2021 ESMO congress

576MO

Health-related quality of life (HRQoL), pain and safety outcomes in the phase III VISION study of 177Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer

K. Fizazi[1], K. Herrmann[2], B.J. Krause[3], K. Rahbar[4], K.N. Chi[5], M.J. Morris[6], O. Sartor[7], S.T. Tagawa[8], A.T. Kendi[9], N.J. Vogelzang[10], J. Calais[11], J. Nagarajah[12], X.X. Wei[13], V.S. Koshkin[14], J-M. Beauregard[15], B. Chang[16], M. DeSilvio[17], R.A. Messmann[18], J. de Bono[19]

[1] Cancer Medicine Department, Gustave Roussy Institute, University of Paris Saclay, Villejuif, France, [2] Nuclear Medicine, University Hospital Essen, Essen, Germany, [3] Department of Nuclear Medicine, Rostock University Medical Center, Rostock, Germany, [4] Clinic for Nuclear Medicine, University Hospital Münster, Münster, Germany, [5] Medical Oncology Department, British Columbia Cancer Agency, Vancouver Centre, Vancouver, BC, Canada, [6] Cancer Centre, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [7] Medical School, Tulane Medical School, New Orleans, LA, USA, [8] Urology, Hematology and Medical Oncology Department, Weill Cornell Medicine, New York, NY, USA, [9] Radiology, Mayo Clinic, Rochester, MN, USA, [10] US Oncology Research, Comprehensive Cancer Centers, Las Vegas, NV, USA, [11] Department of Molecular and Medical Pharmacology, University of California, Los Angeles, CA, USA, [12] Department of Radiology and Nuclear Medicine, Radboud University Medical Center, Nijmegen, Netherlands, [13] Medicine, Dana-Farber Cancer Institute, Boston, MA, USA, [14] Department of Medicine, University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA, [15] Department of Radiology and Nuclear Medicine, CHU de Québec - Université Laval, Quebec, QC, Canada, [16] Radiation Oncology Associates, Parkview Hospital, Ft Wayne, IN, USA, [17] Analytics GDD/CD&A GDD, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, [18] Global Clinical Development R&D, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA[19] Drug Development Unit, The Institute of Cancer Research and Royal Marsden Hospital, London, UK

Background

[^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA-617) delivers β-particle radiation to prostate-specific membrane antigen (PSMA) expressing cells and the surrounding microenvironment. In the phase III VISION study (NCT03511664), ^{177}Lu-PSMA-617 + protocol-permitted standard of care (SOC) prolonged radiographic progression-free survival (rPFS; HR, 0.40; 99.2% CI: 0.29, 0.57), overall survival (OS; 0.62; 95% CI: 0.52, 0.74) and time to first symptomatic skeletal event (SSE; 0.50; 95% CI: 0.40, 0.62) versus SOC (all $p < 0.001$).

Methods

VISION was an international, open-label study of ^{177}Lu-PSMA-617 in adults with PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) previously treated with ≥ 1 androgen receptor pathway inhibitor and 1–2 taxane regimens. Patients were randomized 2:1 to ^{177}Lu-PSMA-617 (7.4 GBq every 6 weeks, ≤ 6 cycles) plus SOC or to SOC alone. rPFS and OS were alternate primary endpoints; time to SSE was a key secondary endpoint. Other secondary endpoints included safety and patient-reported HRQoL (Functional Assessment of Cancer Therapy – Prostate [FACT-P]) and pain (Brief Pain Inventory – Short Form [BPI-SF]). Pre-specified analyses included time to the first occurrence of HRQoL/pain worsening, disease progression or death. *Ad hoc* analyses included time to worsening only (non-inferential).

Results

HRQoL was assessed in the pre-specified rPFS analysis set comprising 581 of the 831 randomized patients (^{177}Lu-PSMA-617 arm, n = 385; control arm, n = 196). HRQoL and pain time-to-worsening analyses favoured the ^{177}Lu-PSMA-617 arm (Table), despite a higher incidence of grade ≥ 3 adverse events versus SOC alone. No new or unexpected safety concerns were noted, including changes in creatinine clearance.Table: 576MO

Hazard ratios for time to worsening in FACT-P and BPI-SF scores

Outcome†	Hazard ratio (95% confidence interval)		
FACT-P			
Total Pain-related subscale Prostate cancer subscale	0.46 (0.35, 0.61)*	0.55 (0.42, 0.71)*	0.59 (0.46, 0.76)*
BPI-SF			
Pain intensity Worst pain intensity Pain interference	0.45 (0.33, 0.60)*	0.49 (0.37, 0.65)*	0.60 (0.45, 0.80)*

† Time to the first occurrence of the following from baseline. ≥ 10 point decrease in FACT-P total ≥ 2 point decrease in FACT-P pain-related subscale ≥ 3 point decrease in FACT-P prostate cancer subscale ≥ 30% or ≥ 2 point increase in BPI-SF pain

intensity, worst pain intensity or pain interference *p < 0.001 (nominal; non-inferential analysis)

Conclusions

^{177}Lu-PSMA-617 plus SOC was generally well tolerated and delayed time to HRQoL and pain worsening versus SOC alone in patients with advanced mCRPC.

