EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

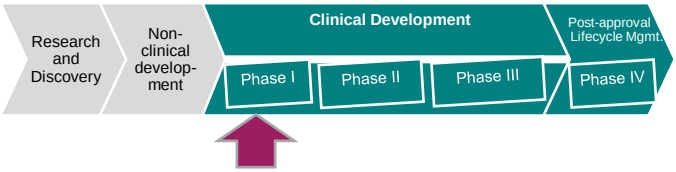
Direct patient insight on Lupus with a focus on cutaneous aspects

Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:

GlaxoSmithKline R&D, Immuno-Inflammation Therapy Area Unit

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective? (max 200 words)

In October 2015, two medical doctors and one scientist from GSK interviewed 5 female patients diagnosed with systemic lupus with cutaneous manifestations, or diagnosed with cutaneous lupus with skin symptoms only - four patients interviewed in Cambridge in the UK, and one patient interviewed over Skype.
The objective was to hear patients' views on their disease and on research because GSK is planning clinical trials of an investigational medicinal product in patients with cutaneous lupus.
Patients described a long history of the disease, and their general symptoms that impact on daily life, for example they become tired very soon, they have painful joints, cold feet and fingers, prolonged mouth ulcers, and they can feel isolated or have depression as they cannot always go outside or to work. With respect to the skin symptoms, the patients consistently reported that exposure to sunlight provokes or aggravates symptoms. This significantly limits outside activities, and they must put on sunscreen even several times a day. Skin lesions are itchy, can be thick, occur anywhere on the body including on the head or face, which can lead to social isolation. The patients indicated that they need several different treatments, all the time.

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
[ ] Other: 1 x EUPATI trainee with experience as a patient with the disease under discussion

Challenges and barriers (and how you have overcome them, or which ones were unresolved) (max 150 words)

The challenge was that the interviews were in Cambridge in the UK. The patients who responded had to consider travelling a considerable distance (from the Netherlands and Spain) to participate and were given the option to participate by telephone, those who decided to travel were provided with support in making arrangements. Nevertheless, it was a tiring activity for the patients. The interviews were structured with similar questions for each interview as far as possible. This may have seemed a little strict but it helped to ensure the areas that were discussed were standard across the patients. Following consent, four interviews were video recorded and all audio recorded. One interview required an interpreter.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

The patients reported a range of general symptoms that are associated with the cutaneous symptoms, and a range of treatments that they have to use every day. They said they would prefer a topical treatment so that they do not have to take another oral treatment. Ideally they would like the topical treatment to contain sunscreen so that they would not have to apply two creams. They would accept intravenous treatment if that meant they would generally be better. They wish a new treatment would prevent or reduce the flares – ideally curing them. With respect to using UV provocation in a research clinical trial, they would think about it and may want reassurance that they would not develop a flare.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

The patients were truly inspirational. They have overcome the challenges that the disease has imposed on their lives, and they wanted to help others by sharing their experience. It was apparent that the impact of the disease is broad. Patients would consider the potential effect of the clinical trial on their disease or their daily routine before considering participating in a trial, to avoid provoking a flare. They understand that research is required to find new treatments, and they also wish to share their experience to help others through patient organisations. The information that patients shared helped the researchers to progress with designing a clinical trial, which is planned to start during 2016.

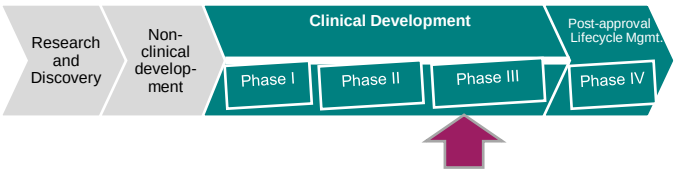
EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

Patient feedback on a draft plain language summary of clinical trial results

Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:
GlaxoSmithKline

RESEARCH/DEVELOPMENT PHASE:



Description of the case (how were patients involved in your R&D project? What was the objective? (max 200 words)

Plain language summaries will be required for all interventional studies (Phase 1 to Phase 4) with a study site in the EU. Patients were asked to review a draft plain language summary from a completed Phase 3 study approximately 1 week in advance of a follow-up discussion. Individual telephone interviews with the patients were conducted by GSK staff members. Six patients were interviewed; two were EUPATI trainees. None of the patients had the condition that was evaluated in the study.

