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Perspectives on Benefit, Risk and Access

Susan Schaeffer
President & CEO
The Patients' Academy for Research Advocacy

@BiotechSusan
@AcadForPatients

Public

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AIDS Crisis: Patients Demand Access

FDA Headquarters, Oct. 11, 1988; Photo source: FDA

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1980s: Ripe for Patient-Driven Reform

- U.S. drug approvals among world's slowest
- Underfunded FDA has huge backlog of drug applications
- Reviews take years

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1990s: System Resets for Access

- PDUFA I eliminates “drug lag”
- Accelerated Approval speeds access in high-need settings
- FDAMA (which includes PDUFA II) expands FDA mandate from “protecting” to “promoting” public health

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Patient Perspectives

"There still is not a cure, but because of some of the new drugs, **a lot of us have been able to get back to work**."

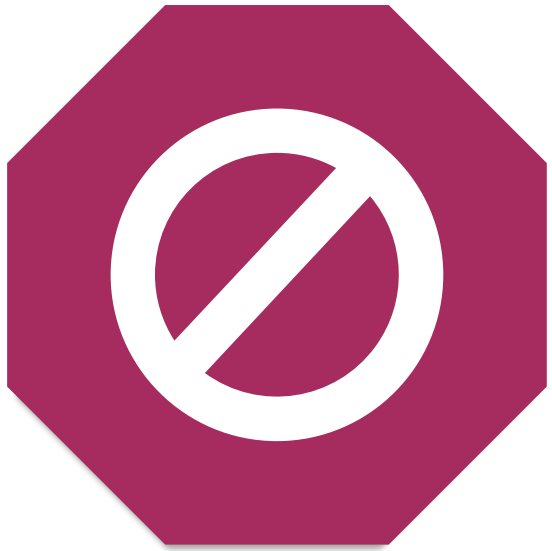
James Swire, AIDS Activist and Health Educator

June 1997

Public

2004: Risk Tolerance Plummets

- Chiron flu vaccine suspended
- Rofecoxib withdrawn
- Antidepressants get black box warning
- Congress pressures FDA to require proof of the absence of risk
- Investment and access suffer



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Natalizumab Sparks Patient-Driven Change

- Accelerated Approval in November 2004 based on reduced relapse rate
- Withdrawn February 2005 due to one confirmed fatal case and one suspected case of PML in trials
- By 2006, 3 confirmed cases in ~3,500 patients treated in trials
- Confirmatory data showed
  - Significant reductions in progression of disability (primary endpoint vs. placebo)
  - Sustained reductions in relapse rates ~2x better than other drugs (based on cross-trial comparisons)

Public

Patient Perspectives

"Roughly 25% of us have been failing on medication, progressing. The aggregate risk of us not having the drug on the market is **far greater** than the risk of PML."

Mike Barron, Patient with MS
February 2006

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Patient Perspectives

"If someone tells me Tysabri will take 10 years off my life but I'll have the quality of life I had a year ago when I was taking it, **I'd take it**."

Bartira Tiburtius, Patient with MS
March 2006

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Patient Perspectives

"People with MS have **the right to decide** what risks are acceptable to us."

Cheryl Bloom, Patient with MS
March 2006

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Today: System Resets Around Patients

"Patients are the experts in living with their disease or condition, the outcomes that are most important to them, and **how they weigh benefits and risks**."

Jeff Shuren, Director of FDA's CDRH

May 2, 2019

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C3G Patients Express Risk Tolerance

BioCentury

REGULATION

FOUNDATION FOR INCLUSION

BY EMILY CUKIER-MEISNER, SENIOR WRITER

"I WILL GO TO PRET... LENGTHS TO PRESE... KIDNEY FUNCTION. ... NUMBER ONE PRIOR...

LINDSEY FULLER, PATIENT

DAMAGE CONTROL

"Across the group, patients were willing to accept increased risks from treatments in exchange for benefits on either [quality of life or altering progression]."

Source: Cukier-Meisner, E., BioCentury 2017

Patient Perspectives

"I will go to pretty great lengths to preserve my kidney function. That is my **number one priority**."

Lindsey Fuller, Patient with C3G
August 2017

Public

Patient Perspectives

"I am home-bound and bed-bound 80% of the time. I am **willing to accept significant risks** to escape from this disease."

