Considerations for Studies in Infectious Diseases of the Genitourinary System

An Area of Significant Unmet Medical Need

Infectious diseases of the genitourinary system compromise quality of life for many women and can lead to serious conditions including pelvic inflammatory disease, infertility and cervical cancer. Women commonly experience genitourinary system infections:

- Bacterial vaginosis has an estimated prevalence of 21.2 million women aged 14-49
- Approximately one-third of women require antibiotic treatment for a urinary tract infection (UTI) by age 24, and half of women experience at least one UTI in their lifetime
- The Centers for Disease Control estimates that there are approximately 20 million new cases of sexually transmitted infections in the United States each year
- Recurrent genitourinary system infections are common

There is a substantial need for novel therapeutics for infectious diseases of the genitourinary system. A variety of bacterial and viral pathogens, fungi and protozoan may cause infections of the reproductive system. Multi-drug resistant bacterial and protozoan STIs and HIV are significant global issues. In the treatment of UTIs, antimicrobial resistance is a challenge. Additionally, existing antivirals are not recommended for human papillomavirus (HPV) infections; therapeutics are primarily ablative or immunomodulatory. Clinical research is necessary to offer alternative treatment options and improve health outcomes in patients experiencing genitourinary system infections.

Operational and Methodological Considerations

Requirements for clinical trials of therapeutics for infectious diseases of the genitourinary system vary depending on many factors, including the type of pathogen, the number of likely sites of infection, diagnostics used in clinical practice, diagnostics required to determine study eligibility, allowable coinfections, stratification requirements for the patient population, site selection and endpoints. For example:

- A study of a novel antibiotic for a bacterial STI like gonorrhea may involve diagnosis by culture and nucleic acid amplification test (NAAT), collection of urethral, cervical, rectal and pharyngeal samples, testing for coinfections by other pathogens and in vitro susceptibility testing
- A study of an investigational therapeutic for a viral pathogen such as HPV or herpes simplex virus 2 (HSV-2) will involve a longer treatment period and efficacy measures such as percent reduction in viral shedding, percent of subjects with
detectable viral shedding, clearance of lesions or percent of days with lesions in a specified follow-up period

- Studies of STIs will likely recruit a sexually active population at urban clinics, including STI clinics, with consideration for enrolling men who have sex with men
- A study of a therapeutic for bacterial vaginosis will likely involve typical OB/GYN sites with patients across a wider age span, eligibility requirements such as a Nugent’s Gram Stain Score of 7-10, and multiple endpoints related to physiological discharge, a whiff test and clue cells as a percentage of total epithelial cells
- A study of a therapeutic for anogenital warts may require consideration of the required number of warts that are nonconfluent, individually isolated and within specific surface-area parameters, potentially creating enrollment challenges
- Endpoints in studies of HSV-2 antivirals are typically based on recurrence frequency and lesion rates, but it may be possible to consider viral shedding rate as a surrogate outcome in a phase 2 trial
- The quality and consistency of sample collection and the roles of local and central labs are often important considerations in studies of infections of the genitourinary system

Key Risks and Corresponding Mitigations

Key risks in studies of diseases of the genitourinary system may include noncompliance of patients and their partners with required dosing and limitations on sexual activity and use of intravaginal products. In addition, especially with young populations that may experience frequent changes of employment and residence, there is a risk of early discontinuation.

Risk 1: High subject discontinuations

Risk of subject discontinuation is heightened in trials enrolling young, sexually active populations who may move more frequently than an older population. Risk of discontinuation is greater when subjects perceive study requirements as burdensome.

Mitigations

- Investigational sites in studies of STI therapeutics must fully inform subjects of requirements for trial participation at the outset, including the timing of the various requirements and the importance of subject compliance and completion of all study obligations.
- Distribute a subject stipend over all visits, including the last visits and all visits at which endpoint data is collected.
- If there is an extensive site network, explore arrangements for transferring patients between sites in event of relocation.

Risk 2: Inconsistency in interpretation of study inclusion criteria and endpoints

In studies with inclusion criteria requiring specific number and size of lesions or condylomas and endpoints requiring reductions in number of lesions or combined surface area, there may be inconsistencies in site performance.

Mitigations

- Precisely define procedures for measuring lesions and surface area and provide visual guides and training for site staff.

For Assistance With Your Development Program

With the increasing prevalence of drug-resistant pathogens, the need for novel therapeutics is great. However, studies of infectious diseases of the genitourinary system can face a variety of operational challenges. As a CRO committed to improving healthcare outcomes for women worldwide, Health Decisions is determined to advance and accelerate clinical development of improved treatments for infectious diseases of the genitourinary system. Please contact us to explore how Health Decisions can assist with efficient, timely development of your investigational treatment.

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