Immunotherapy DCVax – how hopeful is this treatment for people living with a glioblastoma?

What is immunotherapy?
Immunotherapy is a broad term used for one way of treating cancer. It harnesses the power of the body's immune system to treat cancer. There have been some promising reports of a particular type of immunotherapy having an impact on brain cancer. This immunotherapy is called DCVax®-L and is produced by a biotech company called Northwest Biotherapeutics (NWBio).

What is DCVax®-L?
DCVax®-L is an immune therapy made from each patient's dendritic cells and specific biomarkers (antigens) from their glioblastoma tumour (GBM). Dendritic cells are a type of immune cell that help the body's immune system recognise and attack potentially harmful things, such as foreign invaders or tumour cells. A marker or element of the invading microbe or pathogen, or the tumour cell, is called an antigen. It is seen as a threat by the immune system and can stimulate an immune response. Dendritic cells conduct surveillance throughout the body, and when they find an antigen in the body, they alert multiple parts of the immune system to respond, including mobilizing T cells against the antigen and producing antibodies against it.

DCVax®-L is composed of a patient's own dendritic cells. A patient's immature immune cells are obtained through a blood draw, and then are matured into dendritic cells in a lab, and activated and educated to recognize the antigens from the patient's own tumour. These dendritic cells are reintroduced into the patient (by a simple injection in the arm, similar to a flu shot) to mobilise the body's own immune system to attack the GBM tumour. When reintroduced into the body, the DCVax®-L dendritic cell vaccine educates the immune system about which antigens to attack.

What did this research want to find out?
The research had two endpoints. The primary endpoint was to find out if DCVax®-L changed the overall survival of patients with newly diagnosed GBM (nGBM).

The secondary endpoint was to find out if DCVax®-L changed the overall survival of patients with a diagnosed recurrent (late stage) GBM (rGBM).

What stage is the research currently at?
Clinical trials have been completed and the results have been presented at a scientific conference in May 2022. This phase 3 trial enrolled 331 patients from 94 trial sites across the UK, Germany, USA and Canada. Phase 3 is the final phase in the clinical trial process prior to seeking regulatory approval (enabling doctors to prescribe). The last patient was enrolled in November 2015 and long term survival has been followed up to determine the survival "tail".

What do these phase 3 clinical trial results tell us?
Both endpoints were met with statistical significance. This means that DCVax®-L made a difference to the overall survival for some patients with nGBM and rGBM.

Median survival for people with nGBM who are treated with the current standard of care is about 15-17 months from surgery[1]. These phase 3 trial results show a median overall survival of 33 months from surgery for nGBM patients with methylated MGMT, and about 18 months from surgery for patients with unmethylated MGMT. Median survival is the time—expressed in months or years – at which half the patients are expected to be alive. It means that the chance of surviving beyond that time is 50 percent.

Median overall survival for patients with rGBM was 13.2 months from recurrence with DCVax®-L compared to 7.8 months in the control patients who received existing treatments.

These tables reflect another way of showing the survival "tail" in nGBM and rGBM:

Landmark survival rate (%) in nGBM measured from the date of randomisation (3 months after surgery)			
	External (N=1366)	DCVax®-L (N=232)	**Comparative increase**
36 months	15.5%	20.2%	**130%**
48 months	9.9%	15.7%	**159%**
60 months	5.7%	13.0%	**>228%**

Landmark survival rate (%) in rGBM measured from the date of recurrence			
	External (N=640)	DCVax®-L (N=64)	**Comparative increase**
6 months	64.0%	90.6%	**142%**
12 months	30.8%	54.1%	**175%**
18 months	15.9%	31.8%	**200%**
24 months	9.6%	20.7%	**215%**
30 months	5.1%	11.1%	**217%**

How safe is DCVax®-L?

According to Northwest Biotherapeutics, DCVax®-L has shown an excellent safety profile and is very easy to administer by an injection in the arm (similar to a flu shot). Just over 2,150 doses of DCVax®-L were given in the phase 3 trial and only 5 serious adverse events* (SAE) which possibly were related to treatment were recorded. Overall, the side effects were not materially different from the side effects with existing standard of care treatments alone. There were no autoimmune responses or severe immune reactions.

*Serious Adverse Events (SAEs) are serious or life-threatening side effects.

What are the next steps for this therapy?

