Why you should read this article:

- To gain knowledge of the mechanism of action of CDK4 and CDK6 inhibitors and how you could explain this to patients
- To understand the dosing, administration and potential side effects of abemaciclib in the treatment of metastatic breast cancer, and where to find prescribing information: **lillyoncology.co.uk/assets/pdf/verzenios-api-a4-landscape.pdf**
- To count towards revalidation as part of your 35 hours of CPD, or you may wish to write a reflective account (UK readers)
- To contribute towards your professional development and local registration renewal requirements (non-UK readers)

Abemaciclib▼ for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) metastatic breast cancer

Pauline McIlroy

Citation
McIlroy P (2020) Abemaciclib▼ for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) metastatic breast cancer. Cancer Nursing Practice. doi: 10.7748/cnp.2020.e1658

Peer review
This article has been subject to external double-blind peer review and has been checked for plagiarism using automated software

Correspondence
pauline.mcilroy@ggc.scot.nhs.uk

Conflict of interest
The author has received an honorarium for writing this article. Medical writing support during preparation of the article was provided by ISO.health Ltd. Editorial support and funding was provided by Eli Lilly and Company Ltd. PP-AL-GB-0077 July 2020

Accepted
22 January 2020

Published online
August 2020

Abstract

Many patients with metastatic breast cancer develop resistance to endocrine therapy. Therefore, treatments with novel molecular targets have been developed to overcome endocrine resistance in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2–) metastatic breast cancer, including cyclin-dependent kinase 4 and 6 (CDK4 and CDK6) inhibitors. CDK4 and CDK6 inhibitors such as abemaciclib offer a new treatment option for patients with metastatic breast cancer.

Nurses have an important role in providing guidance, education and support to patients with breast cancer. Since more patients are likely to receive abemaciclib, it will become increasingly important for nurses to understand how it works, how to effectively manage potential side effects and how to support patients with adhering to treatment.

This article describes the rationale for the use of CDK4 and CDK6 inhibitors in patients with breast cancer, and provides practical advice on how to manage patients with metastatic breast cancer who have been prescribed abemaciclib.

Author details

Pauline McIlroy, advanced breast clinical nurse specialist, The Beatson West of Scotland Cancer Centre, Glasgow, Scotland

Keywords

breast cancer, cancer, cancer research, cancer treatments, concordance, medicines, medicines management, targeted therapies, tumours

Aims and intended learning outcomes

This article aims to provide an overview of the rationale for cyclin-dependent kinase 4 and 6 (CDK4 and CDK6) inhibitor treatment for patients with metastatic breast cancer, along with information on how to manage these patients. It focuses on abemaciclib, an oral CDK4 and CDK6 inhibitor. Abemaciclib has only recently been approved in the UK, so there are limited real-world treatment data outside the clinical trial setting. This article provides practical advice on how to manage patients with metastatic breast cancer who have been prescribed abemaciclib. After reading this article and completing the time out activities you should be able to:

- Explain the available options for treating metastatic breast cancer treatment and the effect of CDK4 and CDK6 inhibitor availability in the UK.
- Summarise the key efficacy and safety data for abemaciclib.

CPD CONTINUING PROFESSIONAL DEVELOPMENT

- Outline the potential side effects of abemaciclib treatment, as well as how best to monitor, manage and support patients who are experiencing these side effects.
- Understand the correct dosing and administration of abemaciclib and be able to communicate this information to patients to support them in adhering to treatment.

Epidemiology of metastatic breast cancer in the UK

Breast cancer is the most common cancer in the UK, accounting for 15% of all new cancer cases in 2016 (Office for National Statistics 2018). In 2016, almost 46,000 cases of breast cancer were diagnosed in England (Office for National Statistics 2018).

Of patients with newly diagnosed breast cancer, between 3% and 8% will present with metastatic disease at the time of diagnosis, while approximately one third of patients diagnosed with early stage disease will later develop advanced or metastatic disease. The five-year survival rate for these women is approximately 20% (Başaran et al 2018).

There are several subtypes of breast cancer, which are described according to the receptors expressed on the surface of tumour cells, stage of diagnosis and rate of growth. Hormone receptor-positive (HR+) breast cancer includes breast cancer in which the tumours express oestrogen receptors (ER+) and/or progesterone receptors, while human epidermal growth factor receptor 2-negative (HER2–) breast cancer refers to breast cancer that does not overexpress the HER2 gene. HR+/HER2– breast cancer is the most common subset of breast cancer, accounting for approximately 70% of cases (Tong et al 2018).

Approximately one third of all HR+/HER2– patients initially diagnosed with early stage disease experience disease recurrence (van Ommen-Nijhof et al 2018), and as a result the HR+/HER2– subset is responsible for the majority of breast cancer related deaths (van Ommen-Nijhof et al 2018).

The primary treatment for patients with HR+ metastatic breast cancer has been sequential endocrine therapies targeting the ER+, which initially leads to a long-lasting positive reaction to treatment in the form of durable tumour responses in the majority of patients. However, over time, most patients become resistant to these treatments, resulting in disease progression (van Ommen-Nijhof et al 2018). Therefore, there is a need for increasingly effective treatments for these patients.

Use of CDK4 and CDK6 inhibitors for the treatment of metastatic breast cancer

Treatments with novel molecular targets have been developed to overcome endocrine resistance in patients with HR+/HER2– metastatic breast cancer, including inhibitors of CDK4 and CDK6. CDK4 and CDK6 are protein kinases that facilitate the progression of the cell cycle, which results in the multiplying of cells in the body. CDK4 and CDK6 inhibitors prevent cell cycle progression, resulting in reduced cell growth and division, cell cycle arrest and ultimately cell death (Hamilton and Infante 2016).

In normal, non-cancerous cells, CDK4 and CDK6 bind to cyclin-D and other molecules, which facilitates a controlled process of gene and protein activation, resulting in deoxyribonucleic acid (DNA) replication and cell proliferation (Hamilton and Infante 2016). In some cancerous cells, this pathway is faulty and too many CDK4 and CDK6 proteins are activated and bound to cyclin-D, which causes cancer cells to grow and divide rapidly (Hamilton and Infante 2016). Box 1 provides advice for nurses on how they could explain the mechanism of action of CDK4 and CDK6 inhibitors to patients.