Clinical trial identification

PSMA-617-01. 08 July 2019. EudraCT 2018-000459-41.

Editorial acknowledgement

Under the guidance of the authors, Dr Sarah Sabir from Oxford PharmaGenesis provided medical writing support for this abstract, with funding from Advanced Accelerator Applications, a Novartis Company.

Legal entity responsible for the study

Endocyte, Inc., a Novartis company.

Funding

Endocyte, Inc., a Novartis company.

Disclosure

K. Fizazi: Financial Interests, Institutional, Advisory Role: Janssen Oncology; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Institutional, Advisory Role: Astellas Pharma; Financial Interests, Institutional, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Orion Pharma GmbH; Financial Interests, Personal, Advisory Role: Curevac; Financial Interests, Institutional, Advisory Role: AstraZeneca; Financial Interests, Institutional, Advisory Role: ESSA; Financial Interests, Institutional, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Bristol-Myers Squibb; Financial Interests, Personal, Advisory Role: Clovis Oncology; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Janssen; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: MSD; Financial Interests, Institutional, Other, Honoraria: Janssen; Financial Interests, Institutional, Other, Honoraria: Sanofi; Financial Interests, Institutional, Other, Honoraria: Astellas Pharma; Financial Interests, Personal, Other, Honoraria: Bayer. K. Herrmann: Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Advisory Role: Bain Capital; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Advanced Accelerator Applications, a Novartis company; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: BTG; Financial Interests, Personal, Advisory Role: Ipsen; Financial Interests, Institutional, Advisory Role: ITG; Financial Interests, Institutional, Advisory Role: ROTOP Pharmaka; Financial Interests, Personal, Advisory Role: Siemens Healthineers; Financial Interests, Personal, Advisory Role: GE Healthcare; Financial Interests, Personal, Leadership Role: SOFIE; Financial Interests, Personal, Ownership Interest: SOFIE. B.J. Krause: Financial Interests, Institutional, Funding: Advanced Accelerator Applications, a Novartis company; Financial Interests, Institutional, Funding: Endocyte, Inc., a Novartis company; Financial Interests, Institutional, Funding: Novartis. K. Rahbar: Financial Interests, Personal, Other, Honoraria: Advanced Accelerator Applications, a Novartis company; Financial Interests, Personal, Other, Honoraria: Bayer; Financial Interests, Personal, Other, Honoraria: SIRTEX; Financial Interests, Personal, Advisory Role: ABX GmbH; Financial Interests, Personal, Advisory Role: Advanced Accelerator Applications, a Novartis company; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: ABX CRO. K.N. Chi: Financial Interests, Personal, Advisory Role: ESSA; Financial Interests, Personal, Advisory Role: Astellas Pharma; Financial Interests, Personal, Advisory Role: Janssen; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Roche; Financial Interests, Personal, Advisory Role: POINT Biopharma; Financial Interests, Personal, Advisory Role: Daiichi Sankyo; Financial Interests, Personal, Advisory Role: Merck; Financial Interests, Personal, Advisory Role: Constellation Pharmaceuticals; Financial Interests, Personal, Other, Honoraria: Janssen; Financial Interests, Personal, Other, Honoraria: Astellas Pharma; Financial Interests, Personal, Other, Honoraria: Bayer; Financial Interests, Personal, Other, Honoraria: AstraZeneca; Financial Interests, Personal, Other, Honoraria: Roche; Financial Interests, Personal, Other, Honoraria: Merck; Financial Interests, Institutional, Funding: Janssen; Financial Interests, Institutional, Funding: Astellas Pharma; Financial Interests, Institutional, Funding: Bayer; Financial Interests, Institutional, Funding: Sanofi; Financial Interests, Institutional, Funding: Bristol-Myers Squibb; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: Roche; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Novartis; Financial Interests, Institutional, Funding: Pfizer; Financial Interests, Institutional, Funding: ESSA. M.J. Morris: Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Endocyte, Inc., a Novartis Company; Financial Interests, Personal, Advisory Role: Advanced Accelerator Applications, a Novartis Company; Financial Interests, Personal, Advisory Role: ORIC Pharmaceuticals; Financial Interests, Personal, Advisory Role: Johnson & Johnson; Financial Interests, Personal, Advisory Role: Curium Pharma; Financial Interests, Personal, Advisory Role: Athenex; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Endocyte, Inc., a Novartis Company; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Fujifilm; Financial Interests, Institutional, Funding: Bayer; Financial Interests, Institutional, Funding: Sanofi; Financial Interests, Institutional, Funding: Endocyte, Inc., a Novartis

