Severely Affected Patients Respond to B-cell Depletion Therapy

Back in May I attended the 2011 Invest in ME Conference and heard of a potentially important discovery from two Norwegian oncologists, Dr. Øystein Fluge and Professor Olav Mella. Like many keynote medical discoveries in the past, this happened quite by accident. Uniquely though, the research concerned severely affected ME patients.

Among Dr Fluge & Prof Mella’s cancer patients was a person who also had severe ME. They were treating this person with chemotherapy, and unexpectedly found that “major CFS symptom relief” occurred. This spurred a pilot study involving a similar drug, the B-lymphocyte cell depletion agent Rituximab, “which demonstrated significant clinical response in three CFS patients”.

As a result they conducted a small clinical trial involving 30 patients. Invest in ME Conference journal advised:

“The investigators anticipate that severely affected chronic fatigue syndrome patients may benefit from B-cell depletion therapy using Rituximab induction with maintenance treatment. The hypothesis is that at least a subset of chronic fatigue syndrome (CFS) patients have an activated immune system involving B-lymphocytes, and that prolonged B-cell depletion may alleviate symptoms”.

We were asked not to speak about their findings, as the study was not yet published and journals may refuse to publish any material that has been given a public airing in advance. In October that changed, with the appearance of:

Benefit from B-Lymphocyte Depletion Using the Anti-CD20 Antibody Rituximab in Chronic Fatigue Syndrome. A Double-Blind and Placebo-Controlled Study – Fluge Ø et al. 2011; PLoS ONE 6(10): e26358

This study found that …

Major or moderate overall response ... was seen in 10 out of 15 patients (67%) in the Rituximab group and in two out of 15 patients (13%) in the Placebo group (p = 0.003).

… leading to this conclusion:  

The delayed responses starting from 2–7 months after Rituximab treatment, in spite of rapid B-cell depletion, suggests that CFS is an autoimmune disease and may be consistent with the gradual elimination of autoantibodies preceding clinical responses.

Points made by Dr Fluge & Prof Mella in their conference presentation included:

➢ In severely affected patients who do not respond to Rituximab, plasma exchange could be a pre-treatment.

➢ Response to one Rituximab treatment did not persist in the long term – however, there was a major and lasting clinical response with further Rituximab.

➢ Two new studies have been approved – including one on very severe ‘CFS’.

➢ Although the paper refers to ‘CFS’ all but two participants met criteria for ‘ME/CFS’ as set out in the Canadian diagnostic protocol (Carruthers et al., 2003). [NB: all of those who received Rituximab met these diagnostic criteria]

➢ Responding patients quickly adapted to their improved health status without the need for CBT or a graduated activity programme. This undermines the notion that there is a problem with physiological de-conditioning and abnormal illness beliefs that requires to be overcome for patients to progress.
Comments Following Publication …

From Invest in ME: The recent ground-breaking research by Professor Olav Mella and Dr Øystein Fluge *et al.* from Haukeland University in Bergen, Norway, is testament to good science performed by people who look at ME objectively and try to understand it with scientific rigour. Dr Kerr also suggested clinical trials using Etanercept and monoclonal antibodies - one of which is Rituximab - at the IIME conference 2007. … Dr Kerr received no funding to do these trials ... The silence about the Norwegian research from the BBC and UK media and government officials is deafening.

From the European ME Alliance: This research clearly shows the physical basis of ME. It also shows that patients had no difficulty in adjusting to normal life - something which makes redundant the previous attributions to psychological problems in this patient group.

From Bjørn Guldvog, Deputy Director General at the Norwegian Directorate of Health: I think that we have not cared for people with ME to a great enough extent. I think it is correct to say that we have not established proper health care services for these people, and I regret that.

From 25% ME Group Medical Advisor Dr Nigel Speight: In my opinion this research is extremely encouraging and I hope that it can be repeated as soon as possible. I don’t see why doctors in this country should not respond to requests from patients for a trial of this treatment on this study alone. The drug has been used widely by rheumatologists and transplant doctors for 10-20 years. I’ve heard that rituximab is coming off patent next year when its price should fall. The Norwegian team are proceeding with a further study and their Ministry of Health has provided some funds. Charles Shepherd (medical advisor to the ME Association) had urged our Medical Research Council to do the same but had no response. It is worth seeing the Norwegian video* on the girl who got back to cross country skiing.

By Helen Brownlie

* http://www.youtube/watch?v=ZBCXKIRBQ-s and click the ‘cc’ icon on the video bar at the bottom right hand corner of the video clip for English subtitles.

You can access the published study at [http://www.plosone.org/article/info:doi/10.1371/journal.pone.0026358](http://www.plosone.org/article/info:doi/10.1371/journal.pone.0026358)

You can read more about the Invest in ME Conference on the website: www.investinme.org Conference presentations, including the talk by Dr Fluge & Prof Mella, can be viewed on the invest in ME Conference DVD, available for £14 from Invest in ME. You can order via the website, or from Invest in ME, P.O. Box 561, Eastleigh, Hampshire, SO50 0GQ

The pre conference talks by Hillary Johnson and by Dr Iain Gibson were inspirational. Dr Gibson has been instrumental in progressing Invest in ME’s proposal to set up a UK Centre of Excellence for biomedical research into ME and the examination of patients. He said that this was ‘one decision away’. Unfortunately a stumbling block is that the Norfolk and Norwich University Hospital is unwilling to allow a consultant to work on this, despite NHS Norfolk agreeing to fund the post. (Eastern Daily Press 23rd June 2011). You can read more about this on Invest in ME’s website.