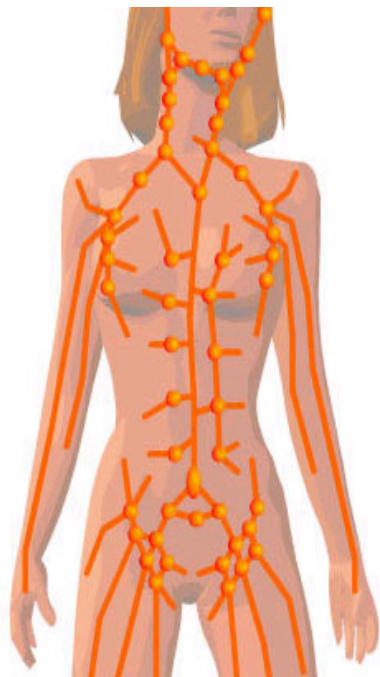


## An Overview of Non-Hodgkin's Lymphoma

### The Lymphatic System



#### Non-Hodgkin's Lymphoma (NHL): At A Glance

- NHL is the most common form of lymphoma<sup>1</sup>
- The introduction of new treatments can:
  - Improve cure rates for aggressive NHL
  - Prolong the life of lymphoma patients
  - Allow for a better quality of life
  - Provide longer time without disease
- NHL has grown in incidence by 80% since the early 1970s<sup>2</sup>
- It is estimated that 360,000 people die each year from the disease<sup>3</sup>
- Of the people diagnosed with NHL each year:
  - 55% have aggressive or fast-growing NHL
  - 45% have indolent NHL, a slow developing, recurring form of the cancer

The lymphatic system is a network of organs (bone marrow, spleen, thymus gland, lymph nodes, tonsils, appendix), tissues and ducts that serves two roles:

1. Draining fluid from cells and tissues back to the bloodstream
2. Fighting infection and cancer by distributing lymphocytes (white blood cells) around the body.

Lymphatic fluid, composed of proteins, fats and lymphocytes, circulates around the lymphatic system through a complicated network of very fine tubes called lymphatic vessels. There are two main types of lymphocytes involved in protecting the body against bacteria and viruses: B-cells and T-cells:

- B-cells mature into plasma cells, which produce antibodies necessary to fight infection
- T-cells are primarily involved in controlling cell-mediated immune reactions and B-cell activation through the production of powerful chemical substances called lymphokines

## **Lymphoma**

Lymphoma is a type of cancer that can develop when an error occurs in the way a lymphocyte is produced. This results in an abnormal cell that becomes cancerous due to endless abnormal cell replication at high speed. Like normal lymphocytes, the cancerous lymphocytes can grow in many parts of the body including the lymph nodes, spleen, bone marrow, blood or other organs.

There are two main types of cancer of the lymphatic system:

1. Hodgkin's lymphoma
2. Non-Hodgkin's lymphoma: A group of closely related cancers that affect the lymphatic system

## **Diagnosis and Symptoms of Non-Hodgkin's Lymphoma**

Non-Hodgkin's lymphoma symptoms include swollen lymph nodes (in the neck, armpits or groin), coughing, shortness of breath, unexplained weight loss, fever, profuse sweating (particularly at night) and/or severe itchiness. These symptoms, however, may also be signs of non-cancerous problems, such as infections. There are no tests for early detection of non-Hodgkin's lymphoma. If these symptoms persist, a medical consultation is essential.

## **Causes of Non-Hodgkin's Lymphoma**

The exact cause of non-Hodgkin's lymphoma remains unknown. However, research has focused on some factors that may contribute to the development of lymphoma, including genetic factors, impaired immune system and viruses, such as HIV.

## **Types of Non-Hodgkin's Lymphoma**

There are more than 30 different sub-types of non-Hodgkin's lymphoma (mainly consisting of malignant B-cells) that are categorised by several factors, including rate of growth, location and certain (histologic) characteristics of the tumour cells themselves. Disease prognosis depends on the tumour burden of the patient, number of areas in the body affected, the patient's age and others factors. These factors are considered when physicians recommend specific treatment regimens. Current treatments for non-Hodgkin's lymphoma include chemotherapy, monoclonal antibody therapy, radiation, biological treatments and bone marrow transplantation.

