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VIM Participant Information Sheet

VIM: A randomised phase II trial of oral **vi**norelbine as second-line therapy for patients with malignant pleural **m**esothelioma

We invite you to take part in a research study called "VIM"

- Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve
- Please take time to read the following information carefully and discuss it with friends, relatives, and your key worker or General Practitioner (GP) if you wish
- You are free to decide whether or not to take part in this research study. If you choose not to take part, this will not affect the standard of care that you will receive
- Ask us if there is anything that is not clear or if you would like more information
- Thank you for reading this information. If you decided to take part you will be given a copy of this information sheet and your signed consent form

Important things that you need to know

- We want to find out if further chemotherapy treatment in patients with progressed mesothelioma is beneficial

- Currently, the aim of treatment once mesothelioma progresses is to control symptoms (also known as active symptom control)
- We are testing a drug called vinorelbine in patients with progressed mesothelioma
- There is some evidence that vinorelbine may be beneficial in patients who have previously had chemotherapy for mesothelioma. However, it is not known whether vinorelbine is better than active symptom control in this situation
- Like all medicines used to treat mesothelioma, the medicines used in this trial can have side effects
- The researchers who have designed this trial have tried to fit the study into your normal treatment to minimise any additional hospital visits
- You can stop taking part in the trial at any time, without giving a reason and without affecting the care or benefits that you receive

1. Why are we doing the VIM study?

We need to find out:

- How well vinorelbine works to control your mesothelioma
- How safe vinorelbine is for the treatment of mesothelioma
- What side effects vinorelbine has in patients with mesothelioma

2. Why have I been asked to take part?

- You are being invited to take part because you have been diagnosed with mesothelioma which has already been treated with chemotherapy, but has now progressed

3. How will my treatment be decided?

- Everyone who agrees to take part in this trial will be put into one of two treatment groups. The only way to make sure that the two groups of patients are as similar as possible is to have your treatment decided upon by chance. This process is called "randomisation"
- In this trial, you will either have active symptom control, or active symptom control with vinorelbine capsules
- One-third (33%) of the patients that agree to take part will have active symptom control, and two-thirds will have the active symptom control plus vinorelbine. This means there will be two patients given vinorelbine in

addition to active symptom control for every one patient who has active symptom control alone

- It is also important to remember that, regardless of the treatment group to which you are allocated, you will receive the standard treatment for your disease, be monitored closely and be given the best possible care

4. What will happen to me if I take part?

- You will see the doctor and have some screening tests. These tests include:
  - Physical examination
  - Blood tests
  - Heart trace (ECG)
  - CT scan (CAT scan) (only if you haven't had one in the last 4 weeks)
  - Chest X-ray (only if needed)
  - Pregnancy test (if appropriate)

- If your doctor looks at the results of these tests and decides that you are suitable for this study and you agree to take part, you will be asked to sign a consent form and be entered into one of the treatment groups in the study

- If you agree to take part in this study, you will be asked for your permission to take an extra blood sample when you first join the study. You will also be asked to give your permission for researchers to have access to your diagnostic biopsy tissue. If this sample is not available you may be asked for a re-biopsy. These samples will be stored and may be used for future research purposes, which may include genetic testing. These samples may help researchers learn more about your cancer type and how best to treat it.

- Vinorelbine is taken once every week, and must be stored in the fridge. Prior to each administration you will need to have a blood test to ensure it is safe for you to have your next dose. You may need to go to hospital for this test or it can sometimes be taken at your GP Surgery.

- During treatment you will see your doctor at least once every 3 weeks and have a set of tests just to make sure that your body is coping ok with the treatment. These tests include:

  - Physical examination
  - Blood tests
  - Heart trace (ECG)
  - CT scan

- It is important that you attend all of your appointments as these hospital visits are part of your standard care. Unfortunately, there is no additional funding to pay for travelling or other expenses

- If your treatment is active symptom control plus vinorelbine capsules, you will be given the vinorelbine capsules at your first visit then you may be given capsules every three weeks at each of your three weekly visits depending on the hospital at which you attend.

