Supplementary Table S1: Per protocol definition of dose-limiting toxicity and maximum tolerated dose

DLTs were defined as any of the following AEs related to the IMPs in the absence of clear evidence to the contrary, after validation by the study committee, and if not related to a disease progression grading, then using NCI CTCAE version 5.0. • Grade ≥3 febrile neutropenia/neutropenia with documented infection • Grade ≥3 hematologic toxicity lasting >72 h (Grade 4 thrombocytopenia/Grade 3 with hemorrhage or requiring transfusion) • Any Grade ≥3 irAEs, except for Grade 3 skin reactions. If an irAE was suspected, then neoplastic, infectious, metabolic, toxin, or other etiologic causes prior to labeling an AE as an irAE were ruled out • Any other Grade ≥3 non-hematological toxicities (excluding Grade 3 nausea, vomiting, and diarrhea, if controlled with adequate anti-diarrheal therapy and resolving to Grade ≤1 within 48 h) • Patient with known liver metastases enrolled with Grade 2 AST or ALT abnormalities at baseline; an increase in AST or ALT was considered a DLT only if the increase was >3 times the baseline and the elevation was confirmed ≥5 days later
MTD was defined as the highest dose level with a true DLT rate during the first 28 days of treatment within the target range of 16%–33% and with <0.25 probability of a true DLT rate >33%. Doses >DL8 were not tested, and if this MAD was found to be safe, it was considered MTD

AE, adverse event; DL, dose level; DLT, dose-limiting toxicity; irAE, immune-related AE; MAD, maximum administered dose; MTD, maximum tolerated dose.