

questionnaire decreased, and that there was some evidence that growing noncompliance introduced bias into the results.

#### 4. Representative List of Clinical Trials

Now that the take-home lessons from the Shepherd study, the Bezjak study, and the Bonomi study, have been reviewed, the following provides study design information regarding HRQoL from these clinical trials, as well as from one additional clinical trial (Table 22.5).

#### g. HRQoL in Breast Cancer

Perry et al. (54) summarized the HRQoL tools, about 20 in all, that have been used in clinical trials on breast cancer. The following narrative focuses on only two trials, the Watanabe study and the Muss study.

#### h. HRQoL in Chronic Lymphocytic Leukemia

The Clinical Study Protocol for a trial for a leukemia drug provides an exemplary account of the use of an HRQoL tool. The HRQoL tool was the FACT-Leu questionnaire, which is configured for use with leukemia patients (55). HRQoL data were used as one of the secondary endpoints. The Protocol

provided the following guidance on how the HRQoL data should be interpreted (56):

Change in HRQL domain and symptom scores based on ... FACT-Leu ... defined as the change from baseline and the time to definitive increments or decrements of 10%, 20%, and 40% from baseline; **time to definitive increment** (better than baseline by the specified amount) is the interval from randomization to the first timepoint when the HRQL measure is consistently better than at baseline ... and **time to definitive HRQL decrement** (worse than baseline by the specified amount) is the interval from randomization to the earliest death or the first timepoint when the HRQL measure is consistently worse than at baseline.

The FACT-Leu questionnaire took the form of rows of checkboxes requesting choice of severity, for questions such as:

- I have lack of energy;
- I have nausea;
- I am forced to spend time in bed;
- I feel close to my friends;
- I get emotional support from my friends;
- My family has accepted my illness;
- I feel sad;
- I feel nervous;
- I worry about dying.

The Clinical Study Protocol also included background information on the evaluation of HRQoL in leukemia clinical trials, which is excerpted below (57). Although it might be

<sup>54</sup>Perry S, Kowalski TL, Chang CH. Quality of life assessment in women with breast cancer: benefits, acceptability and utilization. *Health Qual. Life Outcomes* 2007;5:24–37.

<sup>55</sup>Cella D, et al. Measuring health-related quality of life in leukemia: the Functional Assessment of Cancer Therapy-Leukemia (FACT-Leu) questionnaire. *Value Health* 2012;15:1051–8.

<sup>56</sup>A phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of GS-1101 (CAL-101) in combination with rituximab for previously treated chronic lymphocytic leukemia. Protocol GS-US-312-0116. November 18, 2011.

<sup>57</sup>A phase 3, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of GS-1101 (CAL-101) in combination with rituximab for previously treated chronic lymphocytic leukemia. Protocol GS-US-312-0116. November 18, 2011.