Company; Financial Interests, Institutional, Funding: Progenics; Financial Interests, Institutional, Funding: Corcept Therapeutics; Financial Interests, Institutional, Funding: Roche/Genentech; Financial Interests, Institutional, Funding: Janssen. O. Sartor: Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Dendreon; Financial Interests, Personal, Advisory Role: Constellation Pharmaceuticals; Financial Interests, Personal, Advisory Role: Advanced Accelerator Applications, a Novartis company; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Bristol-Myers Squibb; Financial Interests, Personal, Advisory Role: Bavarian Nordic; Financial Interests, Personal, Advisory Role: EMD Serono; Financial Interests, Personal, Advisory Role: Astellas Pharma; Financial Interests, Personal, Advisory Role: Progenics; Financial Interests, Personal, Advisory Role: Blue Earth Diagnostics; Financial Interests, Personal, Advisory Role: Myovant Sciences; Financial Interests, Personal, Advisory Role: Myriad Genetics; Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Advisory Role: Clarity Pharmaceuticals; Financial Interests, Personal, Advisory Role: Fusion Pharmaceuticals; Financial Interests, Personal, Advisory Role: Isotopen Technologien; Financial Interests, Personal, Advisory Role: Janssen; Financial Interests, Personal, Advisory Role: Noxopharm; Financial Interests, Personal, Advisory Role: Clovis Oncology; Financial Interests, Personal, Advisory Role: Noria Therapeutics; Financial Interests, Personal, Advisory Role: Point Biopharma; Financial Interests, Personal, Advisory Role: TeneoBio; Financial Interests, Personal, Advisory Role: Telix Pharmaceuticals; Financial Interests, Personal, Advisory Role: Theragnostics; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Bayer; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Johnson & Johnson; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Sanofi; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: AstraZeneca; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Progenics; Financial Interests, Personal, Expert Testimony: Sanofi; Financial Interests, Personal, Ownership Interest: Lilly; Financial Interests, Personal, Ownership Interest: GlaxoSmithKline; Financial Interests, Personal, Ownership Interest: Abbvie; Financial Interests, Personal, Ownership Interest: Cardinal Health; Financial Interests, Personal, Ownership Interest: United Health Group; Financial Interests, Personal, Ownership Interest: PSMA Therapeutics; Financial Interests, Personal, Ownership Interest: Clarity Pharmaceuticals; Financial Interests, Personal, Ownership Interest: Noria Therapeutics; Financial Interests, Personal, Ownership Interest: Clovis Oncology; Financial Interests, Institutional, Funding: Bayer; Financial Interests, Institutional, Funding: Sanofi; Financial Interests, Institutional, Funding: Endocyte Inc., a Novartis company; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: InVitae; Financial Interests, Institutional, Funding: Constellation Pharmaceuticals; Financial Interests, Institutional, Funding: Advanced Accelerator Applications, a Novartis company; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Dendreon; Financial Interests, Personal, Funding: SOTIO; Financial Interests, Personal, Funding: Janssen; Financial Interests, Personal, Funding: Progenics; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Endocyte Inc., a Novartis company; Financial Interests, Personal, Advisory Role: Taiho; Financial Interests, Institutional, Funding: Arvinas. S.T. Tagawa: Financial Interests, Personal, Advisory Role: Medivation; Financial Interests, Personal, Advisory