Food and Drug Administration
Center for Drug Evaluation and Research
Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
May 20-21, 2025

Location: FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. The public also had the option to participate via an online teleconferencing and/or video conferencing platform, and the meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform.

Topic: On the morning of May 20, 2025, the Committee discussed supplemental biologics license application (sBLA) 761309/S-001, for COLUMVI (glofitamab) injection, submitted by Genentech, Inc. The proposed indication (use) is in combination with gemcitabine and oxaliplatin for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) who are not candidates for autologous stem cell transplant (ASCT).

On the afternoon of May 20, 2025, the Committee discussed sBLA 761145/S-029, for DARZALEX FASPRO (daratumumab and hyaluronidase) injection, for subcutaneous use, submitted by Janssen Biotech, Inc. The proposed indication (use) is as monotherapy for the treatment of adult patients with high-risk smoldering multiple myeloma (SMM).

On the morning of May 21, 2025, the Committee discussed new drug application (NDA) 215793, for UGN-102 (mitomycin) intravesical solution, submitted by UroGen Pharma, Inc. The proposed indication (use) is for the treatment of adult patients with low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC).

On the afternoon of May 21, 2025, the Committee discussed supplemental new drug application (sNDA) 211651/S-013, for TALZENNA (talazoparib) capsules, submitted by Pfizer Inc. The proposed indication (use) is in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC).

These summary minutes for the May 20-21, 2025 meeting of the Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration were approved on July 15, 2025.

I certify that I attended the May 20-21, 2025 meeting of the ODAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/	/S/	/S/
Jessica Seo, PharmD, MPH Acting Designated Federal Officer, ODAC	Neil Vasan, MD Acting Chairperson, ODAC (Day 1)	Daniel Spratt, MD Acting Chairperson, ODAC (Day 2)

Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
May 20-21, 2025

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on May 20-21, 2025, at FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. The public also had the option to participate via an online teleconferencing and/or video conferencing platform, and the meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA, Genentech, Inc, Janssen Biotech, Inc, UroGen Pharma, Inc, and Pfizer Inc. The meeting was called to order by Neil Vasan, MD (Acting Chairperson) on Day 1, and Daniel Spratt, MD (Acting Chairperson) on Day 2. The conflict of interest statement was read into the record by Jessica Seo, PharmD, MPH (Acting Designated Federal Officer). There were approximately 125 people in attendance in-person on Day 1 and Day 2, and approximately 1205 people online during Day 1, and 896 people online during Day 2. There was a total of 2 Open Public Hearing (OPH) speaker presentations during the Day 1 morning session, 10 OPH speaker presentations during the Day 1 afternoon session, 7 OPH speaker presentations during the Day 2 morning session, and 5 OPH speaker presentations during the Day 2 afternoon session.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda:

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On the afternoon of May 21, 2025, the Committee discussed supplemental new drug application (sNDA) 211651/S-013, for TALZENNA (talazoparib) capsules, submitted by Pfizer Inc. The proposed indication (use) is in combination with enzalutamide for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC).

Attendance:

Oncologic Drugs Advisory Committee Members Present (Voting): Toni K. Choueiri, MD (*via video conferencing platform; May 20 Sessions Only*); Mark R. Conaway, PhD (*All Sessions*); William J. Gradishar, MD (*May 21 Sessions Only*); Ravi A. Madan, MD (*All Sessions*); Daniel Spratt, MD (*All sessions; Acting Chairperson for May 21 Sessions*); Neil Vasan, MD, PhD (*All Sessions; Acting Chairperson for May 20 Sessions*);

Oncologic Drugs Advisory Committee Members Not Present (Voting): Pamela L. Kunz, MD;

Oncologic Drugs Advisory Committee Members Present (Non-Voting): Tara L. Frenkl, MD, MPH (*May 20 Sessions and May 21 Morning Session Only*)

Acting Industry Representative to the Oncologic Drugs Advisory Committee (Non-Voting): Craig Tendler, MD (*May 21 Afternoon Session Only*)

