Canadian Fabry Disease Initiative

Dr. Michael L. West
Division of Nephrology, Department of Medicine
Dalhousie University
Halifax NS
Disclosures

Dr. West has received research funding, speaker’s fees and/or consultant fees from the following:

Alexion  
Amicus  
AvroBio  
Excelsior Pharma  
Glaxo Smith Kline  
Idorsia  
Protalix  
Sanofi-Genzyme  
Shire  
Sumitomo Pharma
CFDI

• Fabry disease inherited lysosomal disease due to decreased activity of enzyme alpha-galactosidase A with accumulation of glycosphingolipids in all tissues resulting in neuropathic pain, kidney failure, decreased sweating, heart failure, strokes with reduced survival

• Rare metabolic disease (except in Nova Scotia)

• 2005 two recombinant human enzymes licensed in Canada; both not recommended by CDR due to lack of clinical outcomes data, high cost

• 82 patients on enzyme replacement therapy (ERT) in special access programs, created national demand for access
CFDI

• Group of Canadian Fabry experts invited in 2016 to create Fabry disease study at request of P/F governments

• Goals
  • Provide ERT to all who will benefit from this therapy
  • Determine safety of ERT
  • Determine clinical outcomes on ERT
  • Compare two versions of ERT: agalsidase-alfa (Replagal®), agalsidase beta (Fabrazyme®)
  • Define the natural history

• Funding evenly shared between government/Shire/Sanofi-Genzyme

• Renewed every 3 years
## CFDI

<table>
<thead>
<tr>
<th><strong>Pro</strong></th>
<th><strong>Con</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>484 patients, 10 years of prospective data on Fabry disease outcomes; 224 patients on ERT</td>
<td>Cost $1M/yr vs. $46.9M/yr ERT</td>
</tr>
<tr>
<td>Established 5 centres of excellence, 9 subsites</td>
<td>Fabry natural history only partially defined</td>
</tr>
<tr>
<td>Formalized Fabry disease treatment guidelines and annual updates</td>
<td>Inadequate statistical support</td>
</tr>
<tr>
<td>All patients vetted to ensure meet treatment guidelines; ERT withdrawal criteria developed</td>
<td>World wide shortage Agalsidase beta 2009-2012; 36 patients switched to Agalsidase alfa 2010</td>
</tr>
<tr>
<td>Annual renewals of drug therapy</td>
<td>CIHR oversight not started until year 2</td>
</tr>
<tr>
<td>Ordering of drug therapy on behalf of participating jurisdictions</td>
<td>Federal government support, CIHR oversight only to year 3</td>
</tr>
<tr>
<td>Sept 2014 all P/T agreed to cover ERT for FD based upon CFDI outcomes data</td>
<td>Delays in contract renewal caused funding interruption of up to 18+ months</td>
</tr>
<tr>
<td>2 publications, 17 abstracts, 2 manuscripts in preparation</td>
<td>Slow publication</td>
</tr>
<tr>
<td>Most complete prospective database on Fabry disease</td>
<td>Agalsidase alfa and beta both unlicensed 2010</td>
</tr>
<tr>
<td>New disease causing GLA genotypes discovered</td>
<td></td>
</tr>
<tr>
<td>Minor outcomes differences identified between ERT versions</td>
<td></td>
</tr>
<tr>
<td>Provide QA data to provinces re ERT use, no safety issues</td>
<td></td>
</tr>
</tbody>
</table>
CFDI

• New paradigm for DRD
• Clinical outcomes data collected at request of government in support of reimbursement; supported re-licensing of agalsidase
• Manufacturers able to ‘sell’ drug before official reimbursement
• Shared costs of CFDI between manufacturers, governments
• Treatment guidelines established, reviewed yearly
• ERT only for those meeting treatment guidelines
• Indirect support for clinical centres of excellence to support patient care
• Supported ERT during periods of no drug licensure, shortage
• Cost reasonable vs. estimated $469M ERT cost over 10 years
CFDI Investigators
Dr. M West, Dr. D Bichet, Dr. M Iwanochko, Dr. A Khan, Dr. S Sirrs

Associate Investigators
Dr. A. Chan
Dr. S. Dyack
Dr. C. Rockman-Greenberg
Dr. S. Jain
Dr. J. MacKenzie
Dr. B. Maranda
Dr. M. Inbar-Feigenberg
Dr. C. Morel
Dr. S. Murphy
Dr. C. Prasad
Dr. L. Turner

Research Coordinators
K. LeMoine
D. Menon
K. Courtney
L. Hebert
K. Rideout
C. Fortier
C. Barr
S. Wasim

DSMB
Dr. D. Moore
Dr. B. Chodirker
Dr. A. Willan

Data Clerks
N. Praught
A. Thomas

Data Analysis
J. Whyte

Metabolite Assays
Dr. C. Auray-Blais

DNA Analysis
Dr. D. Sinasac

Statistical Analysis
S. Doucette

Financial Sponsors
Sanofi-Genzyme
Shire, Amicus

Governments of the Canadian provinces and territories

CIHR grant # 200605FAB-167550-RTC-ADHD-119507

Thank you to the Canadian Fabry Association, patients and their families