Role: Astellas Pharma; Financial Interests, Personal, Advisory Role: Dendreon; Financial Interests, Personal, Advisory Role: Janssen; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Genentech; Financial Interests, Personal, Advisory Role: Endocyte Inc., a Novartis company; Financial Interests, Personal, Advisory Role: Immunomedics; Financial Interests, Personal, Advisory Role: Karyopharm Therapeutics; Financial Interests, Personal, Advisory Role: Abbvie; Financial Interests, Personal, Advisory Role: Tolmar; Financial Interests, Personal, Advisory Role: QED Therapeutics; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Clovis Oncology; Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Advisory Role: POINT Biopharma; Financial Interests, Personal, Advisory Role: Blue Earth Diagnostics; Financial Interests, Personal, Advisory Role: Alkido Pharma; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Sanofi; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Immunomedics; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Amgen; Financial Interests, Institutional, Funding: Lilly; Financial Interests, Institutional, Funding: Sanofi; Financial Interests, Institutional, Funding: Janssen; Financial Interests, Institutional, Funding: Astellas Pharma; Financial Interests, Institutional, Funding: Progenics; Financial Interests, Institutional, Funding: Millennium; Financial Interests, Institutional, Funding: Amgen; Financial Interests, Institutional, Funding: Bristol-Myers Squibb; Financial Interests, Institutional, Funding: Dendreon; Financial Interests, Institutional, Funding: Rexahn Pharmaceuticals; Financial Interests, Institutional, Funding: Bayer; Financial Interests, Institutional, Funding: Genentech; Financial Interests, Institutional, Funding: Newlink Genetics; Financial Interests, Institutional, Funding: Inovio Pharmaceuticals; Financial Interests, Institutional, Funding: AstraZeneca; Financial Interests, Institutional, Funding: Immunomedics; Financial Interests, Institutional, Funding: Novartis; Financial Interests, Institutional, Funding: AVEO; Financial Interests, Institutional, Funding: Boehringer Ingelheim; Financial Interests, Institutional, Funding: Merck; Financial Interests, Institutional, Funding: Stem CentRx; Financial Interests, Institutional, Funding: Karyopharm Therapeutics; Financial Interests, Institutional, Funding: Abbvie; Financial Interests, Institutional, Funding: Medivation; Financial Interests, Institutional, Funding: Endocyte Inc., a Novartis company; Financial Interests, Institutional, Funding: Exelixis; Financial Interests, Institutional, Funding: Clovis Oncology; Non-Financial Interests, Personal, Other: Telix Pharmaceuticals; Non-Financial Interests, Personal, Other: ATLAB Pharma; Non-Financial Interests, Personal, Other: Phosplatin Therapeutics; Financial Interests, Institutional, Funding: POINT Biopharma; Financial Interests, Institutional, Funding: Gilead Sciences. A.T. Kendi: Other, Personal, Principal Investigator, PI at Mayo Clinic Rochester for VISION trial: Endocyte, Inc., a Novartis Company. N.J. Vogelzang: Financial Interests, Personal, Advisory Role: Novartis; Financial Interests, Personal, Speaker's Bureau: Bayer; Financial Interests, Personal, Advisory Board: Bayer; Financial Interests, Personal, Speaker's Bureau: Sanofi adventis; Financial Interests, Personal, Advisory Board: Sanofi adventis; Financial Interests, Personal, Speaker's Bureau: Janssen; Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Speaker's Bureau: Pfizer; Financial Interests, Personal, Advisory Board: Pfizer; Financial Interests, Personal, Advisory Board:

