Incorporating patient preferences in drug development

An Industry Perspective

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Agenda

Industry examples of patient involvement within drug development

Examples of patients and patient organizations involvement determined via the public-private partnership IMI-PREFER

Impact of patient involvement on regulatory decision making
Patient Involvement – current challenges

- Recruitment challenges for training patients with certain diseases
- Lack of awareness and understanding of the different processes
- Capacity for training and education, timing for involvement
- How much used for final decision-making by regulators?
- Individual view may be limited and subjective – how representative for entire patient population?
- Comprehensive approach to capturing patient preferences
- Understanding of best methodologies, when and how to collect preferences to be used by regulators and HTA bodies
Overall strategy

Incorporate the voice of patients in our clinical studies

Develop appropriate communication according to patients’ needs

Use appropriate tools to capture patient preference and needs, PROs & QoL information

Participate to Public-private partnership to provide systematic methodology to include patients perspective

Bring to the patient the right treatment at the right time

Involving patients as partners in Clinical Development

PROs: Patient Reported Outcomes
QoL: Quality of Life Questionnaire
INCORPORATE THE VOICE OF PATIENTS IN OUR CLINICAL STUDIES
Industry Examples – Informed Consent (1/2)

PATIENTS INVOLVED IN INFORMED CONSENT FEEDBACK
E.G. EPILEPSY AND RHEUMATOID ARTHRITIS / UCB

- **Objectives:** to make the informed consent form simpler and easier for the patients to understand

- **Projects**
  
  Part I: patients visited at home and asked to read existing consent forms. Reactions and opinions discussed with them. Feedback was included to modify the informed consent form.
  
  Part II: patient invited to a workshop to put forward the patient perspective on the modified consent form. Readability discussed. A survey was filled out by patients to score the preferences on the layout, text and color of informed consent form.

- **Type(s) of patient (advocates) involved**
  
  Patients with personal disease experience.
  
  Expert patients / patient advocates with good expertise on disease, but little R&D experience

- **Results**
  
  Patients valued being consulted on their preferences
Major changes to the existing documents such as shorter paragraphs and changes to the design features. Sentences deemed to be very important by the patients were highlighted.

‘Quick Guide’ was produced which gave quick facts regarding the trial.

- Challenges and barriers

There were worries that the ethics committees might not approve the suggested format or text.

- In the end, there were not any concerns from the ethics committees and approvals were obtained from many countries, with the comments being very minor.

There could have been potential challenges when trying to take on board all of the patient feedback and translating them into practical solutions (e.g., the color of the text might not have been suitable).

- Learning

The feedback from patients can be dependent on the type of patients involved.

- This means there can be a bias on the information gathered, based on personal experience and expertise.

- Several wishes and suggestions of patients but what is realistically feasible.

The time involved in gathering feedback from the needs, to be factored into the process development stages. The cost also needs to be budgeted.

An open mind is needed to really gain the maximum out of the process (e.g. there was a lot of new and impressive technology on iPad but patients with tremor in hands are not able to use the touchscreen).

9/27/2017

Source: EUPATI
Consultation between Novartis and
  Nurses from different teams (USA, Canada and Brazil),
  Cushing’s disease patients (USA) and caregivers
  Patient organization representatives

Objectives
  Obtain specific feedback on sections of a draft protocol from patients, caregivers, advocates, and research study coordinators on Cushing’s disease clinical trial development

  Identify potential areas of concern from the patient and research community that may impact the Cushing's disease trial accrual process in the future

  Identify ways that Novartis can help support new product development with related tools and educational materials for patients with Cushing’s disease

Types of patient (advocates) involved
  Patients with personal disease experience
  Expert patients / patient advocates with good expertise on disease
  Expert patients / patient advocates without good R&D experience
Industry Examples – Clinical Trial Design (2/2)

