CASE REPORTS
on meaningful patient involvement in industry-led medicines R&D

Cases provided by:

AKU Society - Amgen - Bristol-Myers Squibb - Duchenne Parent Project - EATG - EURORDIS - Genzyme - GSK - Janssen Leukemia Patient Advocates Foundation - Eli Lilly – Merck - MSD Novo Nordisk - Novartis - Sanofi - SMA - UCB

EUPATI WORKSHOP
"MEANINGFUL PATIENT INVOLVEMENT IN INDUSTRY-LED MEDICINES R&D"
23 July 2014, BERLIN

European Patients' Academy on Therapeutic Innovation (EUPATI)
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SUMMARY OF ALL CASE REPORTS

Each participant in the EUPATI Workshop was tasked to do some preparatory work with other people in their organisation that have engaged in collaborative R&D activities between patients and industry R&D. Below is a short summary of all the cases submitted by 7th June 2014.

21 case reports were submitted in total by the following organisations: AKU Society (1), Amgen (2), BMS (1), Duchenne Parent Project (1), EATG (1), EURORDIS (1), Genzyme (1), Eli Lilly (1), GSK (1), Janssen (1), LePAF / CML Advocates Network (1), Merck (1), MSD (1), Novartis (3), Novo Nordisk (2), Sanofi (2), SMA – Spinal Muscular Dystrophy Ukraine (1) and UCB (1).

A wide range of partners were involved and patients and patient advocates were involved. Cases ranged across the various medicines development phases.

Types of cases included:

- A series of three clinical studies whereby the AKU Society ensured patient views were considered at planning stages, and throughout the ongoing studies
- FUNDHEPA staff were the first contact with patients for a trial - they explained the purpose of the clinical trail and the benefits
- Patient organisation involvement across the development of a cure/treatment for Duchenne Muscular Dystrophy
- The patient community playing a key role in achieving a trial which involved the concurrent use of two unregistered compounds for the first time in the HIV area
- The patient community expressing concerns and working towards agreements with industry to exclude patients with fewer than 200 CD4 cells in order to avoid increased risk in phase 2b dose finding studies
- Patient organisations assisting in disseminating information about infantile onset (IO) trials, locating patients around the globe, finding lodging, parent support, recruitment, review of assessments, encouraging retention, presenting at the oral explanation at the EMA (a first) and developing a patient reported outcome survey.
- Face-to-face patient interviews with the objective of increasing understanding of the impact of psoriasis on the lives of patients, patient views of device design concept to potentially deliver drug to the skin and future clinical study endpoints
- Clinical Operations seeking feedback on a parental patient information leaflet (PIL) from a consumer representative group
- HIV patients being actively involved pharmaceutical R&D
- A meeting of CML patient advocates with clinical development and patient relations staff of a major pharmaceutical company to revise a trial protocol
- An Advisory Board with patient organizations to address patient relevant endpoints in psoriasis clinical trials involving 6 National Psoriasis Patient Organizations representatives
- Obtaining specific feedback on sections of a draft protocol from patients, caregivers, advocates, and research study coordinators on Cushing's disease clinical trial development
- Representatives of E-TSC being involved from the first meeting of investigators to design the TuberOus SClerosis Registry to Increase Disease Awareness (TOSCA) to address some of these gaps by collecting data from patients across many countries worldwide
- A framework for a patient sounding board with aims, guidelines and principles developed together with the International Alliance of Patients' Organizations
- A department made up of professional researchers responsible for ensuring the quality and compliance of user research used in early device development
- A qualitative assessment of the existing Written Subject Information (WSI) / Informed Consent Form (ICF) resulting in a review and a practical and concrete template for the use of a Clinical Research Unit Team Members
- A patient committee structured and trained to be able to review informed consent and protocol (review done under confidentiality agreement)
- A pilot clinical trial addressing issues in SMA clinical trials
- Direct feedback on the informed consent form gained from different settings (i.e. not through the usual market research channel).

SUMMARY OF ALL CASE REPORTS

Benefits included:

- Involving patient groups as active partners to lead in tasks such as patient recruitment and patient retention
- Building a new process to ensure the correct approach by the correct person(s) to patient organizations
- Patients being the driving force to speed up research and translation from the lab to the patient (bench to bed)
- The collaboration of two POs from both sides of the Atlantic entering a new, more intensive phase, thus allowing exchange of experience across the communities of people living with HIV
- Establishing a consensus that exposing patients with immediate treatment need and compromised immune systems to dose finding studies was ethically problematic and without benefit for industry
- Patient relevant endpoints being identified e.g. Quality of Life as primary secondary endpoint, efficacy and safety long term, rapidity for young patients
- Knowledge and surveillance on a rare disease and orphan drugs being increased, outcomes being registered, and the effectiveness of treatment being assessed by incorporating patients across the EU
- The input received from a consumer group on a parental patient information leaflet (PIL) resulting in a major revision of the document and consequently to a revision of child and adolescent assent forms. A further benefit was also the shortened review timeline from the Ethical Review Board (just 20 days from ERB meeting to approval being issued) and the very few comments received on the document
- Direct collaboration resulted in a) more targeted development; b) a better understanding of real needs for research and development; c) faster study enrolment; d) closer contact between R&D experts and benificiaries (motivational benefit), and e) better outcomes for patients
- Involving patients into the process of protocol development did not result in delays as serious issues that might have threatened recruitment, trial retention or ethics were uncovered at the design stage, and resolved before submission of the protocol to authorities
- Hearing the impact of disease on day-to-day life really motivated the team to develop new medicines
- The use of user research to understand patients' articulated as well as unarticulated needs, and thereby 'test' whether the technological innovations match and meet real users' real needs
- Placing the patient at the heart of the information system and as the primary recipient of the informed consent document
- A 'Quick Guide' gave quick facts regarding the trial providing patients with an advanced understanding of whether the trial could be right for them.

Challenges and Barriers included:

- Translations add a significant cost to production of patient information
- Several meetings are necessary with patient organisations and industry to reinforce the importance of giving the opportunity to patients to receive an innovative treatment for their disease through participation in a clinical trial. It also takes time to align regarding communication materials such as the invitation for the webpage for a trial
- Pharma may face strict rules that make interacting with patients difficult before a product is on the market
- The use of two experimental compounds was not common practice. Substantial advocacy (political) input was required from the patient community to convince the developer (and in turn FDA, EMA & NCA) of this new strategy
- Despite clarity of objectives it is difficult for a patient organisation to negotiate with three companies at once
- Development teams are given very strict timelines to complete protocols and get trials moving which results in resistance in these teams to add another layer of input into protocol development
- Finding expert advocates with specific knowledge in clinical trials
- The dynamic and communication style of the different board members who met to discuss the registry (TOSCA) had to be adapted to the different scientific knowledge and understanding of the 3 components (investigators, company, PO representatives)
- Patient organisations can be unwilling to work with industry due to their policies
- Making changes to patient information leaflets/consent forms (ICF) is not an easy task and takes additional time and significant discussion with all functions involved
- Professors and experts are not always in favor of having patients on board
- Perceived legal barriers for disclosure of the trial synopsis and protocol (solved by persistence of the patient relations department to agree on NDA).

SUMMARY OF ALL CASE REPORTS

Challenges and Barriers (continued):

- Resistance of the clinical development team to involve patients and agree on a face-to-face meeting with patient advocates, mainly due to the lack of perceived value (these perceptions completely changed as a result of this meeting)
- Patient involvement can have implications for human resources (preparations, delegate involvement, telephone meetings, contracts, administrative work), travel and venue costs (due to global geographical reach)
- Expectation management and the need to clarify upfront how potential use of any advice offered by patients would be fed back
- Lack of specific experience in SMA R&D in Ukraine
- Many internal as well as external rules and regulations. In order to ensure compliance comprehensive guidelines can be developed
- There were worries that the ethics committees might not approve the suggested format or text of amended versions of the informed consent sheet but in the end comments were very minor in many countries.

The main discussions and learnings for EUPATI may be:

- Patient groups are the most involved in understanding how the disease affects patients and so make a good choice for partners in research
- It is important to have early contact between patient organizations and industry in the interest of working together
- POs should collect (and own) natural history data at an early stage
- A trio should be established of academic experts, POs and an internal project physician with rules of communication at the start
- New strategies and uninterrupted work, complete with continuous self-education and rigorous knowledge of the field by the patient community are needed in order to navigate the complex setting of drug development and research
- Better coordination of efforts and more transparency in the complicated field of drug development (further worsened by fierce competition between companies) is an uphill battle for the patient community
- Earlier start (phase II and protocol design phase)
- It could be very useful in the future to involve patient representatives already educated by the EUPATI Platform
- The patients involved want to know how their insight had informed industry so a thank you letter with a high level summary of findings was sent to each patient
- Patient literacy needs to be ensured to optimise feedback
- A short, concise and well-prepared meeting between the clinical development team and an experienced patient advocate can induce a mind set change particularly when initiated, enforced and facilitated by the responsible patient relations person
- Every patient advocate is different and offers a different mix of personal and professional interests, insights and skills
- The anthropological approach to gaining more insights into users' perspectives is extremely valuable in the early phases of development. It is important to understand that people do not express their needs explicitly and can exist on an unarticulated level. Qualitative research methods, and researchers trained in this approach are needed
- The "universality" of the writing system for informed consent leaflets was verified by developing it on studies in Tunisia, Morocco and French-speaking Africa
- All the informed consents are reviewed by the Patient Committee prior to the submission to Ethics Committee
- A key factor for the successful advancement in SMA research is the sufficient number of experienced and motivated researchers as well as patient representatives and R&D EU experts
- The feedback from patients can be dependent on the type of patients involved resulting in a bias, based on personal experience and expertise. There also needs to be a trade-off between the wishes and suggestions of patients and what is realistically feasible.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

DevelopAKUre: An international public-private partnership to cure alkaptonuria (AKU)

PROVIDED BY:
AKU Society (Oliver Timmis, oliver@akusociety.org)

PARTNER(S) INVOLVED:
Industry (Sobi), Patient groups (AKU Society and ALCAP), Hospitals (Royal Liverpool, Hopital Necker, National Institute of Rheumatic Diseases), Academia (Universities of Liverpool and Siena, Institute of Molecular Physiology and Genetics) and SMEs (Nordic Bioscience, PSR and Cudos).

