CLL4 PATIENT INFORMATION SHEET

Introduction

You are invited to take part in a nationwide study designed to establish the best treatment for Chronic Lymphocytic Leukaemia (CLL), which affects the blood, lymph glands and bone marrow.

The trial is a comparison between :-

- the standard treatment with a drug called **chlorambucil** taken by mouth (tablets)
- a relatively new agent, **fludarabine**, which is given intravenously (into a vein) or by mouth (tablets).
- a combination of **fludarabine** and **cyclophosphamide**, both given intravenously or by mouth (tablets).

The treatment you receive will be selected by a process called **randomisation**; that is, it will not be chosen by you or your doctor, but by a computer and it is like the toss of a coin. This is to prevent bias in the results of the trial.

There is already information available suggesting that both fludarabine and its combination with cyclophosphamide may lead to remission, that is clearance of the leukaemic cells, at a higher rate than chlorambucil. However it is not yet known whether there are advantages in long term survival, quality of life and duration of the remission.

What will I have to do?

If you agree to take part in this study, you will be asked to have blood tests, a bone marrow biopsy and x-rays. These will be repeated at certain times during the study which is planned to last 5 years. You will be randomised to one of the three treatments listed above. All three treatments are given every four weeks until maximum response is achieved, then stopped. **Chlorambucil** is taken orally for 7 days each month for up to a year. **Fludarabine** is given as an intravenous injection for 5 days each month for six months, but it is also available in tablet form - you may need to take 6 or 7 tablets a day for 5 days. **Fludarabine plus cyclophosphamide** is given as an intravenous injection for 3 days each month for six months or by mouth spread over 5 days, in total you may need to take between 12 to 14 tablets each day. These treatments may continue for slightly longer if your doctor feels they continue to be beneficial. All the treatment courses will be given as an outpatient. The choice of whether you have oral form (tablets) or intravenously (injections) will depend on you, by agreement with your doctor. The efficiency is the same, but you may have symptoms such as nausea or diarrhoea with the tablets. If the symptoms are severe, the drugs may not be absorbed well and your doctor may advise you to switch to the injections. You will be asked to attend once every 4 weeks for blood tests before each course. You will be assessed each month to see whether or not you are receiving any benefit from the treatment and to make sure that there are no problems.

At the start of the study you will be asked for an extra blood sample to test for any possible faulty genes and to complete a simple questionnaire asking about your quality of life. This information will not be traceable back to an individual patient and will not affect any treatment you may have now or in the future and is intended for a study of the genetic basis of CLL. You will also be asked to complete a Quality of Life questionnaire again at 3, 9 and 12 months and once a year afterwards. This is to give us information about how the treatment affects your everyday activities. The questionnaire takes only a few minutes to complete.

You will be followed up in clinic regularly for five years after the end of the trial treatment. Some of your blood samples may be stored frozen for future research use.

What are the possible risks/benefits?

The risks and benefits apply to all arms of the trial. The major side-effect of these treatments is to lower the number of normal cells made by the bone marrow. Your red blood cells may be decreased, and it may be necessary for you to have a blood transfusion. You may also be more likely to develop infections. If an infection develops you may need to be treated with antibiotics. You may be given prophylactic (preventative) antibiotics. In addition the treatments may cause a sore mouth, nausea, vomiting and diarrhoea, tiredness and skin rashes. We can give you tablets to control most of these problems should they arise. An anti-sickness injection will be given on the first day of the intravenous combination treatment and tablets on the following 2 days. Very rarely, haemorrhagic cystitis (pain and blood on passing urine), and pneumonia have been reported. The side effects may be greater with fludarabine alone or in combination with cyclophosphamide, but this disadvantage may be counterbalanced by greater effectiveness. At present, we do not know whether the potential benefits outweigh the greater risk of infections.

Women of child-bearing potential, and all men, must use effective contraception for the duration of treatment and for six months afterwards.

Second randomisation

If the treatment you are given stops working at any stage, there is a second part to this study designed to investigate the effect of a laboratory test of drug sensitivity to decide the choice of your next treatment. The test is designed to identify which drugs will be effective and which may not be effective against your leukaemia. However, it can delay treatment for 7-10 days while the test is performed and has not been proven to be effective in prolonging survival. Hence this part of the trial will compare by randomisation:

- your physician's choice of treatment, guided by the study protocol,
- treatment guided by the laboratory results, which will be made available to your physician.

Do I have to take part?

Your participation in this study is voluntary. Refusal to participate will not affect your treatment or the relationship with your doctor. If you agree to take part and then change your mind, you may withdraw at any time without giving a reason. Treatment will be stopped if there are any unacceptable side effects or if it is clearly ineffective and alternative treatments will be offered to you. Your legal rights are not affected by giving your consent to take part in this study. Your general practitioner will be informed of your treatment with your permission. It may be necessary for your records to be inspected by regulatory bodies. Personal information about you will be kept strictly confidential and will not be seen by anyone not involved in the study.

What do I do now?

You will be given time to think about the research and discuss it with your family or friends. You can tell the doctor of your decision next time you see him/her.

For further information please contact: