Dear Editor,

The CRESCENDO trial of rimonabant\textsuperscript{1} confirmed the conclusions of previous meta-analyses: rimonabant increases the risk of serious adverse events with no evidence of benefit on major cardiovascular outcomes.\textsuperscript{2-4} According to Topol et al., the trial has been stopped prematurely because the level of serious neuropsychiatric effects was deemed unacceptable by regulatory authorities.\textsuperscript{1} We argue that the trial was terminated too late, not too early. First, CRESCENDO began months after the marketing approval (MA) for rimonabant as a weight-loss drug had been requested in Europe. Testing the efficacy of a drug on hard outcomes after its marketing for uncertain surrogates is a time sequence in the interest of the manufacturer, not of public health. Second, the MA for rimonabant was issued by the EC in June 2006, but withdrawn in November 2008.\textsuperscript{5} However, concerns about an unfavorable benefit-risk balance of rimonabant had already been expressed in 2006, shortly after the MA.\textsuperscript{3} Rimonabant was never marketed in the USA as the application was rejected by the FDA in 2007\textsuperscript{4} (figure). Thus the European Medicines Agency was indeed rather slow in cancelling the MA, and when it did so, it was on the basis of strong evidence and not of concerns as suggested by Topol et al. Last but not least, there is no evidence that a longer duration of CRESCENDO would have demonstrated rimonabant’s benefits. Even with 12190 and 5092 participants at year1 and year2, respectively, not the slightest divergence in survival curves between arms could be detected, a sharp contrast with the absolute 10.9% difference in psychiatric disorders.\textsuperscript{1}
Reference List


Figure 1. Timeline of main procedural steps and available scientific information relative to rimonabant as a weight-loss drug.