Description of the case (how were patients involved in your R&D project? What was the objective?

DevelopAKUre is a series of three clinical studies, funded by the European Commission's FP7 programme. They will investigate the drug nitisinone to find evidence if it works to treat alkaptonuria (AKU). The project involves a dose-response study (SONIA 1), an efficacy study (SONIA 2) to compare no-treatment to treatment, and a cross-sectional study (SOFIA) to determine the best age to begin treatment. Studies take place at three sites across Europe (UK, France and Slovakia).

DevelopAKUre is patient-led, with the AKU Society as a lead partner, ensuring patient views were considered at planning stages, and throughout the ongoing studies. The AKU Society now leads on patient recruitment and support, developing patient information documents and promoting patient retention. The AKU Society raised additional funding from a crowdfunding campaign hosted on Indiegogo in order to be able to provide a high level of patient care throughout DevelopAKUre.

The AKU Society is also coordinating dissemination for the project, ensuring project activities are shared with patients and the public.

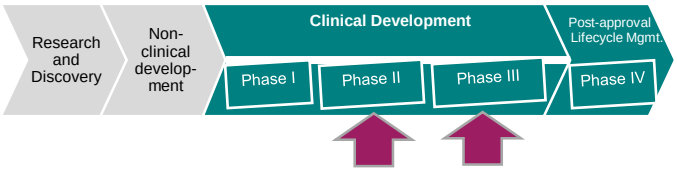
More information at www.DevelopAKUre.eu

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

DevelopAKUre is unique: a truly patient-led clinical trial. We believe it could create a new paradigm in medical research, helping to promote patient involvement in planning and running of clinical trials, and introducing the idea of involving patient groups as active partners who can lead in tasks such as patient recruitment and patient retention.

The involvement of patient groups in planning the clinical trials has improved the patient experience from advocating for a more streamlined expenses reimbursement process and funding carers' travel to making invasive tests optional and reducing the number of visits to test centres

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:
[X] Patients with personal disease experience
[X] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[X] Expert patient / patient advocate with good expertise on disease and good R&D experience

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

1. Funding: we spent several years attempting to raise funding for clinical research. We eventually applied and gained funding of €6 million from the European Commission. As medical research is so expensive, we would find it unlikely national bodies could provide large enough grants for research into rare diseases.
2. Legal/Ethics: The AKU Society are leading on patient information, which requires professional advice on legal and ethical concerns. We rely on other partners (PSR) and review boards for this input.
3. Language: The biggest barrier for patient recruitment in Europe has been language issues. Translations have added a significant cost to production of patient information.
4. Regulatory Issues: resolved through external advice mainly our SME partners, and scientific advice from the EMA.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

We hope to see more patient-led research, where patients are involved in planning and running studies, and patient groups are given an active role. For us, patient groups are the most involved in understanding how the disease affects patients and so make a good choice for partners in research. Additional training (such as from EUPATI) in working with pharma and academics, the drug development process and ethical/legal requirements of trials is needed. Many patient groups need encouragement to show there contribution is valued and important to medical research.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Advisory Board of Expert Melanoma nurses and Melanoma expert patient advocates

PROVIDED BY:
Mary Uhlenhopp, Amgen Europe

PARTNER(S) INVOLVED:
6 expert Melanoma nurses from across Europe and 5 Melanoma expert patient representatives , Amgen Medical Director, Director Regulatory Affairs, Advocacy and Nurse Education leads

Description of the case (how were patients involved in your R&D project? What was the objective?

Advisory Board meeting of Nurse experts and Advocacy group experts held to explore perceptions about novel treatments and scientific developments in the management of melanoma, discussion of oncolytic immunologic therapies; gain insight into the melanoma patient journey from a nursing and patient perspective, and define informational and supportive need of persons with melanoma.

The meeting included discussions about the melanoma patient journey, a presentation on TVEC by the Medical director (legally approved), presentation from experienced clinical trials specialist nurse and their view of the patient experience in that trial. Considerable discussion focussed on the diagnostic journey and access to clinical trials across Europe.

Clear identification and outline of patient informational needs as well as nurses informational needs and areas of collaboration were identified

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

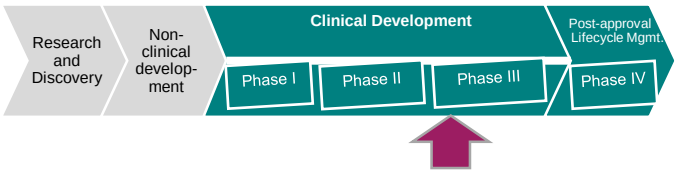
The practical and very 'real world' experiences highlighted in such a meeting can not be replaced by market research or other more remote or non-personal ways of collecting information. Internal team members were able to share these insights directly back to key individuals and decision-makers within the company to assure these voices were heard and the feedback was taken into consideration.

Meeting participants truly highlighted the challenges faced in the clinic setting with fatalistic attitudes toward the disease, reluctance to conduct biomarker tests, and often updated knowledge about where and what trials might be available.

The meeting minutes and outcomes were shared internally with regulatory and R & D leads within the company. Key insights about management and treatment realities and hurdles as well as opportunities were identified in various countries. Varying management and treatment plans exist in country and region. Nursing and Advocacy leads internally advocated for plans and resources to meet these stakeholders and will act as advisors to continue the dialogue and engage with these experts throughout the development process.

Triggered R & D to be aware of Patient needs, and also acknowledge practical realities in the Clinic/hospital setting. Debunk opinion leader thinking about patient experience or perceived patient needs.

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:

[**X**] Patients with personal disease experience

[**X**] Expert patient / patient advocate with good expertise on disease, but little R&D experience (some)

[**X**] Expert patient / patient advocate with good expertise on disease and good R&D experience (some advocates)

[**X**] Other, describe here: Expert nurses with expertise in R & D/Clinical trials

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Tasks (partly challenging)

- mapping and identifying expert nurses in melanoma and melanoma trials
- contacting, partnering and engaging with some melanoma advocate experts only due to time, work and family related constraints (part-time advocates who are full time employees and or care-givers)

Surmountable hurdles: managing expectations and understanding of country level medical and compliance leads to appropriately engage and invite the participants

Working through SOPs and interactions with the assigned agency to make the appropriate arrangements as well as directly with the advocates about the processes and agreements

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

General agreed upon principles across the company at Global, Regional, and Local levels about:

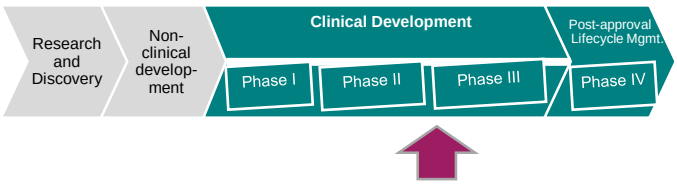
- Why to engage with expert nurses and patients
- How to engage with expert nurses and patients
- Clearly outlined process for all **to find/read** on the above two points
- Action plans and formats-not to reinvent the wheel each time one wants to conduct such a meeting
- For global and regional support to establish more systematic and regular meetings of such key external stakeholders and agree and maintain budgets, and responsible functions/persons to manage ongoing engagement and relationships

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Advisory Board of Expert GYN nurses and Ovarian Cancer patient group experts

PROVIDED BY:
Mary Uhlenhopp, Amgen Europe
PARTNER(S) INVOLVED:
Six expert GYN Oncology nurses from across Europe and 4 Ovarian Ca patient group representatives, Amgen Medical Director, Advocacy and Nurse Education leads

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

An Advisory Board meeting of Nurse experts and Advocacy group experts was held to explore perceptions about novel treatments used in the management of ovarian cancer; gain insight into the advanced ovarian cancer patient journey from a nursing and patient perspective, and define gaps in meeting ovarian cancer patient needs.

The meeting included discussions about the ovarian cancer patient journey, a presentation from a clinical trials specialist nurse and discussion of the patient experience in that trial as well as a presentation about novel agents in the management of ovarian cancer in current Phase II and Phase III trials.

The meeting enabled clear identification and outline of patient informational needs as well as nurses informational needs and areas of collaboration were identified.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

The practical and very 'real world' experiences highlighted in such a meeting cannot be replaced by market research or other more remote or non-personal ways of collecting information. Internal team members were able to share these insights directly back to key individuals and decision-makers within the company to assure these voices were heard and the feedback was taken into consideration.

The meeting minutes and outcomes were shared internally with regulatory and R & D Leads within the company. Key insights about management and treatment realities and hurdles as well as opportunities were identified in various countries. Varying management and treatment plans exist in country and region. Nursing and Advocacy Leads internally advocated for plans and resources to meet these stakeholder-needs and will act as advisors to continue the dialogue and engage with these experts throughout the development process.

The outcomes triggered R & D to be aware of Patient needs, and acknowledged practical realities in the Clinic/hospital setting. Opinion leader thinking about patient experience or perceived patient needs was debunked.

Type of patient (advocates) involved, tick all that apply:

[**X**] Patients with personal disease experience
[**X**] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience
[**X**] Other, describe here: Expert nurses with expertise in R & D/Clinical trials

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Tasks (partly challenging)
- mapping and identifying expert nurses in GYN oncology nurses, as well as ovarian cancer groups or expert ovarian cancer patient advocates

Overcoming this: speaking with many experienced advocates in broader cancer patient groups and gaining insights about how and with whom other industry sponsors in the ovarian space are engaging.

