DESCRIPTION OF THE CLINICAL RESEARCH STUDY

Veristrat testing: If you decide to participate, a 3.5 mL blood sample will be collected for VeriStrat testing before randomization and will be sent to a central laboratory, called Biodesix, in Aurora, Colorado, USA. Neither you nor your doctor will be informed about the result of the test.There is a small possibility that your sample cannot be analyzed due to technical reasons. In this case you will be asked to give one additional blood sample. If this can also not be analyzed you will not be able to participate in this study.

You will have a full medical history taken, physical examination, radiological and lab workout performed at the time you enter the study. If you are a female of child-bearing potential, a pregnancy test will be done on your blood serum within 7 days prior to receiving study treatment.

If you decide to participate in the study and meet the criteria to take part in the study described above, you will receive one of the following treatments:

A: Tarceva®: 150 mg orally, daily. You will take Tarceva tablets every day. Tablets should be taken at a fixed time each day and at least 1 hour before or 2 hours after you eat.

B: Docetaxel: 75mg/m^2 intravenous (IV) infusion received on one day every 3 weeks. Each period of 3 weeks is called a 3-week cycle. To reduce the risk of fluid retention and allergic reaction to this treatments, all patients will receive corticosteroids for 3 days starting one day before every Docetaxel administration.

It is not clear at this time which treatment schedule would be better for you. For this reason, the treatment offered to you will be chosen by a method called randomization. Randomization is a method similar to the “flip of a coin” to assign at random (by chance) a treatment for you. Neither you nor your doctor can choose to which treatment arm you will be allocated: You will have an equal chance of being placed in one of the two groups.

During the study treatment, you must visit your treating physician every 3 weeks for a physical examination. If you have been randomized to receive Tarceva, please bring with you all empty, full and partly used boxes of Tarceva® tablets. Routine blood analyses including liver and kidney function will be carried out every 3 weeks as part of standard medical routine. If you develop side effects, more frequent examinations may be necessary.

Inpatient admission into a hospital is not foreseen, but can potentially become necessary.

Your treating physician will document your general condition and all hospital stays during the clinical research study. He/she will similarly ask you about all side effects you have experienced and about all medications, supplements or treatments you have taken/received since your last visit.

To determine the status of your NSCLC and effects from the treatment, radiological examinations (computer tomography [CT] of the chest) will be conducted at study entry and every 6 weeks thereafter (at the beginning of cycles 3,5,7,9 etc) until your tumour grows again. These examinations are carried out as part of medical routine and may be carried out more frequently, if your treating physician considers this appropriate.

Your doctor may suggest other tests, such as CT of the brain. The regular doctor’s visits are part of your standard medical care and are handled the same way as if you did not take part in the study.

ALTERNATIVE TREATMENTS

Instead of being in this study, your doctor may recommend that you receive Tarceva or another form of treatment (for example chemotherapy and/or radiotherapy) not given as part of this study.

BENEFITS

The ultimate goal of conducting clinical research studies in lung cancer patients is to better understand the behaviour of cancer and to find better ways of treatment. We hope that the treatment under this clinical research study will be of benefit to you and/or that it will help others, although we cannot guarantee this.

RISKS AND DISCOMFORTS

While you receive treatment with the medications being used in the protocol, you are at risk of the side effects of these treatments. Your physician will be checking you closely to see if any of the side effects are occurring. You should report any side effect or symptom that you experience to your physician. Other drugs may be given to make some of these side effects less serious and uncomfortable.

Tarceva®

Very common (≥ 10%):

- Diarrhoea
- Vomiting
- Rash which may occur or worsen in sun exposed areas
- Eye irritation due to conjunctivitis/keratoconjunctivitis and keratitis
- Infection
- Loss of appetite, decreased weight
- Depression
- Headache, altered skin sensation or numbness in the extremities
- Difficulty in breathing, cough
- Nausea
- Mouth irritation
- Stomach pain, indigestion and flatulence
- Abnormal blood tests for the liver function
- Itching, dry skin and loss of hair
- Tiredness, fever, rigors

Common (1 – 10%):

- Bleeding from the nose
- Bleeding from the stomach or the intestines
- Inflammatory reactions around the fingernail
- Cracked skin (skin fissures)

Rare (< 1%)

- Eyelash changes
- Excess body and facial hair of a male distribution pattern
- Eyebrow changes
- Brittle and loose nails

Very rare (< 0.1%)

- Perforation or ulceration of the cornea
- Severe blistering or peeling of skin

Your physician will be checking you closely to see if any of these side effects are occurring. Your doctor may prescribe medication to keep these side effects under control.