Cyclin-D is also the target for endocrine therapies, meaning endocrine therapies and CDK4 and CDK6 inhibitors can be combined to stop the growth and division of cancer cells (Hamilton and Infante 2016, O'Leary et al 2016).

Three CDK4 and CDK6 inhibitors – palbociclib (European Medicines Compendium (EMC) 2020a), ribociclib (EMC 2019a) and abemaciclib (EMC 2020b) – have been approved by the European Medicines Agency for use in specific patients. Abemaciclib is approved for the treatment of women with HR+/HER2– locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received previous endocrine therapy.

Box 1. How nurses could explain the mechanism of action of CDK4 and CDK6 inhibitors to patients

- Many cancers grow rapidly and uncontrollably because the cancer cells override the signals that normally control cell growth and division
- Overactivity of the CDK4 and CDK6 enzymes are reported in various cancers; the increased expression of CDK4 and CDK6 can cause cells to rapidly grow and divide increasing the size of the tumour
- Abemaciclib inhibits CDK4 and CDK6, which in turn halts cancer cell growth and prevents cancer cells from dividing

(Hamilton and Infante 2016)

Key points

- Abemaciclib is an oral CDK4 and CDK6 inhibitor treatment for patients with metastatic breast cancer that has only recently been approved in the UK
- Unlike other CDK4 and CDK6 inhibitors, abemaciclib is given to patients on a continuous dosing schedule
- The most common side effects experienced with abemaciclib are diarrhoea, neutropenia, infections, nausea, fatigue, anaemia, vomiting, decreased appetite, leucopenia and alopecia
- It is important that patients understand the treatments they are being offered, the potential benefits of these treatments and any associated side effects

In premenopausal or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone agonist (EMC 2020b).

In early 2019, abemaciclib was recommended by National Institute for Health and Care Excellence (NICE) (2019a) for the same indication, in combination with an aromatase inhibitor. This followed similar NICE (2017a, 2017b) recommendations for palbociclib and ribociclib in 2017. Later in 2019, NICE (2019b) recommended abemaciclib with fulvestrant to be available for NHS use within the Cancer Drugs Fund.

The Cancer Drugs Fund indication for abemaciclib is for patients with HR+/HER2– locally advanced/metastatic breast cancer who have not received previous treatment with a CDK4 and CDK6 inhibitor (NICE 2019b). This guidance means that abemaciclib is now a second-line treatment option for these patients, following treatment with either (neo)adjuvant endocrine therapy or first-line endocrine therapy for metastatic disease.

For patients to receive the medicine, the Cancer Drugs Fund application for abemaciclib treatment should be made, and the first cycle of treatment should be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy (NICE 2019b).

The Scottish Medicines Consortium (SMC) have also recently recommended abemaciclib for the treatment of patients with breast cancer. For full indications and advice, refer to SMC2179 (SMC 2019a) and SMC2135 (SMC 2019b).

Abemaciclib versus other CDK4 and CDK6 inhibitors

Abemaciclib differs from ribociclib and palbociclib in its structure and in how it interacts with CDK4 and CDK6 (O'Shaughnessy et al 2018). Pre-clinical studies have shown that it is 14 times more selective for CDK4 than for CDK6 (Goetz et al 2017), which in practice has resulted in abemaciclib having a different dosing schedule and different side effects than ribociclib and palbociclib.

Abemaciclib is given to patients on a continuous dosing schedule, whereas ribociclib and palbociclib are given to patients for 21 days followed by seven days without treatment (EMC 2019a, 2020a, 2020b). Pre-clinical data have demonstrated the importance of continuous inhibition of CDK4 and CDK6 for inhibition of cancer cell growth and subsequent cell apoptosis (Torres-Guzmán et al 2017).

TIME OUT 1

Reflecting on your clinical practice, how often do you see patients who have been prescribed a CDK4 and CDK6 inhibitor? Which of the three available CDK4 and CDK6 inhibitors does this tend to be? How comfortable do you feel in differentiating between the three CDK4 and CDK6 inhibitors?

Efficacy of abemaciclib for the treatment of HR+/HER2– metastatic breast cancer

Abemaciclib has been investigated in two Phase III clinical trials in women with HR+/HER2– advanced breast cancer: MONARCH 2 (Sledge et al 2017, 2019) and MONARCH 3 (Goetz et al 2017, Johnston et al 2019). MONARCH 2 investigated abemaciclib in combination with fulvestrant, while MONARCH 3 investigated abemaciclib in combination with an aromatase inhibitor. The results of these studies are detailed in Box 2.

In patients with incurable disease, such as those with advanced breast cancer, a gain in their progression-free survival (PFS) may be countered by a reduction in their functional status and perceived health-related quality of life, and they may not be willing to undergo additional treatments. As such, it is important that patient-reported health-related quality of life is assessed to determine if the efficacy of a treatment has any negative effects on quality of life. In the MONARCH 2 and MONARCH 3 studies, abemaciclib plus endocrine treatment did not result in any statistically significant or clinically meaningful differences in patient-reported global health, functioning or most symptoms compared with placebo plus endocrine treatment. Patients reported that increased gastrointestinal symptoms were transient and consistent with the manageable and reversible side effects associated with abemaciclib (Kaufman et al 2018, Goetz et al 2019).

TIME OUT 2

How might you discuss PFS with a patient? How might you make the information you provide specific to your patients' understanding and level of cancer severity? Based on the information you have read in this article, is there anything new you would now include in your conversations regarding abemaciclib?

Abemaciclib administration, dosing and patient monitoring

Administration of oral cancer therapies

The available CDK4 and CDK6 inhibitors are all given orally. Oral cancer therapies can reduce the burden of treatment for

patients because they can be taken outside of the hospital without the need for nurse administration or intravenous infusion (Greer et al 2016). However, patients do not always adhere to oral therapies for breast cancer, with adherence shown to vary in those receiving oral endocrine therapy (Greer et al 2016). Patients with cancer who do not take their treatment as prescribed on average experience reduced efficacy from their treatment, a higher number of inpatient days, and worse survival (Greer et al 2016). Therefore, it is vital that standard procedures for educating patients on the importance of taking oral medicines as prescribed are developed and put into practice, to ensure that they receive the greatest benefit possible from their treatment. Such procedures may include (Boyle and Bubalo 2007, NICE 2009, Jimmy and Jose 2011):

- Providing appropriate counselling for patients about the risks, benefits and safe administration of their CDK4 and CDK6 inhibitor, ensuring that simple language is used so they can understand the implications of their treatment. This may include:
  - Addressing the important information about their treatment, for example what the medicine is, why they are being prescribed it, when to take it, how to take it and for how long.
  - Informing patients of the common side effects and discussing how the patient would like to manage them.
- Involving patients in their treatment decision making where possible so they have a sense of ownership and become partners in their treatment plan.
- Providing a patient leaflet about the risks, benefits and appropriate dosing of their CDK4 and CDK6 inhibitor, to complement the leaflet that comes with the packaging, which can often be complex and challenging for patients to understand.
- Using medication adherence aids, such as calendars, pillboxes, dosage counters and medication diaries.
- Ensuring adherence assessments are undertaken at follow-up appointments, to assess patient adherence, identify any related challenges or barriers and discuss appropriate actions to improve adherence.

