blood draw, including at 12 and 18 months of age. Investigators used enzyme immunoassay to test for HIV-1 antibodies at 18 months of age. Positive test results were confirmed by an HIV-1 Western blot assay (Cambridge Biotech, Rockville, MD).

Researchers amended the study protocol in February 2000 (Amendment II) in response to findings in other studies that some women could develop viral resistance to NVP, and that some children treated with various antiretroviral drugs in utero or perinatally could possibly experience mitochondrial toxicity. The modification entailed extending follow-up of women in the NVP arm and all children in the 18-month study to 5 years, with yearly evaluations for NVP resistance in women who had received NVP (HIVNET 012 Investigators, 2000).

RESULTS

HIVNET 012 enrolled 645 pregnant women between November 1997 and April 1999, when the study reached its target enrollment. The analysis of the study did not include 19 women randomized to placebo before February 18, 1998.

The first of two papers, published in *The Lancet* in 1999, reported safety and efficacy data through 14–16 weeks of follow-up of the infants (Guay et al., 1999). This paper reported that the study had randomized 313 pregnant women to ZDV, 313 to NVP, and 19 to placebo. Of infants exposed to ZDV and NVP, 307 and 309, respectively, could be evaluated for HIV-1-free survival. The relative risk of HIV-1 infection was 0.53 in the NVP as compared to the ZDV arm (a 47% reduction) (see Table 2.1).[4]

The 1999 *Lancet* paper also analyzed adverse events and toxic effects based on the first 556 mother/infant pairs assigned to treatment with ZDV (279 pairs) and NVP (277 pairs). The authors reported that "the rates of maternal serious adverse events were similar in the two groups (4.4% in the ZDV group and 4.7% in the NVP group)," and that "the occurrence of clinical or laboratory abnormalities in mothers was similar in the two groups." The authors also reported that for infants, "the rate of occurrence of serious adverse events in the two groups was similar up to the 18-month visit (19.8% in the ZDV group and 20.5% in the NVP group)." The "frequency and severity of laboratory-detected toxic effects . . . were similar in the two groups."

[4]The authors report the "efficacy" of NVP compared with ZDV as 47%, which is actually 100*(1-RR)—that is, the percentage reduction in risk. Standard relative risks are reported above.