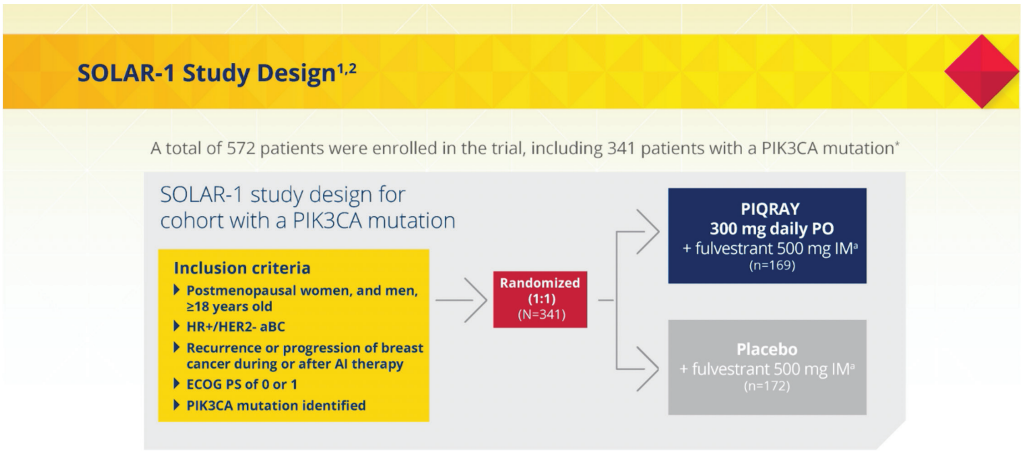
TALKING PIQRAY

SOLAR 1 Continued | Show notes

Show notes

The following table outlines the study design for the SOLAR-1 clinical trial



AI, aromatase inhibitor; ECOG, Eastern Cooperative Oncology Group; IM, intramuscularly; PO, orally; PS, performance status.
*A total of 231 patients did not have a PIK3CA mutation and were included as a separate cohort as proof of concept to evaluate PIQRAY as a biomarker-driven therapy. The proof of concept criteria were not met for this cohort.
[a]Fulvestrant given on day 1 and day 15 of the first 28-day cycle, then day 1 of subsequent 28-day cycles.
References: 1. Piqray® (alpelisib) Core Data Sheet: Version 1.0. Novartis Pharma AG; November 2018. 2. André F et al. *N Engl J Med*. 2019;380(20):1929-1940.

The following table lists the adverse reactions associated with PIQRAY

ARs Occurring in >20% of the Total Population

ARs	PIQRAY + Fulvestrant (N=284)		Placebo + Fulvestrant (N=287)	
	All Grades n (%)	Grade 3-4 n (%)	All Grades n (%)	Grade 3-4 n (%)
Gastrointestinal disorders				
Diarrhea	164 (57.7)	19 (6.7)[d]	45 (15.7)	1 (0.3)[d]
Nausea	127 (44.7)	7 (2.5)[d]	64 (22.3)	1 (0.3)[d]
Stomatitis[a]	85 (29.9)	7 (2.5)[d]	18 (6.3)	0[d]
Vomiting	77 (27.1)	2 (0.7)[d]	28 (9.8)	1 (0.3)[d]
General disorders and administration site conditions				
Fatigue[b]	120 (42.3)	15 (5.3)[d]	83 (28.9)	3 (1.0)[d]
Investigations				
Weight decreased	76 (26.8)	11 (3.9)[d]	6 (2.1)	0[d]
Metabolism and nutrition disorders				
Hyperglycemia	184 (64.8)	105 (37.0)	29 (10.1)	2 (0.7)[d]
Decreased appetite	101 (35.6)	2 (0.7)[d]	30 (10.5)	1 (0.3)[d]
Skin and subcutaneous tissue disorders				
Rash[c]	147 (51.8)	56 (19.7)[d]	21 (7.3)	1 (0.3)[d]

AR, adverse reaction.
[a]Including stomatitis, aphthous ulcer, mouth ulceration. [b]Including fatigue, asthenia. [c]Including rash, rash maculopapular, rash macular, rash generalized, rash papular, rash pruritic. [d]No grade 4 ARs were reported.
Reference: Piqray® (alpelisib) Core Data Sheet: Version 1.0. Novartis Pharma AG; November 2018.