Temporary Members (Voting): Mark W. Ball, MD, FACS (*May 21 Morning Session Only*); Isla P. Garraway, MD, PhD (*May 21 Morning Session Only);* Julie Graff, MD (*May 21 Afternoon Session Only*); Colette Johnston (*via video conferencing platform; Patient Representative; May 21 Morning Session Only*); Terrence "Terry" Kungel, MBA (*Patient Representative; May 21 Afternoon Session Only*); Christopher Lieu, MD (*May 20 Sessions Only*); Paul V. Majkowski, Esq. (*Patient Representative; May 20 Morning Session Only*)*;* Heidi McKean, MD (*All Sessions*)*;* Ajay K. Nooka, MD, MPH (*May 20 Morning Session Only*)*;* Joan Durnell Powell (*Patient Representative; May 20 Afternoon Session Only*);

FDA Participants (Non-Voting): Richard Pazdur, MD (*May 20 Morning Session Only and May 21 Sessions*); Nicole Gormley, MD (*May 20 Sessions Only*); R. Angelo de Claro, MD (*May 20 Sessions Only*); Nicholas Richardson, DO, MPH (*May 20 Sessions Only*); Margret Merino, MD (*May 20 Morning Session Only*); Nicole Sunseri, MD, PhD (*May 20 Morning Session Only*); Bindu Kanapuru, MD (*May 20 Afternoon Session Only*); Payal Aggarwal, DO, MS (*May 20 Afternoon Session Only*); Laleh Amiri-Kordestani, MD (*May 21 Sessions Only*); Daniel Suzman, MD (*May 21 Sessions Only*); Sundeep Agrawal, MD (*May 21 Morning Session Only*); Brian Heiss, MD (*May 21 Morning Session Only*); Jaleh Fallah, MD (*May 21 Afternoon Session Only*); William Maguire, MD, PhD (*May 21 Afternoon Session Only*);

Acting Designated Federal Officer (Non-Voting): Jessica Seo, PharmD, MPH

Open Public Hearing Speakers Present:

Day 1 (morning session): Amanda Berhaupt, PhD (National Center for Health Research); Daneen Sekoni (Cancer Support Community);

Day 1 (afternoon session): Bradley J. Hanson; Louise Miller Lavin; Jeffrey S. Rubin, MD; Kathleen Vallefuoco; Irene Ghobrial, MD; Anne Quinn Young (Multiple Myeloma Research

Foundation); Ken Anderson, MD; Bhavana Bhatnagar, DO; Solly Silwan Chedid, MD; Jonathan Ticku, MD;

Day 2 (morning session): Yazmin Lago; Lisa Malzone; Sandip Prasad, MD; Mark Perlin; Tom Hyland; Meri-Margaret Deoudes; Katherine Lacey Parker;

Day 2 (afternoon session): Amanda Berhaupt, PhD (National Center for Health Research); Thomas Bognanno; Tom Remenick; Courtney Bugler (ZERO Prostate Cancer); Harry Ames;

The agenda was as follows:

May 20, 2025, Morning Session

8:00 a.m.	Call to Order and Introduction of Committee	**Neil Vasan, MD, PhD** Acting Chairperson, ODAC
8:05 a.m.	Conflict of Interest Statement	**Jessica Seo, PharmD** Acting Designated Federal Officer, ODAC
8:10 a.m.	**FDA Opening Remarks**	
	Glofitamab-gxbm	**Nicole Gormley, MD** Director Division of Hematologic Malignancies II (DHM II) Office of Oncologic Diseases (OOD) Office of New Drugs (OND), CDER, FDA
	Glofitamab-gxbm (COLUMVI) BLA 761309	**Margret Merino, MD** Clinical Team Leader DHM II, OOD, OND, CDER, FDA
8:30 a.m.	**APPLICANT PRESENTATIONS**	**Genentech, Inc.**
	Introduction	**Charles Fuchs, MD, MPH** Genentech, Inc.
	DLBCL Background & Unmet Need	**Jeremy Abramson, MD** Massachusetts General Hospital Cancer Center
	STARGLO Efficacy & Safety	**Michelle Boyer, PhD** Genentech, Inc.
	STARGLO Subgroup Analyses	**Venkat Sethuraman, PhD** Genentech, Inc.
	Clinical Perspective	**Krish Patel, MD** Sarah Cannon Research Institute

APPLICANT PRESENTATIONS (CONT.)

