Feasibility study to evaluate capabilities for conducting psychiatric clinical research within the Rwandan mental healthcare system

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ABSTRACT

Objective To evaluate the feasibility of conducting a large clinical trial within the Rwandan mental healthcare system that would establish the safety, efficacy and benefit of paliperidone palmitate once-monthly (PP1M) and once-every-3-months (PP3M) long-acting injectable formulations in adults with schizophrenia.

Study design An open-label, prospective feasibility study.

Setting/Participants 33 adult patients with schizophrenia were enrolled at 3 sites across Rwanda.

Interventions The study design included 3 phases of treatment: an oral run-in to establish tolerability to risperidone (1 week), lead-in treatment with flexibly dosed PP1M to identify a stable dose (17 weeks) and maintenance treatment with PP3M (24 weeks).

Primary and secondary outcome measures Feasibility endpoints included compliance with governmental and institutional requirements, acceptable supply chain delivery and proper onsite administration of risperidone/PP1M/PP3M, adequate site infrastructure, adequate training of clinical staff and successful completion of study procedures and scales. A variety of study scales were administered to assess outcomes relevant to patients, caregivers, clinicians and payers in Rwanda and other resource-limited settings.

Results This study was terminated early by the sponsor because certain aspects of study conduct needed to be addressed to maintain Good Clinical Practice requirements and meet regulatory standards. Results identified areas for improvement in study execution, including study governance, site infrastructure, study preparation and conduct of procedures, study budget and study assessments. Despite the identification of areas in need of adjustment, none of these limitations were considered insurmountable.

Conclusions This work was designed to strengthen global research in schizophrenia by building the capacity of researchers to prepare and conduct pharmaceutical trials in resource-limited settings. Although the study was ended early, modifications motivated by the results will facilitate the successful design and completion of more comprehensive studies, including an ongoing, follow-up interventional trial of PP1M/PP3M in a larger population of patients in Rwanda.

Trial registration number NCT03713658

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study identified key adjustments in administrative procedures, physical infrastructure, logistics and cultural adaptation necessary to conduct successful large-scale mental health clinical trials in Rwanda.

⇒ Findings from this study may facilitate the design and conduct of other clinical studies in countries with limited resources and promote their successful completion.

⇒ Only Rwandan mental healthcare system hospitals deemed to have the capability to conduct a clinical trial were chosen to participate in this feasibility study; therefore, results may not be fully generalisable to other Rwandan mental healthcare system sites or other resource-limited settings.

⇒ Results from this study may not generalise to lower-functioning patients as most of the patients enrolled had relatively mild illness.

⇒ Some key assessments used in this feasibility study were found to be inadequate and had to be replaced by scales that require further validation within this environment before implementation in a larger trial.

INTRODUCTION

Patients with schizophrenia experience symptoms of psychosis, distorted reality, impaired cognition, decreased motivation, diminished interests and emotional blunting. Untreated, these symptoms profoundly impact the quality of life of patients and their families and increase community economic and social burden. The symptoms of schizophrenia are consistent across cultures. However, the full impact of the disease and its treatment differ depending on the cultural, social and economic settings, and treatment interventions may require adaptation to achieve optimal success in each setting.1

Outcomes of patients with severe mental illnesses such as schizophrenia remain
unfavourable in resource-limited settings. A review of 40 studies examining treatment of schizophrenia in eight sub-Saharan African countries found that most patients were treated with a combination of faith/traditional healers and contemporary Western psychiatry. Throughout Africa, few treatment options are available in rural areas where most of the population resides, and initial access to mental healthcare usually involves traditional treatment approaches. Even in larger cities, treatment is generally limited to poorly tolerated first-generation antipsychotics because of their low cost and clinicians’ difficulty in accessing more recent pharmaceutical advances. The unfavourable tolerability of first-generation treatments contributes to low medication adherence and poor treatment outcomes, with continued burden on caregivers and mental healthcare systems.

