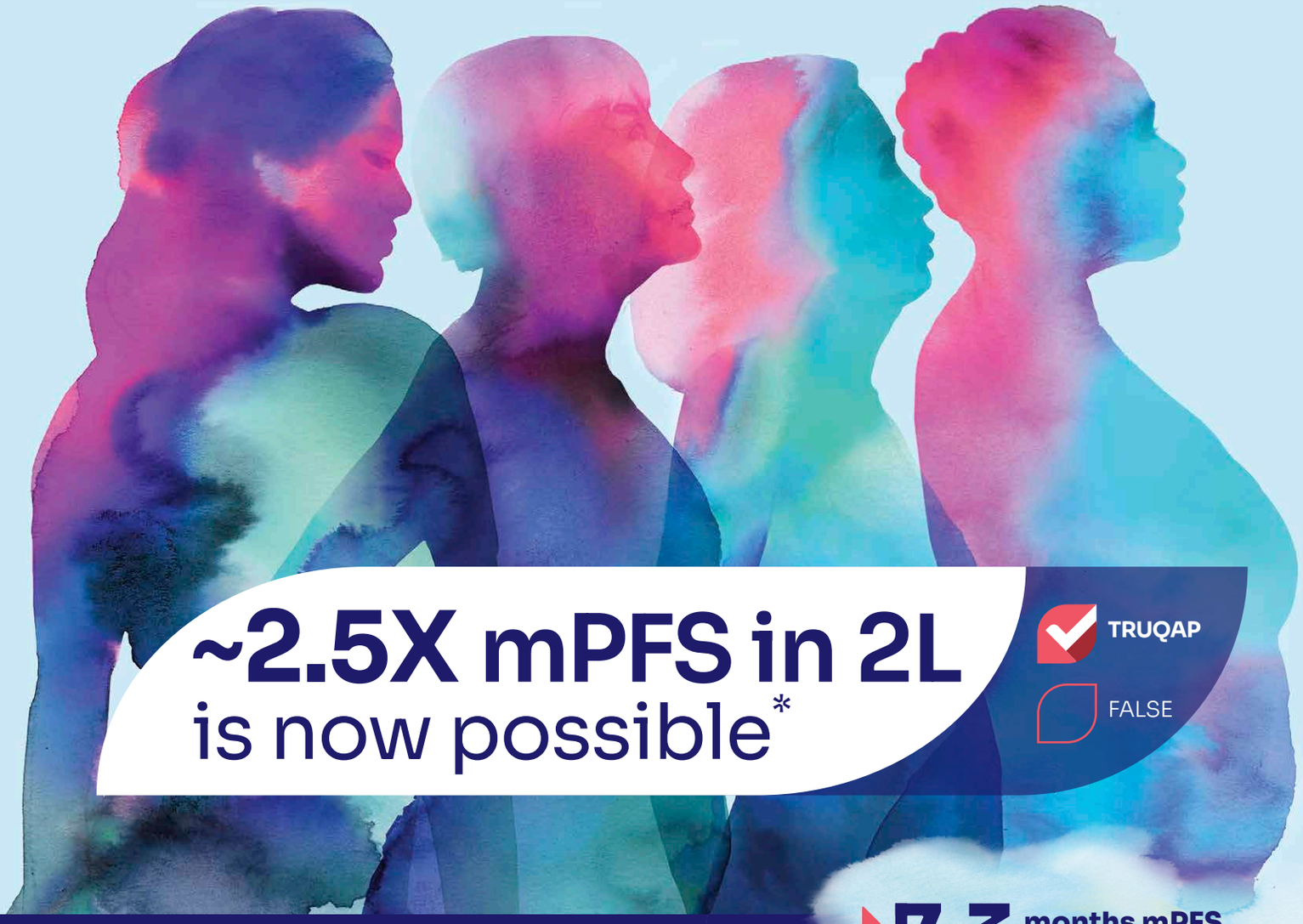
Truqap™
capivasertib
160 mg • 200 mg tablets

NOW APPROVED

In HR+/HER2– aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i



~2.5X mPFS in 2L is now possible*

TRUQAP

FALSE

Introducing TRUQAP + fulvestrant

7.3 months mPFS (95% CI: 5.5-9.0)
with TRUQAP + fulvestrant (n=155)[1]

vs

3.1 months mPFS (95% CI: 2.0-3.7)
with fulvestrant (n=134)[1]

HR=0.50
(95% CI: 0.38-0.65;
P<0.0001)

***The first and only targeted combination to more than double mPFS** vs fulvestrant alone in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations, most having received prior ET + CDK4/6i[1]

TEST for *PIK3CA*, *AKT1*, *PTEN*

TREAT with TRUQAP + fulvestrant

2L=second line; aBC=locally advanced breast cancer not amenable to resection or radiation therapy with curative intent; *AKT1*=serine/threonine protein kinase 1; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; ET=endocrine therapy; HER2–=human epidermal growth factor receptor 2 negative; HR=hazard ratio; HR+=hormone receptor positive; mBC=metastatic breast cancer; mPFS=median progression-free survival; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog.

IMPORTANT SAFETY INFORMATION ABOUT TRUQAP™ (capivasertib) tablets

TRUQAP is contraindicated in patients with severe hypersensitivity to TRUQAP or any of its components.

Hyperglycemia

Severe hyperglycemia, associated with ketoacidosis, has occurred in patients treated with TRUQAP. The safety of TRUQAP has not been established in patients with Type I diabetes or diabetes requiring insulin. Patients with insulin-dependent diabetes were excluded from CAPItello-291.

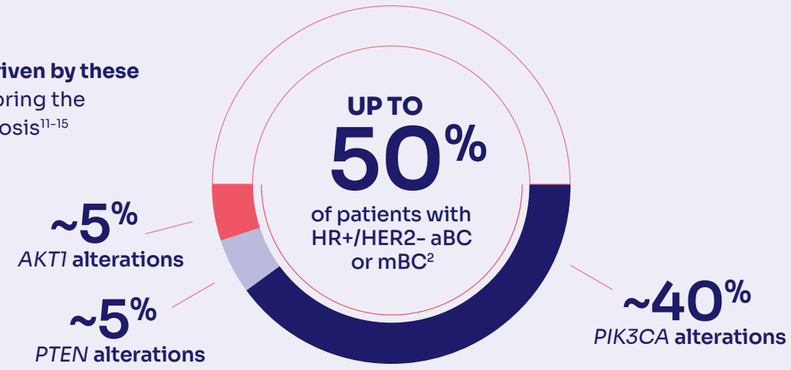
Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

Up to **50% of patients** with HR+/HER2- aBC or mBC have one or more *PIK3CA*, *AKT1*, or *PTEN* alterations[2]

After exposure to 1L ET ± CDK4/6i[3-10]

Better treatment options have been urgently needed to improve outcomes while reducing discontinuation rates due to adverse reactions for patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations.