	Closing Remarks	**Charles Fuchs, MD, MPH**
	FDA WELCOME	**Martin A. Makary, MD, MPH** Commissioner FDA
		Vinayak Kashyap Prasad MD, MPH Director Center for Biologics Evaluation and Research (CBER), FDA
9:15 a.m.	**FDA PRESENTATIONS**	
	Glofitamab-gxbm (COLUMVI) BLA 761309	**Nicole Sunseri, MD, PhD** Clinical Reviewer DHM II, OOD, OND, CDER, FDA
9:55 a.m.	Clarifying Questions	
10:20 a.m.	**BREAK**	
10:30 a.m.	**OPEN PUBLIC HEARING**	
11:00 a.m.	Questions to the Committee/Committee Discussion	
12:00 p.m.	**LUNCH**	

May 20, 2025, Afternoon Session

1:00 p.m.	Call to Order and Introduction of Committee	**Neil Vasan, MD, PhD** Acting Chairperson, ODAC
1:05 p.m.	Conflict of Interest Statement	**Jessica Seo, PharmD** Acting Designated Federal Officer, ODAC
1:10 p.m.	**FDA Opening Remarks**	
	BLA 761145 Daratumumab and hyaluronidase-fihj (Dara SC) (DARZALEX FASPRO)	**Bindu Kanapuru, MD** Supervisory Associate Director for Therapeutic Review DHM II, OOD, OND, CDER, FDA

1:30 p.m.	**APPLICANT PRESENTATIONS**	**Janssen Research & Development, LLC**
	Introduction	**Sen Zhuang, MD, PhD** Vice President, Oncology Research & Development Johnson & Johnson
	Unmet Need	**Sagar Lonial, MD, FACP** Chair and Professor Department of Hematology and Medical Oncology Anne and Bernard Gray Family Chair in Cancer Chief Medical Officer Winship Cancer Institute Emory University School of Medicine
	Efficacy	**Robin Carson, MD** Vice President, Clinical Leader Oncology Johnson & Johnson
	Safety	**Robyn Dennis, MD** Senior Medical Director, Oncology Johnson & Johnson
	Clinical Perspective	**S. Vincent Rajkumar, MD, FRCPC** Edward W. and Betty Knight Scripps Professor of Medicine Mayo Clinic
2:15 p.m.	**FDA PRESENTATIONS**	
	BLA 761145 Daratumumab and hyaluronidase-fihj (DARZALEX FASPRO)	**Payal Aggarwal, DO, MS** Clinical Reviewer DHM II, OOD, OND, CDER, FDA
2:55 p.m.	Clarifying Questions	
3:20 p.m.	**BREAK**	
3:30 p.m.	**OPEN PUBLIC HEARING**	
4:00 p.m.	Questions to the Committee/Committee Discussion	
5:00 p.m.	**ADJOURNMENT**	

May 21, 2025, Morning Session

8:00 a.m.	Call to Order and Introduction of Committee	**Daniel Spratt, MD** Acting Chairperson, ODAC
8:05 a.m.	Conflict of Interest Statement	**Jessica Seo, PharmD** Acting Designated Federal Officer, ODAC
8:10 a.m.	FDA Opening Remarks	
	UGN-102 (Mitomycin)	**Sundeep Agrawal, MD** Clinical Team Leader Genitourinary Malignancies Division of Oncology 1 (DO1) OOD, OND, CDER, FDA
8:35 a.m.	**APPLICANT PRESENTATIONS**	**UroGen Pharma, Inc.**
	Introduction	**Mark Schoenberg, MD** Chief Medical Officer UroGen Pharma, Inc.
	Unmet Need	**Sam S. Chang, MD** Chief, Division of Urologic Oncology Chief Surgical Officer Vanderbilt Ingram Cancer Center
	Efficacy	**Michael J. Louie, MD, MPH, MSc** EVP, Clinical Development and Medical Affairs UroGen Pharma, Inc.
	Safety	**Sunil Raju, MBBS, BSc** Vice President, Clinical Development UroGen Pharma, Inc.
	Clinical Perspective	**Max Kates, MD** Division Director, Urologic Oncology Brady Urological Institute Johns Hopkins Greenberg Bladder Cancer Institute
	Conclusion	**Mark Schoenberg, MD**
9:20 a.m.	**FDA PRESENTATIONS**	
	NDA 215793: UGN-102 (mitomycin intravesical solution)	**Brian Heiss, MD** Clinical Reviewer Genitourinary Malignancies DO1, OOD, OND, CDER, FDA

9:50 a.m.	Clarifying Questions	
10:20 a.m.	**BREAK**	
10:30 a.m.	**OPEN PUBLIC HEARING**	
11:00 a.m.	Questions to the Committee/Committee Discussion	
12:00 p.m.	**LUNCH**	