PATIENTS INVOLVED IN CLINICAL TRIAL DESIGN (PHIII)
E.G. CUSHING’S DISEASE/NOVARTIS

• Benefit of patient involvement (topic discussed)
  Multiple issues to consider when designing a rare disease trial including patient-investigator communication, enrolment, education, psycho-social support, access, tracking, reporting and follow-up

  Study length, transportation and visit schedule were named among the main barriers from the patient perspective

  Working with patient advocate groups in clinical trials is crucial. Patient advocate groups should be used to announce and disseminate information about trials to boost enrolment

  Consideration on the proof of concept and possible importance of the medicine being studied for the patients

• Results
  Trial design was better tailored to patient’s needs
  Different perspectives and insights allowed to better inform a study design
Development of Appropriate communication to patient’s needs - Example: Informed consent...

PART ONE
GENERAL INFORMATION

What is a research study?
A research study is a careful experiment to answer an important medical question. Participating in a research study is not the same as getting regular medical care. The purpose of regular care is to improve your health. The purpose of a research study is to collect and analyze information, which may help patients get better care in the future.

What is systemic lupus erythematosus?
Systemic lupus erythematosus (SLE), also known as lupus, is a systemic autoimmune disease in which the body’s immune system mistakenly attacks healthy tissue. There are many kinds of lupus, but the most common form is systemic lupus erythematosus (SLE), which affects many internal organs in the body (such as the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system). Systemic lupus erythematosus may be chronic and due to an environmental trigger. There is no cure for systemic lupus erythematosus.

Why is Actemra doing this study for people with systemic lupus erythematosus?
The purpose of this study is to test the efficacy of a new drug called ACT-334441. We need to find out if ACT-334441 is safe and effective and what is the best dose to treat people with systemic lupus erythematosus.

ACT-334441 is tested in the study and compared to placebo (containing no medication). ACT-334441 can be used in 4 doses, so the study has 5 different groups (4 ACT-334441 groups with different doses and 1 placebo group).

What is the study drug?
ACT-334441 is a study medicine that increases the number of the white blood cells. The white blood cells are part of your body’s defense system that causes systemic lupus erythematosus.

ACT-334441 is still in the experimental stage and has not yet been approved by the government health authorities to treat systemic lupus erythematosus. This study medicine has already been tested in 58 healthy people (who do not have systemic lupus erythematosus). This is the first time that it will be tested in patients with systemic lupus erythematosus. Further research is needed to determine if the study drug is safe and effective for people with systemic lupus erythematosus.

What is a placebo?
A placebo looks like real medicine but has no drug in it. Sometimes people feel better even when they take a placebo. It is important to compare the study drug with a placebo to find out if the study drug really works.

What do “randomization,” “double-blind,” and “dose response mean?”

Forty-eight participants will take ACT-334441 (0.5 mg, 1 mg, 2 mg or 4 mg daily doses) while 16 participants will take placebo (containing no medicine). You may take ACT-334441 or placebo.

The study is divided into 2 parts. ACT-334441 (0.5 mg, 1 mg, 2 mg daily doses compared to placebo) taken in a first part and ACT-334441 (4 mg daily doses compared to placebo) taken in a second part. The second part will only start after independent medical experts have evaluated the results of the first part of the study.

When will my visits happen?

VISITS

- Screening
- Dosing ACT-334441
- Routine Check up and PK visit
- Routine Check up and PK visit
- Follow-up/Phone call

ACT-334441 is still in the experimental stage and has not yet been approved by the government health authorities to treat systemic lupus erythematosus. This is the first time that it will be tested in patients with systemic lupus erythematosus. Further research is needed to determine if the study drug is safe and effective for people with systemic lupus erythematosus.

ECG

Authorization for use granted by the pulmonary hypertension UK association to Actelion Pharmaceuticals Ltd., for MAESTRO Study AC-655-303, March 2014

To a user-friendly layout...

