CLINICAL MANAGEMENT OF PATIENTS TAKING ABEMACICLIB

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Abemaciclib is Approved for Use in HR+, HER2-, High Risk Early or Advanced/Metastatic Breast Cancer

FDA Prescribing Information[1] >>LINK

In adult patients with HR+, HER2-, node-positive, early breast cancer at high risk of recurrence, abemaciclib is administered:

- **In combination with an endocrine therapy (tamoxifen or an AI)** for the adjuvant treatment of **adult patients**

In patients with HR+, HER2- advanced or MBC, abemaciclib is administered:

- **In combination with an AI as initial endocrine-based therapy** for the treatment of **adult patients**
- **In combination with fulvestrant** for the treatment of adult patients with **disease progression** following ET
- As **monotherapy** for the treatment of adult patients with disease progression following ET and prior chemotherapy in the metastatic setting

HR+ HER2- MBC	NCCN Guidelines[2]
1L	Abemaciclib plus an AI or fulvestrant
2L	Abemaciclib plus fulvestrant if CDK4 & 6 inhibitor not previously used[a]
Beyond 2L	Abemaciclib plus fulvestrant if CDK4 & 6 inhibitor not previously used[a]
	Abemaciclib monotherapy is useful under certain circumstances[a,b]

[a]If there is disease progression while on CDK4 & 6 inhibitor therapy, there are limited data to support an additional line of therapy with another CDK4 & 6-containing regimen. [b]Indicated after disease progression on prior endocrine therapy and prior chemotherapy in the metastatic setting. 1L=First line; 2L=Second Line: AI=Aromatases Inhibitor; CDK=Cyclin Dependent Kinase; ET=Endocrine Therapy; FDA=Food and Drug Administration; HER2=Human Epidermal Growth Factor Receptor 2; HR=Hormone Receptor; MBC=Metastatic Breast Cancer; NCCN=National Comprehensive Cancer Network.1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2023 2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Breast Cancer V.4.2021. Verzenio® is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

Abemaciclib Dosing, Administration and Drug Interactions

Abemaciclib is Continuously Dosed and Supplied as an Oral Tablet

Recommended dosing of abemaciclib

150 mg PO BID
when used in combination
with fulvestrant, tamoxifen or an AI

or

200 mg PO BID
when used as monotherapy

Contraindications: None

- Abemaciclib should be taken at approximately the same time every day and may be administered with or without food[1]
- If the patient misses a dose or vomits, the next dose can be taken at the scheduled time[1]
- Abemaciclib tablets should be swallowed whole[1]
  - Patient should not chew, crush, or split the tablets
  - Patient should not ingest if tablets are broken or cracked
  - If a patient cannot swallow the abemaciclib tablet, the intact tablet may be placed in a glass with at least 10 mL of water. Allow the tablet to break apart (disperse) in the water. Please note that the tablet will not dissolve in the water to a clear solution. Once the tablet has dispersed the patient must drink all of the solution immediately (i.e., within 10 minutes of dispersing it in at least 10 mL of water) [2]

AI=Aromatase Inhibitor; BID=Twice Daily; PO=By Mouth. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Data on file, Eli Lilly and Company.

Abemaciclib Supply and Storage

Abemaciclib is available as tablets and is supplied in 4 strengths[1a]

- **50 mg beige tablets**
  - 1 blister pack (14 tablets)
  - NDC# 0002-4483-54

- **100 mg beige tablets**
  - 1 blister pack (14 tablets)
  - NDC# 0002-4815-54

- **150 mg beige tablets**
  - 1 blister pack (14 tablets)
  - NDC# 0002-5337-54

- **200 mg beige tablets[b]**
  - 1 blister pack (14 tablets)
  - NDC# 0002-6216-54

Store tablets at room temperature between 68 °F to 77 °F (20 °C to 25 °C)[1]
Keep Abemaciclib out of the reach of children[2]

[a]The number of tablets per blister pack may vary by region. [b]Abemaciclib 200-mg tablets are only available in certain regions. NDC=National Drug Code. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2.Verzenio [patient information]. Indianapolis, IN: Eli Lilly and Company; 2019.