Rwanda has emerged as a leader in sub-Saharan Africa for providing mental healthcare. Recognising the significant increase in persons living with mental illness following the 1994 Rwanda genocide against the Tutsi, the Rwandan government has worked to improve mental healthcare throughout the country. These policies have resulted in a strong mental health strategic plan and a consistent annual budget to improve national mental health. Even so, resources remain constrained. In 2021, Rwanda had 12 practicing psychiatrists, most of whom are based in the capital city of Kigali. Although psychiatric nurses and other practitioners also play an important role in the support of psychiatric patients in Rwanda, there are nevertheless too few trained mental health professionals to sufficiently treat a population of nearly 13 million. Access to better-tolerated second-generation antipsychotics, including long-acting injectable (LAI) antipsychotics, remains limited. The burden resulting from these limitations is borne by patients, their caregivers, clinicians and society at large. Most patients and their caregivers have a limited understanding of mental illnesses and often cannot afford the time and costs associated with travel to treatment centres. A cost-consequence model that estimated the benefits of LAIs for schizophrenia treatment in Rwanda found that travel costs, in addition to traditional direct medical costs, make up a significant proportion of patient costs associated with schizophrenia treatment. Clinicians are overburdened with caseloads and are challenged to manage the mass of patients requiring treatment. Consequently, treatment remains inconsistent, outcomes are often poor and societal burden remains high in resource-limited African countries.

LAIs have the potential to address some of the psychiatric healthcare challenges in low-income countries such as Rwanda. Prolonged maintenance of therapeutic blood levels and certain knowledge of treatment adherence have been shown to reduce relapse and improve outcomes while reducing burden on mental healthcare systems. The improved side effect profile of second-generation LAIs promotes better long-term compliance. Another potential benefit is the diminished need for direct patient contact with highly trained healthcare professionals for medication management. This is especially relevant in resource-limited settings because the few available healthcare providers face significant caseload burdens, and patients and their caregivers must take leave of their employment and expend considerable time and expense to travel for psychiatric care. Despite the potential benefits, access to LAIs remains scarce throughout resource-limited settings.

Although the value of LAIs has been demonstrated in high-resource settings, demonstrating value within resource-limited settings such as the Rwandan mental healthcare system presents significant hurdles. Delivery challenges, storage requirements, administration procedures and attitudes toward the use of LAIs may limit their acceptance and diminish their value in these settings. Lack of experience with clinical trials that meet internationally accepted standards and regulatory requirements further complicates efforts to establish convincing evidence of LAI value.

The primary objective of this study was to evaluate the feasibility of conducting a comprehensive, comparative clinical research trial of paliperidone palmitate once-monthly (PP1M) and once-every-3-months (PP3M) long-acting injections in Rwandan patients with schizophrenia. Secondary objectives were to obtain preliminary safety and efficacy data for risperidone, PP1M and PP3M when used within the Rwandan mental healthcare system and to assess the value and feasibility of the Screener for Mental Illness with Lay Evidence (SMILE) scale. Weaknesses and limitations related to study design and clinical conduct that were identified in this feasibility trial were addressed in the preparation and conduct of a larger, ongoing interventional trial of PP1M/PP3M in Rwanda.

METHODS
Study design and treatment
This was an open-label, uncontrolled, multicentre, interventional study in patients with schizophrenia, conducted at three sites in Rwanda: CARAES Ndera Neuropsychiatric Hospital, Ruhengeri Referral Hospital and Kibungo Referral Hospital. The study included four phases: (1) screening; (2) run-in treatment with 3 mg oral risperidone to test tolerability of the active principle in PP1M and PP3M; (3) initiation of LAI treatment with PP1M (50 mg eq, 75 mg eq, 100 mg eq or 150 mg eq) and (4) maintenance LAI treatment with PP3M (175 mg eq, 263 mg eq, 350 mg eq or 525 mg eq) (Figure 1). At the conclusion of the study, participants who wished to continue treatment with PP3M were offered an option to transition into a post-trial access programme.

Participants
Eligible participants were men and women of non-childbearing potential, aged >18 years to <70 years with a DSM-IV (Diagnostic and Statistical Manual of Mental Disorders version IV) diagnosis of schizophrenia.
confirmed by the Mini International Neuropsychiatric Interview. At screening, participants either required treatment initiation with an antipsychotic or a change in their current antipsychotic treatment because of inadequate tolerability or efficacy. Participants were willing and able to consent to the study procedures, including willingness to receive antipsychotic treatment by injection, and had a primary caregiver who was willing to help ensure compliance with study procedures. Participants were also required to speak either Kinyarwanda, French or English and to be eligible for treatment within the Rwandan mental healthcare system. All participants received compensation for travel and time spent at the study site based on fair market value.

The major exclusion criteria were a history of organic brain syndromes, comorbid psychiatric and/or physical illnesses, poor prior response to risperidone or significant comorbid substance abuse that was likely to interfere with understanding of or compliance with study procedures.

