4. Circulating Tumor Cells as a Prognostic Biomarker for Colon Cancer—The Cohen Study

Circulating tumor cells (CTCs) can be used as a biomarker. In a study of colon cancer, Cohen et al. (65) stratified patients according to baseline levels of tumor cells circulating in the bloodstream. Prior to initiating chemotherapy, blood was withdrawn, tumor cells present in the bloodstream were analyzed, and patients were divided into two subgroups. The two subgroups were:

- *First subgroup.* Three or more tumor cells/7.5 mL whole blood.
- *Second subgroup.* Less than three tumor cells/7.5 mL whole blood.

Tumor cells were detected by an immunological method sensitive to cytokeratin. All of the patients were subsequently treated with one of the drugs, bevacizumab, irinotecan, or exaliplatin. There was no placebo group.

The median PFS was 4.5 months (high CTCs) and 7.9 months (low CTCs). The median overall survival was 9.4 months (high CTCs) and 18.5 months (low CTCs). The results demonstrated that lower baseline CTCs, as compared with higher baseline CTCs, are correlated with greater PFS ($P = 0.0002$) and also correlated with greater overall survival ($P < 0.0001$). The authors concluded that the biomarker of CTCs is a strong predictor for PFS and overall survival.

The CTC biomarker test has the following uses. First, it can serve as a stratification factor for clinical trials. Second, it can inform the physician if more aggressive chemotherapy is needed (high CTCs), or if less toxic chemotherapy is acceptable (low CTCs). Third, it can identify patients who can safely have prolonged treatment breaks in chemotherapy versus those who need to resume chemotherapy more quickly.

5. Methodology Tip—Circulating Tumor Cells as a Biomarker

Tumor cells circulating in the bloodstream can be used as a measure of solid tumors present in specific organs, and as a prognostic tool for survival to that solid tumor. It has been reported that all types of solid tumors give rise to CTCs, and that in all types of solid tumors, some of these find residence in the bone marrow (66). Once residing in the bone marrow, these cells may persist over many years and eventually disseminate into other organs. Hence, studies using tumor cells as a biomarker use peripheral blood mononuclear cells (PBMCs) as well as bone marrow as the source of cells. CTCs can be measured directly, using an immunoassay that employs antibodies and a microscope, or indirectly, using PBMCs with detection of tumor cells by a polymerase chain reaction (PCR)-based method (67). PBMCs, used as a source of unpurified lymphocytes by immunologists, also contain CTCs.

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[66]Riethdorf S, Wikman H, Pantel K. Review: biological relevance of disseminated tumor cells in cancer patients. Int. J. Cancer 2008;123:1991–2006.

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