NOVARTIS

PIQRAY® (alpelisib) tablets

Transcript

Presenter	Welcome to this episode of Talking Piqray. Throughout this episode you'll hear a number of medical experts discussing the importance of identifying the PIK3CA mutations in advanced breast cancer patients. We will also detail SOLAR-1, the study that led to the approval of PIQRAY, a PI3Kα inhibitor specifically for advanced Breast Cancer patients with a PIK3CA mutation. Plus, we get insights into the efficacy and safety profile of PIQRAY. And lastly, we have details about dosage and administration as well as patient management considerations. Dr. Joyce O'Shaughnessy features in this episode again – she also spoke in another episode which focused on patient management. She 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. We welcome Dr. Wolfgang Janni back again as well. He spoke to us in another episode, helping us understand the SOLAR-1 study design. Dr. Janni is Professor and Chair of Obstetrics and Gynaecology at the University Hospital of Ulm in Germany. After Dr. Janni, we will hear from 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. In this episode you will also hear Dr. Carlos Barrios who joins us from the Latin American Cooperative Oncology Group and Grupo Oncoclinicas in Brazil. We're delighted to have his input. We're also delighted to welcome back Dr. Fabrice André to share his expertise on the podcast again. Dr. André is the Research Director, Head of INSERM U981 and Professor, Director of Medical Oncology, Institut Gustave Roussy in France. You can hear full disclosures for all our contributors at the end of this episode but it's a busy episode so let's get on with it! To begin, Dr. O'Shaughnessy, what would you like to draw our attention to first please?
Dr. O'Shaughnessy	To begin today's discussion, I'd like to tell you why PIK3CA mutations matter in hormone receptor positive, HER2- breast cancer patients. PIK3CA is one of the most frequently mutated genes in breast cancer, occurring in approximately 40% of hormone receptor positive, HER2 negative breast cancer patients.[1-4]

Transcript

Presenter	And why is PIK3CA of particular importance?
Dr. O'Shaughnessy	PIK3CA is of particular importance because metastatic patients with a PIK3CA mutation face a worse prognosis.[5-8]
Presenter	And, Dr. O'Shaughnessy, could you please tell us a little more about the mechanism of action of PIQRAY?
Dr. O'Shaughnessy	PIQRAY is a bio-marker driven therapy specifically targeting patients with a PIK3CA mutation.
Presenter	Anything else of note?
Dr. O'Shaughnessy	PIQRAY is a potent and selective inhibitor of PI3 kinase alpha, the protein that is activated in PIK3CA-mutated cancer.[9,10] PIQRAY inhibits PI3 kinase alpha 50 times more potently than the other PI3 kinase isoforms.[9,10]
Presenter	Fascinating! And so, Dr. O'Shaughnessy, what should a healthcare provider do to assess whether they need to consider this treatment for their advance breast cancer patients?
Dr. O'Shaughnessy	To ensure your patients are appropriate for treatment with PIQRAY, it's essential to test for PIK3CA mutations.[10-12]
Dr. O'Shaughnessy	Moreover, with PIK3CA mutations implicated in endocrine therapy resistance and poor prognosis in hormone receptor positive, HER2 negative advanced breast cancer, it's important to test for PIK3CA mutations to inform up front treatment strategies.[13]
Presenter	Thank you so much Dr. O'Shaughnessy for that incisive overview.

