

TALKING PIQRAY

MOA | Show notes

Show notes

There are no show notes for this podcast episode. Please see the full transcript below.

Transcript

Presenter Welcome to this episode of Talking Piqray. On this episode of our four-part series, Dr. Fabrice André will explain Piqray's Mechanism of Action.

Dr. Fabrice André is Research Director, Head of INSERM U981 and Professor, Director of Medical Oncology, Institut Gustave Roussy (France).

Presenter To begin, we asked Dr. André to talk about the role of PIK3CA mutations in oncogenesis.

Dr. André Gain-of-function mutations in PIK3CA, an oncogene that encodes the catalytic subunit of PI3 kinase, PI3 kinase alpha, have been implicated in the hyperactivation of PI3 kinase alpha,¹⁻³ driving oncogenic PI3 kinase pathway signaling.^{4,5}

Presenter So why are PIK3CA mutations of particular interest?

Dr. André PIK3CA mutations are of particular importance as it is one of the most frequently mutated genes in breast cancer.⁶⁻⁹

Presenter And approximately in what % of advanced Breast Cancer patients do these mutations occur?

Dr. André Approximately 40% of HR+/HER2- breast cancer.⁶⁻⁹

Presenter And what, Dr. André, is the significance of finding this mutation in advanced breast cancer patients?

Dr. André Patients with a PIK3CA mutation face a worse prognosis.¹⁰⁻¹⁴

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Presenter So, we see that it's essential to identify that mutation as soon as possible. In this next section you will hear the story of a hypothetical patient talking about her experience of her diagnosis.

Presenter And that patient is Kelly, a retired wife and mother, aged 75, who faced this particularly challenging diagnosis.

Finding out that just after 5 months of breast cancer treatment I now have cancer in my liver was so shocking and disappointing.

Kelly (played by Actor) My Oncologist was surprised too — she is having the lab run a new test on my archived breast tissue to see if my cancer shows a mutation. I rely on my daughter to take me to the doctor and to my treatments. I don't want to be a burden. If my tests come back positive for the mutation, what then? Is there a treatment that can help?

With a diagnosis such as this, it can often feel like there is nothing clear when dealing with breast cancer.

Presenter The fact that Kelly's oncologist sent her tissue for testing is a key step. With PIK3CA mutations implicated in poor prognosis in hormone receptor positive, HER2 negative advanced breast cancer,¹⁰⁻¹⁴ it's important to test for PIK3CA mutations to inform up-front treatment strategies.

This is because once the PIK3CA mutation is found, her treatment will be clear.

Dr. André, as our focus today is Mechanism of Action, once an oncologist finds the mutation and prescribes Piqray, what exactly is happening at a cellular level?

Dr. André PIQRAY is a selective inhibitor of PI3 kinase alpha, the protein that is activated in PIK3CA-mutated cancer, specifically targeting the effect of the PIK3CA mutation.^{14,15}

Dr. André PIQRAY inhibits PI3 kinase alpha 50 times more potently than other PI3 kinase isoform.^{14,15}

Presenter Fascinating. So how does the mutation affect cells?

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Dr. André

Mutation in PIK3CA leading to increased PI3 kinase signaling have been shown *in vitro* to drive cell proliferation and also drive tumorigenesis in mouse models of breast cancer.¹⁵

Dr. André

In xenograft models derived from ER-positive, PIK3CA mutated breast cancer cell line, the combination of alpelisib plus fulvestrant demonstrated increased antitumor activity compared to either treatment alone.^{14,15}

Presenter

Ah yes, I understand from reading your article in the New England Journal that Piqray tablets and fulvestrant work synergistically to inhibit both the PI3K and estrogen receptor pathways.¹⁴

So, what is the significance of this evidence?

Dr. André

These *in vitro* and *in vivo* evidences suggest that targeting PIK3CA mutations with PIQRAY may overcome resistance to endocrine-based therapy used in hormone receptor positive, HER2 negative advanced breast cancer and help inform upfront treatment strategies.^{16,17}

Presenter

And after this evidence was gathered, what was done to evaluate the efficacy of alpelisib in targeting PIK3CA mutation in breast cancer patients?

Dr. André

To specifically address targeting of PIK3CA mutation in breast cancer patient, the SOLAR-1 study was designed to evaluate PIQRAY plus fulvestrant in hormone receptor positive, HER2 negative, PIK3CA-mutated advanced breast cancer patient.^{14,15}

Ah yes, the SOLAR-1 study. We have an episode all about the SOLAR-1 study: visit our website www.piqray.com to find that and other episodes. Here you will also find references linked throughout the podcast.

Well, that marks the end of our discussion today.

Presenter

I'd like to thank Dr. André for his expert insights and opinions while also fully sharing the disclosures that at the time of recording this, Dr. André has received grant support from Novartis and also from AstraZeneca, Pfizer and Eli Lilly.

He also received Research funding from Astra Zeneca, Daiichi Sankyo, Lilly, Novartis, Pfizer and Roche.

Presenter

Before you go, we have some safety information about PIQRAY that we would like to share with you.

Important Safety Information FROM THE PIQRAY EU SmPC

The most common ADRs and the most common grade 3 / 4 ADRs (reported at a frequency >20% and $\geq 2\%$ respectively) were plasma glucose increased, creatinine increased, gamma-glutamyltransferase increased, rash, lymphocyte count decreased, nausea, alanine aminotransferase increased, anaemia, fatigue, lipase increased, decreased appetite*, stomatitis, vomiting*, weight decreased, hypocalcaemia, plasma glucose decreased*, activated partial thromboplastin time prolonged*, alopecia** diarrhoea, hypokalaemia, hypertension, nausea, creatinine increased, and mucosal inflammation (*<2% grade 3/4 ADRs reported, ** no grade 3/4 ADRs reported).

Piqray can cause serious side effects such as severe hypersensitivity, severe cutaneous reactions, hyperglycemia, pneumonitis, diarrhoea, and osteonecrosis of the jaw.

The following should be taken into consideration prior to or during treatment with Piqray:

Piqray should be permanently discontinued in patients with serious hypersensitivity reactions.

Piqray should not be initiated in patients with a history of severe cutaneous reactions, should be interrupted if signs or symptoms of severe cutaneous reactions are present, and permanently discontinued if a severe cutaneous reaction is confirmed.

Fasting glucose and HbA1c levels should be monitored frequently in the first 4 weeks of treatment, and patients should be advised of the signs and symptoms of hyperglycaemia.

In case of new or worsening respiratory symptoms, the patient should be evaluated for pneumonitis.

Patients should be advised to notify their physician if diarrhoea occurs.

Caution should be exercised when Piqray and bisphosphonates or denosumab are used together or sequentially. Piqray should not be initiated in patients with ongoing osteonecrosis of the jaw.

The efficacy and safety of Piqray has not been studied in patients with symptomatic visceral disease.

Animal studies suggest that Piqray may cause fetal harm in pregnant women. Therefore, as a precaution, women of childbearing potential should use effective contraception while receiving Piqray during treatment and at least 1 week after stopping treatment. Women should not breast feed for at least 1 week after the last dose of Piqray. Piqray may affect fertility in males and females.

Please see full Prescribing Information for Piqray, available at: www.piqray.com

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