INTERVIEW

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Gavin Giovannoni on why time matters in multiple sclerosis

Gavin Giovannoni* was appointed in November 2006 to the Chair of Neurology, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London and the Department of Neurology, Barts and The London NHS Trust (all UK). In September 2008, he took over as the Neuroscience and Trauma Centre Lead in the Blizard Institute. Gavin did his undergraduate medical training at the University of the Witwatersrand, South Africa, where he graduated *cum laude* in 1987. He moved to the Institute of Neurology, University College London, Queen Square, London (UK) in 1993 after completing his specialist training

in neurology in South Africa. Following 3 years as a clinical research fellow, under Professor Ed Thompson, and 2 years as the Scarfe Lecturer, working for Professor W. Ian McDonald, Gavin was awarded a PhD in immunology from the University of London (UK) in 1998. That year, he was also appointed as a Clinical Senior Lecturer, Royal Free and University College Medical School (UK), and in 1999 he moved back to Institute of Neurology, Queen Square (UK). He was promoted to Reader in Neuroimmunology in 2004. His clinical interests are multiple sclerosis (MS) and other inflammatory disorders of the central nervous system. Gavin is particularly interested in clinical issues related to optimizing disease-modifying therapies in MS. His current research is focused on Epstein–Barr virus as a possible cause of MS, defining the ‘MS endophenotype’, MS-related neurodegeneration, MS biomarker discovery, MS clinical outcomes and immune tolerance strategies. His team focuses on translational research and therefore has an active clinical trial program.

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Q What inspired you to work in the field of inflammatory disorders with a particular interest in multiple sclerosis?

On entering medical school I wanted to specialize in psychiatry, but soon realized it was not the field for me. However, my first encounter with a real patient in 1985, a lady in her mid-40s with multiple sclerosis (MS) was a transformative experience. At this time, there were no treatments for MS, and the uncertainty of life with the disease really struck me. Approximately 18 months later I decided to become a neurologist, and I have since dedicated my career to studying MS and developing effective treatments for people with MS.

Q What would you describe as the biggest achievement of your career to date?

I think that my biggest achievement has been my involvement, as part of the larger community, in clinical trials. Ultimately, delivering highly effective therapies to market is what has transformed MS care.

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Q How has multiple sclerosis care changed over the course of your career?

Massively. Prior to the first disease-modifying treatments all we could offer was diagnosis. We could manage relapses using steroids, but we would ultimately watch people deteriorate over time. Individuals were always on the ward with terrible relapses, undergoing rehabilitation and physiotherapy.

Now we are beginning to see a significant change in the natural history of the disease; it is unusual these days to see disabling attacks if you start individuals on therapy early enough. We are not passive anymore, we are not just watching the disease; we have hope and we can offer our patients hope. Plus, after the latestECTRIMS meeting (7–10 October 2015, Barcelona, Spain) and the positive trial results of ocrelizumab, we can now offer some hope to people with primary progressive MS.

Q Following the release of initial data from the Phase III trial of ocrelizumab, can you tell us a bit more about this trial?

There were three trials, two in relapsing MS and one in primary progressive MS. We expected the relapsing trials to be positive based on the Phase II data. But when the results were confirmed it was even better than we had hoped because, while the efficacy was still very high, the safety profile of the drug was also very favorable.

The third benefit of this particular compound is that the monitoring requirements have dropped compared with those for other therapies in this category. This makes it a real game changer in the sense that we have a high-efficacy drug that looks relatively safe with very little monitoring, making it feasible for widespread use.

Q What will be the next steps in making this drug available?

Well it is now in Roche's hands and they will need to submit it to the European and US regulatory authorities. They will primarily need to clear the hurdle of obtaining a license so that it can be offered as a first-line treatment.

Once it is licensed the company will need to decide how much to charge for the product and for me this is a pivotal issue. Ultimately the payers are concerned with cost-effectiveness, so if ocrelizumab is more expensive than other available drugs there is a real chance it will only be offered to people with very severe MS. In this

case, the majority of people who could benefit from it early would not get the chance. It all comes down to pricing.

