TRUQAP Launch Playbook

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*Market Insights and Brand Strategy are not for use with customers. Use only AZAP-approved messages when discussing TRUQAP with customers.

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

The approval of TRUQAP + fulvestrant marks a new era of advancement in targeted 2L treatment options that extend endocrine therapy for patients with HR+/HER2- aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations.

This Launch Playbook provides you with an overview of the strategic framework, HR+/HER2- treatment landscape, message flow, and a page-by-page CVA overview. This playbook has been designed to help you successfully launch TRUQAP + fulvestrant in a highly competitive and evolving 2L treatment landscape.

All sales calls must use approved materials and include a fair balance of efficacy/benefit and safety/risk.

Campaign overview

Brand personality for TRUQAP

Bold

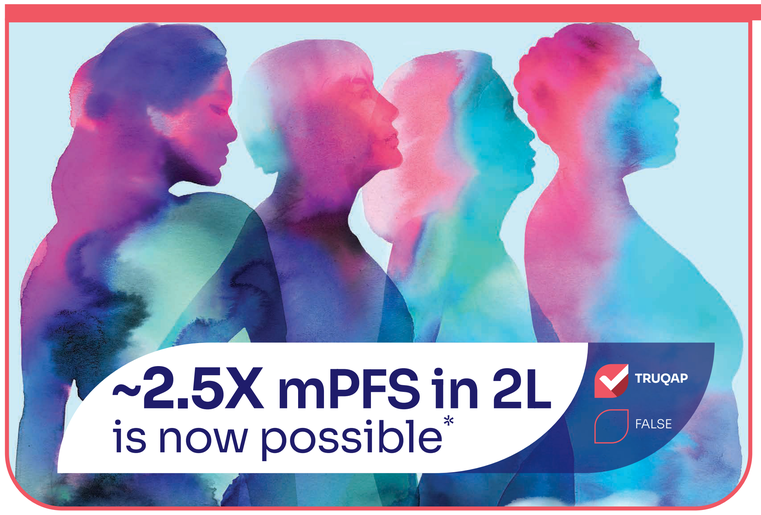
TRUQAP, in combination with fulvestrant, is the first and only combination therapy to use AKT inhibition and ER downregulation to address treatment resistance in patients with aBC or mBC who have progressed on prior endocrine therapy

Genuine

TRUQAP is paving a clear treatment path where before there was unpredictability and uncertainty

Optimistic

TRUQAP + fulvestrant offers the hope for “More Progression-Free Tomorrows”



The bold TRUth

With **“TRU”** in the brand name, the campaign **focuses on a bold promise of TRUth** that is **only possible when TRUQAP + fulvestrant is chosen—more than double mPFS for patients with limited options**

The TRUQAP/FALSE quiz device overlaid on watercolor renderings of a diverse group of women with HR+/HER2- aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i, serves to deliver the gravity of what’s at stake when making 2L treatment choices while celebrating the unique human beings affected by the outcomes of this choice

Market insights for HR+/HER2- aBC or mBC

34% 5-year survival for HR+/HER2- aBC with distant metastases

- Once a patient's disease becomes advanced or metastatic, oncologists go from a place where they can treat with curative intent to a place where they are looking to delay disease progression and extend life as long as possible while balancing treatment-related ARs
- Although ET + CDK4/6i is considered the standard of care in 1L, treatment resistance and disease progression are inevitable. Current 2L treatments either have limited data in patients who have previously had ET + CDK4/6i combinations, have treatment-limiting toxicities, or both, making the right choice unclear
- After patients progress on ET + CDK4/6i, the treatment goal for many HCPs is to extend endocrine-based therapy for treatments without adding significant toxicities
- Personalized medicine and targeted therapies are advancing oncology treatment approaches. And TRUQAP, in combination with fulvestrant, not only addresses a high unmet need as the first and only targeted option for patients with *AKT1* and/or *PTEN* alterations, but also is an NCCN Guidelines Category 1 Preferred option for patients with at least one or more *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression after one or more prior lines of ET, including one line containing a CDK4/6i. TRUQAP is a novel advancement that leverages the central location and regulatory functionality of AKT to deliver targeted inhibition and block oncogenic signaling from *PIK3CA*, *AKT1*, and *PTEN* alterations

2L market will be highly competitive at launch, with similar mPFS post-CDK4/6i + ET

There are no head-to-head studies comparing TRUQAP with any other targeted therapy; comparisons of efficacy or safety cannot be made. This is not a comprehensive comparison but reflects current strategic insights. This chart is not intended to encourage cross-trial comparisons of efficacy or safety.