Dose Adjustments May be Required

- For patients who experience AEs, dose reduction is recommended (50 mg BID/reduction)[1]

Dose Level	Dose (in combination with ET)	Dose (monotherapy)
Recommended starting dose	150 mg BID	200 mg BID
First dose reduction	100 mg BID	150 mg BID
Second dose reduction	50 mg BID	100 mg BID
Third dose reduction	Not applicable	50 mg BID

- For patients with mild or moderate renal and hepatic impairment, no dose adjustments are required[1]
  - For patients with severe renal impairment, with end stage renal disease, or who are on dialysis, the pharmacokinetics of abemaciclib is unknown
  - For patients with severe hepatic impairment, reduce the dosing frequency to once daily

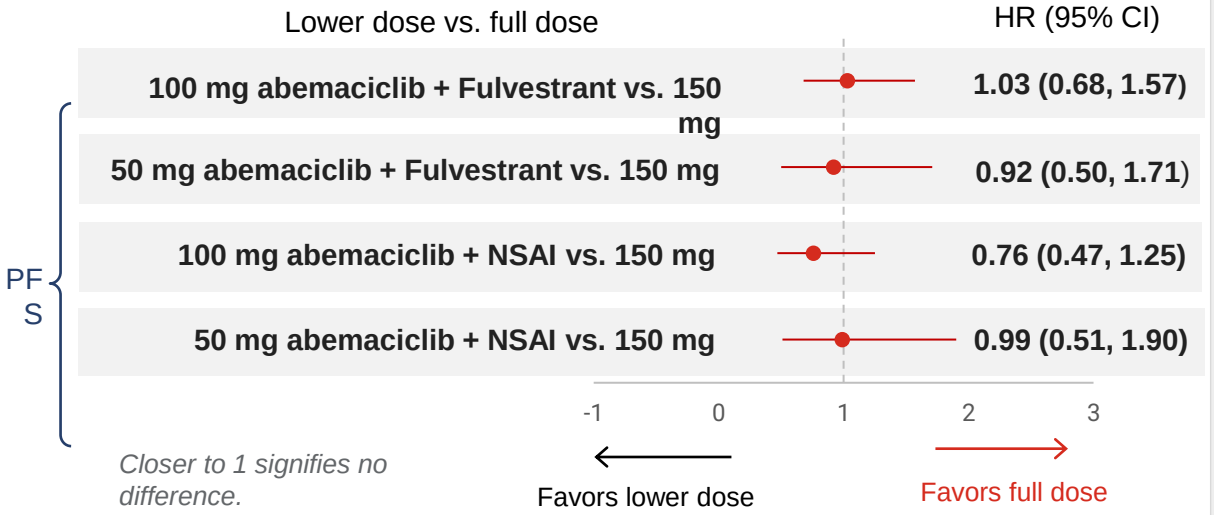
Patients with **MBC** may continue treatment until disease progression or unacceptable toxicity and should discontinue treatment if they are unable to tolerate 50 mg BID[1]

In monarchE, patients with **EBC** were dosed on a continuous schedule for up to 2 years or until disease recurrence or unacceptable toxicity occurs (whichever occurs first)[2]

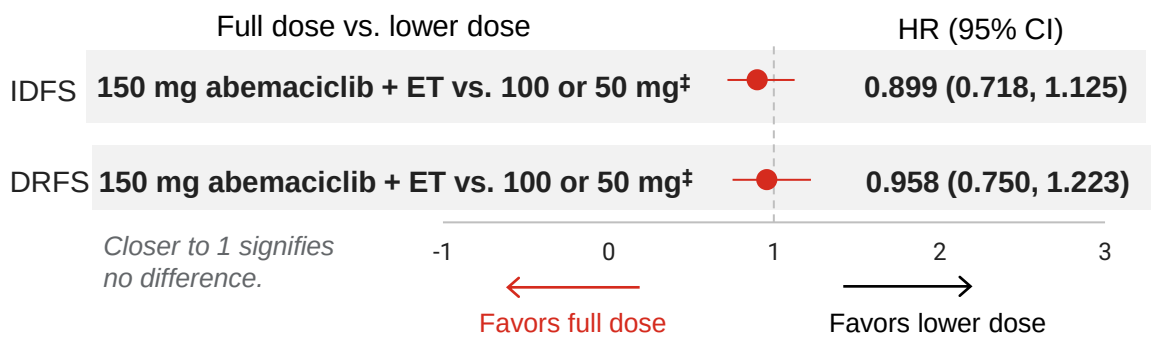
AE=Adverse Events; BID=Twice Daily; EBC=Early Breast Cancer; ET=Endocrine Therapy; MBC=Metastatic Breast Cancer. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Johnston SRD, et al. *J Clin Oncol.* 2020;38:3987-3998.

