

Industry Perspective on Patient Preference Information

FDA/CERSI PPI Workshop



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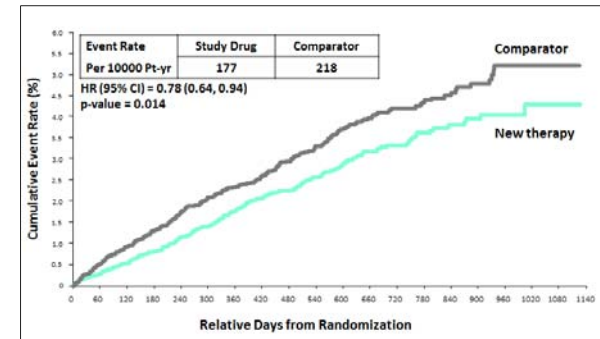
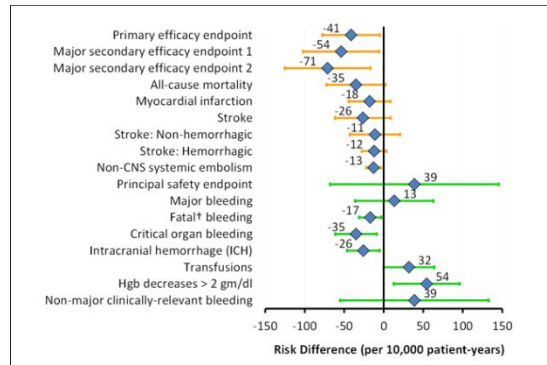
Janssen Research & Development, LLC

Outcome	Drug A	Drug B
Relief of pain	 <p>A horizontal scale with four points: None, Mild, Moderate, and Severe. A red arrow starts at the Severe point and points left towards the Mild point.</p>	 <p>A horizontal scale with four points: None, Mild, Moderate, and Severe. A red arrow starts at the Severe point and points left towards the Moderate point.</p>
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 10,000	No chance
Which medicine would you choose if these were the only medicines available?	<input data-bbox="1012 922 1077 989" type="checkbox"/>	<input data-bbox="1488 922 1554 989" type="checkbox"/>

Outcome	Drug C	Drug B
Relief of pain	 <p>None Mild Moderate Severe</p>	 <p>None Mild Moderate Severe</p>
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 1,000	No chance
Which medicine would you choose if these were the only medicines available?	<input data-bbox="1012 922 1077 989" type="checkbox"/>	<input data-bbox="1488 922 1554 989" type="checkbox"/>

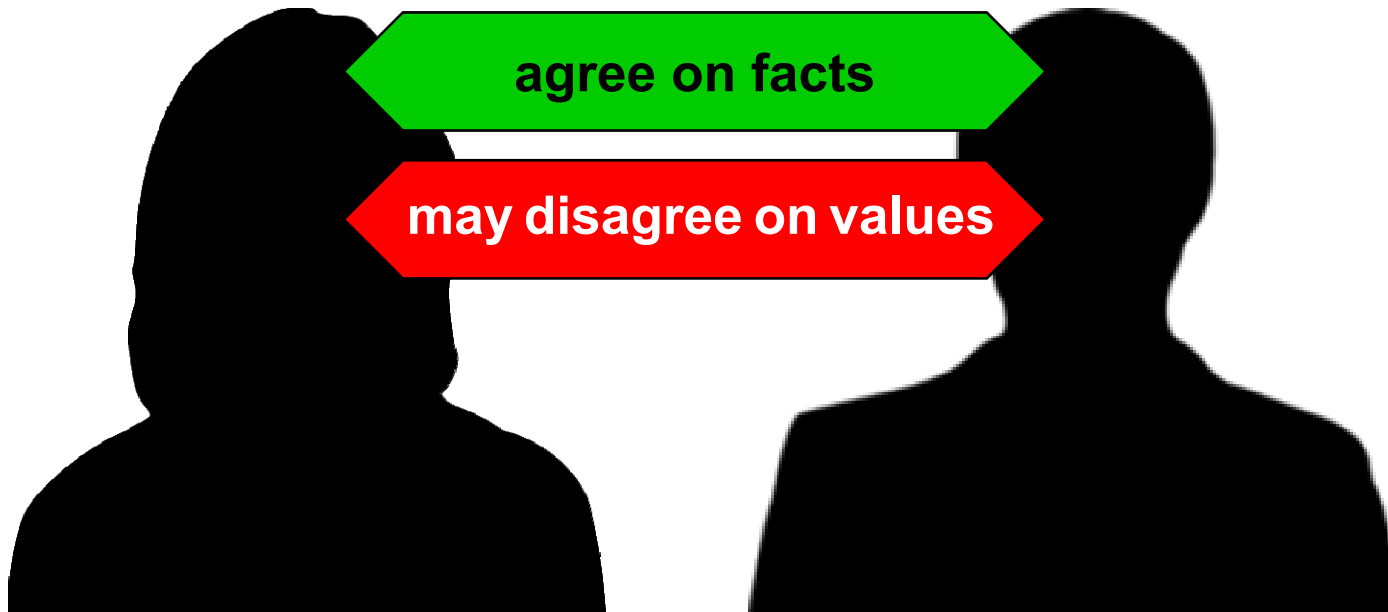
Outcome	Drug D	Drug B
Relief of pain	 <p>None Mild Moderate Severe</p>	 <p>None Mild Moderate Severe</p>
Ability to perform work/school and social activities	No limitations	Cannot work, difficulty with chores and shopping
Annual chance of a heart attack	1 in 100	No chance
Which medicine would you choose if these were the only medicines available?	<input data-bbox="1012 925 1077 987" type="checkbox"/>	<input data-bbox="1491 925 1556 987" type="checkbox"/>

