Background OBP-301 is a novel, oncolytic adenovirus that incorporates the human telomerase reverse transcriptase promoter for replication selectivity. As a single agent, OBP-301 demonstrated immune responses and clinical activity in phase I studies. We examined OBP-301 in combination with pembrolizumab in a multicenter phase II study as a novel mechanism to improve immunotherapy in advanced gastric cancer.

Methods Eligible patients had advanced GEA, progressed on at least 2 lines of prior therapy. Patients received OBP-301 at 2x10^12 viral particles via direct tumor injection every two weeks x 4 injections as well as pembrolizumab 200 mg IV every 3 weeks. The primary endpoint was objective response rate (ORR). The null hypothesis that the ORR is ≤ 15% was tested against the Ha ORR >30%. We used a Simon two-stage design, requiring 3 or more responses in 18 patients in the first stage to proceed to stage two. The study was closed after successfully completing stage one of the Simon’s two stage design to formally examine OBP-301 + pembrolizumab in an immunotherapy (IO) refractory GEA population. Tissue was collected for single cell RNA Sequencing to examine the tumor immune microenvironment pre- and post-OBP-301 injections.

Results From May 2019 to Oct 2022, we enrolled 16 patients, median age 65 (range 43–81), male n=13. OBP-301 direct tumor injection was well tolerated, median OBP-301 injections 3 (range 1–5). Toxicity attributed to OBP-301 included grade 2–3 fatigue/weakness (37.5%), grade 2–3 fever (12.5%), grade 2–3 elevated liver function tests (12.5%). We observed 2 patients (13%) with a partial response and 1 patient with a complete response, thereby meeting the Simon two-stage threshold. The responses were durable; two patients are currently without evidence of disease and the 3rd patient received 16 months of therapy before progression (figure 1). One patient with brain metastases demonstrated regression of metastatic disease following progression on immunotherapy alone. All patients were mismatch repair proficient. Complete response was associated with delayed increase in CD8 cytotoxic T cells, based on single cell RNA Seq expression (figure 2).

Conclusions OBP-301 with pembrolizumab has encouraging activity in GEA, with durable responses and demonstration of activity in immunotherapy refractory disease. Longitudinal single cell RNA seq data of tumor microenvironment will be presented. A formal phase II study of OBP-301 + pembrolizumab in IO refractory GEA patients is underway.