You should tell your doctor:

- if you have sudden difficulty in breathing associated with cough or fever because your doctor may need to treat you with other medicines and interrupt your Tarceva treatment
- if you have diarrhoea;
- immediately, if you have severe or persistent diarrhoea, nausea, loss of appetite, or vomiting;
- if you have severe pain in the abdomen, severe blistering or peeling of skin, or acute or worsening eye problems (for example eye pain).
- if you are also taking a statin and experience unexplained muscle pain, tenderness, weakness or cramps.

Docetaxel

Very common (≥ 10%):

During the infusion at the hospital

- flushing, skin reactions, itching
- chest tightness; difficulty in breathing
- fever or chills
- back pain
- low blood pressure

After the infusion:

- infections, decrease in the number of red (anaemia), or white blood cells and platelets
- fever: if this happens you must tell your doctor immediately
- allergic reactions as described above
- loss of appetite (anorexia)
- insomnia
- feeling of numbness or pins and needles or pain in the joints of muscles
- headache
- alteration in sense of taste
- inflammation of the eye or increased tearing of the eyes
- swelling caused by faulty lymphatic drainage
- shortness of breath
- nasal drainage; inflammation of the throat and nose; cough
- bleeding from the nose
- sores in the mouth
- stomach upsets including nausea, vomiting and diarrhoea, constipation
- abdominal pain
- indigestion
- short term hair loss (in most cases normal hair growth should return)
- redness and swelling of the palms of your hands or soles of your feet which may cause your
- skin to peel (this may also occur on the arms, face, or body)
- change in the colour of your nails, which may detach
- muscle aches and pains; back pain or bone pain
- change or absence of menstrual period
- swelling of the hands, feet, legs
- tiredness; or flu-like symptoms
- weight gain or loss

Common (1 – 10%):

- fungal infection of the mouth (oral candidiasis)
- dehydration
- dizziness
- hearing impaired
- decrease in blood pressure; irregular or rapid heart beat
- heart failure
- oesophagitis
- dry mouth
- difficulty or painful swallowing
- haemorrhage
- raised liver enzymes (hence the need for regular blood tests)

Rare (< 1%)

- fainting
- at the injection site, skin reactions, phlebitis (inflammation of the vein) or swelling
- inflammation of the colon, small intestine; intestinal perforation
- blood clots.

Pregnancy/Birth Control:

All women who participate in the trial and are able to become pregnant must use effective contraception while they receive study medication and 12 months thereafter.

If you are female and are pregnant, or plan to become pregnant, or if you are breastfeeding. you will not be allowed to enter this study. This is because the effects of the drug used in this study to an unborn baby or nursing infant are uncertain. You will also be asked to use a proven contraceptive method (a way to prevent you from becoming pregnant) while you are in this study. Your doctor will discuss with you which methods constitute effective contraception.

If you are a man whose partner can get pregnant, you and your partner will need to use a proven contraceptive method while you are in this study.

If you are female and become pregnant, or if you are male and a partner becomes pregnant, you must tell your study doctor immediately. For female patients, your doctor may discuss with you the possibility of stopping study treatment. Your doctor will need to report this information and the outcome of you or your partner's pregnancy to the ETOP safety office.

NEW INFORMATION ARISING FROM THIS AND OTHER STUDIES

You have the right to be informed of the progress of the clinical research study and of its final results. You have also the right to be informed of all additional results of other studies, which might be important for your treatment or might affect your willingness to continue.

CONFIDENTIALITY

The researchers will need to collect personal information from you such as your age, gender and relevant health information. All information collected is coded in a way that without a key, it will not be possible to link the information to your person.

Any personal or health information that is collected will be kept private and confidential. It will be stored securely. Only authorised persons, who understand that it must be kept confidential, will be able to get access to it. In any report of the research made available to the public you will not be referred to by name.

Representatives of ETOP, Biodesix Inc., health authorities or drug regulatory agencies may require access to personal or health information contained in your medical records to verify clinical trial procedures and/or data. Your personal data will be stored in a database and evaluated at the Data Centre of ETOP. ETOP guarantees that the national and international data protection guidelines are respected.

