Donald B. Sanders

Cost of Drugs for Neuromuscular Disorders

Disclosure

- Dr. Sanders is a consultant to Accordant Health Services and Jacobus Pharmaceutical Co.

Cost of Drugs for Neuromuscular Disorders

- Health care costs for MG & CIDP
- Financial consequences of the Orphan Drug Act
- Potential financial consequences of competing trials for an Orphan Drug

The Estimated Cost of Treating Myasthenia Gravis in an Insured US Population

ESTIMATED COST OF TREATING MYASTHENIA GRAVIS IN AN INSURED U.S. POPULATION

JEFFERY T. GUPTILL, MD,[1] BAL K. SHARMA. PhD.[2] ALEX MARANO. BS.[2] ALISON SOUCY, BS,[2] ANDREW KRUEGER, MD,[2] and DONALD B. SANDERS, MD[1]

Muscle Nerve **45:** 363–366, 2012

- Costs for treating MG paid by US health plans in 2009 were determined from a comprehensive health-care insurance database.
- To determine MG-related costs, 119 MG patients were matched with 339 non-MG patients to determine non-MG related health-care costs for this population.

ESTIMATED COST OF TREATING MYASTHENIA GRAVIS IN AN INSURED U.S. POPULATION

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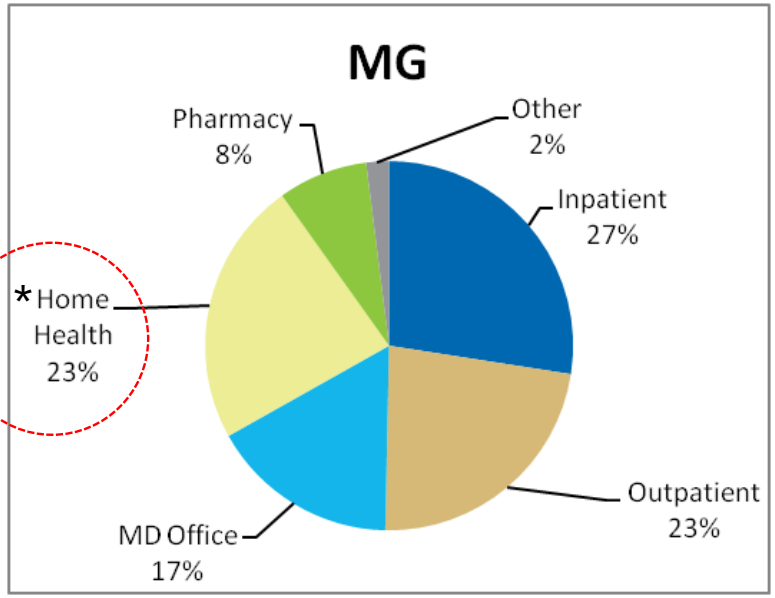
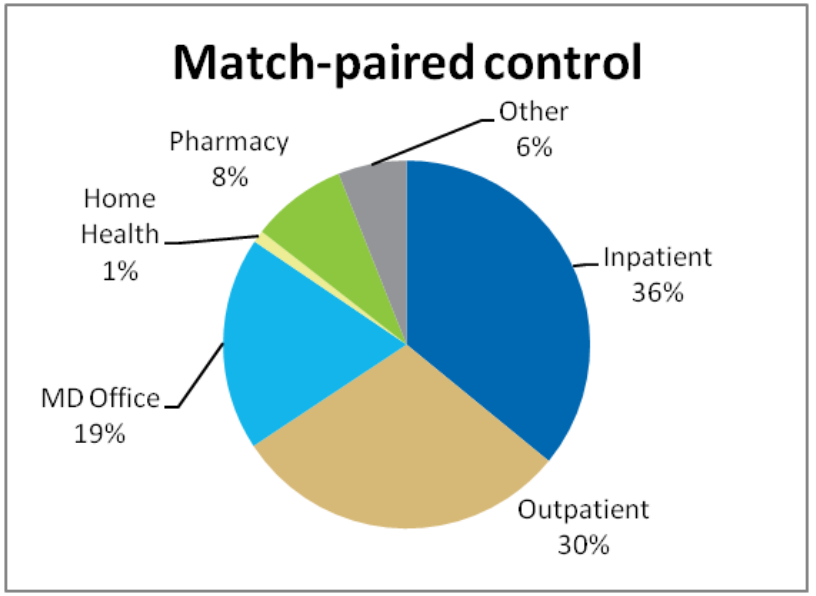
Muscle Nerve **45:** 363–366, 2012

