Abstract 312 Table 1 Treatment efficacy between ipi3 and HDI by subgroup

Group	HR, 95% CI	
	OS	RFS
Female sex	0.60 (0.40, 0.92)	0.66 (0.49, 0.89)
In-transit, LN-ve	0.55 (0.29, 1.02)	0.58 (0.38, 0.88)
Ulceration	0.70 (0.50, 0.98)	0.83 (0.65, 1.07)
Stage IIIC	0.67 (0.48, 0.95)	0.78 (0.61, 1.01)
PS = 1	0.55 (0.32, 0.95)	0.74 (0.49, 1.12)

Trial Registration NCT01274338
Ethics Approval The study protocol was approved by the institutional review board (IRB) of each participating institution and conducted in accordance with Good Clinical Practice guidelines as defined by the International Conference on Harmonisation. This study was monitored by the ECOG-ACRIN DataSafety Monitoring Committee and the NCI.
Consent All patients provided IRB-approved written informed consent.

REFERENCE

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Clinical trials in progress

313 A PHASE 1 EVALUATION OF TEBOTELIMAB, A BISPECIFIC PD-1 X LAG-3 DART® MOLECULE, IN COMBINATION WITH MARGETUXIMAB IN PATIENTS WITH ADVANCED HER2+ NEOPLASMS

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Background Tebotelimab, also known as MGD013, is an investigational, Fc bearing bispecific tetravalent DART molecule designed to bind PD-1 and LAG-3 and sustain/restore the function of exhausted T cells.[1] Margetuximab, an investigational Fc-engineered anti-HER2 monoclonal antibody, has similar HER2 binding and antiproliferative properties to trastuzumab, but with enhanced Fc-mediated effector function. In vitro studies have demonstrated upregulation of LAG-3/PD-L1 expression on immune cells after margetuximab exposure, along with enhanced lytic activity of immune cells primed by margetuximab in the presence of tebotelimab.

Methods This study characterizes safety, PK/PD, and preliminary antitumor activity of tebotelimab plus margetuximab in patients with advanced HER2+ malignancies. A one-step 3+3 dose escalation phase of tebotelimab (300 and 600 mg) combined with margetuximab 15 mg/kg, both every 3 weeks, was followed by cohort expansion of patients with breast, gastric or gastroesophageal, and other HER2+ tumors.
Results At data-cutoff, 31 patients (2.0 median lines of prior therapy; 64.5% with prior HER2-directed therapy) were treated. Median duration of treatment is 10.3 weeks with 17 patients remaining on treatment. No maximum tolerated dose was defined. Treatment-related adverse events (TRAEs) occurred in 23/31 (74.2%) patients, most commonly diarrhea (n=6), nausea, ALT increased (n=5, each), AST increased, and myalgia (n=4, each). The rate of Grade 3 TRAEs was 19.4%, with no Grade 4–5 TRAEs observed. Immune-related AEs were consistent with events observed with anti-PD-1 antibodies and were manageable with supportive treatment. Among 20 response-evaluable patients (i.e., received on-treatment scan), 8 objective responses (6 confirmed) per RECIST v1.1 have been observed, including a confirmed complete response (cholangiocarcinoma) and 7 partial responses (breast [2], microsatellite stable colorectal cancer [2], esophageal adenocarcinoma [1], ovarian cancer [1], and microsatellite stable gastroesophageal junction carcinoma).[1] Immunohistochemistry (IHC) of available baseline tumor specimens (n=17) demonstrated low PD-L1 expression with combined positive scores of either 0 (n=16) or 1 (n=1, colorectal cancer). Investigations into other potential correlative biomarkers, including LAG-3 and PD-1 by IHC and gene expression profiling by NanoString, remain ongoing.
Conclusions Tebotelimab in combination with margetuximab has demonstrated an acceptable safety profile and encouraging early evidence of anti-tumor activity, with a preliminary overall response rate (ORR) of 40% (8/20) [including unconfirmed responses] among late-line patients with various advanced HER2+ malignancies.
Trial Registration NCT03219268
Ethics Approval This study was approved by each Institution's Ethics Board prior to enrollment of subjects.

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315 W0180 NOVEL ANTI-VISTA ANTIBODY: RATIONALE FOR TARGET PATIENT POPULATION AND FIRST-IN-HUMAN TRIAL DESIGN IN MONOTHERAPY AND IN COMBINATION WITH ANTI-PD1 ANTIBODY

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Background V-domain Ig suppressor of T cell Activation (VISTA) is a negative checkpoint regulator of T cell response.[1] VISTA is expressed within the tumor microenvironment, where its blockade can enhance antitumor immune responses.[2] Furthermore, an increase in VISTA expression has been reported after treatment by anti-PD1/L1 and anti-CTLA4.[3,4]