Table 12.4 Bedikian study of melanoma

	Oblimersen plus dacarbazine	Dacarbazine only	Statistics	
			Hazard ratio	P value
	All study subjects			
Median PFS	2.6 months	1.6 months	HR = 0.75	P < .001
Median overall survival	9.0 months	7.8 months	HR = 0.87	P = .077
	Subgroup with normal serum lactate dehydrogenase			
Median PFS	3.1 months	1.6 months	HR = 0.71	P < .001
Median overall survival	11.4 months	9.7 months	HR = 0.79	P = .02

The fact that significant efficacy was found only in the normal LDH subgroup means that baseline LDH value is an appropriate parameter for selecting patients most likely to benefit from treatment with the combination of oblimersen plus dacarbazine.

A number of researchers have addressed the question of whether oblimersen's efficacy in killing melanoma cells is related to levels of Bcl-2 expressed by these cells (85,86) and the question of whether oblimersen acts at targets other than Bcl-2 mRNA (87,88).

IV. SUMMARY

The Maemondo study demonstrated that efficacy of the study drug, as well as the control drug, can first be detected at an earlier time, during the course of a clinical trial, with the endpoint of PFS, when compared to the endpoint of overall survival.

The Gradishar study also demonstrates that efficacy of a drug can be evaluated at an earlier time using the endpoint of PFS, as compared to use of the endpoint of overall survival. This study also demonstrates the utility of reviewing the same radiological data twice, by two separate radiologists.

The Robert study illustrates the use of an inclusion criterion, namely HER2 overexpression, for admitting subjects to a clinical trial. The Robert study further illustrates the utility of subgroup analysis, where the results of all admitted subjects were analyzed according to whether HER2 overexpression was only moderate, or if it was great.

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