- Costs attributed to treating MG: $15,675
- Home health costs were 23% of total
  - Almost exclusively IVIg
- 6 patients had total of 136 IVIg infusions costing $109k/patient/year

Health-plan paid costs by place of service for 113 MG patients and 339 matched controls.





Annual paid/patient:

$20,190 $4,515

**IVIg infusion costs are included in home health costs.*

COST ANALYSIS OF MYASTHENIA GRAVIS FROM A LARGE U.S. INSURANCE DATABASE

Muscle Nerve **44**: 907–911, 2011

JEFFREY T. GUPTILL, MD,[1] ALEXANDER MARANO, BS,[2] ANDREW KRUEGER, MD,[2] and DONALD B. SANDERS, MD[1]

- Costs for treating 1,288 MG patients paid by US health plans from 6/1/2008 to 6/30/2010 were determined from a database containing comprehensive health-care insurance data from 6 million patients.
- “Pharmacy” costs were $9.4M for these patients (43% of total health-care costs).

Medications used most frequently by 1,288 MG patients

Name	% of patients
Acetylcholinesterase inhibitors	80%
Opioid analgesics	51%
Corticosteroids	50%
Ulcer drugs	40%
Lipid-lowering drugs	38%
Anti-hypertensives	38%
Non-corticosteroid immunosuppressives	29%
Azathioprine	17%
Mycophenolate mofetil	13%
Cyclosporine	3.5%
Methotrexate	1.4%
Tacrolimus	0.9%
Cyclophosphamide	0.2%
Antidepressants	29%
Non-steroidal anti-inflammatory drugs	28%
Diuretics	28%
COPD, asthma drugs	24%
Bisphosphonates	23%
Thyroid drugs	19%
Anti-hyperglycemic drugs	17%
Anticonvulsants	17%
Intravenous immunoglobulin	12%
Hematopoietic drugs	7%
Other anti-neoplastic drugs	2.4%

2-year pharmacy costs for 1,288 MG patients

Agent	Used by	% of all pharmacy costs
IVIg	12%	85%
Non-steroidal IS	29%	9.3%
Cholinesterase inhibitors	80%	5.7%
Corticosteroids	50%	0.2%

