Pr Truqap™ capivasertib
160 mg • 200 mg tablets

Discover TRUQAP™

TRUQAP (capivasertib tablets), in combination with fulvestrant, is indicated for the treatment of adult females with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) locally advanced or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN* alterations following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.[1]

Guideline recommendations for capivasertib + fulvestrant

NCCN
CATEGORY 1

Preferred 2L therapy option for HR+/HER2- mBC with *PIK3CA/AKT1/PTEN* activating mutations in adults after disease progression or recurrence after one or more prior lines of endocrine therapy, including one line containing a CDK4/6 inhibitor.[2]

ASCO

2L treatment option for HR+/HER2- mBC appropriate for tumours harboring *PIK3CA* or *AKT1* mutations or *PTEN* inactivation.[3]

2L=second line; *AKT1*=serine/threonine protein kinase 1; ASCO=American Society of Clinical Oncology; CDK4/6=cyclin-dependent kinase 4 and 6; mBC=metastatic breast cancer; NCCN=National Comprehensive Cancer Network; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog.

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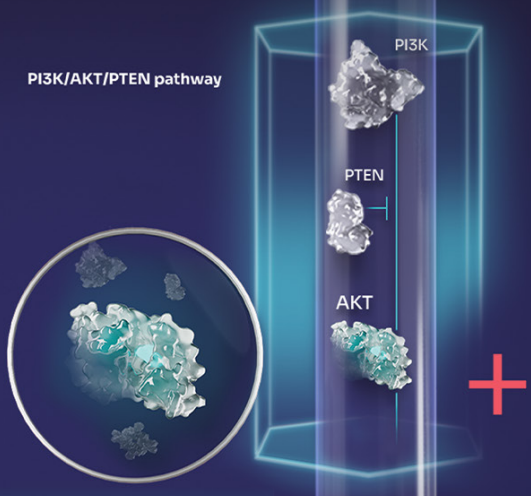
Discover: TRUQAP + fulvestrant combination

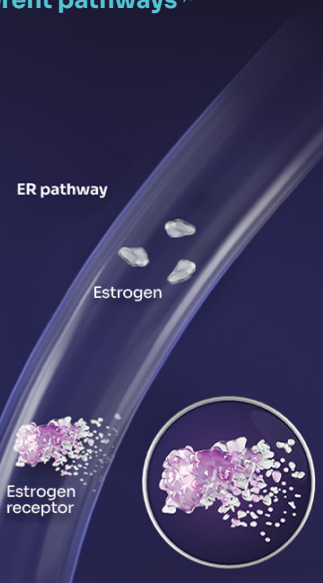
Mechanism of action

TRUQAP - the first and only AKT pathway inhibitor indicated in one or more alterations of *PIK3CA/AKT1/PTEN* in HR+/HER2- locally advanced or metastatic breast cancer, in combination with fulvestrant, a nonagonist estrogen receptor antagonist.[1,3-5]*

TRUQAP and fulvestrant work in different pathways[1,5]



TRUQAP is an inhibitor of the kinase activity of all 3 isoforms of serine/threonine kinase AKT (*AKT1*, *AKT2* and *AKT3*).†

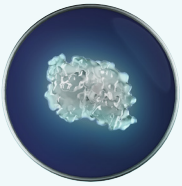


Fulvestrant is an ER antagonist that has a mode of action leading to downregulation of ER protein.†

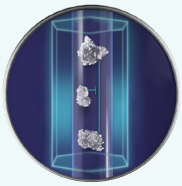
In vitro and *in vivo*, combined with fulvestrant, TRUQAP reduces the growth of ER+ breast cancer models.†

Adapted from the TRUQAP and Faslodex Product Monographs[1,5†]

In tumours, AKT activation occurs as a result of upstream activation by other signalling pathways and also through genetic alterations in *AKT1* phosphatase, *PTEN* and/or *PIK3CA*.[1†]



AKT



PI3K/AKT/PTEN pathway

AKT=serine/threonine protein kinases; *AKT1*=serine/threonine protein kinase 1; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; PI3K=phosphoinositide 3-kinase; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog.
*Comparative clinical significance has not been established.
†Clinical significance has not been established.

