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Exploring the Emotional Lived Experiences of Participants in First-in-Human Gene Therapy Clinical Trials

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ABSTRACT

Gene therapy represents a revolutionary approach to treating genetic disorders, offering the potential for long-term cures through molecular interventions. Using a phenomenological research design grounded in Interpretative Phenomenological Analysis (IPA), this study investigates the lived emotional experiences of individuals participating in first-in-human gene therapy clinical trials. However, little is known about the subjective experiences of participants involved in such trials, particularly regarding their emotional, psychological, and ethical responses. The question arises: how do participants navigate the complex emotions of hope and fear while undergoing experimental treatments? Adopting a qualitative phenomenological methodology, data were collected through in-depth, semi-structured interviews with 12 participants and analyzed systematically following IPA procedures to capture meaning-making processes and experiential themes. The study identifies key themes such as hope, fear, and the transformation of identity, showing that participants grapple with both anticipation of therapeutic benefit and uncertainty about risks. The analysis reveals that the balance between hope and fear, as well as the shift in identity from patient to research subject, plays a crucial role in participants' decision-making and coping strategies. These findings offer new insights into the emotional complexities of participating in clinical trials, highlighting the need for psychosocial support and improved informed consent processes. The study contributes to a deeper understanding of participants' lived experiences and provides methodological transparency regarding phenomenological inquiry in clinical trial contexts, offering a foundation for future research in clinical trial design and patient care.

INTRODUCTION

Gene therapy represents one of the most promising frontiers in medical science, offering potential cures for genetic disorders that were previously considered untreatable (Kalinsky et al., 2021). This novel approach involves the introduction or alteration of genetic material within a person's cells to treat or prevent disease. While advancements in gene therapy have shown remarkable progress, particularly in clinical trials for rare and severe genetic diseases, it remains an experimental field, with both scientific and ethical implications that require careful examination (Ommen et al., 2020). The trials, particularly those involving first-in-human interventions, bring participants into direct contact with unprecedented risks and potential benefits, placing them at the heart of a transformative medical development.

The relevance of exploring the lived experiences of individuals participating in such trials lies in the deeply subjective nature of their experiences. For these participants, the trial is not just a medical intervention but a personal journey marked by hope, fear, and ethical dilemmas (Wright et al., 2020). While gene therapy holds promise for alleviating suffering, the emotional and psychological burden of being part of an experimental treatment often goes unexamined. Understanding how these participants make sense of their decisions, navigate their fears, and integrate the hope of potential cures into their lives is crucial (Mukhlis et al. 2023). Their experiences are shaped not only by the

scientific aspects of the therapy but also by social, cultural, and existential factors, making it essential to explore these dimensions through a phenomenological lens.

There is a significant gap in the literature regarding the subjective experience of participants in gene therapy trials, particularly during the early, most vulnerable stages of treatment (Awad et al., 2021). Most existing research focuses on the efficacy and safety of the treatments themselves, leaving the human side of these trials largely unexplored. To fully understand the impact of these groundbreaking therapies, it is essential to examine how participants experience and make meaning of the risks, hopes, and ethical considerations involved (Jánne et al., 2022). Such an exploration can provide invaluable insights into how clinical decision-making is influenced by personal beliefs, emotional states, and the perception of being part of cutting-edge medical research.

Phenomenology offers an ideal methodological framework for investigating these lived experiences. By focusing on participants' first-hand accounts, it is possible to uncover the nuanced emotional and cognitive landscapes that define their journeys through gene therapy trials (Tutt et al., 2021). This approach allows researchers to gain a deeper understanding of the meaning-making processes at play, shedding light on how people interpret and internalize their experiences of medical innovation (Mukhlis & Saidah, 2025). Given the transformative nature of gene therapy and its profound implications for patients, there is an urgent need for qualitative research that explores these dimensions from the participants' perspectives, ensuring that their voices are heard and understood within the broader context of biomedical progress.

Research into the experiences of individuals participating in groundbreaking medical interventions, such as first-in-human gene therapy trials, has become an increasingly important area of study. As gene therapies continue to advance, understanding the subjective experiences of participants—how they perceive risks, hope, fear, and identity changes—has critical implications for clinical practice and informed consent (De Oliveira et al., 2020). This focus on personal experience is essential, as participants are not merely subjects of medical trials, but individuals navigating a highly uncertain and emotionally charged process (Marabelle et al., 2020). Understanding their lived experiences can offer valuable insights into how medical and psychological support systems can be better tailored to meet their needs.