- You will continue taking the capsules until there is evidence that the disease has progressed further, and you may also stop the capsules at any time if you have unacceptable side effects, or if you want to without giving a reason but you should discuss this with your consultant.

- You will be given a patient pack and a diary to record when you take each tablet and to write down any side-effects that you may have.

- You will be given a card that looks a bit like a business card which you should carry with you at all times as it informs people that you are on this trial, states your trial number and it has the contact details for your hospital doctor should you ever be admitted to hospital.

- Vinorelbine capsules are taken once a week. Your dose will be calculated depending on your body area and will be made up from 2 to 5 capsules of different strengths. Vinorelbine capsules must be swallowed whole with water, without chewing, sucking or dissolving the capsules. It is recommended to take your capsules with some food.

- At every other visit throughout your treatment (i.e every 6 weeks), and at the end of your treatment you will have a CT scan. The CT scan will take a series of X-rays of your body from different angles. A computer puts these together to form a picture. This picture will show your doctor where the cancer is in your body and also how big it is.

- In certain circumstances, your doctor may decide to reduce, delay or even stop your capsules. In most circumstances, where your capsules need to be stopped, your active symptom control can be continued. If this happens, your doctor will tell you and request that you return any capsules that you haven't taken, in their original container at your next appointment.

- At clinic visits during the study, the team looking after you will ask you some extra questions about how you are feeling and if you have noticed any side effects from your treatment. You may be asked additional questions at these visits and for up to one year after your treatment. After your treatment, your doctor will discuss your follow up care with you and make the necessary arrangements. Your participation in the study will end a year after your treatment, but you will continue to be seen by your doctor which would happen as part of your standard care.

5. What are the possible advantages and disadvantages of taking part?

- We hope that vinorelbine will help control the cancer more than standard treatment, however this cannot be guaranteed.

- The information that we get from this study may help us to treat future patients with mesothelioma more effectively.

- If you have private medical insurance and/or life insurance you should contact your provider before you agree to take part in the study. This is to make sure that taking part in the study will not affect your cover.

- The inconvenience, side-effects and impact on quality of life is similar to that of any course of chemotherapy.

- The study requires that you have regular CT scans. Three of the CT scans are additional to the ones that you would receive as part of normal follow-up and as a consequence you will be exposed to slightly more radiation. However, the overall level radiation exposure is still negligible and you will not notice any changes to your health because of it.

- As part of the normal CT scanning process, you will also be given an injection of a dye to help show up your organs and any tumours that might be present. Rarely, this injection can cause an allergic reaction or damage to the kidneys but precautions are routinely taken to minimise this risk.

- You will undergo additional blood tests. These can cause pain, bruising, infection or inflammation at the sampling site, and may make you feel faint.

- Your study assessments could result in your hospital doctor finding a condition that you did not know that you had. If this happens your GP will be informed so that appropriate medical treatment can be offered to you.

- **There will be approximately six extra visits to hospital if you participate in the trial (although this number will vary depending on your response to your treatment). The trial is unable to provide travel expenses, so you would have to pay for your travel yourself. There is no payment to you for taking part in the study.**

6. What are the side effects of vinorelbine?

- All chemotherapy drugs have potential side effects. However, not all patients will experience all side effects and the majority of these may only last a few days. The symptoms can often be helped by medication. Your doctor will

prescribe additional medication e.g. anti-sickness tablets before each dose of vinorelbine to reduce the likelihood of you suffering side-effects i.e. being sick whilst on treatment. You may also benefit from taking laxatives.

- No-one can predict before you start treatment whether you will have any side-effects, or how serious they might be. Therefore, it is important that you record any symptoms that have made you feel unwell in your diary and that you discuss these with your doctor or nurse at each appointment.

- Although serious side-effects are rare, they do occur, so it is important that you seek advice from your research nurse or hospital doctor if you experience any side-effects which make you feel particularly unwell. Their contact details are at the end of this information sheet and also on your trial card.

