Table 13.5 The Meropol study

		Biopsy positive (+) for thymidine phosphorylase	Biopsy negative (−) for thymidine phosphorylase
TTP	Primary tumor	8.7 months	6.0 months
	Metastatic tumor	8.7 months	5.4 months
Overall survival	Primary tumor	28.2 months	14.9 months
	Metastatic tumor	26.2 months	9.8 months

catalyzed by **thymidine phosphorylase**. This enzyme is preferentially expressed by colorectal cancer cells, thus lending specificity of cepecitabine's toxic effects to the cancer cells, rather than to normal tissues. The efficacy of capecitabine is similar to that of 5-fluorouracil. The toxicity of capecitabine is less than the toxicity of bolus 5-fluorouracil, but similar to that with infusional 5-fluorouracil (35).

The goal of the study was to assess the possible correlation of **thymidine phosphorylase** expression with outcome. Thus, this was a study of a predictive biomarker. The difference between a "predictive biomarker" and a "prognostic biomarker" is detailed in this book in the chapter on biomarkers and personalized medicine.

The data demonstrated that increased expression of **thymidine phosphorylase** is an excellent predictor of increased TTP (Table 13.5). Also, the data demonstrated that increased expression was an excellent predictor of increased overall survival.

The data on overall survival were especially dramatic.

All patients (52 patients) provided biopsies of primary tumors. But at the time of diagnosis, only 30 of these patients had metastatic tumors. Most of the metastatic colorectal cancer tumors were located in the liver, lung, and lymph nodes. Hence, data from only 30 patients are available for correlating the biomarker expressing on metastatic tumors with the endpoints.

Regarding the predictive value of **thymidine phosphorylase** found in the Meropol study, it has been suggested that the medical community should select capecitabine versus 5-fluorouracil rationally based on analysis of tumor **thymidine phosphorylase** levels using a simple test for enzyme expression, for example by measuring RNA levels by a PCR-based method, or protein levels by an antibody-based method (36). Meropol's interesting data on the thymidine phosphorglase biomarker justify the following digressions on this biomarker, on the concept of synergy, and on the issue of mRNA expression versus polypeptide expression.

[35] O'Neil BH, McLeod HL. Thymidine phosphorylase and capecitabine: a predictive marker for therapy selection? *J Clin Oncol*. 2006;24:4051–4053.

[36] O'Neil BH, McLeod HL. Thymidine phosphorylase and capecitabine: a predictive marker for therapy selection? *J Clin Oncol*. 2006;24:4051–4053.