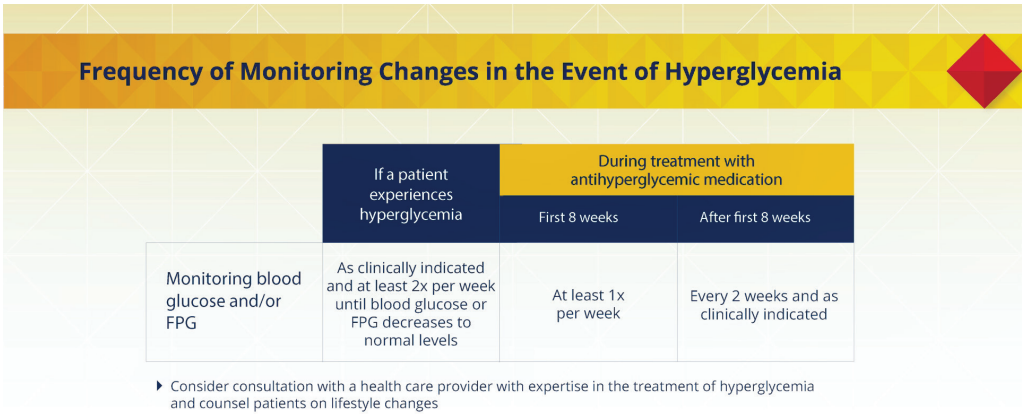
TALKING PIQRAY

MOA Continued | Show notes

Show notes

The following table lists the frequency of monitoring changes in the event of hyperglycemia



Frequency of Monitoring Changes in the Event of Hyperglycemia

	If a patient experiences hyperglycemia	During treatment with antihyperglycemic medication	
		First 8 weeks	After first 8 weeks
Monitoring blood glucose and/or FPG	As clinically indicated and at least 2x per week until blood glucose or FPG decreases to normal levels	At least 1x per week	Every 2 weeks and as clinically indicated

- Consider consultation with a health care provider with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes

Reference: Piqray® (alpelisib) Core Data Sheet: Version 1.0. Novartis Pharma AG; November 2018.

The following table lists the rate and severity of rash decrease using prophylactic antihistamines

Consider prophylaxis with antihistamines prior to onset of rash

- Antihistamines administered prior to rash onset may decrease incidence and severity of rash based on SOLAR-1 trial[1]

Event	Patients receiving prophylactic treatment prior to onset of rash (n=86)	Overall population (n=284)
All grades rash	26.1%	53.9%
Grade 3 rash	11.4%	20.1%
Rash leading to permanent discontinuation of PIQRAY	3.4%	4.2%

Transcript

Presenter	Welcome to this episode of Talking Piqray. To help improve understanding of managing patients who are prescribed PIQRAY, we have brought together a panel of five experts.
Presenter	In this episode you will hear Dr. Dejan Juric. Dr. Juric is a Director of the Henri and Belinda Termeer Centre for Targeted Therapies at Massachusetts General Hospital in the United States.
Presenter	Dr. Joyce O'Shaughnessy is the Celebrating Women Endowed Chair in Breast Cancer Research at Baylor University Medical Center. She is also Chair of the Breast Cancer Research Program, Texas Oncology, US Oncology in the United States.
Presenter	After Dr. O'Shaughnessy, we will hear from Dr. Eva Ciruelos of Medical Oncology, at the University Hospital 12 de Octubre, Grupo SOLTI for Breast Cancer Research in Spain.
Presenter	Then you will hear a familiar voice if you have already been following this podcast. Dr. Fabrice André returns to share his expertise once more. Dr. André is the Research Director, Head of INSERM U981 and Professor, Director of Medical Oncology, Institut Gustave Roussy in France.
Presenter	And finally, Dr. Guy Jerusalem will also share his expertise with us. He is Head of Medical Oncology in the Department of Medicine and Director of the Breast Clinic, CHU in Liège in Belgium.
Presenter	Dr. Juric. could you tell us briefly about any studies undertaken to assess PIQRAY's efficacy please?
Dr. Juric	In the SOLAR-1 Phase III trial, PIQRAY demonstrated a nearly doubling of median progression-free survival versus placebo and a generally manageable safety profile in patients with a PIK3CA mutation.[1]
Presenter	Thank you for that introduction Dr. Juric. And now, turning to you Dr. Joyce O'Shaughnessy, maybe you could tell us what are your key recommendations before starting treatment with PIQRAY?

