Supplementary Table 2. Adverse events requiring treatment discontinuation

Any grade 4 adverse events require permanent treatment discontinuation except for single laboratory values out of normal range that do not have any clinical correlate and resolve to grade ≤1 or baseline grade within 7 days with adequate medical management.
Any grade 3 adverse events require treatment discontinuation except for any of the following: • Transient (≤6 hours) grade 3 flu-like symptoms or fever, which is controlled with medical management. • Transient (≤24 hours) grade 3 fatigue, local reactions, headache, nausea, emesis that resolves to ≤grade 1 or baseline grade. • Tumour flare phenomenon defined as local pain, irritation, or rash localized at sites of known or suspected tumour. • Any grade ≥3 drug-related amylase or lipase abnormality that is not associated with symptoms or clinical manifestations of pancreatitis. The Study Medical Monitor should be consulted for such grade ≥3 amylase or lipase abnormalities. If the amylase or lipase abnormality not associated with symptoms or clinical manifestations of pancreatitis has not resolved to grade ≤1 within the subsequent 2 cycles (28 days), the subject should permanently discontinue treatment unless approved to continue by Medical Monitor after specific request from site investigator. • Grade 3 Hgb decrease (<8·0 g/dL) that is clinically manageable with blood transfusions or erythroid growth factor use does not require treatment discontinuation. During the 21-day-DLT period, a grade 3 Hgb decrease (<8·0 g/dL) requires treatment discontinuation, unless it resolves to at least 9 g/dL within 14 days or changes in associated red blood cell parameters during such a Hgb decrease that resolve within 14 days without blood transfusion or erythroid growth factor use. • Increases in Eastern Cooperative Oncology Group performance status (ECOG PS) ≥ 3 that resolves to ≤2 by Day 1 of the next cycle (infusions should not be given if the ECOG PS is ≥3 on the day of administration and should be delayed until ECOG PS ≤2). • Keratoacanthoma and squamous cell carcinoma of the skin. Any suspicious skin lesion should be biopsied and surgically removed. The Study Medical Monitor should be consulted. • Grade 3 or 4 dermatological immune-related adverse events, treatment should be delayed, and treatment started according to the protocol, if condition improves to grade 1, treatment may be resumed. If ≥2 consecutive doses are missed, the Medical Monitor should be consulted. • Grade 3 or 4 symptomatic endocrinopathies (eg, thyroiditis or hypophysitis), treatment should be delayed, and treatment started according to the protocol, if condition improves to grade 1, treatment may be resumed. If ≥2 consecutive doses are missed, the Medical Monitor should be consulted.

Any grade 2 adverse events should be managed as follows:

- If a grade 2 adverse event resolves to grade ≤1 by the last day of the current cycle, treatment may continue.
- If a grade 2 adverse event does not resolve to grade ≤1 by the last day of the current cycle but it is manageable and/or not clinically relevant, the adverse event should be discussed with the Medical Monitor and based upon discussion it is possible the infusion will be given on the following cycle. If at the end of the following cycle, the event has not resolved to grade 1, discussion should be had with the Medical Monitor about permanently discontinuing treatment.
- Upon the second occurrence of the same grade 2 adverse event in the same subject (except for fatigue and hormone insufficiencies that can be managed by replacement therapy), continuation of treatment has to be discussed with the Medical Monitor and might be permanently discontinued.
- Infusion-related reactions and hypersensitivity reactions (grades 1 to 4) should be handled according to the guidelines provided in the protocol.
- Anemia should be handled according to the guidelines provided in the protocol.
- Immune-related adverse events should be managed according to the protocol.