Surmountable hurdles: managing expectations and understanding of country-level medical and compliance leads to appropriately engage and invite the participants

Working through SOPs and interactions with the assigned agency to make the appropriate arrangements as well as directly with the advocates about the processes and agreements

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

General agreed upon principles across the company at Global, Regional, and Local levels about:
- Why and how to engage with expert nurses and patients
- Clearly outlined process for all **to find/read** on the above two points
- Action plans and formats-not to reinvent the wheel each time one wants to conduct such a meeting
- Establishing more systematic and regular meetings of such key external stakeholders and agree and maintain budgets, and responsible functions/persons ~~to~~ manage ongoing engagement and relationships

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

TREATMENT FOR MEXICAN HEPATITIS C PATIENTS: SYNERGY WITH FUNDHEPA

PROVIDED BY:
Bristol Myers Squibb Mexico
Ana Gabriela Gomez Velázquez
anagabriela.gomezvelazquez@bms.com

PARTNER(S) INVOLVED:
Fundación Mexicana para la Salud Hepatica FUNDHEPA, organization that promotes the hepatic health in Mexico http://www.fundhepa.org.mx

RESEARCH/DEVELOPMENT PHASE:

Type of patient (advocates) involved, tick all that apply:
[√] Patients with personal disease experience
[√] Expert patient / patient advocate with good expertise on disease, but little R&D experience

Description of the case

In México the prevalence of Hepatitis C in general population is 1.4% and almost 60% of patients treated with standard interferon and ribavirin do not respond to treatment. Non treatment or treatment failure can lead to cirrhosis and hepatocarcinoma. Results of clinical trials phase II of BMS hepatitis molecules were very encouraging. Mexico was invited to participate in some phase III hepatitis studies. FUNDHEPA was contacted and several meetings were held with the ultimate goal of giving the opportunity to Hepatitis C patients to receive an innovative treatment that had already proved efficacy. During the meetings the characteristics that patients need to have so they can participate in the clinical trial were review until they were well understood by FUNDHEPA staff because they were going to be the first contact with patients. They were going to give them an explanation of the purpose of the clinical trail and the benefits. An invitation for participating in the Hepatitis C clinical trials was posted in FUNDHEPA's web page. Patients called FUNDHEPA and staff from the organization made some question that help them to refer the patients to the nearest investigational center. *Fifth teen patients were referred and nine of them were included in the clinical studies and received the benefit of the treatment .*

Benefits

BMS mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. In R&D through the conduction of clinical trials we ensure that this happens. With the help of FUNDHEPA, the patients received treatment and at the same time the number of patients who have to be treated to have information regarding efficacy and safety was reached. In BMS Mexico a new process was build to ensure the correct approach by the correct person (s) to this kind of organizations.

Challenges and barriers

This was our first collaboration with an organization that takes actions for the patients benefit. Basically two challenges were present; several meetings with FUNDHEPA staff were needed to reinforce the importance of giving the opportunity to patients to receive an innovative treatment for their disease through the participation in a clinical trial. This made the process longer . The second challenge was the time it took to aligned BMS and FUNDHEPA regarding the text that the invitation that was going to be posted in the web page must have. This text had to be approved by the FUNDHEPA medical committee and by BMS.

Discussion and learnings for you and EUPATI

It´s very important to have an early contact with these organizations in the interest of start working together since there are several points where an agreement has to take place in order to take actions. Sometimes, because of the nature of the organization it will require a greater investment of time for these actions to take place. BMS Mexico currently has a program to contact and work with these organizations or PAG´s before the clinical trials arrives to the country thus giving opportunity to set action plans for the patients benefit. To add value to the program the dissemination of the information regarding clinical study and its benefits must be communicated to patients in advance.

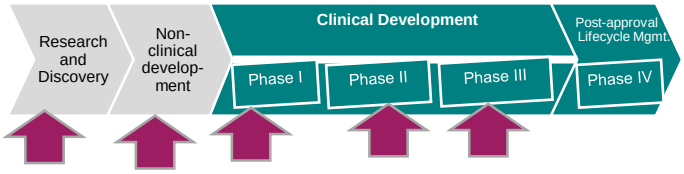
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

DUCHENNE PARENT PROJECT – development of Exonskip technology for Duchenne MD

PROVIDED BY:
DUCHENNE PARENT PROJECT

PARTNER(S) INVOLVED:
DUCHENNE PARENT PROJECT
– LEIDEN UNIVERSITY
– PROSENSA - GSK

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Development of a cure/treatment for Duchenne Muscular Dystrophy

Funded research at the University (Leiden) and Biotech (Prosensa)

Funded the phase 1b trial (local injection)

Was involved in:
- Recruitment and Patient registries for the follow up trials
- Standards of care (needed for Clinical trials)
- Development of Outcome measures
- Information to families and patients
- Regulatory discussions

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

DPP was part of the initiative from day one, without DPP the research project and follow-up probably had never started.

At the end drugs have to be proven 'clinically meaningful' to the patients, so starting from the patients is a very manner to develop drugs. (bed to bench)

Patients are the driving force to speed up research and translation from the lab to the patient (bench to bed).

Type of patient (advocates) involved, tick all that apply:

[x] Patients/Parents with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[x] Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other, describe here: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Collaboration with the Biotech company was 'easy' however when the first product was taken over by 'Big Pharma' GSK, collaboration (such as discussions about trial design, outcome measures and recruitment and other policies) became very difficult as Big Pharma has strict rules not to interact with Patients before a product is on the Market. To have companies design trials for the full spectrum of patients and not only for a small label as at the end when the product comes on the Market it is very likely only authorised for the same small label.

Regulators having very limited knowledge about the disease.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

In retrospective we should have started earlier with the collection of Natural History data. When you want a cure, collecting Natural History data don't sound 'sexy', but it can really help speeding up the process of drug development, cut down the size of the placebo group. When Natural History data are collected (and owned) by PO they can be used by different companies.

Make sure you have outcome measures for all groups. We started and funding initiatives to develop these outcome measures.

Raise awareness among regulators about your disease and the preferences of the patients.

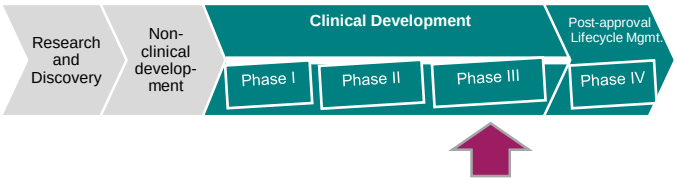
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Patient advocacy for combination of two investigational compounds: DUET 1&2

PROVIDED BY:
European Community Advisory Board of the European AIDS Treatment Group (EATG/ECAB), www.eatg.org

PARTNER(S) INVOLVED:
Pharmaceutical company, AIDS Treatment Activists Coalition Drug Development Committee, USA

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

The pharmaceutical developer Tibotec (now Janssen Therapeutics) designed the DUET 1 & 2 studies in 2005. The DUET phase III trials involved the concurrent use of TMC125 (etravirine) and TMC114 (darunavir) in a HIV treatment experienced population. The unique feature of the trial was that both compounds used had not been licensed at the time of use (2006). This was the first occasion that two yet unlicensed compounds were used in a trial in a treatment experienced setting, albeit only in one arm, while the other arm of the trial remained placebo-controlled.
HIV infection is a yet incurable but manageable disease that requires a relatively rigorous regime of antiretroviral medication (ART) for the patients in order to avoid resistance. Resistance to certain drugs or classes of drugs is more common with treatment experienced patients who therefore need novel or more complex regimens to control virus reproduction in the body.
The patient community played a key role in achieving that – for the first time – a trial involved the concurrent use of two unregistered compounds. Standard procedure is to use a single new compound in a trial.
The objective of this intervention of the patient community was to make sure that a potent novel combination of ART is available as salvage therapy for heavily treatment experienced patients. Compassionate use of the novel treatment regime through the trial was advocated for.

Type of patient (advocates) involved, tick all that apply:
[**X**] Patients with personal disease experience
[**X**] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[**X**] Expert patient / patient advocate with good expertise on disease and good R&D experience

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Providing compassionate use of novel compounds to patients with reduced treatment options was and remains a challenge. The participation in clinical trials is an effective tool for patients to access new drugs.
The use of two experimental compounds was not common practice. Substantial advocacy (political) input was required from the patient community to convince the developer (and in turn FDA, EMA & NCA) of this new strategy.
An important meeting was held with ATAC-DDC, EATG/ECAB and the pharmaceutical company in Antwerp in 2005.The specific objective of the meeting was to convince the company of the usefulness of and need for a new approach to help patients in need.
However, one main challenge remained that the pharmaceutical company decided to design the trial with one placebo-controlled arm, meaning that 50% of the patients received placebo + one investigational compound rather than both new drugs.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

Consultation between the patient community and the pharmaceutical developer matured and evolved during this process significantly. The PO's involved could successfully demonstrate to the industry and the regulators that the knowledge and experience of the patient community can yield substantial input into the development process. The innovative approach of the community infused the development process with a certain degree of "courage" to go apply unconventional strategies when preliminary results from previous trials are convincing enough (both new compounds were already known to be safe and well tolerable at the time).
This new approach led to lasting results and trust between the stakeholders involved. The collaboration of two PO's from both sides of the Atlantic entered a new, more intensive phase, thus allowing exchange of experience across the communities of people living with HIV. The DUET study resulted in overcoming accumulated MDR for thousands of heavily pretreated patients.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

The involvement of patient organisations and expert patients in pharmaceutical development is no longer unique. However, new strategies and uninterrupted work, complete with continuous self-education and rigorous knowledge of the field by the community are needed in order to navigate the complex setting of drug development and research.
More intensive interaction with regulators is required to leverage the political objectives and pressure that PO's want to exert to achieve their objectives; in this case the availability of new treatment options.
Despite all efforts, the PO's could only achieve a partial result: a placebo-controlled arm remained part of the trials concerned. Improvements in this area could, however, be achieved in later study designs developed with patient involvement.
Even better coordination between PO's and a more regular exchange of experience within and outside a specific disease area should improve the effectiveness and efficiency of patient involvement in research.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Own experience as interface between sponsors of clinical trials and participants

PROVIDED BY:
François Houÿez
PARTNER(S) INVOLVED:
[Experience both in rare diseases with EURORDIS (2003-today), and in HIV/AIDS Act Up – Paris (1989-2002), TRT5 (1995-1998) , EATG (1995-2002)

Description of the case (how were patients involved in your R&D project? What was the objective?