Transcript

Presenter	It's widely accepted that many women are devastated when they relapse and fear the worst. In the following case of a hypothetical patient, Irma had an initial relapse with metastases in chest tissue and throughout her nodes. After a short time on a CDK4/6 inhibitor and an aromatase inhibitor, Irma reported back pain to her doctor. Her doctor ordered a bone scan which, unfortunately, confirmed new bone metastases. With her active work and home life, Irma is hoping for a treatment that will likely reduce her tumor burden. Irma was very interested in her test results showing her positive PIK3CA mutation status. Now, she wants to know what this means for her treatment options:
Irma	Hearing my scans came back with new metastases was so disappointing. I'm now really worried about the next treatment being able to reduce my tumors. My doctor decided to run another test that came back showing my cancer tested positive for the PIK3CA mutation. I asked my doctor if there's a treatment designed specifically to help patients like me, that test positive for this mutation? Can it help reduce my tumors?
Presenter	Certainly, this is worrying, but once Irma's doctor confirmed the PIK3CA mutation her treatment could be clear and PIQRAY was prescribed.
Presenter	It's always interesting to hear patient stories. As it is always important to recognize that no two patients are the same… but one factor that can tie these patients together is the PIK3CA Mutation presence. About 40% of patients with HR+/HER2- advanced breast cancer have a PIK3CA mutation[1-4] and as Dr. O'Shaughnessy mentioned, it's important to do that test because metastatic patients like Irma with a PIK3CA mutation face a worse prognosis.[5-8]
Presenter	Next we spoke with Dr. Wolfgang Janni about the SOLAR-1 study and how it was designed to evaluate the efficacy and safety of PIQRAY. He talks in more detail on this topic in the episode focusing on SOLAR-1 which you can find at www.piqray.com. Dr. Janni, can you please give us a high-level introduction to SOLAR-1?

Transcript

Dr. Janni	SOLAR-1 is a phase 3, randomized, double-blind, placebo-controlled study evaluating PIQRAY in combination with fulvestrant in postmenopausal women, and men, with hormone receptor positive, HER2- locally advanced and metastatic breast cancer whose disease had progressed or recurred on or after an aromatase-inhibitor-based treatment.[9]
Presenter	And how many patients were involved in SOLAR-1?
Dr. Janni	In the SOLAR-1 trial, 572 patients were enrolled into two cohorts - patients with or patients without a PIK3CA mutation. The 341 patients with a PIK3CA mutation were randomized one-to-one to receive either PIQRAY plus fulvestrant or placebo plus fulvestrant.[9,10]
Presenter	And what about the cohort of patients without a PIK3CA mutation?
Dr. Janni	The cohort without a PIK3CA mutation consisted of 231 patients, also randomized one to one, and were included as a separate cohort as proof of concept. The proof of concept criteria were not met for this cohort.[9,10]
Presenter	Was there any variability in baseline characteristics?
Dr. Janni	Demographics of patients included in SOLAR-1 were well balanced and included patients receiving PIQRAY as first or second line treatment after progressing on endocrine based therapy.[9,10]
Presenter	Thank you Dr. Janni for detailing the design of SOLAR-1 for us. In addition, a table detailing this can be found in the show notes for this episode online at www.piqray.com.
Presenter	Next, we spoke with Dr. Dejan Juric to find out more about what the SOLAR-1 study indicates about the efficacy of PIQRAY. Dr. Juric, I understand that certain benefits were seen with PIQRAY for patients with a PIK3CA mutation?

Transcript

Dr. Juric	We can see that in patients with a PIK3CA mutation there is a significant and clinically meaningful benefit - the median PFS for these patients nearly doubled from 5.7 months to 11 months with PIQRAY plus fulvestrant versus fulvestrant alone. The separation of the PFS curve was apparent as early as 2 months.[9,10] Furthermore, we see a substantial increase in the overall response rate in patients with a PIK3CA mutation who had measurable disease, more than doubling from 16.2% to 35.7% with PIQRAY plus fulvestrant versus fulvestrant alone.[9,10]
Presenter	After reviewing PIQRAY's efficacy, what does its safety profile look like and what are the most common adverse reactions?
Dr. Juric	The most common adverse reactions in patients taking PIQRAY plus fulvestrant were hyperglycemia, diarrhea, rash, nausea, fatigue and asthenia, as well as decreased appetite, stomatitis, vomiting and weight decrease.[9]
Presenter	Interesting... And the most serious adverse reactions?
Dr. Juric	Serious adverse reactions associated with PIQRAY include hypersensitivity including anaphylactic reaction, severe cutaneous reactions, hyperglycemia, and pneumonitis.[9]
Presenter	Thank you again Dr. Juric for your contribution. More information about adverse reaction and several common laboratory abnormalities are detailed in a table in the show notes at www.piqray.com
Presenter	Next, we reached out to Dr. Carlos Barrios MD to take us through the dosage and administration of PIQRAY. Dr. Barrios, what is the recommended dose and how should patients take PIQRAY?
Dr. Barrios	The recommended dose of PIQRAY is 300 mg taken orally, once daily, with food, at approximately the same time each day.[9]

