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Oncologic Drugs Advisory Committee (ODAC) Meeting

April 30, 2026

New Drug Application (NDA)# 218197/Supplement 004

Drug name: capivasertib

Applicant: AstraZeneca UK Limited

Combined FDA and Applicant ODAC Briefing Document

Errata

Section 2.3.7, Table 9, Page 37

The FDA conducted the analysis "rPFS event for receiving a new anti-cancer therapy," not the Applicant.

Section 2.3.10, Table 11, Page 41

Table 11 is corrected and clarified below.

- **Footnote added to clarify that the data in the table reflects efficacy data available at the time of approval of the mHSPC indication.**
- **TITAN: Supportive secondary endpoint was the delay to initiation of cytotoxic chemotherapy (not initiation of subsequent therapies).**
- **ARCHES: OS HR of 0.66 (CI 0.53, 0.81) was the final OS, which is now clarified in the footnote. At the time of approval, the OS HR was 0.81 (0.53, 1.25). Supportive secondary endpoint was time to new antineoplastic (not time to cytotoxic chemotherapies).**
- **ARANOTE: No supportive secondary endpoints included in labeling.**

Table 11. FDA – Historical Context: Approvals in mHSPC

Trial	Treatment Arm vs. Control Arm	Basis of Approval[1] HR (95% Confidence Interval)	Supportive secondary endpoints[2]
TITAN	Apalutamide + ADT vs Placebo + ADT	rPFS HR 0.48 (0.39, 0.60); OS HR 0.67 (0.51, 0.89)	Time to initiation of cytotoxic chemotherapy
ARCHES	Enzalutamide + ADT vs Placebo + ADT	rPFS HR 0.39 (0.30, 0.50); OS HR 0.81 (0.53, 1.25)[3]	Time to initiation of new antineoplastic therapy
ARANOTE	Darolutamide + ADT vs Placebo + ADT	rPFS HR 0.54 (0.41, 0.71); OS HR 0.78 (0.58, 1.05)[4]	None
AMPLITUDE	Niraparib + AAP + ADT vs. Placebo + AAP + ADT	(*BRCA2* only) rPFS HR 0.46 (0.32, 0.66)[5]; OS events 22% [niraparib] vs. 34% [placebo][3]	Time to pain progression
LATITUDE	AAP + ADT vs Placebo + ADT	OS HR 0.62 (0.51, 0.76)	None
ARASENS	Darolutamide + Docetaxel + ADT vs. Placebo + Docetaxel + ADT	OS HR 0.68 (0.57, 0.80)	Time to symptomatic progression

[1]Efficacy data available at the time of initial approval of the mHSPC indication.
[2]Supportive secondary endpoints are secondary endpoints that were statistically significant and included in product labeling.
[3]OS not mature at time of approval. Final OS for ARCHES was 0.66 (95% CI: 0.53, 0.81).
[4]Not statistically significant.
[5]Not formally tested.
Abbreviations: AAP: abiraterone acetate + prednisone; CI: confidence interval; HR: hazard ratio; OS: overall survival; rPFS: radiographic progression-free survival

FDA Appendix 13, Table 35, Page 89

Table 35 is corrected below. Rows 2-4 were based on analyses without the condition of "in the absence of (or prior to) PD/death." The results presented in the table are unchanged.

Table 35. FDA – CAPItello-281: Treatment Discontinuation Prior to Progression or Death

	C+AAP N=507	P+AAP N=505
Patients who discontinued both study treatments in the absence of (or prior to) PD/death, n (%)	128 (25.2)	92 (18.2)
Discontinued capivasertib/placebo due to AE or clinical progression, n (%)	121 (23.9)	60 (11.9)
Discontinued capivasertib/placebo due to AE, n (%)	93 (18.3)	24 (4.8)
Discontinued abiraterone due to AE, n (%)	48 (9.5)	27 (5.3)

Source: Applicant's response to IR dated 03/06/2026 and CSR Table 14.1.1

Abbreviations: C+AAP: capivasertib + abiraterone acetate + prednisone; CI: confidence interval; P+AAP: placebo + abiraterone acetate + prednisone; PD: progression of disease

FDA Appendix 13, Table 36, Page 89

Table 36 is corrected below. The 95% confidence intervals for "PTEN loss >=95" row, "No" columns were corrected.