TRUQAP was studied in a global, phase 3, randomized, double-blind, multicenter, placebo-controlled trial (N=708)[1,6†]

CAPItello-291

289 patients (40.8%) in the overall population had tumours with *PIK3CA/AKT1/PTEN* alterations[1,6]

Select Inclusion Criteria:[1,6]

- HR+/HER2− (defined as IHC 0 or 1+, or IHC 2+/ISH−) locally advanced (inoperable) or metastatic breast cancer
- Men[‡] and pre-/post-menopausal women[§]
- Evidence of progression on prior AI-based treatment in the metastatic setting or recurrence on or within 12 months of completing (neo)-adjuvant treatment with an AI
- ≤2 lines of prior ET for locally advanced (inoperable) or metastatic disease
- ≤1 line of chemotherapy for locally advanced (inoperable) or metastatic disease
- Prior CDK4/6i allowed (at least 51% required)
- HbA1c <8.0% (63.9 mmol/mol) and diabetes not requiring insulin allowed

Randomized 1:1 (n=289)[1†]

(n=155)

TRUQAP
400 mg twice daily

+

fulvestrant
500 mg (2 injections)

TRUQAP and placebo: each dosed on Days 1 to 4 in each week of a 28-day treatment cycle.[1]

Fulvestrant: dosed on Days 1 and 15* of Cycle 1, and then on Day 1 of each cycle thereafter.[1,7]

(n=134)

placebo
400 mg twice daily

+

fulvestrant
500 mg (2 injections)

*Day 15 is Week 3 Day 1 of Cycle 1.

Stratification factors: Liver metastases, prior CDK4/6i, and region[1,6¶]

Dual primary endpoints

- Investigator-assessed PFS in:
  - overall population** and
  - subgroup with *PIK3CA/AKT1/PTEN*-altered tumours

Key secondary endpoints

- OS
- ORR

To learn about patient demographics and baseline characteristics from the CAPItello-291 trial, click the QR code.

AI=aromatase inhibitor; *AKT1*=serine/threonine protein kinase 1; CDK4/6=cyclin-dependent kinase 4 and 6; HbA1c=hemoglobin A1c; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; IHC=immunohistochemistry; ISH=*in situ* hybridization; LHRH=luteinizing hormone-releasing hormone; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog.

† In CAPItello-291, a total of 708 patients were randomized 1:1 to receive either 400 mg of TRUQAP (N=355) or placebo (N=353) given twice daily for 4 days followed by 3 days off treatment each week of a 28-day treatment cycle. Fulvestrant 500 mg was administered on Cycle 1 Days 1 and 15 and then at Day 1 of a 28-day cycle. In total, 289 patients had tumours with eligible *PIK3CA/AKT1/PTEN* alterations.

‡ TRUQAP is not indicated in men.

§ Pre- or peri-menopausal women also received an LHRH agonist for the duration of the study treatment.