Transcript

Presenter	Important advice. It always helps to keep a routine when taking medication. But what should a patient do if they do miss a dose?
Dr. Barrios	If a dose of PIQRAY is missed, it can be taken with food within 9 hours after the time it's usually taken. After more than 9 hours, skip the dose for that day. The next day, take PIQRAY at the usual time.[14]
Presenter	And what about patients who are prescribed fulvestrant in addition to PIQRAY?
Dr. Barrios	When coadministered with PIQRAY, the recommended dose of fulvestrant is 500 mg administered on days 1, 15, and 29, and once monthly thereafter.[9]
Presenter	Thank you, Dr Barrios... lastly, we asked Dr Fabrice André to comment on management of hyperglycemia in the SOLAR-1 trial.
Dr. André	In SOLAR-1, hyperglycemia was reported in 64% of patients.[9]
Dr. André	Hyperglycemia is an expected, on-target effect of treatment with a PI3K inhibitor.[9,15]
Presenter	And how were the patients who experienced this managed?
Dr. André	Hyperglycemia was managed in SOLAR-1 with dose reduction, interruption, and/or additional therapy with antihyperglycemic medication.[9]
Presenter	What happened once those with hyperglycemia completed their PIQRAY treatment?

Transcript

Dr. André	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.[9]
Presenter	Any other adverse events that oncologists should look out for when prescribing PIQRAY?
Dr. André	Additionally, rash events were reported in 53% of patients in SOLAR-1. The majority of rash event were mild to moderate and responsive to therapy.[9]
Presenter	And how were the rash events managed?
Dr. André	Rash was managed in SOLAR-1 with the use of topical or oral corticosteroids, antihistamine, and/or PIQRAY dose adjustment.[9]
Presenter	Is there any other approach to managing any grade of rash events that you would recommend to those prescribing PIQRAY?
Dr. André	It is important to consider prophylactic antihistamine before initiating treatment with PIQRAY because prophylactic use decreases the likelihood your patient will develop severe rash event.[14]
Presenter	Oh yes that's a great recommendation to prevent any grade of rash in these patients. And I think you also mentioned that there was another adverse event to look out for in patients?
Dr. André	Finally, I would like to mention that 57% of patient treated with PIQRAY in SOLAR-1 experienced diarrhea but there were no reports of grade 4 diarrheal event.[9]
Presenter	OK… any advice to help patients with this adverse event?

Transcript

Dr. André	Anti-diarrheal medication, and/or PIQRAY dose adjustment were used in SOLAR-1 to manage symptom in appropriate patient.[9]
Presenter	Good advice. Thanks again Dr. André for your contribution.
Presenter	And 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 exactly apelisib interacts with the PIK3CA mutation. That mutation is the key here: if you find it in your advanced breast cancer HR+/ HER2- patients, her treatment can be clear. Other episodes further detail safety and efficacy. We also have an episode with a lot more information about the SOLAR-1 Study design. Each of those episodes, with charts, tables and graphs and transcripts of all four episodes can be found at www.piqray.com. Remember, PIQRAY is the first and ONLY treatment specifically for advanced breast cancer patients with a PIK3CA mutation. To learn more please go to www.PIQRAY.com. 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 in Novartis. 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 Corporation, Eisai, Genentech, Genomic Health, GRAIL, Immunimedics, 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. Dr. Carlos Barrios talked us through dosing and administration today. Dr. Barrios receives research funding from AstraZeneca. He also receives speaker honoraria from and holds an advisory role with AstraZeneca, Boehringer INgelheim, Bristol-Myers Squibb, Eisai, GSK, Libbs Farmacêutica, MSD, Novartis, Roche, and Pfizer.

