HERIZON: A PHASE 1B/2 OPEN-LABEL STUDY OF IMU-131 HER2/NEU PEPTIDE VACCINE PLUS STANDARD OF CARE CHEMOTHERAPY WITH RANDOMIZATION IN PHASE 2 IN PATIENTS WITH HER2/NEU OVEREXPRESSING METASTATIC OR ADVANCED ADENOCARCINOMA OF THE STOMACH OR GASTROESOPHAGEAL JUNCTION

Updated Interim Analysis Results

Marina Maglakelidze[1], Dinara Ryspayenva[2], Iurie Bulat[3], Zoran Andric[4], Ivan Nikolic[5], Tanuj Chawla[6], Rajnish Nagarkar[7], Vaibhav Choudhary[8], Giri Venkata[9], Rajesh Kumar Singh[10], Davorin Radosavljevic[11], Zoran Petrovic[12], Ursula Wiedermann[13] , Leslie Chong[14], Rita Laeufle[14] Nicholas Ede[14], Bonnie NIxon[14], Anthony J. Good[14]

[1]ARENSIA Exploratory Medicine, Tbilitsi, Georgia, [2]ARENSIA Exploratory Medicine, Kiev, Ukraine, [3]ARENSIA Exploratory Medicine, Chisinau, Moldova, [4]Republic of, Clinical Hospital Center Bezanijska Kosa, Belgrade, Serbia, [5]Oncology Institute of Vojvodina, Sremska Kamenica, Serbia, [6]Tata Medical Centre, Kolkata, India, [7]HCG Manavata Cancer Centre, Nashik, India, [8]HCG NCHRI Cancer Centre, Nagpur, India, [9]Victoria Hospital, Bangalore, India, [10]Regional Cancer Centre Indira Gandhi Institute of Medical Sciences, Patna, India, [11]Institute of Oncology and Radiology of Serbia, Belgrad, [12]Serbia, Military Medical Academy, Belgrad, Serbia, [13]Medical University, Vienna, Austria, [14]Imugene, Sydney, Australia,

INTRODUCTION

HER-Vaxx (IMU-131) is a **B-cell activating immunotherapy** consisting of three fused B-cell epitopes (p467) from the HER2/neu extracellular domain coupled to CRM197 and administered with the adjuvant Montanide.

This is an update on the previous reported IA (*Maglakelidze et al: abstract CT107, AACR 2021*). The Phase 2 part of the study hypothesizes that active immunization with HER-Vaxx (IMU-131) will replicate or improve efficacy and safety of the approved monoclonal antibodies that target HER2 in patients with confirmed HER2+ advanced or metastatic Gastric Cancer. In the Phase 1b dose finding part of the study tumor response of patients who received 50µg dose strongly correlated with antibody levels with 50µg selected as the Phase 2 dose *(Wiedermann et. al., Clin Cancer Res (2021))*.

BACKGROUND

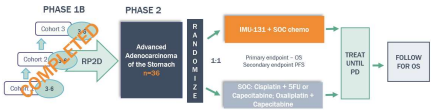

Figure 1: IMU.ACS.001 Study Design

In part 2 of study IMU.ACS.001, patients are randomized into two arms of either HER-Vaxx plus standard chemotherapy or standard chemotherapy alone.

The study is conducted in countries with limited access to trastuzumab in Asia and Eastern Europe.

The primary endpoint is overall survival, with progression-free survival and safety as secondary endpoints. Immune related endpoints include values and changes from randomization in humoral and cellular immunogenicity data.

METHODS

IMU-131 plus chemotherapy treated patients received 50µg dose of IMU-131 at Baseline/Day 0, Day 14, Day 35, Day 77 and then every 63 days until disease progression.

RESULTS

This update presents the ORR in addition to safety and efficacy results from the 1st interim analysis (OS and PFS) in a total of 27 patients after 15 progression events.

Overall survival is in favor for patients who received HER-Vaxx plus chemotherapy with a HR of 0.418 (2 sided 80% CI: 0.186, 0.942) and a 1-sided p-value of 0.083. PFS showed that 9 patients progressed on the control arm and 6 patients on the HER-Vaxx plus chemotherapy arm with a HR of 0.532 (2 sided 80% CI 0.267, 1.060) and a 1-sided p-value of 0.086.

Endpoint	Overall Survival Intent to Treat (Primary)		Progression Free Survival Intent to Treat (Secondary)	
Treatment	Her-Vaxx + Chemotherapy	Chemotherapy Only	Her-Vaxx + Chemotherapy	Chemotherapy Only
All Patients n=27	14	13	14	13
Events	4	8	6	9
HR	0.418		0.532	
2-sided 80%CI	(0.186,0.942)		(0.267,1.060)	
Log-rank Test (1-sided p-value) *	0.083*		0.086*	