	AstraZeneca	NOVARTIS	NOVARTIS	Stemline®	NOVARTIS
	Capivasertib + Fulv (AKTi + SERD) *PIK3CA/AKT1/PTEN* altered	**Alpelisib + Fulv** (PI3Ki + SERD) *PIK3CAm*	**Everolimus + Exem** (mTORi + AI) All-comer	**Elacestrant** (Oral SERD) *ESR1m*	**Ribociclib + Fulv/Exem** (CDK4/6i + SERD/AI) Re-challenge All-comer
Trial	CAPItello-291 (Phase 3)	SOLAR-1 (Phase 3)	BOLERO-2 (Phase 3)	EMERALD (Phase 3)	MAINTAIN (Phase 2)
Prior CDK4/6i (%)	Yes (71%)	Yes (6%*)	No	Yes (100%)	Yes (100%)
mPFS (months)	mPFS: **7.3**	mPFS: **11.0**	mPFS: **7.8**	mPFS *ESR1*: **3.8**	mPFS: **5.3**
Discontinuation rate due to ARs (%)	10	25.6†	24	6	8.3

For background information only. Brand strategy is not for use with customers. Use only AZAP-approved messages when discussing TRUQAP with customers.

*The ongoing phase 2 BYLieve trial is evaluating alpelisib plus endocrine therapy (fulvestrant or letrozole) in patients with HR+/HER2– *PIK3CA*-mutated aBC or mBC who have progressed on or after prior treatment with a CDK4/6i. Only Cohorts A and B of the BYLieve trial required prior CDK4/6i exposure (67% of total trial population); in both cohorts, all patients had prior CDK4/6i exposure.

†21% discontinued Piqray alone; 4.6% discontinued both Piqray and fulvestrant.

Fragmented 2L treatment landscape focused on extending time on ET for HR+/HER2– aBC and mBC

Current NCCN Clinical Practice Guidelines for 1L and 2L treatments

1L treatment	2L treatment
ET + CDK4/6i	ET + AKTi
ET monotherapy	ET + CDK4/6i, if not previously used
Chemotherapy*	ET monotherapy
PARPi†	ET + mTORi
	ET + PI3Ki‡
	Oral SERD§
	PARPi†
	Chemotherapy*

Key factors for 2L treatment decisions:

- Prior 1L treatment
- Anticipated benefit from further ET
- Performance status
- Biomarkers

NCCN

CATEGORY 1 PREFERRED

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer recommends capivasertib (TRUQAP™) + fulvestrant as a Category 1 Preferred treatment option for HR+/HER2- aBC or mBC with at least one or more *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression after one or more prior lines of ET, including one line containing a CDK4/6i

*If patient is in visceral crisis or endocrine refractory.
†PARPi is an option for patients with *gBRCAm*, who are in visceral crisis, or whose disease is endocrine refractory.
‡Alpelisib is indicated for the 2L treatment of postmenopausal women or adult men with HR+, HER2–, *PIK3CA*-mutated aBC or mBC.
§Elacestrant is indicated for the 2L treatment of postmenopausal women or adult men with ER+, HER2–, *ESR1*-mutated aBC or mBC.

Winning strategy to maximize patient impact

Establish TRUQAP + fulvestrant as the 2L SoC for HR+/HER2- aBC or mBC with one or more *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i, to extend ET with precision medicine

IDENTIFY

Ensure all eligible patients are identified at diagnosis

ESTABLISH

Differentiate and drive adoption of TRUQAP + fulvestrant as 2L SoC for *PIK3CA*, *AKT1*, and/or *PTEN* alterations

OPTIMIZE

Provide proactive AR and dosing support

NOTE: Brand strategy is not for use with customers. Use only AZAP-approved messages when discussing TRUQAP with customers.

Reinforce the core story

Unmet Need/MOD

- Post-CDK4/6i, better treatment options that balance efficacy/ tolerability have been needed
- Up to 50% of patients have one or more *PIK3CA*, *AKT1*, or *PTEN* alterations

MOA

- First and only AKT inhibitor
- TRUQAP targets AKT and blocks signaling driven by *PIK3CA*, *AKT1*, *PTEN* alterations, inhibiting tumor growth

Efficacy

- Only phase 3 targeted combo trial with majority of patients having received prior ET + CDK4/6i
- 2.5X median PFS versus fulvestrant alone in *PIK3CA*, *AKT1*, *PTEN*-altered HR+/HER2- aBC or mBC (7.3 vs 3.1 mo; HR=0.50) following progression on or after ET ± CDK4/6i