Study site selection and training procedures

Study sites were selected in consultation with the Rwanda Biomedical Centre, the healthcare implementation agency of the Rwanda Ministry of Health. After identification, sites were visited by the study team to evaluate capabilities for completing protocol assessments, storing, dispensing and administering oral antipsychotic treatments and PP1M and PP3M in accordance with product labels. Participating principal investigators and staff were psychiatrists, psychiatric nurses and other mental health workers within the Rwandan mental healthcare system. They were trained on study procedures and assessments at a 2-day, in-person investigators’ meeting and at site initiation visits. All training was given in English with translation provided as needed for trainees. Simulated trainings on administration of PP1M/PP3M were provided before participant randomisation. Continued support for study conduct was provided by site monitors and other staff from the sponsor for the duration of the trial as per the study monitoring plan.

Assessments

Assessments were chosen to capture outcomes relevant to patients, caregivers, treating and research clinicians and payers (government and private insurers) in Rwanda and other resource-limited settings. Nine scales were included to determine which would be most feasible and informative for inclusion in a larger, more comprehensive trial with LAIs in patients with schizophrenia in these settings. All assessments were paper based, and data were later entered into the RAVE electronic data capture system. Full descriptions of each scale are listed in online supplemental table 1. The full SMILE scale can be found in online supplemental table 2.

Study endpoints

Endpoints were full compliance with governmental and institutional requirements, including successful contracting with the local hospital sites and the sponsor; acceptable supply chain delivery of risperidone/PP1M/PP3M; adequate site infrastructure; adequate training of clinical staff; proper administration of risperidone/PP1M/PP3M; successful completion of study procedures and adequacy and successful completion of study scales. At the study’s conclusion, a structured review addressing satisfaction with the study was obtained from the investigators.

Statistical methods

The proposed sample size was based on identifying a convenience sample to assess the feasibility of conducting a future pragmatic clinical study with similar design in this environment. A sample size of 30 participants was considered adequate to evaluate study endpoints with an acceptable degree of precision. Qualitative analysis for each of the study endpoints included evaluation of whether a problem existed for that endpoint and identifying its potential impact on the conduct of the follow-on pragmatic clinical study. Descriptive statistics are presented for all endpoints.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination of this research.

RESULTS

Patient disposition and baseline demographics

A total of 33 participants were enrolled in this study; their demographic data are summarised in Table 1. Of the 33

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**Figure 1** Schematic overview of the study. PP1M, paliperidone palmitate once-monthly; PP3M, paliperidone palmitate once-every-3-months. *Risperidone run-in was not required for patients who had previously been treated with risperidone and showed no allergic reaction.*
enrolled participants, 1 participant was discontinued due to disease relapse, 1 participant withdrew consent to participate in the study and 2 participants completed the study. The remaining participants (n=29) were discontinued when the study was terminated early by the sponsor based on recognition that certain aspects of study conduct needed to be addressed to maintain Good Clinical Practice (GCP) requirements and that these could not be adequately addressed while the study was ongoing. Prior to study termination, 97% (32/33) of participants had received treatment with PP3M and had tolerated the study medication well. Because the treatment was well tolerated and participants were clinically stable on study medication, the sponsor made treatment available to the 31 study participants who completed the study or were discontinued at early study termination through a post-trial access programme.

Feasibility endpoints

Compliance with governmental and institutional requirements

Review of study preparation and conduct procedures suggests that these procedures were not sufficiently explained and practiced in a mock trial setting during presstudy meetings. This resulted in significant protocol deviations during the trial, many of which were related to timely entry and review of the clinical data for this study. Amelioration of problems, once identified, was considered slow or inadequate by those affected. Feedback from some of the institutional participants indicated that the complex and rigorous requirements for study completion, in addition to an already taxing clinical schedule, resulted in rater exhaustion, burnout and delays in the completion of study evaluations.

Acceptability of supply chain and preparation administration of risperidone/PP1M/PP3M to participants

Risperidone, PP1M and PP3M were reliably supplied as labelled study medication to each of the sites and stored adequately in the hospital pharmacies for the duration of the study. Overall, PP1M and PP3M were administered without difficulty by study staff.