Further detailed information on educating patients on their oral cancer treatments is available from the Multinational Association of Supportive Care in Cancer (2016) Oral Agent Teaching Tool.

TIME OUT 3

When considering patients you have treated previously, have there been any groups of patients who have been more adherent to their treatment than others? How have you developed strategies in partnership with patients to assist them to incorporate taking medicines into their daily routine, thus supporting adherence? What strategies do you have in place to monitor adherence?

Abemaciclib dosing

Abemaciclib is given as a 150mg tablet taken twice daily in combination with endocrine therapy on a continuous 28-day dosing schedule, where each cycle is 28 days (EMC 2020b). The abemaciclib dosing schedule differs from that of palbociclib and ribociclib, which are given as once daily doses on an intermittent dosing schedule of 21 days on

Box 2. Results of the MONARCH 2 and MONARCH 3 studies

MONARCH 2 study

Women whose disease had progressed while receiving previous endocrine therapy, and who were treated with abemaciclib plus fulvestrant, had a significantly longer progression-free survival (PFS) (the period when the cancer is stable and does not progress) versus those treated with fulvestrant plus placebo ($P<0.001$). The median PFS of women who received abemaciclib as part of their treatment was 16.9 months versus 9.3 months for patients who did not receive abemaciclib. Overall survival was 46.7 months for women receiving abemaciclib plus fulvestrant versus 37.3 months in the placebo group, which is a 9.4-month improvement (hazard ratio 0.757, $P=0.01$). Additionally, in patients with measurable cancer, the objective response rate – the percentage of patients whose cancer shrunk (partial response) or disappeared (complete response) after treatment – was 48% in the abemaciclib arm versus 21% in the placebo arm ($P<0.001$)

MONARCH 3 study

Women who had not yet received any treatment for their advanced breast cancer, and who were given abemaciclib with a non-steroidal aromatase inhibitor, had a significantly longer PFS than those treated with placebo plus a non-steroidal aromatase inhibitor ($P<0.001$). The median PFS of women who received abemaciclib plus an aromatase inhibitor was 28.2 months versus 14.8 months with placebo plus aromatase inhibitor. This means that women who were given abemaciclib as part of their treatment, on average, lived without their breast cancer progressing for an additional 13.4 months compared with those who did not receive abemaciclib. Additionally, in patients with measurable cancer, the objective response rate was 61% in the abemaciclib arm versus 46% in the placebo arm ($P=0.003$)

(Johnston et al 2019, Sledge et al 2019)

FURTHER RESOURCES

Summary of Product Characteristics
medicines.org.uk/emc/product/9532/smpc

Abemaciclib Prescribing Information
lillyoncology.co.uk/assets/pdf/verzenios-api-a4-landscape.pdf

treatment and seven days off treatment (EMC 2019a, 2020a). Abemaciclib tablets are available in three different doses: a 150mg yellow tablet of 7.5×13.7mm; a 100mg white tablet of 6.6×12.0mm; and a 50mg beige tablet of 5.2×9.5mm. Patients should continue to receive their abemaciclib treatment for as long as they are experiencing clinical benefit or until unacceptable side effects occur. This, along with dose reductions for side effects, are discussed in the management of abemaciclib side effects section of this article.

Patient monitoring

To determine the appropriate dose of abemaciclib before initiating treatment, and during treatment, patients should have a full blood count and liver function tests – alanine aminotransferase (ALT) and aspartate aminotransferase (AST) – before starting their treatment, every two weeks for the first two 28-day cycles, monthly for the next two cycles, and then as clinically indicated, for example if they are experiencing side effects. Before treatment initiation, the patient's absolute neutrophil count should be ≥1,500/mm3, platelet count ≥100,000/mm3 and haemoglobin level ≥8g/dL (EMC 2020b).

Communicating information about abemaciclib to patients

It is important that patients fully understand the correct dosing and administration of abemaciclib to ensure maximum efficacy.

Box 3 outlines some important information to communicate to patients about abemaciclib. Patients should know who to contact if they experience any side effects so that a plan can be implemented to reduce the risk of patients missing or reducing their dose without input from the healthcare team. Plans may include appropriate prophylactic treatments and/or dose interruptions and reductions. For further details, refer to the section of this article on management of abemaciclib side effects.

Management of abemaciclib side effects

The most common side effects experienced with abemaciclib are diarrhoea, neutropenia, infections, nausea, fatigue, anaemia, vomiting, decreased appetite, leucopenia and alopecia (EMC 2020b).

Side effects such as diarrhoea are generally manageable when patients are informed of them in advance and are educated on how best to manage and cope with them. However, side effects are specific to each individual, and what is manageable for one patient may not be manageable for another patient. Providing advice and information tailored to the patient is important in assisting them to manage any side effects so they can achieve the greatest benefit from their treatment.