The patients provided valuable feedback about the wording, structure, and content of the plain language summary.

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
[x] Expert patient / patient advocate with good R&D experience
[x] Other: EUPATI trainees and future trainees with experience as patients, but not with COPD, the condition evaluated in the example study.

Challenges and barriers (and how you have overcome them, or which ones were unresolved) (max 150 words)

[The only challenge was to ensure the activity was accessible to patients who responded to the posting. Initially we were planning to run a focus group in London however it became quickly evident, mainly due to location of patients and their availability, this wasn't going to be the best approach. Flexibility and agility was key; we were able to quickly change our plans and hold individual telephone based interviews with a set interview guide to obtain input. Each interview was audio recorded so feedback could be aggregated with key conclusions drawn plus the wider GSK team could hear the feedback.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

We used the comments from the patients to make some changes to the structure and format of our plain language summaries. For example, we have added headings to the document to make it easier for the reader to find information. We confirmed that the tables were preferable to text explanations of adverse event results. We added clarifying language to help the reader understand more about clinical research.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

Every patient brought a different perspective, skill, expertise and level of knowledge. Each raised interesting questions which provoked follow on in-depth discussion both within the interview but also with the GSK team, particularly around the question "what happens after plain language summaries are released – what happens next for the patient who took part/the medicine/the research?" As a result, in addition to receiving similar points in each interview around reporting the key study finding, we also obtained a wide range of suggestions for overall improvement of the plain language summary document. Beyond this from insights shared, we were able to consider how patients may seek and retain the information provided by GSK.

EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

LYMPHOMA PATIENT REPRESENTATIVE AT EMA JOINT HTA SCIENTIFIC ADVICE

Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:

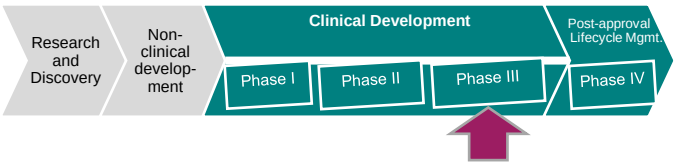
Susanna Leto di Priolo, Novartis Oncology Region Europe

PARTNER(S) INVOLVED:

Lymphoma Patient Organisation Expert

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? (max 200 words)

INVOLVING A PATIENT EXPERT WITH EMA
We invited a Lymphoma Patient expert to attend a "EMA-HTA Parallel Scientific Advice Meeting" to discuss a protocol in lymphoma.
The patient involved is leader of a local Lymphoma patient organisation, experienced the disease, got trained in clinical development.
The patient collaborates as well with local authorities.

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
[ ] 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) (max 150 words)

Novartis involvement was very intense:
2 face to face meetings, preparation with Medical and Regulatory, email, TC conversation. The treatment to be discussed was however quite complex and need the patient to understand it well.
The Expert patient has the impression not be included anymore by EAM in advice because of this first collaboration with industry.
Lesson-Learned from the Novartis Patient Relations perspective:

- Speak as early as possible to the specific NOVARTIS Drug Regulatory Affairs and Clinical Trial Leaders (6 months in advance of the SA)
- Needs of preparation efforts, quite intense
- EMA as well involved an expert patient, but no direct questions to both from EMA
- A slide with the patient perspective was in any case included in the slide deck sent to EMA
- Identify the appropriate expert which has no conflict of interest with EMA
- Inform the patient group network (in that case Lymphoma Coalition Europe)

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

1. INTERNAL EXPOSURE TO PATIENT NEEDS
For the first time the Unit engaged an expert patient fro EMA SA meeting.
Several Novartis people, from medical, drug regulatory affairs, commercial met the patient, understood the needs, asked for input in the protocol, specifically on Patient Reported Outcomes.
2. LEARNING HOW TO PREPARE FOR AN EMA SA WHEN INCLUDING THE PATIENT
The experience will drive and streamline future activities of this type

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

In general this was a good first Novartis experience and learning for the future.
We should work better with EMA and ask them to put a specific time allocated to the invited (by the company and/or by EMA) patient experts.
It would be good EMA to send the patient expert specific questions in advance.
Clarify in advance with EMA and the patient expert invited by the company if the expert patient will be in the future also asked by EMA to collaborate, or if this first collaboration with industry will make impossible for the expert patient to be involved by EMA in the future.