From a complex document...
...with new ways of providing similar information

Ongoing assessment of electronic informed consent solution

Features and Benefits

- Mitigating Regulatory Risks
- Improving Patient Comprehension and Understanding
- Enhancing Efficiency
- Saving Time and Costs
- Upgrading Audit Trails
- Ensuring Version Control

eConsent offers researchers numerous benefits, including:

Improving Patient Comprehension & Understanding

- eConsent solutions should utilize diverse multimedia, tailored information delivery and interactive assessments to explain all aspects of the clinical trial to participants, guiding them through a significant amount of complex information. For example, eConsent solutions can feature pop-ups to definitions of unfamiliar medical terms or videos of test procedures.

- eConsent also provides participants with the ability to pause and check in with how their comprehension is going, tracking where they have questions and documenting the Q&A session to analyze their capacity to consent as they progress. Participants should also be able to ask questions so that a doctor can review and clarify understanding later on.

- By enhancing patient understanding and verifying that they truly comprehend the consent information, study teams can streamline enrollment, improve site engagement of potential participants, improve compliance documentation, and reduce costly subject dropouts. Prior to the investigator and/or delegate signing the consent, reviewing the subject’s eConsent audit trail enables better assessment of a participant’s readiness for study enrollment.
Applying quantitative methodologies: Patient preferences in multiple sclerosis

- **Study**
  - Oral Ponesimod vs. Teriflunomide in Relapsing Multiple Sclerosis

- **Trial Medication**
  - Ponesimod 20 mg, teriflunomide 14 mg

- **Primary outcome**
  - Annualized relapse rate (ARR)

- **Sample size**
  - 1100

Source: Actelion Pharmaceuticals Ltd
Sub-Study to Elicit Patient Preferences

- **Data collected in 18 countries -> USA + Western European countries**
- **Target enrollment -> 360 MS patients**
- **Patients asked to give preferences for 7 benefit or risk outcomes**
- **Preferences elicited at 3 time-points in the study -> 2 at Baseline; 1 at EOS**
  
  Baseline to provide data on short-term stability/ reproducibility of the preferences
  
  Difference between Baseline and EOS measures (by treatment group)
  
  - show impact of treatment on patient preferences in long-term (overall and by treatment)
- **Data collected on hand-held device given to patients**
- **Patient training at screening and online patient guide to support completing the questionnaire**
Example of questionnaire on mobile device

Section 7 of 9

Monitoring of the Heart

Completion time: 10 minutes

Begin

Monitoring of the Heart

Some MS drugs require heart monitoring in a hospital on the day of the first dose of the drug or when re-starting the drug.

Your Patient Guide includes a section called Monitoring of the Heart which includes more information about this section.
Expected Results

- Show change in patient preferences long-term (overall and by treatment)
- Ranking of the importance of the outcomes from the patients’ perspective (Weighting)
- Regression analyses to estimate predictive models for preferences (overall and by treatment):
  - **Demographic characteristics** such as age, gender, socio-economic status may predict preferences
    - e.g. age differences in willingness to spend time in hospital for monitoring
  - **Disease characteristics** such as severity of disease, time since diagnosis may also predict preferences for treatment outcomes
- Analyses of treatment outcomes versus changes in patient preference
www.imi-prefer.eu

This work has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking PREFER grant n° 115966.
About PREFER

- PREFER will establish recommendations to support development of guidelines for industry, Regulatory Authorities and HTA bodies:
  - how and when to include patient perspectives on benefits and risks of medicinal products

- Aim over the next five years:
  - Conduct of patient preference studies in both academic and industry settings
  - To gain a better understanding of best-practice approach recommendation of patient-preference studies
  - To show how patient preference studies can give valuable information to support regulators and HTA bodies decision making

http://www.imi-prefer.eu/
Patient Preference Case Study in PREFER

- **Historical Case Studies**
  - 23 patient preference case studies have been collected in Work Package 3
  - Study designs follow both qualitative and quantitative designs