[1] Fernandes C, Costa A, Osório L, et al. Current Standards of Care in Glioblastoma Therapy. In: De Vleeschouwer S, editor. Glioblastoma [Internet]. Brisbane (AU): Codon Publications; 2017 Sep 27. Chapter 11. Available from: https://www.ncbi.nlm.nih.gov/books/NBK469987/ doi: 10.15586/codon.glioblastoma.2017.ch11

Now that the data is mature and the results have shown a significant statistical difference for patients who are newly diagnosed, or at recurrence, the next step would be to seek regulatory approval e.g. from MHRA. If MHRA approves the therapeutic vaccine, then the final step is negotiation with the National Institute for Health and Care Excellence (NICE) for reimbursement and delivery through NHS. NWBio hopes this treatment can become widely available – NWBio does not want DCVax®-L to be seen as a niche product which is only accessible by a very few people. It has recently opened a production plant near Cambridge so that production can be matched to need. NWBio is also working on automation of the manufacturing of these personalised living immune cells, in order to bring the cost of this manufacturing down so that the costs of the treatment can be reduced over time.

When will this therapy be available?
We don't know. What we do know is that completion of the clinical trial brings DCVax®-L closer to being able to be made available as a treatment for those patients for whom it is appropriate., subject to regulatory approval. NWBio is working hard and fast to make this happen.

What can I do if I want to access this treatment in the UK now?
DCVax®-L can be accessed privately on a compassionate use basis if your physician feels it would be potentially helpful and appropriate. Please discuss with your clinical team and ask them to contact NWBio if your team would like more information. You can contact NWBio here:

Contact Northwest Biotherapeutics:
https://www.nwbio.com/contact-us/
Phone +1-240-497-9024

Is this treatment available for children?
As far as we are aware, no. These results are from an adult trial and we do not have any information about a trial of DCVax®-L for children with glioblastoma.

Will DCVax®-L work for other types of brain cancers/tumours?
DCVax®-L is designed to treat all types of operable solid tumors, but the phase 3 trial was for patients with a newly diagnosed GBM (nGBM) and for patients with recurrent GBM (rGBM).

What else do we know?

- In order to produce DCVax-L, a small sample of a patient's tumour is needed: ideally, about 2 grams, but smaller amounts (even less than 1 gram) can be used. The tumour sample can be a fresh sample at the time of surgery, or a frozen sample from a surgery already performed (but not a prior sample embedded in paraffin).
- The study took 8 years to recruit 331 patients (there was a 4-year funding gap). 92% of patients were enrolled between 2012 – 2015. Patients were followed since then for survival.
- 1599 were screened for the trial:
  - 306 patients were ineligible for the trial because pathology analysis of tumour tissue confirmed the patient did not have a GBM
  - A further 250 screened patients showed possible evidence of disease progression prior to being randomised and so could not join the trial. NWBio elected to follow 55 of these patients in an 'information arm' (outside of the phase 3 trial). Results for this population of patients who typically do poorly were encouraging.

  - 337 patients did not successfully make the vaccine, mainly due to insufficient viable tumour tissue.
  - 331 patients enrolled in the trial, so 20.7% patients who were screened.

- Those patients who have a good surgical resection of the tumour tend to do better.
- Progression free survival (PFS) was not significantly different between the DCVax®-L arm and the placebo arm. This may be because DCVax®-L caused pseudo-progression, where tumours looked like they were growing on MRI scans, but actually it was just inflammation or immune cells infiltrating the tumour site to fight the tumour (imaging technology today cannot tell the difference between real tumour progression vs. inflammation or immune cells).
- DCVax®-L is suitable for combinations with a wide range of other treatments.
- DCVax®-L can be administered in community settings as well as major cancer centres.
- When a DCVax®-L patient has recurrence, new batches of DCVax®-L can be made and the patient can continue the treatment.

See our commentary here https://brainstrust.org.uk/brain-tumour-support/navigating-your-pathway/treatment-information/therapies/#3

What does this mean?

Bottom line?

For the first time in 17 years this is the first systemic treatment that extends overall survival in people with nGBM. For the first time in 27 years, this is the first treatment of any kind that extends overall survival in rGBM. It has an excellent safety profile and noteworthy long tails of survival with 13% of people in the trial living for 5 years or more.

Ask yourself

- What specifically am I struggling with?
- What do I want to know?
- What have I found out for myself?
- What makes it hard?
- What's on the horizon?
- What are the sources of information that will help me fill in the gaps?
- Who can help me?
- How can *brainstrust* help me?

Contact hello@brainstrust.org.uk or call 01983 292405 if you'd like to speak to someone.

Other helpful links

Expertly checked and updated May 2022