Disease progression can be driven by these common alterations, underscoring the importance of testing at diagnosis[11-15]



AKT is an important target for inhibition[11,12,16]

As **the central regulating protein** of the PI3K/AKT/PTEN pathway, **AKT can mediate amplified signaling from other proteins**, including effects from PI3K and PTEN.

AKT inhibition blocks oncogenic signaling from the following alterations associated with tumor growth:

✓ ***PIK3CA*** ✓ ***AKT1*** ✓ ***PTEN***

TEST patients for *PIK3CA*, *AKT1*, and *PTEN* alterations at aBC or mBC diagnosis

1L=first line; AKT=serine/threonine protein kinase; ER=estrogen receptor; mTOR=mammalian target of rapamycin; PI3K=phosphoinositide 3-kinase.

IMPORTANT SAFETY INFORMATION (continued)

Hyperglycemia

Hyperglycemia occurred in 18% of patients treated with TRUQAP (n=355). Grade 3 (insulin therapy initiated; hospitalization indicated) or Grade 4 (life-threatening consequences; urgent intervention indicated) hyperglycemia occurred in 2.8% of patients. Diabetic ketoacidosis occurred in 0.3% of patients and diabetic metabolic decompensation in 0.6% of patients. Dose reduction for hyperglycemia was required in 0.6% and permanent discontinuation was required in 0.6% of patients. The median time to first occurrence of hyperglycemia was 15 days (range: 1 to 367).

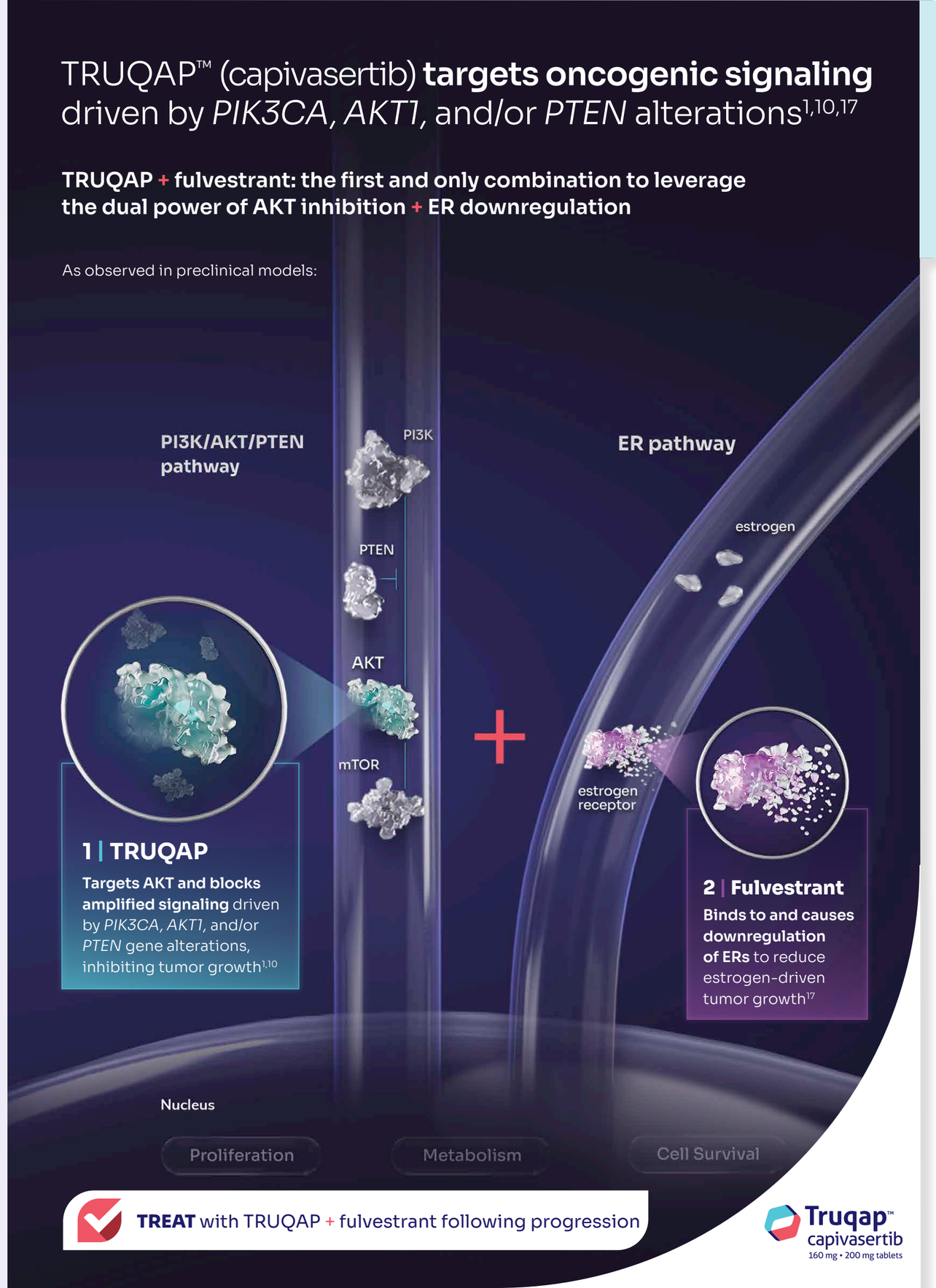
In the 65 patients with hyperglycemia, 45% required treatment with anti-hyperglycemic medication (insulin in 15% and metformin in 29%). Of the 29 patients who required anti-hyperglycemic medication during treatment with TRUQAP, 66% (19/29) remained on these medications at treatment discontinuation or last follow-up.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

TRUQAP™ (capivasertib) **targets oncogenic signaling** driven by *PIK3CA*, *AKT1*, and/or *PTEN* alterations[1,10,17]

TRUQAP + fulvestrant: the first and only combination to leverage the dual power of AKT inhibition + ER downregulation

As observed in preclinical models:



TREAT with TRUQAP + fulvestrant following progression

Truqap™ capivasertib
160 mg • 200 mg tablets

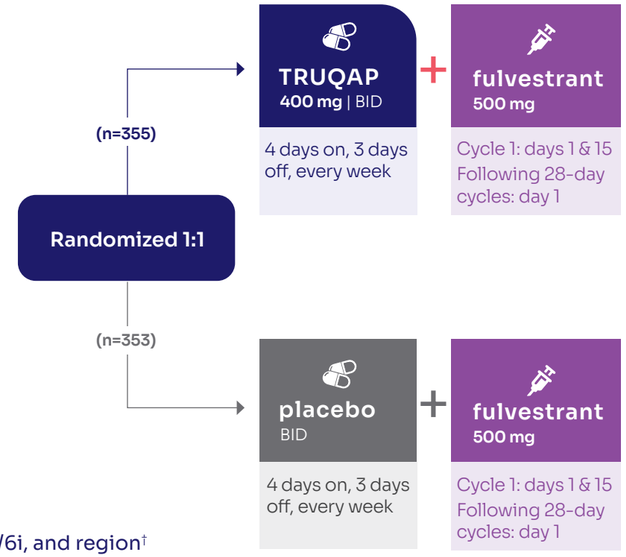
In combination with fulvestrant,

TRUQAP™ (capivasertib) was studied in a global, phase 3, randomized, double-blind, multicenter trial with **70% of patients having prior CDK4/6i**[1,18]