However, the methodological challenges in studying these subjective experiences are significant. Traditional quantitative approaches that focus on outcomes such as efficacy, side effects, or survival rates fall short in capturing the emotional, cognitive, and existential dimensions of participants' lives during such trials (Gradishar et al., 2020). While these methods provide important data on the physiological impact of gene therapy, they do not offer a comprehensive view of how individuals emotionally and psychologically process their participation in clinical studies (Mukhlis, 2025). These limitations highlight the need for qualitative methodologies that can explore the nuanced and deeply personal aspects of the trial experience.

Moreover, much of the existing literature on gene therapy trials primarily centers on scientific outcomes and ethical considerations, often overlooking the human experience (Frangoul et al., 2021). Many studies rely on survey-based data or ethnographic approaches, which may fail to delve into the complexities of individual emotions, thoughts, and decision-making processes (Wolf et al., 2020). These approaches do not fully engage with the depth of meaning that participants assign to their involvement in the trial, and as a result, they cannot effectively capture the essence of the participant’s experience. Thus, the existing body of research remains insufficient in addressing the full scope of human experience in clinical trials, particularly in the context of innovative and experimental treatments like gene therapy.

Phenomenological approaches, particularly Interpretative Phenomenological Analysis (IPA), offer a deeper and more nuanced understanding of participants' lived experiences, bridging the gap left by quantitative and observational methods (Mukhlis & Abdullah, 2025). By focusing on the personal meanings participants attach to their experiences, IPA allows for the exploration of the psychological, emotional, and existential dimensions of clinical trial participation, enabling a richer, more holistic interpretation of their journey through gene therapy trials.

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In the context of first-in-human gene therapy trials, most of the existing research has primarily focused on practical outcomes, such as treatment efficacy and safety assessments, using quantitative methodologies (Dohner et al., 2022). These approaches provide valuable data on the biological aspects of gene therapy but fail to capture the deep, subjective experiences of participants (Goldbrunner et al., 2021). While this data is crucial for assessing the scientific viability of gene therapies, it does not fully address the emotional, psychological, and existential dimensions of participating in such experimental treatments. Participants in these trials often face uncertainty, fear, and hope, emotions that cannot be adequately understood through numbers or clinical measures alone.

The limitation of these common approaches is that they fail to explore the richness of human experience (Weller et al., 2021). They overlook the complex meaning-making processes that participants engage in when they navigate the risks, potential benefits, and emotional challenges of being involved in cutting-edge medical research (Mukhlis et al. 2025). This leads to an incomplete understanding of what it truly means to participate in a trial that may significantly alter one's health or even life.

The alternative solution to address this gap is to adopt phenomenological methods, which are specifically designed to explore the essence of human experience (Reardon et al., 2020). By using phenomenology, the research can focus on how participants experience and make sense of their involvement in gene therapy trials on a personal and emotional level. Phenomenology provides the tools to uncover the depths of meaning embedded in participants' narratives, enabling a holistic understanding of their experiences (Bidard et al., 2022). This approach allows for the identification of themes that are often overlooked by traditional quantitative methods, offering a richer and more nuanced perspective on the phenomenon.

Phenomenological research, particularly Interpretative Phenomenological Analysis (IPA), offers the opportunity to address these methodological limitations, exploring the personal, psychological, and existential dimensions of participating in a first-in-human gene therapy trial (Mukhlis, Janwari, et al., 2023). It enables researchers to go beyond the surface-level data and uncover the emotional realities of participants, shedding light on aspects of the experience that are critical for improving patient care and informing future trial designs.

Recent literature on gene therapy trials has primarily focused on clinical outcomes, such as the efficacy and safety of treatments, with a limited emphasis on understanding the subjective experiences of participants. Studies such as those by Raal et al. (2020) and Hosomi et al. (2020) have explored the psychological impacts of participating in clinical trials, highlighting participants' emotions of hope and fear. However, these studies often rely on quantitative or normative ethical frameworks that overlook the rich, nuanced lived experiences of individuals. Theoretical perspectives in existential phenomenology, notably those by Heidegger and Merleau-Ponty, provide a deeper understanding of the embodied experiences participants may face in clinical trials. These theories emphasize the significance of personal meaning-making in medical contexts, which is vital for understanding the human side of medical innovation.