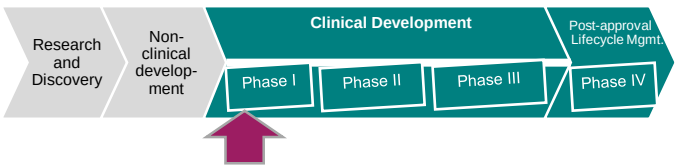
This question is probably written for sponsors of clinical trials who enrol patients in their projects, more than for patients' advocates.
This being said, the numbers of clinical trials in the design, conduct, DSMB, results analysis and communication of which I was personally involved approximates 77. This includes trials with a few hundreds to a few thousand patients.

Methods:
- TRT5: SOP approved by the national AIDS research agency (ANRS) according to which all protocols of clinical trials in AIDS/HIV (including opportunistic diseases), viral hepatitis and other viral diseases have to be discussed with patients' advocates prior to their submission to ethics committee, and progress review for each of them all along the clinical trials;
- In parallel TRT5 also met with private sponsors (industry) but on a voluntary basis;
- EATG/European Community Advisory Board: from 1996 to 2002, on a voluntary basis, clinical trials run by industry or public research organisations (e.g. INITIO trial by HIV Connect)
- EURORDIS: implementation of the Charter for Clinical Trials in Rare Diseases signed by 7 companies, one of which has signed a memorandum of understanding with relevant patients' organisations (working together on 2 clinical trials and one compassionate use programme)

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

No systematic evaluation of the processes and results in the methods explained above.
However this whole process made possible:
- Substantial changes in CT protocols: discussion on the therapeutic index led a sponsor to add one arm to a phase III trial testing a dose that wasn't initially proposed by the investigators. This dose turned out to be the authorised dose when was authorised;
- Substantial changes in the product development plan: trials which had not been planned by the company but proposed by advocates were added and successfully conducted;
- Interruption of trials: trials which had been authorised and approved by ethics committees were finally interrupted as patients advocates expressed ethical issues after the trial had started;
- Choice of the relevant outcome: for rare diseases, when no or little clinical research has been conducted before, it is essential to listen to patients for the identification/adaptation/creation of a relevant outcome.

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:
[✓] Patients with personal disease experience
[✓] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[✓] Expert patient / patient advocate with good expertise on disease and good R&D experience
[✓] Other, describe here: Patient advocate with no expertise on the disease and good R&D experience

Challenges and barriers (and how you have overcome them, or which ones were unresolved)
- Table of decisions & follow-up: it is essential to keep track of all discussions, text modifications and proposals made - a good secretariat managed by the patients;
- Confidentiality undertaking: signed documents are essential. If no confidentiality documents signed, don't even meet with sponsor, this is waste of time;
- Insider trading: ensure this risk is reduced, have participants sign an agreement not to use the information to buy or sell shares on the stock exchange
- Consistency of the opinion given: ensure long term commitment of patients' advocates and a pool of volunteers/staff with a good communication between all (see also first point above);
- Conflicts of interest prevention: transparency, share the agenda/minutes of the meeting with regulatory authorities;
- Transparency with the patients' community at large: define what will be discussed, agree what will be confidential and what won't be
- Adequate training / mentorship

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)
- Whom to interact with exactly? For public sponsors usually the main investigator. Private sponsors can mean (1) public relations and marketing department, (2) research team, (3) a mix. Only (2) should be considered.
- How to make sure decision makers interact with the advocates? And not simply go-between with little if no capacity to influence the sponsor's senior management?
- For international trials, how to coordinate with advocates across the world?
- Head-to-head comparisons ort multifactorial design trials where cooperation between competitors is needed: this is typically not happening, and yet very much needed. How to improve this?
- Dialogue on R&D is not just about obtaining marketing authorisation and/or reimbursement. How to open dialogue on the company's corporate responsibility at large?
- CT results and how to inform the trials' participants at the same time than investigators

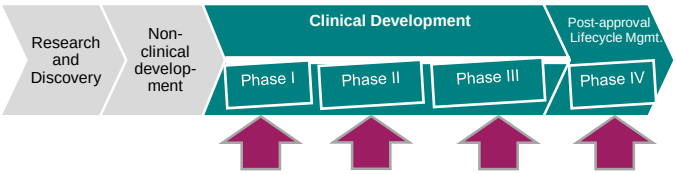
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Working with a patient organisation and academia in the development of a treatment for an ultra-orphan disease (Pompe disease)

PROVIDED BY: A. Dillon, K. Paradis, Genzyme, a Sanofi company. Annamarie.dillon@genzyme.com

PARTNER(S) INVOLVED:
International Pompe Association (IPA); UK, Dutch, and US Pompe patient associations, Erasmus Medical Center, Duke University

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Pompe disease is a rare inherited neuromuscular disease due to deficiency of a lysosomal enzyme. Babies with <1% of GAA enzyme present as the infantile onset (IO) form and usually die within the first year of life, while individuals with some residual GAA activity may present from infancy to late adulthood with neuromuscular weakness, ambulatory and respiratory issues. Work carried out at Erasmus Medical Center (EMC) and Duke University in the 1990's with knock-out Pompe mice showed promise with enzyme replacement therapy as a treatment. Clinical and manufacturing development was discussed on a regular basis jointly with the academic centers and patient organisations (PO). Clinical trials first began with the IO babies due to the extreme rapidity of disease progression. However due to the rarity of the disease (~1:40.000 births) recruitment was challenging. The POs assisted in disseminating information about the trials, locating patients around the globe, finding lodging, parent support etc. For the trials in children and adults, POs assisted in recruitment, review of assessments with Genzyme and investigators, and encouraging retention in these long placebo controlled trials (18 months) even after approval. A patient representative of IPA also presented at the oral explanation at the EMA (a first).The IPA in collaboration with EMC (supported financially by Genzyme) developed a patient reported outcome survey independently from industry years before treatment was available which has proven to be important in supporting reimbursement discussions.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

There is regular communication with POs for rare diseases on our development plans as well as some reviews of protocol assessments. This has become much more difficult recently with the rules of conduct that have been implemented. We do not (yet) have the patient collaboration implemented in standard operating procedures.

Type of patient (advocates) involved, tick all that apply:

[✓] Patients with personal disease experience
[✓] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[✓] Other, describe here: [professional patient advocate]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Development teams on the programs are given very strict timelines to complete protocols and get trials moving. There is often resistance in these teams to add another layer (on top of senior management from science, development, regulatory, safety, toxicology, clinical pharmacology etc.) of input into protocol development. By ensuring timely input from the PO and illustrating the benefits in the long-run in terms of recruitment, fewer screen failures, better completion of assessments etc., one can convince internal project teams that this is worthwhile. Another challenge in some countries is the difficulty of direct contact; in that case we asked the investigator to contact the national PO and review the protocol with them for input. Internal concerns about maintaining confidentiality was overcome with a confidentiality agreement with PO, which allowed for free and frank communication. Lastly, the IPA patient survey, although it has provided valuable Patient Reported Outcomes (PRO) and many publications, it is not considered as credible to regulatory authorities and payors due to lack of source data verification, a lesson which could be applied in the future.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Lessons learned: **1**. Establish a trio of academic experts, PO and internal project physician with rules of communication at the start **2**. Ensure that a PRO instrument is created and validated for the disease (what is the most important thing for the patient), with appropriate measures to ensure the data is robust and will satisfy regulatory and payor requirements **3**. Start a natural history study, with the PRO, years before the treatment will be available in order to be able to compare **4**. The most valuable input into the protocol is reviewing assessments, their feasibility etc. and should be standard. **5**. Keep community appropriately informed by providing program updates for dissemination through PO.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

PSORIASIS

PROVIDED BY:
Kay Warner, Focus on the Patient, Medical Platforms, GSK
kay.j.warner@gsk.com

PARTNER(S) INVOLVED:
Seven individual patients: one a Psoriasis Association representative

RESEARCH/DEVELOPMENT PHASE:
[Move the arrow left/right to mark the key phase where patient input was incorporated. Multiple phases = duplicate the arrow!]

Description of the case (how were patients involved in your R&D project? What was the objective?

Our Biopharm Discovery Medicine plus the Commercial Strategy teams working on developing a topical treatment for psoriasis sponsored a series of seven separate face-to-face patient interviews with the objective of:

- a greater understanding of the impact of psoriasis on the lives of patients
- patient view of device design concept
- future clinical study endpoints

These interviews were held at GSK Stevenage Medicines Research Centre from Dec 2012 to Jan 2013 and conducted by a GSK physician. Topics discussed were diagnosis, living with psoriasis, how patients are treated, problems with existing treatments and a discussion about the potential device and dosing techniques. Each interview was video-recorded as well as observed by one member from each sponsor team.

This insight was required at an early stage in the research and discovery phase before the novel device was further developed and to confirm that indeed the device concept would appeal to patients.

Type of patient (advocates) involved, tick all that apply:
[✓] Patients with personal disease experience
[✓] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience
[✓] Other, describe here: [GSK employees x 2 – not from R&D]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Due to the nature of the condition and its impact on an individuals' confidence, the main challenge was identifying patients who would be willing to come forward and speak about their experiences. During this activity, we learnt that many patients with the condition hide away so in recognition of this we extended the time period for these sessions to allow more time for patient identification. Our intended sample was 8-10 patients; no specific selection criteria applied.

During our outreach to identify patients through various different channels, we encountered one patient organisation who due to their policy were unwilling to work with industry.

The patients we interviewed were glad they were involved and offered to help again the future.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)
Understanding psoriasis from the patient's view point has influenced our program team and strategy moving forward. Hearing the impact of disease on day-to-day life really motivated the team to develop new medicines for psoriasis.

A number of important observations about psoriasis were drawn from this activity and patients raised many practical questions about the new treatment ideas which we talked about. This was one of the most useful outcomes from the interviews; these are exactly the kinds of questions we need to answer during our clinical trials.