- The side-effects commonly reported by patients who have received treatment with vinorelbine are listed below:

    - Tiredness or weakness
    - Feverishness
    - Nausea (sickness) or vomiting
    - Poor appetite
    - Sore mouth
    - Constipation or diarrhoea
    - Numbness or tingling in the hands and feet which may be permanent
    - Anaemia, which may require a blood transfusion
    - Reduced white blood cells, increasing the risk of infection

- Uncommon side effects:

    - Allergic reaction
    - Hair loss
    - Low blood platelets, increasing the risk of bruising or bleeding
    - Shortness of breath
    - Pain in the joints or muscles
    - Chest pain
    - Headache
    - Pain in the abdomen

7. More information about taking part

Effect of treatment on fertility and contraception

- It is not known what effect vinorelbine will have on the ovaries or testes. Vinorelbine may cause permanent infertility (inability to have a child).

- There is risk to an unborn child from vinorelbine. It is possible for women to become pregnant, and men to father a child during treatment. Therefore, you

and your partner should use effective methods of contraception* during treatment and for six months after treatment, because of the risk to the unborn child. You would be advised to do this even if you were not taking part in this trial.

- In the event that you or your partner becomes pregnant while you are taking part in the study you should consult your doctor immediately and inform your research nurse. Your research nurse will then report the pregnancy to the Wales Cancer Trials Unit who are running the study. Should you or your partner become pregnant during the study you will be provided with additional information.

  *Suitable contraceptive methods include:

  - Oral contraceptive together with condom
  - Intra-uterine device (coil) together with condom
  - Diaphragm (cap) with spermicide together with condom
  - Vasectomy
  - Tubal occlusion

What happens when the research study stops?

You will receive the standard treatment you would have been given if you had not agreed to take part in the study.

What if I change my mind?

If you do decide to take part in VIM then you are still free to withdraw at any time without giving a reason. This will not affect your future care in any way but we would still like to know how you are, and with your permission, will request this information from your doctor. This is so that the overall quality of the study is not impaired. Please let your doctor know if you wish to withdraw and he/she will carry on your care in the normal way.

If you withdraw, you will be asked to clarify which part of the trial you are withdrawing from. You may withdraw from some parts or all parts. Depending on your response, we will know what information we can keep and whether we can still collect information on your progress.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw, your doctor will make arrangements for your normal care to continue. If you decide to continue in the study you will be asked to sign a new consent form.

Also, on receiving new information, your doctor might consider it to be in your best interest to withdraw you from the study. He/she will explain the reasons and arrange for your usual care to continue.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [Please add site contact details].

In the event that something does go wrong and you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms are available to you. Details can be obtained from your hospital.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. Your GP will be notified of your participation in the trial if you choose to take part.

Your research nurse will supply information to the WCTU which is co-ordinating the trial. They will use your date of birth, initials, and a participant trial number specific to you in this study. This information will be securely stored at the office of the WCTU on paper and electronically under the provisions of the 1998 Data Protection Act. Any information about you that leaves the hospital will have your full name and address removed so that you cannot be recognised from it.

Staff at the WCTU, staff at the University of Leicester as sponsor of the study and people who monitor and audit trials such as the IRB/IEC and the UK regulatory authorities may look at your medical records to check that the study is being done properly. All will have a duty of confidentiality to you as a research participant.

We will contact your hospital over the years to find out how you are getting on. Ideally, we would like to do this for life, but patients often change address and or GP or lose touch with their hospital. If this happens, we would like to access the national records, which are kept on everyone's health status to find out how you are. We will need to give them enough information to identify you, usually your name, date of birth and NHS number. Any details that we receive from any source are confidential and will only be used for the purposes of the VIM study. It is up to you to decide whether or not to consent to this optional part of the study.

What will happen to the results of the research study?

The results of this study may be shown at medical meetings and submitted to major cancer research journals for publication. You will not be identified in any way in any report or publication arising from the study. Where feasible, publications will be

made available to the general public on the WCTU website (www.WCTU.org.uk). They will also be brought to the attention of Macmillan Cancer Support. If you wish to know the results at the end of the study, please access the WCTU's website or contact MacMillan Cancer Support.