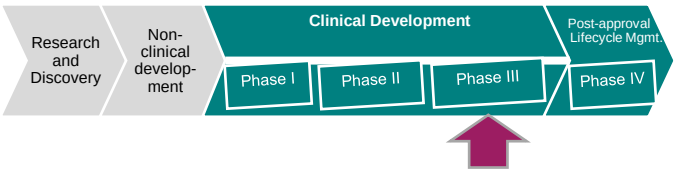
EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

[Patients Organizations and access to information on clinical trials]

PROVIDED BY:
Susanna Leto di Priolo on behalf of Polish Country Novartis Communications and Patient Relations Department Oncology Business Unit

PARTNER(S) INVOLVED:
Local Patient Organization strongly supporting Patients with Breast Cancer

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? (max 200 words)

- Patient Organization turned to the company for information on conducted clinical trial in advanced breast cancer with the aim to publish the information on their webpage and Facebook.
- Prepared information sheet fitted to the requirements of social media tools and webpage (based on translated information from clinicaltrials.gov) as well as the aim to share it with Patient Organization was approved by Bioethical Committee.
- Investigators were informed about Patient Organization request and agreed for contact with Patient Organization.
- Patient Organization published the information using mentioned tools and making the information more accessible for 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: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved) (max 150 words)

- Regulations regarding the access to the information on clinical trial are barriers so giving the information in the responsible way should not only be reactive but also prepared in the clear, easy to understand way and what is the most important must be approved by (Regulator's Entity) Bioethical Committee.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

- The activity improved access to information on clinical trials for patients.
- Ability to publish information on clinical trials by PAG was perceived as attempt to increase transparency in the access to information.
- The interest in such information was shown by the high amount of shares (over 190) and webpage entries (over 60 000).

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

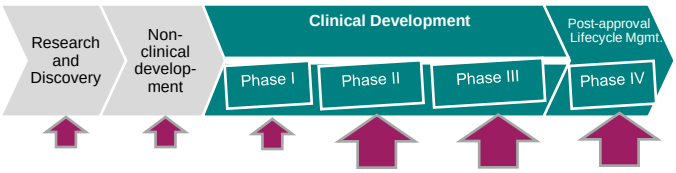
- Clinicaltrials.gov is a tool out of which Patients Organizations can not benefit because of highly complicated terminology and language barrier.
- There is a need to educate and build awareness with the general public about clinical trials.
- When the external entity approval process is included in the activity it impacts the timing of activity.

EUPATI CASE REPORT on meaningful patient involvement in industry-led medicines R&D:
HIV PATIENTS ACTIVELY INVOLVED BY JANSSEN R&D Please note this document is EUPATI confidential unless consented for public release. For EUPATI consortium members only.

PROVIDED BY:
Janssen, Pharmaceutical Company of Johnson&Johnson

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

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? (max 200 words)

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
[ ] Other, describe here: [ ]

Challenges and barriers (and how you have overcome them, or which ones were unresolved) (max 150 words)

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) (max 150 words)

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) (max 150 words)

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

Patient literacy needs to be ensured to optimise feedback

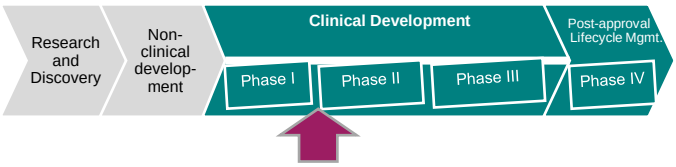
Ability to replicate this collaboration across more patient groups and advocates to increase knowledge on different topics, amongst other, Health Economics.

EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:
Patient input into breast cancer study design
Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:
Paul Robinson

PARTNER(S) INVOLVED:
Commercial Service provider

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? (max 200 words)

Breast cancer is a new disease area for MSD.