Transcript

Dr. O'Shaugnessy	Before your patient starts on PIQRAY, it is important to advise them on the signs and symptoms of possible serious adverse reactions associated with PIQRAY.
Dr. O'Shaugnessy	Serious adverse reactions associated with PIQRAY include hypersensitivity including anaphylactic reaction, severe cutaneous reactions, hyperglycemia, pneumonitis, diarrhea, and embryo-fetal toxicity.[1]
Presenter	Great information to consider before treatment with PIQRAY. Thank you, Dr. O'Shaughnessy.
Presenter	Let's now hear from Dr. Ciruelos about the most common adverse reaction during treatment with PIQRAY.
Dr. Ciruelos	The most common adverse reactions in patients taking PIQRAY plus fulvestrant were hyperglycemia, diarrhea, rash, nausea, fatigue and asthenia, decreased appetite, stomatitis, vomiting and weight decreased.[1]
Presenter	Now turning to Dr. Fabrice André. Dr. André, could you please outline for us the dosing and administration of PIQRAY?
Dr. André	PIQRAY is given in combination with fulvestrant. The recommended dose of PIQRAY is 300 mg taken orally, once daily, with food, at approximately the same time each day.[1]
Presenter	According to the prescribing information PIQRAY should be taken in combination with Fulvestrant 500mg dose on days 1, 15 and 29 during the first month of treatment, and then afterwards, 500mg dose once monthly.[1]
Presenter	And Dr. André, if there are certain adverse reactions can the prescribing doctor adjust the dosage?

Transcript

Dr. André	PIQRAY may require dose interruption, reduction, or discontinuation and may be reduced in 50mg increments.[1]
Presenter	Next we return to Dr. Dejan Juric to delve into the topic of monitoring patients during treatment.
Presenter	Dr. Juric, can you outline for us the most relevant monitoring follow-up that might be required for patients during treatment?
Dr. Juric	While additional therapy may be needed for management of adverse reactions, the only laboratory monitoring needed for patients on PIQRAY is fasting plasma glucose, or FPG, and hemoglobin A1c. Before initiating treatment with PIQRAY, FPG and hemoglobin A1c should be measured and blood glucose levels corrected.[1]
Presenter	And then - as treatment continues?
Dr. Juric	Monitor hemoglobin A1c every three months.[1,2]
Presenter	So in what circumstances would the frequency of this monitoring change?
Dr. Juric	If your patient experiences hyperglycemia while taking PIQRAY or begins treatment with antihyperglycemic medications, the frequency of needed FPG and/or blood glucose monitoring changes.[1]
Presenter	A table detailing the frequency of FPG and / or blood glucose monitoring in this situation is available in this episode's show notes on our site www.piqray.com. It is also recommended that a health care provider with expertise in hyperglycemia is consulted and patients are advised on lifestyle changes.

