Society of Gynecologic Oncology
ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

Antitumor Activity and Safety of Dostarlimab Therapy in Patients with Endometrial Cancer by Age Subgroups: a Post Hoc Analysis from the GARNET Trial

Ana Oaknin, MD[1]; Lucy Gilbert, MD[2]; Anna V. Tinker, MD[3]; Renaud Sabatier, MD[4]; Jubilee Brown, MD[5]; Cara Mathews, MD[6]; Valentina Boni, MD[7]; Vanessa Samouelian, MD[8]; David M. O'Malley, MD[9]; Andrea Jewell, MD[10]; Susana Banerjee, MD, PhD[11]; Grace Antony, PhD[12]; Jennifer Veneris, MD, PhD[13]; Bhavana Pothuri, MD[14]

[1]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [2]Division of Gynecologic Oncology, McGill University Health Centre, Montreal, Quebec, Canada; [3]BC Cancer–Vancouver, Vancouver, British Columbia, Canada; [4]Department of Medical Oncology, Institut Paoli Calmettes, Aix-Marseille University, Marseille, France; [5]Division of Gynecologic Oncology, Levine Cancer Institute, Atrium Health, Charlotte, NC, USA; [6]Women and Infants Hospital of Rhode Island, Providence, RI, USA; [7]START Madrid CIOCC (Centro Integral Oncológico Clara Campal), Hospital Universitario HM Sanchinarro, Madrid, Spain; [8]Gynecologic Oncology Service, Department of Obstetrics and Gynecology, Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada; [9]The Ohio State University College of Medicine, Columbus, OH, USA; [10]University of Kansas Medical Center, Kansas City, KS, USA; [11]The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [12]GlaxoSmithKline, London, UK; [13]GlaxoSmithKline, Waltham, MA, USA; [14]Gynecologic Oncology Group (GOG) and Department of Obstetrics/Gynecology, Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA.

Background

- Although median age of diagnosis of endometrial cancer (EC) is 63 years, most deaths from EC occur in patients older than 65 years, with a median age at death of 70 years[1]
- Older patients may have poor tolerance of the toxicity from conventional standard-of-care chemotherapy
  - Better tolerated and more effective regimens remain an unmet need for older patients with EC
- Dostarlimab is a programmed death receptor 1 (PD-1)–blocking antibody that is approved in the US as a monotherapy in adult patients with:
  - Mismatch repair deficient (dMMR) recurrent or advanced EC that has progressed on or following prior treatment with a platinum-containing regimen[2]
  - dMMR recurrent or advanced solid tumors that have progressed on or following prior treatment and who have no satisfactory alternative treatment options[2]
- In the EU, dostarlimab is approved as a monotherapy in adult patients with recurrent or advanced dMMR/microsatellite instability–high (MSI-H) EC that has progressed on or after treatment with a platinum-containing regimen[3]

Conclusions

- Dostarlimab's antitumor activity and safety for patients with dMMR/MSI-H EC and mismatch repair proficient (MMRp)/microsatellite stable (MSS) EC were generally comparable across age groups
  - Objective response rates were similar across age groups for patients in both the dMMR/MSI-H EC and the MMRp/MSS EC cohorts
  - Incidences of grade ≥3 treatment-related adverse events (TRAEs) were low across all subgroups
- Older patients with advanced/recurrent dMMR/MSI-H EC experienced broadly similar treatment benefits as younger patients
- Dostarlimab can be used safely in older patients with advanced/recurrent dMMR/MSI-H EC

Poster #210

Scan to download a copy of this poster

Presenting author email: aoaknin@vhio.net

Presented at the Society of Gynecologic Oncology (SGO) Annual Meeting on Women's Cancer; March 18–21, 2022; Phoenix, AZ

Acknowledgments

This study (NCT02715284) was funded by GlaxoSmithKline (Waltham, MA, USA). Writing and editorial support, funded by GlaxoSmithKline and coordinated by Heather Ostendorff-Bach, PhD, of GlaxoSmithKline, were provided by Shannon Morgan-Pelosi, PhD, and Jennifer Robertson, PhD, of Ashfield MedComms, an Ashfield Health company (Middletown, CT, USA)

