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First-in-Human Study of a Novel Nonpeptide Drug Conjugate (CRN09682) in Patients With Somatostatin Receptor 2-Expressing Tumors

Daneng Li, MD[1]; Mohammed Najeeb Al Hallak, MD, MS[2]; Lowell Anthony, MD[3]; Emily Baiyee Toegel, MD[4]; Sreenivasa R. Chandana, MD, PhD[5]; Arvind N. Dasari, MD, MS[6]; Farshid Dayyani, MD, PhD[7]; Michael J. Demeure, MD, MBA[8]; Jennifer R. Eads, MD[9]; Rocío Garcia-Carbonero, MD, PhD[10]; Thorvardur R. Halfdanarson, MD[11]; Jason T. Henry, MD[12]; Tatiana Hernández, MD, PhD[13]; Jorge Hernando, MD[14]; Mary A. Maluccio, MD, MPH[15]; Ruoyu Miao, MD[16]; Manuel Pedregal, MD, MSc[17]; Matthew J. Reilley, MD[18]; Sheena Sahota, MD[19]; Michael M. Song, MD, PhD, PharmD[20]; Alexander I. Spira, MD, PhD[21]; Rohit Thummalapalli, MD[22]; Dylan M. Glatt, PhD[23]; Dongli Zhou, PhD[23]; David C. Metz, MD[23]; Bin Zhang, MD, MSc[23]; Emily Bergsland, MD[24].

[1]City of Hope Comprehensive Cancer Center, Duarte, California, USA; [2]Karmanos Cancer Institute and Wayne State University, Detroit, Michigan, USA; [3]University of Kentucky, Lexington, Kentucky, USA [4]University of Colorado Cancer Center, Aurora, Colorado, USA; [5]START Midwest and The Cancer & Hematology Centers, Grand Rapids, Michigan, USA; [6]The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; [7]University of California Irvine, Orange, California, USA; [8]Hoag Family Cancer Institute, Newport Beach, California, USA; [9]Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA; [10]Hospital Universitario 12 de Octubre, Imas 12, UCM, Madrid, Spain; [11]Mayo Clinic, Rochester, Minnesota, USA; [12]Sarah Cannon Research Institute at HealthOne, Denver, Colorado, USA; [13]START Barcelona, HM Nou Delfos Hospital, Barcelona, Spain; [14]Vall d'Hebron University Hospital, Barcelona, Spain; [15]LSU Health Sciences Center, New Orleans, Louisiana, USA; [16]Emory University, Atlanta, Georgia, USA; [17]Hospital Universitario Fundación Jiménez Díaz START, Madrid, Spain; [18]University of Virginia Health System, Charlottesville, Virginia, USA; [19]NEXT Oncology, Austin, Texas, USA; [20]NEXT Oncology, Dallas, Texas, USA; [21]NEXT Oncology, Fairfax, Virginia, USA; [22]Memorial Sloan Kettering Cancer Center, New York, New York, USA; [23]Crinetics Pharmaceuticals, Inc., San Diego, California, USA; [24]University of California San Francisco, San Francisco, California, USA.

BACKGROUND

Somatostatin receptor 2 (SSTR2) is an established target for the treatment of neuroendocrine tumors (NETs) and a possible target for other solid tumors expressing SSTR2, including breast cancer, melanoma, small cell lung cancer, and meningioma. CRN09682 is a novel, nonradioactive, nonpeptide drug-conjugate (NDC) targeting SSTR2-expressing tumors with a monomethyl auristatin E (MMAE) payload. Here, we report the study design and methodolgy for the first-in-human evaluation of CRN09682.

METHODS

This phase 1/2, multicenter, open-label, nonrandomized study consists of two phases: dose escalation and dose expansion. In the dose escalation phase, the primary objective is to evaluate the safety and tolerability of CRN09682, while secondary objectives include evaluation of CRN09682 pharmacokinetics, identification of the maximum tolerated dose (MTD), and selection of the expansion phase dose. Eligible patients with progressive metastatic/unresectable SSTR2-expressing tumors (confirmed by SSTR imaging) will be enrolled in the dose escalation phase. CRN09682 will be administered every 3 weeks via intravenous infusion, at a starting dose based on ICH S9 guidelines. Dose escalation will utilize a BOIN design to establish the MTD. The recommended dose for expansion

will be based on the totality of data, including available exposure response from the dose escalation phase. The dose expansion phase will enroll cohorts of patients with SSTR2-expressing neoplasms, including: well-differentiated grade 1-3 pancreatic NETs; well-differentiated grade 1-3 extra-pancreatic NETs; poorly differentiated neuroendocrine carcinomas (NECs; including small- and large-cell pulmonary carcinomas, extrapulmonary NECs, and Merkel cell carcinoma); and, if feasible, relapsed or refractory non-neuroendocrine SSTR2-expressing tumors. Patients will continue therapy until disease progression, unacceptable toxicity, or other discontinuation criteria are met. The primary endpoints in the dose expansion phase are safety and tolerability (eg, incidence of adverse events, dose interruptions). Secondary endpoints include assessments of antitumor activity (eg, objective response rate, duration of response, and disease control rate, based on RECIST 1.1 criteria; progression-free survival, overall survival) and pharmacokinetic assessments.

RESULTS

N/A

CONCLUSIONS

Results of this study will be used to inform subsequent clinical trials to investigate the efficacy and safety of CRN09682 for patients with metastatic or locally advanced/unresectable neuroendocrine neoplasms or other SSTR2-expressing tumors.

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