INFORMATION SHEET

Name of the participant:

STUDY TITLE: A RANDOMIZED CONTROL TRIAL OF RITUXIMAB VS MODIFIED PONTICELLI REGIMEN IN THE TREATMENT OF PRIMARY MEMBRANOUS NEPHROPATHY – A PILOT STUDY

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Place of study: Muljibhai Patel Urological Hospital, Nadiad

What is the purpose of this study?

Membranous nephropathy is one of the most frequent causes of nephrotic syndrome in adults. Nephrotic syndrome is a condition where there is protein leak in the urine in excess of 3.5g per day and is characterized by edema, high cholesterol levels and increased risk of infection and clotting in vessels. MN is an immune mediated disease where antibodies affect the patient's nephrons. There are two types – primary/idiopathic and secondary. The primary MN which we will be studying this trial is usually characterized by the presence of specific antibodies called the Anti-PLA2R antibodies in 70-80% of cases. Apart from the presentation of nephrotic syndrome, patients with MN also have high risk of progression to end-stage renal disease (ESRD) when untreated.

The KDIGO (Kidney Diseases International Global outcomes) guidelines in 2012 recommended the Modified Ponticelli regimen for treatment of this disease. This therapy consists of a 6-month cycle of alternating steroids and the oral drug cyclophosphamide. While it was effective in reducing protein in urine, cyclophosphamide has several side effects including low blood counts, infection, infertility and hemorrhagic cystitis affecting the bladder. The long-term risk of cancer is also present with this drug.

Rituximab is newer drug which targets the B cells in the body that produce antibodies. Several large studies have shown that this drug is effective in reducing proteinuria in patients with IMN. The main side effect of this drug is reaction during infusion which can be prevented by premedication.

There are no studies which have done a head-to-head comparison of the two regimens in IMN. We will attempt to compare the outcomes in two groups of patients with IMN with one receiving the modified Ponticelli regimen and the other receiving rituximab. We will attempt to assess whether rituximab is non-inferior to modified Ponticelli regimen in producing remission of proteinuria 6 months after therapy.

Why have you been chosen for this research?

All patients with biopsy proven membranous nephropathy are eligible for the study provided they are positive for Anti-PLA2R on either biopsy or serology or secondary causes of MN have been rule out.

Do you have to take part in it?

Participation in this trial is purely voluntary and you may withdraw from the trial at any period. You will still receive all the services you would usually receive whether you choose to participate or not.

What is the procedure during participation in this trial?

All patients with primary MN will be given a 3 month observation period to watch for spontaneous resolution of proteinuria. Patients with severe symptoms or those with persistent proteinuria will be randomized into one of the two groups and will receive either rituximab or modified Ponticelli regimen. The rituximab group will receive two injections of rituximab 375mg/m2 on days 1 and 15. Their CD19 which indicates B cell levels will be checked at 1 and 6 months. The modified Ponticelli regimen consists of steroids in months 1, 3 and 5 which will include 3 injections of methylprednisolone on days 1-3 followed by wysolone tablet at 0.5mg/kg/day. Cyclophosphamide tablet will be given in months 2, 4, and 6 at 2mg/kg/day. All patients will undergo routine blood and urine investigations as recommended for patients with MN. This would involve drawing 5-10ml of blood during follow-up visits and providing urine sample. All patients will also undergo AntiPLA2R titres at baseline, 3 and 6 months.

What is the duration of the study including treatment and follow-up?

All patients with MN require long-term follow-up to watch for remission and relapses. Patients participating in the study will be followed up throughout the study period and for a minimum of 6 months from the start of therapy. During the initial 6 months, you will have to come monthly for reviewing the course of your disease which is routinely done in all IMN patients.

What are the passible risks to the participants?

All drugs used in this study have an established role in treatment of MN and all are associated with specific side effects. Steroids can cause weight gain, hyperglycemia, bone weakness and muscle wasting and increase risk of infections. Cyclophosphamide can cause infections, infertility, bladder problems, low blood counts as well as cancer. Rituximab is typically associated with reactions during infusion including flushing, itching and sometimes low blood pressure.

What are the benefits of the study?

The participants would receive two regimens of therapy which are routinely being used in our centre for the treatment of this disease. The study could benefit the community in assessing whether rituximab is not inferior to modified Ponticelli regimen in IMN treatment. Change in therapy from one group to another due to non-response of side effects will be at the discretion of the treating physician who will be independent of the study investigators.

What are the incentives to the participants?

There are no specific incentives in the study. However, in view of the cost of rituximab, the drug cost will be reimbursed or free samples will be arranged for patients who are unable to purchase the medication.

Whom to contact?

You can contact the following persons for more details regarding the study:

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