Background Most patients fail to respond to checkpoint blockade, partly due to a lack of preexisting anti-tumor immunity. Cancer vaccines aim to induce de novo anti-tumor immune responses against tumor neoantigens. We previously described an in situ vaccine approach combining intratumoral (IT) Flt3L, low dose irradiation (XRT), and IT polyICLC to, respectively, mobilize, antigen-load, and activate IT DC1 in patients with advanced stage indolent non-Hodgkin’s lymphoma (iNHL), yielding partial and complete remissions lasting months to years. Pre-clinical modeling revealed this combination induced tumoral PD-L1 expression, potentially explaining resistance, and addition of PD-1 blockade to the vaccine improved cure rates.1

Methods In this Phase 1/2 trial, patients with iNHL, metastatic breast cancer (MBC) or head and neck squamous cell carcinoma (HNSCC) received local XRT on Days 1-2, IT Flt3L to the same tumor for 9 days, followed by 8 IT injections of poly-ICLC over 6 weeks. On Day 23 patients received their first of 8 doses of intravenous (IV) pembrolizumab q3wk (figure 1).

Phase 1 enrolled 6 patients to assess safety. In Phase 2, tumor-specific cohorts are enrolling, each with a Simon’s Two-Stage design (figure 2). Here, we report interim results from the first 10 patients.

Results Between April 2019 and July 2022, 10 patients were enrolled; 6 with MBC, 3 with iNHL and one patient with HNSCC have completed their first disease response assessment. All patients experienced TRAEs, mostly low-grade injection-site reactions and flu-like symptoms related to poly-ICLC. Two patients experienced Grade 3 TRAEs, one experienced self-resolving grade 3 fever after poly-ICLC, another experienced grade 3 pembrolizumab-related colitis. Of ten evaluable patients, 1 patient had a CR, 2 achieved partial response, one had SD, and six had PD. One patient with ER/PR+ breast cancer had received 12 prior lines of therapy with non-response to two prior chemotherapies, achieved PR—without evidence of new or recurrent disease at 6 months, including regression of (distant) bulky left adrenal metastasis (figure 3) and other metastatic sites.

Conclusions In situ vaccination with Flt3L, XRT, poly-ICLC and pembrolizumab is well tolerated, with early signs of efficacy in patients with relapsed/refractory NHL and MBC, warranting expansion of this approach. Analysis of biopsies and blood from patients to define determinants of response to this in situ vaccine approach is ongoing.

Trial Registration NCT03789097

REFERENCE