AR/Dosing

- Proven safety profile with low discontinuation rate due to ARs (10%)
- Optimized dosing schedule (4 days on, 3 days off, every week)

Call to Action

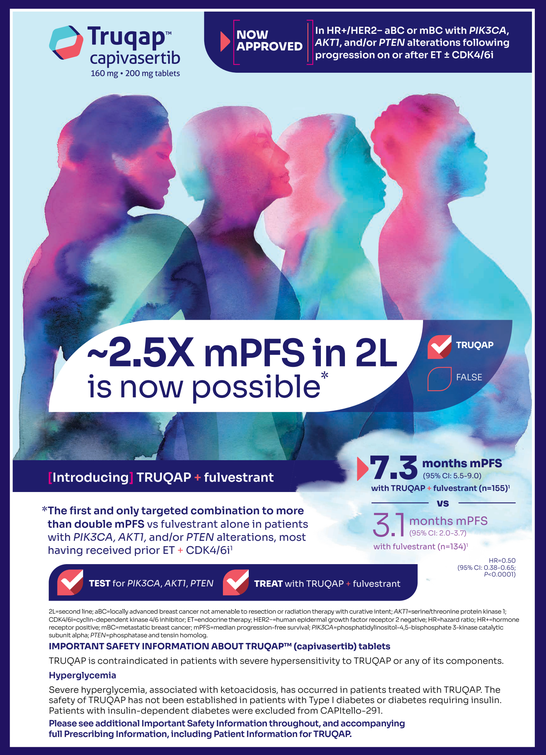
- TEST for *PIK3CA*, *AKT1*, *PTEN* alterations at advanced or metastatic diagnosis
- TREAT with TRUQAP + fulvestrant following progression on or after endocrine therapy to more than double mPFS with proven safety profile

CVA guidance

Detailing the CVA
The Core Visual Aid (CVA) serves as the primary resource for TRUQAP, providing essential information to communicate key attributes and establish a consistent brand story for TRUQAP, highlighting what differentiates TRUQAP from its competitors.

Please see the following pages for guidance to best detail from the CVA when discussing TRUQAP + fulvestrant with HCPs, as well background information and insights.

Short-call verbalization
Be sure to speak to the Important Safety Information for TRUQAP. As always, you are required to offer the current version of the Prescribing Information, including Patient Information, for TRUQAP. Please see prior slide for full core story.



Campaign overview

With “TRU” in the brand name, the campaign focuses on a bold promise of TRUth that is only possible when TRUQAP with fulvestrant is chosen—more than double mPFS in patients with HR+/HER2- aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations, most having received prior ET + CDK4/6i, who have limited options

The TRUQAP/FALSE quiz device overlaid on watercolor renderings of a diverse group of women with HR+/HER2- aBC or mBC with *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i, serves to deliver the gravity of what’s at stake when making 2L treatment choices while celebrating the unique human beings affected by the outcomes of this choice

Communication goals

Share the approval of a new treatment option, TRUQAP + fulvestrant, for HR+/HER2- aBC or mBC with *PIK3CA/AKT1/PTEN* alterations following progression on or after ET ± CDK4/6i

Establish TRUQAP + fulvestrant as 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 prior ET + CDK4/6i

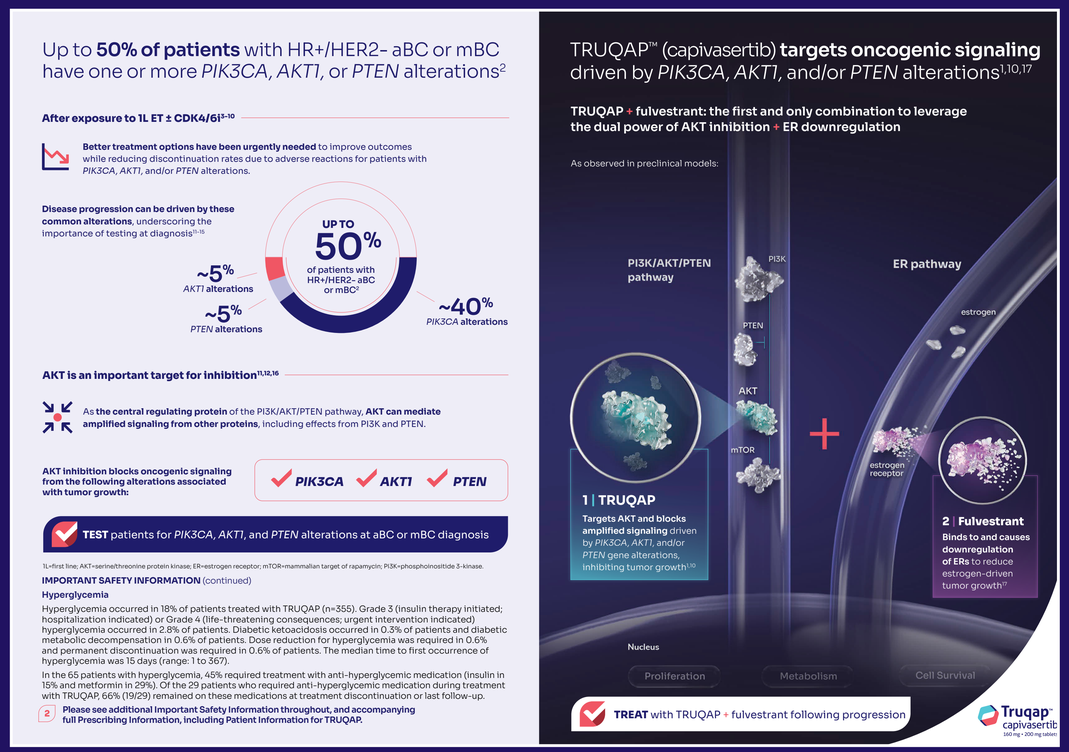
Test for *PIK3CA/AKT1/PTEN* and treat with TRUQAP + fulvestrant

