Incorporation of measures for monitoring and assessment of the female reproductive system in a 52-week toxicity study in the minipig

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We performed a 52-week toxicity study in minipigs by daily oral gavage dosing. The female reproductive system was identified in earlier rodent studies as a potential target for toxicity of the drug. In this study, we incorporated a number of observations and measurements to assess the reproductive system in the females in order to identify potential signals for toxicity as early as possible. The purpose of these measurements was to avoid the need to sacrifice groups of animals periodically during the study to enable assessment of the relevant organs macroscopically and microscopically. Evaluations undertaken were: evaluation of the estrus cycle, regular blood sampling for progesterone, periodic (every 3 months) ultrasound scanning of the ovaries and post-mortem evaluation (macroscopic, organ weight and microscopic changes). Through these investigations, we gained useful information concerning measurement and observation of the reproductive behaviour of the animals. Normal cycling (estrus cycle length of ca 19 to 20 days) was seen in all but 1 animal which was found, both by scanning and by post-mortem examination, to have ovarian cysts. Ultrasound scanning was useful to monitor the normal size and morphology of the ovaries in-life, and could identify those animals that were shown to have abnormalities post-mortem. We conclude that the battery of tests incorporated into this study is useful to detect possible changes in the female reproductive system in minipigs during the course of a study. A significant benefit was avoiding use of interim kills to detect the timing of potential changes in ovarian morphology.