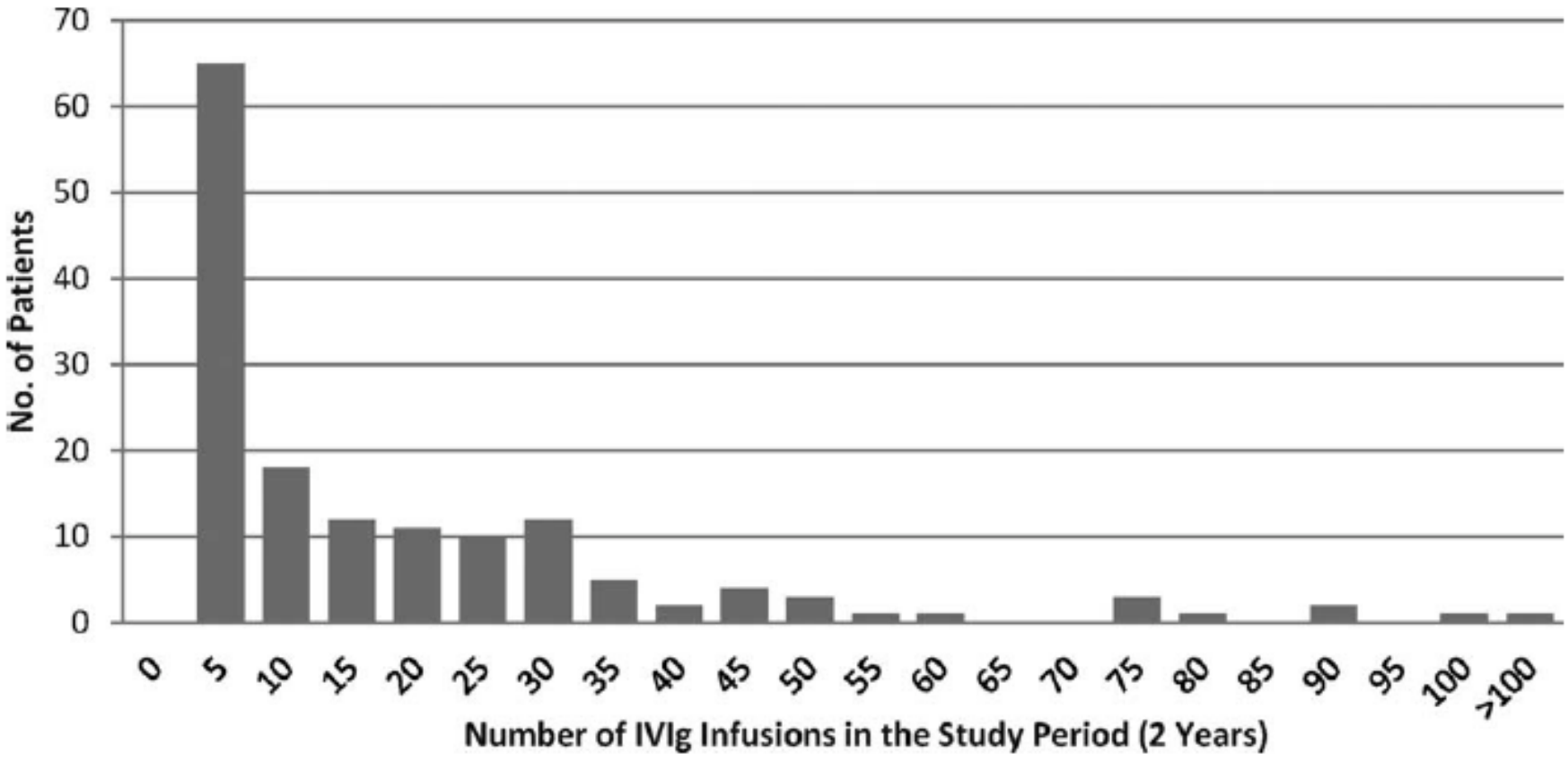
COST ANALYSIS OF MYASTHENIA GRAVIS FROM A LARGE U.S. INSURANCE DATABASE

Muscle Nerve **44**: 907–911, 2011

JEFFREY T. GUPTILL, MD,[1] ALEXANDER MARANO, BS,[2] ANDREW KRUEGER, MD,[2] and DONALD B. SANDERS, MD[1]