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

** TRUQAP is only indicated for patients with *PIK3CA/AKT1/PTEN* alterations.

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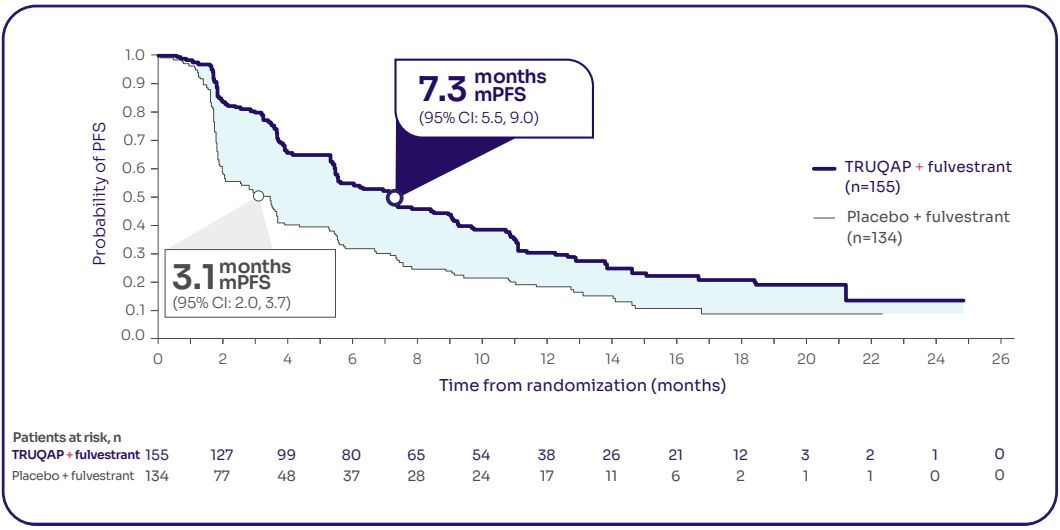
TRUQAP + fulvestrant demonstrated statistically significant improvement in PFS vs. placebo + fulvestrant*

TRUQAP + fulvestrant demonstrated:

50% reduction in risk of progression or death with TRUQAP + fulvestrant
vs. fulvestrant alone

HR=0.50† (95% CI: 0.38, 0.65; *p*<0.001‡)

Number of events (%):
TRUQAP + fulvestrant 121 (78.1)
vs. fulvestrant 115 (85.8)



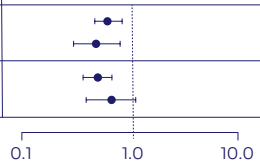
Adapted from the TRUQAP Product Monograph[1]

AKT1=serine/threonine protein kinase 1; CI=confidence interval; HR=hazard ratio; mPFS=median PFS; PFS=progression-free survival; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog; RECIST=Response Evaluation Criteria in Solid Tumours.
*Analysis was performed by investigator assessment determined by RECIST 1.1.
†Stratified Cox proportional hazards model. A hazard ratio <1 favours capivasertib + fulvestrant.
‡Stratified log-rank test.

Subgroup analysis of PFS in *PI3KCA/AKT1/PTEN*-altered tumours (exploratory analyses)

Improvement in PFS observed across all pre-specified subgroups

Subgroup		TRUQAP + fulvestrant	Placebo + fulvestrant	Hazard ratio (95% CI)
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)
Prior use of CDK4/6 inhibitors	Yes	93/114 (81.6%)	85/94 (90.4%)	0.49 (0.36, 0.66)
	No	28/41 (68.3%)	30/40 (75.0%)	0.65 (0.38, 1.08)



Adapted from Turner NC, *et al*. 2023.[8]

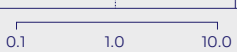
Improvement in PFS for patients treated with TRUQAP + fulvestrant was also observed in the non-altered tumour population which comprised patients with a confirmed non-altered tumour and those with no testing result available.[1]*

71% of patients received prior CDK4/6i (total population in patients with *PIK3CA/AKT1/PTEN*-altered tumours)[1]

Additional data from subgroup analysis of PFS

The data that follows is from an exploratory analysis and should be interpreted with caution.

Subgroup		TRUQAP + fulvestrant	Placebo + fulvestrant	Hazard ratio (95% CI)
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%)	0.53 (0.33, 0.86)
Race	Asian	35/48 (72.9%)	30/35 (85.7%)	0.59 (0.36, 0.96)
	White	60/75 (80.0%)	65/76 (85.5%)	0.59 (0.42, 0.84)
	Other	26/32 (81.3%)	20/23 (87.0%)	0.41 (0.22, 0.75)
Region	United States, Canada, Western Europe, Australia, and Israel	67/80 (83.8%)	68/76 (89.5%)	0.48 (0.34, 0.68)
	Latin America, Eastern Europe, and Russia	21/29 (72.4%)	18/24 (75.0%)	0.80 (0.43, 1.52)
	Asia	33/46 (71.7%)	29/34 (85.3%)	0.58 (0.35, 0.96)
Menopausal status (females only)	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)
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)
Bone-only metastases	Yes	17/25 (68.0%)	13/16 (81.3%)	0.47 (0.23, 1.00)
	No	104/130 (80.0%)	102/118 (86.4%)	0.58 (0.44, 0.76)
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 chemotherapy for locally advanced/ metastatic disease	Yes	25/30 (83.3%)	20/23 (87.0%)	0.55 (0.31, 1.01)
	No	96/125 (76.8%)	95/111 (85.6%)	0.56 (0.42, 0.74)