Exactly which course of therapy a physician recommends depends on the following three critical factors:

### 1. Stage

There are four stages of non-Hodgkin's lymphoma according to the Ann Arbor Classification, which characterise where the cancer has spread in the body:

- |           |  |
|-----------|--|
| Stage I   | Involves a single area or region, often a single lymph node and the area surrounding it. There are typically no symptoms.                    |
| Stage II  | Involves more than one lymph node area on one side of the diaphragm or one lymph node region, plus a nearby area or organ.                   |
| Stage III | Involves lymph node regions on both sides of the diaphragm and one organ or area near the lymph nodes, the spleen, or another organ or area. |
| Stage IV  | Involves one or more organs and the bone marrow or skin.   |

### 2. Bulk

Tumours that are large in size are called bulky tumours or bulky disease.

### 3. Treatment

Non-Hodgkin's lymphoma is generally classified into two groups (aggressive or indolent) with significantly different prognosis and treatment strategies for both tumour groups:

- Aggressive (intermediate/high grade) lymphomas rapidly divide and multiply in the body and, if left untreated, can be fatal within six months. However, patients who are diagnosed and treated in the early stages of aggressive disease are more likely to be cured and are less likely to have late recurrences. Traditionally, treatment for aggressive non-Hodgkin's lymphoma has been standard CHOP (cyclophosphamide, hydroxydoxorubicin, vincristine and prednisone) chemotherapy and/or high dose chemotherapy and autologous transplantation. The use of the monoclonal antibody MabThera (rituximab), in combination with standard (CHOP) chemotherapy, was approved by European Regulatory Authorities (EMA) in 2002. The approval, based upon results from a randomised phase III study, which demonstrated that treatment with MabThera plus CHOP prolongs survival and increases the chance of cure for patients compared to CHOP chemotherapy alone, has led to MabThera plus CHOP becoming the standard treatment for aggressive non-Hodgkin's Lymphoma patients.

- Indolent (low-grade) lymphomas slowly divide and multiply in the body, making initial diagnosis more difficult. Follicular lymphoma is the most common form of indolent non-Hodgkin's lymphoma. Patients may live many years with the disease, but in contrast to aggressive NHL, standard treatments cannot cure the disease. Generally, patients have high response rates with their first course of therapy, but are expected to have repeated recurrences of the cancer. Typically, a patient with follicular non-Hodgkin's lymphoma can expect to be treated five to six times over his/her life span. However, patients usually experience lower response rates with each subsequent treatment. Median survival of this form of non-Hodgkin's lymphoma, where patients eventually succumb to the disease or its complications, is approximately 6 - 10 years. In August of 2004, the EMEA approved MabThera (rituximab) in combination with CVP (cyclophosphamide, vincristine, prednisolone) chemotherapy for the first-line treatment of follicular non-Hodgkin's lymphoma. The approval was based on data from a phase III randomised study comparing MabThera plus CVP chemotherapy versus CVP chemotherapy alone, which showed that MabThera plus CVP chemotherapy significantly improved Time to Treatment Failure (TTF), Time to Progression (TTP), Overall Response Rate (ORR) and Complete Response Rate (CR) when compared to treatment with CVP chemotherapy alone.<sup>5</sup> On 6 July 2006, MabThera was approved by the EMEA as maintenance therapy for follicular non-Hodgkin's lymphoma. The approval was based on a phase III study which showed that the risk of death is halved (50% reduction) for patients with follicular NHL who received MabThera maintenance, compared to those who received no maintenance treatment, regardless of their initial therapy. The best outcome was seen in patients receiving induction therapy which included MabThera followed by MabThera maintenance: at 33 months follow-up, overall and progression-free survival were approximately 90% and 70%.<sup>6</sup>

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