Some patients may experience side effects to an extent that they require their dose

Box 3. Information to communicate to patients about abemaciclib

Abemaciclib administration and dosing
- Abemaciclib should be taken twice daily at approximately the same times every day
- Abemaciclib can be taken with or without food but should not be taken with grapefruit or grapefruit juice
- Tablets should be swallowed whole, not chewed, split or crushed
- If the patient vomits after taking abemaciclib or a dose is missed, they should take their next dose as scheduled and should not take another dose to compensate for the missed dose
- Abemaciclib is contraindicated for patients with hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 of the Summary of Product Characteristics. For further details about this and any special warnings and precautions for use, refer to the Summary of Product Characteristics, available at: medicines.org.uk/emc/product/9532/smpc

Patient monitoring
- Patients will be monitored through blood tests while taking abemaciclib to reduce complications from severe side effects that may be associated with abemaciclib, for example neutropenia, anaemia, leucopenia or reduced liver function
- Patients will have their blood taken to evaluate their haematological status and liver function before the start of treatment, every two weeks for the first two months, monthly for the next two months, then as clinically indicated. This would be clinically indicated in patients who are experiencing side effects such as neutropenia, anaemia, leucopenia, fever or reduced liver function

Enhancing patient adherence
- Patients should be provided with appropriate contact details so they can discuss any concerns they have, or for advice on managing side effects
- Patients should understand that there are several ways to relieve side effects they experience, including additional over-the-counter medicines and/or dose reductions
- Refer to the section of this article on the management of abemaciclib side effects for further information

(European Medicines Compendium 2020b)

of abemaciclib to be reduced. For patients experiencing any side effects and who require a dose reduction, it is recommended that the first dose reduction should be to 100mg twice daily, followed by a further dose reduction to 50mg twice daily if required (EMC 2020b).

Table 1 details the most frequent side effects reported in Phase III studies of abemaciclib in combination with endocrine therapy.

TIME OUT 4

Fatigue can be a common side effect for many patients undergoing various cancer treatments. Reflecting on the conversations you have had with patients receiving cancer treatment, how often do you discuss fatigue? What interventions and suggestions do you usually advise for this side effect? Can you think of any other ways for patients to manage fatigue?

Diarrhoea

Diarrhoea is a common side effect associated with cancer treatments. Patients who experience diarrhoea may also experience stomach cramps, bloating and nausea (Andreyev et al 2014), and it can lead to dehydration and low levels of salt and potassium (National Cancer Institute 2018). Table 2 details the Common Terminology Criteria for Adverse Events grading of diarrhoea.

Grades 3 and 4 diarrhoea can be serious and life-threatening and may require hospitalisation (National Cancer Institute 2017). Therefore, although some patients may find it challenging to talk about diarrhoea, it is important for them to report this side effect as soon possible if they start to experience it.

Diarrhoea was the most commonly reported side effect in the MONARCH 2 and MONARCH 3 studies, occurring in between 82-86% of patients receiving abemaciclib (Sledge et al 2017, Johnston et al 2019). Most of these cases were of low grade and occurred early in the first treatment cycle, with a median time to first onset of six to eight days (EMC 2020b). The majority of patients (>70%) did not require a dose modification (Sledge et al 2017, Johnston et al 2019).

When discussing diarrhoea with patients, nurses should assess the frequency and severity of episodes and ask about other symptoms. As long as diarrhoea is not caused by another underlying condition, it can be effectively managed through patient education and medicines. Before patients are initiated onto abemaciclib treatment, they should be informed that diarrhoea is a common side effect and that they should begin treatment with an antidiarrhoeal medicine, such as loperamide hydrochloride, at the first sign of loose stools; or an antispasmodic when

Table 1. Most frequent side effects reported in Phase III studies of abemaciclib in combination with endocrine therapy (*n*=768)

Side effect	All grades (%)	Grade 3 toxicity (%)	Grade 4 toxicity (%)
Diarrhoea	84.6	11.7	0
Neutropenia	45.1	22.9	2.5
Infections*	43.6	5.2	1.0
Nausea	43.5	2.1	0
Fatigue	40.5	2.3	0
Anaemia	30.1	7.0	0.1
Vomiting	27.7	1.2	0
Decreased appetite	26.4	1.3	0
Leucopenia	25.7	8.5	0.3
Alopecia	20.7	0	0

*Infections includes all preferred terms that are part of the System Organ Class Infections and infestations

(European Medicines Compendium 2020b)

Table 2. Common Terminology Criteria for Adverse Events grading of diarrhoea

Grade	Description	Management recommendations
Grade 1	Increase of <4 stools per day over baseline; mild increase in ostomy output compared with baseline	» No dose reduction required
Grade 2	Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared with baseline; limiting instrumental activities of daily living	» If toxicity does not resolve within 24 hours to Grade 1 or below, suspend the dose until resolution. A dose reduction is not required » If Grade 2 toxicity persists or recurs after resuming the same dose despite maximal supportive measures, suspend the dose until the toxicity resolves to Grade 1 or below and resume at the next lower dose
Grade 3	Increase of ≥7 stools per day over baseline; hospitalisation indicated; severe increase in ostomy output compared with baseline; limiting self-care activities of daily living	» Suspend the dose until the toxicity resolves to Grade 1 or below » Resume the drug at the next lower dose
Grade 4	Life-threatening consequences; urgent intervention indicated; requires hospitalisation	

(National Cancer Institute 2017, European Medicines Compendium 2020b)

experiencing spasms. Dose reductions are recommended for patients experiencing persistent Grade 2, Grade 3 or Grade 4 diarrhoea. Patients should keep a record of the number of stool movements and the dose and amount of antidiarrhoeal medicines taken to enable the healthcare team to assess the severity of their symptoms and develop appropriate management strategies.

Box 4 outlines a stepped approach to managing diarrhoea in patients taking abemaciclib.

Haematological side effects

Severe neutropenia has frequently been reported in studies of palbociclib and ribociclib, and was a dose-limiting toxicity. This means that neutropenia leads to the use of dose interruptions and intermittent dosing schedules for these treatments, for example 21 days on treatment, seven days off treatment (Flaherty et al 2012, Juric et al 2015, Cristofanilli et al 2016, Hortobagyi et al 2018). Like the other two CDK4 and CDK6 inhibitors, abemaciclib can cause neutropenia, but it was not a dose-limiting toxicity and therefore patients can be continuously dosed without the need for a week off treatment. In the MONARCH 2 and MONARCH 3 studies, neutropenia of any grade occurred in 45% of patients receiving abemaciclib, with 25% of patients experiencing Grade 3 or Grade 4 neutropenia (EMC 2020b).

Before commencing abemaciclib treatment, patients should have a full blood count and throughout treatment, patients should be appropriately monitored. If a haematological toxicity occurs, such as neutropenia, patients should be managed with dose reductions according to the Summary of Product Characteristics (EMC 2020b).

Abnormal or impaired liver function

Abnormal liver function can occur in some patients receiving abemaciclib. Most causes of abnormal liver function do not result in any side effects for patients; however, symptoms such as fatigue, loss of appetite or in extreme cases jaundice can occur (NHS 2017a).

