Improving the clinical trial experience for patients and investigators through a simulated trial in palmoplantar pustulosis (PPP)

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Involving patients in trial design can help overcome challenges of clinical trial recruitment and retention, which are particularly relevant for rare diseases, and improve patient outcomes. This simulated trial shows that patients value clear, concise, and non-technical literature, efficient trial visits, and the option to continue effective treatment after study completion

PURPOSE

To evaluate the experiences and perceptions of patients with PPP participating in a simulated clinical trial and inform and enhance future, patient-centric trial designs.

INTRODUCTION

- Seeking and implementing patient feedback on clinical trial design can enhance the patients' experience and improve outcomes by reducing drop-out rates and associated costs, and allowing collection of more robust data[1–4]
- Challenges in recruiting and retaining patients are amplified in rare diseases, where there are fewer patients across a wider geographic spread,[5] making appropriate trial design even more important
- PPP, a rare, debilitating disease,[6–8] is an ideal candidate for conducting a simulated trial to refine the design before initiating recruitment for a full clinical trial

CONCLUSIONS

- Barriers to recruitment that were highlighted by patients with PPP in this simulated clinical trial included pre-trial literature, likelihood of assignment to placebo, visit schedules and logistics, and outcome measures
- Solutions were to develop study materials with simpler language and visual aids; incorporate open-label extensions or cross-over options; reduce the number and increase the efficiency of study visits; and provide greater financial support
- These simple patient- and investigator-focused improvements may inform future PPP trial designs, optimize the patient experience, and support generation of robust data
- Importantly, these insights are potentially applicable to other therapeutic areas and could be used for wide-ranging improvements to trial design

METHODS

PATIENT REVIEW OF PPP CLINICAL TRIAL MATERIALS AND DESIGN
Patient participants recruited through patient organizations and participating investigators (N=9)
Aged >18 years; diagnosis of moderate-to-severe PPP

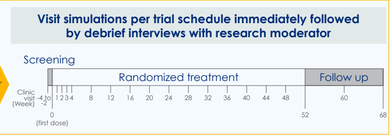
At-home assignments

Review of trial documentation	Review of PRO questionnaires
ICF	5 × disease-specific measures*
Trial recruitment poster (n=3 Japanese patients)	2 × general health-related quality of life*
Trial recruitment brochure (n=6 European and US patients)	3 × new pain NRS*

Virtual trial visit simulation and debrief

Visit simulations per trial schedule immediately followed by debrief interviews with research moderator

In-depth conversation with physician, based on trial discussion guide



ADVISORY BOARDS†

Patients and patient representatives (N=14) attended two virtual advisory boards to discuss and enrich results from the trial simulation

Canada/USA/Europe: n=11
Japan: n=3

*Questionnaires included disease-specific measures (BASDAI, DLQI, PSS, ppQLI, and PBI-S), general health-related quality of life measures (SF-36, EQ-5D-5L), and three newly developed pain NRS; †The participants included 3 members of the patient advisory committee involved in development of the simulated trial, 7/9 patients who participated in the virtual trial simulation, and 4 additional patient representatives.

RESULTS

Demographic and clinical characteristics of patient participants

- Nine patients participated in the trial simulation, and 14 patients or patient representatives took part in the advisory boards, of whom 10 were living with PPP
- Patients participating in the trial simulation were mostly female (n=8, 88.9%) and had not participated in a clinical trial (n=7, 77.8%); mean (range) age at diagnosis was 42.6 years (25–73); mean (range) duration of disease was 16.4 years (4–35); and most were currently receiving PPP treatment with biologics (n=4, 44.4%) or topicals (n=4, 44.4%)

Patient feedback on the ICF and recruitment materials

"I kind of get lost, glazed over, when I start reading about all of that coding of your data. You could just say, 'We do this' or, 'We do that' instead of saying it in longhand"

"There are so many words that I didn't understand"

"I have been in the clinical trial but I didn't read the consent form. I had no time to read"

"An animated video what is the clinical trial, what is the placebo, what is the consent form, what is the highlights from the consent form. So instead of a brochure I think it's better a video"

Patients felt the ICF was too long and recommended using less technical language and visual media for recruitment materials; discussion with an HCP was considered beneficial

Patient feedback on the trial visit schedule and logistics

"The duration of the visit. Because I thought that was crazy, ridiculous. Three and a half hours for a maintenance visit. Nobody's going to spend half a day at the doctors"