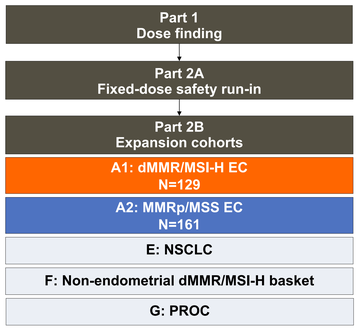
Objective

- To report on a post hoc analysis of the antitumor activity and safety of dostarlimab by age subgroup in patients with dMMR/MSI-H EC and MMRp/MSS EC

Methods

- GARNET is a phase 1, multicenter, open-label, single-arm study of dostarlimab monotherapy in patients with advanced or recurrent solid tumors (Figure 1)

Figure 1. GARNET Trial Design



Key inclusion/exclusion criteria for cohorts A1 and A2:

- Patients must have progression on or after platinum doublet therapy
- Patients must have received ≤2 prior lines of treatment for recurrent or advanced disease
- Patients must have measurable disease at baseline
- Patients must be anti–PD-(L)1 naive
- Patients could be screened based on local MMR/MSI testing results using IHC, PCR, or NGS performed in a certified local laboratory, but patient cohort assignment was by MMR IHC results
- Patients must submit 2 scans demonstrating PD on or after the latest systemic anticancer therapy based on RECIST v1.1 per BICR prior to the first dose of dostarlimab

BICR, blinded independent central review; dMMR, mismatch repair deficient; EC, endometrial cancer; IHC, immunohistochemistry; MMR, mismatch repair; MMRp, mismatch repair proficient; MSI, microsatellite instability; MSI-H, microsatellite instability–high; MSS, microsatellite stable; NGS, next-generation sequencing; NSCLC, non–small cell lung cancer; PCR, polymerase chain reaction; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PROC, platinum-resistant ovarian cancer; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

- MMR status was determined by local immunohistochemistry
- Patients received 500 mg of intravenous dostarlimab every 3 weeks for 4 cycles, followed by 1000 mg every 6 weeks until discontinuation (Figure 2)

Figure 2. GARNET Study Dosing Schedule

	500 mg Q3W (1 cycle = 3 weeks)				1000 mg Q6W until disease progression or unacceptable toxicity (1 cycle = 6 weeks)			
Cycle	1	2	3	4	5	6	7	Continue dosing Q6W
Week	1	4	7	10	13	19	25	

Q3W, every 3 weeks; Q6W, every 6 weeks.

- The primary endpoints were evaluation of antitumor activity (in terms of objective response rate and duration of response by Response Evaluation Criteria in Solid Tumors version 1.1 per blinded independent central review), safety, and tolerability
- The data cutoff date was March 1, 2020

Results

- 129 patients with dMMR/MSI-H EC and 161 patients with MMRp/MSS EC were enrolled and treated as of the data cutoff date of March 1, 2020; these patients constitute the safety population of cohorts A1 and A2, respectively (Table 1)
- The efficacy population included those patients with ≥1 measurable lesion at baseline and the opportunity for ≥24 weeks of follow-up as of the data cutoff date
  - 105 patients with dMMR/MSI-H EC and 156 patients with MMRp/MSS EC met these criteria

Table 1. Demographics and Baseline Characteristics

Characteristic	dMMR/MSI-H EC N=129			MMRp/MSS EC N=161		
	<65 years n=66	≥65 years to <75 years n=51	≥75 years n=12	<65 years n=70	≥65 years to <75 years n=72	≥75 years n=19
Age, median (range), years	58.5 (39–64)	68.0 (65–74)	76.0 (75–80)	59.0 (30–64)	68.0 (65–74)	78.0 (75–86)
FIGO stage at diagnosis, n (%)[a]						
Stage I or II	26 (39.4)	28 (54.9)	3 (25.0)	17 (24.3)	34 (47.2)	8 (42.1)
Stage III or IV	40 (60.6)	23 (45.1)	9 (75.0)	53 (75.7)	38 (52.8)	10 (52.6)
Histology, n (%)						
Endometrioid carcinoma type I (grade 1 or 2)	44 (66.7)	33 (64.7)	8 (66.7)	23 (32.9)	11 (15.3)	3 (15.8)
Endometrial carcinoma type II	22 (33.3)	17 (33.3)	4 (33.3)	47 (67.1)	61 (84.7)	16 (84.2)
Serous	2 (3.0)	2 (3.9)	1 (8.3)	14 (20.0)	35 (48.6)	10 (52.6)
Clear cell	1 (1.5)	0	0	6 (8.6)	4 (5.6)	0
Squamous carcinoma	0	1 (2.0)	0	0	3 (4.2)	0
Undifferentiated	2 (3.0)	3 (5.9)	0	4 (5.7)	0	0
Carcinosarcoma	0	0	0	1 (1.4)	1 (1.4)	0
Mixed carcinoma	5 (7.6)	2 (3.9)	0	5 (7.1)	5 (6.9)	2 (10.5)
Unspecified	9 (13.6)	6 (11.8)	2 (16.7)	12 (17.1)	9 (12.5)	4 (21.1)
Other[b]	3 (4.5)	3 (5.9)	1 (8.3)	5 (7.1)	4 (5.6)	0
Unknown	0	1 (2.0)	0	0	0	0