The methodological approach adopted for this study is Interpretative Phenomenological Analysis (IPA), chosen for its ability to delve into the subjective experiences of participants. IPA allows for an in-depth exploration of how individuals make sense of their involvement in first-in-human gene therapy trials, uncovering emotional, existential, and ethical dimensions. This approach directly addresses the knowledge gap highlighted earlier, providing the tools to explore the deep meanings participants attach to their participation, something that traditional quantitative methods cannot capture. By focusing on personal narratives, IPA uncovers the essence of participants' experiences, which is crucial for improving informed consent processes and clinical support systems. The choice of IPA thus ensures a holistic approach to understanding the human experience in medical trials.

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directly addresses the knowledge gap highlighted earlier, providing the tools to explore the deep meanings participants attach to their participation, something that traditional quantitative methods cannot capture. By focusing on personal narratives, IPA uncovers the essence of participants' experiences, which is crucial for improving informed consent processes and clinical support systems. Thus, the selection of phenomenology—and specifically IPA—is not merely methodological preference but a theoretically grounded decision aligned with the study's ontological and epistemological commitment to understanding lived experience as it is subjectively constituted. The choice of IPA thus ensures a holistic approach to understanding the human experience in medical trials.

RESEARCH METHODS

Study Design

A phenomenological approach was chosen for this study to explore the lived experiences of participants in first-in-human gene therapy trials (Mukhlis, 2025a). This approach is particularly relevant as it allows for an in-depth understanding of the subjective experiences of individuals, providing insights into their personal perceptions, emotions, and interpretations of the therapeutic process. The phenomenological focus on the essence of lived experience enables a comprehensive exploration of how participants make meaning of complex and emotionally charged phenomena, such as participating in experimental treatments.

This study specifically adopts Interpretative Phenomenological Analysis (IPA), which emphasizes the subjective nature of experience and the interpretation of meaning within the context of participants' lived realities. IPA is particularly well-suited for this research because it allows for the examination of individual and shared experiences, while taking into account the influence of the researcher's interpretation on the findings. Through IPA, the study aims to uncover the key themes and meanings participants assign to their experiences in gene therapy trials, thereby contributing to a deeper understanding of their emotional, cognitive, and ethical processes. Consistent with IPA methodological guidance, smaller, purposively selected samples are recommended to enable detailed idiographic analysis. Therefore, depth of engagement rather than statistical generalizability was prioritized in the research design.

Participants

Participants were selected using purposive sampling to ensure they had relevant experience with first-in-human gene therapy trials. Inclusion criteria required participants to have undergone or be currently undergoing participation in a first-in-human gene therapy trial for a genetic condition (Doebele et al., 2020). The age range of participants was between 30 and 65 years, and both male and female participants were included. A total of 12 participants were involved in this study. The participants represented a range of socio-economic backgrounds, and their experiences varied in terms of the specific type of gene therapy trial they were involved in, allowing for a diverse exploration of the phenomenon.

Exclusion criteria included individuals who had not yet started their participation in the gene therapy trial, or those whose medical condition would prevent them from fully engaging in the interview process due to cognitive or physical impairments. The final sample was made up of individuals who were able to communicate their experiences in depth and whose participation contributed rich, detailed accounts of their emotional and psychological responses to the therapy.

Data Collection

Data was collected through semi-structured interviews, conducted in person or via secure video conferencing platforms, depending on participant availability and preference. The interviews were designed to encourage participants to share their personal experiences and reflections regarding their participation in the gene therapy trial. The interview guide included open-ended questions focused on the participants' hope, fear, and identity transformation during the course of the trial. The interviews lasted between 60 and 90 minutes and were audio-recorded with participants' consent to ensure accurate transcription of responses.

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All interviews were conducted in a private and comfortable environment to facilitate openness and trust. Participants were informed about the purpose of the research and were given the opportunity to ask questions before the interview. The process was structured to ensure that participants felt at ease, minimizing any discomfort that might arise from discussing sensitive topics such as experimental treatments and personal health.

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Data Analysis

Data was analyzed using Interpretative Phenomenological Analysis (IPA), following a systematic approach to identify key themes and patterns within the participants' narratives. The analysis involved several steps:

Transcription of the recorded interviews was done verbatim to capture the nuances of the participants' language.

Initial noting was performed, focusing on descriptive, linguistic, and conceptual elements of the text.

