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

<table>
<thead>
<tr>
<th>Group</th>
<th>HR, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OS</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.60 (0.40, 0.92)</td>
</tr>
<tr>
<td>In-transit, LN-ve</td>
<td>0.55 (0.29, 1.02)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>0.70 (0.50, 0.98)</td>
</tr>
<tr>
<td>Stage IIIc</td>
<td>0.67 (0.48, 0.95)</td>
</tr>
<tr>
<td>PS = 1</td>
<td>0.55 (0.32, 0.95)</td>
</tr>
</tbody>
</table>

**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**


**Clinical trials in progress**

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


**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. 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-1 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). 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.

**REFERENCE**


315 WO180 NOVEL ANTI-VISTA ANTIBODY: RATIONALE FOR TARGET PATIENT POPULATION AND FIRST-IN-HUMAN TRIAL DESIGN IN MONOTHERAPY AND IN COMBINATION WITH ANTI-PD1 ANTIBODY


**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.

**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.

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**Trial Registration** NCT03219268

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This confirms that VISTA may play a key role as a mechanism of resistance to the currently used immunotherapies. VISTA/PSGL1 pH-selective biochemical interaction has been recently demonstrated.\(^6\) VISTA and PSGL1 expression pattern, their correlation and their relationship to myeloid infiltrates have been evaluated in samples from patients with solid tumors. K01401-020 (W0180) is a novel anti-VISTA antibody that has the potential to activate T cells when given as a monotherapy,\(^6\) and thus to generate added activity when combined with anti-PD1/L1 antibodies in cancer patients.

**Methods**

This phase I/IIb for W0180 consists of 2 parts: an initial dose escalation phase I followed by an expansion cohorts phase IIb. In the dose escalation phase, 2 cohorts of patients will be assessed in parallel: the first cohort will be given W0180 as a single agent and the second cohort will receive W0180 in combination with pembrolizumab. The first dose and the schedule of administration of W0180 in combination with pembrolizumab will be determined using safety and pharmacokinetic data generated in monotherapy. The phase I will allow to determine the Maximum Tolerated Dose and Schedule (MTDS), to characterize Dose-Limiting Toxicities (DLTs) and explore pharmacodynamic activity of W0180 in monotherapy and combination with pembrolizumab. The dose-toxicity relationships will support the dose escalation process and will be used to assess the MTDS and recommended doses for expansion. Following completion of the dose escalation phase, the expansion phase will enroll cohorts of patients with homogeneous tumors to validate the dose/schedule, assess preliminary activity and to explore the potential relationship with VISTA and PSGL1 expression.

**Results**

N/A

**Conclusions**

N/A

**Trial Registration**

N/A

**Ethics Approval**

The study was approved by National French Ethnic committee (CPP Ile de France V) and National Spanish Ethnic committee (Comité Ético de Investigación Clínica de Navarra) and was registered in the European database (EudraCT: 2019-002299-15).

**Consent**

N/A

**REFERENCES**


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**Abstracts**

**EVICTON STUDY: PRELIMINARY RESULTS IN SOLID TUMOR PATIENTS WITH ICT01, A FIRST-IN-CLASS, GAMMA9 DELTA2 T CELL ACTIVATING ANTIBODY TARGETING BUTYROPHILIN-3A**


**Background**

Gamma9 Delta2 (γ9Δ2) T cells are an important component of the innate anti-tumor immune response whose infiltration into solid tumors has been associated with a positive prognosis, making γ9Δ2 T cells an attractive target for the next generation of cancer immunotherapy. Butyrophilins (BTNs) are a family of immune checkpoint molecules that regulate γ9Δ2 T cell activity, including BTN3A that is a potent endogenous activator of γ9Δ2 T cells following phosphoantigen (pAg) binding to the intracellular domain of BTN3A. This observation led to the design and development of ICT01, a humanized, monoclonal antibody that binds all 3 isofoms of BTN3A/AA/A2/A3 and induces pAg-independent γ9Δ2 T cell activation, for the treatment of patients with solid or hematologic tumors.

**Methods**

EVICTON (www.clinicaltrials.gov NCT04243499; EudraCT Number: 2019-003847-31) is a first-in-human, two-part, open-label, clinical study to assess the safety, tolerability and activity of intravenous doses of ICT01 as monotherapy and in combination with pembrolizumab, in patients with advanced-stage, relapsed/refractory cancer. Following Competent Authority and Ethics Committee approvals, the study is being conducted at cancer centers in France, Belgium, Spain, Germany, and the UK. Patients provide signed informed consent prior to screening. Eligible patients receive ICT01 (Range: 20 μg to 200 mg) every 3 weeks with blood samples collected at multiple timepoints for immunophenotyping and cytokine analysis (IFNy, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-13, TNFα). Tumor biopsies are collected at baseline and Day 28 and stained by immunohistochemistry for BTN3A, γ9Δ2 T cells and other markers of anti-tumor immunity.

**Results**

Cohort 1 comprising 6 patients with solid tumors (3 Colorectal, 1 Pancreatic, 1 Ovarian, 1 Melanoma) has been enrolled and treated with ICT01 doses ranging from 20 to 700 μg. No dose-limiting toxicities or related SAEs have been reported. Target occupancy on T cells at 4 hours post first dose was 10% at 70 μg (n=1), 31% at 200 μg (n=2) and 34% at 700 μg (n=2), which was reflected at 24 hours post dose by a 73%, 91% and 97% decrease from baseline in the number of circulating γ9Δ2 T cells, respectively. On Day 7, γ9Δ2 T cells remained decreased by 37%, 75% and 76%, respectively. There were no effects on CD4 or CD8 T cells, NK cells, or B cells. Transient increases in IFNy, secreted by activated γ9Δ2 T cells, were observed in 4/6 patients. No cytokine release syndrome was observed. Data from the paired tumor biopsies are still being generated and will be presented.

**Conclusions**

The preliminary results demonstrate that ICT01 has the potential to activate the innate anti-tumor potential of γ9Δ2 T cells through BTN3A.

**Acknowledgements**

Trial Registration www.clinicaltrials.gov NCT04243499; EudraCT Number: 2019-003847-31

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