[a]One patient with MMRp EC had disease status/stage unknown; [b]Includes adenocarcinoma and adenocarcinoma with ambiguous differentiation.
dMMR, mismatch repair deficient; EC, endometrial cancer; FIGO, International Federation of Gynecology and Obstetrics; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable.

Results *(cont'd)*

- The objective response rate was similar across age groups for patients in both the dMMR/MSI-H EC and the MMRp/MSS EC cohorts (Table 2)

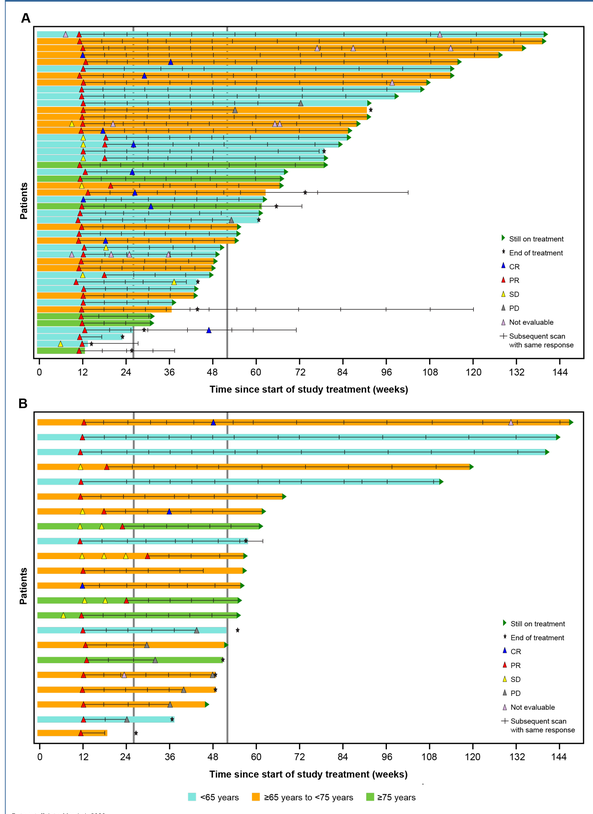
Table 2. Primary Endpoint Analysis

Variable	dMMR/MSI-H EC N=105			MMRp/MSS EC N=156		
	<65 years n=53	≥65 years to <75 years n=41	≥75 years n=11	<65 years n=66	≥65 years to <75 years n=71	≥75 years n=19
Median follow-up time, mo	13.7	19.2	14.5	27.8	13.8	11.2
Confirmed responses, n	24	18	5	6	12	4
ORR, % (95% CI)[a]	45.3 (31.6–59.6)	43.9 (28.5–60.3)	45.5 (16.7–76.6)	9.1 (3.4–18.7)	16.9 (9.0–27.7)	21.1 (6.1–45.6)
CR, n (%)	6 (11.3)	3 (7.3)	2 (18.2)	0	1 (1.4)	2 (10.5)
PR, n (%)	18 (34.0)	15 (36.6)	3 (27.3)	6 (9.1)	11 (15.5)	2 (10.5)
SD, n (%)	8 (15.1)	3 (7.3)	2 (18.2)	10 (15.2)	16 (22.5)	6 (31.6)
PD, n (%)	16 (30.2)	19 (46.3)	4 (36.4)	40 (60.6)	37 (52.1)	8 (42.1)
NE, n (%)	5 (9.4)	1 (2.4)	0	10 (15.2)	6 (8.5)	1 (5.3)
Disease control rate, % (95% CI)[b]	60.4 (46.0–73.5)	51.2 (35.1–67.1)	63.6 (30.8–89.1)	24.2 (14.5–36.4)	39.4 (28.0–51.7)	52.6 (28.9–75.6)
Response ongoing, n (%)	21 (87.5)	17 (94.4)	4 (80.0)	4 (66.7)	7 (58.3)	3 (75.0)
Duration of response, median (range), mo	NR (2.79+ to 28.09+)	NR (4.34+ to 27.66+)	NR (2.63 to 13.47+)	NR (2.79 to 27.89+)	NR (1.54 to 30.36+)	NR (5.55 to 8.48+)
Kaplan-Meier estimated probability of remaining in response, %						
At 6 mo	100.0	100.0	80.0	83.3	81.8	75.0
At 12 mo	84.6	100.0	80.0	66.7	56.1	NR
At 18 mo	74.0	90.0	NR	66.7	56.1	NR