CAPItello-291 (N=708)[1]*

Key inclusion criteria[1]

- HR+/HER2– (defined as IHC 0 or 1+ or IHC 2+/ISH–) aBC or mBC
- Recurrence while on or <12 months from end of neoadjuvant or adjuvant AI or progression while on prior AI for aBC or mBC
- ≤2 lines of prior ET for aBC or mBC
- ≤1 line of chemotherapy for aBC or mBC
- Prior CDK4/6i allowed (at least 51% required)
- HbA1C <8% (63.9 mmol/mol) and diabetes not requiring insulin allowed



Stratified by: Liver metastases, prior CDK4/6i, and region†

Dual primary endpoints[1]

- PFS in overall population (investigator assessed)
- PFS in patients with *PIK3CA/AKT1/PTEN* alterations (investigator assessed)

Key secondary endpoints[1]

- Overall survival
- ORR (Investigator assessed)
- Safety
- DoR

Pathway alteration status was determined centrally using next-generation sequencing in tumor tissue with the FoundationOne® CDx assay. Patients were treated until disease progression or unacceptable toxicity.[1]

*Overall population (N=708); *PIK3CA/AKT1/PTEN*-altered population (n=289; TRUQAP + fulvestrant n=155; placebo + fulvestrant n=134).[1]

†Region 1: United States, Canada, Western Europe, Australia, and Israel; Region 2: Latin America, Eastern Europe, and Russia; Region 3: Asia.[1]

IMPORTANT SAFETY INFORMATION (continued)

Hyperglycemia

If a patient experiences hyperglycemia after initiating treatment with TRUQAP, monitor FG as clinically indicated, and at least twice weekly until FG decreases to normal levels. During treatment with anti-hyperglycemic medication, continue monitoring FG at least once a week for 8 weeks, followed by once every 2 weeks and as clinically indicated. Consider consultation with a healthcare practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes. Withhold, dose reduce, or permanently discontinue TRUQAP based on severity.

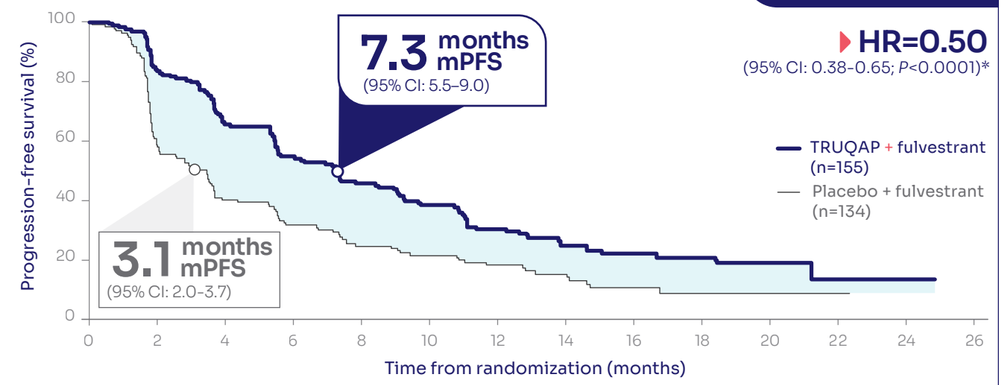
Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

In combination with fulvestrant,

TRUQAP—**the first and only AKT inhibitor to more than double mPFS** vs fulvestrant alone[1]

mPFS in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations (n=289)[1]

~2.5X mPFS



Patients at risk, n

TRUQAP + fulvestrant	155	127	99	80	65	54	38	26	21	12	3	2	1	0
Placebo + fulvestrant	134	77	48	37	28	24	17	11	6	2	1	1	0	0

In CAPItello-291, both primary endpoints, PFS in the overall population (N=708) and PFS in patients with *PIK3CA, AKT1,* and/or *PTEN* alterations (n=289), reached statistical significance.

An exploratory analysis of PFS in 313 (44%) patients who did not have *PIK3CA, AKT1,* and/or *PTEN* alterations showed an HR of 0.79 (95% CI: 0.61–1.02), indicating the improvement in PFS in the overall population was primarily due to the PFS results in patients with alterations. FDA approval of TRUQAP + fulvestrant was therefore based on the PFS results seen in patients with *PIK3CA, AKT1,* and/or *PTEN* alterations.[1]

TEST for *PIK3CA, AKT1, PTEN* **TREAT** with TRUQAP + fulvestrant following progression

*Stratified Cox proportional hazards model. A hazard ratio <1 favors TRUQAP + fulvestrant. The log-rank test and Cox model stratified by presence of liver metastases (yes vs no) and prior use of CDK4/6i (yes vs no).[1]

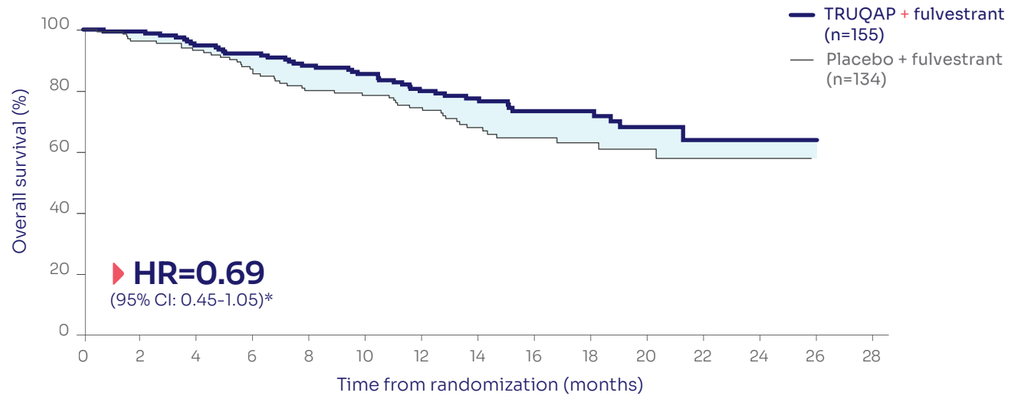
AI=aromatase inhibitor; DoR=duration of response; HbA1C=glycated hemoglobin; IHC=immunohistochemistry; ISH=in situ hybridization; ORR=objective response rate; PFS=progression-free survival.

