

Information sheet and consent forms

Appendix 10

Patient Information Sheet
(Hospital Headed Paper)**A Phase II study of efficacy of VEPEMB in older patients with Hodgkin's Lymphoma**

You have been diagnosed with Hodgkin's lymphoma and your doctor believes that you will benefit from treatment with chemotherapy. We would like to ask you to consider taking part in a research study which hopes to confirm results from elsewhere that a particular mixture of drugs might be the best for older patients with Hodgkin's lymphoma .

Before you decide whether to take part it is important for you to understand why the research is being done. Please take time to read the following information carefully and to discuss it with friends, relatives and your GP if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES) publish a leaflet entitled Medical Research and you. This leaflet gives information about medical research and looks for some questions you may want to ask. A copy may be obtained at a charge directly from CERES, P.O. Box 1365, London, N16 OBW. Alternatively, your Doctor or Study Nurse can arrange to give you a copy which has been supplied by the Study Central Office in Newcastle, free of charge.

Thank you for reading this.

What is the purpose of the study?

Hodgkin's lymphoma is an unusual cancer in that it is usually found in younger patients. However about one in five patients who develop this disease are over 60 years of age. Over the last twenty years younger patients have had improved survival due to being able to tolerate more intensive treatment but older patients are usually excluded from studies of these treatments and therefore the manner in which they are treated and the clinical outcome is not well described.

The reasons for this lack of tolerance of intensive treatment is probably due to a combination of factors including the difficulty of completing all the planned courses of treatment on time because of problems with the treatment due to the increased toxicity of the drugs in older patients.

Since 1996, The Italian Intergroup Study Group for Lymphoma has treated 100 patients aged > 65 years with a combination therapy, VEPEMB, this includes 7 drugs (vinblastine, cyclophosphamide, procarbazine, prednisolone, etoposide, mitroxantrone and bleomycin) given in part by injection into a vein and in part by

mouth. All these drugs have been utilised or are utilised for treatment of Hodgkin's lymphoma in other studies and are known to be effective in this disease. In this new VEPEMB combination, the doses of the drugs have been adjusted in the light of experience in their use in individuals over the age of 60 years, to make sure that they provide the best outcome with the least number of problems due to toxicity. All anti-cancer drugs have side-effects which relate to the effect on the bone marrow and hair follicles. In this combination all of the drugs will cause side-effects, as described in the section entitled "What are the side effects of any treatment received when taking part?"

Worldwide, conventional treatment for Hodgkin's lymphoma is to give consecutive cycles of chemotherapy (ABVD) involving four drugs (adriamycin, bleomycin, vinblastine and dacarbazine) but this can be very difficult to give in older patients. One of the main issues of this study is to try to avoid drugs such as adriamycin in this ABVD schedule which can cause further damage in patients with heart disease. Also, the drug dacarbazine, used in the ABVD schedule is very problematic to give, even in younger patients, because of inflammation caused to the veins in the arm. It was, therefore, considered inappropriate to recommend this treatment for patients in the elderly age group.

In order to confirm that VEPEMB is associated with less toxicity problems and gives improved results in older patients we have proposed the current study. This new VEPEMB combination appears to be well tolerated and to give similar results to the ABVD combination.

Secondly, as it can be difficult to diagnose this particular form of lymphoma, an important part of this study is to investigate tumour specimens, which are routinely collected, using new techniques. From this we hope to learn more about the characteristic features of this disease, and whether these features can be used to identify groups of patients with a better or worse than average chance of cure. This will help us decide whether some groups of patients should be treated differently in future.

Another part of the study will address the problem of whether it is possible to predict patients who will not tolerate the treatment.

Why have I been invited to take part?

You have been invited to take part in this study as the pathologist at your local hospital has made a diagnosis of Hodgkin's lymphoma on a biopsy specimen and you are aged ≥ 60 years.

Do I have to take part?

It is up to you to decide whether or not to take part, and it is possible for you to agree to take part in the clinical study, but not the pathology sub-study if you wish. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide not to take part you will receive standard treatment for your disease and the standard of your care will not be affected.

If you do decide to take part you are still free to change your mind at any time, without giving a reason.

What will happen to me if I take part?

Whether or not you take part in this study the treatment you receive will be very similar. Involvement in the study will not involve any extra visits or time in hospital, therefore your expenses in travelling from home to the hospital will not be reimbursed.

Before starting treatment it will be necessary for your doctor to establish how advanced your Hodgkin's lymphoma is, we call this "staging". This will involve routine blood tests, in particular to check your kidney and liver function, CT scans and if indicated a bone marrow biopsy.

At the end of treatment the above tests, performed before starting treatment, will be repeated in order to fully assess your clinical response to the treatment drugs.