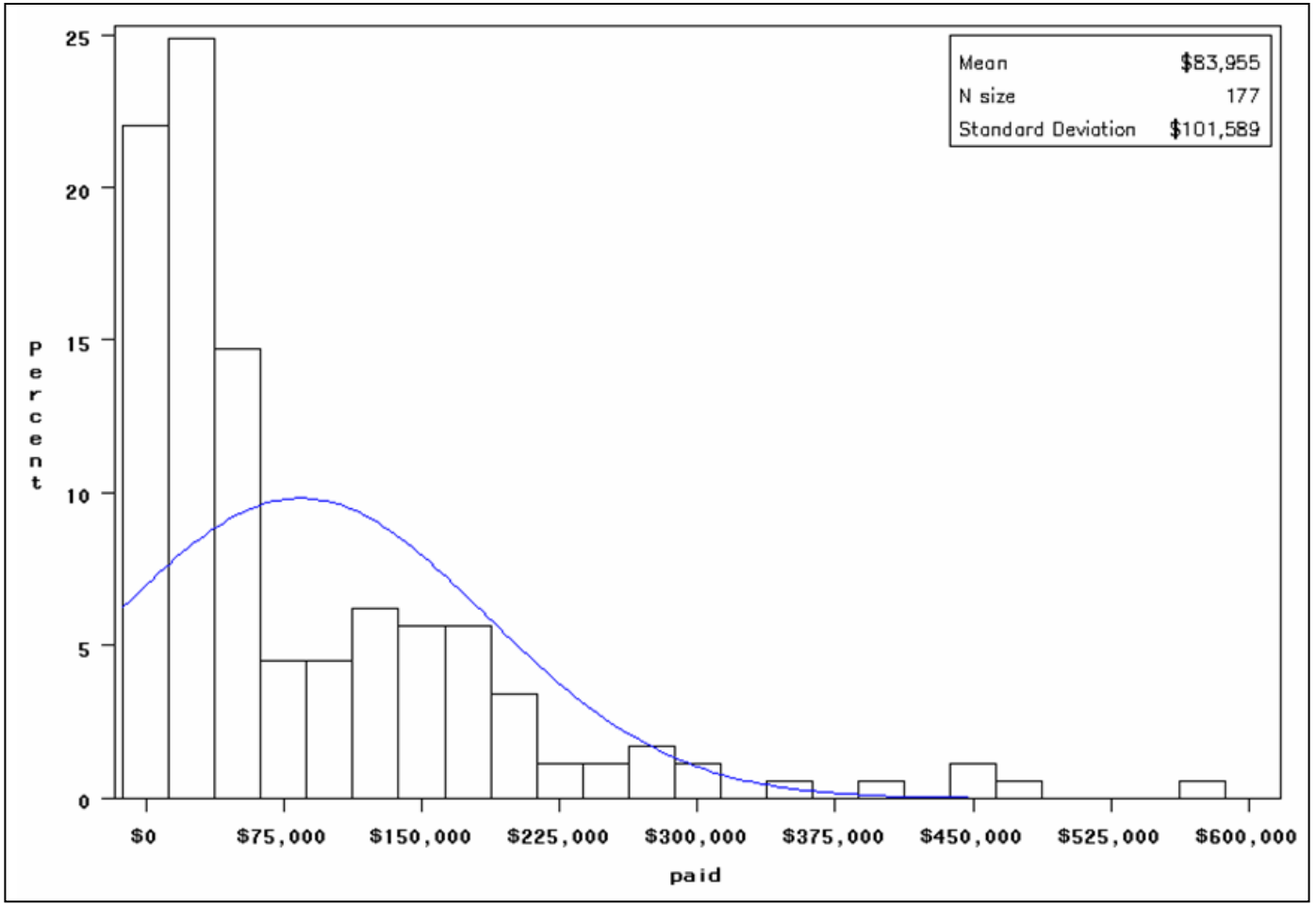
- Health-care insurance paid an average of $3,484 for each IVIg infusion and $1,306 for each PLEX.
- Paid costs for a course of IVIg vs PLEX:
  - PLEX x 5 - **$6,530**
  - IVIg x 2 days **- $6,968**
- A small number of patients had very high use of IVIg.

Number of IVIg infusions in 24 months



1288 MG patients

Patients who received >20 IVIg infusions in 2 years accounted for 60% of all MG-related pharmacy costs