Truqap™ capivasertib
160 mg • 200 mg tablets

In combination with fulvestrant,

Overall survival with TRUQAP™ (capivasertib) at **30% maturity**[18]

Overall survival in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations (n=289)[18]



Patients at risk, n															No. of events
TRUQAP + fulvestrant	155	153	144	139	131	125	111	83	60	45	30	14	3	1	0	**41**
Placebo + fulvestrant	134	127	122	112	101	99	87	62	46	31	22	13	3	0	0	46

At the time of data cutoff, **a sufficient number of events had not been reached to yield an overall survival rate**[1,18]

*Stratified Cox proportional hazards model. The log-rank test and Cox model stratified by presence of liver metastases (yes vs no) and prior use of CDK4/6i (yes vs no).[1]

IMPORTANT SAFETY INFORMATION (continued)

Diarrhea

Severe diarrhea associated with dehydration occurred in patients who received TRUQAP (n=355).

Diarrhea occurred in 72% of patients. Grade 3 or 4 diarrhea occurred in 9% of patients. The median time to first occurrence was 8 days (range: 1 to 519). In the 257 patients with diarrhea, 59% required antidiarrheal medications to manage symptoms. Dose reductions were required in 8% of patients and 2% of patients permanently discontinued TRUQAP due to diarrhea. In patients with Grade ≥ 2 diarrhea (n=93) with at least 1 grade improvement (n=89), median time to improvement from the first event was 4 days (range: 1 to 154).

Monitor patients for signs and symptoms of diarrhea. Advise patients to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea while taking TRUQAP. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity.

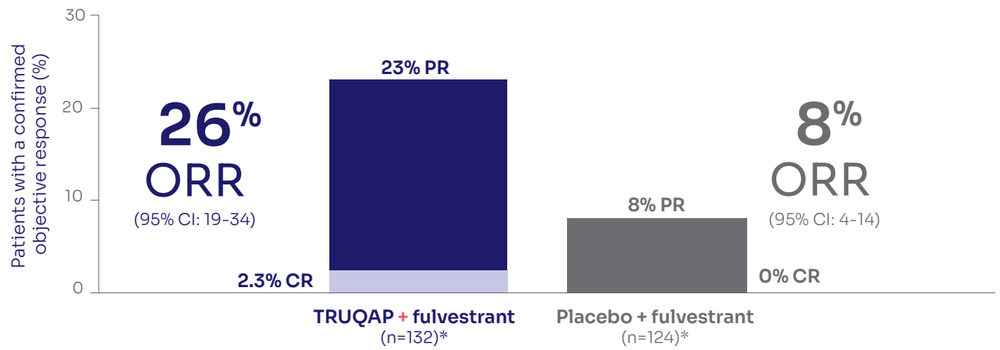
6

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

In combination with fulvestrant,

TRUQAP delivered an **objective response rate of 26%**—fulvestrant alone was 8%[1,18]

ORR in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations (investigator assessed)



- CBR=CR+PR+SD sustained for 24 weeks with TRUQAP + fulvestrant was 56% (n=155) —fulvestrant alone was 28% (n=134)[18]
- Median duration of response was 10.2 months (95% CI: 7.7-NC) with TRUQAP + fulvestrant —fulvestrant alone was 8.6 months (95% CI: 3.8-9.2)

*ORR is calculated based on patients with measurable disease at baseline.

CBR=clinical benefit rate; CR=complete response; NC=not calculable; PR=partial response; SD=stable disease.

Truqap™ capivasertib 160 mg • 200 mg tablets

In combination with fulvestrant,

TRUQAP™ (capivasertib) delivered **consistent PFS benefit across subgroups**[18]*

Investigator-assessed PFS by subgroup

Subgroup		TRUQAP + fulvestrant	Placebo + fulvestrant	HR (95% CI)
		n events/n patients (%)		
All patients		121/155 (78.1)	115/134 (86.4)	0.50 (0.38-0.65)
Age	<65 years	89/110 (80.9)	79/89 (88.8)	0.58 (0.43-0.79)
	≥65 years	32/45 (71.1)	36/45 (80)	0.53 (0.33-0.86)
Menopausal status	Pre/peri	19/23 (82.6)	25/29 (86.2)	0.83 (0.45-1.50)
	Post	100/130 (76.9)	90/105 (85.7)	0.49 (0.37-0.66)
Race	Asian	35/48 (72.9)	30/35 (85.7)	0.59 (0.36-0.96)
	White	60/75 (80)	65/76 (85.5)	0.59 (0.42-0.84)
	Other	26/32 (81.3)	20/23 (87)	0.41 (0.22-0.75)
Bone-only metastases	Yes	17/25 (68)	13/16 (81.3)	0.47 (0.23-1.00)
	No	104/130 (80)	102/118 (86.4)	0.58 (0.44-0.76)
Liver metastases	Yes	59/70 (84.3)	50/53 (94.3)	0.47 (0.32-0.70)
	No	62/85 (72.9)	65/81 (80.2)	0.57 (0.40-0.81)
Visceral metastases	Yes	84/103 (81.6)	85/98 (86.7)	0.60 (0.45-0.82)
	No	37/52 (71.2)	30/36 (83.3)	0.47 (0.29-0.78)
Endocrine resistance†	Primary	47/60 (78.3)	46/55 (83.6)	0.56 (0.37-0.85)
	Secondary	74/95 (77.9)	69/79 (87.3)	0.56 (0.40-0.78)
Prior use of CDK4/6i	Yes	93/114 (81.6)	85/94 (90.4)	0.49 (0.36-0.66)
	No	28/41 (68.3)	30/40 (75)	0.65 (0.38-1.08)
Prior chemotherapy for aBC or mBC	Yes	25/30 (83.3)	20/23 (87)	0.55 (0.31-1.01)
	No	96/125 (76.8)	95/111 (85.6)	0.56 (0.42-0.74)

*Exploratory analysis of prespecified subgroups. Study was not powered to show statistical significance across subgroups.[18]

†Per ESO-ESMO guidelines: Primary endocrine resistance=relapse while on the first 2 years of adjuvant ET, or PD within first 6 months of 1L ET for mBC, while on ET. Secondary resistance=relapse while on adjuvant ET after the first 2 years, or relapse within 12 months of completing adjuvant ET, or PD ≥6 months after initiating ET for mBC, while on ET.[19]

IMPORTANT SAFETY INFORMATION (continued)

Cutaneous Adverse Reactions

Cutaneous adverse reactions, which can be severe, including erythema multiforme (EM), palmar-plantar erythrodysesthesia, and drug reaction with eosinophilia and systemic symptoms (DRESS), occurred in patients who received TRUQAP (n=355).

