

In a study of **colorectal cancer** by Van Cutsem et al. (24) subjects in the control arm received only best supportive care, where this care was described as, “BSC was defined as the best palliative care per investigator excluding antineoplastic agents.”

In a study of **liver cancer** by Barbare et al. (25) subjects in the control arm received only best supportive care, as described, “[a]ll patients in the study group and in the control group received best supportive care and appropriate management of the liver disease as usually practiced in the individual centers.”

VII. CLASH BETWEEN BEST SUPPORTIVE CARE AND THE ENDPOINT OF HRQoL

Typically, clinical trials in oncology include the endpoints of objective response, overall survival, and HRQoL. Where HRQoL is one of the endpoints, and where the control arm receives only best supportive care, it is critical that the study drug arm also receives best supportive care. To provide an instructive example, in a study of pancreatic cancer, Glimelius et al. (26) used HRQoL as one of their endpoints. The control arm received best supportive care only. These authors were careful to state that both study arms had received best supportive care, that is, the study drug arm and also the control arm received best supportive care. Interference of best supportive care with the endpoint of HRQoL has been documented in the clinical trial of Smith et al. (27) “[o]ur data did not show improved quality of life associated with...therapy, possibly owing to the high proportion of patients with advanced disease receiving palliative care.” Data collected on quality of life can be a deciding factor, in comparing efficacy and safety of the study drug group and control group (28).

VIII. ETHICS OF PLACEBOS

The following provides a context when contemplating the ethics of placebos. In a classic book on study design, E.B. Wilson wrote that, “[t]he use of controls in medical and

²⁴ Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol.* 2007;25:1658–1664.

²⁵ Barbare JC, Bouché O, Bonnetain F, et al. Randomized controlled trial of tamoxifen in advanced hepatocellular carcinoma. *J Clin Oncol.* 2005;23:4338–4346.

²⁶ Glimelius B, Hoffman K, Sjöden PO, et al. Chemotherapy improves survival and quality of life in advanced pancreatic and biliary cancer. *Ann Oncol.* 1996;7:593–600.

²⁷ Smith RE Jr, Aapro MS, Ludwig H, et al. Darbepoetin alpha for the treatment of anemia in patients with active cancer not receiving chemotherapy or radiotherapy: results of a phase III, multicenter, randomized, double-blind, placebo-controlled study. *J Clin Oncol.* 2008;26:1040–1050.

²⁸ Efficace F, Bottomley A, Osoba D, et al. Beyond the development of health-related quality-of-life (HRQOL) measures: a checklist for evaluating HRQOL outcomes in cancer clinical trials – does HRQOL evaluation in prostate cancer research inform clinical decision making? *J Clin Oncol.* 2003;21:3502–3511.