Endpoint	Study Drug/ 10,000 pt-yrs	Comparator Rate/ 10,000 pt-yrs	HR (95% CI)	Risk Difference / 10,000 pt-yrs
Primary efficacy (Stroke + embolism)	177	218	0.78 (0.65, 0.94)	-41 (-78, -5)
Secondary efficacy 1 (stroke, embolism + vascular death)	318	371	0.85 (0.73, 0.98)	-54 (-102, -6)
Secondary efficacy 2 (stroke, embolism + vascular death + MI)	396	467	0.84 (0.73, 0.95)	-71 (-125, -17)



regulator

patient



What Did Migraine Patients Say?

Stated choice conjoint preference survey of 200 adult migraine patients

- **Relieving all functional limitations was twice as important as relieving all migraine pain**

Maximum Acceptable Risk = maximum level of treatment-related 1-year heart attack risk patients would accept for a given improvement in migraine symptoms

- **Patients would accept up to a 2/1000 (95% CI 1.6 – 2.4) annual heart attack risk in exchange for restoring their ability to function during migraines**

Three Types of Patient Preference Information

Type	What it Measures
Attributes	<u>What Matters</u>
Relative Importance	<u>How much</u> it matters
Tradeoffs	<u>What tradeoffs</u> patients are willing to make between benefits, harms, and other aspects

Where Can Patient Preferences Inform the Development Lifecycle?

Commercial viability
/ Patient needs

Trial design

What endpoints do patients care most about?

TPP

What is the relative importance of benefits, risks and other treatment features to patients?

Approval & reimbursement

How do patients vary in these properties (heterogeneity)? Are there distinct subgroups?

Ph 2a/b

Ph 3

Reg

Post-approval

What level/rate of endpoints are critical to patients?

Effect size

Maximum acceptable risk, minimum required benefit, choice share?

