

Recommendation to DACHDNC for Screening for Pompe Disease

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Decision Matrix

Net Benefit	Certainty	Feasibility	Readiness		
			Ready	Developmental	Unprepared
Significant	High	High or Moderate	A1	A2	A3
		Low		A4	
	Moderate				
Zero to Small	High or Moderate				
Negative					
	Low				

Infantile Form

- **Screening results in earlier diagnosis than clinical identification**
- **Earlier treatment with enzyme replacement therapy (ERT) results in better outcomes for infants**
- **Infants identified through screening and treated with ERT have better outcomes than historical controls**

Screening test function

- **Extremely high sensitivity for infantile form**
- **With two stage confirmation, extremely high specificity (e.g. Taiwan)**

Applying Decision Matrix to Infantile Form

- **Significant benefit**
 - 13 lives saved in birth cohort of 4 million
 - 26 individuals survival off ventilator
- **High certainty**
 - Likelihood that additional science will change results very small
- **Test highly sensitive and specific**
- **Move to feasibility**

Considering “Late Onset”

- **What is the appropriate threshold/criteria in considering impact of identification of later onset?**
 - **A. Significant benefit/high or moderate certainty or**
 - **B. Any non-negative benefit, moderate certainty (i.e., moderate certainty of absence of harm), or**
 - **C. Any non-negative benefit, moderate certainty (i.e., moderate certainty of absence of harm) with guidance to undertake studies to assess optimal management**
- **We recommend “C” as the appropriate threshold**

Benefit/harm of identification of late onset

- No direct data on impact of treatment prior to onset of symptoms
- Treatment after diagnosis results in improved function (PFT's and walking distance)
- Biologic plausibility of benefit of early treatment
- Harm of treatment vs. placebo:
 - Overall similar symptom profile
 - + allergic reaction
 - + antibody development

Additional Considerations for “Late Onset”

- Credible hypothesis that treatment prior to symptoms or clinical diagnosis beneficial (but no data)
- Harms likely minimal (although non-zero) given safety record
- Lived experience of difficulty of prolonged diagnostic odyssey and preference for early knowledge
- This provides optimal context for trial of alternative strategies re: early treatment

Readiness/feasibility

- **No major impediments to implementation**
- **Limitations exist in current state readiness**
 - **Training, staffing**
 - **Purchasing or modifying equipment**
 - **Arranging treatment referral network**

Overall Recommendation

- **Add to RUSP (A2) based on significant benefit of identifying infants**
- **1-5 year roll out to enable states to obtain equipment, train staff and develop referral networks**
- **Support trial/study of alternative strategies re: early treatment of late onset disease**