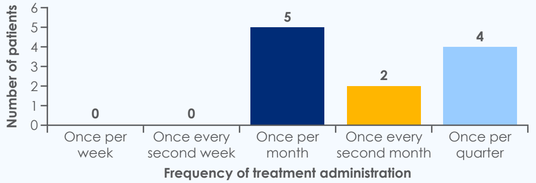
"Sometimes you're just waiting for a long, long, long time and I do not want that. I'm not willing to invest that time into such a trial"

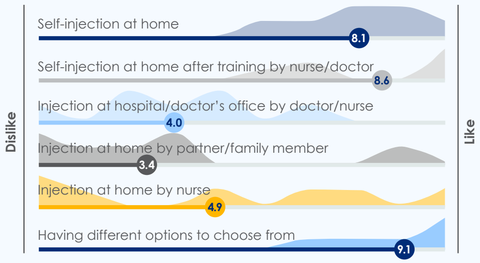
"…how many appointments are in one year? Maybe 12 or 18? [A participant] would have to take so many days off. Let's just imagine 18 days, you would have to think about what kind of options are there [and] how to compensate somebody for that"

"It's just an infringement on my day-to-day life. So, those visits would determine my life living, that is not what I like"

Asking patients to attend 20 visits lasting approximately 2–3 hours each was considered excessive, especially as waiting times are often long. Patients felt that logistical and financial support were crucial in enabling trial participation

Patient preferences regarding frequency and method of treatment administration





Patient responses to a question on acceptable injection frequency, and weighted mean Likert scale outcome values (with distribution of responses) to a question on treatment administration processes.

Most patients indicated a preference to self-inject treatment at home (monthly or quarterly), or to be given options to choose from

Patient feedback on therapies and disease management during the trial

"You're requested to stop using certain medication and that might be for a good treatment of the PPP. So especially stopping is something that I find very difficult"

"If you were to have said you can't put anything on your skin then that would be an out for me, I wouldn't do the trial because you have to have something that softens up the cuts and things like that on your hand, the fissures"

"The fact that you have to do all this and then still might end up only getting the placebo, that's difficult for me, difficult to accept"

"We are all concerned. What will happen if we take the placebo? For the patients who have PPP, it's very difficult to live everyday life. For me, it was very difficult to walk"

Patients expressed concern about receiving a placebo and having to stop using existing medications and pain relief

Most important questions relating to the simulated clinical trial for patients, among participants at the Canada, USA, and Europe advisory board (n=8)

*Patients preferred the wording "How do we think the drug will work in PPP?".

Patients were most concerned about managing their condition if it worsened and not being able to continue treatment after study completion, if it was effective; both patients and physicians recommended an open-label extension

Patient treatment goals and appropriateness of outcome measures

Patients wanted to be independent and take part in normal daily activities without pain or fear of remission

Outcome measures were generally acceptable to patients, but could be improved by ensuring questions are not duplicated between questionnaires and including questions that capture measures of both peak and average pain, as well as the limitations and daily burden caused by the disease

Abbreviations

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DLQI, Dermatology Life Quality Index; HCP, healthcare professional; ICF, informed consent form; NRS, numerical rating scale; PBI-S, Patient Benefit Index – Standard; PPP, palmoplantar pustulosis; ppQLI, Palmoplantar Quality of Life Instrument; PRO, patient-reported outcomes; PSS, Psoriasis Symptom Scale; SF-36, Short Form 36.

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Disclosures & Acknowledgements

The study was supported and funded by Boehringer Ingelheim. **DT** has no conflicts of interest to disclose. **AP** has worked as an investigator and/or speaker and/or advisor for AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Boehringer Ingelheim, Celgene, Celltrion, GlaxoSmithKline, Eli Lilly, Galderma, Hexal, Janssen, LEO Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, and UCB. **CBH** has attended advisory boards and received honoraria from AbbVie, Boehringer Ingelheim, and La Roche-Posay. **SK** received research grants from Kyowa Kirin and honoraria from AbbVie, Eli Lilly, Janssen, Maruho Pharmaceutical, Novartis, and Taiho Pharmaceutical. **SBe** served as Chief Scientific & Medical Officer for the National Psoriasis Foundation during the time of the study. **KK**, **TG**, **NY**, **SBr**, **YD**, **FB**, and **ECB** are employees of Boehringer Ingelheim. **PvdK** received fees for consultancy service or lectureships from Almirall, AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant Sciences, Eli Lilly, Janssen, LEO Pharma, Novartis, and UCB. The authors met criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of the poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy, as well as intellectual property considerations. Holly Baker, PhD, and Derah Saward-Arav, PhD, of OPEN Health Communications (London, UK) provided writing, editorial, and formatting support, which was contracted and funded by Boehringer Ingelheim.

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