Data on the treatment you receive and your progress will be reported in confidence to the trial organisers, the SHIELD (Study of Hodgkin's lymphoma In the Elderly/Lymphoma Database) Trial Study Unit, who will put this together with data from all the other patients in the study, without identifying anyone individually.

Analysis of Samples Before Treatment

With your permission we would like to send some of the tumour sample collected routinely by your hospital to be examined by an expert pathologist at the Pathology Department, Royal Victoria Infirmary, Newcastle upon Tyne (this is the "pathology sub-study"). As part of this study, new techniques will be used to examine tumour cells in more detail. This will not affect your treatment in any way (and you will not benefit financially), but by collecting similar information on lots of patients we may be able to identify features which allow us to predict more accurately how patients will respond to different treatments in the future. The tumour sample would be anonymised, but would be identified by a numerical code so that when, and only when, the pathologist's report on the sample is sent to the study organisers (the SHIELD Study Group) they will be able to link the pathology details to details of your treatment and progress. When the study is completed, the biopsy sample will be returned to your local hospital.

We would also like to ask your permission to take a serum blood sample at diagnosis to be stored in Newcastle for possible use in future projects relating to the diagnosis and treatment of Hodgkin's lymphoma, as new techniques become available. These may be carried out by researchers other than those in Newcastle. This blood sample may be fully used in the research or in subsequent research and will be considered as a 'gift' from you to the research team. No one involved with this study would benefit financially if this were to happen. All further research using such stored samples will require approval from yourself and an appropriate Research Ethics Committee. When the research tests have been completed, any of the blood sample still remaining will be kept centrally at the Study Centre in Newcastle.

What is the drug or procedure that is being tested?

Depending on how advanced your disease is you will be given a different number of courses of your chemotherapy (VEPEMB). In “early stage” disease (i.e. disease is localised) you will receive 3 courses of treatment followed by radiotherapy to the areas originally involved.

If your disease is more extensive “advanced stage” you will be given 6 courses of treatment and (possibly) radiotherapy to any disease that remains or sites of initial bulky disease.

Each course of treatment lasts 4 weeks and you will need to attend the hospital weekly during the treatment phase. Full written details of the different drugs, how they act and any specific side-effects, will be provided for you by your Consultant or the medical/nursing team at the time of pre-treatment assessment. Your treatment will take approximately 5 months if you have early stage disease and 9 months if it is more advanced. These treatments are normally given on an outpatient basis. The treatment is complicated and will be discussed with you in detail by one of the clinical team involved in your care.

Some patients do not have blood vessels in their arms which are capable to withstand 5 months of treatment with this form of intravenous chemotherapy. It is possible that your medical advisors will suggest that you have a special plastic tube inserted into a major blood vessel which can be used during treatment as an easy access point for the administration of the drugs and for blood sampling. These tubes are called Hickman lines or catheters.

What are the side effects of any treatment received when taking part?

As with all chemotherapy, your treatment will result in side effects. The drugs can cause nausea and vomiting but you will be given treatment to prevent this. You are likely to lose your hair but this will be temporary and we can provide a wig. The most important clinical side effects involve those affecting your blood. Your white cells (which fight infection) can become very low and you will be given prophylactic antibiotics if this occurs. If your haemoglobin level drops (due to decreased numbers of red cells) you may need a blood transfusion and, in some patients, your platelets (which help blood clot) may be low and you may require platelet transfusions. Additional common side effects are tiredness, a sore mouth related to the treatment and tingling in the fingers and toes. More details will be provided of this by your doctor and nursing staff. Once chemotherapy is completed virtually all these side effects completely disappear.

What are the alternatives for diagnosis or treatment?

Hodgkin's lymphoma is a cancer for which chemotherapy would always be the treatment of choice, giving the maximum chance of cure. Chemotherapy used for the younger patients (ABVD) is too toxic for older people. However, the seven drugs used in the VEPEMB schedule are well known and have been sequenced to allow best effect, with as little side-effects as possible. We are not making any comparisons of treatments in this study but aiming to assess the protocol in a large number of patients (150), in an organised way.

What are the possible advantages and risks of taking part?

Although Hodgkin's lymphoma is a cancer which, untreated, usually causes death within a period of months, drug treatment like that recommended in this study results in cure in over half of patients. Combination chemotherapy is strongly recommended, whether or not you take part in this study. To achieve these cure rates, we have to give fairly intensive chemotherapy, which does have side effects as described above; however you will be monitored closely throughout your treatment so that any side effects can be treated promptly.

Male patients should use contraception (if relevant) during the course of this study as it is possible the treatment may interfere with the normal functioning of male sperm.

What are the possible benefits of taking part?

It is expected that receiving treatment with VEPEMB will cure a substantial proportion of patients with this form of lymphoma. We hope that the results of this study will mean that in future patients will receive effective, but perhaps less toxic treatment than before.