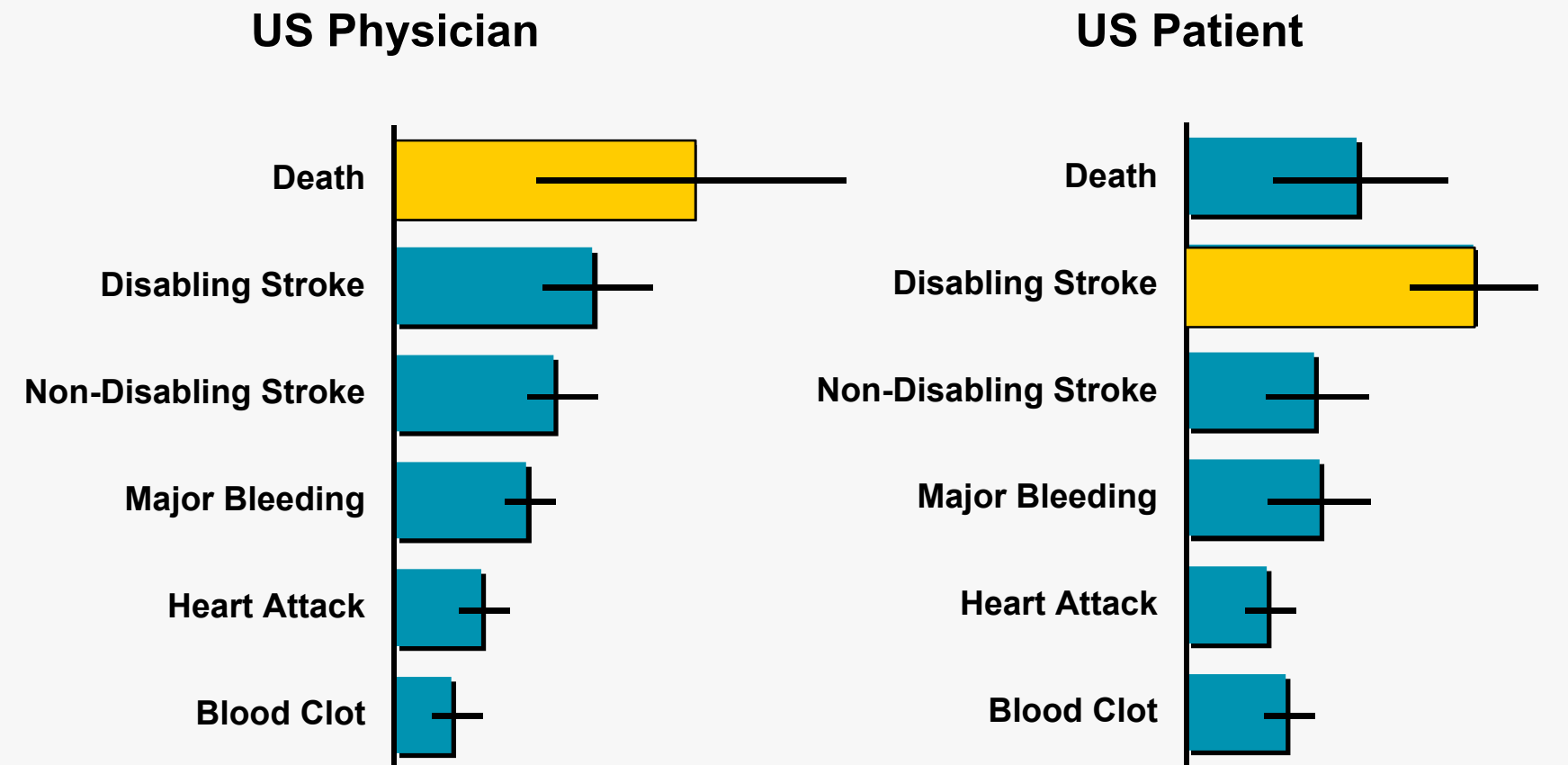
Defensible B-R

Are there important differences between stakeholders?