Some patients receiving abemaciclib in combination with endocrine treatment experienced increased levels of liver enzymes (ALT and AST); this was reported in 15% (ALT) and 14% (AST) of patients (EMC 2020b). Severe Grade 3 or Grade 4 increases in ALT or AST elevations were uncommon, affecting 4-6% of patients (EMC 2020b). Grade 3 is an increase of >5.0-20.0 times the upper limit of normal, while Grade 4 is an increase of >20.0 times the upper limit of normal. If a patient's liver function is abnormal, dose reductions should be performed. If a patient experiences an elevation in AST and/or ALT >3 times the upper limit of normal with total bilirubin >2 times the upper limit of normal, in the absence of cholestasis, or if they have a Grade 4 increase in ALT or AST, abemaciclib treatment should be discontinued (EMC 2020b).

Although abnormal liver function is not a common side effect of abemaciclib treatment, patients should be informed that there is a risk, and that they should report any relevant symptoms that they experience. The Child-Pugh score is a system for assessing the prognosis of chronic liver disease, primarily cirrhosis (Peng et al 2016). In patients with severe hepatic impairment (Child-Pugh C), a decrease in dosing frequency to once daily is recommended. This recommendation is based on an increase in abemaciclib exposure observed in patients who had Child-Pugh C hepatic impairment (EMC 2020b).

Other side effects

Other side effects associated with abemaciclib treatment include fatigue, nausea and vomiting. Interstitial lung disease, which can cause shortness of breath, has also been reported in patients taking abemaciclib (EMC 2020b). It is important that patients are aware that they should inform the healthcare team about these or any other side effects that they are concerned about, to ensure that a plan can be implemented to support

Box 4. Stepped approach to managing diarrhoea in patients taking abemaciclib

1. Expect – diarrhoea is a common side effect of abemaciclib. If diarrhoea occurs, patients will likely experience it within the first month of treatment
2. Plan – plan ahead of time. Ensure patients have antidiarrhoeal medicines available to them before they start taking abemaciclib. Inform patients that antidiarrhoeal medicines are not for prophylactic use
3. Act – develop a 24-hour plan with the patient. Patients should start treatment with antidiarrhoeal medicines at the first sign of loose stools, and should increase oral fluids and notify the healthcare team
4. Follow up – follow up with the patient after the first 24 hours. If the diarrhoea does not resolve to Grade 1 or below within 24 hours, the nurse may need to suspend the dose, and possibly reduce it when resuming treatment

(European Medicines Compendium 2020b)

them with managing these issues. If a patient experiences any other non-haematological side effects of Grade 1 or Grade 2 in severity (National Cancer Institute 2017), they should be supported according to local hospital guidelines, for example providing antiemetics for nausea. If the side effect is Grade 2 and persistent or recurrent, and does not resolve with support to baseline or Grade 1 within seven days, abemaciclib treatment should be stopped until the side effect resolves to Grade 1 or below and an abemaciclib dose reduction should be recommended (EMC 2020b).

The patient's healthcare team should be informed of the side effect so that other causes can be ruled out. Investigations for other causes of the side effect might include: blood tests to evaluate the patient's full blood count and to rule out haematological causes; liver function tests to eliminate hepatic causes; appropriate tests for bacterial infections, since nausea and/or diarrhoea may be caused by bacterial infection; and evaluation of other treatments the patients may be receiving, for example diarrhoea may be caused by antibiotic use.

Serum creatinine

While not a side effect, abemaciclib increases serum creatinine levels without affecting renal function due to inhibition of renal tubular secretion transporters. Serum creatinine increases occur within the first month of treatment, remain elevated but stable throughout treatment, are reversed on treatment discontinuation, and are not accompanied by changes in markers of renal function, such as cystatin C (EMC 2020b). Therefore, it should be expected that patient serum creatinine levels will rise when treatment with abemaciclib is initiated and this should not cause concern or result in patients being taken off treatment. If serum creatinine levels are not stable and continue to rise throughout treatment, further investigations should be performed and patients may be required to discontinue their abemaciclib treatment.

Risk of venous thromboembolism

Venous thromboembolism was reported in around 5% of patients treated with abemaciclib plus fulvestrant or an aromatase inhibitor, compared with less than 1% of patients treated with placebo plus fulvestrant or an aromatase inhibitor (EMC 2020b). It is important to monitor patients for signs and symptoms of deep vein thrombosis and pulmonary embolism and treat as medically appropriate.

Communicating abemaciclib side effects to patients

It is important that potential side effects are communicated to patients effectively without causing them concern, because this may decrease their willingness to take the medicine as prescribed (Sawant and Sansgiry 2018). Box 5 provides suggestions for discussing abemaciclib side effects with patients.

Management of co-administration with CYP3A4 inhibitors

Abemaciclib is primarily metabolised by the enzyme CYP3A4, so use of strong CYP3A4 inhibitors co-administered with abemaciclib should be avoided to prevent increased plasma concentrations of abemaciclib. Examples of strong CYP3A4 inhibitors include clarithromycin, itraconazole, ketoconazole,

Box 5. Suggestions for discussing abemaciclib side effects with patients

It is important to inform patients that:

- Most patients receiving abemaciclib will experience some side effects. However, these are generally of low severity and can be well managed
- They should discuss any side effects they experience with the healthcare team to assist with managing and alleviating symptoms
- Additional medicines can be prescribed to alleviate side effects, and in some circumstances the dose of abemaciclib can be reduced
- It is important that they take abemaciclib at the correct dose to maximise the chance of the medicine being effective against their breast cancer
- It is important that they do not change their dose without speaking to the healthcare team

Diarrhoea

If a patient is experiencing diarrhoea, it is important to ensure it is not caused by an underlying issue and to discuss how best to manage it. At the first sign of loose stools, nurses should advise patients to:

- Take an antidiarrhoeal medicine such as loperamide hydrochloride. Patients should take two tablets of 2mg loperamide after the first loose stool, followed by one tablet of 2mg loperamide after subsequent loose stools, up to a maximum of 6mg or 12mg per day
- Maintain an optimal fluid intake by taking small, frequent sips of water
- Eat small, light meals and avoid fatty or spicy foods. Examples of suitable foods include potatoes, rice, bananas, soup and boiled vegetables

If the patient also experiences spasms, advise that they take an antispasmodic such as hyoscine butylbromide, in addition to an antidiarrhoeal medicine

Haematological side effects

If the patient has a high temperature, pyrexia, feels unusually tired or fatigued or has any signs of skin rash or signs of infection, nurses should encourage them to report this immediately to ensure there are no additional issues causing these symptoms. Specific signs nurses should advise patients to look for include:

- High temperature of 38°C or above
- Low temperature of 36°C or below
- Chills and shivering
- Sore throat
- Recurrent mouth ulcers
- Toothache
- Skin rashes
- Excessive or chronic tiredness – more than usual
- Flu-like symptoms

(National Institute for Health and Care Excellence 2012, 2017c, NHS 2017b, NHS Inform 2020, European Medicines Compendium 2019b, 2019c)

lopinavir/ritonavir, posaconazole and voriconazole. The patient should also be advised to avoid grapefruit or grapefruit juice, because this is also a potential CYP3A4 inhibitor.