PATIENT DEMOGRAPHICS AND HEALTH PLAN PAID COSTS IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

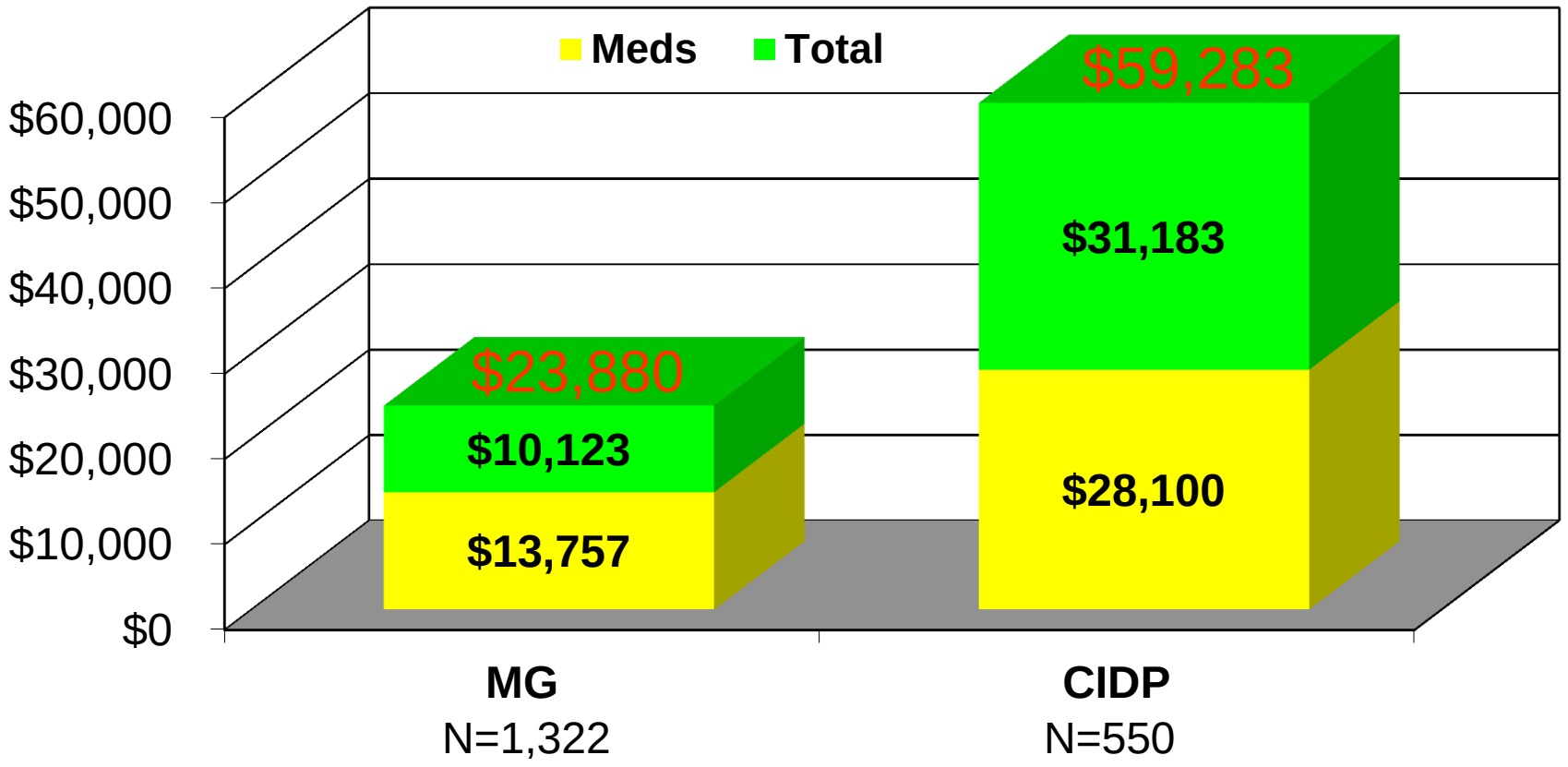
JEFFREY T. GUPTILL, MD,[1] MARK B. BROMBERG, MD, PhD,[2] LI ZHU, PhD,[3] BAL K. SHARMA, PhD,[3]
AMY R. THOMPSON, MBA,[3] ANDREW KRUEGER, MD,[3] and DONALD B. SANDERS, MD[1] *Muscle Nerve* 50: 47–51, 2014

- Costs for treating CIDP paid by US health plans in 2011 were determined from a comprehensive health-care insurance database covering 6.5M patients.
- The annual paid health-costs was $56,953
  - Drugs were the major cost (57%)
  - IVIg was 90% of drug cost

Medications used most frequently by 73 CIDP patients

Name	% of patients
Gabapentin	26
IVIg	26
Prednisone	16
Azithromycin	14
Amoxicillin	10
Lisinopril	10
Omeprazole	10
Oxycodone/acetaminophen	10
Clonazepam	8
Doxycycline hyclate	8
Fluticasone propionate	8
Noncorticosteroid immunosuppressive	
Mycophenolate mofetil	4
Azathioprine	3

Average annual total health-care costs paid: MG vs CIDP (11/1/07-10/30/09)



Financial Consequences of the Orphan Drug Act

An Act to amend the Federal Food, Drug, and Cosmetic Act to facilitate the development of drugs for rare diseases and conditions, and for other purposes.