May 21, 2025, Afternoon Session

1:00 p.m.	Call to Order and Introduction of Committee	**Daniel Spratt, MD** Chairperson, ODAC
1:05 p.m.	Conflict of Interest Statement	**Jessica Seo, PharmD** Acting Designated Federal Officer, ODAC
1:10 p.m.	**FDA OPENING REMARKS**	
	Talazoparib with Enzalutamide for Metastatic Castration-Resistant Prostate Cancer (mCRPC)	**Jaleh Fallah, MD** Clinical Team Leader (Acting) Genitourinary Malignancies DO1, OOD, OND, CDER, FDA
1:30 p.m.	**APPLICANT PRESENTATIONS**	**Pfizer, Inc.**
	Introduction	**Johanna Bendell, MD** Chief Development Officer Oncology Research and Development Pfizer, Inc**.**
	Treatment Landscape	**Pedro Barata, MD, MSc, FACP** Associate Professor of Medicine Case Western Reserve University School of Medicine Case Comprehensive Cancer Center Cleveland, Ohio
	Efficacy and Safety	**Dana Kennedy, PharmD, BCOP** **Vice President** Genitourinary Therapeutic Area Head Oncology Research and Development Pfizer, Inc.

	APPLICANT PRESENTATIONS (CONT.)	
	Clinical Perspective	**Neeraj Agarwal, MD, FASCO** Professor of Medicine & Presidential Endowed Chair of Cancer Research Huntsman Cancer Institute University of Utah
	Closing Remarks	**Johanna Bendell, MD**
2:15 p.m.	**FDA PRESENTATIONS**	
	Talazoparib with Enzalutamide for Metastatic Castration-Resistant Prostate Cancer (mCRPC)	**William Maguire, MD, PhD** Clinical Reviewer Genitourinary Malignancies DO1, OOD, OND, CDER, FDA
2:55 p.m.	Clarifying Questions	
3:20 p.m.	**BREAK**	
3:30 p.m.	**OPEN PUBLIC HEARING**	
4:00 p.m.	Questions to the Committee/Committee Discussion	
5:00 p.m.	**ADJOURNMENT**	

Questions to the Committee:

May 20, 2025 - Morning Session

1. **DISCUSSION:** Discuss how the differential results observed in the Asian and Non-Asian regions impact the overall interpretation of the STARGLO trial results and the generalizability to a U.S. patient population.

   Committee Discussion*: In discussing their interpretation of the STARGLO trial results, panel members expressed general agreement that while the trial met its primary endpoint with a 40% reduction in the risk of death overall, the significant differences observed in the Asian and Non-Asian regions created substantial uncertainty about the generalizability of the results to the U.S. population. Committee members cited the small U.S. sample size of only 25 patients, the lack of regional stratification in the study design, and potential imbalances in patient characteristics as sources of skepticism for applying these findings to U.S. patients. Possible explanations for the differential results were discussed, including differences in subsequent treatments between regions and the impact of COVID-19 on enrollment, but were not considered fully explanatory. Concerns were also raised about the*

applicability and safety of glofitamab treatment and the need for more certainty of the its safety and effectiveness for use in the community oncology setting. A couple of panel members highlighted the overall positive effect of the treatment and its potential benefit for U.S. patients, especially given the lack of standard treatments for this population.

Please see the transcript for details of the Committee's discussion.

2. **VOTE**: Are the STARGLO population and trial results applicable to the proposed U.S. patient population?

   Vote Result: Yes: 1 No: 8 Abstain: 0

   ***Committee Discussion**: The Committee members were in near unanimous agreement that the STARGLO population and trial results are not applicable to the proposed U.S. patient population. Panel members who voted "no," cited several concerns. These included the limited number of U.S. patients enrolled in the trial, inconsistencies in results between Asian and non-Asian populations, and the lack of adherence to ICH E17 guidelines for multi-regional clinical trials. Some panel members noted that while the primary endpoint was met, the subgroup analyses showed inferior results in non-Asian populations across multiple endpoints (OS, PFS, ORR, and CR). Doubts were also expressed about whether the trial met the FDA's standard of enrolling a sufficient number of participants to support a robust assessment of safety and effectiveness in US patients. The panel member who voted "yes" prioritized the patient perspective and emphasized that the trial met its primary endpoint. The panel concluded that overall, more data from U.S. patients would be necessary to prove the therapy's efficacy and safety in the U.S. population.*

   Please see the transcript for details of the Committee's discussion.