Efficacy of Abemaciclib at Reduced Doses- MBC and EBC

MBC



EBC†



Summary

- **Abemaciclib dose reductions were commonly and effectively implemented to manage side effects of therapy**
- **Based on multiple analyses, the efficacy of abemaciclib was not compromised by dose reductions in HR+/HER2- early or metastatic breast cancer***
- **All patients receiving abemaciclib should be carefully monitored for toxicity, with dose adjustments as needed, with a goal of maximizing adherence to maintain benefit**

The results (MBC/EBC) were based on exploratory analyses assessing the impact of dose reductions on efficacy. These analyses were not statistically powered or alpha-controlled for testing significance. Note that full dose favorability is indicated below 1 for EBC and above 1 for MBC. *The analyses results were from time-dependent Cox Proportional Hazards model that compared the efficacy of staying at full dose level with being reduced to a lower dose level in monarchE, MONARCH 2 and MONARCH 3; †Data presented are for monarchE Cohort 1 (91% of ITT). ‡Up to 2 abemaciclib dose reductions (100 or 50 mg) were permitted prior to discontinuation.

CI: confidence interval; DRFS: distant relapse-free survival; ET: endocrine therapy; EBC: early breast cancer; HR: hazard ratio; IDFS: invasive disease-free survival; ITT: intent-to-treat; MBC: metastatic breast cancer; NSAI: nonsteroidal aromatase inhibitor PFS: progression-free survival.

1. Rugo HS et al. Oncologist. 2021;26(1):e53-65. 2. O'Shaughnessy J et al. Poster presented at ESMO Congress, Madrid, Spain, October 20-24, 2023.

CYP3A Inhibitors and Inducers Affect Abemaciclib Exposure Levels

Abemaciclib concentration

CYP3A Inhibitors

Abemaciclib coadministration with strong and moderate CYP3A4 inhibitors can **increase** the body's exposure to abemaciclib and its active metabolites, which may lead to an increase in toxicity

- **Avoid taking abemaciclib with ketoconazole and grapefruit products**
- When taking abemaciclib with a **strong CYP3A inhibitor**, dose reductions are recommended[a]
- When taking abemaciclib with a **moderate CYP3A inhibitor**, monitor for adverse reactions and consider dose reductions[b]

CYP3A Inducers

Abemaciclib coadministration with strong and moderate CYP3A inducers can lead to a **decrease** in the body's exposure to abemaciclib and its active metabolite, which may lead to reduced activity

- **Avoid use of strong or moderate CYP3A inducers with abemaciclib**

Please refer to the full prescribing information or SmPC for information on how to appropriately use abemaciclib

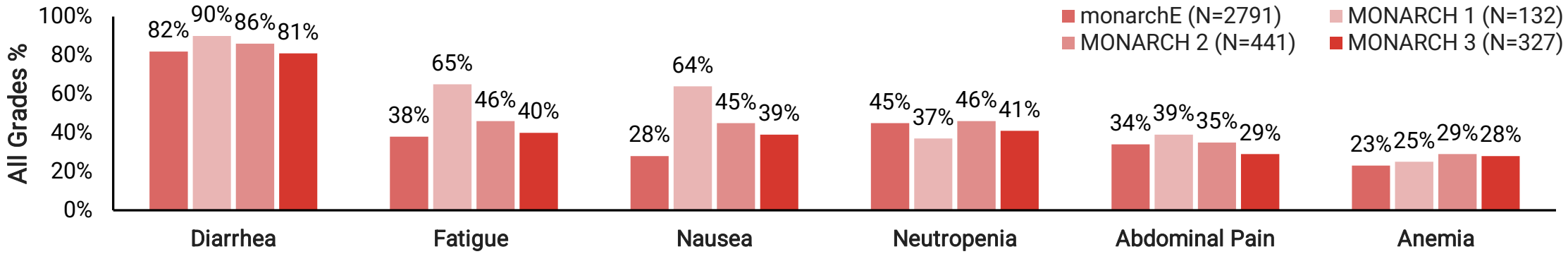
[a]In patients taking abemaciclib in concomitant with a strong CYP3A inhibitor (other than ketoconazole) with a starting abemaciclib dose of 200 mg BID/150 mg BID, reduce the dose to 100 mg BID. If the patient had a dose reduction to 100 mg BID due to adverse reactions, further reduce dose to 50 mg BID. If the patient discontinues taking the strong CYP3A inhibitor, the original abemaciclib dosage prior to concomitant use of the strong CYP3A inhibitor may be resumed. [b]In patients taking abemaciclib in concomitant with a moderate CYP3A inhibitor, consider reducing abemaciclib dose in 50 mg decrements.
BID=Twice Daily; CYP3A4=Cytochrome P450 3A4; SmPC=Summary of Product Characteristics. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021.