Orphan Drug Act of 1983

ODA 1983

- Drugs, vaccines and diagnostic agents qualify for **orphan status** if they were intended to treat a disease affecting fewer than 200,000 U.S. citizens.
- Provided these financial incentives:
  - **7 year market exclusivity** for companies that developed an orphan drug
  - **tax credits** equal to half of the development costs, later changed to a fifteen-year carry-forward provision and a three-year carry-back
  - **fast-track approvals** of drugs indicated for rare diseases
  - expanded access to the Investigational New Drug Program
  - later amended to waive user fees

Market exclusivity

- Begins when FDA approves the indication, not when the drug is patented
- Independent of drug's current patent status
- Potential competing drugs must be shown to be therapeutically superior

- Creates a monopolistic market for approved drugs

Consequences of ODA

- Positive:
  - 2,116 orphan compounds designated
  - >378 orphan drugs approved as of 2012
  - 200 orphan diseases had approved treatments
  - 1/3 of FDA-approved agents are now orphan products
  - ~10% were for neurological or psychiatric conditions
  - Orphan-designated drugs had shorter average FDA review time
  - FDA has approved orphan drugs without RCTs
- Negative:
  - "*The [pharmaceutical] industry has taken advantage of the incentives to charge excessive profits and to reap windfalls far in excess of their investments in the drug*." Henry Waxman, primary sponsor of the ODA
  - *"Orphan product exclusivity can reduce patient access to existing drugs….Costs of each new drug are arguably unsustainable…"* Murphy et al, Ann Neurol 2012

21st Century Cures Act
July 10, 2015

- Additional $8.75B for NIH:
  - The NIH Innovation Fund for development and implementation of a strategic plan, early stage investigators, and high-risk, high-reward research.
  - The FDA must define "precision" drugs and the evidence needed to support their use in a subset of patients. …the FDA may rely upon data previously submitted for a different approved drug or indication.
- Extends market exclusivity rights by 6 months for drugs repurposed to treat a rare disease.

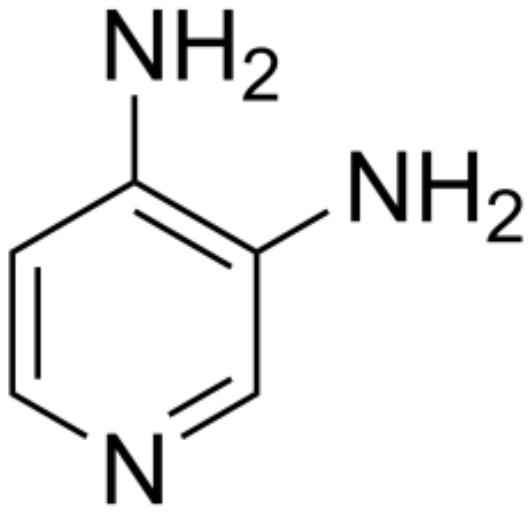
21st Century Cures Act

- Clinical testing of medical devices or drugs no longer requires the informed consent of the subjects if the testing poses no more than minimal risk and includes safeguards.
- Removes the requirement that manufacturers of medical products report payments to physicians for certain educational activities.

Competing Clinical Trials of an Orphan Drug in Lambert-Eaton Myasthenic Syndrome

3,4-Diaminopyridine

- 3,4-DAP is a simple organic molecule that blocks K^+ channels on nerve terminals in the open state, prolonging action potential duration, thus enhancing transmitter release.
- >80% of LEMS patients get clinically significant improvement in weakness from 3,4-DAP.