Q Can you tell us a bit about the MS Brain Health initiative, & your role within it?

The MS Brain Health initiative [1] is a consensus campaign calling for widescale changes in the management of MS, and I am the chairman of the committee that runs it. I was invited to be the lead author by Oxford Health Policy Forum, the policy practice of Oxford PharmaGenesis. They had been following my blog [2] and realized that the MS space could benefit from a policy document, particularly because of the multitude of issues around delays in providing people with treatment and access to more effective therapies. We developed a business case, brought together a group of interested individuals and succeeded in securing funding. The underlying premise is that MS, like any other neurodegenerative disease, needs to be treated early before brain loss has progressed too far – there is much to gain from starting a therapy early in the disease.

Q 'MS Brain Health' recently published a consensus report. Can you outline some of its aims and recommendations?

The aim of the document is to help reduce the delays in getting people with MS onto appropriate therapies in order, essentially, to protect their brains. The main recommendation is early diagnosis, which means reviewing the delays in getting people into the system. The second recommendation is to focus on disease-modifying treatments but also on the lifestyle factors that adversely affect brain health, including lack of exercise, poor diet and poor sleep. Finally, a major global problem is poor access to treatments, owing to high costs; we are trying to encourage the community to find cost-effective solutions so that people can access effective drugs.

Q You mention improving the speed of diagnosis for MS patients in order to intervene early; how can this be achieved?

We need to work on efficient systems of referral. Obviously it is a resources issue, so healthcare systems need to make more money available to pay for neurologists, MS experts and diagnostic tools. In resource-rich countries it is not really an issue; we just need to invest in MS services.

Q In terms of treatments for MS, do any recent or forthcoming advances have you excited?

Apart from ocrelizumab for primary progressive MS (which is obviously a tremendous advance), we are generally not treating the progressive phase of the disease adequately. The exciting next phase of our treatment paradigm is the generation of emerging drugs that could be used in combination with existing anti-inflammatory drugs to try to delay this progressive phase.

Q What should be the priorities in MS over the next 5–10 years?

One of our biggest problems is the slow adoption of innovation. A large number of neurologists are very conservative: they are not prescribing therapies for MS actively enough and it is hard to re-educate the community. The MS Brain Health document I mentioned earlier also deals with the problem of education; how do we make people aware of the issues and get them to adopt innovation more quickly? The next phase will be the development of combination therapies targeting different processes occurring in MS, what I call the therapeutic pyramid: we need to build on anti-inflammatory drugs to provide neuroprotection. Above that we will need remyelination strategies, which are being developed right now. Finally, we need something that helps to restore function (this is largely science fiction at the moment but there are people working on neurorestorative therapies).

We must not forget that there is a whole tranche of people living with MS in low-income countries who do not have access to even the

most basic diagnostic tools or to high-cost drugs. This is the big elephant in the room: how do we address the treatment needs of people in resource-poor countries? One solution would be for ‘big pharma’ to provide these expensive drugs cheaply, but I think it needs a policy or a lobbying initiative in these countries. Of course, there are a lot of effective therapies that have never been licensed because they are off-patent, so how do we repurpose and get people to use these off-patent drugs in MS without the financial incentive to invest in them to get a license?

Disclaimer

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Financial & competing interests disclosure

G Giovannoni is a steering committee member for AbbVie’s daclizumab trials, Biogen-Idec’s BG12 and daclizumab trials, Novartis’ fingolimod and siponimod trials, Teva’s laquinimod trials and Roche’s ocrelizumab trials. He has received consultancy fees from Biogen-Idec, Merck-Serono, Novartis and Genzyme-Sanofi advisory board meetings, GSK’s Phase 3 MS trial programme and Synthon BV DSMB activities. He has received honoraria for speaking at Genzyme-Sanofi and Biogen-Idec meetings. G Giovannoni has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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