A Phase 1/1b Open-Label, First-in-Human, Single Agent, Dose Escalation and Expansion Study of a HER2-Targeted T Cell Engager (SAR443216) in Patients With Relapsed/Refractory HER2-Expressing Solid Tumors

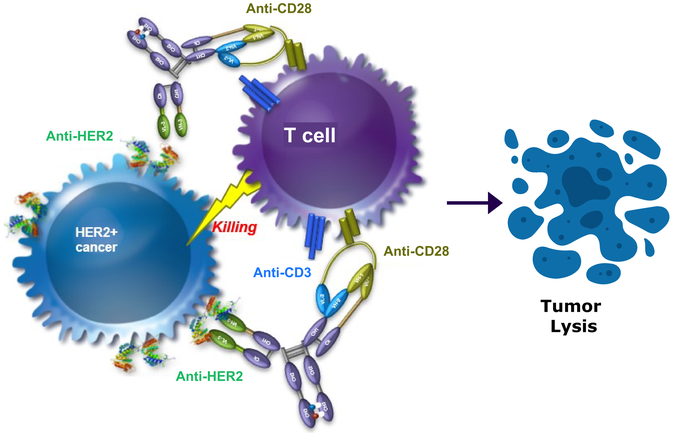
Ecaterina E. Dumbrava[1], Emiliano Calvo[2], Elena Garralda[3], Min-Hee Ryu[4], Do-Youn Oh[5], Li-Yuan Bai[6], Wei-Pang Chung[7], Katerin Rojas L[3], Ozlem Yildirim[8], Serena Masciari[8], Kingston Kang[8], Barbara Buday[8], Faiza Rharbaoui[8], Giovanni Abbadessa[8], Victor Moreno[9]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; [3]Hospital Vall d'Hebron, Barcelona, Spain; [4]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [5]Seoul National University Hospital, Seoul, South Korea; [6]China Medical University Hospital, and China Medical University, Taichung, Taiwan; [7]National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [8]Sanofi, Cambridge, MA, USA; [9]START Madrid-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain.

BACKGROUND

- SAR443216 is a trispecific T-cell engager, designed to target human epidermal growth factor receptor 2 (HER2) expressing cancer cells
  - HER2, a tyrosine kinase receptor, is overexpressed in multiple cancer types, including breast, gastric, lung, gastroesophageal, ovarian, bladder, colon, and others[1]
  - Clinically, HER2 is a validated tumor target evidenced by approved therapies of HER2-targeting antibodies and small molecule inhibitors[1]
- SAR443216 contains one HER2 binding domain, one CD3 binding domain for T cell binding and activation, and a CD28 binding domain that provides a co-stimulatory signal to the T cells
- The primary mode of action employed by SAR443216 against cancer cells is through the binding to HER2 expressed on tumor cells along with co-engagement of CD3 and CD28 receptors on T cells. This interaction leads to the activation of T cells, ultimately resulting in the killing of cancer cells by T cell-mediated cytotoxic activity **(Figure 1)**

Figure 1: Cytolytic granules are released by T cells to kill tumors[2,3]



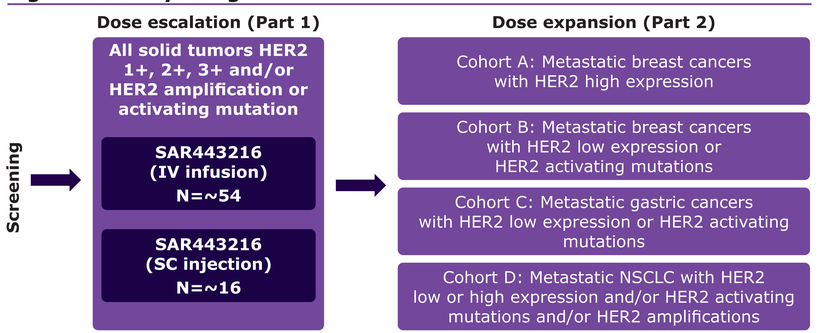
CD, cluster of differentiation; HER2, human epidermal growth factor receptor 2

- SAR443216 utilizes T cells of the adaptive immune system to eradicate HER2-expressing cancers, differentiates from other approved HER2 therapies[4]
- A phase 1/1b study is being conducted to evaluate the safety, pharmacokinetics (PK), pharmacodynamics, and preliminary clinical efficacy of intravenous (IV) or subcutaneous (SC) SAR443216 in patients with HER2-expressing advanced solid tumors (EudraCT 2021-00008632/NCT05013554)

STUDY DESIGN

- This is a first-in-human, multicenter, open-label, non-randomized Phase 1/1b single-agent dose escalation and expansion study **(Figure 2)**

Figure 2: Study design



HER2, human epidermal growth factor receptor 2; IV, intravenous; NSCLC, non-small cell lung cancer; SC, subcutaneous

