



Figure S1: The simulation for the PK profiles of total and unbound vismodegib in the plasma was based on 150mg daily dose for 12-weeks with 24-weeks washout using the published popPK model. The actual age and body weight (from the 74 patients in the dataset), and the typical value of AAG ($30 \mu\text{M}$) were used in the simulation as PK covariate; 500 simulations with 200 patients for each simulation (sampling with replacement from the 74 patients) were conducted. The shaded areas are the 95% prediction intervals. The observed proportion of grade ≥ 1 muscle spasm over time (red cycle) was from the cohort 2.