CHAPTER

21

Endpoints for Infections

I. INTRODUCTION

Infections include bacterial infections, protozoal infections, and viral infections. Endpoints used in clinical trials for infections can include direct measurements of the infecting agent, measurements of physiological functions that are impaired by the infecting agent, and measurements of immune responses against the infecting agent.

Infections are not necessarily fatal. For example, regarding Chagas' disease, which is caused by infections with *Trypanosoma cruzi*, "the disease enters the chronic phase, which usually involves a clinically latent period ... lasting 10–30 years, although it may be lifelong" (1). Thus, endpoints that track survival, such as overall survival or progression-free survival, may be irrelevant in clinical trials on infections. Another issue in determining drug efficacy is that there may not exist any test to determine a cure. In the words of Molina et al. (2) "[o]ne of the limitations of clinical trials ... in chronic Chagas' disease is that there is no definite test to determine cure." For these reasons, surrogate endpoints may be the only available endpoint available for clinical trials on infectious diseases.

This chapter establishes a context for understanding endpoints for clinical trials on infectious diseases by detailing the physiology of hepatitis C virus (HCV) infections, and endpoints used for clinical trials on HCV. HCV infections are often chronic and fatal.

II. CLINICAL AND IMMUNOLOGICAL FEATURES OF HCV INFECTIONS

Hepatitis C virus (HCV) was identified in 1989 (3). About 170 million people worldwide are infected with HCV, with about 4 million of

[1]Pérez-Molina JA, Pérez-Ayala A, Moreno S, et al. Use of benznidazole to treat chronic Chagas' disease: a systematic review with a meta-analysis. J. Antimicrob. Chemother. 2009;64:1139–47.

[2]Molina I, Prat J, Salvador F, et al. Randomized trial of posaconazole and benznidazloe for chronic Chagas' disease. New Engl. J. Med. 2014;370:1899–908.

[3]Rehermann B. Hepatitis C virus versus innate and adaptive immune responses: a tale of coevolution and coexistence. J. Clin. Invest. 2009;119:1745–54.

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