Cutaneous adverse reactions occurred in 58% of patients. Grade 3 or 4 cutaneous adverse reactions occurred in 17% of patients receiving TRUQAP. EM occurred in 1.7% of patients and DRESS occurred in 0.3% of patients. Dose reduction was required in 7% of patients and 7% of patients permanently discontinued TRUQAP due to cutaneous adverse reactions.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

In CAPItello-291,

Baseline characteristics were balanced between treatment arms[18]

In patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations

Baseline characteristics		TRUQAP + fulvestrant (n=155)	Placebo + fulvestrant (n=134)
Median age, years (range)		58 (36-84)	60 (34-90)
Female, n (%)		153 (98.7)	134 (100)
Postmenopausal, n (%)		130 (83.9)	105 (78.4)
Race, n (%)	White	75 (48.4)	76 (56.7)
	Asian	48 (31)	35 (26.1)
	Black	2 (1.3)	1 (0.7)
	Other	30 (19.4)	22 (16.4)
Disease characteristics			
Metastatic sites, n (%)	Bone only	25 (16.1)	16 (11.9)
	Liver	70 (45.2)	53 (39.6)
	Visceral	103 (66.5)	98 (73.1)
Endocrine resistance,† n (%)	Primary	60 (38.7)	55 (41)
	Secondary	95 (61.3)	79 (59)
Prior treatments			
No. of prior ET for aBC, n (%)	0	13 (8.4)	20 (14.9)
	1	131 (84.5)	96 (71.6)
	2	11 (7.1)	18 (13.4)
Previous CDK4/6i, n (%)	Adjuvant/neoadjuvant	0	2 (1.5)
	aBC	113 (72.9)	91 (67.9)
Previous chemotherapy, n (%)	Adjuvant/neoadjuvant	79 (51)	67 (50)
	aBC	30 (19.4)	23 (17.2)
Alterations[18]			
***PIK3CA*,* n (%)**		116 (74.8)	103 (76.9)
***AKT1* (only), n (%)**		18 (11.6)	15 (11.2)
***PTEN* (only), n (%)**		21 (13.5)	16 (11.9)

76% of patients with alterations in CAPItello-291 **had a *PIK3CA* alteration**[1,18]

*Includes patients whose tumors have both *PIK3CA* + *AKT1* and *PIK3CA* + *PTEN* alterations.

ESO-ESMO=European School of Oncology-European Society for Medical Oncology; PD=progressive disease.

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In CAPItello-291,

Adverse reactions were mostly Grade 1 or 2[1]*

ARs in ≥10% (all Grades) of patients

Adverse reactions	TRUQAP + fulvestrant (n=155)		Placebo + fulvestrant (n=133)	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders				
Diarrhea	77	12	19	0.8
Nausea	35	1.3	14	0.8
Stomatitis†	25	1.9	5	0
Vomiting	21	1.9	7	0.8
Skin and subcutaneous tissue disorders				
Cutaneous adverse reactions‡	56	15	16	0.8
General disorders and administration site conditions				
Fatigue†	38	1.9	27	1.5
Metabolism and nutrition disorders				
Hyperglycemia§	19	1.9	4.5	0
Decreased appetite	17	0	8	0.8
Nervous system disorders				
Headache†	17	0	13	0.8
Infections and infestations				
Urinary tract infections†	14	0.6	5	0
Renal and urinary disorders				
Renal injury‖	11	2.6	1.5	0.8

CAPItello-291 allowed for patients with HbA1C <8% and diabetes not requiring insulin

Other clinically relevant ARs reported in fewer than 10% of patients in the TRUQAP™ (capivasertib) + fulvestrant group included: Anemia, hypersensitivity (including anaphylactic reaction), dysgeusia, dyspepsia, pneumonia, and pyrexia

*134 patients with *PIK3CA/AKT1/PTEN* alterations were randomized to the placebo + fulvestrant arm. The safety population in this arm (n=133) excluded 1 patient who was randomized but did not receive treatment.

†Includes other related terms.

‡Cutaneous adverse reaction includes butterfly rash, dermatitis, allergic dermatitis, dry skin, eczema, erythema multiforme, hand dermatitis, palmar-plantar erythrodysesthesia syndrome, pruritus, rash, erythematous rash, maculopapular rash, papular rash, skin discoloration, skin fissures, skin reaction, skin ulcer, urticaria, purpura, erythema, and drug eruption.

§Hyperglycemia includes hyperglycemia, blood glucose increased, glycosylated hemoglobin increased, glucose tolerance impaired, and diabetes mellitus.

‖Renal injury includes acute kidney injury, renal failure, renal impairment, glomerular filtration rate decreased, increased creatinine and proteinuria.

IMPORTANT SAFETY INFORMATION (continued)

Cutaneous Adverse Reactions

Monitor patients for signs and symptoms of cutaneous adverse reactions. Early consultation with a dermatologist is recommended. Withhold, dose reduce, or permanently discontinue TRUQAP based on severity.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

In CAPItello-291,

Safety and tolerability profile[1]

Laboratory abnormalities (≥10% of patients)

Laboratory abnormality	TRUQAP + fulvestrant*		Placebo + fulvestrant†	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Glucose metabolism				
Increased random glucose	58	9	17	0
Increased fasting glucose	37	0.6	29	0
Hematology				
Decreased lymphocytes	49	11	14	2.3
Decreased hemoglobin	47	2	22	2.3
Decreased leukocytes	35	0.6	23	0
Decreased neutrophils	25	1.9	16	0.8
Decreased platelets	12	1.9	6	0.8
Other				
Increased triglycerides	30	0.7	22	0.9
Increased alanine aminotransferase	23	2.6	13	0
Electrolytes/Renal				
Decreased corrected calcium	19	0.6	8	0
Increased creatinine	19	1.3	4.6	0.8
Decreased potassium	17	4.5	8	0

Rates of dose discontinuation/reduction due to ARs[1]

TRUQAP discontinuation due to ARs occurred in 10% of patients

- The most frequent (≥2%) AR leading to discontinuation was cutaneous adverse reactions (6%)

Dose reductions due to ARs occurred in 21% of patients receiving TRUQAP + fulvestrant

- The most frequent (≥2%) ARs leading to dose reduction were diarrhea and cutaneous adverse reactions (8% each)

Had a **low rate of discontinuation** due to ARs (10%)

Among 155 patients who received TRUQAP, 61% were exposed for 6 months or longer, and 30% were exposed for greater than 1 year.

*The denominator used to calculate the rate varied from 129 to 155 based on the number of patients with a baseline value and at least one post-treatment value.

†The denominator used to calculate the rate varied from 109 to 131 based on the number of patients with a baseline value and at least one post-treatment value.

AR=adverse reaction.

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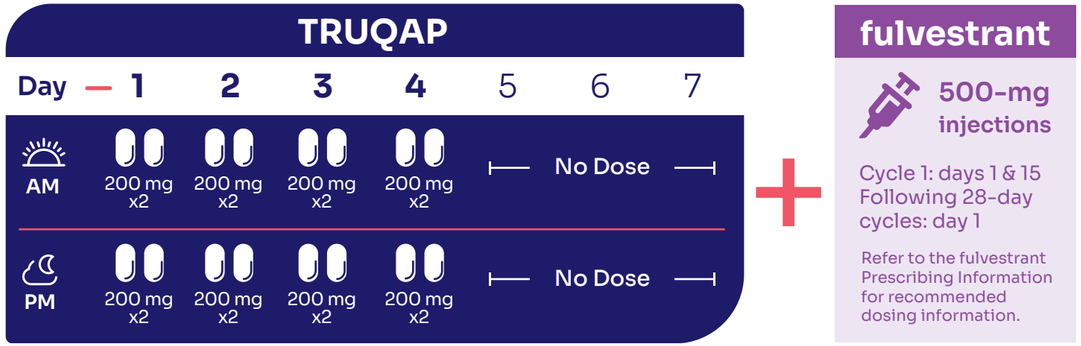
In combination with fulvestrant,

TRUQAP™ (capivasertib) has an optimized dosing schedule[1]

Benefit-risk balance achieved with 4 days on, 3 days off, every week

The recommended dose of TRUQAP is
400 mg taken orally twice daily, approximately 12 hours apart



+

fulvestrant

500-mg injections

Cycle 1: days 1 & 15
Following 28-day cycles: day 1

Refer to the fulvestrant Prescribing Information for recommended dosing information.