If the use of strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose should be reduced to 100mg twice daily. If a patient already has a dose reduction to 100mg twice daily, for example as a result of an existing side effect, and co-administration of strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose should be further reduced to 50mg twice daily.

In patients who have had their dose reduced to 50mg abemaciclib twice daily and in whom co-administration of strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose may be continued with close monitoring for signs of side effects. Alternatively, the abemaciclib dose may be reduced to 50mg once daily or discontinued. If the CYP3A4 inhibitor is discontinued, the abemaciclib dose should be increased to the dose used before the initiation of the CYP3A4 inhibitor, but only after three to five half-lives of the CYP3A4 inhibitor (EMC 2020b).

CYP3A4 inducers

Co-administration of abemaciclib with CYP3A4 inducers should also be avoided because of the risk of decreased efficacy of abemaciclib. For example, co-administration of abemaciclib with the strong CYP3A4 inducer rifampicin decreased the plasma concentration of abemaciclib by 95% (EMC 2020b). Other examples of strong CYP3A4 inducers include carbamazepine, phenytoin and St John's wort (EMC 2020b).

TIME OUT 5

There are several medicines that should not be co-administered with abemaciclib, some of which are available over the counter or may be prescribed by a GP. How can you ensure your patient understands the risk of taking these medicines with abemaciclib and knows which medicines should be avoided?

Effect of abemaciclib on current patients with metastatic breast cancer

It is important that patients understand the treatments they are being offered, the potential benefits of these treatments and any associated side effects. Appropriate clinical practice and management guidelines should be implemented to provide information and support for patient decision-making, treatment planning and psychological support.

NHS England (2017) recommends that patients should be actively involved in their treatment decisions and healthcare, which has been shown to improve patient satisfaction, health outcomes, quality of life, adherence to treatment and cost effectiveness of services (Vahdat et al 2014).

Similarly, The Scottish Government (2016) is working to improve the experience and outcomes for people affected by cancer through a person-centred approach. This involves finding out what is important to the patient, working with the individual and their family and friends to support their decisions, and providing the information they require to be fully involved in care decisions at a level that they can understand.

TIME OUT 6

Take the opportunity to familiarise yourself with your local guidelines on the care and treatment of breast cancer, so that you can fully understand the treatment options available to the patients you care for

Conclusion

CDK4 and CDK6 inhibitors represent one of the most exciting recent developments for women with HR+/HER2– metastatic breast cancer, potentially providing a new standard of care for these patients. Abemaciclib offers a new, effective treatment option, both in the first-line advanced setting and following cancer progression on previous endocrine therapy. Although no direct comparison studies have been undertaken, patients treated with abemaciclib experience a higher rate of diarrhoea than other CDK4 and CDK6 inhibitors, but also lower rates of haematological side effects that enables continuous dosing and simplified blood monitoring (NICE 2019a). The efficacy of abemaciclib in early stage breast cancer is being evaluated and results in this patient population are awaited (ClinicalTrials.gov 2019, NCT03155997).

TIME OUT 7

Consider how using abemaciclib for the treatment of HR+/HER2– metastatic breast cancer relates to The Code: Professional Standards of Practice and Behaviour for Nurses, Midwives and Nursing Associates (Nursing and Midwifery Council 2018) or, for non-UK readers, the requirements of your regulatory body

TIME OUT 8

Now that you have completed the article, reflect on your practice in this area and consider writing a reflective account: **rcni.com/reflective-account**

References

Andreyev J, Ross P, Donnellan C et al (2014) Guidance on the management of diarrhoea during cancer chemotherapy. The Lancet Oncology. 15, 10, e447-e460. doi: 10.1016/S1470-2045(14)70006-3

Başaran G, Twelves C, Diéras V et al (2018) Ongoing unmet needs in treating estrogen receptor-positive/HER2-negative metastatic breast cancer. Cancer Treatment Reviews. 63, 144-155. doi: 10.1016/j.ctrv.2017.12.002

Boyle D, Bubalo J (2007) Enhancing patient adherence to improve outcomes with oral chemotherapy. Proceedings from a symposium at the 2007 Hematology/Oncology pharmacy association annual conference. US Pharmacist. 32, 10, 1-8.

ClinicalTrials.gov (2019) Endocrine Therapy With or Without Abemaciclib (LY2835219) Following Surgery in Participants With Breast Cancer (monarchE). clinicaltrials.gov/ct2/show/NCT03155997 (Last accessed: 13 March 2020.)

Cristofanilli M, Turner N, Bondarenko I et al (2016) Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncology. 17, 4, 425-439. doi: 10.1016/S1470-2045(15)00613-0

European Medicines Compendium (2019a) Kisqali 200mg Film-Coated Tablets. medicines.org.uk/emc/product/8110/smpc (Last accessed: 13 March 2020.)

European Medicines Compendium (2019b) Loperamide 2mg Hard Capsules (PL 29831/0381). medicines.org.uk/emc/product/1207/smpc (Last accessed: 13 March 2020.)

European Medicines Compendium (2019c) Buscopan 10 mg Tablets. medicines.org.uk/emc/product/1775/smpc (Last accessed: 13 March 2020.)

European Medicines Compendium (2020a) IBRANCE 75mg Hard Capsules. medicines.org.uk/emc/product/4449/smpc (Last accessed: 13 March 2020.)

European Medicines Compendium (2020b) Verzenios 50mg Film-Coated Tablets. medicines.org.uk/emc/product/9532/smpc (Last accessed: 13 March 2020.)