We now understand for which patients such a device would be most suitable. Feedback on the device has also influenced the design and new prototypes are currently being evaluated.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Allow more time for outreach and patient identification

Greater and wider emphasis placed on the opportunity for patients and patient organisations to work with industry and the benefits this can bring to all stakeholders

The patients involved wanted to know how their insight had informed GSK; thank you letter with high level summary of findings was sent to each patient

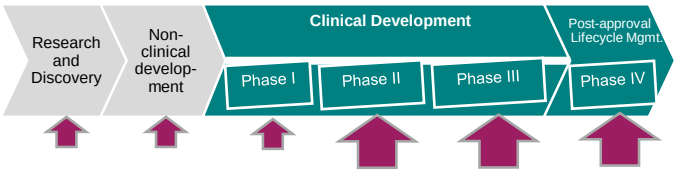
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

HIV PATIENTS ACTIVELY INVOLVED BY JANSSEN R&D

PROVIDED BY:
Janssen, Pharmaceutical Company of Johnson&Johnson

PARTNER(S) INVOLVED:
EATG – ELPA – TREATMENT ACTION GROUP

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Patient were involved as follows:
- Protocol design and review
- Informed Consent Form (ICF) review
- Participation in Drug Safety Monitoring Board (DSMB)
- Participation in Investigator Meeting
- Building capacity in the area of Health Economics

Janssen initiated also a collaboration with the London School of Economics and a talior-made eductaional program was constructed for the EATG members. Afterwards, the course was handed over for further capacity building within their organization without further company involvement.

Type of patient (advocates) involved, tick all that apply:
[**X**] Patients with personal disease experience
[**X**] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[**X**] Expert patient / patient advocate with good expertise on disease and good R&D experience

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

In disease areas outside HIV, professors and experts not always in favor of having patients on board.
We have discussed with them and showed EATG success example as model.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

Thanks to this collaboration we obtained:

- More targeted development.
- Better understanding of real needs for research and development.
- Faster study enrolment.
- Closer contacts between R&D experts and benificiaries (motivational benefit).
- Better outcomes for patients.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Need to structure the process to ensure continuing process beyond individuals.

Patient literacy needs to be ensured to optimise feedback

Ability to replicate this collaboration across more patient groups and advocates to increase knowledge on different topics, amongst other, Health Economics.

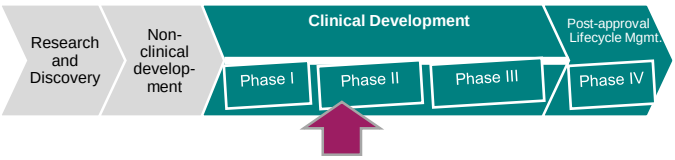
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Patient feedback on a trial protocol of a paediatric CML study

PROVIDED BY:
Jan Geissler <jan@cmladvocates.net>

PARTNER(S) INVOLVED:
A major pharmaceutical company.
CML Advocates Network / Leukemia Patient Advocates Foundation (represented by Jan Geissler, jan@cmladvocates.net).

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

A major pharmaceutical company prepared a phase 1/2 study of the pharmacokinetics, safety and efficacy of a new targeted drug in paediatric patients with a chronic myeloid leukemia (CML) with resistance or intolerance to other drugs. By the time of this protocol design, the drug was in phase III trials aiming for approval in adult use.

Paediatric CML is an ultra-rare condition which affects only about 20 children a year in a population of 80 million. Barely any larger pediatric center has more than 1-2 paediatric CML patients. Hence, recruitment into trials is difficult. By the time of the protocol review, 2 other drugs were approved for paediatric use.

The patient relations department set up a 2 hours meeting between

- an experienced patient / patient advocate with personal disease experience as well as advocacy experience in medicines R&D in CML, and
- clinical development staff involved in the protocol design.

The trial synopsis (16 pages) was shared with the patient advocate 14 days prior to the meeting, subject to non-disclosure agreements. The advocates' written comments were returned by the patient advocate to the clinical development 2 days prior to the meeting, and were then discussed face to face.

Feedback provided by the patient advocate focused on in/exclusion criteria (e.g. unnecessary exclusion of children <10 years, required ability to swallow pills despite dissolvability of the drug), access to the drug after the study conclusion, diagnostics (e.g. necessity of quite invasive bone marrow biopsies), dosing (e.g. number of pills given in paediatric use vs. difficulties in paediatric admission), involvement of parents in creation of informed consent / assent documents.

Type of patient (advocates) involved, tick all that apply:
[X] Patients with personal disease experience
[X] Expert patient / patient advocate with good expertise on medicines R&D

The development process was not delayed by involving patients, as the consultation was incorporated into the process of protocol development. Serious issues that might have threatened recruitment, trial retention or ethics were uncovered at design stage, and resolved before submission of the protocol to authorities.

Given there has been little prior exposure of the clinical development team to real (adult) CML patients and no prior experience with paediatric CML patients or their parents, a number of issues had surfaced that, according to our assessment, would have prevented parents from enrolling their children into those trials, or might have caused serious rates of trial drop-outs. According to clinical development, much of the feedback "was covering issues that we should have really thought about, but have not surfaced in discussions both within the team and with investigators prior to the meeting".

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

- Perceived legal barriers for disclosure of the trial synopsis and protocol (solved by persistence of the patient relations department to agree on NDA)
- Resistance of the clinical development team to involve patients and agree on a face-to-face meeting with patient advocates, mainly due to the lack of perceived value (these perceptions completely changed as a result of this meeting)

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

According to direct feedback of the clinical development team at the conclusion of the meeting, as well as feedback received by the patient relations department days later, the input received was perceived as "invaluable" and has led to significant modification of the trial protocol.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

This is a good example of a mind set change induced by a short, concise and well-prepared meeting between the clinical development team and an experienced patient advocate, initiated, enforced and facilitated by the responsible patient relations person.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Patient Friendly Informed Consent Document

PROVIDED BY:

Eli Lilly

Petra Kraus

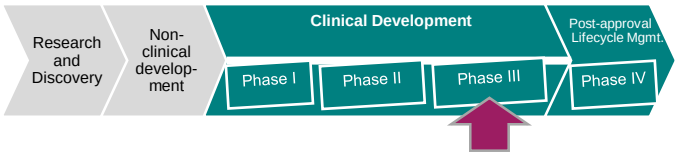
European Clinical Operations Manager

Werner-Reimers-Str 2-4, 61352 Bad Homburg, Germany

PARTNER(S) INVOLVED:

Patient Consumer Group [part of National Institute for Health Research (NIHR), Clinical Research Network]

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:

[ ] Patients with personal disease experience

[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience

[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience

[X] Other, describe here**: [consumer representative group (parent experienced in reviewing PILs)]**

Description of the case (how were patients involved in your R&D project? What was the objective?

In the UK, the National Institute for Health Research (NIHR) was established in April 2006 to provide the framework through which the Department
of Health could position, maintain and manage the research, research staff and research infrastructure
of the NHS in England as a national research facility. The NIHR's mission is to maintain a health research system in which the NHS supports outstanding individuals working in world-class facilities, conducting leading-edge research focused on the needs of patients and the public.
For a clinical study involving children aged 7 to 14 years, via the Medicines for Children Research Network (part of the NIHR), Lilly UK Clinical Operations sought feedback on a parental patient information leaflet (PIL) from a consumer representative group.
The input received from the consumer group resulted in a major revision of the document and consequently to a revision of the child and adolescent assent forms. Whilst connecting with the NIHR Clinical Research Networks has become common practice for the planning, set-up and enrolment of clinical trials, the involvement of consumer and patient advocacy groups is only just starting to happen.

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Making changes to patient information leaflets/consent forms (ICF) is not an easy task since we have an ICF creation process with mandatory templates and wording. To accommodate the suggestions from the consumer group, parts of the compound documents well as the local ICF template needed to be adjusted/ modified, and changes internally approved, which took additional time and significant discussion with all functions involved.

Although the consumer group reviewer had a very short turn around time of 2 weeks, the whole process with obtaining feedback, incorporation into our documents, internal discussion and approval of changes etc. took some additional time which resulted in a delayed ERB submission of approximately 1 month against the original planned date.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

Obtaining feedback from the consumer group on how they would like to see a PIL was very helpful for Lilly on our journey to move into a patient centric organisation. This collaboration led Lilly and CRO partner to recreate the documents with much more patient friendly wording, avoiding business, technical and medical terminology (e.g. sponsor, vendor, subject) that might be difficult for someone outside of the field of clinical research to understand.
Besides the appreciation from the patient point of view, the benefit for Lilly was also the shortened review timeline from the Ethical Review Board (just 20 days from ERB meeting to approval being issued) and the very few comments received on the documents.
ERBs are becoming increasingly interested in how patients are being involved in the research process. A question exists in the ERB application form to capture this, and although patient involvement is currently not a requirement, it is something ERBs like to see.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Understand upfront how the review process works for the consumer/patient advocacy group in question – what is the expected turnaround time and do they meet according to a fixed schedule (eg. ad hoc or monthly meetings)?

Upfront planning very early in the set-up process to allow sufficient time for the consumer group consultancy step thereby avoiding any delay to the ERB submission timeline. Early communication of the plan to the Lilly study team members who will be called upon for input to support the ICF development.

The ideal would be to create a standard process to include consumer representative/patient advocacy groups for the majority of Lilly clinical studies in the UK and have discussions with other EU affiliates to learn from this process and find synergies.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

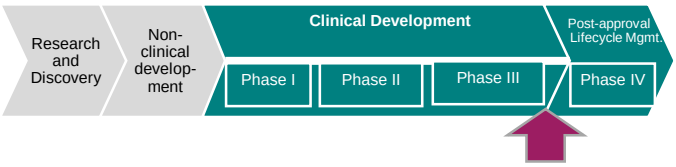
Patient Medication Labeling (USA)

PROVIDED BY:
Jeanne M. Regnante, Office of the Chief Medical Officer
1.267.305.1297 - jeanne.regnante@merck.com

Laurie Myers, Leader, Health Literacy and Healthcare Disparities Strategy
1.267.305.2376 – laurie_myers@merck.com
Merck & Co., Inc.

PARTNER(S) INVOLVED:
Northwestern University, Emory University

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:
[x] Patients with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[X] Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other, describe here: [ ]

Description of the case (how were patients involved in your R&D project? What was the objective?