Select patients based on an FDA-approved test for detection of *PIK3CA*, *AKT1*, and *PTEN* alterations.

Advise patients on the following when taking TRUQAP:

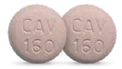
- Can be taken with or without food
- Swallow whole
- Do not chew, crush, or split tablets prior to swallowing. Do not take tablets that are broken, cracked, or otherwise not intact
- Do not consume grapefruit products
- If a patient misses a dose within 4 hours of the scheduled time, instruct the patient to take the missed dose. If a patient misses a dose by more than 4 hours of the scheduled time, instruct the patient to skip the dose and take the next dose at its usual scheduled time
- If a patient vomits a dose, instruct the patient not to take an additional dose and to take the next dose at its usual scheduled time
- For pre-/perimenopausal women, administer an LHRH agonist according to current clinical practice standards. For men, consider administering an LHRH agonist according to current clinical practice standards

Continue treatment until disease progression or unacceptable toxicity occurs.

In combination with fulvestrant,

Recommended dosage modification of TRUQAP for ARs[1]

First dose reduction
320 mg twice daily for 4 days followed by 3 days off



Two 160-mg tablets BID

Not actual size.

Second dose reduction
200 mg twice daily for 4 days followed by 3 days off

One 200-mg tablet BID

Not actual size.

- Permanently discontinue TRUQAP if unable to tolerate the second dose reduction
- Avoid concomitant use with strong CYP3A inhibitors. If concomitant use with a strong CYP3A inhibitor cannot be avoided, reduce the dosage of TRUQAP to 320 mg orally twice daily for 4 days followed by 3 days off
- When concomitantly used with a moderate CYP3A inhibitor, reduce the dosage of TRUQAP to 320 mg orally twice daily for 4 days followed by 3 days off
- After discontinuation of a strong or moderate CYP3A inhibitor, resume the TRUQAP dosage (after 3 to 5 half-lives of the inhibitor) that was taken prior to initiating the strong or moderate CYP3A inhibitor
- Avoid concomitant use of TRUQAP with strong or moderate CYP3A inducers

LHRH=luteinizing hormone-releasing hormone.

IMPORTANT SAFETY INFORMATION (continued)

Hyperglycemia

Evaluate fasting blood glucose (FG) and hemoglobin A1C (HbA1C) and optimize blood glucose prior to treatment. Before initiating TRUQAP, inform patients about TRUQAP's potential to cause hyperglycemia and to immediately contact their healthcare professional if hyperglycemia symptoms occur (eg, excessive thirst, urinating more often than usual or greater amount of urine than usual, or increased appetite with weight loss). Evaluate FG at least every two weeks during the first month and at least once a month starting from the second month, prior to the scheduled dose of TRUQAP. Monitor HbA1C every three months. Monitor FG more frequently during treatment with TRUQAP in patients with a medical history of diabetes mellitus and in patients with risk factors for hyperglycemia such as obesity (BMI ≥ 30), elevated FG of >160 mg/dL (>8.9 mmol/L), HbA1C at or above the upper limit of normal, use of concomitant systemic corticosteroids, or intercurrent infections.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

Truqap™ capivasertib
160 mg • 200 mg tablets

Recommended dosage modifications for ARs[1]

Hyperglycemia	
FG > ULN–160 mg/dL or FG > ULN–8.9 mmol/L or HbA1C > 7%	Consider initiation or intensification of oral antidiabetic treatment
FG 161–250 mg/dL or FG 9–13.9 mmol/L	Withhold TRUQAP™ (capivasertib) until FG decrease ≤160 mg/dL (or ≤8.9 mmol/L) If recovery occurs in ≤28 days, resume TRUQAP at same dose If recovery occurs in >28 days, resume TRUQAP at one lower dose
FG 251–500 mg/dL or FG 14–27.8 mmol/L	Withhold TRUQAP until FG decrease ≤160 mg/dL (or ≤8.9 mmol/L) If recovery occurs in ≤28 days, resume TRUQAP at one lower dose If recovery occurs in >28 days, permanently discontinue TRUQAP
FG > 500 mg/dL or FG > 27.8 mmol/L or life-threatening sequelae of hyperglycemia at any FG level	For life-threatening sequelae of hyperglycemia or if FG persists at ≥500 mg/dL after 24 hours, permanently discontinue TRUQAP If FG ≤500 mg/dL (or ≤27.8 mmol/L) within 24 hours, then follow the guidance in the table for the relevant grade

Consider consultation with a healthcare practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.

Diarrhea*	
Grade 2	Withhold TRUQAP until recovery to ≤Grade 1 If recovery occurs in ≤28 days, resume TRUQAP at same dose or one lower dose as clinically indicated If recovery occurs in >28 days, resume at one lower dose as clinically indicated For recurrence, reduce TRUQAP by one lower dose
Grade 3	Withhold TRUQAP until recovery to ≤Grade 1 If recovery occurs in ≤28 days, resume TRUQAP at same dose or one lower dose as clinically indicated If recovery occurs in >28 days, permanently discontinue TRUQAP
Grade 4	Permanently discontinue TRUQAP

*Grading according to CTCAE Version 5.0.

Cutaneous adverse reactions*	
Grade 2	Withhold TRUQAP until recovery to ≤Grade 1 Resume TRUQAP at the same dose Persistent or recurrent: reduce TRUQAP by one lower dose
Grade 3	Withhold TRUQAP until recovery to ≤Grade 1 If recovery occurs in ≤28 days, resume TRUQAP at same dose If recovery occurs in >28 days, resume TRUQAP at one lower dose For recurrent Grade 3, permanently discontinue TRUQAP
Grade 4	Permanently discontinue TRUQAP

Monitor patients for signs and symptoms of cutaneous adverse reactions. Early consultation with a dermatologist is recommended. Withhold, dose reduce, or permanently discontinue TRUQAP based on severity.

Other adverse reactions*	
Grade 2	Withhold TRUQAP until recovery to ≤Grade 1 Resume TRUQAP at the same dose
Grade 3	Withhold TRUQAP until recovery to ≤Grade 1 If recovery occurs in ≤28 days, resume TRUQAP at same dose If recovery occurs in >28 days, resume TRUQAP at one lower dose
Grade 4	Permanently discontinue TRUQAP

*Grading according to CTCAE Version 5.0.