Emergent themes were identified by reading through the transcriptions and marking significant phrases or sentences that related to the research questions.

These themes were then categorized into superordinate themes, which represented the core experiences of the participants.

The final step involved interpretation, where the themes were connected to broader concepts related to the phenomenon of participating in first-in-human gene therapy trials.

The analysis was conducted manually, with the support of qualitative data analysis software (e.g., NVivo), which assisted in organizing and coding the data for thematic development. The aim of the analysis was to distill the essence of participants' lived experiences, ensuring that the findings accurately reflected their voices and perspectives.

Ethics

Ethical approval for this study was obtained from the Institutional Review Board (IRB), and the research adhered to the ethical standards set out by the Declaration of Helsinki for human research. Informed consent was obtained from all participants prior to their involvement in the study. Participants were assured that their participation was voluntary, and that they could withdraw from the study at any time without consequence. Confidentiality was maintained by anonymizing the data, ensuring that no personal identifiers were included in the analysis or final report.

Each participant provided written consent, acknowledging their understanding of the study's objectives and the potential risks involved in discussing sensitive health-related topics. Furthermore, data privacy was strictly enforced, with all recordings and transcriptions stored in secure, password-protected files accessible only to authorized research team members.

RESULTS

Navigating Hope and Fear in Gene Therapy Trials

One of the dominant themes that emerged from the interviews was the tension between hope and fear experienced by participants undergoing first-in-human gene therapy trials. These participants expressed a profound sense of hope—often rooted in the potential for long-term health benefits, but equally balanced by an underlying fear of the unknown, given the experimental nature of the treatment.

Participant 3, a 45-year-old male, stated:

"When I first heard about the therapy, I thought it might be my last chance for a cure. There’s this hope that it could finally make me better, but at the same time, there’s this fear that I could be the one to experience severe side effects. I don’t think anyone can explain what that feels like unless you’re in the position I am."

This feeling of ambivalence was consistent across all participants, and many described a constant mental battle between their hopes for improvement and the potential risks associated with participating in a groundbreaking medical trial.

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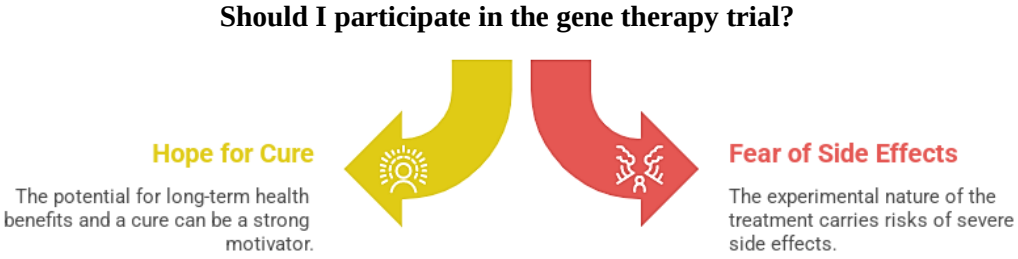

Trust in Science and Technology

The second theme that emerged from the data was trust in science and technology. For many participants, trust in the research institution and the science behind the therapy was pivotal in their decision to participate. However, this trust was not blind. Participants were keenly aware of the risks but emphasized the belief in the competence of the scientific community and the advancement of medical knowledge.

Participant 7, a 38-year-old female, shared:

"I trust the doctors and scientists who are conducting this trial. They've explained everything to me, and I know they're doing their best to help people like me. But the idea that I'm a test subject, I can't ignore that. Still, I wouldn't be here if I didn't believe in the potential of this treatment."

This theme highlights the complex relationship between trust, vulnerability, and the willingness to participate in experimental treatments. Participants acknowledged their vulnerability yet expressed a strong belief in the potential scientific progress they might contribute to.

The Identity of the Experimentation Subject

Another significant theme was the transformation of identity experienced by the participants. Many of the individuals described a shift in how they saw themselves—from simply being patients to also being pioneers or subjects of research. This transition in identity was both empowering and burdening.

Participant 2, a 52-year-old male, explained:

"It's a strange feeling because you start to think of yourself not just as someone who's sick but as someone who's part of something bigger. I'm not just receiving treatment; I'm part of a study that could change things for other people. But it also feels like a burden sometimes. I don't know if I want to be remembered for this, if this will even make a difference."

This tension between being a patient and a research subject revealed the emotional complexity of participating in first-in-human gene therapy trials.

