Background S-488210/S-488211 is a cancer peptide vaccine composed of 5 human leukocyte antigen (HLA)-A*02:01-restricted epitope peptides derived from 5 cancer-testis antigens: DEPDC1, MPHOSPH1, URC10, CDCA1 and KOC1. These antigens were shown to be highly and differentially expressed in a range of solid tumours. A vaccine composed of HLA-A*24:02 restricted epitopes of the same antigens previously demonstrated safety and immunogenicity. This study aimed to evaluate the safety and immunological responses of S-488210/S-488211 in patients with HLA-A*02:01, the most prevalent HLA subtype in Europe and the US.

Methods An open-label, single centre, first-in-human phase I study (NCT04316689) was conducted. Eligible patients had unresectable recurrent or metastatic malignancies of the lung, oesophagus, mesothelium, head and neck or urinary tract and had exhausted conventional treatment options. Patients who were HLA-A*02:01 positive, performance status 0-1 and had a lymphocyte count ≥10% received S-488210/S-488211 (1 mg of each of 5 peptides mixed with Montanide ISA 51 VG) subcutaneously weekly for 4 weeks, then every 2 weeks for up to 8 weeks. The primary objective was to evaluate the safety and tolerability with adverse events classified by CTCAE version 4.03. The secondary objective was to evaluate cytotoxic T lymphocyte (CTL) induction rate during treatment, defined as the proportion of patients who showed increased CTL activity for ≥1 peptide. An exploratory objective was to assess disease control rate (DCR; CR+PR+SD) at 12 weeks.

Results 7 patients were enrolled between 30/7/19 and 9/7/21. One patient did not receive treatment due to a decline in performance status and was excluded from the safety analysis. Median age was 57, 5/6 patients were male and 5/6 were white. All patients experienced at least 1 adverse event (AE), most commonly a Grade 1 injection site reaction. There were 2 Grade 3 treatment-related AEs (hypertension and injection site reaction), neither of which met the dose-limiting toxicity criteria. There were no treatment-related serious AEs. 3/6 patients received the full planned treatment (9 doses) and 3/6 patients were withdrawn due to disease progression or death. The CTL induction rate was 100% in the 5 evaluable patients and was highest for the DEPDC1 (100%), MPHOSPH1 (60%) and URC10 (40%) peptides. The DCR at 12 weeks was 16.7% (1/6 patients with SD).

Conclusions S-488210/S-488211 was generally well tolerated and led to a robust CTL response in a range of solid tumours. S-488210/S-488211 is being taken forward in a phase 2 study in combination with PD-L1 blockade.

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Trial Registration NCT04316689

Ethics Approval The study was approved by Ethical Committee on Clinical Trial of Shionogi (held on 27 Oct 2018)