Setting Priorities and Taking the Next Steps

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State of Play

Progress in treating DMD
• Corticosteroids
• Neurohumoral modifiers for CHF (Congestive Heart Failure)

Progress in potential for treating DMD
• Ultimate therapies – gene therapy, stem cell therapies
• Customised therapies – AON (antisense oligonucleotides), PTC (post-transcriptional control)
• Muscle therapies – promoting muscle growth
  - impairing muscle breakdown
  - reducing muscle inflammation
What we have discussed

Needs
Considerations
Limitations
Next Steps
Biomarkers of disease progression possibilities include:

- **SCK** (serum creatine kinase)
- **Osteopontin** (glycoprotein and phosphoprotein secreted by NKT cells)
- **cTn1** (cardiac troponin 1)
NEED

Functional outcomes

- What are the endpoints?
- Animal models
  - does treatment improve function?
  - how well could it translate?
NEED

Functional markers
- Echo vs MRI?
- QMT (quantitative muscle testing) vs MMT (manual muscle testing) vs walking vs stair climbing

Clinical endpoints
- What is our benchmark? Is it steroids?
LIMITATION

Limited number of patients and some are “specific trial focussed”

- 15% interested in PTC and gentamycin trials
- hot spot mutations interested in AON trials
- steroid naïve trials??
CONSIDER

Introduction of culture for:
- rationale involvement in clinical trials
- tissue biopsies - standards need to be developed and agreed upon for appropriate tissue collection, repository and distribution especially as biopsies are required less for genetic diagnosis
- tissue harvesting (autopsy) – is this feasible? -How would this be dealt with from an ethical and emotional perspective?
Next Steps

What is the goal of therapy?

- To buy time
- Consider treatment for a chronic illness
- Can we delay onset of symptoms?
  - Prednisone
  - ACE inhibitors
  - Anti-inflammatory therapies in Multiple Sclerosis?
Next Steps

When do we intervene?
- Th1 (helper T) cells are involved in acute phase
- Th2 (helper T) cells are involved in adult phase
- P188 (triblock copolymer) considered initially for acute events
- Lessons from steroids – starting younger and younger
  
  ACE inhibitors?

This should drive research efforts with respect to age of mice that we utilise
Next Steps

Cardiac

- absence of reserve
- effect of fibrosis
- extent of inflammation at specific ages
Next Steps

What can we learn from other diseases?
- Rheumatoid Arthritis, Multiple Sclerosis, myositis etc
- Cardiomyopathy researchers are investigating cytokine therapies in addition to neurohumoral blockade.

What drugs are being used successfully?
- ie benefit:risk/adverse-effects ratio

What about TNFα (tumor necrosis factor) antagonists?
- Skeletal vs cardiac benefits.

Ideally treatment should improve both
- Satisfactory for drug to improve one and be neutral to the other
- Unsatisfactory for drug to improve one and be detrimental to the other