Abemaciclib Adverse Event Evaluation and Management

Common Abemaciclib-Associated AEs

- Common (incidence ≥20%) abemaciclib-associated AEs in patients with MBC include diarrhea, neutropenia, nausea, abdominal pain, infections, fatigue, anemia, leukopenia, decreased appetite, vomiting, headache, alopecia, and thrombocytopenia[1]
- Common AEs observed in both patients with MBC and EBC across abemaciclib clinical trials include diarrhea, fatigue, nausea, neutropenia, abdominal pain, and anemia[1,2]

Common abemaciclib-associated AEs in MBC and EBC Populations[1,2]



AE=Adverse Event; EBC=Early Breast Cancer; MBC=Metastatic Breast Cancer. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Johnston SRD, et al. *J Clin Oncol.* 2020;38:3987-3998.

Notable Abemaciclib-Associated AEs Leading to Dose Modifications or Discontinuation

	monarchE (N=2791)[1,2]	MONARCH 1 (N=132)[3,4]	MONARCH 2 (N=441)[3,4]	MONARCH 3 (N=327)[3,4]
Treatment change due to diarrhea, n (%)				
Dose reduction of study drug	474 (17.0)	27 (20.5)	83 (18.8)	45 (13.8)
Dose omission	530 (19.0)	32 (24.2)	83 (18.8)	50 (15.3)
Treatment discontinuation	141(5.1)	1 (0.8)	13 (2.9)[a]	6 (1.8)
Treatment change due to neutropenia, n (%)				
Dose reduction of study drug	217 (7.8)	14 (10.6)	44 (10.0)	42 (12.8)
Dose omission	427 (15.3)	21 (15.9)	72 (16.3)	57 (17.4)
Treatment discontinuation	26 (0.9)	0	7 (1.6)	9 (2.8)
Treatment change due to fatigue, n (%)				
Dose reduction of study drug	124 (4.4)	-	-	-
Dose omission	135 (4.8)	-	-	-
Treatment discontinuation	53 (1.9)	1 (0.8)	1 (0.2)	1 (0.3)
Treatment change due to nausea, n (%)				
Dose reduction of study drug	-	2 (1.5)	14 (3.2)	5 (1.5)
Dose omission	-	-	-	-
Treatment discontinuation	11 (0.4)	0	2 (0.5)	5 (1.5)

[a]Eight of 13 patients who discontinued treatment due to diarrhea had initiated abemaciclib treatment at 200 mg. AE=Adverse Event. 1. Rastogi P, et al. Abstract presented at: *SABCS 2020*. Abstract GS1-01. 2. Rugo HS, et al. Abstract presented at: *St. Gallen 2021*. Abstract PO13. 3. Rugo HS, et al. Abstract presented at: *ESMO 2018*. Abstract 339P. 4. Data on file, Eli Lilly and Company.

Common Abemaciclib-Associated AEs: Diarrhea

	Diarrhea Reported by Grade[1,2] ■ Grades 3 and 4 (%) ■ Any Grade (%)	Time to Onset[3,4] (any grade, median)	Dose Reduction[3,5]	Dose Omission[3,5]	Treatment Discontinuation[3,5]
monarchE (N=2791)	8%[b] 84%	8 days	17.0%	19.0%	5.1%
MONARCH 1 (N=132)	20% 90%	7 days	20.5%	24.2%	0.8%
MONARCH 2 (N=441)	13% 86%	6 days	18.8%	18.8%	2.9%
MONARCH 3 (N=327)	9% 81%	8 days	13.8%	15.3%	1.8%

CTCAE Grade: Diarrhea[6]

Grade 1 (Increase of <4 stools per day over baseline)

Grade 2 (Increase of 4-6 stools per day over baseline)

Grade 3 (Increase of ≥7 stools per day over baseline)

Grade 4 (Life-threatening consequences/ urgent intervention indicated)

Grade 5 (Death)

