545 A PHASE 2 STUDY OF RETIFANLIMAB IN PATIENTS WITH ADVANCED OR METASTATIC MERKEL CELL CARCINOMA (MCC) (POD1UM-201)

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Background Retifanlimab (INCMGA00012) is a humanized, hinge-stabilized immunoglobulin G4 kappa (IgG4κ), anti-programmed cell death protein (PD)-1 monoclonal antibody with safety and clinical pharmacology that are characteristic for the class. Evaluation of retifanlimab in solid tumors is under investigation in phase 2 and 3 studies. POD1UM-201 is an open-label, single-arm, multicenter, phase 2 study evaluating the efficacy and safety of retifanlimab in patients with chemotherapy-naïve or chemotherapy-refractory advanced/metastatic Merkel cell carcinoma (MCC). Updated results from the chemotherapy-naïve cohort are reported here.

Methods Eligible patients were ≥18 years of age, had metastatic or recurrent unresectable loco-regional MCC, Eastern Cooperative Oncology Group performance status ≤1, measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, and had not received prior systemic treatment for MCC. Retifanlimab 500 mg IV every 4 weeks (Q4W) was administered for up to 2 years. The primary endpoint was overall response rate (ORR) assessed by independent central review per RECIST v1.1. Secondary endpoints included duration of response, disease control rate (DCR; defined as proportion of patients with either an objective response or stable disease lasting at least 6 months), progression-free survival, overall survival, safety, and pharmacokinetics.

Results As of April 16, 2021, 87 patients with chemotherapy-naïve advanced/metastatic MCC had received retifanlimab. Per protocol, the primary efficacy analyses are based on the first 65 patients assessed. At the data cutoff, 34 of these 65 patients (52.3%) were on treatment; 4 (6.2%) had completed treatment; and 27 (41.5%) had discontinued treatment for reasons including disease progression (18 [27.7%]), adverse event (AE; 7 [10.8%]), death (1 [1.5%]), and physician decision (1 [1.5%]). The ORR in these patients was 46.2% (n=30: complete response, 8 [12.3%]; partial response, 22 [33.8%]). The DCR was 53.8% (n=35). Other secondary efficacy results are not yet mature. Among all treated patients (n=87), 66 (75.9%) had a treatment-emergent AE (TEAE), 25 (28.7%) had a grade ≥3 TEAE, and 12 (13.8%) had a grade ≥3 treatment-related AE. Twenty-three patients (26.4%) had an immune-related AE (irAE), and 8 (9.2%) had a grade ≥3 irAE. Four patients (4.6%) discontinued treatment due to irAEs (peripheral sensorimotor neuropathy, pancreatitis, eosinophilic fasciitis, and polyarthritis [each n=1]). One patient (1.1%) had a grade 3 infusion reaction.

Conclusions These data from the POD1UM-201 trial show that retifanlimab monotherapy at 500 mg Q4W continues to demonstrate promising clinical activity and safety in patients with advanced/metastatic chemotherapy-naïve MCC. Updated results will be presented at the meeting.

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Ethics Approval The study was approved by institutional review boards or independent ethics committees in Canada (McGill University Health Center-Research Ethics Board [MP-37-2019-5103, MEO-37-2019-1616]; Ontario Cancer Research Ethics Board [1728]; Health Research Ethics Board of Alberta – Cancer Committee [HREBA.CC-19-0004, HREBA.CC-19-0020]); Czech Republic (Eticka komise Fakultni nemocnice Kralovske Vinohrady, Eticka komise IKEM a FTNsP, Eticka komise Nemocnice Na Bulovce, Statni ustav pro kontrolu leciv, Eticka komise FN a LF UP Olomouc [169/18MEK24, LEK/04/07/2018, (L-18-85) 8522/23.3.2021, 22.3.2021/9965/EK-Z]); France (Comité de Protection des Personnes Ile de France X [CNRIPH : 18.11.19.49212/Id. 2043]; Agence Nationale de Sécurité du Médicament et des Produits de Santé); Germany (Ethik-Kommission der Medizinischen Fakultaet der Universitaet Duisburg-Essen [18-8371-AF]; Bundesamt fuer Strahlenschutz; Paul-Ehrlich Institute); Hungary (Egeszsegugyi Tudomanyos Tanacs Klinikai Farmakologiai Etikai Bizottsaga [IV/2407-0/2021-EKL, OGYÉI/11697-2/2021]; Orszagos Gyogyszereszeti es Elelmezes-egeszsegugyi Intezet); Italy (Comitato Etico IRCCS Pascale Napoli [116/21 E - 87/18]; Comitato Etico IRCCS di Candiolo [232/2021]; Istituto Tumori Giovanni Paolo II IRCCS Ospedale Oncologico Bari [736/CE]; Comitato Etico Locale per la Sperim. Clin. dei Medicinali dell'Az. Osp.ra Univ.ria Senese di Siena [14107]; Comitato Etico dell'IRCCS Istituto Nazionale per la Ricerca sul Cancro di Genova [389/2018 - 24/05/2021]; Comitato etico degli IRCCS Istituto Europeo di Oncologia e Centro Cardiologico Monzino [IEO 948 - RE3065/IB Edition 7 dated 10Nov2020 (SA7)]; Comitato Etico, Fondazione IRCCS Istituto Nazionale dei Tumori, .c. Medicina Oncologica 1 – Fondazio [INT 01/19]; Comitato Etico IRCCS Istituto Oncologico Veneto di Padova [EM 109/2021]; Comitato Etico dell'IRCCS Istituto Dermopatico dell'Immacolata Ospedale Generale S. Carlo di Roma [550/7]; AIFA – Agenzia Italiana del Farmaco [0040152-01/04/2021-AIFA-AIFA_USC-P]; Comitatao Etico Policlinico di Modena [1017/2018/FARM/AOUMO - EMENDAMENTO SOSTANZIALE IB EDIZIONE 7 DEL 10/11/20 (201800162739-010) (p. 9869/21)]); Poland (Komisja Bioetyczna przy Centrum Onkologii [no. 55/2019]; Office for Registration of Medicinal Products, Medical Devices and Biocidal Products [UR/DBL/D/328/2019]); Spain (CEIC Hospital General Universitario Gregorio Marañon [280/18]; Agencia Española del Medicamento y Productos Sanitarios); Switzerland (Kantonale Ethikkommission Zürich (KEK-Zürich) [2019-00200]; Swissmedic [2019DR2035]); United Kingdom (North East – York Research Ethics Committee [248465]; Medicines and Healthcare products Regulatory Agency; Health Research Authority); United States (Copernicus Group IRB; Western Institutional Review Board [20181738, Work order number -– IQV1-18-309];

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