Shared decision-making

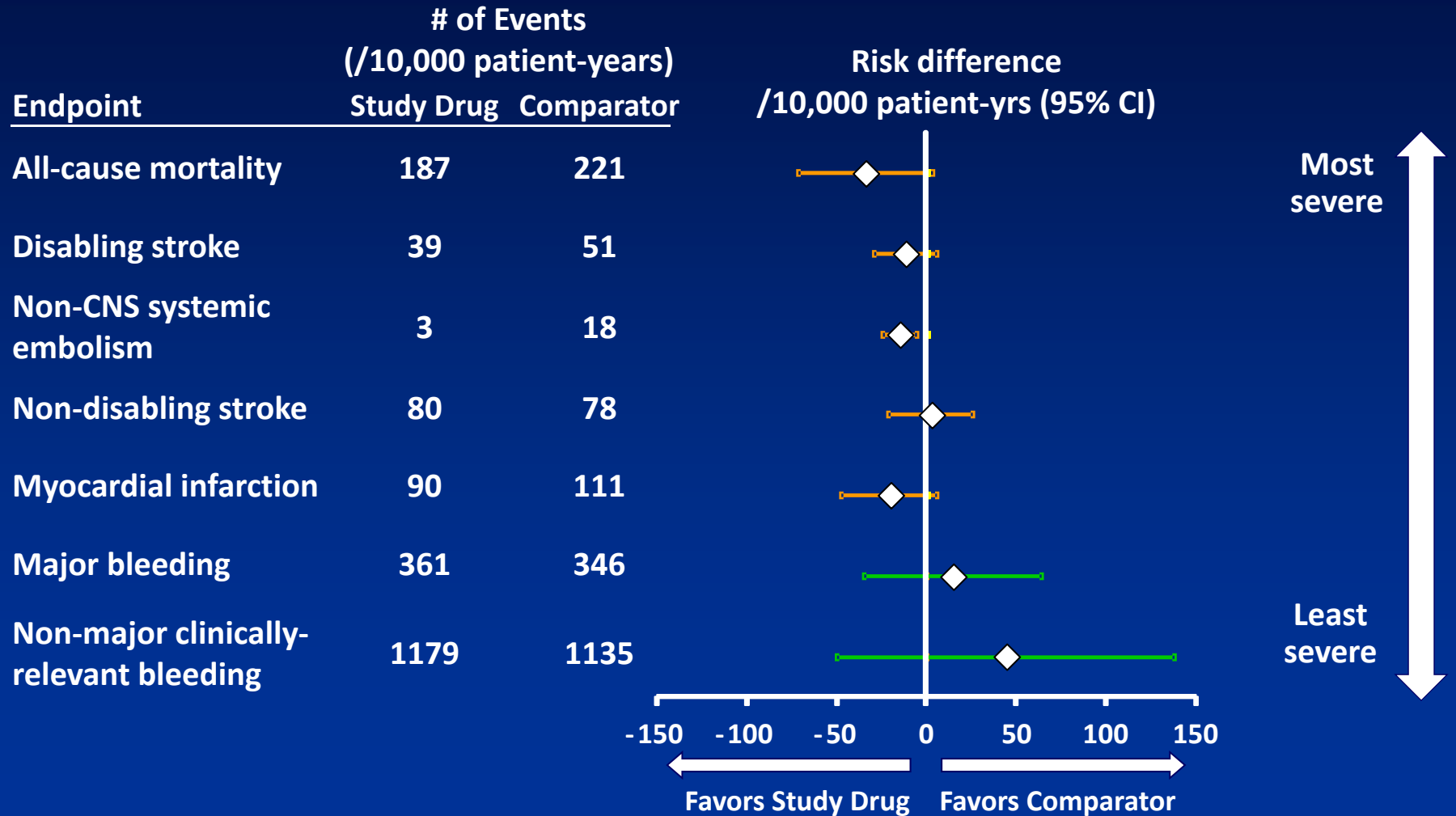
Identifying Differences Between Key Stakeholders