CTCAE=Common Terminology Criteria for Adverse Events; FG=fasting glucose; ULN=upper limit of normal.

IMPORTANT SAFETY INFORMATION (continued)

Embryo-Fetal Toxicity

Based on findings from animals and mechanism of action, TRUQAP can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRUQAP and for 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRUQAP and for 4 months after the last dose.

TRUQAP is used in combination with fulvestrant. Refer to the full Prescribing Information of fulvestrant for pregnancy and contraception information.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

Truqap™ capivasertib 160 mg • 200 mg tablets

AstraZeneca Access 360™

Helping patients access the care they need

The AstraZeneca Access 360™ program provides personal support to help streamline access and reimbursement for TRUQAP

Access 360 provides:

- **Assistance with understanding patient insurance coverage and pharmacy options**
- **Prior authorization support**
- **Claims and appeal process support**
- **Eligibility requirements and enrollment assistance with AstraZeneca's Patient Savings Programs**
- **Referrals to AZ&Me™ Prescription Savings Program, AstraZeneca's patient assistance program**
- **Information about independent charitable patient assistance foundations**

To learn more about the Access 360 program, please call 1-844-ASK-A360 (1-844-275-2360), Monday through Friday, 8 AM - 6 PM ET or visit www.MyAccess360.com

TRUQAP Patient Savings Program

The TRUQAP Patient Savings Program can help eligible commercially insured patients with their out-of-pocket costs

PATIENTS MAY PAY AS LITTLE AS

$0*

PER MONTH

- **Patients may pay as little as $0 per month for TRUQAP.** There are no income requirements to participate in the program
- You can help enroll your patients in the program and file claims on their behalf. For more information and eligibility requirements, visit **AstraZenecaSpecialtySavings.com** or call AstraZeneca Access 360™ at 1-844-ASK-A360 (1-844-275-2360)*

*Terms and conditions apply. See site for full eligibility and terms of use.

TRUQAP acquisition information

Connect with select Specialty Pharmacy Partners (SPPs) and Specialty Distributors. These SPPs also provide support to help patients with their prescribed treatments

Specialty Pharmacy Providers

BIOLOGICS BY MCKESSON
p: 1-800-850-4306
f: 1-800-823-4506
biologicsinc.com

ONCO360 ONCOLOGY PHARMACY
p: 1-877-662-6633
f: 1-877-662-6355
onco360.com

Specialty Distributors

AMERISOURCEBERGEN

ASD Healthcare
p: 1-800-746-6273
f: 1-800-547-9413
asdhealthcare.com

Oncology Supply
p: 1-800-633-7555
f: 1-800-248-8205
oncologysupply.com

CARDINAL HEALTH SPECIALTY DISTRIBUTION
p: 1-855-740-1871
f: 1-888-345-4916
specialtyonline.cardinalhealth.com

CURASCRIPT SD
p: 1-877-599-7748
f: 1-800-862-6208
curascriptsd.com

DAKOTA DRUG, INC.
p: 1-866-210-5887
f: 1-763-421-0661
dakdrug.com

DMS PHARMACEUTICAL
p: 1-877-788-1100
f: 1-847-518-1105
dmspharma.com

MCKESSON SPECIALTY

McKesson Specialty Health (MD Offices)
p: 1-800-482-6700
f: 1-800-289-9285
mscs.mckesson.com

McKesson Plasma and Biologics (Hospitals, IDNs, VA)
p: 1-877-625-2566
f: 1-888-752-7626
mckesson.com/plasmabiologics

If you have any questions regarding TRUQAP acquisition or reimbursement, please contact us:

1-844-ASK-A360
(1-844-275-2360)

1-844-FAX-A360
(1-844-329-2360)

www.Access360.com

Access360@AstraZeneca.com

One MedImmune Way, Gaithersburg, MD 20878

IMPORTANT SAFETY INFORMATION ABOUT TRUQAP™ (capivasertib) tablets

TRUQAP is contraindicated in patients with severe hypersensitivity to TRUQAP or any of its components.

Hyperglycemia

Severe hyperglycemia, associated with ketoacidosis, has occurred in patients treated with TRUQAP. The safety of TRUQAP has not been established in patients with Type I diabetes or diabetes requiring insulin. Patients with insulin-dependent diabetes were excluded from CAPItello-291.

Hyperglycemia occurred in 18% of patients treated with TRUQAP (n= 355). Grade 3 (insulin therapy initiated; hospitalization indicated) or Grade 4 (life-threatening consequences; urgent intervention indicated) hyperglycemia occurred in 2.8% of patients. Diabetic ketoacidosis occurred in 0.3% of patients and diabetic metabolic decompensation in 0.6% of patients. Dose reduction for hyperglycemia was required in 0.6% and permanent discontinuation was required in 0.6% of patients. The median time to first occurrence of hyperglycemia was 15 days (range: 1 to 367).

In the 65 patients with hyperglycemia, 45% required treatment with anti-hyperglycemic medication (insulin in 15% and metformin in 29%). Of the 29 patients who required anti-hyperglycemic medication during treatment with TRUQAP, 66% (19/29) remained on these medications at treatment discontinuation or last follow-up.

Evaluate fasting blood glucose (FG) and hemoglobin A1C (HbA1C) and optimize blood glucose prior to treatment. Before initiating TRUQAP, inform patients about TRUQAP's potential to cause hyperglycemia and to immediately contact their healthcare professional if hyperglycemia symptoms occur (eg, excessive thirst, urinating more often than usual or greater amount of urine than usual, or increased appetite with weight loss). Evaluate FG at least every two weeks during the first month and at least once a month starting from the second month, prior to the scheduled dose of TRUQAP. Monitor HbA1C every three months. Monitor FG more frequently during treatment with TRUQAP in patients with a medical history of diabetes mellitus and in patients with risk factors for hyperglycemia such as obesity (BMI ≥ 30), elevated FG of > 160 mg/dL (> 8.9 mmol/L), HbA1C at or above the upper limit of normal, use of concomitant systemic corticosteroids, or intercurrent infections.

If a patient experiences hyperglycemia after initiating treatment with TRUQAP, monitor FG as clinically indicated, and at least twice weekly until FG decreases to normal levels. During treatment with anti-hyperglycemic medication, continue monitoring FG at least once a week for 8 weeks, followed by once every 2 weeks and as clinically indicated. Consider consultation with a healthcare practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes. Withhold, dose reduce, or permanently discontinue TRUQAP based on severity.

Diarrhea

Severe diarrhea associated with dehydration occurred in patients who received TRUQAP (n=355).

Diarrhea occurred in 72% of patients. Grade 3 or 4 diarrhea occurred in 9% of patients. The median time to first occurrence was 8 days (range: 1 to 519). In the 257 patients with diarrhea, 59% required antidiarrheal medications to manage symptoms. Dose reductions were required in 8% of patients and 2% of patients permanently discontinued TRUQAP due to diarrhea. In patients with Grade ≥ 2 diarrhea (n=93) with at least 1 grade improvement (n=89), median time to improvement from the first event was 4 days (range: 1 to 154).