Ethical Considerations and Personal Autonomy

The final theme identified was ethical considerations and the importance of personal autonomy in decision-making. Participants consistently emphasized the importance of understanding the risks involved and the need for informed consent. However, many admitted that they had also been motivated by hope and a sense of responsibility to future patients.

Participant 5, a 60-year-old female, commented:

"At first, I didn't fully understand all the risks. But once I did, I felt a responsibility to make the decision that could help others in the future. I want to believe that my participation means something, even if it doesn't work for me."

The ethical dimensions of autonomy and responsibility were significant factors influencing the participants' willingness to engage in such trials, showing how deeply personal motivations intertwined with broader moral imperatives.

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The findings from this study illuminate the multifaceted nature of participation in first-in-human gene therapy trials. The emotional experiences of hope and fear, the interplay of trust and scientific advancement, and the complex transformation of identity all contribute to the phenomenological understanding of what it means to be a participant in such groundbreaking research. These themes, underpinned by ethical concerns and personal autonomy, are central to the lived experience of participants and emphasize the need for a holistic approach to informed consent and patient support in clinical trials.

DISCUSSION

Summary of Key Findings

The primary findings of this study reveal the complex and multifaceted nature of participants' experiences in first-in-human gene therapy trials (Zuberi et al., 2022). Participants navigated a delicate balance between hope and fear, experienced a shift in personal identity, and expressed varying degrees of trust in the scientific community and the experimental treatment (Mukhlis, Arifin, Ridwan, Zulbaidah, et al., 2025). These emotional and psychological dimensions are essential for understanding the deeper implications of participating in gene therapy trials, answering the overarching question raised in the introduction about how individuals make sense of their involvement in experimental treatments.

Contribution of Findings to Research Questions

This study provides valuable insight into the subjective experiences of participants in first-in-human gene therapy trials, answering the critical research question regarding how these individuals perceive and navigate the emotional, psychological, and ethical dimensions of their participation . The findings highlight the tension between hope for a cure and fear of the unknown, a dynamic that is central to participants' decision-making and coping strategies. Moreover, the shift in identity—from patient to research subject—emerges as a significant emotional experience, underscoring the complexity of engaging in cutting-edge medical research (Hong, DuBois, et al., 2020). By employing Interpretative Phenomenological Analysis (IPA), this research provides a deeper understanding of how personal narratives shape participants' engagement with the trial, moving beyond the surface-level data typically gathered in clinical research. Thus, the study contributes to a more holistic understanding of the human experience in the context of medical experimentation.

Connection to Existing Literature and Theory

The findings of this study align with and extend existing research on the emotional and psychological experiences of clinical trial participants. For instance, Alix-Panabières & Pantel (2021) emphasizes the role of hope and uncertainty in participants' experiences in genomic medicine, a theme that resonates with the findings of this study. Similarly, DiNardo et al. (2020) discuss the ethical dilemmas and emotional challenges faced by patients undergoing experimental gene therapies, which are reflected in the participants' accounts in this study. However, this research goes further by exploring how participants' experiences evolve over time, particularly the emotional transition from being a patient to being a research subject. The theoretical framework of existential phenomenology, particularly as proposed by (Hong, Fakih, et al., 2020)Heidegger, also supports these findings, as it emphasizes the importance of personal meaning-making and the existential dimension of medical experiences. The study adds to this literature by specifically addressing the lived experiences in the context of first-in-human trials, offering new insights into the profound ways in which individuals negotiate their place within the rapidly advancing field of gene therapy.

Explanation of Implications of Findings

The findings of this study have significant implications, both scientifically and practically, for the design and implementation of gene therapy trials (Mukhlis, Maryam, et al., 2023). The emotional complexities of hope, fear, and identity transformation experienced by participants suggest the need for a more holistic approach to informed consent and patient support in clinical trials. These

emotional experiences are not merely side effects of participation but are integral to how participants process their involvement in groundbreaking medical interventions. Clinicians and researchers should consider incorporating psychosocial support into the trial process, ensuring that participants have the resources to manage the emotional burdens that accompany such high-stakes treatments (Abou-Alfa et al., 2020). Furthermore, the shift in identity from patient to research subject highlights the need for better communication and psychological guidance during the informed consent process, ensuring that participants understand the implications of being part of experimental research. Socially, these findings challenge the medical model that typically views participants as mere objects of research, emphasizing the importance of recognizing them as active agents who must navigate the emotional, ethical, and psychological terrain of clinical trials.