Preferences for Anticoagulants in Atrial Fibrillation

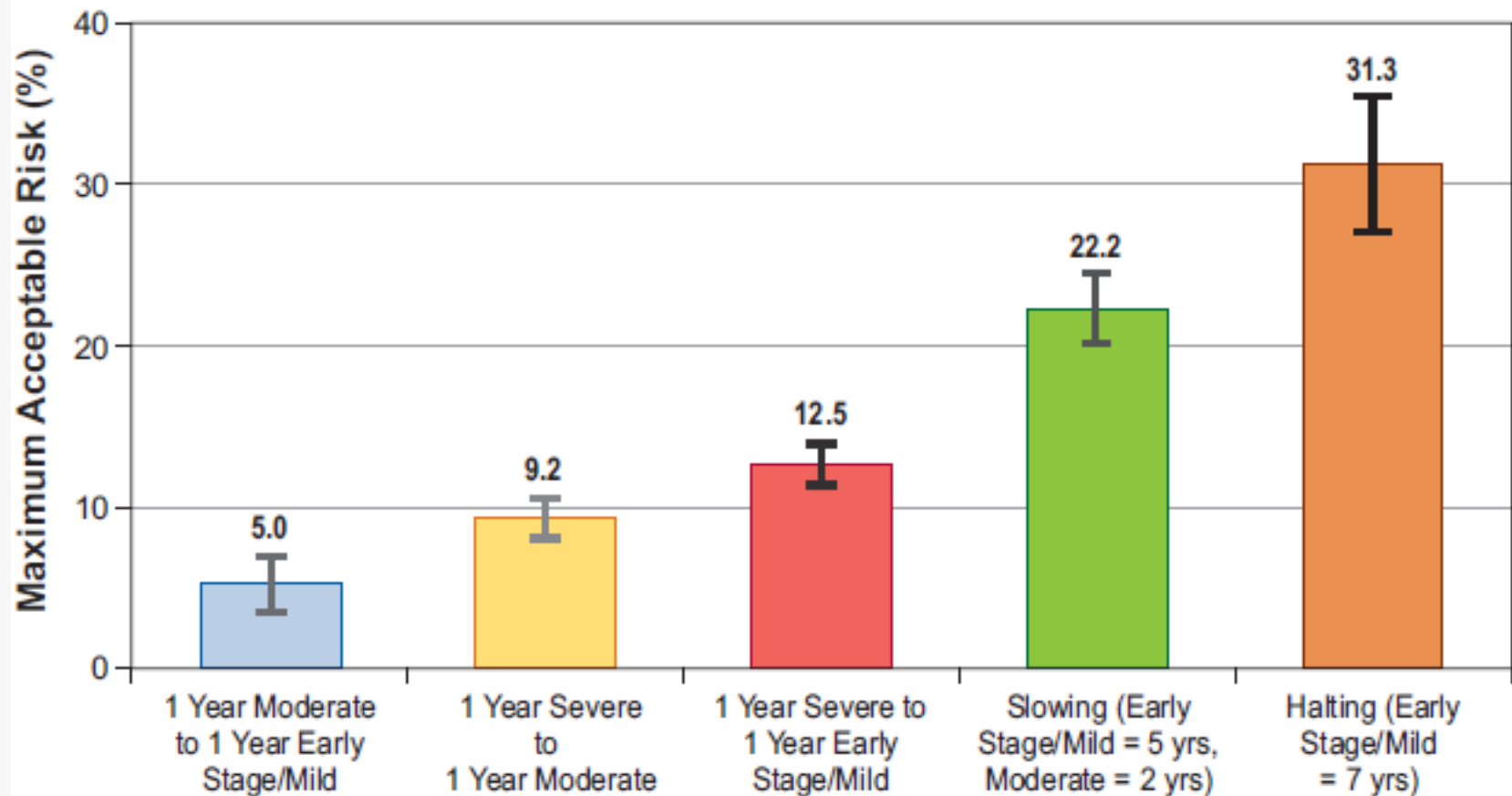


Risk Differences by Clinical Severity/Impact

Atrial Fibrillation Example (mock data)



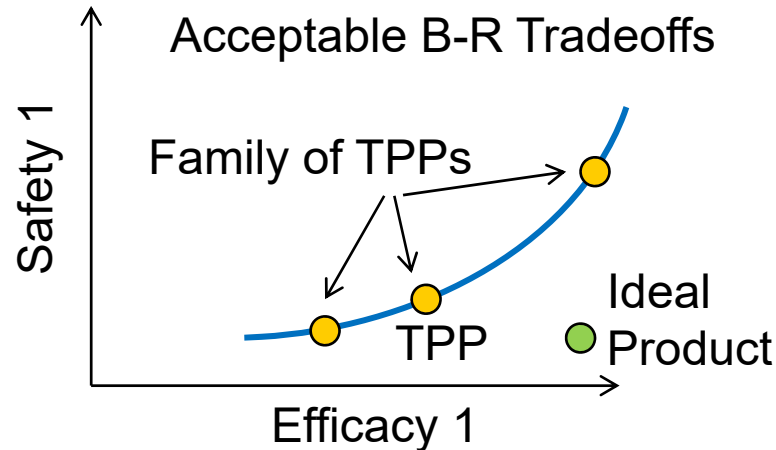
Maximum Acceptable Risk of treatment-related death or permanent severe disability due to stroke



Hauber AB, Johnson FR, Fillit H, et al. Older Americans' risk-benefit preferences for modifying the course of Alzheimer disease. *Alzheimer Dis Assoc Disord.* Jan-Mar 2009;23(1):23-32

Patient Preference Studies Can Inform Target Product Profiles

- Consider TPP a point on a continuum of B-R tradeoffs
- Preference studies given many acceptable tradeoffs
- Can generate a family of viable TPPs
- Provides much greater proactive flexibility for alignment between compound and TPP goals



Early Development

Compound Target Product Profile Date
Please note any changes from previous version in the Notes page of this slide

Indication: Target Patient Population:

Endpoints that lead to Compound TPP Key Value Drivers	Base Case	Performance Threshold for Continued Development
Efficacy (1)		
Efficacy (2)		
Efficacy (3)		
Safety (1)		
Safety (2)		
Tolerability		
Payer Value (1)		
Payer Value (2)		
Patient Reported Outcomes		Patient Reported Outcomes
Dosing/Presentation* (1)		
Companion Diagnostic**/Biomarker		

What Sponsors Worry About When Considering A Patient Preference Study

Do we really need it?

