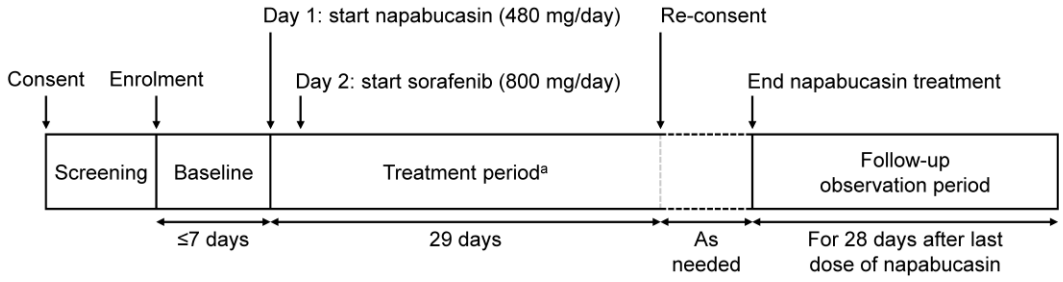
Supplementary Files

Online Resource 1 Study design

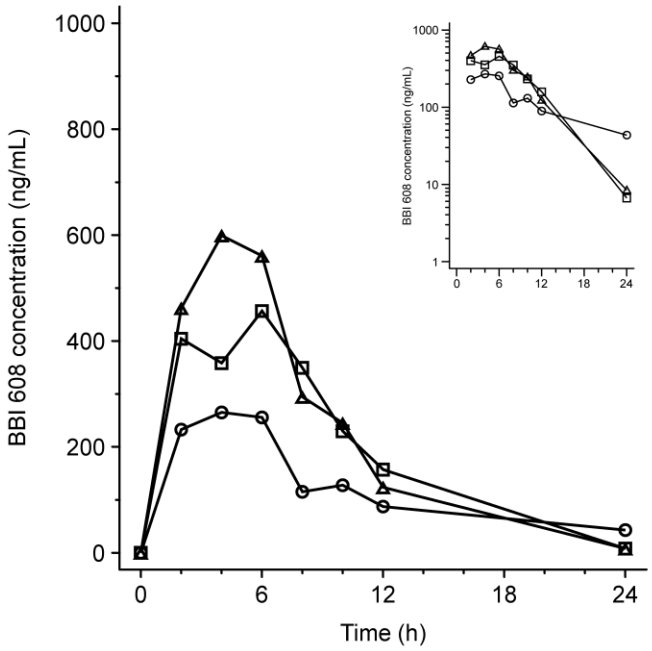


[a]For the initial cohort, this included the DLT evaluation. Patients were hospitalized from day 1 to the morning of day 4, and from day 29 to the end of day 30 examination. PK assessments were conducted on days 1, 2, 29, and 30. For the expansion cohort, hospitalization was not mandated, and DLT and PK evaluation was not performed. Following re-consent (required for the DLT cohort only), napabucasin administration could be continued until treatment was no longer clinically beneficial (per the discretion of the investigator). Treatment with napabucasin could also continue even if sorafenib was discontinued due to a sorafenib-associated adverse event. If a subsequent treatment was administered within 28 days after the last dose of napabucasin, the final observation/examination visit occurred at that time

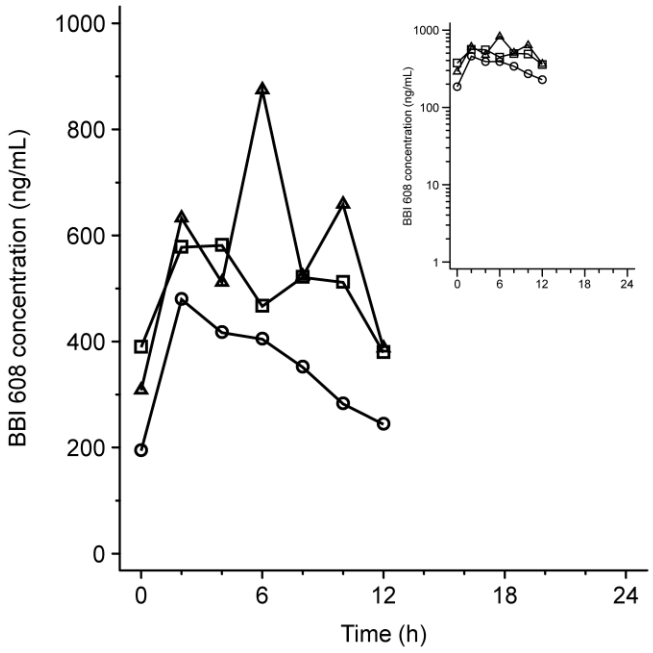
DLT dose-limiting toxicity, *PK* pharmacokinetic

Online Resource 2 Individual plasma napabucasin concentrations over time after **a** single dose administration on day 1 and **b** repeated dose administration on day 29 (pharmacokinetic population)

a



b



Main graph shows linear scale, inset shows logarithmic scale