Participant study guide for the

EMERALD-Y90 Study

EMERALD-Y90

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Welcome

Thank you for taking part in the **EMERALD-Y90 Study** and helping us learn more about possible treatment opportunities for hepatocellular carcinoma. By taking part in medical research, you may help other people with this type of liver cancer.

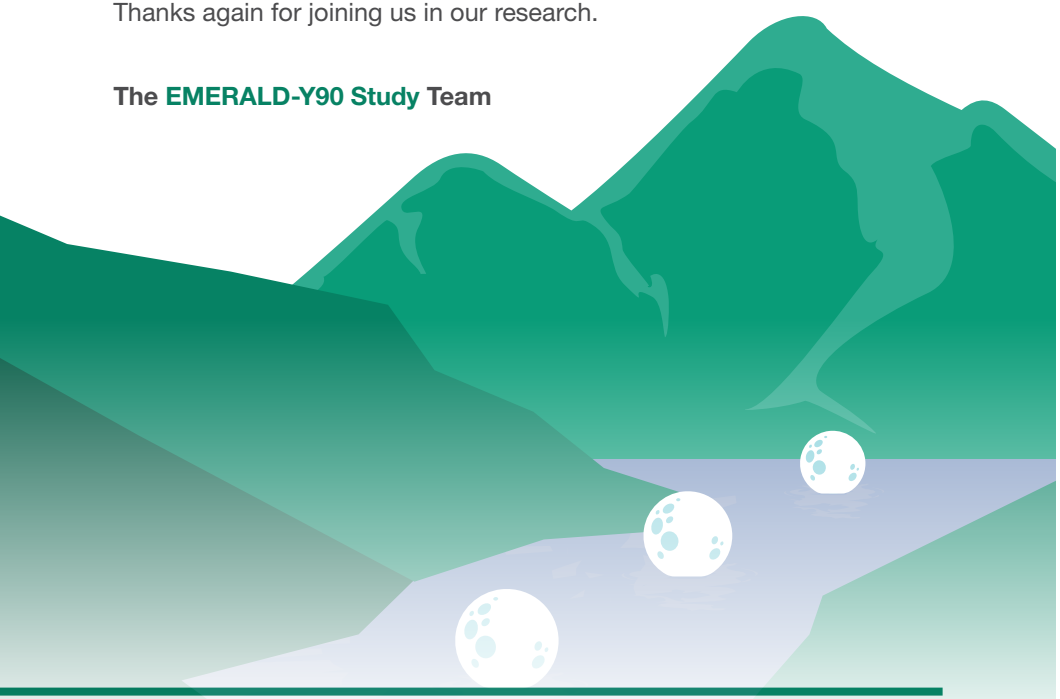
We want to make sure that everyone taking part understands the **EMERALD-Y90 Study** and what it involves, every step of the way. This guide has been provided to help you while you are in the study and help you prepare for each study visit. You should also refer to the informed consent form (ICF) for further information.

Throughout the study, you will have a team of doctors, nurses, and other healthcare staff looking after your well-being. To make sure everybody's efforts count, we need you to come to all scheduled study center visits. If you cannot attend a visit, please get in touch with the study team as soon as possible to let us know.

If you have any questions or worries during the study, we are here to help and will be happy to talk to you at any time.

Thanks again for joining us in our research.

The EMERALD-Y90 Study Team

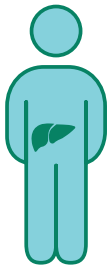


An introduction to clinical research studies

The aim of clinical research studies is to assess whether an investigational treatment is safe and effective for treating a particular medical condition. 'Investigational' means that the treatment has not been approved for a particular medical use and is still being assessed in studies. Clinical research studies also check for any side effects that may develop while taking the investigational treatment.

Clinical research studies are carried out according to strict guidelines. These make sure that the safety and well-being of all participants are always the priority.

The EMERALD-Y90 clinical research study



EMERALD-Y90 is a clinical research study for people with a type of liver cancer known as **hepatocellular carcinoma**. It is assessing the combination of **durvalumab** and **bevacizumab** given after the **TARE Y90** procedure.