We sought patient input into draft phase II (proof of concept) study design to improve probability of success in terms of generating patient-relevant data, whilst also meeting current regulatory needs.

Two face-to-face focus groups were held. The first was relatively 'pragmatic' selecting women who were available on the day. The second was consciously chosen to be ethnically diverse and representative of North American population likely to be recipients of the treatment.

The sessions were organised and mediated by a third party provider. Initially, the name of the sponsor was NOT shared, to avoid any pre-conceptions about the company, but our R&D staff were involved in person.

Feedback was collated into themes and taken into consideration as the protocol was developed.

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) (max 150 words)

- How best to organise this – Do It Yourself, Third part provider
- Practical arrangements – payment, confidentiality, ratio of patients to Pharma Company staff, representative sample size
- Influence of any pre-conceptions of the company or the product (high profile media product in US)
- Willingness of clinical team to engage, in particular if patient suggestions were not incorporated

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

Feedback fell into three broad themes:

- the choice of comparator
- the timing of unblinding of an individual patient
- the option for crossover at point of progression

Two of these were readily incorporated into the protocol, the third formed part of discussions with regulators prior to protocol finalisation.

None of the issues was a surprise but the patient contribution influenced the final design.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

The input was generally considered a positive experience and influenced final study design. Whether that leads to a better protocol, faster recruitment, better adherence, higher probability of success at regulators or reimbursement etc remains to be seen

External guidance on best practice will be helpful – contracting, fair-market value, confidentialty needs etc.

How best to 'select' patients.

How to engage beyond US.

Are there shared learnings …. Maybe a publication on "what women with breast cancer want from a clinical trail" to reduce the need for each company to repeat.

EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

Inclusion of a patient expert on Pfizer's External Bioethics Advisory Panel

Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:

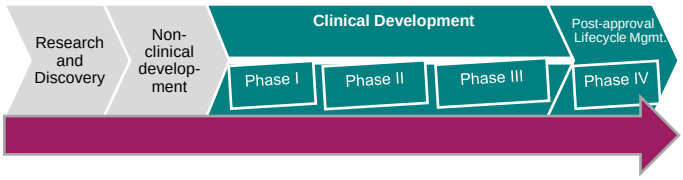
Roslyn F. Schneider Roslyn.f.Schneider@Pfizer.com /Pfizer

PARTNER(S) INVOLVED:

Doris C. Schmitt, Doctor-Patient-Communication Consultant and Trainer, Medical Journalist, Board member Breast Cancer Biobank Foundation PATH, Konstanz, Germany

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? (max 200 words)

Pfizer's External Bioethics Advisory Panel (BAP) is a small group of global ethics experts convened to provide insights on emerging medical, scientific and ethical issues globally, to help inform the company's clinical research planning and policies and ensure that the clinical trials Pfizer sponsors are conducted according to the highest ethical standards. The lens of a patient expert may provide a more inclusive perspective on these issues.

Meetings of the Bioethics Advisory Panel cover topics such as ethical considerations and patients' rights in conducting clinical trials in developing areas; the role of accreditation in positioning research sites to conduct clinical trial; and how informed consent should be structured in an environment of broader clinical data sharing and access, including the use of biological data and material in research. As our aim is to advance patient centricity more systematically in everything we do at Pfizer, in 2015 we proposed to the existing panel adding a patient expert to serve as a standing member so that a representative patient view would be included in consideration of all topics brought to the panel. There was unanimous agreement to include a patient expert.

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
[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) (max 150 words)

A challenge is that one patient expert cannot comprehensively represent every patient or patient experience. Including more panel members would enhance the diversity of representation but may reduce the conversational and interactive nature of the meetings.
It was useful that we already had expectations of the panelists and expertise outlined. When we proposed possible patient experts to the existing panel they and we were able to look to that outline to help ensure alignment with the experience of the patient expert who was selected.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