*Pre-specified alpha at 0.10
* Statistically Significant

Table 1: IMU.ACS.001 Phase 2 Overall Survival & Progression Free Survival

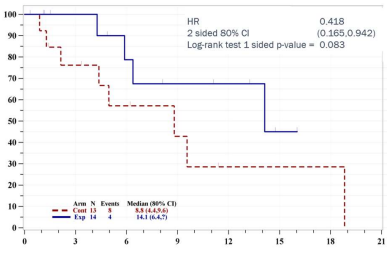

Figure 2 : IMU.ACS.001 KM-Curve Overall Survival Primary Endpoint

The overall response rate in patients who received HER-Vaxx in addition to chemotherapy corresponds to the OS and PFS results *(Table 2)*

Overall Response Rate

Treatment	PR	SD and PD	Rate
CHEMOTHERAPY ALONE	2	5	0.2857143
IMU-131 PLUS CHEMOTHERAPY	4	4	0.5000000

Table 2: IMU.ACS.001: Overall Response Rate (ORR)

No new safety concerns have been identified in the ongoing study. Safety between the two treatment arms is equivalent, suggesting HER-Vaxx does not add toxicity to SOC chemotherapy (*Table 3*). Detailed adverse events previously reported did not change. In addition, two patients received a higher dose of 100µg HER-Vaxx for 2-3 doses respectively, without any significant treatment related toxicity.

Total (n=27)	HERvaxx + Chemotherapy n=14		Chemotherapy Only n=13	
	n	%	n	%
Patients with at least one TEAE	13	92.9%	12	92.3%
Grade 1	2	14.3%	3	23.1%
Grade 2	5	35.7%	2	15.4%
Grade 3	6	42.9%	4	30.8%
Grade 4	0		2	15.4%
Grade 5	0		1	7.7%

Table 3: IMU.ACS.001: Safety Overview of Treatment Emergent Adverse Events (TEAE)

Left ventricular ejection fraction (LVEF) was measured at baseline for all patients and subsequently during the study. The measurements revealed in two patients on chemotherapy alone and in two patients on IMU-131 and chemotherapy, a drop of 10% or higher from baseline. No patients had a drop below 50%. None of the patients experienced an adverse event associated with change of LVEF. LVEF is continued to be monitored for all patients in the currently ongoing study.

Injection site reactions were monitored across the study with only three grade 1 injection site reactions in two patients reported at IA.

By week 6 HER2-AB were developed by the patient's immune system as response to HER-Vaxx vaccinations and remained high during treatment with every 63 days maintenance vaccinations only *(Figure 3)*.

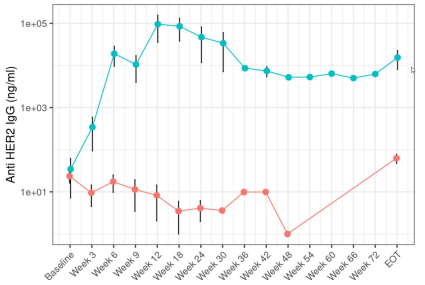

Figure 3 : IMU.ACS.001 HER2-AB Development in both treatment arms

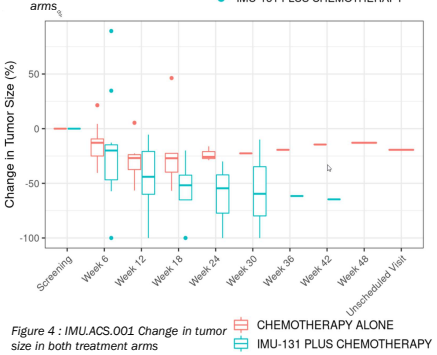

Figure 4 : IMU.ACS.001 Change in tumor size in both treatment arms

Reduction in tumor size in patients that received HER-Vaxx + chemotherapy is increased compared to patients that received chemotherapy alone. This observation confirms the ORR results and supports the OS results of the study (*Figure 4*).

In addition, tumor response is correlated with the amount of antibody development. Patients with AB levels above 1050ng/ml received a tumor reduction of >50% compared to those patients with AB levels below 1050% (Figure 5)

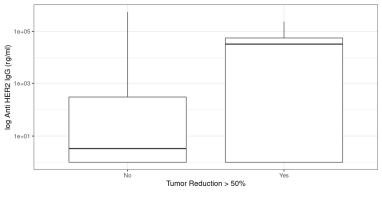

Figure 5 IMU.ACS.001 PHASE 2 - Tree regression on response above/below 1050ng/ml

The study has completed enrollment and final data on PFS and OS is awaited later in 2021 and early 2022, respectively.

CONCLUSIONS

These data demonstrate HER-Vaxx may provide treatment benefits consistent with traditional monoclonal antibodies with a corresponding adaptive immune response without added toxicity. HER-Vaxx will be further investigated in patients with HER2+ GC and in combination with checkpoint-inhibitor.

REFERENCES

Wiedermann et al:, Clinical and Immunologic Responses to a B-Cell Epitope Vaccine in Patients with HER2/neu-Overexpressing Advanced Gastric Cancer—Results from Phase Ib Trial IMU.ACS.001, Clin Cancer Res, 2021, DOI: 10.1158/1078-0432.CCR-20-3742

DISCLOSURES

Study is sponsored by Imugene Limited

B-cell peptide vaccine (IMU-131) was developed at the Medical University of Vienna