Insights

- In research, the directness of the “~2.5X” and/or “more than doubling” mPFS had stopping power and compelled HCPs to want to learn more about TRUQAP
- A differentiator for TRUQAP vs Piqray® (alpelisib) is the much higher percentage of patients in the phase 3 clinical trial who had been previously treated with ET + CDK4/6i
- In research, HCPs appreciated that the patient population (*PIK3CA*, *AKT1*, and/or *PTEN* altered) and the call to action were very clear

Probing questions

- How do you sequence treatment following progression on 1L?
- What are the drivers of treatment decision-making once patients progress on 1L ET ± CDK4/6i?
- How often do you use biomarker results when making 2L treatment decisions?
- What prompts you to test patients for biomarkers?
- Is there any reason you wouldn't use biomarker testing?



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.

2 **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

Communication goals

MOD

- Up to 50% of patients have one or more of these alterations—up to 40% of whom have *PIK3CAm*
- There has been an unmet need for better treatment options after progression

MOA

- After establishing AKT as the central regulating protein and an important target in patients with *PIK3CA/AKT1/PTEN* alterations, speak to how TRUQAP targets oncogenic signaling driven by *PIK3CA*, *AKT1*, and/or *PTEN* alterations
- TRUQAP + fulvestrant: the first and only combination to leverage the dual power of AKT inhibition + ER downregulation

Insights

- Oncologists agree there is a persistent unmet need for safe and effective treatments following progression on 1L treatment for patients with these alterations
- Familiarity with *AKT1* and *PTEN* alterations is limited, as well as the understanding that an AKT-targeting therapy can affect oncogenic activity from multiple alterations within the PI3K/AKT/PTEN pathway, underscoring the importance of educating HCPs on the TRUQAP MOD/MOA story, as well as using the “PI3K/AKT/PTEN pathway” lexicon
- The MOA story tested well in research. HCPs said the language was clear and compelled them to prescribe TRUQAP
- HCPs often compared TRUQAP to competitors, seeking differentiators

Probing questions

- How does this novel MOA impact your understanding that, by targeting AKT with TRUQAP, you could also affect oncogenic activity from *PIK3CA* and *PTEN* alterations?
- What prompts you to test patients for additional biomarkers?
- Once patients have progressed on 1L therapy, how important is it to use a 2L therapy with a different MOA? What has your experience been with agents that target the PI3K/AKT/PTEN pathway?

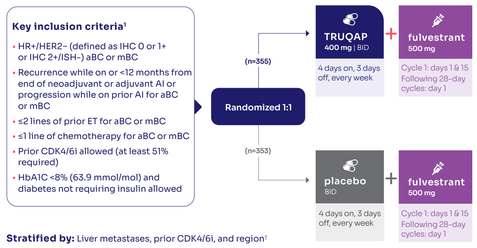
Truqap™ capivasertib 160 mg • 200 mg tablets

Trial design

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]*



Stratified by: Liver metastases, prior CDK4/6i, and region[1]

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.

