**SUPPLEMENTARY DATA**

**Table S1.** Dose-limiting toxicities

|  |  |  |  |
| --- | --- | --- | --- |
| **Dose Cohort** | **DLT** | **Identified as SAE** | **Led to Study Discontinuation** |
| 2-3 mg | Lipase increased | No | No |
| 60 mg | Hypophosphatemia | No | No |
| 100 mg | Pain of skin | No | No |
| Rash, papular | Yes | No |
| 160 mg | Diarrhea | No | Yes |
| 160 mg | Presyncope | Yes | No |
| 160 mg | Somnolence | Yes | Yes |
| Rash, macular | Yes | Yes |

DLT, dose-limiting toxicity; SAE, serious adverse event

**Table S2.** Multiple-dose pharmacokinetic parameters (geometric mean (%CV) of BAY 86-9766 and metabolite M17 on Course 1, Day 22 (representing exposure after 15 days of continuous dosing) for once-daily dosing cohorts

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **BAY 86-9766 Dose (mg)** | **n** | **BAY 86-9766 parameters** | | | **M17 parameters** | | |
| **Tmaxa  (h)** | **Cmax  (ng/mL)** | **AUC0-24 (ng∙h/mL)** | **Tmaxa  (h)** | **Cmax  (ng/mL)** | **AUC0-24 (ng∙h/mL)** |
| 2 | 1 | 2.0 | 31.9 | 202 | 3.1 | 8.9 | 86.6 |
| 4 | 3 | 3.0 (1.1-3.0) | 100 (49%) | 1277 (64%) | 3.0 (1.6-3.0) | 9.0 (57%) | 100 (30%) |
| 6 | 2 | 1.8 (1.5-2.0) | 186 (9%) | 2066 (6%) | 2.3 (1.5-3.1) | 18.0 (44%) | 177 (33%) |
| 10 | 4 | 2.0 (1.0-2.0) | 216 (12%) | 1942 (32%) | 2.5 (1.5-3.0) | 27.0 (45%) | 243 (26%) |
| 20 | 3 | 1.6 (1.5-2.4) | 371 (19%) | 4842 (35%) | 2.1 (2.0-4.4) | 43.5 (90%) | 583 (52%) |
| 30 | 3 | 2.0 (1.0-2.0) | 482 (58%) | 4242 (71%) | 2.0 (1.5-8.0) | 108 (15%) | 1010 (17%) |
| 40 | 3 | 2.0 (1.5-2.1) | 907 (26%) | 11932(24%) | 2.0 (2.0-2.1) | 104 (94%) | 1185 (128%) |
| 60 | 3 | 3.1 (2.0-4.0) | 1254 (37%) | 13040(39%) | 3.0 (2.0-3.1) | 77.4 (97%) | 756 (143) |
| 100b | 3 | 3.0 (3.0-23.7) | 1442 (10%) | 17975(37%) | 3.0 (2.1-3.0) | 317 (70%) | 4343 (53%) |
| 100c | 7 | 2.1 (2.0-8.1) | 1201 (56%) | 13812(58%) | 3.0 (1.5-4.0) | 240 (102%) | 2767 (124%) |

amedian value (minimum value – maximum value); bincludes 1 patient whose dose was reduced from the 160 mg dose; cexpanded MTD cohort (PK on Day 15)  
AUC0-24, area under the curve from 0 to 24 hours; Cmax, maximum plasma concentration; CV, coefficient of variation; MTD, maximum tolerated dose; Tmax, time to maximum plasma concentration

**Table S3.** Multiple-dose pharmacokinetic parameters of BAY 86-9766 and metabolite M17 on Course 1, Day 22 (representing exposure after 15 days of continuous dosing) for twice-daily dosing cohorts

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **BAY 86-9766 Dose** | **n** | **BAY 86-9766 parameters** | | | **M17 parameters** | | |
| **Tmaxa (h)** | **Cmax (ng/mL)** | **AUC0-12 (ng∙h/mL)** | **Tmaxa (h)** | **Cmax (ng/mL)** | **AUC0-12 (ng∙h/mL)** |
| 50 mg BID | 4 | 3.0 (2.0-6.0) | 1240 (22%) | 11,346 | 3.0 (2.0-6.0) | 204 (60%) | 2369 (38%) |
| 80 mg BID | 1 | 4.1 | 1780 | ND | 4.1 | 444 | ND |
| 50 mg BIDb | 7 | 2.0 (1.6-6.0) | 1197 (35%) | 9969 (22%) | 3.0 (1.6-4.1) | 217 (76%) | 1871 (54%) |

amedian value (minimum value-maximum value); bexpanded MTD cohort (PK on Day 15)

Tmax, time to maximum plasma concentration; Cmax, maximum plasma concentration; AUC0-12, area under the curve from 0 to 12 hours; CV, coefficient of variation; ND, not determined; MTD, maximum tolerated dose