Although all three treatments are approved for use in hepatocellular cancer, typically alongside other treatments, this approach is investigational, so has not been approved for use outside of a clinical study.

Approximately **125 people** with hepatocellular carcinoma will join the **EMERALD-Y90 Study** in around **20 study** centers across the **USA**.

Study treatment

EMERALD-Y90 includes three study treatment steps, given in the following order:

1	2	3
TARE procedure	**Durvalumab** – single treatment session	**Durvalumab plus bevacizumab** – combination treatment sessions

STEP 1: TARE procedure

TARE (which stands for *transarterial radioembolization*) is a standard treatment for hepatocellular carcinoma that cannot be treated using surgery.

TARE is a procedure that delivers tiny beads holding radioactive particles (known as *yttrium-90*) directly to liver tumors to kill cancer cells. It involves a thin tube being inserted into a blood vessel in the groin and then guided to the liver. You will be sedated during this procedure. The injected radioactive particles get deposited in the tumor tissue, reducing blood flow to cancer cells, and then giving off radiation to that area. The radiation gradually disappears.

You will also undergo an imaging test, known as a *computed tomography* (CT) scan, after the TARE procedure and further screening tests to confirm whether you can move to the next stage of the study.

STEP 2: Durvalumab – single treatment session

Durvalumab is a type of anticancer drug that helps your immune system to attack and kill cancer cells. It is approved for use in certain cancers including hepatocellular cancer.

You will be given **one dose of durvalumab** via a plastic tube into a vein (known as an *intravenous infusion*), 2 weeks after the TARE procedure.

STEP 3: Durvalumab plus bevacizumab – combination treatment sessions

After a further 2 weeks, you will begin **durvalumab plus bevacizumab** via intravenous infusions. This study treatment will be repeated **every 3 weeks**. The study doctor will decide how many sessions (known as *cycles*) of this study treatment you receive, depending on how you respond.

Bevacizumab is an anticancer drug that reduces blood flow to the tumor to starve the cancer of the nutrients it needs to grow. It is approved for use in certain cancers including hepatocellular cancer.

Other treatments

While you are in the study, you won't be allowed to use some medications and treatments. Please check with the study team **before** starting any new medications or treatments, including vaccines, radiotherapy, other anticancer treatments, herbal remedies, supplements, and complementary therapies.

In particular:

- Do not take any **over-the-counter medications** without checking with the study team first.
- Use of **warfarin** (at any dose) or **aspirin (above 325 mg per day) is not allowed** during the study.

Monitoring your health throughout the study and beyond

Follow-up study center visits

The study team will assess your health using medical tests and questionnaires every time you visit the study center for your study treatment.

When you finish the study treatment, there will be 4 additional follow-up study center visits to continue this monitoring. The first will occur when you stop treatment. This is known as the end of treatment (EoT) visit. The remaining 3 follow-up visits will be arranged for 30, 60, and 90 days after the EoT visit.

Follow-up telephone calls

After the last follow-up study center visit, the study team will contact you by telephone every 12 weeks to check on your well-being.

Tests and procedures

The study will include the following:

Questions about your health in the past, and your current level of functioning and ability to engage in everyday activities.

Physical examination – including measurements of your height and weight.

Pregnancy test (if appropriate).

Assessment of liver health – involving blood tests and assessment of symptoms.

Blood tests – involving a small sample of blood being taken from a vein in your arm.

Urine samples may be taken, if needed.

Electrocardiogram (ECG), if needed – measuring the heart's electrical activity; involves having sticky pads attached to your skin.

Vital signs – measuring body temperature, heart rate, and blood pressure.

Questions abouct adverse events – to assess whether you have experienced any side effects from the study treatment. The study team may also telephone you between study visits to enquire about adverse events.

Questions about other treatments you have used since the previous visit, and other anticancer treatments received after stopping study treatment. The study team may also telephone you between study visits to enquire about these other treatments.

Tumor imaging – to provide images of your tumor, typically using magnetic resonance imaging (MRI). Other scans could include a bone scan, CT scan, positron emission tomography (PET) scan, or X-ray. Scans involve lying very still inside/below the scanner while an image is taken. Some scanners make loud clicking noises, but you cannot feel the image being taken.

