

A statistician can translate the responses to these questions into statistical assumptions which can be utilized to determine a sample size or a range of sample sizes that could be considered for the trial based on statistical principles. These values are then reviewed with the clinical trial design team to set the sample size for the study. For this reason, it is important to have a basic understanding of these terms to ensure productive conversations around sample size determination.

a. What Is the Primary Objective of the Study?

Clinical trial objectives are concise statements of the major and minor questions that the trial is designed to answer. Statement of the objective should include specific details about the purpose of the trial (2). The primary objective of the study is typically related to the assessment of efficacy. For example, CEL-SCI initiated a phase III, open-label, randomized, controlled, multicenter study to evaluate the effects of Multikine Plus Standard of Care (Surgery + Radiotherapy or Surgery + Concurrent Chemoradiotherapy) in Subjects with Advanced Primary Squamous Cell Carcinoma of the Oral Cavity and Soft Palate Versus Standard of Care Only. The Clinical Study Protocol stated primary objective is, “to evaluate the efficacy of peri-tumoral and perilymphatic injection of the investigational Multikine therapy given prior to Standard of Care (SOC) (as currently defined by the NCCN Guidelines).” For this study, efficacy will be evaluated using overall survival (3). It should be

noted that primary objectives of clinical trials can be related to the determination of safety or a combination of multiple endpoints. In these cases, the required sample size may be larger than would have been required for the primary efficacy objective alone (4). The concept of “Standard of Care” is defined in Chapter 7.

b. What Measure Will be Used to Determine This Outcome for a Given Subject?

The measure used to determine the primary objective is often referred to as the primary endpoint. This measurement should be accepted as clinically relevant or exhibiting important treatment benefit in the subject population under evaluation. It should be a measurement that can be obtained or observed for each subject participating in the clinical trial. Using the Multikine study discussed earlier, the primary efficacy endpoint is overall survival. Here, each subject will be observed for the duration of the study and overall survival recorded.

c. What Is the Clinically Meaningful Difference?

The clinically meaningful difference is the difference generally regarded as clinically important or meaningful to a patient or clinician. The determination of clinically meaningful differences is an evolving science, specifically in the development of patient-reported outcomes. For objective measurements of response (ie, survival, changes in

²Spilker B. Guide to clinical trials. Philadelphia, PA: Lippincott Williams & Wilkins; 1991.

³CelSci Corporation, Vienna, VA. http://www.cel-sci.com/multikine_phase_3_clinical_trial_design.html [accessed 28.07.15].

⁴Stenger M. ASCO Committee defines clinically meaningful goals for clinical trials in pancreas, breast, lung, and colorectal cancers. The ASCO Post. May 15, 2014, vol. 5, issue 8, Harborside Press. <http://www.ascopost.com/issues/may-15-2014/asco-committee-defines-clinically-meaningful-goals-for-clinical-trials-in-pancreas,-breast,-lung,-and-colorectal-cancers.aspx> [accessed 28.07.15].