- **Prospective Case Studies**
  - Industry consortium members are encouraged to submit a case study to PREFER beginning at Month 15
  - A case study from MSD has been submitted and included as a pilot to develop process needed for combining industry and PREFER objectives

http://www.imi-prefer.eu/
How will results inform

HEALTH AUTHORITIES AND HTA BODIES

• In marketing authorization, clinical results can be complemented by quantitative B/R perspective of patients
• Patient preferences can support the qualitative B/R assessment done by regulators
• Results provide relevant patient information to HTA bodies
### PFDD meetings for FY 2013-2017

<table>
<thead>
<tr>
<th>Fiscal Year 2013</th>
<th>Fiscal Year 2014</th>
<th>Fiscal Year 2015</th>
<th>Fiscal Year 2016-2017</th>
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<tr>
<td>Chronic fatigue syndrome/myalgic encephalomyelitis</td>
<td>Sickle cell disease</td>
<td>Female sexual dysfunction</td>
<td>Non-tuberculous mycobacterial lung infections</td>
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<td>HIV</td>
<td>Fibromyalgia</td>
<td>Breast cancer</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Pulmonary arterial hypertension</td>
<td>Chagas disease</td>
<td>Neuropathic pain associated with peripheral neuropathy (June 10)</td>
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<tr>
<td>Narcolepsy</td>
<td>Inborn errors of metabolism</td>
<td>Functional gastrointestinal disorders</td>
<td>To be announced</td>
</tr>
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<td></td>
<td>Hemophilia A, B, and other heritable bleeding disorders</td>
<td>Parkinson’s disease and Huntington’s disease</td>
<td>Alopecia areata</td>
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<tr>
<td></td>
<td>Idiopathic pulmonary fibrosis</td>
<td>Alpha-1 antitrypsin deficiency</td>
<td>Autism</td>
</tr>
</tbody>
</table>

*To be announced*:
- Alopecia areata
- Autism
- Hereditary angioedema
- Patients who have received an organ transplant
- Sarcopenia
A sample of what we ask

- Which symptoms have the most significant impact on your daily life?... On your ability to do specific activities?

- How well does your current treatment regimen treat the most significant symptoms of your disease?

- What specific things would you look for in an ideal treatment for your condition?

- What factors do you take into account when making decisions about using treatments? ... Deciding whether to participate in a clinical trial?
Meeting output

- Each meeting results in a **Voice of the Patient** report that faithfully captures patient input from the multiple streams
  
  *http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm*

- This input can support FDA staff, e.g.:
  - Conducting B-R assessments for products under review
  - Advising drug sponsors on their drug development programs
  - Identify opportunities for further dialogue (e.g., future workshops)

- It might also support drug development more broadly:
  - Help identify areas of unmet need in the patient population
  - Help identify or develop tools that assess benefit of potential therapies
  - Help raise awareness within the patient community

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Document issued on August 24, 2016. This document will be in effect as of October 23, 2016.

The draft of this document was issued on May 18, 2015.

For questions about this document regarding CDRH-regulated devices, contact the Office of the Center Director (CDRH) at 301-796-5900 or Anindita Saha at 301-796-2537 (Anindita.Saha@fda.hhs.gov).
Impact of patient preferences
FDA Example in Obesity

- FDA approved in 2015 the Maestro Rechargeable System for certain obese adults, the first weight loss treatment device that targets the nerve pathway between the brain and the stomach that controls feelings of hunger and fullness.

- The clinical study did not meet its original endpoint, which was that the experimental group lose at least 10 percent more excess weight than the control group.

- In considering the benefits and risks of the device in its review of the Maestro Rechargeable System, the FDA considered the clinical study and the Panel’s recommendations. Additionally, the Agency looked at an FDA-sponsored survey relating to patient preferences of obesity devices that showed a group of patients would accept risks associated with this surgically implanted device for the amounts of weight loss expected to be provided by the device.

www.fda.gov
Summary

- Increasing examples of industry listening and involving their stakeholders
- Evidence that the regulatory agencies in EU and USA are developing their own initiatives
- Evidence that while regulatory decision making relies on strong efficacy and safety data, in areas of doubt, patient data can be useful to support the process
Thank You