Adapted from Turner NC, *et al*. 2023.[8]

AKT1=serine/threonine protein kinase 1; CDK4/6=cyclin-dependent kinase 4 and 6; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; PFS=progression-free survival; *PTEN*=phosphatase and tensin homolog.
*TRUQAP is only indicated for patients with *PIK3CA/AKT1/PTEN* alterations.

Safety profile for the CAPItello-291 trial

Adverse drug reactions* occurring in ≥10% (All Grades) of patients

Adverse drug reaction frequencies presented in the table below are those considered to **be causally related to treatment based on assessment by the investigator.**

System Organ Class (SOC) / Adverse reactions	TRUQAP + fulvestrant n=355		Placebo + fulvestrant n=350	
	All Grades (%)	Grade 3-4 (%)	All Grades (%)	Grade 3-4 (%)
Gastrointestinal disorders				
Diarrhea[a]	239 (67.3)	33 (9.3)	46 (13.1)	0
Nausea	97 (27.3)	2 (0.6)	37 (10.6)	2 (0.6)
Vomiting	56 (15.8)	5 (1.4)	9 (2.6)	2 (0.6)
Stomatitis[b]	58 (16.3)	6 (1.7)	11 (3.1)	0
General disorders and administration site conditions				
Fatigue[c]	78 (22.0)	5 (1.4)	47 (13.4)	0
Skin and subcutaneous tissue disorders				
Cutaneous adverse reactions[d]	165 (46.5)	60 (16.9)	38 (10.9)	1 (0.3)
Metabolism and nutrition disorders				
Hyperglycemia[e]	50 (14.1)	8 (2.3)	7 (2.0)	1 (0.3)
Decreased appetite	38 (10.7)	1 (0.3)	8 (2.3)	1 (0.3)

Adapted from the TRUQAP Product Monograph[1]

Please consult the TRUQAP Product Monograph for a full listing of adverse drug reactions.

MedDRA=Medical Dictionary for Regulatory Activities; PT=MedDRA Preferred Term.
*Adverse drug reaction frequencies are those considered to be causally related treatment based on assessment by the investigator.

Median time to first event for selected adverse reactions

Among TRUQAP-treated patients who experienced one of the adverse reactions below, the median time to first event was[1]

Management of adverse drug reactions

Please refer to the Product Monograph for all recommendations and recommended dose modifications for hyperglycemia, diarrhea, cutaneous and other adverse drug reactions. Management of adverse drug reactions may require temporary dosing interruption, reduction and/or discontinuation of TRUQAP. The dosing reduction recommendations are listed in the Product Monograph. A maximum of 2 dosing reductions are recommended after which the patient should be discontinued from treatment with TRUQAP.[1]

To learn about TRUQAP dose modifications, click the QR code.

