

## **Herceptin video script**

### **Slide 1**

Worldwide, 1.6 million new cases of breast cancer are diagnosed each year, with over half a million deaths.

([http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx))

40 years ago in the UK, the five year survival rate following diagnosis was 50%. Today that figure is 80% thanks to advances in treatment and screening.

One of these advances is Herceptin, a breast cancer drug that reduces the chance of the cancer returning by over a third.

### **Slide 2**

Herceptin is a breast cancer drug and was the first humanised monoclonal antibody used to successfully treat cancer. Antibodies are a type of protein produced by the immune system that attaches itself tightly to a specific target, known as an antigen. Herceptin is designed to attach to another protein known as HER2.

### **Slide 3**

HER2 makes cancer cells grow and replicate faster. Herceptin prevents HER2 from working properly and causes the cancer cells to die. However, this only works for patients whose cancer has high levels of HER2 protein. These are known as HER2-positive cancers and make up around one in five breast and stomach cancers.

Herceptin was originally just used to treat metastatic breast cancer, but is now applied to early stage breast cancer. It is given alongside chemotherapy and halves the risk of the cancer coming back.

### **Slide 4**

The HER2 protein was discovered in 1982 in neurological tumours of rats.

In 1985, the first monoclonal antibodies to target against HER2 in mice showed they could reduce tumour growth and prolong survival.

### **Slide 5**

In 1987 researchers showed that extra HER2 in women with breast cancer is linked with a shorter time to relapse and lower survival rate. This meant that not only could this gene be used as a marker for prognosis, but that a monoclonal antibody could work in humans just as it did in mice.

Ref: Slamon DJ, Clark GM, Wong SG et al. Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene Science 1987; 235: 177-82

## **Slide 6**

To develop an antibody treatment to target HER2, researchers began by injecting a sample of the protein into a mouse. The mouse develops an immune response which tries to get rid of the HER2 protein by developing antibodies – Y-shaped molecules that specifically target a certain molecule.

## **Slide 7**

The B lymphocyte cells that manufacture antibodies are extracted from the mouse's spleen. These cells, like all healthy cells, have a limited lifespan. This means that they cannot be grown in lab enough to produce enough antibodies for testing. To get around this, the spleen cells are fused with human myeloma cells. These myeloma cells can replicate indefinitely and are regularly used by scientists for research.

The fused cells are called hybridomas. Once the cells have grown enough, they are screened to find a cell that produces an antibody targeting HER2 specifically. This is the hallmark of monoclonal antibodies: they are produced from a single original cell. This means that there is no mixture of different types of antibodies and all of the antibodies given to patient will work in the same way and reduce side effects.

## **Slide 8**

If this mouse antibody is given directly to humans it can trigger an immune reaction. This is because the immune system recognises that it isn't human. To get around this, the genes for producing the antibody are altered to make them more like human antibodies. By going through this, Herceptin contains 95% human sequence and 5% from mice. This is enough to evade the immune system, but keeps the important section at the tips of the antibody that recognise and target HER2.

## **Slide 9**

The newly humanised gene for the antibody is then placed inside Chinese hamster ovary cells, a common set of cells used in research. These cells can be grown in unlimited amounts and the antibodies are extracted from them and given to patients.

## **Slide 10**

Herceptin was developed in 1991, but before it could be tested in humans it was important to understand how Herceptin behaves in a living system. Monkeys and mice were used to check if Herceptin was safe and to look for dangerous side-effects. Studies in cynomolgus monkeys showed that Herceptin can pass through to embryos or foetuses in pregnant patients and can also pass through to breast milk in nursing mothers. This means that Herceptin is not routinely recommended for women in these situations.

Following these studies and clinical trials, Herceptin was first approved for treatments in 1998.

## **Slide 11**

Since 1998, Herceptin has been given to more than 1.3 million patients worldwide. Research continues to expand this to more people and to make it easier to administer the drug. In September

2013, a new formulation of Herceptin was approved in Europe that allows it to be given to patients by injection within 5 minutes rather than by the usual intravenous drip that can take up to 90 minutes.