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

Communication goals

Establish how the TRUQAP + fulvestrant combination was studied in CAPItello-291, a phase 3, randomized, double-blind, multicenter trial with the majority of patients having prior ET + CDK4/6i

Explain that CAPItello-291 had dual primary endpoints of PFS in the overall population (N=708) and PFS in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations (n=289; TRUQAP + fulvestrant n=155; placebo + fulvestrant n=134)

Point out that the inclusion criteria included patients with an HbA1C of <8% (63.9 mmol/mol) and those with diabetes not requiring insulin

Insights

- HCPs appreciated that CAPItello-291 was a phase 3 clinical trial in a clinically relevant population, a clear differentiator for TRUQAP
- In research, HCPs were satisfied with the trial design, but questioned fulvestrant monotherapy as a comparator. For more information, please refer to the US-80020 TRUQAP HCP RTCF
- In the phase 3 SOLAR-1 trial for Piqray (the only other available agent that targets an alteration in the PI3K/AKT/PTEN pathway, ie., *PIK3CA*), only 6% of patients had prior 1L CDK4/6i exposure
  - The phase 2 BYLieve trial included a population exposed to CDK4/6i, but the study lacked a comparator arm
- Because hyperglycemia is an AR of clinical interest, the high A1C inclusion threshold (<8%) in CAPItello-291 provides a key point of differentiation vs Piqray, as SOLAR-1 trial had an A1C inclusion threshold of ≤6.5%

Probing questions

- How do you sequence treatment following progression on 1L ET, including CDK4/6i?
- What are the drivers of treatment decision-making once patients progress on 1L ET + CDK4/6i?
- How often do you use biomarker testing when making 2L treatment decisions?
- What prompts you to test patients for additional biomarkers?
- What percentage of your patients are on 1L ET + CDK4/6i? How do you compare the CAPItello-291 inclusion criteria vs other 2L options?

Truqap™ capivasertib
160 mg • 200 mg tablets

Communication goals

Introduce TRUQAP as the first and only AKT inhibitor, in combination with fulvestrant, to more than double mPFS vs fulvestrant alone in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations, while highlighting the hazard ratio–median PFS 7.3 months with TRUQAP + fulvestrant vs 3.1 months with fulvestrant alone (HR=0.50)

Explain that the FDA approval of TRUQAP + fulvestrant was based on the PFS results seen in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations, as 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

Insights

- The early separation of the curves is impressive and showcases the benefit of TRUQAP + fulvestrant
- HCPs may compare mPFS benefit seen in CAPItello-291 to mPFS benefit demonstrated with other therapies without consideration of differences in patient populations across clinical trials

Probing questions

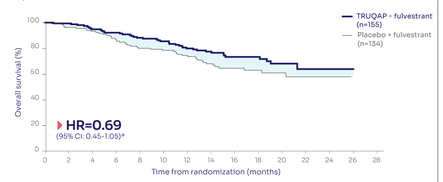
- What are your 2L treatment goals for HR+/HER2- aBC or mBC?
- What are your major considerations when making treatment decisions?
- Based on the efficacy data that you see here, how would you change your treatment approach for patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations?

Key secondary endpoints

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)

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).

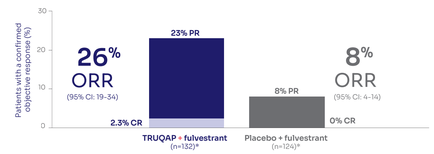
Monitor patients for signs and symptoms of diarrhea. Advise patients to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea while taking TRUQAP. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity.

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

Communication goals

Establish the OS data, a key secondary endpoint, as immature, explaining that not enough patient events have occurred to perform the final OS calculation

ORR data (CR + PR): 26% with TRUQAP + fulvestrant and 8% with fulvestrant alone

Please note: CBR is calculated by adding CR + PR + SD (sustained for 24 weeks)

Insights

- In research, HCPs were curious about OS data, and many were impressed by the early separation of the KM curves when it was presented
- The OS Interim Analysis is expected to occur at 56% maturity, and the OS Final Analysis will take place when ~70% maturity has been observed in the overall population and in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations

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Subgroup PFS

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)

Favors TRUQAP + fulvestrant ◀▶ Favors placebo + fulvestrant

0.1 1.0 10.0

*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.

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

Communication goals

Highlight consistent PFS results across subgroups

Emphasize subgroups that, in research, HCPs were very interested in: bone/liver metastases, primary or secondary endocrine resistance, or prior chemotherapy/ CDK4/6i use

This interest stems from the comparability of the patients they see in everyday practice

Identify that these data are from an exploratory analysis of prespecified subgroups and that the study was not powered to show statistical significance

Insights

- CAPItello-291 Analysis by gene alteration presented at SABCS 2023:
  - Compared with fulvestrant alone, the addition of TRUQAP to fulvestrant provided consistent PFS results across alterations in all 3 key genes (*AKT1*, *PIK3CA*, and *PTEN*) within the PI3K/AKT/PTEN pathway
  - This was an exploratory analysis
- In research, HCPs appreciated that these data showed consistent results across subgroups

Probing questions

- How do these data further establish the efficacy of TRUQAP + fulvestrant in patients with *PIK3CA*, *AKT1*, and/or *PTEN* alterations you have treated in your practice?