Dose reductions

18.6%

of TRUQAP + fulvestrant patients had their dose reduced due to adverse reactions

The most frequent adverse reactions (≥2%) leading to dose reductions

- Diarrhea (7.9%)
- Cutaneous adverse reactions (6.5%)

Low discontinuation rate reported

10.4%

of TRUQAP + fulvestrant patients discontinued due to adverse reactions

The most frequent adverse reactions (≥2%) leading to treatment discontinuation

- Cutaneous adverse reactions (6.5%)
- Diarrhea (2.0%)
- Vomiting (2.0%)

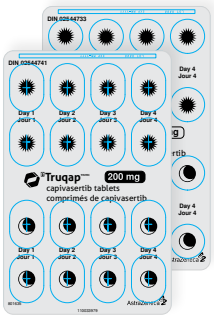
a Diarrhea includes PTs of diarrhea and frequent bowel movements.
b Stomatitis includes PTs of stomatitis, aphthous ulcer, lip ulceration, mouth ulceration and mucosal inflammation.
c Fatigue includes PTs of fatigue, malaise and asthenia.
d Cutaneous adverse reaction includes the PTs of dermatitis allergic, acne, butterfly rash, dermatitis, drug reaction with eosinophilia and systemic symptoms, dry skin, eczema, erythema multiforme, papule, pruritus, rash, rash erythematous, rash follicular, rash macular, rash maculo-papular, rash papular, rash pruritic, skin discoloration, skin fissures, skin hyperpigmentation, skin reaction, skin ulcer, urticaria, rash pustular, purpura, erythema, drug eruption, dermatitis exfoliative generalized.
e Hyperglycemia includes PTs of hyperglycemia and blood glucose increased.

TRUQAP's 4 days on / 3 days off weekly dosing schedule

The recommended dose of TRUQAP is:

- **400 mg (two 200 mg tablets) taken orally twice daily,** approximately 12 hours apart (total daily dose of 800 mg),
- **for 4 days followed by 3 days off treatment.**

Treatment with TRUQAP should continue until disease progression or unacceptable toxicity occurs.[1]



Morning Dose
Take 2 x 200 mg tablets

Evening Dose
Take 2 x 200 mg tablets

Blister packs are labelled to help patients keep track of the 4 consecutive days part of TRUQAP's weekly dosing schedule (for select doses of 400 mg and 320 mg twice daily).

TRUQAP + fulvestrant dosing

TRUQAP

Day	1	2	3	4	5	6	7
AM	200 mg x2	200 mg x2	200 mg x2	200 mg x2	No Dose		
PM	200 mg x2	200 mg x2	200 mg x2	200 mg x2	No Dose		

+

fulvestrant

Recommended dose of fulvestrant is

500 mg
(2 injections [each injection = 250 mg/5 mL])

on Days 1 and 15† of Cycle 1 and on Day 1 of each cycle thereafter.

TRUQAP and fulvestrant are both started on the same day (Day 1 Cycle* 1).

Discuss the choice of a start date with your patients.

*Each cycle has a duration of 28 days.
† Day 15 is Week 3 Day 1 of Cycle 1.

EXAMPLE FOR WEEK 1 CYCLE 1						
MONDAY	**TUESDAY**	**WEDNESDAY**	**THURSDAY**	**FRIDAY**	**SATURDAY**	**SUNDAY**
TRUQAP + fulvestrant	TRUQAP	TRUQAP	TRUQAP			

Correct glucose levels in patients with abnormal glucose levels before initiating TRUQAP. Due to the potential of TRUQAP to cause hyperglycemia, patients should be tested for fasting blood glucose (FG) levels and HbA1c prior to treatment and at regular intervals during treatment.

In pre-/peri-menopausal women, TRUQAP + fulvestrant should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.[1]

Please see the TRUQAP Product Monograph for complete dosing and administration information including dosing considerations.

Important safety information for TRUQAP

Clinical use:

No pediatric data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

Safety analyses suggest a higher incidence of severe adverse reactions in those >65 years of age compared to younger patients.

Contraindications:

TRUQAP is contraindicated in patients who are hypersensitive to capivasertib or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

Most serious warnings and precautions:

Cutaneous adverse reactions including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Erythema Multiforme (EM) and palmar-plantar erythrodysesthesia. Patients should be monitored for signs and symptoms of cutaneous reactions and based on severity, TRUQAP dosing may be interrupted, reduced, or permanently discontinued. Early consultation with a dermatologist is recommended.

