Degarelix - Query on PSA progression or death post hoc analysis in the CS21 study

ERG response: 25 November 2013

On page 71 of the MS, the manufacturer stated that "*Patients receiving degarelix had a lower risk of PSA progression (recurrence/failure) or death compared with patients in the leuprorelin group; this difference was statistically significant (log-rank test, p=0.05)"* and referenced to the study from Tombal *et al.,* (2010).

However the Tombal *et al.,* (2010) study goes on to state: *"Adjusting for baseline disease stage and PSA resulted in a hazard ratio (HR) of 0.664 (95% CI, 0.385–1.146; Fig. 1)."* This information was not included within the MS so was not picked up by the ERG.

In the MS the hazard ratio for PSA progression is derived by fitting a parametric curve to the degarelix arm and assuming proportional hazards for the leuprorelin arm. This results in a reported hazard ratio for degarelix versus leuprorelin of 1.71 (CI 1.00-2.93) (MS Table 24). Whilst it is not explicitly mentioned it appears than the two quoted HRs are reciprocals (with the reciprocal of the 1.71 HR being 0.58). The MS does not mention any adjustment for baseline disease stage in these analyses.

The ERG believe that baseline disease stage is a relevant issue and should be adjusted for in analyses if possible. The Tombal (2010) study indicated that the difference in PSA recurrence or death is not statistically significant when baseline disease stage is adjusted for. Additionally the p-value from the original analysis without adjusting for baseline disease stage was 0.05, which was at borderline and therefore relatively weak evidence. After adjusting the covariate, the 95% CI included "1", which showed even weaker evidence. This information together suggests that the ERG's scenario analysis in which degarelix and LHRH agonists are assumed to have equal efficacy in terms of PSA progression and death may be the most appropriate scenario.