Health questionnaires – with questions about your symptoms and how these impact your everyday activities.

Visit schedule

This table shows when the various tests and procedures will occur. If you cannot attend a visit, please make sure that you let the study team know straight away.

		Study treatment			Follow-up study center visits				Follow-up telephone calls
		TARE	Durvalumab	Durvalumab + bevacizumab	Follow-up 1/EoT	Follow-up 2	Follow-up 3	Follow-up 4	
			Around 2 weeks after TARE	Around 2 weeks after durvalumab treatment, and then every 3 weeks	When you stop study treatment	30 days after EoT	60 days after EoT	90 days after EoT	Every 12 weeks after Follow-up 4
									
	Questions about your health	●	●	●	●	●	●	●	
	Physical examination and weight	●	●	●	●	●	●		
	Pregnancy test (if appropriate)		●	●	●				
	Assessment of liver health	●	●	●	●	●	●	●	
	Blood tests	●	●	●	●	●	●	●	
	Urine test	As needed							
	ECG	As needed							
	Vital signs	●	●	●	●	●	●	●	

Visit schedule (continued)

		Study treatment			Follow-up study center visits				Follow-up telephone calls
		TARE	Durvalumab	Durvalumab + bevacizumab	Follow-up 1/EoT	Follow-up 2	Follow-up 3	Follow-up 4	
			Around 2 weeks after TARE	Around 2 weeks after durvalumab treatment, and then every 3 weeks	When you stop study treatment	30 days after EoT	60 days after EoT	90 days after EoT	Every 12 weeks after Follow-up 4
									
	Questions about adverse events	●	●	●	●	●	●	●	
	Questions about other treatments	●	●	●	●	●	●	●	●
	Tumor imaging	● A CT scan will be taken within 24 hours after the TARE	● 12 weeks after TARE; and then every 9 weeks for the first 48 weeks, then every 12 weeks						
	Health questionnaires	●	●	●	●				
	Check on your well-being								●
	TARE therapy	●							
	Durvalumab infusion		●	●					
	Bevacizumab infusion			●					

Adverse events=unwanted side effects of the study drugs (your ICF will have a full list); CT=computed tomography (medical scanning technique); ECG=electrocardiogram (measures electrical activity of the heart); EoT=end of treatment; TARE=transarterial radioembolization (anticancer procedure).

Study duration

The study duration will be different for each participant, but could be an average of around 2 years, not including the follow-up telephone calls.

Leaving the study early

You are free to leave the study at any time, for any reason. If you withdraw, there will be no penalty or loss of benefits regarding your future healthcare. You will be asked to return to the study center to undergo the tests performed at the EoT visit.

Your participation in the study may be discontinued for various reasons, including if:

- You develop a medical condition, or the results of tests show that it is better for you not to continue.
- You experience a severe reaction to the study treatment.
- You do not follow instructions given by the study team.
- You start a treatment that is not allowed during the study.
- You have a positive pregnancy test result (female participants).
- The study doctor decides that continuing in the study is not in your best interests.
- The Sponsor (the company carrying out the study), or another group monitoring the research, decides to stop the study.

If you have any questions about withdrawal or removal from the study, please contact the study team.

Reminders

The reminders below will help your participation run as smoothly as possible:

- Keep your study center visit appointments. If you are unable to attend, let the study team know as soon as possible so the visit can be rescheduled.
- Tell the study doctor immediately if you experience worsening symptoms or any side effects.
- Remember to use suitable contraception throughout the study.
- Do not take part in any other clinical research study while you are on this study. Tell your regular doctor that you are taking part in this study.

Thank you

Clinical research studies such as the **EMERALD-Y90 Study** could not take place without people like you. We really appreciate your time and commitment.

You are making a valuable contribution to clinical research that may help us learn more about hepatocellular carcinoma.

Study team contact details

Study center:

Study doctor name:

Study coordinator name:

Address:

Telephone:

Website:

Opening hours:

Out-of-hours emergency contact number:

Email:

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