3,4-Diaminopyridine

- 3,4-DAP is an orphan drug and has been used to treat LEMS (& congenital myasthenic syndromes) for more than 25 years.
- Several small controlled trials have demonstrated safety & efficacy, but it has never been submitted to the US FDA for regulatory approval.

3,4-DAP in LEMS trials

3,4-DIAMINOPYRIDINE IN THE TREATMENT OF LAMBERT–EATON MYASTHENIC SYNDROME

KATHLEEN M. MCEVOY, M.D., PH.D., ANTHONY J. WINDEBANK, M.D., JASPER R. DAUBE, M.D., AND PHILLIP A. LOW, M.D.

New Engl J Med 1989;321;1567

A randomized trial of 3,4-diaminopyridine in Lambert-Eaton myasthenic syndrome

Donald B. Sanders, Janice M. Massey, Linda L. Sanders and Lloyd J. Edwards

Neurology 2000;54;603

Efficacy of 3,4-Diaminopyridine and Pyridostigmine in the Treatment of Lambert-Eaton Myasthenic Syndrome: A Randomized, Double-blind, Placebo-Controlled Crossover Study

Wirtz P.W, Verschuuren J., van Kijk J.G., de Kam M.L., etc

Clin Pharmacol Ther 86:44-48, 2009

3,4-DIAMINOPYRIDINE IS MORE EFFECTIVE THAN PLACEBO IN A RANDOMIZED, DOUBLE-BLIND, CROSS-OVER DRUG STUDY IN LEMS

SHIN J. OH, MD, GWENDOLYN G. CLAUSSEN, MD, YUKI HATANAKA, MD, and MARLA B. MORGAN, MD

Muscle Nerve **40**: 795–800, 2009

3,4-DAP in LEMS

- 80% of patients obtain significant clinical benefit from DAP
- No significant side-effects at usual clinical doses
- Complemented by pyridostigmine
- Available from compounding pharmacies or under a "compassionate use" IND.

3,4-DAP: Formulations

- 3,4-DAP base
  - Jacobus Pharmaceutical Co. (US, Canada, etc.) - FDA approved under "Compassionate Use" INDs for LEMS & CMS
  - Compounding pharmacies in U.S., several European countries
- Firdapse® – phosphate salt
  - BioMarin Pharmaceutical Inc (Europe)
  - EMEA approved for LEMS & CMS in Europe

- FDA: Two drugs that differ by peripheral chemical components can be defined as members of the same general "class" as a previously approved product.

Firdapse

- In 2010, the phosphate salt of amifampridine was licensed as "Firdapse®" by Biomarin Pharmaceutical Co.
- Based on previously reported trials Firdapse was approved for clinical use in Europe as an orphan drug.
- In UK, the annual cost increased from <$1,600 to $60,000.

Firdapse

- UK NHS commissioners network declined to pay for Firdapse, stating:

"There is no reason in principle why the NHS should be required to prescribe a more expensive licensed drug when a pharmacologically identical drug is unlicensed for the treatment in question."

- Now UK patients must pay for Firdapse or find an alternative source.

3,4-DAP: U.S. clinical trials for FDA approval

- In 2011, Catalyst Pharmaceutical Partners and Jacobus Pharmaceutical Co. each began RCTs to evaluate the efficacy & safety of 3,4-DAP in LEMS.
- Both trials have been successfully completed.
- This is a unique situation, in which two companies will be applying for FDA licensing of the same active agent.

Competing trials of 3,4-DAP in LEMS

- Catalyst is a publically-owned company, with fiduciary responsibility to maximize profits for its stock holders.
- JPC is a family-owned corporation with no external financial responsibilities.
- Under current ODA, the winning license-holder will have exclusive U.S. marketing rights for 7 years.

Potential outcomes

- Clinical trials competing for regulatory approval for the same drug is a unique situation, only possible for orphan drugs.
- Is there a precedent or appropriate regulation to deal with this situation?
- Which will the FDA approve?
  - Earliest?
  - Most conclusive results?
  - Most clinically relevant outcome measures?