Transcript

Presenter	Dr. Juric, are there any patient groups where the safety of PIQRAY is unknown?
Dr. Juric	The safety of PIQRAY in patients with Type 1 and uncontrolled Type 2 diabetes has not been established as these patients were excluded from SOLAR-1.[1,2]
Presenter	I understand that there's a reason why hyperglycemic events are expected side effects when prescribing PIQRAY?
Dr. Juric	These events of hyperglycemia are an expected, on-target effect of treatment with a PI3 kinase inhibitor and were reported in 64.8% of patients in SOLAR-1.[1,3]
Dr. Juric	Among the patients who had grade 2 or higher hyperglycemia in SOLAR-1, the median time to first occurrence was 15 days, median time to improvement by at least one grade was 8 days, and median duration was 10 days.[1]
Presenter	And for those who experienced elevated FPG, did they remain hyperglycemic once they had finished their treatment with Piqray?
Dr. Juric	Of the 54 patients with elevated FPG who continued fulvestrant treatment after discontinuing PIQRAY 96%, or 52 patients, had FPG levels that returned to baseline.[1]
Presenter	And how were the patients that experienced hyperglycemia while on PIQRAY treatment managed?
Dr. Juric	In SOLAR-1, 87% of patients with hyperglycemia were managed with antihyperglycemic medication. In SOLAR-1 most patients reported use of metformin as a single agent or in combination with other antihyperglycemic medications.[1]

Transcript

Presenter	And during the SOLAR-1 how many patients discontinued treatment with PIQRAY due to hyperglycemia?
Dr. Juric	6% of patients in SOLAR-1 taking PIQRAY plus fulvestrant discontinued treatment due to hyperglycemia.[1]
Presenter	Would you have any last recommendations in relation to hyperglycemia?
Dr. Juric	In the event of hyperglycemia, your patient may require PIQRAY dose adjustments or interruption and use of antihyperglycemic treatment.[1]
Presenter	Many thanks, Dr. Juric, for simplifying what is important to monitor or follow up, especially in relation to hyperglycemic events. During treatment with Piqray hyperglycemia is an expected, on-target effect of treatment with a PI3 kinase inhibitor. Good to know.
Presenter	Next in this episode of Talking Piqray, we spoke with Dr. Guy Jerusalem. Dr. Jerusalem is Head of Medical Oncology in the Department of Medicine and Director of the Breast Clinic in CHU of Liège in Belgium.
Presenter	Welcome Dr. Jerusalem, can you please tell us about the occurrence of rash events as observed in patients who participated in the SOLAR-1 study?
Dr. Jerusalem	Rash events were reported in 53.9% of patients in SOLAR-1 and the majority were mild to moderate and responsive to therapies. The median time to first onset of grade 2 or 3 rash was 12 days.[1]
Presenter	And what treatment would be recommended to address a rash?

Transcript

Dr. Jerusalem	For the treatment of rash, corticosteroids are recommended based on the severities as well as antihistamines to manage symptoms.[1] Antihistamines may also be considered prior to the onset of rash and at the time of initiation of treatment with PIQRAY.[1]
Presenter	Is there any evidence that prophylaxis with antihistamines helps with the frequency of patients having a rash?
Dr. Jerusalem	In the SOLAR-1 study, a subgroup of 86 patients received prophylaxis, including antihistamines, prior to onset of rash. In these patients, rash was reported less frequently than in overall population.[1]
Presenter	Thank you very much for those details from the SOLAR-1 study, Dr. Jerusalem. A table showing the rate and severity of rash decrease using prophylactic antihistamines is available in our show notes for this Episode at www.piqray.com.
Presenter	In addition to hyperglycemia and rash, is there any other adverse event of note? We put this question to Dr. Joyce O'Shaughnessy...
Dr. O'Shaughnessy	And the final adverse event I'd like to mention today is diarrhea. In SOLAR-1, 58%, of patients experienced diarrhea. 18.3% of patients experienced grade 2 diarrhea while 6.7% of patients experienced grade 3 diarrhea. There were no reported cases of grade 4 diarrhea.[1]
Presenter	And what kind of timeframe was observed for the onset of diarrhea?
Dr. O'Shaughnessy	The median time to onset of grade 2 or 3 diarrhea was 46 days.[1]

