

'BRAINSTORMING' ENZYME REPLACEMENT THERAPY & NEW for LYSOSOMAL STORAGE DISORDERS

Group 2:

MPS-II (Hunter syndrome)

As with MPS-I, there is a wide spectrum of clinical severity in MPS-II, from physical symptoms to progressive brain disease.

Clinical trials of enzyme replacement therapy for MPS-II are being planned.

Group 3:

MPS-III (Sanfilippo syndromes)

MPS-III comprises a sub-group of four disorders, commonly known as types A, B, C and D. Whilst all four disorders exhibit physical problems, this group is primarily characterised by progressive brain disease.

Clinical trials of enzyme replacement therapy are currently not being planned for these disorders.

Group 4:

*MPS-I (Scheie syndrome);
MPS-II (Hunter syndrome);
MPS-IV (Morquio syndrome);
MPS-VI (Maroteaux-Lamy syndrome)*

Some MPS disorders exhibit primarily physical symptoms, such as bone and joint problems, without progressive brain disease. Because of this, these disorders are commonly referred to as 'mild'. This is a largely artificial division, however, which does not accurately reflect the progressive severity of clinical problems experienced by this group of patients. This group includes some patients affected by MPS-I. Both forms of MPS-IV are characterised by significant bone and skeletal changes and short stature, as is MPS-VI.

Clinical trials of enzyme replacement therapy have commenced for MPS-I and MPS-VI, and are being planned for MPS-II.

Q: Who would avail themselves of enzyme replacement therapy, if available?

Participant comments: The majority of participants stated that they would take-up the opportunity of enzyme replacement therapy, if available. The potential for an improved quality of life was seen as its primary benefit, particularly increased independence, decreased pain and halting or reversing disease progression. It is generally seen as a step towards a permanent cure, not a cure in itself, but one that would prolong the life of a child and reduce their disease burden until such time as a permanent cure is available.

Those who indicated they would decline enzyme replacement therapy were concerned that it may adversely affect the rate of deterioration. Further concerns related to the financial, social and emotional costs that may be associated with treatment.

There were general concerns associated with enzyme replacement therapy. In particular, this centred around the uncertainty that still exists with this therapy, its benefits and risks, and the lack of available data on its efficacy. Many felt that enzyme replacement therapy did not yet offer a 'cut and dried' solution.

Q: What are your major issues concerning enzyme replacement therapy?

Participant comments: Enzyme replacement therapy was generally considered by participants to pose less medical risk than bone marrow transplantation. There were concerns about its implications, however, such as the absence of data on its side-effects and long-term effects, the safety of the treatment, and mortality and treatment complication rates.

Other issues of concern that were highlighted include:

- the perception that many children seem to be beyond the age where therapy could be of benefit; this was also expressed in terms of eligibility for receiving treatment if the child is beyond a certain age;
- access to therapy may ultimately be a financial one for families;
- medical ethics and accountability of those proposing the treatment;
- pressure to start therapy and remain on it, irrespective of personal beliefs and decisions;
- the frequency of enzyme infusion and the effects of mutations upon its effectiveness and use;
- the need to have an idea of disease severity and progression;
- problems related to extending life expectancy;
- being at the 'cutting-edge' and the reliance of patients and parents on medical 'pioneers' in this field

Group 1 participants drew attention to the political aspects of therapy, such as issues concerned with financial support to enable access to therapy; 'fast-tracking' drug availability; the use of the media in promoting lysosomal storage disorders, and drawing experience from other groups (e.g. HIV/AIDS activists).

Groups 2 and 3 had particular concerns about the practicalities of administering enzyme to a child where behavioural problems are a prominent issue, and the continued impact upon family resources this would entail, for example one parent having to remain at home for this purpose.

Q: What is your reaction to enzyme replacement therapy if it prolonged your child's life without demonstrating much improvement in quality of life?

Participant comments: A variety of responses were received to this question. A parallel was drawn between the option of enzyme replacement therapy and a time when parents were in the dilemma of considering bone marrow transplantation for their child.

The central issue of concern is the potential for enzyme replacement therapy to prolong life and improve the disease burden in body tissues, but not necessarily halt progressive brain disease.

Group 2 noted that studies to date do not provide an answer as to the likelihood of this particular outcome.

In Group 3, 80% of participants stated they would not use enzyme replacement therapy

in this situation. Some felt that since enzyme replacement therapy for MPS disorders with progressive brain disease seemed to be a "long way off", research into other, more practical options may be more beneficial. These options included developing more effective calming techniques and behavioural management.

Participants in Group 3 considered that their current "path" is somewhat clearer than for families with MPS-I for example, where therapy is being trialed and may offer benefit to some patients, but possibly not those with neurological dysfunction. This was seen as a cause of significant "distress" to parents. It also raised a potential point of conflict between the 'haves' and 'have nots', and the difficulties this could raise in families with more than one affected child.

Some participants felt that the option of taking up enzyme replacement therapy in this situation may depend upon the stage of the disorder, and the hope that it offered to prolong life with the expectation of the development of more effective treatments.

On-going access to professional assistance is seen as important, particularly in relation to expectations of disease progress and assisting families in decision-making. The need for professional honesty is an important issue. It is recognised that decisions about whether to commence or prolong therapy under these circumstances are personal and should be respected, irrespective of the outcome, but it was noted that pressure may arise to adopt the course towards therapy because "others are doing it". Group 2, in particular, noted that if it becomes clear that enzyme replacement is not having a beneficial effect upon brain disease, families would like the right to withdraw from treatment.

Concerns were raised in Group 2 about the on-going community cost of using therapy that is unlikely to result in an improved quality of life, and philosophical questions about the value of human life. This reflected a general concern amongst the groups that decision-makers may rely on the financial aspects of treatment rather than on medical/social/emotional grounds when making a decision about whether to commence or continue treatment, without considering the potential impact upon the patient and family.

A particular concern of families where progressive brain disease is a significant problem relates to the increased life expectancy offered by enzyme replacement therapy, and the on-going difficulties parents would face without continued support and respite services. There is recognition that the burden of care may not decrease as both the child and parents age.

Q: Reflect on your own position. Newborn screening: what would you think of having the diagnosis completed at one-month of age?

Participant comments: Most participants would wish to have the option of newborn screening if therapy was available for a particular disorder, or if the promise of therapy was on the horizon. There was recognition that early diagnosis would require accurate knowledge of the disorder and its likely progression. The impact on families of individuals missed on newborn