SUPPLEMENTAL MATERIALS

First-in-human phase 1/2, open-label study of the anti-OX40 agonist INCAGN01949 in patients with advanced solid tumors

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Supplemental Table S1 Definition of DLT (28-day DLT observation period)

Nonhematologic toxicity • Any grade ≥3 nonhematologic toxicity EXCEPT the following: – Transient (≤72 hours) abnormal laboratory values without associated clinically significant signs or symptoms – Nausea, vomiting, and diarrhea adequately controlled with supportive care within 48 hours – Changes in cholesterol and triglycerides – An event clearly associated with the underlying disease, disease progression, a concomitant medication, or comorbidity – Asymptomatic changes in lipid profiles – Asymptomatic changes in amylase and lipase – Singular or nonfasting elevations in blood glucose (ie, blood glucose excursions will be considered toxicities if fasting blood glucose is elevated on two separate occasions)
Hematologic toxicity • Grade 3 thrombocytopenia with clinically significant bleeding (ie, requires hospitalization, transfusion of blood products, or other urgent medical intervention) • Grade 4 thrombocytopenia • Grade ≥3 febrile neutropenia (absolute neutrophil count $<1.0\times10^9$/L and fever >101°F/38.3°C) • Grade 4 neutropenia that does not recover to grade ≤2 in ≤3 days after interrupting study drug • Grade 4 anemia not explained by underlying disease or some other concomitant disorder
Immune-related toxicity[a] • Grade ≥2 ocular irAEs will be considered a DLT • Grade 3 irAEs that do not improve to baseline or at least grade 1 in <5 days with appropriate care or with corticosteroid therapy will be considered a DLT • Grade 4 irAEs will be considered a DLT regardless of duration

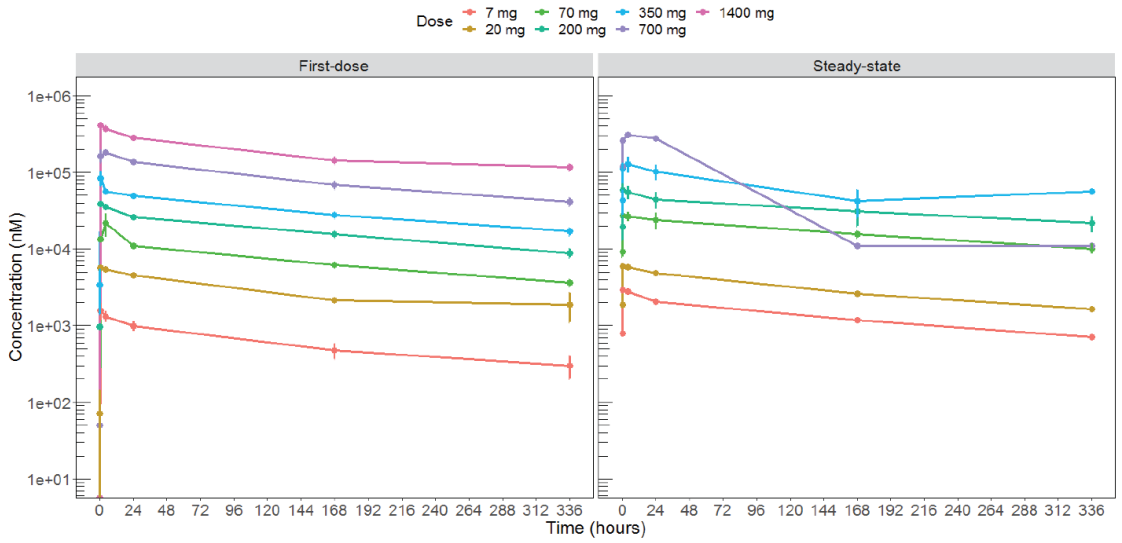
General • Inability to receive the planned number of doses within the 28-day DLT period due to toxicity, regardless of grade, will be considered a DLT
MTD • In Part 1 of the study, the MTD will be defined as one dose level below that at which ≥ one-third of patients in a particular cohort have DLTs • In Part 2 of the study, toxicities will continue to be monitored. If the cumulative incidence of DLTs occurs in ≥33% of patients after 6 patients have been observed for at least 28 days, further enrollment may be interrupted, and the investigators and sponsor will meet and reassess the MTD. All AEs, regardless of the time of occurrence on study, may be considered in DLT determination purposes
MNTD • For each dose and schedule explored, if >33% of patients (minimum of 6 patients) experience a grade ≥3 toxicity related to study drug after completing ≥4 cycles, then treatment will be stopped and the MNTDs will be determined in conjunction with the investigators and sponsor based on all available safety data. All AEs, regardless of the time of occurrence on study, may be considered in DLT determination decisions

Transient (≤72 hours) abnormal laboratory values without associated clinically significant signs or symptoms based on investigator determination will not be considered DLTs.

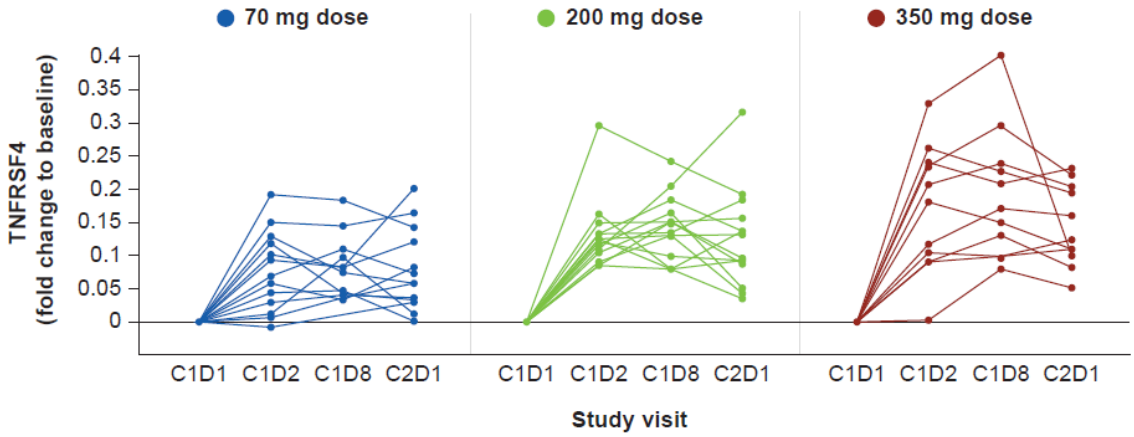
[a]irAEs are a diagnosis of exclusion, after alternative etiologies have been ruled out.

AE, adverse event; DLT, dose-limiting toxicity; irAE, immune-related adverse event; MTD, maximum tolerated dose; MNTD, maximum number of tolerated doses.

Supplemental Figure S1 Mean (± standard error) INCAGN01949 concentration over time after the first dose (cycle 1) and at steady state (cycle 6).



Supplemental Figure S2 Soluble OX40 receptor (TNFRSF4) levels in the plasma of patients treated with INCAGN01949. C, cycle; D, day.



Supplemental Figure S3 Polyfunctional frequency (PFF) and polyfunctional strength index (PSI) of $CD4^+$ and $CD8^+$ T cells before and after INCAGN01949 treatment. C, cycle; D, day.