Baseline characteristics

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 Asian Black Other	75 (48.4) 48 (31) 2 (1.3) 30 (19.4)	76 (56.7) 35 (26.1) 1 (0.7) 22 (16.4)
Disease characteristics			
Metastatic sites, n (%)	Bone only Liver Visceral	25 (16.1) 70 (45.2) 103 (66.5)	16 (11.9) 53 (39.6) 98 (73.1)
Endocrine resistance,† n (%)	Primary Secondary	60 (38.7) 95 (61.3)	55 (41) 79 (59)
Prior treatments			
No. of prior ET for aBC, n (%)	0 1 2	13 (8.4) 131 (84.5) 11 (7.1)	20 (14.9) 96 (71.6) 18 (13.4)
Previous CDK4/6i, n (%)	Adjuvant/neoadjuvant aBC	0 113 (72.9)	2 (1.5) 91 (67.9)
Previous chemotherapy, n (%)	Adjuvant/neoadjuvant aBC	79 (51) 30 (19.4)	67 (50) 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.

Truqap™ capivasertib 160 mg • 200 mg tablets

Communication goals

Describe the CAPItello-291 baseline patient population as balanced between treatment arms in their disease characteristics

Establish that the patient population reflects the clinical heterogeneity seen in today's clinical practice

Emphasize the *PIK3CA/AKT1/PTEN*-altered population of CAPItello-291 as having:

- 76% with *PIK3CA* alteration
- 71% with prior ET + CDK4/6i
- 51% with prior adjuvant/neoadjuvant chemotherapy
- 70% with visceral metastases
- 14% with bone-only metastases

Insights

- Some HCPs may be unfamiliar with our competitors' baseline characteristics and may need to be reminded of the challenges of treating patients after progression on or after ET + CDK4/6i

Probing questions

- How is this patient population similar or different to whom you see in your practice?

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.

10 **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.

Truqap™ capivasertib 160 mg • 200 mg tablets

Communication goals

Remember to present comprehensive safety data

Establish that the majority of reported ARs in the trial were Grades 1 and 2

Highlight the incidence of Grade 3/4 hyperglycemia was 1.9% in the TRUQAP + fulvestrant arm and the CAPItello-291 threshold for HbA1C was <8%

Emphasize the low discontinuation rate due to ARs of 10%

Insights

- HCPs saw the safety profile as favorable and described adverse reactions as common and manageable
- CAPItello-291 study protocol did not allow for primary prophylaxis for instances of diarrhea or rash, and in research, some HCPs noted that giving primary prophylaxis would reduce ARs (for more information, please see RTCF)
- HCPs recognize that hyperglycemia is to be expected when using an agent that targets the PI3K/AKT/PTEN pathway, but they are optimistic with the low rates seen with TRUQAP
- The laboratory abnormalities do not present any notable concerns

Probing questions

- Is the incidence of these adverse reactions typical of or different from what you would expect from this type of treatment? How so?
- How would the combination of efficacy shown earlier and this safety and tolerability affect your decision to recommend TRUQAP + fulvestrant?
- Which, if any, of these ARs concern you? And why?
- Do the low rates of Grade 3/4 hyperglycemia help alleviate concerns you may have with an agent targeting the PI3K/AKT/PTEN pathway?

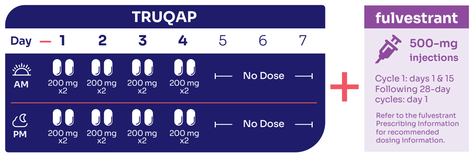
Dosing

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



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

12 **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

Communication goals

Establish that the dosing schedule was designed for an optimal benefit/risk profile and briefly explain how TRUQAP should be taken

Inform HCPs that 2 dose reductions are available that can be used as needed due to ARs to help patients stay on TRUQAP

Insights

- Many HCPs welcome the idea of giving patients a 3-day break from treatment
- Some expressed concern with adherence. Inform HCPs there are resources to help with patient adherence, for example, the starter kit, which includes US-80041 TRUQAP Patient Brochure, US-74956 TRUQAP Patient treatment booklet and side effect tracker, and US-75474 TRUQAP Pill Box
- Refer to the recommended dose modifications for ARs section of the CVA for more specific guidance