According to the National Assessment of Adult Literacy, only 12% of adults possess “proficient” health literacy. Some 14% are estimated to be “below basic” in health literacy, an estimated 30 million people. Groups most vulnerable include those over age 65, recent immigrants who don’t speak English, people with limited educations, and those with limited incomes.

The patient label is important because it provides patients information about dosing, potential side effects, and conditions for which the product is used. It also forms the basis for communications to patients about our medications. This may include patient education materials, product websites, print advertisements, and direct to consumer TV advertising.

The simplified label is the result of a two-year cross-divisional effort within Merck and in partnership with health literacy experts at Emory and Northwestern universities to create a labeling format that nearly everyone – including people with limited health literacy levels – can understand.

We are working with the FDA to share our data and hope to result in a new standard for patient labeling.

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

In the past, Merck has had extremely small or no representation from individuals with limited literacy in our market research. By working with external experts at Northwestern and Emory, and our own marketing research team, we learned how to recruit this population for our patient labeling research.

Developing a new standard meant tapping into groups that do not typically self-select to participate in research and are not in recruiter databases: people whose health literacy levels are limited.

For example, the initiative required creative new approaches to finding study participants, including recruiting from literacy centers and senior centers. Patient research commonly excludes people over the age of 75 from studies. Those over 75, however, typically have the greatest burden of multiple chronic diseases requiring prescription drugs, and are more likely to have limited health literacy.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

The comprehension test used in the research sought to measure, among other things, whether the subjects understood what condition the medicine was meant to treat, how it was dosed, and possible side effects. Research by Northwestern and Emory had shown a significant gap in comprehension between limited health literacy and adequate health literacy respondents. Testing of our new format showed we virtually eliminated differences in comprehension between low-literacy populations and the general population. In addition, comprehension of the draft patient label was very strong for both limited health literacy (86%) and adequate health literacy (95%) respondents.

The best practices developed during Merck’s efforts could be a significant public health benefit when companies and other organizations understand how to identify the right populations for testing their products and services.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Compared to historic comprehension testing trials performed within this one pharmaceutical company, the application of health literacy evidence-based practices via partnership with an academic research team led to unprecedented performance in its evaluation, especially among those with limited health literacy. This partnership should be viewed as a model that could be adapted by other pharmaceutical companies as well as other industries in healthcare (i.e. health insurers, medical device makers), and perhaps health systems that generate patient-facing communications.

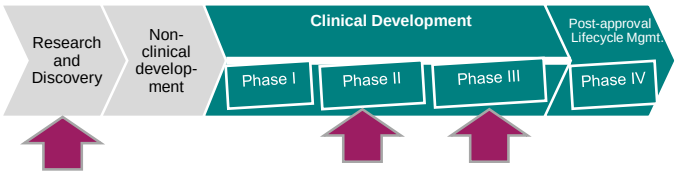
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Patient Input Forum

PROVIDED BY:
Merck & Co.
Jeanne M. Regnante | Office of the CMO | phone: 1.267.305.1297 | mobile: 215.738.6527 | jeanne.regnante@merck.com

PARTNER(S) INVOLVED:
Alzheimer's Disease
Treating Neurologist, Patient and Caregiver

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Consistent with the corporate strategy to enhance human health and focus on the patient, the primary objective of the Patient Input Forum (PIF) is to expose the company's workforce to "real world" patients and hear their perspective on living with a disease in a key therapeutic area where we are working. The patient (and caregiver) input will provide meaningful insight for company employees as they work to optimize, develop, and launch innovative products and services with a focus on the patient.

The company engages with physician facilitators based in the U.S. who in turn will identify patients who are willing to share their experiences with their illness, including their overall treatment experience and systems of care, and to respond to questions submitted in advance , and from the audience of Merck employees. The physician will serve as the patient interviewer. The meeting lasts approximately one hour and will be conducted at a company site as a webcast (with a live audience of employees). The physician, patient and caregiver also participated in an informal meeting with invited members of the company team to gain deeper understanding on the disease burden from PIF participants.

Type of patient (advocates) involved, tick all that apply:

[X] Patients with personal disease experience
[X] Other, describe here: [Caregiver]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Evaluation of the appropriate policies and development of guidance documents to define process and procedures for an event involving patients. Identification of patient and caregiver who were willing to participate and had the courage and communication skills to engage in meaningful dialog.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

This event happened very recently. Feedback from employees highlighted value to hear first-hand the impact of an AD diagnosis and about living day to day with the difficult challenges of the disease. Also the clinical team heard important input related to clinical protocol/ trial design and aspects of trial conduct that could be more patient-friendly. The consideration of whether or not to participate in clinical trials was especially insightful as well as how the caregiver obtains the information she uses to make such decisions. Her sense of responsibility for the patient was quite powerful and the importance of trust and good communication with the treating physician was evident. The R and D team was left with a feeling of the significance and urgency for the work that they do as well as the gratitude from the patient and family for all the ongoing work to advance novel treatments.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Given the internal feedback from this event, one outcome is that we will consider to doing more of these across various therapeutic areas and perhaps stages of disease as it really catalyzed discussion and energy for the work ongoing in R and D organization. Also feedback from the physician and caregiver were that it was a meaningful experience, including meeting the people within the company who are working to "make a significant impact in the fight against AD". Sharing of best practices and various approaches to obtain patient input should continue to be supported externally.

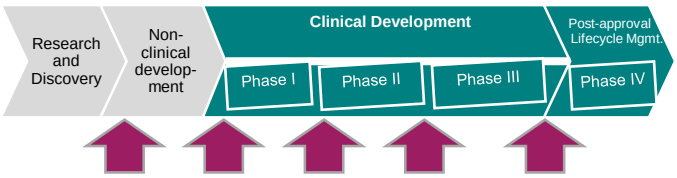
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Patient sounding board

PROVIDED BY:
Novo Nordisk A/S

PARTNER(S) INVOLVED:
International Alliance of Patients' Organisations and local patient organisations

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Objectives
- To ensure that patient perspectives on Novo Nordisk's work are explored and acted upon, so the company can better address patient needs as expressed by patients and patient representatives and facilitate ongoing dialogue between patients, patient organisations and Novo Nordisk.
- To apply a full cycle involvement approach (scoping, strategy, implementation and evaluation) and develop learnings for future use.

Methodology
A framework for the patient sounding board with aims, guidelines and principles were developed together with the International Alliance of Patients' Organizations.

10–16 board members consisting of people with diabetes and haemophilia, family members of people with diabetes or haemophilia and patient organisations from different regions and continents were invited.

Implementation
- Meetings of 1-2 days duration were held.
- Representatives from R&D and other parts of the organisation were engaged in advance to propose priority questions/topics of interest. Topics of particular relevance and interest to the sounding board were covered.
- Minutes outlined the conclusions and implications.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

New important perspectives related to patient-centricity were identified by the various representatives from different parts of the organisation who took part in different sessions.

Specific global projects were concretely adjusted to optimise particular aspects from a patient's perspective in accordance with detailed inputs from the sounding board.

There was improved understanding that it is possible and of great value to obtain the patients perspective on a range of issues.

Type of patient (advocates) involved, tick all that apply:
X Patients with personal disease experience
X Expert patient / patient advocate with good expertise on disease, but little R&D experience
X Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other, describe here: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Challenge:
It is resource demanding:
- Human resources (preparations, delegate involvement, telephone meetings, contracts, administrative work)
- Travel and venue costs (due to global geographical reach)

Solution:
- Do meetings less frequently, use fewer persons tailored for the specific questions
- Consider electronic communication opportunities

Legal and contractual paper work could not be diminished.

Challenge:
Expectation management

Solution:
- Clarify upfront how potential use of any advice offered by the sounding board would be fed back

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

"Everyone is different"
Every patient advocate is different and offers a different mix of personal and professional interests, insights and skills.

It is essential to:
- Understand each person's interests and unique contribution areas
- Carefully ensure that the profile of the patient expert matches the specific requirements for input in each case. E.g. considering age, professional experience background, patient advocacy experience, specialisation in certain topics, geography, etc.

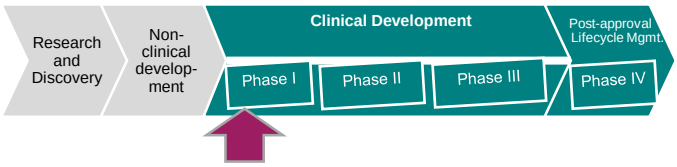
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Using User Research – Training in the anthropological approach

PROVIDED BY:
Novo Nordisk

PARTNER(S) INVOLVED:
Patients

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

In Novo Nordisk Device R&D we do user research with patients.

The purpose of user research is to enhance understanding of users in order to develop products that meet users' needs. More specifically, user research within Device R&D is performed in order to:

- Gain or refine an understanding of user needs
- Get feedback on product and/or service concepts
- Evaluate the usability of devices and packaging material.

The user research is designed to the specific project's needs and methods are decided accordingly.

We have a department made up of professional researchers, responsible for ensuring the quality and compliance of user research used in early device development.

Type of patient (advocates) involved, tick all that apply:
[x] Patients with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other, describe here: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

There are many internal as well as external rules and regulations. In order to ensure compliance we have developed comprehensive guidelines for user research, which describes the process flow which all user research has to follow.

The department conducts the research and when project members (e.g. engineers) are invited to participate in the research – they will be trained beforehand in the anthropological approach and in rules and regulations.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

Through user research we try to understand patients' articulated as well as unarticulated needs, and thereby 'test' whether the technological innovations we are conducting match and meet real users' real needs.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

We learned that it takes a lot of resources to ensure compliance with rules and regulations.

Another learning is that the anthropological approach to gaining more insights into users' perspective is extremely valuable in the early phases of development. It is important to understand that people do not express their needs explicitly – most of the issues interesting for us exist on an unarticulated level – therefore qualitative research methods, and researchers trained in this approach are needed.

