CHAPTER 10

Introduction to Endpoints for Clinical Trials in Pharmacology

I. INTRODUCTION

Endpoints are used to assess efficacy of a drug, medical device, counseling, physical exercise, or other form of treatment under evaluation in a given clinical trial. Typically, in designing a clinical trial, an investigator includes more than one type of endpoint. Endpoints include efficacy endpoints and sometimes safety endpoints.

a. Phase I clinical trial endpoints

Phase I clinical trials are primarily conducted for arriving at an optimal dose, for use in Phase II and III clinical trials, but only secondarily, if at all, for acquiring data on efficacy. In comments about Phase I trials in the context of oncology, Llovett et al. (1) find that, "[i]n current oncological practice, phase 1 studies are intended to define appropriate dosage by using endpoints such as dose-limiting toxicity, maximum tolerated dose, pharmacokinetic profile, and pharmacodynamic profile. The primary endpoint of these studies is the safety profile or change in measures that reflect relevant biologic processes."

b. Clinical endpoints

The endpoints that are most relevant to the study subject are events of which the study subject is aware or afraid of, such as death, a heart attack, loss of vision, or the arising need for a liver transplant due to viral infection (2). These endpoints are classified as *clinical endpoints*. In clinical trials on life-threatening disorders, the most common clinical endpoint is overall survival (OS). But, according to Le Tourneau et al. (3) "[t]he main drawback of overall survival is that it usually requires larger patient numbers and longer follow-up than surrogate time-to-event end points."

c. Surrogate endpoints

Another class of endpoints is *surrogate endpoints*. Where the natural time course of a particular disease is extremely long, or where the window of drug therapy is extremely

[1] Llovet JM, Di Bisceglie AM, Bruix J, et al. Design and endpoints of clinical trials in hepatocellular carcinoma. *J Natl Cancer Inst*. 2008;100:698–711.

[2] Fleming RT, DeMets DL. Surrogate end points in clinical trials: are we being misled? *Ann Intern Med*. 1996; 125:605–613.

[3] Le Tourneau C, Michiels S, Gan HK, Siu LL. Reporting of time-to-event end points and tracking of failures in randomized trials of radiotherapy with or without any concomitant anticancer agent for locally advanced head and neck cancer. *J Clin Oncol*. 2009;27:5965–5971.

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