When should we do it?

Work with a patient group?

Who is involved?

Will regulators pay attention?

What can we do with it?

Can we publish?

How much does it cost?

How long will it take?

How rigorous?

Whose preferences?

Can we trust the results?

What method?

How do we design it?

Who can help us?

Many Methods for Assessing Preferences

Group	Method
Structured-weighting	<ul style="list-style-type: none">• Simple direct weighting• Ranking exercises• Swing weighting• Point allocation• Analytic hierarchy process• Outranking methods
Health-state utility	<ul style="list-style-type: none">• Time tradeoff• Standard gamble
Stated-preference	<ul style="list-style-type: none">• Direct-assessment questions• Threshold technique• Conjoint analysis and discrete-choice experiments• Best-worst scaling exercises
Revealed-preference	<ul style="list-style-type: none">• Patient-preference trials• Direct questions in clinical trials

Factors Influencing Whether Patient Preference Information May Be Valuable for Regulatory Review

- **Patient's perspective**

- ▶ Important differences in preferences of patients and other stakeholders
- ▶ Important differences in preferences of subgroups of patients
- ▶ Understanding the patient experience requires considerable familiarity with the disease (e.g. very subjective endpoints, lifestyle indication, rare disease)

- **Benefit-risk tradeoffs (preference sensitive)**

- ▶ Clear benefit with rare serious risks compared to alternatives
- ▶ Harms occur early/benefits occur later (e.g. secondary prevention)
- ▶ Considerable uncertainty whether a patient will realize the benefit or risks

- **Novelty**

- ▶ New mechanism of action or type of device
- ▶ Lack of precedent

What do you want to know?

Two basic approaches to patient-preference studies

- **Product-evaluation (top-down) approach**

- Assess patient preferences for known features of treatment options to make decisions
- Applies to existing products or services or those in development
- Example: CDRH weight-loss preference study (*Ho et al., 2015*)

Survey pretest similar to cognitive debriefing

- **Issues-identification (bottom-up) approach**

- Patients define relevant features, priorities, or needs
- Preference methods used to quantify the relative importance of features
- Not necessarily specific to the features of an existing product
- Example: PPMD Duchenne Muscular Dystrophy Studies (*Hollin et al., 2015; Peay et al.,*

Survey development similar to concept elicitation

Many Open Questions on Preference Work

- **Technical / methodological questions**

- ▶ Methods, population, bias, internal validity, external validity, ...
- ▶ E.g. MDIC framework gap analysis

- **Regulatory standards in development**

- ▶ Design requirements
- ▶ Sample requirements
- ▶ Internal validity

- **Avenues for regulatory communication**

- ▶ ICH update to common technical document – place for pref studies
- ▶ Label - Limited opportunity for benefit-risk or patient preferences

* Levitan, Hauber, Damiano, Jaffe and Christopher, “The Ball is in your Court: Agenda for Research to Advance the Science of Patient Preferences in the Regulatory Review of Medical Devices in the United States,” Patient, August, 2017 (online)

Huge Growth of Initiatives on Methodology, Policy and Application of Patient Preference Studies

Regulatory/Govt

Trade Orgs

Pub Private/Prof

Patient Groups



FasterCures
A CENTER OF THE MILKEN INSTITUTE



Innovative Medicines Initiative



**Parent Project
Muscular Dystrophy**

LEADING THE FIGHT TO END DUCHENNE



NATIONAL
HEALTH COUNCIL



EUROPEAN MEDICINES AGENCY
SCIENCE. MEDICINES. HEALTH.



PATIENT FOCUSED
MEDICINES DEVELOPMENT



21st
Century
Cures

Selected sample

**THE MICHAEL J. FOX FOUNDATION
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Future Direction: Consortium Approach to Preference Studies

- **Multiple stakeholders (e.g. industry, patient group, academia, regulatory) collaborate on a preference study**
- **Pool resources and expertise**
- **Lessen covert bias**
- **Larger sample size**
- **Greater acceptance**

Goal

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