Accurate diagnosis of this disease is extremely important. The pathology part of the study will not benefit you directly but we hope it will benefit future patients with this condition by giving them better information on their chances of cure, and in helping to decide the most appropriate treatment.

What if new information becomes available?

In the event that a new treatment for Hodgkin lymphoma becomes available which is of advantage to you this will of course be shared with you. If a new form of therapy would be beneficial to you then this will be discussed with you and it would be possible for you to withdraw from the present study. If you chose to continue, you may be asked to sign an updated consent form.

What happens when the research study stops?

Since the study does not include new drugs and all the drugs are available for routine care, it is anticipated that the treatment schedule may become a standard treatment for Hodgkin's lymphoma in elderly patients. If it does become a standard treatment then it may be used for comparison if a new treatment were to come along in the future.

What if something goes wrong?

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 should be available to you. If you are harmed by taking part in this research project, there are no special compensation programme. 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.

What do I have to do?

The information about the treatment you received for the study will be collected from your doctor. We do not know if participation in this study will benefit you but we hope it will benefit patients in the future by giving better information on their chances of

cure and helping to decide on the most appropriate treatment. However, we would ask that you will be involved in the study by filling in a questionnaire about how you feel.

It is becoming increasingly important for doctors to be able to compare the side effects of different treatments and also to learn how patients are coping with their disease and treatment (we call this "Quality of Life" assessment). A questionnaire has been designed to obtain this information from the patient's point of view. Our intention would be to collect this information four times: before treatment, immediately after treatment has finished, 1 year after diagnosis and 5 years after diagnosis. In future this information could be used to develop support systems for patients as well as influencing treatment.

We would ask you to fill in the questionnaire both before treatment and at the follow up visits. If the questionnaire is not given to you, please help by reminding your doctor or nurse about it.

Will my taking part in this study be kept confidential

If you consent to take part in a research study such as this one, relevant aspects of your medical records will be sent, in confidence, to the SHIELD Study Group Trials Unit (SSTU). They are registered under the Data Protection Act to hold patient information in secure storage, to be accessed only by appropriate staff involved with this study. Once registered in this study, the SSTU will give your doctor an identification number which uniquely identifies you, so that your full name need not be kept on the main study database. Similarly, with your agreement, some small pathology specimens will be sent to the Department of Pathology in Newcastle. Your name and address will be removed from such specimens and any blood samples, so that you will not be identifiable other than to the SSTU, and all information from the study will be kept strictly confidential. No individual patients will be identified when the results of the study are published. Your General Practitioner will however be informed of your participation in the study.

What will happen to the results of the research study?

Approximately one to two years after the study has been completed (it is anticipated this will take at least 3-4 years) the results will be published in a recognised medical journal. The results will be available to you at this time as will a copy of the published results if you would like this. You will not be identified in any report or publication.

Who has reviewed the study?

A Multi-centre Research Ethics Committee will have approved this study, as will the Local Research Ethics Committee for your hospital.

Who is the organising this research?

The study is being organised by the SHIELD Study Group. Your clinical care will be paid for by the usual National Health Service mechanism. Your doctor will not be paid for including you in this study.

Contact for further information

Should have worries or concerns about your treatment we recommend that you contact _____ who can be contacted on the telephone number _____

Thank you for considering taking part in this study.

PLEASE NOTE: Please let your Physician know if you have any eyesight problems which prevent you for reading this document clearly. Arrangements can be made to have it read to you in an appropriate and understandable way. Similarly, if English is your second language, an interpreter can be provided.

Participant Consent Form

A phase II study VEPMB in patients with Hodgkin Lymphoma aged \geq 60 years.

The participant should complete the whole of this sheet him or herself.
 (please write your initials in the following boxes if you agree with the statement).

Please
initial here

1. I confirm that I have read and understood the information sheet dated 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, and without it affecting my medical care or legal rights.	
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from the trial team or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	
4. I understand that tumour samples collected routinely will be examined by an expert Pathologist at the Royal Victoria Infirmary, Newcastle upon Tyne and that a serum blood sample will be taken at diagnosis to be stored in Newcastle for possible use in future projects relating to the diagnosis and treatment of Hodgkin's lymphoma, as new techniques become available. These samples may be carried out by researchers other than those in Newcastle. This blood sample may be fully used in the research or in subsequent research and will be considered as a 'gift' from me to the research team. Any unused blood sample will be stored at the Study Centre in Newcastle. <u>Any new research with my blood sample will be reviewed by an Ethics Committee.</u>	
5. I agree to my General Practitioner being informed of my participation in the study.	
6. I agree to take part in the above study.	

Name of Patient _____ **Date** _____

Signature _____

Name of Person taking consent _____ **Date** _____
 (if different from researcher)

Signature _____

Researcher _____ **Date** _____

Signature _____

1 copy for patient; 1 copy for researcher; 1 copy to be kept with hospital notes.