The desired effect of the administered growth factor is prevention of neutropenia (268). The prophylactic administration of the growth factor reduces the need for chemotherapy dose reductions and delays that may limit chemotherapy dose intensity. By reducing the need for dose reductions, the administered growth factor increases the potential for prolonged disease-free and overall survival in the curative setting (269).

Neutropenia is the primary dose-limiting toxicity in patients treated with chemotherapy that suppresses the formation of white blood cells (myelosuppressive chemotherapy), leading to morbidity and mortality, and disrupting treatment with curative regimens. The use of granulocyte G-CSFs, as primary prophylaxis starting in the first cycle of chemotherapy, can reduce the rates of febrile neutropenia and neutropenia-related hospitalization.

However, the undesired effect of the growth factor is that the antiapoptotic effect of G-CSF or GM-CSF saves cancer cells from chemotherapy-induced killing, thereby permitting the cancer cells to develop into a myeloid cancer.

Administration of these growth factors has been associated with increased risks for cancer as well as dysplasia. Dysplasia refers to abormalities of chromosomal structure that can be precursors to cancer. The use of G-CSF was associated with a doubling in the risk of subsequent AML or MDS among the population that we studied, although the absolute risk remained low. Growth factors have also been administered to enhance immune response against an anticancer vaccine (270). In any situation where the data suggest that a growth factor can be used as a drug against cancer, researchers and the FDA have been unusually cautious.

e. Paradox With Antidepressants and Depression

Antidepressants can have the effect of increasing depression and inducing suicide (271). This adverse drug reaction can occur when initiating therapy with the antidepressant. For example, fluoxetine (Prozac®) can result in increased depression and increased suicide risk in children and adolescents (272,273). This effect, which has been extensively documented, is distinguished by the following time line:

- May 2003: Manufacturer of notifies FDA of clinical trial data indicating an increased risk of suicidal thoughts and actions in children and adolescents.
- Oct. 2003: FDA issues a public health advisory on possible safety risks related to use of antidepressants.

[268]Rader M. Granulocyte colony-stimulating factor use in patients with chemotherapy-induced neutropenia: clinical and economic benefits. Oncology (Williston Park) 2006;20(5 Suppl. 4):16–21.

[269]Lyman GH. Guidelines of the National Comprehensive Cancer Network on the use of myeloid growth factors with cancer chemotherapy: a review of the evidence. J. Natl Compr. Canc. Netw. 2005;3:557–71.

[270]Parmiani G, Castelli C, Pilla L, Santinami M, Colombo MP, Rivoltini L. Opposite immune functions of GM-CSF administered as vaccine adjuvant in cancer patients. Ann. Oncol. 2007;18:226–32.

[271]Friedman RA, Leon AC. Expanding the black box-depression, antidepressants, and the risk of suicide. New Engl. J. Med. 2007;356:2343–6.

[272]Busch SH, Barry CL. Pediatric antidepressant use after the black-box warning. Health Aff. (Millwood) 2009;28:724–33.

[273]Leon AC. The revised warning for antidepressants and suicidality: unveiling the black box of statistical analyses. Am. J. Psychiatry 2007;164:1786–9.