Flaherty K, Lorusso P, Demichele A et al (2012) Phase I, dose-escalation trial of the oral cyclin-dependent kinase 4/6 inhibitor PD 0332991, administered using a 21-day schedule in patients with advanced cancer. Clinical Cancer Research. 18, 2, 568-576. doi: 10.1158/1078-0432.CCR-11-0509

Goetz M, Johnston S, Martin M et al (2019) Abstract P6-16-01: health-related quality of life in MONARCH 3: abemaciclib plus an aromatase inhibitor as initial therapy in women with HR+, HER2– advanced breast cancer. Cancer Research. 79, 4, P6-16-01. doi: 10.1158/1538-7445.SABCS18-P6-16-01

Goetz M, Toi M, Campone M et al (2017) MONARCH 3: abemaciclib as initial therapy for advanced breast cancer. Journal of Clinical Oncology. 35, 32, 3638-3646. doi: 10.1200/JCO.2017.75.6155

Greer JA, Amoyal N, Nisotel L et al (2016) A systematic review of adherence to oral antineoplastic therapies. Oncologist. 21, 3, 354-376. doi: 10.1634/theoncologist.2015-0405

Hamilton E, Infante J (2016) Targeting CDK4/6 in patients with cancer. Cancer Treatment Reviews. 45, 129-138. doi: 10.1016/j.ctrv.2016.03.002.

Hortobagyi G, Stemmer S, Burris H et al (2018) Updated results from MONALEESA-2, a phase III trial of first-line ribociclib plus letrozole versus placebo plus letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. Annals of Oncology. 29, 7, 1541-1547. doi: 10.1093/annonc/mdy155

Jimmy B, Jose J (2011) Patient medication adherence: measures in daily practice. Oman Medical Journal. 26, 3, 155-159. doi: 10.5001/omj.2011.38

Johnston S, Martin M, Di Leo A et al (2019) MONARCH 3 final PFS: a randomized study of abemaciclib as initial therapy for advanced breast cancer. NPJ Breast Cancer. 5, 5. doi: 10.1038/s41523-018-0097-z

Juric D, Hamilton E, Estévez L et al (2015) Abstract P5-19-24: phase Ib/II study of LEE011 and BYL719 and letrozole in ER+, HER2– breast cancer: safety, preliminary efficacy and molecular analysis. Cancer Research. 75, 9, P5-19-24. doi: 10.1158/1538-7445.SABCS14-P5-19-24

Kaufman PA, Toi M, Neven P et al (2018) Health-related quality of life (HRQoL) in MONARCH 2: abemaciclib plus fulvestrant in women with HR+, HER2– advanced breast cancer (ABC) who progressed on endocrine therapy. Journal of Clinical Oncology. 36, Suppl 15, 1049. doi: 10.1200/JCO.2018.36.15_suppl.1049

Multinational Association of Supportive Care in Cancer (2016) MASCC Oral Agent Teaching Tool (MOATT) User Guide. mascc.org/assets/Guidelines-Tools/moattuserguide_sept2016_update_usletter.pdf (Last accessed: 13 March 2020.)

National Cancer Institute (2017) Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0. ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf (Last accessed: 13 March 2020.)

National Cancer Institute (2018) Diarrhea and Cancer Treatment. cancer.gov/about-cancer/treatment/side-effects/diarrhea (Last accessed: 13 March 2020.)

National Institute for Health and Care Excellence (2009) Medicines Adherence: Involving Patients in Decisions about Prescribed Medicines and Supporting Adherence. Clinical guideline No. 76. NICE, London.

National Institute for Health and Care Excellence (2012) Neutropenic Sepsis: Prevention and Management of Neutropenic Sepsis in Cancer Patients. Clinical guideline No. 76. NICE, London.

National Institute for Health and Care Excellence (2017a) Palbociclib with an Aromatase Inhibitor for Previously Untreated, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer. Technology appraisal guidance No. 495. NICE, London.

National Institute for Health and Care Excellence (2017b) Ribociclib with an Aromatase Inhibitor for Previously Untreated, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer. Technology appraisal guidance No. 496. NICE, London.

National Institute for Health and Care Excellence (2017c) Sepsis: Recognition, Diagnosis and Early Management. NICE guideline No. 51. NICE, London.

National Institute for Health and Care Excellence (2019a) Abemaciclib with an Aromatase Inhibitor for Previously Untreated, Hormone Receptor-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer. Technology appraisal guidance No. 563. NICE, London.

National Institute for Health and Care Excellence (2019b) Abemaciclib with Fulvestrant for Treating Hormone Receptor-Positive, HER2-Negative Breast Cancer After Endocrine Therapy. Technology appraisal guidance No. 579. NICE, London.

NHS (2017a) Liver Disease. nhs.uk/conditions/liver-disease (Last accessed: 13 March 2020.)

NHS (2017b) Low White Blood Cell Count. nhs.uk/conditions/low-white-blood-cell-count (Last accessed: 13 March 2020.)

NHS England (2017) Involving People in their own Health and Care: Statutory Guidance for Clinical Commissioning Groups and NHS England. england.nhs.uk/wp-content/uploads/2017/04/ppp-involving-people-health-care-guidance.pdf (Last accessed: 13 March 2020.)

NHS Inform (2020) Diarrhoea. nhsinform.scot/illnesses-and-conditions/stomach-liver-and-gastrointestinal-tract/diarrhoea#treating-diarrhoea (Last accessed: 13 March 2020.)

Nursing and Midwifery Council (2018) The Code: Professional Standards of Practice and Behaviour for Nurses, Midwives and Nursing Associates. NMC, London.

Office for National Statistics (2018) Cancer Registration Statistics, England: 2016. ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancerregistrationstatisticsengland/final2016#breast-prostate-lung-and-colorectal-cancers-continue-to-be-the-most-common (Last accessed: 13 March 2020.)

