

#### d. Relatively objective endpoints versus relatively subjective endpoints

The following chapters concern endpoints used in clinical trials on solid tumors, hematological cancers (non-solid tumors), immune disorders, and infections. Following these accounts are chapters on health-related quality of life (HRQoL). HRQoL refers to subjective information collected from study subjects by way of questionnaires. HRQoL data may be used, as an endpoint, in efforts to gain FDA approval for various drugs and medical devices.

Publications that systematically address the utility and reliability of HRQoL questionnaires include the following. The publications are cited for studies of cancers, including breast cancer (16) colorectal cancer (17) lung cancer (18) melanoma (19) and liver cancer (20) as well as for diseases that are not cancer, such as hepatitis C virus (21) tuberculosis (22,23) multiple sclerosis (24,25) and asthma (26).

At the objective end of the endpoint spectrum is overall survival (death), while at the subjective end of the spectrum is HRQoL. Regarding survival, Slamon et al. (27) refer to this as “an end point free of ascertainment bias.”

Endpoints that reside at intermediate points in this spectrum include endpoints that rely on tumor size and number. Even though tumor size and number seem straightforward, these are often determined by measurements by an independent radiologist, and by the investigator’s radiologist, and they are often determined at a given time point, and then confirmed at a later time point. Other endpoints can reside in between the far-objective and far-subjective ends of the spectrum. For Patient-Reported Outcomes

<sup>16</sup> Twelves CJ, Miles DW, Hall A. Quality of life in women with advanced breast cancer treated with docetaxel. *Clin Breast Cancer*. 2004; 5:216–222.

<sup>17</sup> Cornish D, Holterhues C, van de Poll-Franse LV, Coebergh JW, Nijsten T. A systematic review of health-related quality of life in cutaneous melanoma. *Ann Oncol*. 2009;20(Suppl 6):51–58.

<sup>18</sup> Gridelli C, Ardizzoni A, Le Chevalier T, et al. Treatment of advanced non-small-cell lung cancer patients with ECOG performance status 2: results of a European Experts Panel. *Ann Oncol*. 2004;15:419–426.

<sup>19</sup> Cornish D, Holterhues C, van de Poll-Franse LV, Coebergh JW, Nijsten T. A systematic review of health-related quality of life in cutaneous melanoma. *Ann Oncol*. 2009;20(Suppl 6):51–58.

<sup>20</sup> Yeo W, Mo FK, Koh J, et al. Quality of life is predictive of survival in patients with unresectable hepatocellular carcinoma. *Ann Oncol*. 2006;17:1083–1089.

<sup>21</sup> Gutteling JJ, de Man RA, Busschbach JJ, Darlington AS. Overview of research on health-related quality of life in patients with chronic liver disease. *Neth J Med*. 2007;65:227–234.

<sup>22</sup> Guo N, Marra F, Marra CA. Measuring health-related quality of life in tuberculosis: a systematic review. *Health Qual Life Outcomes*. 2009;7:14.

<sup>23</sup> Marra CA, Marra F, Colley L, Moadebi S, Elwood RK, Fitzgerald JM. Health-related quality of life trajectories among adults with tuberculosis: differences between latent and active infection. *Chest*. 2008;133:396–403.

<sup>24</sup> Ramp M, Khan F, Misajon RA, Pallant JF. Rasch analysis of the Multiple Sclerosis Impact Scale MSIS-29. *Health Qual Life Outcomes*. 2009;7:58.

<sup>25</sup> Mowry EM, Beheshtian A, Waubant E, et al. Quality of life in multiple sclerosis is associated with lesion burden and brain volume measures. *Neurology*. 2009;72:1760–1765.

<sup>26</sup> Ehlers PO, Nokela M, Stållberg B, Hjemdahl P, Wikström Jonsson E. Brief questionnaires for patient-reported outcomes in asthma: validation and usefulness in a primary care setting. *Chest*. 2006;129:925–932.

<sup>27</sup> Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *New Engl J Med*. 2001;344:783–792.