

RSR-13 dosing guidelines

Brief background to facilitate discussion on the proposed dosing strategy is provided here. Detailed results are available for the ODAC discussion.

Sponsor's proposed dosing strategy

- Proposed per kg dosing leads to lower total mg dose in heavier patients (> 95 kg males, > 70 kg females) and higher total mg dose in lighter patients.
- For a given dose of RSR-13, apparently higher concentrations of RSR-13 in RBCs were observed in a limited number of higher body weight patients in comparison to lower body weight patients.
 - The apparent volume of distribution of RSR-13 in RBCs is claimed to increase disproportionately with body weight.

Inferences from FDA's population pharmacokinetics and p50 Analysis

- Concentrations of RSR-13 in RBC's appear not to be significantly different in
 - Obese (BMI>30 kg) versus non-obese patients.
 - Male versus female patients.
- The volume of distribution of RSR-13 appears to increase proportionately with total body weight.
- Simulations suggest that per kg and sponsor's proposed dosing might not offer considerable advantage over fixed mg dosing. This is so because the unexplained variability is higher than that explained by body weight.
- Fixed dosing (mg) might be worthwhile to consider in future trials.