**Table 4.1** ECOG performance status[a]

| Grade | ECOG performance status |
|---|---|
| 0 | Fully active, able to carry on all pre-disease performance without restriction |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours |
| 3 | Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours |
| 4 | Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair |
| 5 | Dead |

[a] Oken MM, Creech RH, Tormey DC., et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5:649–655.

## j. Irreversible and cumulative toxicity as a basis for exclusion

Although most chemotherapeutic agents have an associated toxicity, reversible side effects impose fewer limitations on future treatment options (58). Topotecan's toxicity (neutropenia; leukopenia) is reversible and non-cumulative (59). Trastuzumab's toxicity (cardiotoxicity) tends to be reversible. According to Perez (60) "in contrast to anthracycline-induced cardiac toxicity, trastuzumab-related cardiac dysfunction does not appear to increase with cumulative dose or to be associated with ultrastructural changes in the myocardium and is generally reversible."

But, the toxicity of anthracyclines, such as doxorubicin, tends to be irreversible and cumulative. Doxorubicin's irreversible cardiac toxicity is well documented (61,62). In the words of Montemurro et al. (63) "[a] steep increase in the risk for irreversible cardiotoxicity for cumulative doses of doxorubicin and epidoxorubicin…represents the main limitation to rechallenge with these drugs."

Carboplatin can produce irreversible toxicity. Where carboplatin is used for treating a particular cancer, and where the cancer returns and where carboplatin is administered again, the result can be a hypersensitivity reaction in the form of tachycardia (64).

[58] Dunton CJ. Management of treatment-related toxicity in advanced ovarian cancer. *The Oncologist*. 2002;7(suppl 5):11–19.

[59] Dunton CJ. Management of treatment-related toxicity in advanced ovarian cancer. *The Oncologist*. 2002; 7(suppl 5):11–19.

[60] Perez EA. Cardiac toxicity of ErbB2-targeted therapies: what do we know? *Clin Breast Cancer*. 2008; 8(suppl 3):S114–S120.

[61] Chan S, Friedrichs K, Noel D, et al. Prospective randomized trial of docetaxel versus doxorubicin in patients with metastatic breast cancer. *J Clin Oncol*. 1999;17:2341–2354.

[62] Armenian SH, Sun CL, Francisco L, et al. Late congestive heart failure after hematopoietic cell transplantation. *J Clin Oncol*. 2008;26:5537–5543.

[63] Montemurro F, Rossi V, Nolè F, et al. Underuse of anthracyclines in women with HER-2 + advanced breast cancer. *Oncologist*. 2010;15:665–672.

[64] Markman M, Kennedy A, Webster K, et al. Clinical features of hypersensitivity reactions to carboplatin. *J Clin Oncol*. 1999;17:1141–1145.