Adequacy of site infrastructure

Although infrastructure requirements were reviewed at an investigator meeting and evaluated at site initiation visits, a more thorough review was needed to ascertain the full extent of the resource requirements for the study. Some important resource limitations were identified several months into the study. For example, sites may have had computers that could be used for the study, but they may not have been adequate for the work that was planned or may not have been regularly available for study work. Internet access was not always sufficient at most sites due to poor network coverage and/or lack of access altogether, and some of the expected clinical laboratory assays were not regularly available to address protocol requirements.

Adequacy of clinical staff training

One major finding was that more comprehensive preparation and study-specific training were needed to ensure that GCP was maintained because the investigators involved in the study did not have prior experience with interventional clinical trials. More comprehensive training in research methodology and GCP requirements, combined with timely review and feedback from supporting study site monitors, are necessary to support this type of clinical study. In some cases, language barriers and time constraints interfered with clear communication and ability to train personnel. The complexities of a clinical trial were added to an already heavy clinical workload, and site personnel had difficulties balancing the additional burdens brought on by this study with their already busy day-to-day activities.

Successful completion of study procedures

Eligible patients who were willing to participate in this study and complete the necessary procedures were readily identified. Patient responses on the Intent to Attend-Plus questionnaire regarding intent to attend follow-up visits were concordant with their actual practice. Most patients said they would return and did; two patients indicated that they would not be able to attend and did not.

However, some issues arose surrounding the timely completion of data documentation forms and, once these forms were completed, query resolution was slow. Additionally, study monitors had significant difficulties with the source data verification. Ultimately, deviations from

Table 1 Patient demographic and baseline (OL) characteristics

<table>
<thead>
<tr>
<th>Participant demographics* n=33</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>18–25 years</td>
</tr>
<tr>
<td>21 (63.6%)</td>
</tr>
<tr>
<td>26–50 years</td>
</tr>
<tr>
<td>21 (63.6%)</td>
</tr>
<tr>
<td>51–65 years</td>
</tr>
<tr>
<td>&gt;65 years</td>
</tr>
<tr>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Median (range)</td>
</tr>
</tbody>
</table>

*All values are n (%) unless otherwise noted. BMI, body mass index; OL, open-label.
GCP, including inadequate study documentation and delays in response to queries, contributed to the study’s early termination.

**Adequacy and successful completion of study scales**

Although outcomes obtained from the study scales were perceived as useful and needed for appropriate participant evaluation (data from several of the efficacy measures are summarised in **table 2**), most of the scales were deemed burdensome by participants and site staff. The scales used in the study were considered poorly translated into Kinyarwanda and both study participants and staff had difficulty understanding them. In particular, the health economics assessments (Clinical Service Receipt Inventory15 and Cost Assessment Questionnaire16) were considered to be poorly adapted to economic drivers for many Rwandans. A scale that more adequately and concisely captures the economic realities in developing countries (including Rwanda) is needed to capture the economic burden of schizophrenia in the context of a clinical trial.

**Exploratory efficacy**

Patient improvement was assessed on the SMILE (patient and caregiver versions), the Clinical Global Impression-Severities17 and the Sheehan Disability Scale18 (**table 2**). Patient and caregiver-reported measures of illness severity (SMILE) showed significant (~65%) improvement at endpoint (week 21) compared with baseline.

**Patient, caregiver and clinician/site personnel satisfaction**

Patients and caregivers were generally satisfied with the study and accepting of LAIs (online supplemental table 3). Only one patient and their caregiver withdrew consent to participate in the study. At the conclusion of the study, a scorecard was provided to investigators for feedback on the study’s strengths and limitations. Clinician satisfaction was generally high throughout the study, with an overall mean (SD) score of 4.8 (0.36) at baseline and 5.0 (0.0) at week 21 (score of 4=satisfied; 5=very satisfied). The consensus of raters results is summarised in **table 3**.

## Safety and tolerability

Overall, LAIs were well tolerated among enrolled participants. Adverse events (AEs) were transient and resolved quickly. AEs were consistent with those reported in other studies.12 19–22 Twelve participants (36.4%) who received PP1M/PP3M reported at least one treatment-emergent AE: gastrointestinal disorders (12.1%, n=4); general disorders and administration site conditions (9.1%, n=3); infections and infestations (6.1%, n=2); metabolism and nutrition disorders (6.1%, n=2); nervous system disorders (6.1%, n=2) and psychiatric disorders (6.1%, n=2). One participant (3.0%) reported a serious AE of hyperglycaemia during the maintenance phase of the study. The participant was hospitalised, and study treatment was discontinued. The event was reported as resolving and deemed related to study treatment by the investigator.