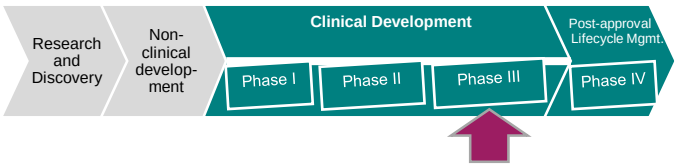
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

INPUT OF PATIENTS ORGANISATIONS INTO CUSHING'S DISEASE CLINICAL TRIAL DESIGN

PROVIDED BY:
Susanna Leto di Priolo Patient Relations Novartis Oncology

PARTNER(S) INVOLVED:
Nurses from USA, Canada and Brazil; USA Cushing patients, caregivers and patient organisations representatives

RESEARCH/DEVELOPMENT PHASE:
[Move the arrow left/right to mark the key phase where patient input was incorporated. Multiple phases = duplicate the arrow!]



Description of the case (how were patients involved in your R&D project? What was the objective?

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

Type of patient (advocates) involved, tick all that apply:
V Patients with personal disease experience
V Expert patient / patient advocate with good expertise on disease, but little R&D experience
V Expert patient / patient advocate with good expertise on disease and good R&D experience
V Other, describe here: nurses

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

No specific barrier

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

The following topics were discussed and then given to the development team

- 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 Duration, Transportation and Visit Schedule were named among the main barriers from the patient perspective
- Working with PAGs in clinical trials is crucial. PAGs should be used to announce and disseminate information about trials to boost enrollment

Consideration on the proof of concept and possible importance of the drug being studied for the patients
Results:

- Trial design was better tailored to patients needs
- Different perspectives and insights allowed to better inform a study design

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

Prepare better the advocates to the discussion, such as

What a clinical trial is
Why a clinical trial is important
What to expect in a clinical trial, along with the time commitment it requires
Why certain tests in a clinical trial are essential, potentially providing tips to facilitate management of these tests
What a trial crossover means, and why it is needed

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Advisory Board on Psoriasis Clinical Trials

PROVIDED BY:
Novartis Pharma AG, Region Europe

PARTNER(S) INVOLVED:

RESEARCH/DEVELOPMENT PHASE:

Advisory Board with Patient Organizations to address patient relevant endpoints in psoriasis clinical trials involved 6 National Psoriasis Patient Organizations representatives (Germany, Italy, France, Spain, Sweden and Switzerland) to discuss patient relevant endpoints in psoriasis clinical trials.

Type of patient (advocates) involved, tick all that apply:
[X] Patients with personal disease experience
[X] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[X] Expert patient / patient advocate with good expertise on disease and good R&D experience.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

- Patient relevant endpoints identified e.g. Quality of Life as primary secondary endpoint, efficacy and safety long term, rapidity for young patients
- PASI is not relevant for patients ,important is location of plaques
- Patient friendly materials and trained nurses to support treatment self –administration, compliance and trial participants' awareness of e.g. concomitant therapies are requested.

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

Find expert Advocates with a specific knowledge in a clinical trials.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

- Earlier start (ph II and protocol design phase)
- Multi-stakeholders Advisory Board (with Key Opinion Leaders s and/or payers).

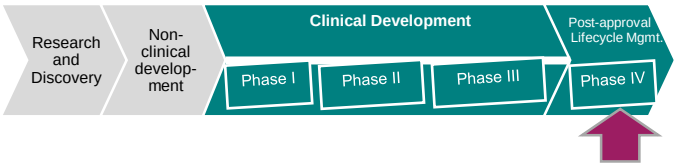
EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

INPUT OF PATIENTS ORGANISATIONS ON A RARE DISEASE REGISTRY: TOSCA

PROVIDED BY:
Susanna Leto di Priolo Patient Relations Novartis Oncology

PARTNER(S) INVOLVED:
European Tuberous Sclerosis Complex Patient Organisations (E-TSC)

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective?

Tuberous sclerosis complex (TSC) is an autosomal dominant genetic disorder with a birth incidence of 1 in 6000.1
—It is a multisystem disorder characterized by benign tumors (hamartomas) that arise in multiple organs, including the brain, kidneys, skin, eyes, lungs, heart, and liver.1-3
• Although considerable information on TSC has been obtained through recent research, gaps still exist in our understanding of the course of TSC manifestations and their prognostic role, rare symptoms and co-morbidities, interventions, treatments and their outcomes, and quality of life.
—Large-scale data on TSC are not available and longitudinal data are very limited. Hence, very little is known about the natural history of TSC across the lifespan
• **T**uber**O**us **SC**lerosis Registry to Incre**A**se Disease Awareness (TOSCA) has been designed to address some of these gaps by collecting data from patients across many countries worldwide.
Representatives of E-TSC were involved since the first meeting of investigators to design the registry.

Type of patient (advocates) involved, tick all that apply:
[ ] Patients with personal disease experience
[v] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience
[v] Other, describe here: [Doctors]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

The only challenge was identify inside the E-TSC the right representatives able to explain the point of view of patients. In this particular disease the representatives are all parents/caregivers.

The dynamic and communication style of the different board members who met to discus the registry had to be adapted to the different scientific knowledge and understanding of the 3 components (investigators, company, PO representatives).

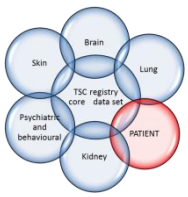
Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

There was a clear consensus to establish an European registry to address some of the gaps in understanding TSC by collecting data from patients across Europe
Collaborative working with an academic steering committee, 3 representatives of E-TSC (UK, ITALY, FRANCE) and the pharmaceutical company was a key component of the registry.
TOSCA is:
- A multicenter, international disease registry
- Designed to collect data from patients with TSC across many countries worldwide
- Aims to address the gaps in understanding the clinical course of TSC and the therapeutic outcomes

Benefits for E-TSC were:
- E-TSC has always felt that data collection is fundamental and should come before anything else
- To date, quality information collected across the nation is severely lacking and problems encountered and similarities in cases may not be accessed and compared
- By incorporating patients with TSC across the EU, knowledge and surveillance on a rare disease and orphan drugs will be increased, outcomes will be registered, and the effectiveness of treatment will be assessed
- This registry could provide the healthcare professionals with an excellent instrument for research

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

The early involvement was positive, one part of the registry is dedicated to patient needs in particular:
- To create a TSC socio-economics specific questionnaire for the patients/family
- To evaluate the impact of the disease in the real life of the involved families
- To measure the quality of life of TSC patients using validated questionnaires



It could be very useful in the future involve patient representative already educated by the EUPATI Platform

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Informed Consent Form: An Innovative Approach
GR56: Guide du Rédacteur (Writer's guide) – 5 Recommendations – 6 Rules

PROVIDED BY:
Sanofi - CSU-France: Luc Duchossoy
(contact:dominique.roome@sanofi.com)

PARTNER(S) INVOLVED:
Ethics Committees, Investigating Centres,
Patients' Associations, National Commission of Ethics Committees (CNCP)

Description of the case

Good Clinical Practice requires the provision of clear and understandable written information. On this basis, Sanofi-France decided in 2005 to launch a qualitative assessment of the existing Written Subject Information (WSI) / Informed Consent Form (ICF) which highlighted five major defects:

(1) Confusion between the situation of research and the situation of care (2) Poorly organised document (3) The Ethics Committee as the primary recipient of the document (4) Little consideration given to patient (5) No connection between the written and the verbal information given to patients.

Sanofi-France decided then to totally review its way of writing WSI/ICF for its clinical trials. In September 2006, on the basis of this report, Sanofi-France published a guide of recommendations on good clinical practices for writing WSI/ICF – Based on this guide, a practical and concrete template has been quickly developed for the use of Clinical Research Unit Team Members from Sanofi-France. This template proposes an innovative approach in form, substance and quality of writing.

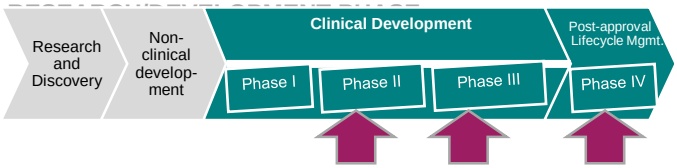
Benefits

A- Innovative Form

- Format of the document = A5 booklet connected to an ICF in triplicate A4 format on one page and connected to a patient card – NB: signatures only on the ICF
- Use of cardboard inserts (particularly in case of multiple WSI or ICF for a same study) to distinguish between sections
- Presence of a table of content with colour codes
- Presence of a colour marker corresponding to the table of contents
- Use of glossary covering terms that cannot be simplified
- Use of diagrams and of a calendar (at the backend of the document) covering the steps and examinations of the study

B- Innovative in Substance

- Distinction between care and research
- Choice of pertinent information that the patient needs to know to make the decision in an informed manner
- Identifying the patient being capable, independent and rational
- Placing the patient at the heart of the information system and as the primary recipient of the document
- An homogeneous information system, avoiding redundancies and organizing information with the patient in mind



Type of patient (advocates) involved, tick all that apply:

[ ] Patients with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[√] Expert patient / patient advocate with good expertise on disease and good R&D experience
[√] Other: patients participating to clinical trials

Benefits (ct'd)

C- Innovative in Quality of Writing

- Writing for people having reached no more than "end of 1st year of high school"
- Using short and simple sentences (only one idea per sentence; 15 to 20 words on average)
- Using common sentence structure (subject-verb-object)
- Using locutions to organize the sentence (logical connectors)
- Using no ambiguous sentences
- Avoiding negative and passive turns of phrase

Challenges and barriers

- No specific challenges and barriers for conducting this project outside necessary alignment between the different partners at the beginning of the project, as well as finding the appropriate medical writing expertise. This template has been used for all studies of Sanofi-France since September 2007.
- The Ethics Committees, Investigating Centres, Patients' Associations and the National Commission of ethics Committees very quickly adhered to the model and gave Sanofi-France their formal approval.
- This template changed since the start of its implementation. Remarks from Ethics Committees, Investigators and auditors, as well as Sanofi internal discussion and objectives of simplification are improving it constantly.

