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Daily Oral Everolimus Activity in Patients with Metastatic Pancreatic Neuroendocrine Tumors after Failure of Cytotoxic Chemotherapy: A Phase II Trial

James C. Yao,[1] Catherine Lombard-Bohas,[2] Eric Baudin,[3] Larry K. Kvols,[4] Philippe Rougier,[5] Philippe Ruszniewski,[6] Sakina Hoosen,[7] Jessica St. Peter,[7] Tomas Haas,[8] David Lebwohl,[7] Eric Van Cutsem,[9] Matthew Kulke,[10] Timothy J. Hobday,[11] Thomas M. O'Dorisio,[12] Manisha H. Shah,[13] Guillaume Cadiot,[14] Gabriele Luppi,[15] James A. Posey,[16] Bertram Wiedenmann[17] for the RADIANT-1 Study Group

[1] *M.D. Anderson Cancer Center, Houston, TX, United States*
[2] *H. E. Herriot, Hospices Civils de Lyon, Lyon, France*
[3] *Institut Gustave Roussy, Villejuif, France*
[4] *H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, United States*
[5] *Hôpital Ambroise Paré, Boulogne Billancourt, France*
[6] *Hôpital Beaujon, Clichy, France*
[7] *Novartis Oncology, Florham Park, NJ, United States*
[8] *Novartis Pharma AG, Basel, Switzerland*
[9] *University Hospital Gasthuisberg/Leuven, Leuven, Belgium*
[10] *Dana-Farber Cancer Institute, Boston, MA, United States*
[11] *Mayo Clinic, Rochester, MN, United States*
[12] *University of Iowa, Iowa City, IA, United States*
[13] *Ohio State University Comprehensive Cancer Center, Columbus, OH, United States*
[14] *Hôpital Robert Debré, Reims, France*
[15] *Azienda Ospedaliero-Universitaria di Modena, Modena, Italy*
[16] *University of Alabama at Birmingham, Birmingham, AL, United States*
[17] *Charité-Universitaet Berlin/Campus Virchow Klinikum, Berlin, Germany.*

Background: No established treatment exists for pancreatic neuroendocrine tumor (NET) progression after failure of chemotherapy. Everolimus (RAD001), an oral inhibitor of mTOR, in combination with octreotide has demonstrated encouraging antitumor activity in patients with NETs.

Methods: This open-label, phase II study assessed the clinical activity of everolimus in patients with metastatic pancreatic NETs progressing on or after chemotherapy. Patients were stratified by prior octreotide therapy (stratum 1: everolimus 10 mg/day [n = 115]; stratum 2: everolimus 10 mg/day plus octreotide long-acting release [LAR; n= 45]). Tumor assessments (RECIST) were performed every 3 months. Chromogranin A (CgA) and neuron-specific enolase (NSE) were assessed monthly if elevated at baseline. Trough concentrations of everolimus and octreotide were assessed.

Results: By central radiology review, in stratum 1, there were 11 (9.6%) partial responses (PR), 78 (67.8%) stable disease (SD), and 16 (13.9%) progressive disease (PD); median progression-free survival (PFS) was 9.7 months. In stratum 2, there were 2 (4.4%) PR, 36 (80%) SD and 0 PD; median PFS was 16.7 months. Patients with an early CgA or NSE response had a longer PFS compared with patients without an early response. Co-administration of octreotide LAR and everolimus did not impact exposure to either drug. Most adverse events were mild to moderate and were consistent with those previously seen with everolimus.

Conclusion: Daily everolimus, with or without concomitant octreotide LAR, demonstrates antitumor activity as measured by ORR and PFS and is well tolerated in patients with advanced pancreatic NETs after failure of prior systemic chemotherapy.

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