COLLECTION OF BIOLOGICAL MATERIAL

About blood samples

Blood samples (3.5 mL or 1 teaspoon) will be collected for VeriStrat testing and will be sent to a central laboratory called Biodesix in Aurora, CO, USA. After performing the test the sample will be destroyed (no collection).

EXPENSES / REMUNERATION

VeriStrat will be provided free of charge by Biodesix, Inc.

Tarceva® and Docetaxel as well as all other expenses, for example, routine standard examinations, will be handled as if you were receiving standard treatment and not participating in the clinical study.

You will receive no payment for taking part in this study.

TERMINATION OF THE STUDY

You might stop receiving study treatment without your consent for the following reasons:

a) If your lung cancer worsens or a new tumour develops.

b) If the doctors treating you detect side effects that they consider dangerous.

c) If you refuse to have the treatments or follow-up examinations and tests needed to determine whether the treatment is safe and effective.

d) If the early analyses of study data show insufficient benefit or a significant potential harm of the treatment.

INSURANCE

The ETOP will compensate you for any damage you may suffer during the course of the clinical trial. For this purpose the ETOP has arranged insurance for clinical trials with XX.
If you notice any health problems or other damage during or after the clinical trial, please contact the responsible doctor without delay. He/She is familiar with the valid legislation, has the relevant documentation and will take the necessary steps for you.

CONTACT PERSONS

The physician in charge of this study is *(give name, telephone number of PI)*. If you need more information about this study before you decide to join, or at any other time, you may wish to contact him/her. In the event that you do decide to participate, he/she should also be called if there are severe side effects from the treatment.

PATIENT INFORMED CONSENT FOR CLINICAL RESEARCH

- Please read this form carefully.
- Please ask if there is anything you do not understand or would like to know.

Clinical trial number: EMPHASIS-lung/ ETOP 3-12
Title of clinical trial: A randomized phase III trial of erlotinib versus docetaxel in patients with advanced squamous cell non-small cell lung cancer who failed first line platinum based doublet chemotherapy stratified by VeriStrat Good vs VeriStrat Poor
Location of clinical trial:
Trial investigator:
Surname and forename:
Patient:
Surname and forename: Date of birth:

- The undersigned doctor has explained to me verbally and in writing the objectives, the procedure of the trial with Tarceva® or Docetaxel, the expected effects, possible advantages and disadvantages and potential risks.
- I have read and understood the written Patient Information Leaflet issued for the above-mentioned trial (see footer for date). My questions related to the participation in this trial have been answered to my satisfaction. I may retain the written information leaflet and have been given a copy of my informed consent form.
- Other possible treatments and treatment methods have been explained to me.
- I have had enough time to make my decision.
- I have been informed that there is insurance to cover any damage that may arise during the course of the trial.
- I agree that my GP is being informed of my participation in the trial.
- I take note that my blood sample will be used for VeriStrat® testing.
- I know that my personal details and sample will only be used in anonymised form for research purposes. I give my consent for the relevant experts from the ETOP, the authorities and the ethics committee to have access to my original data for inspection and review purposes, but provided that strict confidentiality is maintained.
- I am participating voluntarily in this clinical trial. I may withdraw my consent to participate at any time without giving reasons and without any disadvantage to my continued medical care. If I do withdraw my consent, I will undergo a final medical examination.
- I am aware that the requirements and restrictions detailed in the patient information leaflet must be observed during the clinical trial. In the interests of my health, the trial investigator may exclude me from the trial at any time. Furthermore I will report to the investigator any concurrent treatment I receive and any medication I am taking (whether it was prescribed by the doctor or I bought it myself).

Place, Date	Patient's signature:

Confirmation by trial investigator:

I hereby confirm that I have explained the nature, significance and implications of the trial to this patient. I undertake to meet all the obligations arising in connection with this clinical trial. If at any time during the conduct of the trial I learn of aspects that might influence the patient's willingness to participate in the trial, I will notify her of these immediately.

Place, Date	Investigator's signature:

PLEASE RETAIN A COPY OF THE SIGNED INFORMED CONSENT FORM. DO NOT SEND THE SIGNED INFORMED CONSENT FORM TO ETOP.