Discussion and learnings for you and EUPATI

- The writing of WSI/ICF of Sanofi-France studies is now being done by the service provider company that has accompanied the company since the start of this adventure.
- Sanofi-France has developed templates for specific cases: pharmacogenomy, pharmacokinetics, children, caregiver, patients unable to express their consent etc.
- Sanofi-France was also able to verify the "universality" of the system by developing it on studies in Tunisia, Morocco and French-speaking Africa (Note: for Morocco and Tunisia, coexistence of a French version and an Arabic version).
- Sanofi has made a document explaining to the patient the process and the rules of information and consent in clinical studies; this film is broadcasted on an institutional site external to Sanofi-France and on the Sanofi website:

http://moss-intranet.sanofi-aventis.com/ClinShare2/clinshare/Pages/EditoPatientICFvideo.aspx

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

Collaboration with a French Patient Association in Oncology Trials: "Toujours Plus Loin"

PROVIDED BY:
Sanofi - CSU-France: Isabelle David, Aude Bardiot, Emmanuelle Corbier, Luc Duchossoy, Véronique Lotz (contact: dominique.roome@sanofi.com)

PARTNER(S) INVOLVED:
La Ligue Contre Le Cancer (http://www.ligue-cancer.net/)
Unicancer (http://www.unicancer.fr/)

Description of the case

Two years ago, the Sanofi-French Clinical Study Unit (CSU) began a fruitful collaboration with a French Patient Association called "La Ligue Contre Le Cancer".

The success factors of this collaboration were:

- "La Ligue Contre le Cancer" established a specific Patient Committee in collaboration with the National Institute of Research Against Cancer. The objective was to respond to the French "Plan Against Cancer II" launched by the National Authorities requesting patient involvement in clinical studies. This Patient Committee has been structured and trained to be able to review informed consent and protocol (review done under confidentiality agreement).
- Sanofi-French CSU already created a patient oriented informed consent template, recognized as a gold standard (used for 10 years with clear presentation, glossary, adapted wording).

This collaboration was aiming primarily to involve patients in reviewing Sanofi informed consents prior to submission to Ethics Committee. A second objective was to contribute to a survey about patient participation in clinical studies in oncology to collect patients insights and better understand their needs.

Benefits

The feedback from the Patient Committee is concrete and pragmatic. The wording and vocabulary were adapted accordingly for better understanding of the information consent by the patients.
(see examples of advices & recommendations received)

« What are plasmocytes? White cells? A definition is needed »

« The treatment details need to be more specific: is it an injection? What is the frequency? »

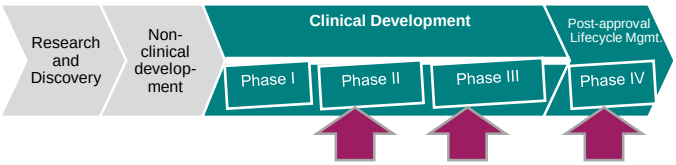
« Is there a rest period between 28 days cycles? »

« What is the participation duration? Can you provide the information earlier in the document? »

« Can you give more details about the different types of visits? Should we plan a half day or entire day for the intravenous infusion? An hospitalization? »

We also started to give this Patient Committee the opportunity to review our study protocol extended synopsis: the first experience with a phase-III trial protocol was positively perceived from the Patient Committee and led to three recommendations taken into account by Sanofi: (1) a critical point on the study design, (2) an emotional approach about the study protocol (3) an advice on the informed consent presentation.

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved, tick all that apply:
[ ] Patients with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[√] Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other

Challenges and barriers

No specific challenges and barriers for conducting this project outside necessary alignment between the different partners at the beginning of the project.

Discussion and learnings for you and EUPATI

Beyond the need to better informed the patients at the time of their consent, the results of the survey highlighted other difficulties encountered by the patients in participating to clinical trials in oncology and gave important directions to be taken into account in the future.

- At the beginning of the study: the complexity of the informed consent process; a step with potential misunderstandings because patients are often looking for better treatments
- During the study: issues and constraints faced by the patients and not always addressed e.g. time to get reimbursement of transport fees, time spent at hospital, lack of knowledge about their where they are in the course of the protocol, need to speak with medical representatives etc.
- At the end of the study: the need for patients to get the results and to be better prepared to what will happen after the study

Today all the informed consents from Sanofi-French CSU for clinical trials in Oncology are reviewed by the Patient Committee prior to the submission to Ethics Committee.

The following statement on the document acknowledges the Patient Committee review step: "*This informed consent has been reviewed by the Patient Committee from the Ligue Contre le Cancer*".

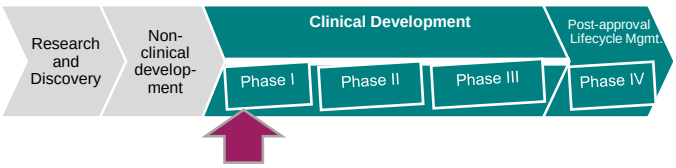
Sanofi has been the first company in France to implement this process in 2014. We now plan to continue this collaboration, expand it to future protocols and other therapeutic areas and implement some concrete actions following the patient survey results.

Charitable Foundation "Children with spinal muscular atrophy" PROMOTE PHASE I CLINICAL TRIAL IN COLLABORATION WITH ACADEMIC INSTITUTION IN UKRAINE

PROVIDED BY:
Charitable Foundation "Children with SMA", Vitaliy Matyushenko, President. www.csma.org.ua Gogolia str 7, Kharkiv, Ukraine, 61057; +380503640673; info@csma.org.ua

PARTNER(S) INVOLVED:
Andriy Shatillo, State Institution "Institute of Neurology, Psychiatry and Narcology of NAMS of Ukraine"; shatil@ukr.net

RESEARCH/DEVELOPMENT PHASE:



Type of patient (advocates) involved:
[√] Patients with personal disease experience
[ ] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[√] Expert patient / patient advocate with good expertise on disease and good R&D experience

Description of the case

Although specific medications with clear clinical benefit is absent for treatment of patients with spinal muscular atrophy (SMA) is absent now, both physicians and patients' families widely use numerous off-label medications and physiotherapeutic interventions in Ukraine. The second problem is SMA-patients' lack of mobility due to health risks and infrastructure restrictions. Also there are commonly accepted difficulties with treatment outcome measuring in SMA.
The listed above problems are complicated by unwillingness of pharmaceutical companies to conduct either clinical trials or preclinical research in Ukraine, as well as lack of state investments in rare disease research.
Our organization, CSMA, establish contacts with academic institution, State Institution "Institute of Neurology, Psychiatry and Narcology of NAMS of Ukraine", which provide us with expert-volunteer who designed a pilot clinical trial addressing most of the listed above issues in SMA clinical trials. Also our collaboration provide us with access to institutional Ethic Committee which allow independent ethical assessment of our projects by experts.
Main objectives of the trial which will start in January -February 2015 is to prove possibility of conduction SMA clinical trials in Ukraine and to find most convenient forms and designs for their organization. Protocol of the trial has been already approved by Ethic Committee.

Challenges and barriers

Most obvious challenges and barriers are lack of specific experience in SMA R&D in Ukraine, low motivation of researchers or relevant institutions, and incompetence of representatives majority of patient community in evidence based on medicine principles, as well as in general questions of R&D.

Benefits

Our project's main benefits are promotion R&D in SMA, optimization of study designs, and developing collaboration between academic/research institutions and patient organizations in Ukraine. As far as such experience is absent in Ukraine we are looking forward to obtain valuable information about specific national pitfalls and obstacles in SMA research.

Discussion and learning's

At this stage of the project it is possible to state that despite of sufficient scientific and medical infrastructure in Ukraine, motivation for SMA R&D, both in industry and in academic researchers, is low and key factor for successful advance in SMA research is sufficient number of experienced and motivated researchers as well as patient representatives and R&D EU experts.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:

BETTERING THE INFORMED CONSENT FORM BY USING PATIENT PERSPECTIVES

PROVIDED BY:
UCB [Daphnee Pushparajah]

PARTNER(S) INVOLVED:
Patients with epilepsy and rheumatoid arthritis

RESEARCH/DEVELOPMENT PHASE:

Description of the case (how were patients involved in your R&D project? What was the objective?

It was thought that potential subjects were put off from entering a clinical trial because they could not understand the details surrounding the clinical trial. Therefore, the project was to make the informed consent form simpler and easier for the patients to understand.

In the first part of the project, patients were visited at home and asked to read existing consent forms. The staff observed their reactions and also discussed their opinions with them. The feedback from the patients was taken on to modify the informed consent form.

In the second part, a patient was invited to a workshop and asked put forward the patient perspective on the modified informed consent form. The readability of the form was discussed as the intention was to make it easy for everyone to comprehend. There was also a survey which was filled out by patients on which they scored their preferences on the layout, text and colour of informed consent form.

Although readability studies are normally carried out at the beginning of the developmental process, in this instance, valuable and direct feedback was gained from different settings (i.e. not through the usual market research channel).

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change)

The experience demonstrated that patients valued being consulted on their preferences. The results of the survey were used to update the format of the informed consent sheet. There were some 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.

There was also a 'Quick Guide' produced which gave quick facts regarding the trial. This meant that patients did not have to read the entire informed consent sheet before finding out if they were eligible. They might get an advanced understanding of whether the trial could be right for them.

There are definite plans to involve more patients to gather feedback throughout the department. It is also thought that it will be easier to match the correct patients to the trials.

Type of patient (advocates) involved, tick all that apply:

[✕] Patients with personal disease experience

[✕] Expert patient / patient advocate with good expertise on disease, but little R&D experience
[ ] Expert patient / patient advocate with good expertise on disease and good R&D experience
[ ] Other, describe here: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved)

There were worries that the ethics committees might not approve the suggested format or text. The regulated environment meant that the amended versions of the informed consent sheet had to gain approvals from the ethics committees.

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. For example, the colour of the text might not have been suitable.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change)

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. There also needs to be a trade-off between the wishes and suggestions of patients and what is realistically feasible.

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

An open mind is needed to really gain the optimum out of the process. Going with a particular perception might prevent gathering a useful insight. For example, there was a lot of new and impressive technology on iPad but patients with tremor in hands are not able to use the touchscreen. This feedback was given very clearly by the patients themselves.