Who is organising and funding the research?

The study is being organised by the Wales Cancer Trials Unit on behalf of the Chief Investigator, Professor Dean Fennell who is a consultant oncologist at University Hospitals of Leicester. The study has been funded by Cancer Research UK and Pierre Fabre Ltd, which makes vinorelbine, has provided the drug and its distribution costs for free.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC) to protect your safety, rights, well-being and dignity. This study has been reviewed by the Wales REC 3 and the Medicines and Healthcare Products Regulatory Authority (MHRA). It has also received independent peer review by the National Cancer Research Network (NCRN) Chemotherapy and Pharmacy Advisory Service (CPAS) group.

Further information and contact details

If you consent to join this study you will be given the telephone number of the hospital, which you can contact at any time if you feel unwell or have questions. We would like you to keep this information sheet and if you find it helpful please use it to discuss treatment with your family, friends or your General Practitioner. If you have any further questions or concerns regarding the study please contact

Dr: .....
Tel: .....

or

Research Nurse/Radiographer: .....
Tel: .....

Thank you for taking the time to read this information sheet and for considering participating in this study.

If you or your relatives have any questions about the VIM study you may wish to contact an organisation that is independent of the hospital at which you are being treated, for example:

Mesothelioma UK
c/o Hospital Management Offices, Glenfield Hospital, Leicester LE3 9QP
Email: mesothelioma.uk@uhl-tr.nhs.uk Free phone 0800 169 2409

Macmillan Cancer Support is a registered charity providing information about all aspects of cancer for patients and their families. They can provide useful booklets on lung cancer, the treatments for lung cancer and medical research in general. You may contact their specialist cancer nurses on **0808 800 1234**. You can also access their web site at **www. http://www.macmillan.org.uk**.

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VIM PARTICIPANT CONSENT FORM

VIM: A randomised phase II trial of oral **vi**norelbine as second-line therapy for patients with malignant pleural **m**esothelioma

Version:	3.0
Date:	15th October 2014
ClinicalTrials.gov:	NCT02139904
EudraCT:	2014-001992-30
SPONSOR:	Leicester University
SPONSORSHIP No:	UNOLE 0329
CRUK Trial No:	CRUK/12/056

Patient ID Number for this trial: Date:

Name of Principal Investigator: Centre Number:

Please **initial** boxes:

1 I confirm that I have read and understand the information sheet dated (version no……..date……) for the above study and have had the opportunity to ask questions. ☐

2 I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3 I understand that sections of any of my medical notes may be looked at by responsible individuals from the Wales Cancer Trials Unit, from the University of Leicester, or from regulatory authorities or the NHS, where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐

4 I consent to the storage of personal information (including electronic) for the purposes of this study. I understand that any information that could identify me will be kept strictly confidential and that no personal information will be included in the study report or other publication. ☐

5 I understand that only my date of birth, initials and VIM participant trial number will be used to identify me on the case report forms that are sent to the Wales Cancer Trials Unit. ☐

6 I agree to provide my diagnostic sample to the VIM study. ☐

7 I consent to give research blood sample(s) for use in laboratory research studies including genetic analysis:

Blood ☐
DNA (extracted from blood) ☐

8 I give permission for my GP to be informed of my participation in this study. ☐

9 I agree to take part in the VIM study. ☐

10 OPTIONAL: I agree for my details to be registered with the National Health Service Information Centre or equivalent for which my name and NHS number must be used in order for my health status to be followed up. (If yes, please complete NHS IC tracing sheet). ☐

11 OPTIONAL: I agree to provide a second biopsy for research purposes if my cancer progresses ☐

12 OPTIONAL: If a second biopsy is taken for clinical reasons, I agree to provide this for research purposes ☐

Name of Patient	Date	Signature
Name of person taking consent (if different from Principal Investigator)	Date	Signature
Name of Principal Investigator	Date	Signature

(Copies: 1 for patient; 1 for researcher; 1 to be kept with hospital notes)