Exelixis; Financial Interests, Personal, Speaker's Bureau: Dendreon; Financial Interests, Personal, Advisory Board: Dendreon. J. Calais: Financial Interests, Personal, Other, Honoraria: Advanced Accelerator Applications, a Novartis company; Financial Interests, Personal, Advisory Role: Blue Earth Diagnostics; Financial Interests, Personal, Advisory Role: Curium Pharma; Financial Interests, Personal, Advisory Role: GE Healthcare; Financial Interests, Personal, Invited Speaker: IBA RadioPharma; Financial Interests, Personal, Advisory Role: Janssen Pharmaceuticals; Financial Interests, Personal, Advisory Role: POINT biopharma; Financial Interests, Personal, Advisory Role: Progenics / Lantheus; Financial Interests, Personal, Principal Investigator: Progenics / Lantheus; Financial Interests, Personal, Other, Honoraria: Radiomedix; Financial Interests, Personal, Invited Speaker: Telix Pharmaceuticals; Financial Interests, Personal, Other, Honoraria: Progenics / Lantheus. J. Nagarajah: Financial Interests, Institutional, Principal Investigator: Novartis; Financial Interests, Personal, Advisory Role: Curium. X.X. Wei: Financial Interests, Institutional, Principal Investigator: BMS; Financial Interests, Institutional, Funding: BMS. V.S. KOSHKIN: Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Clovis; Financial Interests, Personal, Advisory Role: Janssen; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: EMD Serono; Financial Interests, Personal, Advisory Role: Seattle Genetics / Astellas; Financial Interests, Personal, Advisory Role: Dendreon; Financial Interests, Institutional, Funding: Endocyte Inc., a Novartis company; Financial Interests, Institutional, Funding: Nektar; Financial Interests, Institutional, Funding: Clovis; Financial Interests, Institutional, Funding: Janssen; Financial Interests, Institutional, Funding: Taiho; Other, Personal, Other: Prostate Cancer Foundation. J. Beauregard: Non-Financial Interests, Personal and Institutional, Principal Investigator: Advanced Accelerator Applications, a Novartis company; Non-Financial Interests, Personal and Institutional, Principal Investigator: Ipsen; Non-Financial Interests, Personal, Advisory Role: Ipsen. M. DeSilvio: Financial Interests, Personal, Full or part-time Employment: Novartis Pharmaceuticals; Financial Interests, Personal, Ownership Interest: Novartis Pharmaceuticals. R.A. Messmann: Financial Interests, Personal, Full or part-time Employment: Novartis Pharmaceuticals; Financial Interests, Personal, Ownership Interest: Novartis Pharmaceuticals. J. de Bono: Financial Interests, Personal, Full or part-time Employment: Institute of Cancer Research; Financial Interests, Personal, Advisory Role: AstraZeneca; Financial Interests, Personal, Advisory Role: Sanofi; Financial Interests, Personal, Advisory Role: Genentech/Roche; Financial Interests, Personal, Advisory Role: Astellas Pharma; Financial Interests, Personal, Advisory Role: Bayer; Financial Interests, Personal, Advisory Role: Pfizer; Financial Interests, Personal, Advisory Role: Merck Sharp & Dohme; Financial Interests, Personal, Advisory Role: Merck Serono; Financial Interests, Personal, Advisory Role: Boehringer Ingelheim; Financial Interests, Personal, Advisory Role: Sierra Oncology; Financial Interests, Personal, Advisory Role: Menarini Silicon Biosystems; Financial Interests, Personal, Advisory Role: Taiho Pharmaceutical; Financial Interests, Personal, Advisory Role: Daiichi Sankyo; Financial Interests, Personal, Advisory Role: Janssen Oncology; Financial Interests, Personal, Advisory Role: Genmab; Financial Interests, Personal, Advisory Role: GlaxoSmithKline; Financial Interests, Personal, Advisory Role: Orion Pharma GmbH; Financial Interests, Personal, Advisory Role: Eisai; Financial Interests, Personal, Advisory Role: BioXCel therapeutics; Financial Interests, Personal, Advisory Role: Amgen; Financial Interests, Personal, Advisory Role: Astellas Pharma; Financial Interests, Personal, Advisory Role: CellCentric; Financial Interests, Personal, Advisory Role: Harpoon; Financial Interests, Personal, Advisory Role: Qiagen; Financial Interests, Personal, Advisory Role: Terumo; Financial Interests, Personal, Advisory Role: Sanofi Aventis GmbH; Financial Interests, Personal, Advisory Role: Vertex; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: AstraZeneca; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Astellas Pharma; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: GlaxoSmithKline; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Orion Pharma GmbH; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Sanofi; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Genmab; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Taiho Pharmaceutical; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Qiagen; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Vertex; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Amgen; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Bayer; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Bioexcel Therapeutics; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Boehringer Ingelheim; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Cellcentric; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Daiichi Sankyo; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Eisai; Financial Interests, Personal, Other, Travel/Accommodations/Expenses: Genentech/Roche; 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Financial Interests, Personal, Other, Honoraria: Janssen Oncology; Financial Interests, Personal, Other, Honoraria: Menarini Silicon Biosystems; Financial Interests, Personal, Other, Honoraria: Daiichi Sankyo; Financial Interests, Personal, Other, Honoraria: Sierra Oncology; Financial Interests, Personal, Other, Honoraria: BioExcel; Financial Interests, Personal, Other, Honoraria: Amgen; Financial Interests, Personal, Other, Honoraria: Bayer; Financial Interests, Personal, Other, Honoraria: Boehringer Ingelheim; Financial Interests, Personal, Other, Honoraria: CellCentric; Financial Interests, Personal, Other, Honoraria: Eisai; Financial Interests, Personal, Other, Honoraria: Genmab; Financial Interests, Personal, Other, Honoraria: GlaxoSmithKline; Financial Interests, Personal, Other, Honoraria: Harpoon; Financial Interests, Personal, Other, Honoraria: Merck Serono; Financial Interests, Personal, Other, Honoraria: Merck Sharp & Dohme; Financial Interests, Personal, Other, Honoraria: Orion; 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