Matina Nicholson, Person with CFS
April 2013

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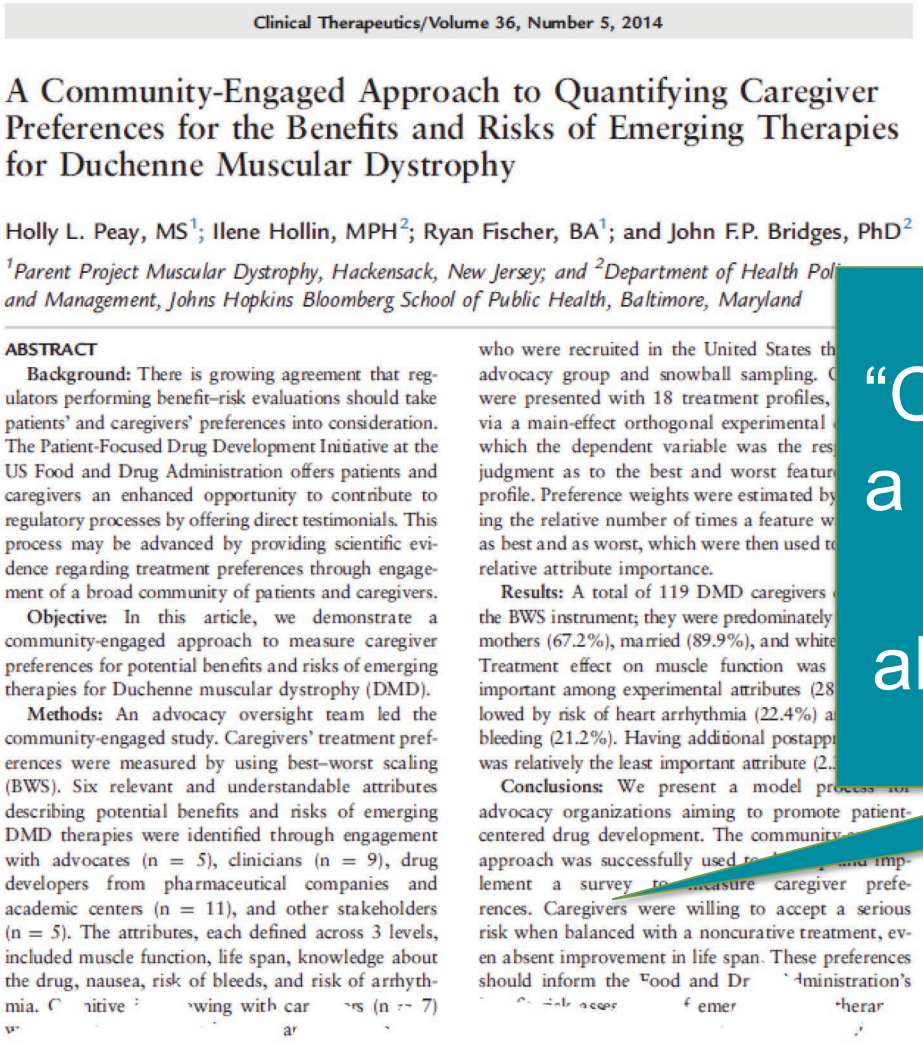
Patients Quantifying Preferences



Clinical Therapeutics/Volume 36, Number 5, 2014

A Community-Engaged Approach to Quantifying Caregiver Preferences for the Benefits and Risks of Emerging Therapies for Duchenne Muscular Dystrophy

Holly L. Peay, MS[1]; Ilene Hollin, MPH[2]; Ryan Fischer, BA[1]; and John F.P. Bridges, PhD[2]

[1]*Parent Project Muscular Dystrophy, Hackensack, New Jersey; and* [2]*Department of Health Pol... and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland*

ABSTRACT

Background: There is growing agreement that regulators performing benefit–risk evaluations should take patients' and caregivers' preferences into consideration. The Patient-Focused Drug Development Initiative at the US Food and Drug Administration offers patients and caregivers an enhanced opportunity to contribute to regulatory processes by offering direct testimonials. This process may be advanced by providing scientific evidence regarding treatment preferences through engagement of a broad community of patients and caregivers.

Objective: In this article, we demonstrate a community-engaged approach to measure caregiver preferences for potential benefits and risks of emerging therapies for Duchenne muscular dystrophy (DMD).

Methods: An advocacy oversight team led the community-engaged study. Caregivers' treatment preferences were measured by using best–worst scaling (BWS). Six relevant and understandable attributes describing potential benefits and risks of emerging DMD therapies were identified through engagement with advocates (n = 5), clinicians (n = 9), drug developers from pharmaceutical companies and academic centers (n = 11), and other stakeholders (n = 5). The attributes, each defined across 3 levels, included muscle function, life span, knowledge about the drug, nausea, risk of bleeds, and risk of arrhythmia. C...nitive ...ewing with car...rs (n = 7) w... ar...

who were recruited in the United States th... advocacy group and snowball sampling. ... were presented with 18 treatment profiles, ... via a main-effect orthogonal experimental ... which the dependent variable was the res... judgment as to the best and worst featur... profile. Preference weights were estimated by ... ing the relative number of times a feature w... as best and as worst, which were then used t... relative attribute importance.

