

OrphaNews Europe: 15 July 2005

Interview with Dr Bruce Morland, paediatric oncologist and Clinical Director at Birmingham Children's Hospital, UK

1) What are the main problems encountered by clinicians wishing to conduct clinical trials in rare diseases?

BM - By definition because of the rarity of these conditions it is essential to build up networks of clinicians in order to have sufficiently large numbers of patients to conduct trials. Clinical trials need numbers. To date we've not been very good at looking at new methodologies for conducting trials with small numbers and this needs to change. Many of us though have a traditional grounding in large trials and lack the knowledge to undertake small trials. There also needs to be a wider recognition within peer groups and regulatory bodies that small trials in rare diseases can be powerful and informative. The world of academia is competitive e.g. the push to publish first on a topic. This "culture" is somewhat counterintuitive when it comes to collaborative links necessary to run trials. We struggle to organise collaborative clinical trials in major disease groups e.g. adult cancer, where numbers are never an issue, why is this?

2) Are academics reticent to develop collaborations with industry in this field?

BM - Absolutely not! It is impossible for academic groups to develop drugs for humans without the input from industry. The regulations around medicinal product manufacture means it's a very expensive process which academic groups simply can not afford. Long gone are the days when you could squirt something into patients you cooked up in your lab earlier that day! (Thank goodness!). However are industry really interested in rare diseases? Many would say no, they're after big bucks, and whilst orphan designation addresses this to some degree it's interesting big Pharma companies haven't engaged with rare diseases to a great extent....why? Putting industry in contact with the right clinical research teams and visa versa is not easy. It usually relies on ad hoc individual person-person contact and is too unstructured to be efficient. Networks clearly help but even where they exist linking to industry is haphazard.

3) How can clinical trials networks for rare diseases be encouraged in Europe?

BM - Pick one or two disease groups that have potential. i.e. already some academic links, pharma engaged, patients keen, perceived need and invest centrally from the EU without the need for several Brazilian rainforests to be destroyed in the process! There needs to be some strategic co-ordinated vision. FP6/7 doesn't step back and look at the bigger picture. A European childhood cancer network would be a great example to work with because a lot of the individual components are there already but needing some "glue" to stick all the pieces together. The lessons learnt from establishing such networks could then be applied to many other disease groups. Perhaps "rare" diseases could be made less rare by pooling together with other rare disease with common themes making much more efficient use of funding. In my field for example a network of childhood cancer would be much more powerful than a single network for neuroblastoma, another for Wilms tumour, another for medulloblastoma etc.

4) What effect has the EU directive on clinical trials had on the promotion of clinical trials in rare diseases?

BM - In a word disaster! The hoops necessary to open a clinical trial today are much greater. I'm not convinced what we were doing previously was honestly any worse in terms of safety to patients! However what has happened is that significantly fewer patients have had access to new experimental therapy since the regulation was implemented!

However the amount of red tape is the same for a trial of 10 patients with a rare disease compared to a big trial of 1000 patients. This can't be right. Individual research groups who may only enter 1 or 2 patients with a rare condition into a trial just don't have the time/energy to prioritise these small trials and patients are therefore getting ignored in the process. My intelligence tells me that in the last year even the numbers of big clinical trials opening has significantly reduced because of the bureaucracy involved. What hope is there for small trials in rare diseases?

5) What, in your view, needs to happen to encourage more academics to play their part in translating new discoveries into safe and effective treatment for rare diseases?

BM - Funding is the key to any academic programme. Recognition of the importance of rare diseases in the overall health economy is vital, and I think that message is getting across slowly. However there are literally thousands of rare diseases, so how do we prioritise research strategies? If, for example there is a very strong and powerful research group looking into rare disease "A" they are likely to attract funding, especially if they are publishing work in peer reviewed journals. Success tends to breed success. But from a health economy rare disease "A" may not be seen as a priority. There may already be effective therapy, or conversely no hope of a major breakthrough in therapy in the foreseeable future. Perhaps we should invest in rare disease "B" where a small single-handed researcher is on the cusp of a major discovery that will lead to new, and so far unavailable therapy? But how does the small voice of researcher B get heard over that of major researcher A? As a society how do we decide that B is a better investment than A in terms of resource? Clearly any patient with either A or B will have strong opinions! But research is not simply about treatments. Other forms of academic research such as epidemiology, basic biology, prevention etc. have a role too. So how do we prioritise these over therapeutic research?

I would favour a focus on significant investment into a few rare diseases where it is felt a particular research strategy would have REAL benefits to patients. This needs to be hypothesis-driven research with clear aims at the start, not some hopeful fishing exercise for an answer! This I recognise has serious implications in that if you are not one of the "chosen few" rare diseases you will understandably be upset. However the ability to translate generic lessons learned from focused research into a few will I feel be of long term benefit to the whole.