### Discussion

Bringing advances in treatment for major psychiatric diseases to patients in resource-limited settings is an important global public health goal. Although the efficacy and safety of existing treatments have been established elsewhere, the benefits of these treatments must still be established for resource-limited settings. Establishing this benefit requires testing in local environments by clinicians, staff and patients under the resource constraints that are locally available. Because conduct of psychiatric treatment RCTs are unfamiliar to most persons in these regions, extra preparation is necessary to be sure that trials are conducted within the framework of GCP. This preparation includes identifying the necessary resources, providing additional training to study staff on data collection and documentation, and ensuring all data collected are reliable and meet local regulatory and international ethical/scientific standards.

The primary objective of the study was achieved and key areas in need of improvement in order to conduct a large schizophrenia treatment trial in the Rwandan mental healthcare system were identified. Multiple adjustments to study implementation were noted but could all be achieved with additional preparation. Despite operational challenges, significant clinical improvement on

### Table 2 Patient/caregiver outcome measures

<table>
<thead>
<tr>
<th>Scale</th>
<th>Visit 2 (baseline), n=33</th>
<th>Week 21 (endpoint*), n=33</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMILE—patient version,† mean (SD)</td>
<td>7.9 (8.54)</td>
<td>2.8 (3.09)</td>
<td>−5.1 (7.33)***</td>
</tr>
<tr>
<td>SMILE—caregiver version,† mean (SD)</td>
<td>8.9 (9.85)</td>
<td>2.9 (3.20)</td>
<td>−6.0 (8.90)***</td>
</tr>
<tr>
<td>CGI-S,‡ mean (SD)</td>
<td>3.1 (0.90)</td>
<td>2.7 (0.65)</td>
<td>−0.4 (1.12)‡</td>
</tr>
<tr>
<td>SDS,¶ mean (SD)</td>
<td>7.8 (7.13)</td>
<td>4.6 (4.01)</td>
<td>−3.1 (8.68)**</td>
</tr>
</tbody>
</table>

*Endpoint includes last available data collection, including scores from week 21.
†Baseline scores were captured at screening visit. Higher scores denote greater severity of clinical symptoms.
‡Baseline scores were captured during the run-in period.
§p=0.051, **p<0.05 and ***p<0.001 are based on paired t-tests on change scores.
¶Baseline scores were captured at week 0 immediately before the first PP1M injection. Higher scores indicate greater degree of disability.
CGI-S, Clinical Global Impression-Severity; SDS, Sheehan Disability Scale; SMILE, Screener for Mental Illness with Lay Evidence.
Table 3  Site satisfaction score card

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Grade</th>
<th>Adequate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study governance and administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Governmental and regulatory compliance</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Institutional compliance</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Management of communication and other challenges unique to the Rwandan mental healthcare system</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Study preparation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staff training adequacy</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Site infrastructure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequacy of study space and equipment</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Resource availability</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Medication supply chain and administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supply chain adequacy</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Study drug administration</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Study conduct</td>
<td></td>
<td></td>
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<tr>
<td>Screening and consenting procedures</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Compliance with study procedures</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Demographic documentation</td>
<td>X</td>
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<tr>
<td>Safety documentation</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Documentation for source data verification</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Adequacy of medication administration</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Relevance/adequacy of study assessments</td>
<td></td>
<td></td>
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<tr>
<td>MINI</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>SMILE</td>
<td>X</td>
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</tr>
<tr>
<td>CGI-S</td>
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<tr>
<td>WHO QoL BREF23</td>
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<tr>
<td>ITA-Plus</td>
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<tr>
<td>SDS</td>
<td>X</td>
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</tr>
<tr>
<td>CAQ</td>
<td>X</td>
<td></td>
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<tr>
<td>CSRI</td>
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</tr>
<tr>
<td>Satisfaction scales</td>
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<td>Study satisfaction</td>
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</tr>
<tr>
<td>Site administration</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Staff satisfaction</td>
<td>X</td>
<td></td>
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<tr>
<td>Patient/participant satisfaction</td>
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<td></td>
</tr>
<tr>
<td>Caregiver satisfaction</td>
<td>X</td>
<td></td>
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</tbody>
</table>

CAQ, Cost Assessment Questionnaire; CGI-S, Clinical Global Impression-Severity; CSRI, Client Service Receipt Inventory; ITA-Plus, Intent to Attend-Plus; MINI, Mini International Neuropsychiatric Interview; SDS, Sheehan Disability Scale; SMILE, Screener for Mental Illness with Lay Evidence; WHO QoL BREF, WHO Quality of Life BREF.

three of four clinical measures was observed and PP1M/PP3M demonstrated good safety and tolerability.