[a]Responses required confirmation at a subsequent scan: SD had to be observed at ≥12 wk on study to qualify as SD; [b]Includes confirmed CR, PR, or SD at ≥12 wk.
CR, complete response; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; mo, months; MSI-H, microsatellite instability–high; MSS, microsatellite stable; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; wk, weeks.

- The duration of response among responders was long (not reached for all subgroups), and the majority of responders remained in response as of the data cutoff date (Figure 3)

Figure 3. Duration of Treatment in Responders with (A) dMMR/MSI-H and (B) MMRp/MSS EC



Data cutoff date: March 1, 2020.
CR, complete response; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; PD, progressive disease; PR, partial response; SD, stable disease.

- Dostarlimab was well tolerated, with an AE profile characteristic of anti–PD-1s (Table 3)

Table 3. Safety Summary

Parameter, n (%)	dMMR/MSI-H EC N=129			MMRp/MSS EC N=161		
	<65 years n=66	≥65 years to <75 years n=51	≥75 years n=12	<65 years n=70	≥65 years to <75 years n=72	≥75 years n=19
Any-grade TEAE	63 (95.5)	49 (96.1)	11 (91.7)	70 (100)	72 (100)	19 (100)
Grade ≥3 TEAE	27 (40.9)	28 (54.9)	7 (58.3)	43 (61.4)	41 (56.9)	6 (31.6)
Any-grade TRAE	43 (65.2)	34 (66.7)	5 (41.7)	50 (71.4)	53 (73.6)	11 (57.9)
Grade ≥3 TRAE	9 (13.6)	7 (13.7)	1 (8.3)	16 (22.9)	14 (19.4)	1 (5.3)
Treatment-related SAE	6 (9.1)	6 (11.8)	0	8 (11.4)	5 (6.9)	0
Any TRAE leading to discontinuation	1 (1.5)	3 (5.9)	1 (8.3)	5 (7.1)	6 (8.3)	0
TRAE leading to death	0	0	0	0	0	0

dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

- Few grade ≥3 TRAEs occurred, and these events were generally similar between age groups
  - Patients aged ≥75 years did not seem to have an increased incidence of grade ≥3 TRAEs compared with younger age groups (Table 4)