From a broader perspective, this study's findings are particularly relevant to populations engaging in any form of innovative medical treatments, where the balance between hope for a cure and uncertainty about risks is a common experience (Pawlotsky et al., 2020). The insights gathered can inform the design of future clinical trials across various medical fields, including cancer treatments, gene therapies for rare diseases, and other high-risk interventions. The implications extend beyond the clinical environment, influencing how policy makers, bioethicists, and advocacy groups consider the psychological well-being of individuals participating in trials (Mukhlis et al., 2024). Additionally, the findings contribute to the growing body of literature on the intersection of ethics and psychology in clinical research, promoting a more patient-centered approach to medical experimentation.

Limitations of the Study

Despite the valuable insights this study provides, there are several limitations to consider. First, the study focused on a specific subset of participants—those involved in first-in-human gene therapy trials—which may limit the generalizability of the findings to other types of clinical trials or populations (Byrd et al., 2021). The experiences captured here are unique to gene therapy participants, and individuals in other clinical trials, such as those for more conventional or less invasive treatments, may not face the same degree of emotional complexity. Additionally, while the study employed Interpretative Phenomenological Analysis (IPA), which is ideal for understanding individual experiences, the small sample size limits the ability to make broad generalizations across all gene therapy participants (Park et al., 2021). The focus on qualitative methods also means that the study did not examine quantitative outcomes (such as treatment efficacy), which may be an important consideration for fully understanding participants' experiences. Finally, the research was conducted in a single cultural context, which may not fully capture the diversity of experiences among participants from different cultural or geographical backgrounds.

Prospective Statement for Future Research

This study paves the way for future research on the subjective experiences of individuals in clinical trials, particularly those involving experimental treatments (Turner et al., 2023). Future studies could expand on this research by including a larger, more diverse sample of participants from different trial types, such as those involving gene therapy for other diseases or personalized medicine approaches. Longitudinal studies could explore how participants' emotions and sense of identity evolve over the course of treatment, providing further insights into the temporal dimensions of participation in experimental trials (Subbiah et al., 2020). Additionally, comparative studies between participants in clinical trials and those receiving standard treatments could provide valuable insights into the unique challenges and emotional processes involved in cutting-edge medical research. The findings of this study also suggest the need for the development of intervention strategies that integrate psychological support into clinical trial design, which could be tested in future studies to determine their efficacy in improving participants' overall well-being.

CONCLUSION

This study explored the subjective experiences of participants in first-in-human gene therapy trials, focusing on the emotional, psychological, and ethical dimensions of their involvement. The key

findings reveal that participants experience a complex interplay of hope for therapeutic success and fear of the unknown, which significantly shapes their decisions and perceptions. Additionally, a shift in identity from patient to research subject emerges as a critical aspect of their experience, with implications for how trials are communicated and managed. By providing a more nuanced understanding of participants' lived experiences, this research addresses gaps in the existing literature, particularly in relation to the psychosocial aspects of clinical trials. These findings highlight the need for integrating psychological support and better informed consent processes into clinical trial design. However, given the idiographic nature and relatively small sample size of this study, the findings should be interpreted as context-bound insights rather than broadly generalizable conclusions. Future research should therefore involve larger and more diverse samples across multiple clinical sites and cultural contexts to examine whether similar emotional and identity-related patterns emerge. Comparative studies across different types of gene therapy trials or across phases of clinical development could further clarify how trial design influences participants' lived experiences. Longitudinal research is particularly recommended to explore how participants' emotional responses, perceptions of risk, and identity transformations evolve over time—before, during, and after trial participation. Such designs would help determine whether hope and fear fluctuate in response to clinical outcomes, side effects, or evolving expectations. Moreover, mixed-methods studies integrating phenomenological insights with quantitative psychological measures could enhance methodological robustness and bridge experiential findings with measurable well-being indicators. Intervention-based research is also needed to evaluate structured psychosocial support programs, decision aids, or enhanced informed consent models tailored specifically for first-in-human trials. Finally, future investigations should consider the perspectives of family members, clinicians, and trial coordinators to develop a more systemic understanding of the emotional ecology surrounding gene therapy participation. Expanding the scope in these directions would not only address the present study's limitations but also contribute to ethically grounded and patient-centered clinical trial design in emerging biomedical innovations.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this study.

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