Informed Consent Form

Comparison of paclitaxel in combination with cisplatin (TP), carboplatin (TC) or fluorouracil (TF) concurrent with radiotherapy for patients with local advanced esophageal squamous cell carcinoma: a three-arm phase III randomized trial (ESO-Shanghai 2)

You are being asked to take part in a clinical study. **Please take your time to make your decision about taking part. If you have any questions, you can ask your study doctor for more explanation.**

You are being asked to take part in this study because you have local advanced esophageal squamous cell carcinoma.

Why is this study being done?

Concurrent chemoradiation is the standard therapy for patients with local advanced esophageal carcinoma unsuitable for surgery. Paclitaxel is an active agent against esophageal cancer and it has been proved as a potent radiation sensitizer. There have been multiple studies evaluating paclitaxel-based chemoradiation in esophageal cancer, the results of which are inspiring. However, which regimen, among paclitaxel in combination with cisplatin (TP), carboplatin (TC) and fluorouracil (TF) concurrent with radiotherapy, provides best prognosis with minimum adverse events is still considered far from resolved and very few studies focus on this field. The purpose of this study is to confirm the priority of TF to TP or TC concurrent with radiotherapy in terms of overall survival and propose a feasible and effective plan for patients with local advanced esophageal cancer.

How many people will take part in the study?

About 321 people will take part in this study.

What will happen if I take part in this research study?

You will be randomized and allocated in a 1:1:1 ratio to the three treatment groups (TF, TP or TC). You will receive radiotherapy combined with concurrent chemotherapy. Radiotherapy will begin on day 1, concurrent with the beginning of cycle 1 of chemotherapy.

Radiation therapy

Same radiation therapy will be delivered in all three treatment groups. Radiotherapy will be delivered with photons (≥6 MV) to a total dose of 61.2Gy in 34 fractions. You will be treated 5 days per week at 1.8Gy/d.

Chemotherapy

Arm A (TP)

If you are in arm A, you will receive 4 courses of TP every 4 weeks. Details are as follows:

Paclitaxel: 175mg/m^2/d, ivgtt over 3 hours, d1; Cisplatin: 25mg/m^2/d, ivgtt, d1-3;

Arm B (TF)

If you are in arm B, you will receive 6 courses of TF concurrent with radiotherapy every week and 2 courses of TF adjuvant chemotherapy every 4 weeks. Details are as follows:

Concurrent: paclitaxel 50mg/m^2/d, ivgtt over 3 hours, d1; 5-FU 300mg/m^2, civ 96h, d1-4

Adjuvant: paclitaxel 175 mg/m^2/d, ivgtt over 3 hours, d1; 5-FU 1800mg/m^2, civ 72h, d1-3

Arm C (TC)

If you are in arm C, you will receive 6 courses of TC concurrent with radiotherapy every week and 2 courses of TC adjuvant chemotherapy every 4 weeks. Details are as follows:

Concurrent: paclitaxel 50mg/m^2/d, ivgtt over 3 hours, d1; carboplatin AUC=2, ivgtt, d1

Adjuvant: paclitaxel 175 mg/m^2/d, ivgtt over 3 hours, d1; carboplatin AUC=5, ivgtt, d1

During each treatment, blood tests will be performed to monitor blood counts, kidney function, liver function and electrolyte levels. Ultrasound, barium swallow and CT scan with contrast will be performed to evaluate the status of disease.

How long will I be in the study?

After your treatment is completed, you will be seen in follow-up visits with your doctor every 3 months in years 1-2, every 6 months in years 3-5 and then once a year for your lifetime.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so he or she can evaluate any risks from the treatment. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. There also is a risk of death.

Risks and side effects related to the chemoradiotherapy

- Soreness in throat or esophagus
- Cough
- Vomiting
- Nausea
- Fatigue
- Anorexia (loss of appetite)
- Diarrhea
- Numbness in arms and legs
- Allergic reaction
- Hair loss
- Redness of irritation of the skin in the treatment area
- Decrease in white blood cell counts and high risk of infection
- Renal insufficiency,

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While researchers hope these treatment regimens will be more useful against cancer compared to the usual treatment, there is no proof of this yet. We do know that the information from this study will help researchers learn more about these combinations of drugs as a treatment for cancer. This information could help future cancer patients.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our center.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, Kuaile Zhao, at 021-64175590.

Signature

I have been given a copy of all 5 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant:

_____	_____	_____
Name of Participant	Signature	Date

Researcher:

_____	_____	_____
Name of Participant	Signature	Date