The study highlights the need for systematic evaluation of the research capacity in settings with limited research experience. It is essential to identify the existing gaps and develop strategies to correct them before committing major resources. Several of the endpoints for this study, including administrative procedures, physical infrastructure, training and logistic components, required adjustment and/or more extensive preparation. This work provides a strong basis to prepare for the planned follow-up study.

This study evaluated the level of adaptation to local practices that was required to complete a large clinical trial within the Rwandan mental healthcare system, a system with limited experience in the conduct of drug-treatment clinical trials and the use of LAIs. Because Rwandan mental healthcare system hospitals in isolated rural areas were not chosen to participate in this feasibility study, results of this work may not be generalisable to settings within Rwanda with different cultural-economic characteristics or to other resource-limited African countries.

A critical need persists for conducting quality clinical trials in resource-limited settings. The findings from this feasibility study provide guidance for such future studies and can be applied to other therapeutic areas as well. Although the study was small, key limitations were identified that can provide insight for the development of future studies. This study demonstrated that additional time and resources are needed to improve training and verify the adequacy of site resources to ensure the success of large interventional clinical trials in resource-limited settings. Multiple adjustments have been implemented for the follow-up interventional trial to address issues identified by this feasibility study, including:

► Inclusion of a national principal investigator to improve communication between the sponsor and the sites, to identify study conduct considerations from participating sites and to coordinate concerns/responses between the sponsor and the sites.

► Implementation of a comprehensive training programme in GCP and research methodology for all sites, including both e-learning modules and in-person training.

► Inclusion of Rwanda-based site monitors, preferably local citizens, to provide consistent, in-person oversight.

► Introduction of health economic scales that more adequately reflect the Rwandan social-economic setting.

► Improved pre-study infrastructure assessment and ensuring availability of required equipment and supplies that meet the study’s requirements.

► Clinical team building and logistical planning that considers investigators’ regular hospital work schedules.

This work highlights the need for small preliminary studies in resource-limited countries to assess the feasibility of planned work, so problems with design and logistics can be addressed before committing to large trials and improve the likelihood of success.

CONCLUSION

This feasibility study proved to be an important first step toward the development of large mental health clinical trials within resource-limited African countries. The work highlighted key areas in need of improvement and emphasised
the need for more careful and extensive preparation for future studies. Despite the challenges identified for the study, sound relationships with key study leaders helped each of the stakeholders in the development and execution of the study to effectively work together to resolve the challenges revealed in the feasibility study and make progress toward development of the full-scale clinical trial.

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Contributors LA, BM, VS, S, AK, EA, AS, JDJ, YK and RB contributed to the design of the study. LA, BM, VS, S, AK, EA, AS, EH and RB contributed to the conduct of the study. LA, VS, S, IT, AK, AS, BM and EA contributed to the analysis of the study. BM is responsible for the overall content as the guarantor.

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Competing interests AK is an employee of Janssen Scientific Affairs, LLC. IT is an employee of Janssen Research and Development, LLC, and EA is an employee of Johnson & Johnson Global Public Health; all hold stock in Johnson & Johnson, Inc. EH was an employee of Janssen Research and Development, LLC, at the time the trial was conducted. AS was an employee of Janssen Research & Development, Belgium, at the time the trial was conducted and holds stock in Johnson & Johnson, Inc. LA was an employee of Janssen Scientific Affairs, LLC, at the time the trial was conducted and is currently employed by Denovo Biopharma, LLC; he holds stock in Johnson & Johnson, Inc., and Denovo Biopharma, LLC. BM and VS were employees of Johnson & Johnson Global Public Health at the time the trial was conducted and hold stock in Johnson & Johnson, Inc. JDJ, YK and RB report no conflicts of interest.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The protocol was reviewed and approved by the Rwanda National Ethics Committee and each hospital’s ethics committee. All study procedures were conducted in compliance with the Declaration of Helsinki and were consistent with Good Clinical Practice and applicable regulatory requirements. Written informed consent in the participant’s preferred language (Kinyarwanda, French or English) was obtained from all participants before enrolment (IRB 00001497). Participants gave informed consent to participate in the study before taking part.

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Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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