May 20, 2025 - Afternoon Session

1. **DISCUSSION:** Discuss the clinical meaningfulness of the efficacy endpoints assessed in the AQUILA trial.

   ***Committee Discussion**: In discussing the clinical meaningfulness of the efficacy endpoints in the AQUILA trial, panel members commented on several nuances and complexities. Panel members acknowledged that while there were signals of benefit from treatment with daratumumab and hyaluronidase, particularly in PFS and a trend towards improved OS, concerns were raised about the maturity of the data and the appropriateness of these endpoints for an asymptomatic condition. Some panel members noted that the PFS endpoint might be clinically meaningful as it delayed the need for more intensive combination therapies, while others questioned whether treating all patients upfront was justified when only about half would progress to requiring treatment in the control arm. The discussion touched on the difficulty of balancing the potential benefits against the risks of overtreatment and side effects in patients who might never progress to active multiple myeloma. In addition,*

panel members discussed whether SMM should be considered cancerous or precancerous, which impacted their interpretation of the endpoints' clinical meaningfulness. Comparisons were also drawn to solid tumor oncology, where similar endpoints are sometimes accepted for drug approval. Overall, while the panel members acknowledged signals of efficacy from the AQUILA trial, there was no clear consensus on clinical meaningfulness of these signals.

Please see the transcript for details of the Committee's discussion.

2. **DISCUSSION:** Discuss the benefit-risk of daratumumab hyaluronidase (Dara SC) for the intended high-risk smoldering multiple myeloma (SMM) population.

***Committee Discussion**: Panel members touched on several facets and complexities in their discussion on the benefit-risk of Dara SC for the high-risk SMM population. Some panel members questioned whether SMM should be considered a precursor condition or an early stage of malignancy, noting different implications for the treatment approach. Several panel members also compared SMM to other cancer types, discussing the challenges of using PFS as an endpoint in this setting. In addition, panel members questioned whether the treatment was preventing or merely delaying disease progression, and whether the benefits outweighed the risks of lifelong therapy started earlier. There were concerns raised about potential overtreatment, especially as more aggressive combination therapies might be developed in the future. However, there was acknowledgement that the study met its primary endpoint, showing significant overall response rate and potential overall survival benefit. Panel members emphasized the need for better identification of high-risk patients who are more likely to progress.*

Please see the transcript for details of the Committee's discussion.

3. **VOTE**: Do the results from the AQUILA trial provide sufficient evidence to support a favorable benefit-risk profile for Dara SC for patients with high-risk SMM?

Vote Result: Yes: 6 No: 2 Abstain: 0

***Committee Discussion**: The majority of Committee members agreed that the results from the AQUILA trial provided sufficient evidence to support a favorable benefit-risk profile for Dara SC for patients with high-risk SMM. Those who voted "Yes" generally agreed that the benefits outweighed the risks, citing trends in overall survival, the need for treatment options, and the importance of patient choice. There was acknowledgement that the trial was well-designed and provided evidence that the progression to multiple myeloma could be delayed. However, panel members also emphasized the need for better definition of "high-risk" patients and for continued follow-up for overall survival data.*

Those who voted "No" expressed concerns about potential overtreatment of patients who may not need it, citing that only 40.5% of enrolled patients were classified as high-risk when applying contemporary criteria. They also pointed out the similar rates of severe

complications between treatment and control groups, and the lack of clear signals in progression-free survival or overall survival to justify the toxicities experienced by treated patients.

There was overall agreement from the panel members on the complexity of their decision and the need for further refinement in patient selection and risk stratification. The importance of clear labeling and guidance for use, if approved, was also emphasized, as well the need for continued research to better identify patients who would benefit most from early treatment with Dara SC.

Please see the transcript for details of the Committee's discussion.

May 21, 2025 - Morning Session

1. **DISCUSSION:** Given uncertainty regarding interpretation of duration of response in low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC), discuss whether randomized trials should be required in the future to assess the effectiveness of therapies in this disease setting.