Ms. Schmitt's participation has been an invaluable enhancement to the conversations during the first three meetings she participated in. Her contributions as a patient, a Board member of a tissue bank, an advocacy group and as an expert in communications among health care professionals and the patient community regularly highlight nuances that others on the panel and among Pfizer attendees had not considered or voiced.
In addition to enhancing these discussions that help inform our R&D and policies, Pfizer leaders who attend as standing or agenda-driven meeting participants have seen the added richness of the discussion from involving a patient expert. This helps address the question some may have about whether patients have the appropriate expertise for involvement in complex scientific discussions. The example demonstrated on this panel supports leaders as they are catalyzing the culture shift at Pfizer to have more systematic patient involvement across the lifecycle of development.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

Next time we might include patient expert representation in a committee such as this from the outset. There should be recognition of the enhancement of outcomes of advisory committees when patients are involved. There should be an understanding of processes in place and that may need to be developed for engaging patients who are experts in an appropriate manner (consistent with law, regulation and culture).

EUPATI CASE REPORT on meaningful patient involvement in R&D and regulatory affairs:

Ethnography and advocacy involvement to inform clinical development in Sickle Cell Disease

Please note this document is EUPATI confidential unless consented for public release.

PROVIDED BY:

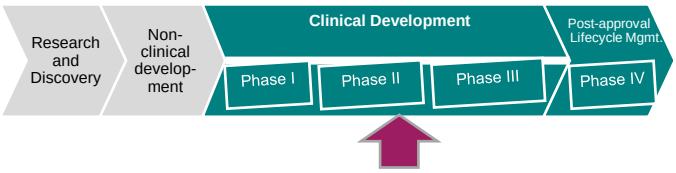
Roslyn F. Schneider Roslyn.f.Schneider@Pfizer.com/Pfizer

PARTNER(S) INVOLVED:

External consultancy firm, patient advocates

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? (max 200 words)

Clinical trials in people living with sickle cell disease are generally slow to enroll, enroll fewer than expected participants, and many studies are terminated due to slow enrollment.* As a phase II trial was ongoing and a phase III was planned the clinical team knew they needed a new approach to recruitment to advance the program for a new potential medicine. The anchor to that new approach was to gain new insights into the world of what it's like to live with sickle cell disease, to have painful crises, and what they might consider if they were to think about joining a clinical trial.

Trained medical anthropologists were matched with 25 people with sickle cell disease by race, age and gender. They spent almost every waking moment shadowing their assigned patient, from breakfast to bedtime for at least two days. They learned how these patients viewed themselves, how they made decisions about their healthcare, and what they thought of healthcare practitioners. The ethnographer's videotapes and notes were coded and used to identify common themes that may be helpful in recruitment and other aspects of planning for phase III.

In addition, the study team engaged sickle cell disease advocates for feedback.

*https://ash.confex.com/ash/2013/webprogram/Paper65249.html

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) (max 150 words)

The nature of ethnography research is resource intensive and time consuming to sort through the identified themes and apply them to planning.

Some insights gained cannot be integrated in a manner that is compliant with regulations or codes of practice. For example the suggestion that spirituality lends itself to messages of "hope" for example from phase II work would not be an appropriate representation of potential risks, benefits and uncertainties of participation in a clinical trial. Feedback to advocates was provided as to why it would not be possible to integrate all of their insights.

Benefits (how has this collaboration improved R&D process(es) and the R&D outcome(s) or triggered R&D organisational change) (max 150 words)

The Pfizer team learned that clinical trial education and the beginning of the informed consent process should be in advance of when a person is having a painful crisis with recruitment in venues other than emergency room settings. We understood more about the language patients used to describe their pain, about the fatigue patients experienced and attempted to design the trial to be more convenient for participants. This patient community trusted each other more than other resources and social media (from people with SCD) methods of learning about clinical trials. As spirituality was important to this group consideration was given to including inspirational quotes in recruitment materials.

Discussion and learnings for you and EUPATI (what would you do differently next time, what are external factors that should change) (max 150 words)

As we gain additional experience with various types of patient engagement at key points in the lifecycle we may be able to better match circumstances that warrant more resource intensive engagement such as ethnography. We might also consider this type of engagement before phase II and even when we don't anticipate as much of a challenge with enrollment. The insights gained may improve the participant experience as well as potentially having an effect on improving recruitment or retention.