Results: A total of 119 DMD caregivers ... the BWS instrument; they were predominately ... mothers (67.2%), married (89.9%), and white ... Treatment effect on muscle function was ... important among experimental attributes (28... lowed by risk of heart arrhythmia (22.4%) a... bleeding (21.2%). Having additional postapp... was relatively the least important attribute (2...

Conclusions: We present a model pr...ess for advocacy organizations aiming to promote patient-centered drug development. The community-... approach was successfully used to ... and implement a survey to measure caregiver preferences. Caregivers were willing to accept a serious risk when balanced with a noncurative treatment, even absent improvement in life span. These preferences should inform the Food and Dr... Administration's ... risk asses... f emer... therar...

"Caregivers were willing to accept a serious risk when balanced with a noncurative treatment, even absent improvement in life span."

Source: Peay, H. et al., Clinical Therapeutics 2014

Intense Desire for Access

BioCentury, THE BERNSTEIN REPORT ON BIOBUSINESS MARCH 31, 2014 PAGE A7 OF 23

Regulation

Josh Hardy chronicles

By Steve Usdin
Washington Editor

The Josh Hardy story puts a human face on both the lifesaving potential of compassionate use programs and the wrenching decisions company executives must make about who receives access to compounds in clinical development.

The Hardy family's social media campaign to gain access to an experimental therapy has apparently saved the seven-year-old boy's life.

But along the way, television news programs depicted the situation as a simple case of corporate bad behavior that was corrected by the righteous attention of the media combined with the power of millions of people who became aware of Josh

marketed by **Gilead Sciences Inc.** to treat cytomegalovirus (CMV) retinitis in AIDS patients. Potentially fatal nephrotoxicity caused by Vistide has limited its use.

Chimerix created brincidofovir using a technology that makes it possible to create oral formulations of IV drugs with improved potency and reduced systemic exposure (see *BioCentury, Feb. 24, 2003*).

> *"Our extremely high-risk patient exhibited complete response to treatment with CMX001."*
> *Journal of Clinical Virology*

Chimerix started approving compassionate use applications in 2009, CEO Kenneth Moch told BioCentury. Using funding from **HHS**'s Biomedical Advanced Research and Development Authority (BARDA), between 2011 and 2012 the company provided the compound to more than 200 patients under emergency INDs in the U.S. or equivalent regulations outside the U.S.

Whitehouse.gov

6:08 PM PST | FEB 10, 2017 | BIOCENTURY | POLITICS, POLICY & LAW

Right to try prairie fire

WHY INDUSTRY CAN DO LITTLE ABOUT RIGHT-TO-TRY LEGISLATION

BY STEVE USDIN, WASHINGTON EDITOR

EDITORS' COMMENTARY

DON'T SKIP DMD PATIENTS

BY STEVE USDIN, WASHINGTON EDITOR
AND SUSAN SCHAEFFER, EDITOR, *BIOCENTURY*

The skimpy NDA for eteplirsen to treat Duchenne muscular dystrophy has FDA wedged between the rock of inconclusive data and the hard place of a well-informed patient community that understands the limitations of the data and still demands access to the compound. There are very good arguments for rejecting eteplirsen, but they are outweighed by the possibility that the compound might help and is very unlikely to harm boys who have no other hope.

In the interest of patients, FDA should grant accelerated approval to eteplirsen for DMD that is amenable to exon 51 skipping. The agency should couple the approval with stringent requirements for Sarepta Therapeutics Inc. to rigorously confirm clinical efficacy, as well as an unambiguous understanding that approval will be withdrawn if efficacy is not confirmed.

At the eteplirsen advisory committee meeting on April 25, Janet Woodcock, director of FDA's Center for Drug Evaluation and Research (CDER), was correct to highlight the impact of regulatory decisions on patients, and the imperative to give patients a greater say in how the

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REGULATION

FDA TO FACILITATE ACCESS TO UNAPPROVED DRUGS

BY STEVE USDIN, WASHINGTON EDITOR

Patients' Academy Perspective

- Decisions with respect to benefit-risk should rest with patients
- Patients should be consulted early on in R&D, as partners with unique knowledge that can improve programs
- Patients with life-threatening or debilitating illness OFTEN prioritize access over risk
- BUT preferences and risk tolerance change over time in ways that cannot be assumed
- Patients must be properly informed in order to make benefit-risk decisions

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Thank You

Susan Schaeffer

President & CEO

The Patients' Academy for Research Advocacy

susan@patients-academy.org

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