KEY INCLUSION CRITERIA

- Age ≥18 years
- Eastern Cooperative Oncology Group performance status 0-1
- Body weight within 45–150 kg (inclusive)
- **Dose escalation Part 1**
  - Histologically or cytologically confirmed diagnosis of metastatic solid tumors
  - With HER2 expression in tumor tissue (IHC [immunohistochemistry] 3+, IHC 2+ or IHC 1+) and/or with HER2 aberration detected in tumor or blood
- **Dose expansion Part 2**
  - Participants in cohort A, B, C and D: Tumor type and HER2 expression as described in **Figure 2**

KEY EXCLUSION CRITERIA

- Any clinically significant cardiac disease
- History of or current interstitial lung disease or pneumonitis
- Uncontrolled or unresolved acute renal failure
- Prior solid organ or hematologic transplant
- Known positivity with human immunodeficiency virus (HIV), known active hepatitis A, B, and C, or uncontrolled chronic or ongoing infectious requiring parenteral treatment
- Receipt of a live-virus vaccination within 28 days of planned treatment start
- Participating in another clinical study while receiving treatment
- Inadequate hematologic, hepatic and renal function

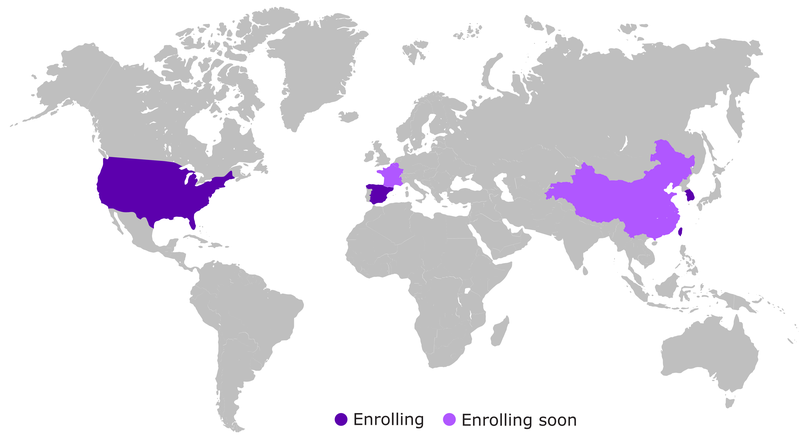
STUDY ENDPOINTS[5]

	Dose escalation (Part 1)	Dose expansion (Part 2)
Primary Endpoints	• Incidence of DLT during DLT evaluation window • Incidence of TEAEs, SAEs and lab abnormalities*	• ORR† • DoR†
Secondary Endpoints	• ORR† • DoR† • PFS† • Plasma concentrations and PK (C_{max}, C_{trough}, $t_{1/2}$, AUC_{0-T}) • Incidence of ADAs	• Incidence of TEAEs, SAEs and lab abnormalities* • PFS† • Plasma concentrations and PK (C_{max}, C_{trough}, $t_{1/2}$, AUC_{0-T}) • Incidence of ADAs

*as per NCI CTCAE v5.0; †as per RECSIST 1.1.
AUC_{0-T}, area under the curve from time 0 to the last measurable concentration; ADAs, antidrug antibodies; C_{max}, maximum observed plasma concentration; CTCAE, common terminology criteria for adverse events; C_{trough}, plasma concentration observed just before treatment administration during repeated dosing; DLT, dose limiting toxicities; DoR, duration of response; NCI, National Cancer Institute; ORR, overall response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SAE, serious adverse events; $t_{1/2}$, elimination half-life; TEAEs, treatment emergent adverse events.

STUDY STATUS

- The study is open and currently enrolling participants in the United States of America, Republic of Korea, Spain and Taiwan
- The study will be open soon in France, Belgium and China



ACKNOWLEDGMENTS:
Medical writing for this poster was provided by Padmanabham Salla of Sanofi.

DISCLOSURES:
- EED: Consulting or advisory role in Bolt Therapeutics. Research funding for institution from Bayer, Immunocore, Amgen, Aileron Therapeutics, Compugen, TRACON Pharma, Unum Therapeutics, Bolt Biotherapeutics, Aprea Therapeutics, Bellicum Pharmaceuticals, PMV Pharma, Triunvira Immunologics Inc, Seagen, Mereo BioPharma, Sanofi, Astex Pharmaceuticals, Immunomedics/Gilead; Rain Therapeutics and Gateway Foundation

Presented at European Society of Medical Oncology (ESMO) Annual Meeting 2023 – Madrid, Spain, October 20-24, 2023.

FUNDING:
This study is sponsored by Sanofi

REFERENCES:
1. Bartsch R, et al. *Biologics*. 2007;1(1):19-31
2. Sha W, et al. Presented at: AACR 2021; April 9–14, 2021; Virtual Annual Meeting. Poster 1825
3. Sanofi, data on file
4. Seung E, et al. *Nature*. 2022;603:328-334
5. NCT05013554. https://clinicaltrials.gov/ct2/show/NCT05013554. Accessed on 04 July, 2023

QR code:
If you have questions about this poster, please email Ecaterina E. Dumbrava (eeileana@mdanderson.org) or Ozlem Yildirim (ozlem.yildirim@sanofi.com). Copies of this poster obtained through QR (Quick Response) are for personal use only and may not be reproduced without written permission of the authors.