Table 4. Most Common TRAEs

Parameter, n (%)	dMMR/MSI-H EC N=129			MMRp/MSS EC N=161		
	<65 years n=66	≥65 years to <75 years n=51	≥75 years n=12	<65 years n=70	≥65 years to <75 years n=72	≥75 years n=19
Most common any-grade TRAE seen in more than 15 patients, n (%)						
Fatigue	5 (7.6)	11 (21.6)	1 (8.3)	12 (17.1)	19 (26.4)	3 (15.8)
Diarrhea	13 (19.7)	7 (13.7)	1 (8.3)	6 (8.6)	11 (15.3)	2 (10.5)
Nausea	7 (10.6)	6 (11.8)	3 (25.0)	9 (12.9)	14 (19.4)	1 (5.3)
Asthenia	11 (16.7)	6 (11.8)	1 (8.3)	6 (8.6)	7 (9.7)	0
Anemia	6 (9.1)	3 (5.9)	0	7 (10.0)	10 (13.9)	1 (5.3)
Hypothyroidism	6 (9.1)	2 (3.9)	1 (8.3)	7 (10.0)	7 (9.7)	2 (10.5)
Vomiting	2 (3.0)	3 (5.9)	0	6 (8.6)	9 (12.5)	2 (10.5)
Arthralgia	5 (7.6)	5 (9.8)	1 (8.3)	3 (4.3)	5 (6.9)	2 (10.5)
Rash	3 (4.5)	4 (7.8)	0	2 (2.9)	10 (13.9)	2 (10.5)
AST increased	2 (3.0)	2 (3.9)	1 (8.3)	6 (8.6)	7 (9.7)	2 (10.5)
ALT increased	2 (3.0)	2 (3.9)	1 (8.3)	6 (8.6)	6 (8.3)	1 (5.3)
Decreased appetite	2 (3.0)	2 (3.9)	1 (8.3)	8 (11.4)	3 (4.2)	2 (10.5)
Pruritus	3 (4.5)	6 (11.8)	0	1 (1.4)	5 (6.9)	2 (10.5)
Amylase increased	2 (3.0)	2 (3.9)	0	3 (4.3)	6 (8.3)	2 (10.5)
Grade ≥3 TRAEs seen in more than 2 patients, n (%)[a]						
Anemia	5 (7.6)	0	0	1 (1.4)	2 (2.8)	0
Amylase increased	0	1 (2.0)	0	0	3 (4.2)	0
ALT increased	0	2 (3.9)	0	1 (1.4)	1 (1.4)	0
Diarrhea	1 (1.5)	1 (2.0)	0	0	2 (2.8)	0
Fatigue	0	0	0	2 (2.9)	2 (2.8)	0
Lipase increased	2 (3.0)	1 (2.0)	0	0	1 (1.4)	0
AST increased	0	0	0	1 (1.4)	2 (2.8)	0
Hyperglycemia	0	0	0	2 (2.9)	1 (1.4)	0
Colitis	2 (3.0)	0	0	0	0	0
Constipation	0	1 (2.0)	0	0	1 (1.4)	0
Hypertension	0	1 (2.0)	0	0	1 (1.4)	0
Nausea	0	0	0	1 (1.4)	1 (1.4)	0
Pulmonary embolism	0	1 (2.0)	0	1 (1.4)	0	0
Transaminase increased	0	1 (2.0)	1 (8.3)	0	0	0

[a]One patient with dMMR/MSI-H EC in the ≥75 years subgroup had a transaminase increase of grade ≥3, and 1 patient with MMRp/MSS EC in the ≥75 years subgroup had a rash of grade ≥3.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; TRAE, treatment-related adverse event.

References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: uterine cancer. https://seer.cancer.gov/statfacts/html/corp.html. Accessed January 21, 2022.
2. GlaxoSmithKline. Jemperli. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761223s000lbl.pdf. Accessed January 12, 2022.
3. European Medicines Agency. Jemperli. https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli. Accessed February 1, 2022.

