

BL 125518/0

Information Request on Updated Primary Analysis on Overall Survival

2014-12-24

The Agency sent you an Information Request (IR) on November 20, 2014 requesting an update on the survival status of 10 subjects whose observations were censored in your primary analysis of Overall Survival (OS). Your response on December 12, 2014 seems to indicate that all these 10 subjects were alive as of the analysis cut-off date of March 31, 2014. It appears that in the primary analysis of OS you submitted in your clinical study report (CSR), you treated most of these observations as being censored soon after randomization. For example, Subjects #015013, #015020, and #015012 had a censoring time of 1, 1, and 16 days, respectively. We performed an updated primary analysis of the OS endpoint, updating the censoring times for these 10 subjects with March 31, 2014 as the last date that they were known to be alive. We will refer to your analysis as the “current analysis” and our updated analysis as the “updated analysis” in what follows. The updated analysis does not change the point estimates and confidence intervals of the medians. However, the p-value for the comparison between treatment groups has changed from 0.051 to 0.155. There is also a visible separation of the OS curves for the GM-CSF Arm between the current and updated analysis (Figure included). For your reference, the identification numbers of the 10 subjects are included below. We request that you verify and confirm that the “updated analysis” should be reported as the primary analysis for the OS endpoint. Or, if you disagree with this request, please provide your justification.

List of the 10 subjects

1. 015013
2. 015020
3. 015012
4. 003008
5. 003004
6. 003026
7. 079002
8. 009008
9. 069024
10. 066020

Overall Survival Primary Analysis: using March 31, 2014 for Censorin