Transcript

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, Daiichi Sankyo, Lilly, Novartis, Pfizer and Roche. His travel, accommodation and expenses are covered by AstraZeneca, GlaxoSmithKline, Novartis and Roche. Finally, Dr. Wolfgang Janni received grant support from 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. The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature.* 2012;490(7418): 61-70. **2.** Tolaney S, Toi M, Neven P, et al. Clinical Significance of PIK3CA and ESR1 mutations in ctDNA and FFPE Samples From the MONARCH 2 Study of Abemaciclib Plus Fulvestrant. Presented at: 2019 American Association for Cancer Research (AACR) Annual Meeting; March 29-April 3, 2019; Atlanta, GA. **3.** Di Leo A, Johnston S, Seok Lee K, et al. Buparlisib plus fulvestrant in postmenopausal women with hormone-receptor-positive, HER2-negative, advanced breast cancer progressing on or after mTOR inhibition (BELLE-3): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2018;19(1):87-100. **4.** Moynahan ME, Chen D, He W, et al. Correlation between PIK3CA mutations in cell-free DNA and everolimus efficacy in HR+, HER2- advanced breast cancer: results from BOLERO-2. *Br J Cancer.* 2017;116(6):726-730. **5.** Sobhani N, Roviello G, Corona SP, et al. The prognostic value of PI3K mutational status in breast cancer: a meta-analysis. *J Cell Biochem.* 2018;119(6):4287-4292. **6.** Li YL, Rong M, Grieu F, Iacopetta B. PIK3CA mutations in breast cancer are associated with poor outcome. *Breast Cancer Res Treat.* 2006;96(1):91-95. **7.** Lai YL, Mau, BL, Cheng WH, Chen HM, Chiu HH, Tzsen CY. PIK3CA exon 20 mutation is independently associated with a poor prognosis in breast cancer patients. *Ann Surg Oncol.* 2008;15(4):1064-1069. **8.** Mosele F, Verret B, Jusque A, et al. Natural history and outcome of patients presenting a metastatic breast cancer with PIK3CA mutation. Abstract presented at: American Association for Cancer Research (AACR) Annual Meeting 2019; March 29-Apr 3, 2019; Atlanta, GA. **9.** Piqray® (alpelisib) Core Data Sheet: Version 1.0. Novartis Pharma AG; November 2018. **10.** André F, Ciruelos E, Rubovszky G, et al. Alpelisib for PIK3CA mutated, hormone receptor-positive advanced breast cancer. *N Engl J Med.* 2019;380(20):1929-1940. **11.** Arthur LM, Turnbull AK, Renshaw L, et al. Changes in PIK3CA mutation status are not associated with recurrence, metastatic disease or progression in endocrine-treated breast cancer. *Breast Cancer Res Treat.* 2014;147(1):211-219. **12.** Li H, Xu Y, Zhao F, et al. Plasma PIK3CA ctDNA specific mutation detected by next generation sequencing is associated with clinical outcome in advanced breast cancer. *Am J Cancer Res.* 2018;8(9):1873-1886. **13.** Thomssen C, Lüftner D, Untch M, et al. International Consensus Conference for Advanced Breast Cancer, Lisbon 2019: ABC5 Consensus - Assessment by a German Group of Experts. *Breast Care* (Basel). 2020;15(1):82-95. **14.** Piqray® (alpelisib) EU Summary of Product Characteristics. Novartis; August 2020. **15.** Goncalves MD, Hopkins BD, Cantley LC. Phosphatidylinositol 3-kinase, growth disorders and cancer. *N Engl J Med.* 2018;379 (21):2052-2062.

NOVARTIS

PIQRAY® (alpelisib) tablets

Novartis Pharma AG
CH-4002 Basel Switzerland