Transcript

Presenter	Any special advice for patients who are being treated with PIQRAY who present with diarrhea?
Dr. O'Shaughnessy	Patients should be managed according to local standard of care medical practice.
Presenter	Thank you, Dr. O'Shaughnessy. That's good to know that diarrhea as an adverse event is manageable. Another aspect of prescribing any medication that we always have to be cognizant of are drug interactions. I put it to Dr. Fabrice André… do you have some particular advice in this area?
Dr. André	There are a few drug interactions to be aware of when your patient begin treatment with PIQRAY. Closely monitor patients when coadministering PIQRAY with BCRP inhibitor, CYP3A4 substrates, CYP2C9 substrate with narrow therapeutic index and CYP2B6 sensitive substrates with narrow therapeutic index.
Presenter	Very clear recommendations… thank you Dr. André. For detailed information on drug interactions please refer to the website at www.piqray.com, where you can also find our show notes. Thanks to you and your colleagues, Dr. André, for sharing your thoughts on how to manage patients undergoing treatment with PIQRAY.
Dr. André	Thank you for joining me and I hope this brief introduction to PIQRAY patient management helps you and your patient during the treatment journey with PIQRAY.
Presenter	That is all for this episode. We also have episodes that cover the mechanism of action of PIQRAY where you can hear Dr. Fabrice André detailing how apelisib specifically addresses PIK3CA mutations. PIK3CA mutation is the key here: if you find it in your advanced breast cancer HR+/ HER2- patients, her treatment can be clear.[1]
Presenter	In this episode we heard from Dr. Dejan Juric who acts in a consulting and advisory role with Eisai, EMD Serono, Genentech as well as here in Novartis.

Transcript

Presenter	We also got details about patient management from Dr. Joyce O'Shaughnessy. She is currently the recipient of honoraria for consulting and advisory boards with AbbVie Incorporated, Agendia, Amgen Biotechnology, AstraZeneca, Bristol-Myers Squibb, Celgene Coporation, Eisai, Genentech, Genomic Health, GRAIL, Immunimedis, Heron Therapeutics, Ipsen Biopharmaceuticals, Jounce Therapeutics, Lilly, Merck, Myriad, with us here in Novartis and also Odonate Therapeutics, Pfizer, Puma Biotechnology, Prime Oncology, Roche, Seattle Genetics, Syndax Pharmaceuticals and Takeda.
Presenter	Dr. Fabrice André also shared his expertise and he receives grant support from us here in Novartis, from AstraZeneca, Pfizer and Eli Lilly. His research funding comes from AstraZeneca, Daiich Sankyo, Lilly, Novartis, Pfizer and Roche. His travel, accommodation and expenses are covered by AstraZeneca, GlaxoSmithKline, Novartis and Roche.
Presenter	Dr. Guy Jerusalem received grants outside the submitted work from us here in Novartis and from Pfizer and Roche. He receives non-financial support outside the submitted work from Amgen, AstraZeneca, Bristol-Myers Squibb, Lilly, Novartis, Pfizer and Roche. Guy Jerusalem also received personal fees outside the submitted work from AbbVie, Amgen, Astra-Zeneca, BMS, Celgene, Daiichi Sankyo, Lilly, Novartis, Pfizer, Puma Technology and Roche. He received personal fees during the conduct of the study from us here at Novartis.
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 ≥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

References: 1. Piqray® (alpelisib) Core Data Sheet: Version 1.0. Novartis Pharma AG; November 2018.
2. Andre F et al. Alpelisib for PIK3CA-Mutated, Hormone Receptor–Positive Advanced Breast Cancer. *N Eng J Med.* 2019;380(20);1929-1940. **3.** Goncalves MD et al. Phosphatidylinositol 3-Kinase, Growth Disorders, and Cancer. *N Eng J Med.* 2018;379(21);2052-2062.

NOVARTIS

PIQRAY® (alpelisib) tablets

Novartis Pharma AG
CH-4002 Basel Switzerland