   Committee Discussion*: In discussing whether randomized trials should be required for assessing therapies in LG-IR-NMIBC, there was a general consensus that randomized trials are the gold standard and provide the highest level of evidence. However, panel members varied on whether they believe randomized trials should be strictly required. Some panel members argued that randomized trials are feasible and necessary in this disease setting, given its prevalence and the need for robust data on efficacy, duration of response, and safety. Others cautioned against using the word "required," suggesting that each case should be evaluated individually, considering factors such as patient recruitment, heterogeneity of the disease, and potential obstacles to conducting randomized trials, although none, including the urologists on the panel, considered randomization (e.g. against a TURBT-based control) to be infeasible in this disease setting.*

   Please see the transcript for details of the Committee's discussion.

2. **VOTE**: Is the overall benefit-risk of the investigational therapy UGN-102 favorable in patients with recurrent LG-IR-NMIBC?

   Vote Result: Yes: 4 No: 5 Abstain: 0

   Committee Discussion*: In the determining the favorability of the overall benefit-risk of UGN-102 treatment in patients with recurrent LG-IR-NMIBC, the panel members were split, with a slight majority of panel members that voted "No." These panel members cited uncertainties in the data and study design, and expressed concerns about the lack of a randomized controlled trial, which they felt was necessary to accurately assess the true benefits and risks. Comments also included the short-term nature of the primary endpoint (3-*

month complete response), limited long-term follow-up data, and uncertainties about the impact on subsequent salvage therapies and quality of life. In addition, it was noted the treatment did not significantly reduce the need for TURBT procedures beyond three months or impact more serious outcomes like cystectomy or disease progression. However, panel members who voted "Yes" emphasized the importance of having a non-surgical option for patients, particularly those with comorbidities, and felt the demonstrated efficacy was encouraging with an acceptable toxicity profile. They also highlighted the potential to delay or avoid TURBT procedures.

Please see the transcript for details of the Committee's discussion.

May 21, 2025 - Afternoon Session

1. **DISCUSSION**: Discuss whether efficacy should be formally evaluated in a biomarker-negative population when the biomarker is predictive of response and the prevalence of the biomarker-negative group is high.

   Committee Discussion*: In discussing whether efficacy should be formally evaluated in a biomarker-negative population when the biomarker is predictive of response and the prevalence of the biomarker-negative group is high, panel members expressed an overall consensus that formal evaluation is necessary and important. Historical examples were cited such as trastuzumab in breast cancer, where retrospective analyses suggested efficacy in biomarker-negative patients, but prospective trials proved otherwise. The panel members emphasized the importance of proper prospective biomarker testing and the advancements in companion diagnostics that now allow for more comprehensive and efficient testing. Concerns were raised about toxicity, both medical and financial, especially in the context of prostate cancer treatments. Panel members stressed the need for clear evidence of benefit in the appropriate patient population before expanding treatment to biomarker-negative groups and highlighted the importance of considering various efficacy endpoints beyond overall survival, such as quality of life and time to symptomatic progression. The panel members noted that TALAPRO-2 was not powered to specifically assess the biomarker-negative subgroup and formal evaluation of efficacy in biomarker-negative populations would be needed for ensuring appropriate patient care.*

   Please see the transcript for details of the Committee's discussion.

2. **VOTE**: Are the results from TALAPRO-2 sufficient to conclude a favorable benefit-risk profile for adding talazoparib to enzalutamide in patients with non-homologous recombination repair mutated (non-HRRm) metastatic castration-resistant prostate cancer (mCRPC)?

   Vote Result: Yes: 0 No: 8 Abstain: 0

Committee Discussion*: The Committee members were in unanimous agreement that the results from the TALAPRO-2 trial are not sufficient to conclude a favorable benefit-risk profile for adding talazoparib to enzalutamide in patients with non-HRRm mCRPC. The panel members cited several reasons for their decision, including concerns about the study design, lack of pre-specification for the non-mutant population, insufficient statistical power to test efficacy in non-HRRm patients, and the high level of toxicity observed. Panel members also noted that while the combination therapy showed promise in HRRm patients, the data for non-HRRm patients was not robust enough to support approval. The importance of balancing the potential benefits with the significant toxicities was emphasized, particularly in an older patient population. Concerns were also raised about the impact on quality of life, the lack of clear survival benefit, and the potential for overtreatment in the context of evolving diagnostic techniques. While acknowledging the need for more treatment options in mCRPC, the panel concluded that the current data did not support a favorable benefit-risk profile for this specific patient population.*

Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 4:56 p.m. ET on Day 1 and approximately 4:40 p.m. ET on Day 2.