Monitor patients for signs and symptoms of diarrhea. Advise patients to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea while taking TRUQAP. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity.

Cutaneous Adverse Reactions

Cutaneous adverse reactions, which can be severe, including erythema multiforme (EM), palmar-plantar erythrodysesthesia, and drug reaction with eosinophilia and systemic symptoms (DRESS), occurred in patients who received TRUQAP (n=355).

Cutaneous adverse reactions occurred in 58% of patients. Grade 3 or 4 cutaneous adverse reactions occurred in 17% of patients receiving TRUQAP. EM occurred in 1.7% of patients and DRESS occurred in 0.3% of patients. Dose reduction was required in 7% of patients and 7% of patients permanently discontinued TRUQAP due to cutaneous adverse reactions.

Monitor patients for signs and symptoms of cutaneous adverse reactions. Early consultation with a dermatologist is recommended. Withhold, dose reduce, or permanently discontinue TRUQAP based on severity.

Embryo-Fetal Toxicity

Based on findings from animals and mechanism of action, TRUQAP can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRUQAP and for 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRUQAP and for 4 months after the last dose.

TRUQAP is used in combination with fulvestrant. Refer to the full Prescribing Information of fulvestrant for pregnancy and contraception information.

ADVERSE REACTIONS

Among the 355 patients who received TRUQAP in CAPItello-291, the most common (≥ 20%) adverse reactions, including laboratory abnormalities, were diarrhea (72%), cutaneous adverse reactions (58%), increased random glucose (57%), decreased lymphocytes (47%), decreased hemoglobin (45%), increased fasting glucose (37%), nausea and fatigue (35% each), decreased leukocytes (32%), increased triglycerides (27%), decreased neutrophils (23%), increased creatinine (22%), vomiting (21%), and stomatitis (20%).

In the 155 patients with *PIK3CA/AKT1/PTEN* alterations treated with TRUQAP + fulvestrant, dose reductions due to adverse reactions were reported in 21% of patients. Permanent TRUQAP discontinuation due to an adverse reaction occurred in 10% of patients. Dose interruptions of TRUQAP occurred in 39% of patients.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Avoid concomitant use with a strong CYP3A inhibitor. If concomitant use cannot be avoided, reduce the dose of TRUQAP and monitor patients for adverse reactions.

Moderate CYP3A Inhibitors: When concomitantly used with a moderate CYP3A inhibitor, reduce the dose of TRUQAP and monitor patients for adverse reactions.

Strong or Moderate CYP3A Inducers: Avoid concomitant use of TRUQAP with strong or moderate CYP3A inducers.

INDICATION AND USAGE

TRUQAP in combination with fulvestrant is indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN* alteration as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

Please see accompanying full Prescribing Information, including Patient Information for TRUQAP.

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, call 1-800-FDA-1088.

References: 1. TRUQAP™ (capivasertib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2023. **2.** Miricescu D, Totan A, Stanescu-Spinu II, Badoiu SC, Stefani C, Greabu M. *Int J Mol Sci*. 2020;22(1):173. doi:10.3390/ijms22010173 **3.** Hui R, de Boer R, Lim E, Yeo B, Lynch J. *Asia Pac J Clin Oncol*. 2021;17(suppl 1):3-14. doi:10.1111/ajco.13555 **4.** Cogliati V, Capici S, Pepe FF, et al. *Life (Basel)*. 2022;12(3):378. doi:10.3390/life12030378 **5.** Piqray® (alpelisib) [prescribing information]. Novartis Pharmaceuticals Corp; 2022. **6.** Afinitor® (everolimus) [prescribing information]. Novartis Pharmaceuticals Corp; 2022. **7.** Lynce F, Shajahan-Haq AN, Swain SM. *Pharmacol Ther*. 2018;191:65-73. doi:10.1016/j.pharmthera.2018.06.008 **8.** George MA, Qureshi S, Omene C, Toppmeyer DL, Ganesan S. *Front Oncol*. 2021;11:693104. doi:10.3389/fonc.2021.693104 **9.** Chang DY, Ma WL, Lu YS. *Ther Clin Risk Manag*. 2021;17:193-207. doi:10.2147/TCRM.S251668 **10.** Ribas R, Pancholi S, Guest SK, et al. *Mol Cancer Ther*. 2015;14(9):2035-2048. doi:10.1158/1535-7163.MCT-15-0143 **11.** Davies BR, Greenwood H, Dudley P, et al. *Mol Cancer Ther*. 2012;11(4):873-887. doi:10.1158/1535-7163.MCT-11-0824-T **12.** Hinz N, Jücker M. *Cell Commun Signal*. 2019;17(1):154. doi:10.1186/s12964-019-0450-3 **13.** Millis SZ, Ikeda S, Reddy S, Gatalica Z, Kurzrock R. *JAMA Oncol*. 2016;2(12):1565-1573. doi:10.1001/jamaoncol.2016.0891 **14.** Papadimitriou MC, Pazaiti A, Iliakopoulos K, Markouli M, Michalaki V, Papadimitriou CA. *Biochim Biophys Acta Mol Cell Res*. 2022;1869(12):119346. doi:10.1016/j.bbamcr.2022.119346 **15.** Osborne CK, Schiff R. *Annu Rev Med*. 2011;62:233-247. doi:10.1146/annurev-med-070909-182917 **16.** Manning BD, Toker A. *Cell*. 2017;169(3):381-405. doi:10.1016/j.cell.2017.04.001 **17.** FASLODEX® (fulvestrant) [prescribing information]. AstraZeneca Pharmaceuticals LP; 2020. **18.** Turner NC, Oliveira M, Howell SJ, et al. *N Engl J Med*. 2023;388:2058-2070. doi:10.1056/NEJMoa2214131 **19.** Cardoso F, Senkus E, Costa A, et al. *Ann Oncol*. 2018;29(8):1634-1657. doi:10.1093/annonc/mdy192

Truqap™
capivasertib
160 mg • 200 mg tablets

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In HR+/HER2- aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i

TRUQAP + fulvestrant: the first and only targeted combination to more than double mPFS vs fulvestrant alone in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations, most having received prior ET + CDK4/6i[1]

7.3 months mPFS
with TRUQAP + fulvestrant (n=155)[1]
(95% CI: 5.5–9.0)

vs

3.1 months mPFS
with fulvestrant (n=134)[1]
(95% CI: 2.0–3.7)

~2.5X mPFS

HR=0.50 (95% CI: 0.38–0.65; *P*<0.0001)

Low rate of discontinuation due to ARs (10%)[1]

To extend time on ET,

TEST for *PIK3CA*, *AKT1*, *PTEN*

TREAT with TRUQAP + fulvestrant[1]

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Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Patient Information for TRUQAP.

AstraZeneca