Figure S4. Qualification of the **(A)** Constant + Gompertz hazard model for grade 3 hand-foot skin reactions (HFSR), **(B)** Gompertz hazard model for grade ≥4 adverse events (AEs), and **(C)** constant hazard model for grade ≥3 hypertension stratified by prediction-corrected visual predictive check (pc-VPC). The pc-VPC shows 5 prediction bins at 50, 100, 200, 300, and 400 days (vertical dashed lines) after start of sorafenib treatment. For each time bin, gray fields represent the 90% prediction interval of the 1,000 simulated event rates for **(A)** grade 3 HFSR events in patients with average dose, **(B)** grade ≥4 AEs in all patients, and **(C)** grade ≥3 hypertension events in patients with average area under the curve (AUC) over the 12-hour dosing interval during the entire treatment period (AUC_{12AV}). Light gray fields represent those below the population median, and dark gray fields represent those above the population median. Black horizontal bars indicate the respective simulated medians, and red horizontal bars show the observed rates of AEs in the 2 strata. Event rates are calculated cumulatively up to the time of the bin. Each of the 1,000 simulated trials used all 413 patients, of whom 207 received placebo initially; 155 of these 207 patients (75%) were crossed over to sorafenib after disease progression.