Recommended dosage modifications for ARs

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

Communication goals

Introduce recommended dose modifications due to specific ARs for TRUQAP: hyperglycemia, diarrhea, cutaneous ARs, and other ARs

Establish how the management of ARs may help keep patients on therapy

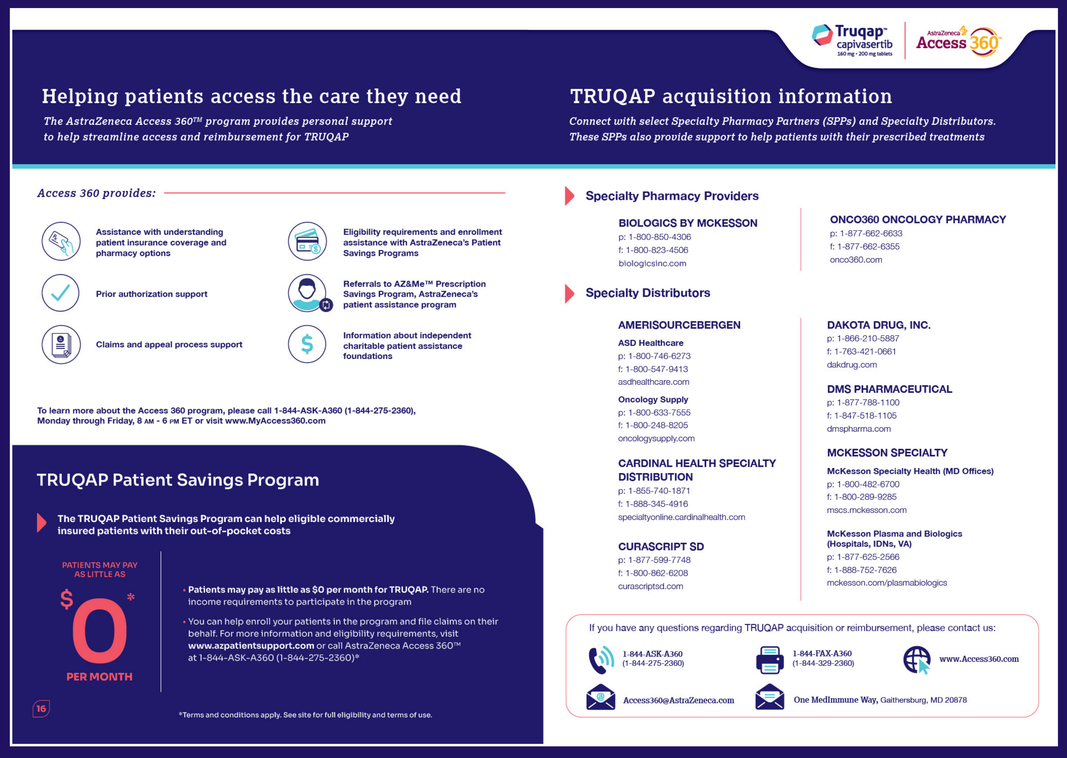
Insights

- Hyperglycemia: Among the 65 patients with hyperglycemia, less than half (45%) required treatment with metformin or insulin, and the majority of those patients (66%) remained on antihyperglycemic medication at treatment discontinuation or last follow-up
- Diarrhea: 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 the 93 patients with Grade ≥2 diarrhea with at least 1 grade improvement (n=89), median time to improvement from the first event was 4 days (range 1 to 154)
- Cutaneous ARs: Among the 204 patients with cutaneous ARs, less than half (90/204) required corticosteroid treatment, with the majority receiving topical corticosteroids (76/204). In patients with Grade ≥2 cutaneous ARs (n=116) with at least 1 grade improvement (n=104), median time to improvement from the first event was 12 days (range 2 to 544)
- For more detailed information about AR management, please refer to the RTCF

Probing questions

- Which, if any, of these ARs concern you? And why?
- Do these recommendations help alleviate concerns you have over any of these ARs?
- Will these recommendations change your management approach?

Patient support



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
- Eligibility requirements and enrollment assistance with AstraZeneca's Patient Savings Programs
- Prior authorization support
- Referrals to AZ&Me™ Prescription Savings Program, AstraZeneca's patient assistance program
- Claims and appeal process support
- 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 **www.azpatientsupport.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.