Conflicts of Interest

Dr. Oaknin reports consulting fees from AstraZeneca, Bristol Meyers Squibb, Deciphera Pharmaceutical, Genmab, GlaxoSmithKline, ImmunoGen, Mersana Therapeutics, Roche, and SUTRO; institutional grants from Abbie Deutchland, Ability Pharmaceuticals, Advaxis Inc, Aeterna Zentaris, Amgen SA, Aprea Therapeutics AB, Clovis Oncology Inc, Eisai Ltd, F. Hoffmann–La Roache Ltd, GlaxoSmithKline, ImmunoGen Inc, Merck Sharp & Dohme de Espana SA, Millennium Pharmaceuticals Inc, PharmaMar, and Regeneron Pharmaceuticals; and travel support from AstraZeneca, Clovis Oncology, PharmaMar, and Roche.
Dr. Gilbert reports institutional grants from Alkermes, AstraZeneca, Clovis, Esperas, ImmunoGen Inc, IMV, Karyopharm, Merck Sharp & Dohme, Mersana, Novocure GmbH, OncoQuest Pharmaceuticals, Pfizer, Roche, and Tesaro; consulting fees from Merck; honoraria from Alkermes, AstraZeneca, Eisai, Eisai-Merck, and GlaxoSmithKline.
Dr. Tinker reports honoraria from GlaxoSmithKline; institutional grants from AstraZeneca; and personal fees from AstraZeneca and Eisai.
Dr. Sabatier reports institutional grants from AstraZeneca and Eisai; personal fees from AstraZeneca, GlaxoSmithKline, Novartis, Pfizer, and Roche; and nonfinancial support from Amgen, AstraZeneca, Pfizer, and Roche.
Dr. Brown reports consulting/advisory roles at Caris, Clovis, Eisai, and GlaxoSmithKline; and research funding from Genentech and GlaxoSmithKline.
Dr. Mathews reports research grant funding to her institution from Astellas, AstraZeneca, Deciphera, GlaxoSmithKline, Modema, Regeneron, and Seattle Genetics; and advisory board honoraria from IMAB Biopharma.
Dr. Boni reports consulting or advisory roles at Guidepoint Global and OncoArt; speakers' bureau fees from Solti; travel support from START; honoraria from IDEAYA Biosciences and Loxo; and institutional grants from Abbvie, Adaptimmune, Alkermes, Amgen, Array BioPharma, AstraZeneca, Bayer, BioNTech AG, Boehringer Ingelheim, Boston Biomedical, Bristol Myers Squibb, CytomX Therapeutics, Genmab, GlaxoSmithKline, Incyte, Janssen Oncology, Kura Oncology, Lilly, Loxo, Merck, Menarini, Merus, Novartis, Pfizer, Pumo Biotechnology, Roche/Genentech, Sanofi, Seattle Genetics, Synthon, and Zenith Epigenetics. Dr. Boni is currently employed at NEXT Oncology Madrid, Hospital Universitario Quironsalud Madrid, Spain.
Dr. O'Malley reports personal fees from consulting and/or advisory board membership from Abbvie, Agenus, Ambry, Amgen, AstraZeneca, Clovis, Eisai, Elevar, Genentech/Roche, GOG Foundation, Immunogen, Iovance Biotherapeutics Inc, Janssen/J&J, Merck, Mersana, Myriad Genetics, Novartis, Novocure, Regeneron, Rubis, SeaGen, Tarveda, and Tesaro/GlaxoSmithKline; research funding (all funding to institution) from Abbvie, Agenus, Ajinomoto Inc., Amgen, Array Biopharma, AstraZeneca, BBI, Bristol Myers Squibb, Cerulean Pharma, Clovis, Eisai, EMD Serono, Ergomed, Genentech/Roche, GenMab, GOG Foundation, Immunogen, INC Research, inVentiv Health Clinical, Iovance Biotherapeutics Inc, Janssen/J&J, Ludwig Cancer Research, Merck, Mersana, NCI, New Mexico Cancer Care Alliance, Novocure, Pra Intl, Regeneron, SeaGen, Serono Inc, Stemcentrx Inc, Tesaro/GlaxoSmithKline, Tracon Pharmaceuticals, VentiRx, and Yale University.
Dr. Banerjee reports honoraria from Amgen, AstraZeneca, Clovis Oncology, GlaxoSmithKline, Pfizer, and Takeda; consulting fees from Amgen, AstraZeneca, GenMab, GlaxoSmithKline, Immunogen, Merck Serono, Mersana, MSD Oncology, Oncxerna, Pfizer, and Roche; institutional grants from AstraZeneca and GlaxoSmithKline; and travel support from NuCana BioMed.
Dr. Samouëlian reports consulting/advisory roles at GlaxoSmithKline and Merck.
Dr. Jewell has nothing to disclose.
Drs. Antony and **Veneris** are employees of GlaxoSmithKline.
Dr. Pothuri reports institutional grant support from AstraZeneca, Celsion, Clovis Oncology, Genentech/Roche, Karyopharm, Merck, Mersana, Incyte, Sutro, and Tesaro/GlaxoSmithKline; and advisory board fees from AstraZeneca, Celsion, Clovis Oncology, Deciphera, Eisai, Elevar Therapeutics, Imab, Merck, Mersana, Sutro Biopharma, Tesaro/GlaxoSmithKline, and Toray.