Hyperglycemia, including diabetic ketoacidosis. Some cases have been fatal. Patients must be tested for fasting blood glucose (FG) levels and HbA1c prior to treatment with TRUQAP and at regular intervals during treatment. Blood glucose should be optimized prior to initiation of treatment. Before initiating treatment with TRUQAP, patients should be informed about the potential of TRUQAP to cause hyperglycemia, and to contact their healthcare professional immediately if hyperglycemia symptoms occur. Consider consultation with a healthcare practitioner with expertise in the treatment of hyperglycemia. Based on the severity of hyperglycemia, TRUQAP dosing may be interrupted, reduced, or permanently discontinued.

Severe diarrhea associated with dehydration and acute kidney injury. Advise patients to start antidiarrheal treatment at the first sign of diarrhea and to increase oral fluids if diarrhea symptoms occur while taking TRUQAP. Based on the severity of diarrhea, TRUQAP may be interrupted, reduced, or permanently discontinued.

Other relevant warnings and precautions:

- Caution when driving or operating machinery
- Testing for fasting blood glucose (FG) levels and HbA1c
- Monitoring of ketones and other metabolic parameters
- Use effective contraception during treatment and for at least 4 weeks after completion of treatment with TRUQAP
- Rule out pregnancy before treatment and avoid becoming pregnant
- Do not breastfeed
- Teratogenic risk

For more information:

Please consult the TRUQAP Product Monograph at truqap-en.azpm.ca for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling 1-800-668-6000.

References: 1. TRUQAP Product Monograph. AstraZeneca Canada Inc. January 3, 2025. **2.** National Comprehensive Cancer Network®. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Breast Cancer. Version 2.2025 March 5, 2025. **3.** Burstein HJ, *et al*. Endocrine and Targeted Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer—Capivasertib-Fulvestrant: ASCO Rapid Recommendation Update. *J Clin Oncol* 2024;42:1450-1453. **4.** Data on file. **5.** FASLODEX Product Monograph. AstraZeneca Canada Inc. November 15, 2019. **6.** Turner NC, *et al*. Capivasertib in hormone receptor-positive advanced breast cancer. *N Engl J Med*. 2023;388(22):2058-2070. **7.** Data on file. **8.** Turner NC, *et al*. Capivasertib in hormone receptor-positive advanced breast cancer [Supplementary Appendix]. *N Engl J Med*. 2023;388(22):2058-2070.

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TEST for *PIK3CA/AKT1/PTEN* alterations

in HR+/HER2- locally advanced or metastatic breast cancer following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

CONSIDER TREATING with TRUQAP + fulvestrant[1]

Demonstrated efficacy and tolerability profile

CAPItello-291 trial: in patients with *PIK3CA/AKT1/PTEN* alterations, TRUQAP + fulvestrant demonstrated:

50% reduction
HR=0.50* (95% CI: 0.38, 0.65; $p<0.001$)†

in risk of progression or death with TRUQAP + fulvestrant vs. fulvestrant alone;

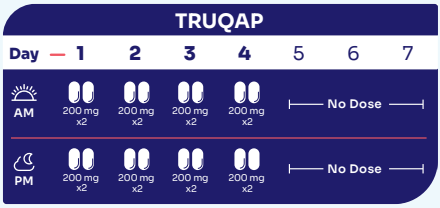
Number of events (%): TRUQAP + fulvestrant 121 (78.1) vs. fulvestrant 115 (85.8)

Low discontinuation rate reported

- 10.4% of patients discontinued due to adverse reactions

TRUQAP's 4 days on / 3 days off weekly dosing schedule

Discuss the choice of a start date with your patients.



Click to visit **TRUQAP.ca** and access resources and support materials

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AKT1=serine/threonine protein kinase 1; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; *PIK3CA*=phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*=phosphatase and tensin homolog.
*Stratified Cox proportional hazards model. A hazard ratio <1 favours capivasertib + fulvestrant.
†Stratified log-rank test.

AstraZeneca

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REVIEWED BY PAAB

Pr Truqap™ capivasertib
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