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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

Communication goals

Reassure physicians that AstraZeneca Access 360™ may be able to help patients access the care they need

Emphasize that this is personalized support that can help support access and reimbursement

Walk physician through top-line services of Access 360 and direct them to learn more by calling or visiting the website

Raise awareness of the Specialty Pharmacy Providers available to assist in accessing and providing support for patients seeking TRUQAP

Insights

- Competitor patient support programs offer comparable access and resources

Probing questions

- Are you familiar with the AstraZeneca Access 360 program?

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.

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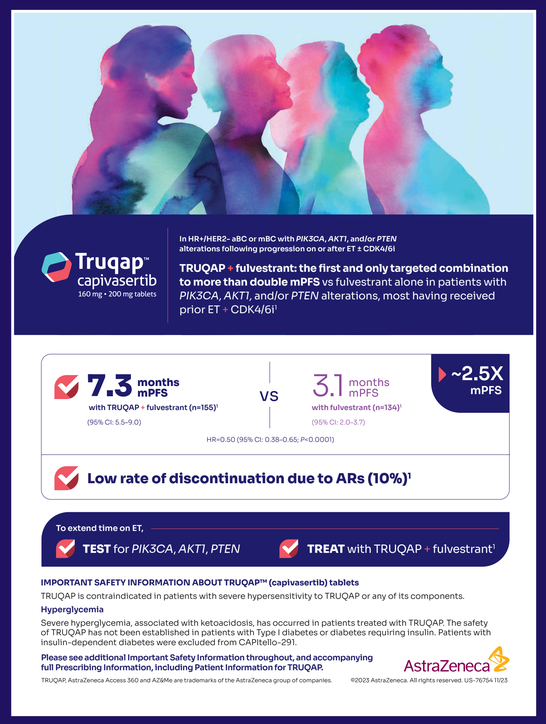
Truqap™ capivasertib 160 mg • 200 mg tablets

Communication goals

Review the Indication and Important Safety Information for TRUQAP

Probing question

- Do you have any questions about the information presented here?



Call verbalization

Doctor, TRUQAP + fulvestrant is the first and only AKT inhibitor combination to achieve 2.5X mPFS vs fulvestrant alone in patients with aBC and mBC whose tumors have *PIK3CA*, *AKT1*, and/or *PTEN* alterations following progression on or after ET ± CDK4/6i.

In addition, TRUQAP + fulvestrant exhibited a low discontinuation rate of 10% due to ARs.

Remember, TRUQAP is indicated in patients with one or more *PIK3CA*, *AKT1*, and/or *PTEN* alterations, so remember to check your patients for all 3 alterations, not just *AKT1*.

Given all the compelling reasons I shared with you today, would you choose TRUQAP in combination with fulvestrant as your preferred treatment for your next eligible patient?

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Abbreviations

1L=first line

2L=second line

aBC=locally advanced breast cancer not amenable to resection or radiation therapy with curative intent

AI=aromatase inhibitor

AKT=serine/threonine protein kinase

AKT1=serine/threonine protein kinase 1

AKTi=serine/threonine protein kinase inhibitor

AR=adverse reaction

ASCO=American Society of Clinical Oncology

AZAP=AstraZeneca Review Process

CBR=clinical benefit rate

CDK4/6i=cyclin-dependent kinase 4/6 inhibitor

CR=complete response

CVA=core visual aid

ER=estrogen receptor

ESR1=estrogen receptor 1

ESR1m=*ESR1* mutation

ET=endocrine therapy

Exem=exemestane

Fulv=fulvestrant

gBRCAm=breast cancer susceptibility gene mutant

HbA1C=glycated hemoglobin

HCP=healthcare provider

HER2–=human epidermal growth factor receptor 2 negative

HER2+=human epidermal growth factor receptor 2 positive

HR=hazard ratio

HR+=hormone receptor positive

KM=Kaplan-Meier

mBC=metastatic breast cancer

MOA=mechanism of action

MOD=mechanism of disease

mPFS=median progression-free survival

mTOR=mammalian target of rapamycin

mTORi=mammalian target of rapamycin inhibitor

NCCN=National Comprehensive Cancer Network

ORR=objective response rate

OS=overall survival

PARPi=poly-ADP ribose polymerase inhibitor

PFS=progression-free survival

PI3K=phosphoinositide 3-kinase

PI3Ki=phosphoinositide 3-kinase inhibitor

PIK3CA=phosphatidylinositol-4, 5-bisphosphate 3-kinase catalytic subunit alpha

PIK3CAm=*PIK3CA* mutation

PR=partial response

PTEN=phosphatase and tensin homolog

RTCF=response to customer feedback

SABCS=San Antonio Breast Cancer Symposium

SERD=selective estrogen receptor degrader

SD=stable disease

SoC=standard of care