Table 36. FDA - CAPItello-281: Exploratory Efficacy Analysis of Subgroups Defined by Different PTEN Loss Cutoffs

Endpoint	rPFS by INV		OS	
PTEN loss >=90 (ITT)	N=1012		N=1012	
Median (C+AAP vs. P+AAP), months	33 vs 26		NE vs NE	
HR (95% confidence interval)	0.81 (0.66, 0.98)		0.9 (0.71, 1.15)	
PTEN loss >=95 (n, proportion of ITT)	Yes (n=814, 80%)	No (n=198, 20%)	Yes (n=814, 80%)	No (n=198, 20%)
Median (C+A vs. P+A), months	33 vs 23	38 vs NE	NE	43 vs NE
HR (95% confidence interval)	0.77 (0.62, 0.95)	1.25 (0.77, 2.05)	0.8 (0.62, 1.05)	1.72 (0.93, 3.30)
PTEN loss >=99 (n, proportion of ITT)	Yes (n=401,40%)	No (n=611, 60%)	Yes (n=401,40%)	No (n=611, 60%)
Median (C+A vs. P+A), months	34 vs 22	33 vs 29	NE	NE
HR (95% confidence interval)	0.71(0.51, 0.96)	0.94 (0.72, 1.21)	0.77 (0.53, 1.11)	1.02 (0.74, 1.39)
PTEN loss =100 (n, proportion of ITT)	Yes (n=331, 33%)	No (n=681, 67%)	Yes (n=331, 33%)	No (n=681, 67%)
Median (C+A vs. P+A), months	34 vs 22	33 vs 29	NE	NE

Abbreviation: C+A: capivasertib + abiraterone acetate+ prednisone; HR: hazard ratio, ITT: intent-to-treat; NE: not evaluable; OS; overall survival; P+A: placebo+ abiraterone acetate+ prednisone; rPFS: radiographic progression-free survival

Section 3 Safety

Section 3.3.1, Table 19, Page 54

Table 19 title is revised below to clarify that it includes analyses from laboratory data. Footnote added to clarify the approach to laboratory abnormality analyses.

Table 19 FDA – Day 120 Safety Update: Most Common (Any Grade >=20%) Adverse Events and Laboratory Abnormalities

Treatment arm	C+AAP N=503		P+AAP N=503	
	Any Grade N (%)	Grade 3-4 N (%)	Any Grade N (%)	Grade 3-4 N (%)
Any Adverse Event	499 (99)	318 (63)	469 (93)	192 (38)
Infections*	286 (57)	91 (18)	222 (44)	32 (6)
Skin reactions*	267 (53)	87 (17)	84 (17)	2 (0.4)
Diarrhea*	265 (53)	33 (7)	45 (9)	2 (0.4)
Hyperglycemia*	257 (51)	74 (15)	80 (16)	6 (1.2)
Musculoskeletal pain*	138 (27)	8 (1.6)	152 (30)	7 (1.4)
Fatigue*	132 (26)	6 (1.2)	93 (18)	6 (1.2)
Decreased hemoglobin†	293/500 (59)	29/500 (6)	220/500 (44)	12/500 (2.4)
Decreased potassium†	236/500 (47)	77/500 (15)	175/500 (35)	42/500 (8)
Hypertension	124 (25)	37 (7)	133 (26)	44 (9)

Abbreviations: C+AAP: capivasertib + abiraterone + prednisone/prednisolone; P+AAP: placebo + abiraterone + prednisone/prednisolone
*Includes multiple terms
†Based on laboratory data. The rate is based on the number of patients with a baseline value and at least one post-treatment value.

Section 3.3.1, Table 20, Page 54

"AE leading to death in first 3 months of therapy" refers to "fatal adverse events with onset in the first 3 months of therapy," not deaths in the first 3 months of therapy. Among patients treated with C+AAP, 13 (2.6%) had fatal adverse events with onset in the first 3 months of therapy, not 14 (2.8%).

"Ischemic cardiovascular events" includes cardiovascular and cerebrovascular events.

Section 4 Clinical Outcome Assessment Analyses

Section 4.1.1, Third paragraph, Page 59

The sentence "FDA notes 10% of patients in the capivasertib arm reported severe bother defined as 'quite a bit' or 'very much' bother" refers to the Week 4 time point.