A study to see if a new generic form of primaquine is the same as the one currently on the market

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We conducted a classic, two sequence, crossover study, with a 10-day wash out period, of 15 mg of IPCA-produced test primaquine tablets and 15 mg of Sanofi reference primaquine tablets. Healthy volunteers, aged 18–45 years, without glucose-6-phosphate dehydrogenase deficiency, a baseline haemoglobin ≥ 11 g/dL, creatinine clearance ≥ 70 ml/min/1.73ms, and body mass index (18.5–30 kg/m^2) were randomised to either test or reference primaquine, administered on an empty stomach with 240 mL of water. Plasma primaquine and carboxyprimaquine concentrations were measured at baseline, then 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 1.75, 2.0, 2.333, 2.667, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 8.0, 10.0, 12.0, 16.0, 24.0, 36.0, 48.0 and 72.0 hours by liquid chromatography coupled to tandem mass spectrometry.

Primaquine pharmacokinetic profiles were evaluated by non-compartmental analysis and bioequivalence concluded if the 90% confidence intervals (CI) of geometric mean (GM) ratios of test vs. reference formulation for the peak concentrations (C_{max}) and area under the drug concentration-time (AUC_{0-t}) were within 80.00 to 125.00%.

Results

A total of 50 volunteers were dosed and 47 of 50 volunteers, median age 33 years, completed both dosing rounds and were included in the bioequivalence analysis. For primaquine, GM C_{max} values for test and reference formulations were 62.12 vs. 59.63 ng/mL, resulting in a GM ratio (90% CI) of 104.17% (96.92%–111.96%); the corresponding GM AUC_{0-t} values were 596.56 vs. 564.09 ngxh/mL, for a GM ratio of 105.76% (99.76%–112.08%). Intra-subject coefficient of variation was 20.99% for C_{max} and 16.83% for AUC_{0-t}. Median clearances and volumes of distribution were similar between the test and reference products: 24.6 vs. 25.2 L/h, 189.4 vs. 191.0 L, whilst the median half-lives were the same, 5.2 h.

There were no reported clinical adverse events. Four mild laboratory adverse events were reported and were considered to be unlikely to be primaquine related. These were increases in: (i) total white cell count (n=2), (ii) baseline eosinophil count, and (iii) ALT.

Conclusion

IPCA primaquine was bioequivalent to the Sanofi primaquine. This opens the door to prequalification, registration in malaria endemic countries, and programmatic use for malaria elimination.