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Positron emission tomography response evaluation from a randomized phase III trial of weekly *nab*-paclitaxel plus gemcitabine versus gemcitabine alone for patients with metastatic adenocarcinoma of the pancreas†

R. K. Ramanathan[1*], D. Goldstein[2], R. L. Korn[3], F. Arena[4], M. Moore[5], S. Siena[6], L. Teixeira[7], J. Tabernero[8], J.-L. Van Laethem[9], H. Liu[10], D. McGovern[10], B. Lu[10] & D. D. Von Hoff[11]

[1]Division of Hematology/Oncology, Mayo Clinic, Scottsdale, USA; [2]Department of Medical Oncology, Prince of Wales Hospital, Sydney, Australia; [3]Diagnostic Radiology, Scottsdale Medical Imaging, Ltd, Scottsdale; [4]Hematology/Oncology, NYU Langone Arena Oncology, Lake Success, USA; [5]Provencial Health Services Authority, BC Cancer Agency, Vancouver, Canada; [6]Falck Division of Oncology, Department of Oncology and Hematology, Niguarda Cancer Center, Ospedale Niguarda Ca' Granda and Università degli Studi di Millano, Milan, Italy; [7]Department of Medical Oncology, Hôpital Saint-Antoine, Paris, France; [8]Department of Medical Oncology, Vall d'Hebron University Hospital and Institute of Oncology (VHIO), Universitat Autònoma de Barcelona, Barcelona, Spain; [9]University Clinic of Brussels, Hôpital Erasme, Brussels, Belgium; [10]Biostatistics and Research and Design, Celgene Corporation, Summit; [11]Clinical Research, Translational Genomics Research Institute and Honor Health, Scottsdale, USA

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Background: In the phase III MPACT trial, *nab*-paclitaxel plus gemcitabine (*nab*-P + Gem) demonstrated superior efficacy versus Gem alone for patients with metastatic pancreatic cancer. We sought to examine the feasibility of positron emission tomography (PET) and to compare metabolic response rates and associated correlations with efficacy in the MPACT trial.

Patients and methods: Patients with previously untreated metastatic adenocarcinoma of the pancreas were randomized 1:1 to receive *nab*-P + Gem or Gem alone. Treatment continued until disease progression by RECIST or unacceptable toxicity.

Results: PET scans were carried out on the first 257 patients enrolled at PET-equipped centers (PET cohort). Most patients (252 of 257) had ≥2 PET-avid lesions, and median maximum standardized uptake values at baseline were 4.6 and 4.5 in the *nab*-P + Gem and Gem-alone arms, respectively. In a pooled treatment arm analysis, a metabolic response by PET (best response at any time during study) was associated with longer overall survival (OS) (median 11.3 versus 6.9 months; HR, 0.56; $P < 0.001$). Efficacy results within each treatment arm appeared better for patients with a metabolic response. The metabolic response rate (best response and week 8 response) was higher for *nab*-P + Gem (best response: 72% versus 53%, $P = 0.002$; week 8: 67% versus 51%; $P = 0.014$). Efficacy in the PET cohort was greater for *nab*-P + Gem versus Gem alone, including for OS (median 10.5 versus 8.4 months; hazard ratio [HR], 0.71; $P = 0.009$) and ORR by RECIST (31% versus 11%; $P < 0.001$).

Conclusion: Pancreatic lesions were PET avid at baseline, and the rate of metabolic response was significantly higher for *nab*-P + Gem versus Gem alone at week 8 and for best response during study. Having a metabolic response was associated with longer survival, and more patients experienced a metabolic response than a RECIST-defined response.

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Key words: pancreatic cancer, positron emission tomography, *nab*-paclitaxel, gemcitabine, metabolic response

introduction

Pancreatic cancer bears an extremely poor prognosis as evidenced by the only 20% of patients who survive ≥1 year after diagnosis [1]. Thus, it is crucial to identify early markers of treatment efficacy. Positron emission tomography (PET) imaging, a technique that uses radioactively labeled glucose 18F-fluorodeoxyglucose (^{18}F-FDG), has been used for the study of cancer, as both a diagnostic tool and, increasingly, as a measure of tumor response to treatment [2–8]. Compared with conventional radiographic means of gauging tumor response based on diameter, metabolic response by PET may represent a more functional measure of tumor response or progression by directly assessing the degree of metabolic activity [6, 9].

*Correspondence to: Dr Ramesh K. Ramanathan, Division of Hematology/Oncology, Mayo Clinic, 13400 E. Shea Blvd, Scottsdale, AZ 85259, USA. Tel: +1-480-301-8000; E-mail: ramanathan.ramesh@mayo.edu

†Previous presentations: ASCO 2013, ESMO 2013, ASCO GI 2014.