

National Institute for Health and Clinical Excellence
Review of TA 110:
rituximab for the first-line treatment of stage III-IV follicular lymphoma

Submission from the Lymphoma Association

The Lymphoma Association is the only national UK charity specialising in providing emotional support and information to people affected by lymphoma, their families and friends. We provide a freephone helpline, free literature, an informative website, nationwide support groups, a buddy scheme and publish a quarterly newsletter with a circulation of over 8,000.

Our constant contact with patients and their families through our helpline, messageboards, chatroom and social networking sites mean that we have a sound understanding of patients' experience and views on all aspects of their treatment and care.

The use of rituximab in combination with chemotherapy is the gold standard treatment around the world for people with stage III-IV follicular lymphoma. Not only has it been shown to improve overall survival, it has made a huge impact on the quality of life of people affected by this debilitating disease.

What is like to have follicular lymphoma?

Most people have advanced stage disease before symptoms develop and 80 – 85% of patients with follicular lymphoma have stage III or IV disease when they are first seen by their doctor. They might still be relatively symptom-free and able to lead a normal life, except that they have the burden of knowing they have a disease that cannot currently be cured. They might be aware that their lymphoma will almost certainly advance and need treatment and that their disease will follow a relapsing and remitting course. Current life expectancy for advanced disease is between 8-10 years depending on prognostic indicators such as age, performance status and disease burden.

Until patients diagnosed with follicular lymphoma become symptomatic, they are put on a watchful waiting regimen and may stay on this for many years before needing treatment. Some patients tell us that they find 'watch and wait' very difficult to cope with. This is a frequent topic of discussion on our message boards.

"Today it's a year since I was told I had follicular non-Hodgkin lymphoma and was placed on watch and wait. Apart from the odd cold and virus and a few more lumps here and there, I don't feel too bad physically. However, mentally I still seem to struggle with the whole situation. I still look at my children and wonder if I will see them grow up, leave school or go to uni, get married etc."

- posting from October 2010 on the Lymphoma Association messageboard

Advanced follicular lymphoma can cause a range of symptoms.

Most people experience **fatigue**, an experience that can be extremely debilitating and can have a significant impact on quality of life.

Fatigue can prevent a person from being able to care for themselves: it can prevent people from climbing the stairs to the bathroom; it can make it difficult to get in and out of a bath; it can make it hard to prepare a meal. Even if these things are

accomplished, an individual with this kind of tiredness might be left without the energy for other daily activities.

Fatigue results in reduced capacity to work, reduced ability to care for others, increased irritability and anxiety, increased risk of depression, reduced libido, reduced capacity for social interaction and reduced enjoyment of life.

Given the advanced age of many people with follicular lymphoma, fatigue exacerbates the problems of ageing, frailty and social isolation.

Other symptoms are wide ranging. Follicular lymphoma can involve the bone marrow, resulting in reduced blood cell production. This can result in several blood-related problems;

- A shortage of red cells which causes **anaemia** – which will worsen symptoms of fatigue
- A shortage of platelets (**thrombocytopenia**) – which can increase an individual's risk of bruising and bleeding
- A shortage of white blood cells (**neutropenia**) –which can increase an individual's risk of developing bacterial infection.

Other symptoms of lymphoma also include, drenching **night sweats, fevers**, and **weight loss**.

Follicular lymphoma can affect many sites around the body and symptoms will depend on what parts of the body are involved. For example, involvement of lungs can result in pleural effusion, causing acute chest **pain** and **difficulty breathing**. Involvement of abdominal nodes or the gastro-intestinal tract can cause **pain, change in bowel habit, indigestion** or **anorexia**.

Living with uncertainty

One of the principal psychological burdens of follicular lymphoma is uncertainty. Those with advanced follicular lymphoma live with a life-threatening condition that may never really go away.

These uncertainties can be a constant source of anxiety. Depression is a common problem for people with follicular lymphoma. Uncertainty and loss of hope in the future make it difficult for people to enjoy life.

What are the outcomes that matter most to patients?

Above all, patients want to hear most of all that they are in complete remission and that it will last as long as possible. Survival for as long as possible and getting back to as near normal a life as they can are their main hopes. The quality and duration of remission are therefore key.

The people we speak to are prepared to cope with the side effects of their treatment because the evidence shows that they can achieve increasingly long periods of progression free survival¹. Nowadays, many people live long and fulfilling lives following treatment.

No longer feeling so tired that a pint of milk is too heavy to lift up, having the energy to return to work and look after one's own children or just manage to live independently are what matter to patients.

¹ J Clinical Oncology 2008/Oct 1st Vol 26 (28): 453 – 458, Marcus et al.

What difference does the technology make?

Before rituximab was added to the standard chemotherapy regime, survival rates were considerably lower.

In addition, by selectively attacking the CD20 antigen, rituximab does not cause side effects associated with damage to other healthy cells.

People today enjoy better quality remissions that last longer and as time goes by, it is likely that people are living longer with the disease.

Research has clearly demonstrated that the addition of rituximab to combination chemotherapy is superior to chemotherapy alone. It means increased response rates to treatment, increased progression-free survival and, most importantly, better overall survival with improved quality of life.

We welcome the expansion of the product licence for rituximab to include the combination of rituximab with any chemotherapy regimen. This allows for greater tailoring of therapy, which can be based even more effectively on the individual patient's disease features, their tolerance of different classes of chemotherapy drugs and their co-morbidities.

Side effects

A patient with follicular lymphoma treated with 6 x R-CHOP at 3-weekly intervals from September 2007 wrote:

"I lost all of my hair and as the treatment progressed, I got more and more tired and my taste began to change. Fortunately I had no sickness but I did have a little constipation. The longest-lasting side-effect was peripheral neuropathy in my hands and feet, which even today hasn't totally gone away...In June 2009, I was given the chance to take early retirement and haven't looked back since. I lead a normal life where I play golf four or five times a week and generally enjoy life!" – [REDACTED]
(personal experience from the Lymphoma Association website)

www.lymphomas.org.uk

The side effects of chemotherapy depend on the individual drugs given. Common side effects might include neutropenia, anaemia, thrombocytopenia, sore mouth, loss of appetite and change in taste, nausea and vomiting, fatigue, hair loss, sore skin, peripheral neuropathy, bladder and kidney problems, reduced fertility.

The additional side effects of the addition of rituximab might be shivers, fevers, headache and flu-like symptoms, but these are most common with the first infusion and the use of paracetamol and antihistamines can prevent these side effects.

Occasionally, people can have more serious side effects to treatment and people with heart problems or high blood pressure need to make this clear to their medical team. There is also the risk of infection as healthy B-cells are damaged as well as cancerous ones. Symptoms of temperature, pain when passing urine, diarrhoea or suddenly feeling generally unwell need to be dealt with urgently as they can lead to life-threatening neutropenic sepsis if not treated swiftly.

Treatment with rituximab can also cause a recurrence of previous viral infections such as hepatitis.

Rituximab is not recommended for pregnant or breastfeeding women.

Using the technology

Rituximab is usually given with each chemotherapy cycle as an infusion over a period of 4 – 5 hours. Some hospitals suggest that patients stay in hospital overnight for their first infusion but the remaining doses can be given over a shorter period. This is generally no more inconvenient for patients than having stand alone chemotherapy.

Conclusion

Rituximab used in combination with chemotherapy is the gold standard treatment for advanced follicular lymphoma around the world. It improves overall survival and it has transformed the lives of many thousands of patients by giving them back their quality of life and longer periods of remission than had previously been possible.

Lymphoma Association
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