ONLINE EXCLUSIVE ARTICLE

Well-Being of Child and Family Participants in Phase 1 Pediatric Oncology Clinical Trials

Stacey Crane, PhD, RN, CPON®, Joan E. Haase, PhD, RN, FAAN, and Susan E. Hickman, PhD

PROBLEM IDENTIFICATION: Pediatric oncology phase 1 clinical trials (P1Ts) are essential to developing new anticancer therapies; however, they raise complex ethical concerns about balancing the need for this research with the well-being of participating children. The purpose of this integrative review was to synthesize and appraise the evidence of how P1T participation, which begins with consent and ends with the transition off the P1T, can affect the well-being (either positively or negatively) of children with cancer. The Resilience in Individuals and Families Affected by Cancer Framework, which has an outcome of well-being, was used to synthesize findings.

LITERATURE SEARCH: Articles on the experiences of child (n = 21) and adult (n = 31) P1T participants were identified through systematic searches.

DATA EVALUATION: Articles were evaluated on rigor and relevance to P1T participant experiences as high, medium, or low.

SYNTHESIS: Minimal empirical evidence was found regarding the effect of P1T participation on the well-being of children with cancer. Adult P1T participant experiences provide insights that could also be important to children's P1T experiences.

IMPLICATIONS FOR PRACTICE: To achieve a balanced approach in P1T consent discussions, nurses and healthcare providers who work with children considering participation in a P1T should share the potential effect of participation on participants' well-being.

KEYWORDS clinical trials; pediatric; ethics
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Cancer remains the leading cause of death by disease in children aged 14 years and younger (Siegel, Miller, & Jemal, 2016). Although five-year survival rates for pediatric cancers have improved overall to 83%, for some pediatric cancers, the five-year survival rate is only 67% (Siegel et al., 2016). New therapies are needed to improve outcomes for children with cancer. Phase 1 clinical trials (P1Ts) are the first step in testing new medical therapies in humans and are essential to the development of innovative therapies for children with cancer (Kim et al., 2008; Lee, Skolnik, & Adamson, 2005).

Although the need for P1Ts is generally accepted, P1Ts raise ethical concerns (Agrawal & Emanuel, 2003; Berg, 2007; Crites & Kodish, 2013; de Vries et al., 2011; Ekert, 2013; Estlin, Cotterill, Pratt, Pearson, & Bernstein, 2000; Hazen, Zyzanski, Baker, Drotar, & Kodish, 2015; Kearns & Morland, 2014; Miller & Joffe, 2008; Oberman & Frader, 2003; Weinfurt et al., 2012). Goals of P1Ts are traditionally to determine the maximum-tolerated dose of the therapy, describe the action of the therapy in humans, and reveal side effects (Kim et al., 2008; Lee et al., 2005). The National Cancer Institute updated P1T templates to include preliminary determination of efficacy as a secondary trial objective (Weber et al., 2015). P1Ts are primarily conducted to determine how innovative therapies may safely be given. Although not intended to directly benefit participants, healthcare providers and researchers hope that P1Ts will directly benefit at least some participants. The Declaration of Helsinki requires that "while the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects" (World Medical Association, 2013, p. 2). The ethical challenge of P1Ts is to ensure that the well-being of participants is supported throughout the trial.

Ethical concerns regarding P1Ts are more complex in children with cancer, in part because children