O'Leary B, Finn R, Turner N (2016) Treating cancer with selective CDK4/6 inhibitors. Nature Reviews Clinical Oncology. 13, 7, 417-430. doi: 10.1038/nrclinonc.2016.26

O'Shaughnessy J, Goetz M, Sledge G et al (2018) Abstract CT099: the benefit of abemaciclib in prognostic subgroups - an update to the pooled analysis of MONARCH 2 and 3. Cancer Research. 78, 13, CT099. doi: 10.1158/1538-7445.AM2018-CT099

Peng Y, Qi X, Guo X (2016) Child–Pugh versus MELD score for the assessment of prognosis in liver cirrhosis. Medicine. 95, 8, e2877. doi: 10.1097/MD.0000000000002877

Sawant R, Sansgiry S (2018) Communicating risk of medication side-effects: role of communication format on risk perception. Pharmacy Practice. 16, 2, 1174. doi: 10.18549/PharmPract.2018.02.1174

Scottish Medicines Consortium (2019a) SMC2135: Abemaciclib 50mg, 100mg and 150mg Tablets (Verzenios). scottishmedicines.org.uk/media/4377/abemaciclib-verzenios-final-april-2019-1-for-website.pdf (Last accessed: 13 March 2020.)

Scottish Medicines Consortium (2019b) SMC2179: Abemaciclib 50mg, 100mg and 150mg Tablets (Verzenios). scottishmedicines.org.uk/media/4378/abemaciclib-verzenios-final-april-2019-2-for-website.pdf (Last accessed: 13 March 2020.)

Sledge GW, Toi M, Neven P et al (2017) MONARCH 2: abemaciclib in combination with fulvestrant in women with HR+/HER2– advanced breast cancer who had progressed while receiving endocrine therapy. Journal of Clinical Oncology. 35, 25, 2875-2884. doi: 10.1200/JCO.2017.73.7585

Sledge GW, Toi M, Neven P et al (2019) The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor-positive, ERBB2-negative breast cancer that progressed on endocrine therapy-MONARCH 2: a randomized clinical trial. JAMA Oncology. doi: 10.1001/jamaoncol.2019.4782

The Scottish Government (2016) Beating Cancer: Ambition and Action. gov.scot/publications/beating-cancer-ambition-action/#res-1 (Last accessed: 13 March 2020.)

Tong C, Wu M, Cho W et al (2018) Recent advances in the treatment of breast cancer. Frontiers Oncology. 8, 227. doi: 10.3389/fonc.2018.00227

Torres-Guzmán R, Calsina B, Hermoso A et al (2017) Preclinical characterization of abemaciclib in hormone receptor positive breast cancer. Oncotarget. 8, 41, 69493-69507. doi: 10.18632/oncotarget.17778

Vahdat S, Hamzehgardeshi L, Hessam S et al (2014) Patient involvement in health care decision making: a review. Iranian Red Crescent Medical Journal. 16, 1, e12454. doi: 10.5812/ircmj.12454

van Ommen-Nijhof A, Konings I, van Zeijl C et al (2018) Selecting the optimal position of CDK4/6 inhibitors in hormone receptor-positive advanced breast cancer – the SONIA study: study protocol for a randomized controlled trial. BMC Cancer. 18, 1, 1146. doi: 10.1186/s12885-018-4978-1

Abemaciclib for metastatic breast cancer

TEST YOUR KNOWLEDGE BY COMPLETING THIS MULTIPLE-CHOICE QUIZ

1. Which statement is true?

a) Cyclin-dependent kinase 4 and 6 (CDK4 and CDK6) inhibitors cannot be combined with endocrine therapies ☐
b) Over time, patients can become resistant to endocrine therapies ☐
c) Cyclin D is targeted by CDK4 and CDK6 inhibitors, but not endocrine therapies ☐
d) CDK4 and CDK6 are protein kinases that halt the progress of the cell cycle ☐

2. Which of these is a CDK4 and CDK6 inhibitor that should be given on a continuous dosing schedule?

a) Abemaciclib ☐
b) Ribociclib ☐
c) Palbociclib ☐
d) Aspirin ☐

3. One of the most common side effects experienced by patients taking abemaciclib is:

a) Increased energy ☐
b) Constipation ☐
c) Increased appetite ☐
d) Diarrhoea ☐

4. How are CDK4 and CDK6 inhibitors administered?

a) Intravenously ☐
b) Orally ☐
c) Topically ☐
d) Rectally ☐

5. Which of the following could be implemented as part of standard procedures to improve patient adherence?

a) Providing counselling about the risks, benefits and safe administration of their treatment ☐
b) Using medication adherence aids such as calendars and pillboxes ☐
c) Undertaking adherence assessments at follow-up appointments ☐
d) All of the above ☐

6. To determine the appropriate dose of abemaciclib before and during treatment, patients should have:

a) A full blood count and liver function tests ☐
b) A gait analysis ☐
c) A lumbar puncture ☐
d) An eye test ☐

7. In the Common Terminology Criteria for Adverse Events grading of diarrhoea, Grade 3 diarrhoea is described as:

a) No increase in the number of stools ☐
b) Increase of <4 stools per day over baseline ☐
c) Increase of 4-6 stools per day over baseline ☐
d) Increase of ≥7 stools per day over baseline ☐

8. Abemaciclib should not be taken with:

a) Water ☐
b) Milk ☐
c) Grapefruit juice ☐
d) Orange juice ☐

9. To identify potential haematological side effects of abemaciclib, nurses should advise patients to look for:

a) Chills and shivering ☐
b) Sore throat ☐
c) Toothache ☐
d) All of the above ☐

10. Which statement is false?

a) Abemaciclib is primarily metabolised by the enzyme CYP3A4 ☐
b) Co-administration of abemaciclib with CYP3A4 inducers should be avoided ☐
c) Abemaciclib should be co-administered with strong CYP3A4 inhibitors ☐
d) If the use of strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose should be reduced ☐

How to complete this assessment

This multiple-choice quiz will help you test your knowledge. It comprises ten multiple choice questions broadly linked to the previous article. There is one correct answer to each question.

You can read the article before answering the questions or attempt the questions first, then read the article and see if you would answer them differently.

You may want to write a reflective account. Visit rcni.com/reflective-account

Go online to complete this multiple-choice quiz and you can save it to your RCNi portfolio to help meet your revalidation requirements. Go to **rcni.com/cpd/test-your-knowledge**

This multiple-choice quiz was compiled by **David Swan**

The answers to this **multi-choice quiz** *are:*

1. b, 2. a, 3. d, 4. b, 5. d, 6. a, 7. d, 8. c, 9. d, 10. c

This activity has taken me ___ minutes/hours to complete. Now that I have read this article and completed this assessment, I think my knowledge is:

Excellent ☐ Good ☐ Satisfactory ☐ Unsatisfactory ☐ Poor ☐

As a result of this I intend to: _____

_____

_____

_____