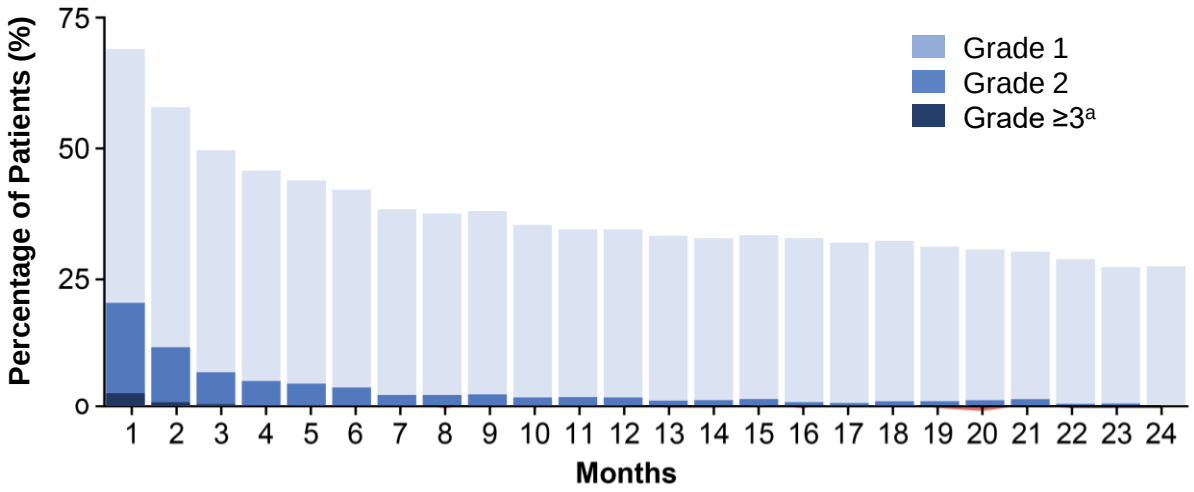
[a]AEs related to ET are reported elsewhere. [b]One Grade 5 event was reported[5]. AE=Adverse Event; CTCAE=Common Terminology Criteria for Adverse Events; ET=Endocrine Therapy.

1. Harbeck N, et al. *Annals Oncol*. 2021;32(12):1571-1581. 2. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 3. Rugo HS, et al. Abstract presented at: *ESMO 2018*. Abstract 339P. 4. Rugo HS, et al. Abstract presented at: *St. Gallen 2021*. Abstract PO13. 5. Rastogi P, et al. Abstract presented at: *SABCS 2020*. Abstract GS1-01. 6. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009.

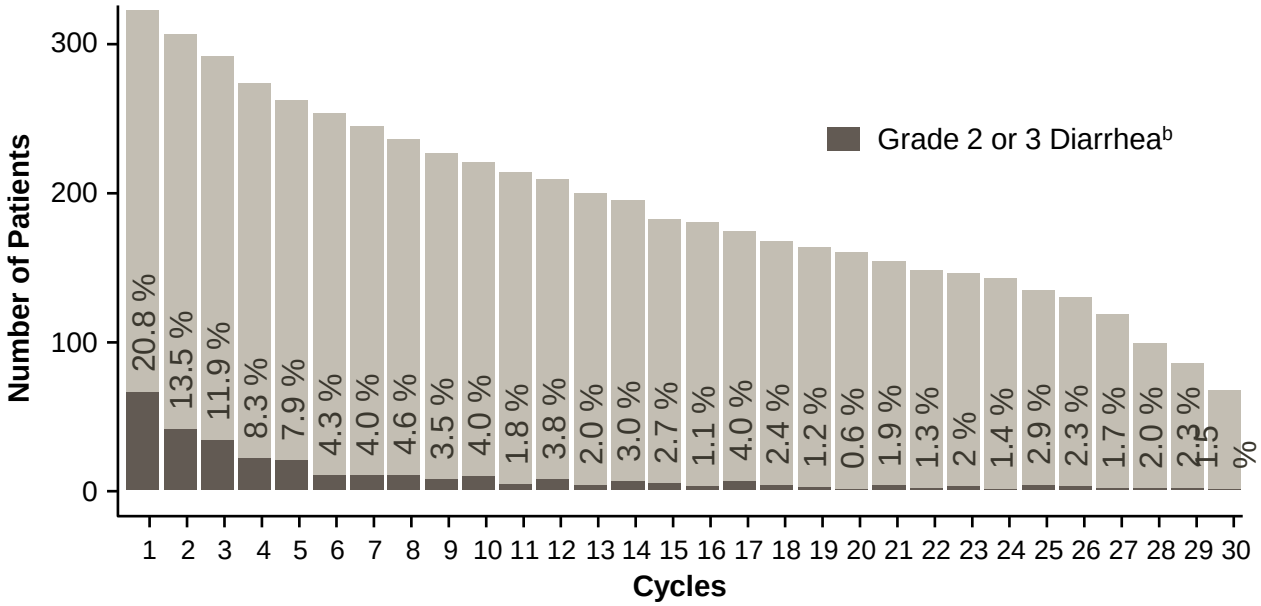
Common Abemaciclib-Associated AEs: Diarrhea

Diarrhea frequency and severity decreased over time in clinical trials

Incidence of diarrhea in monarchE[1]

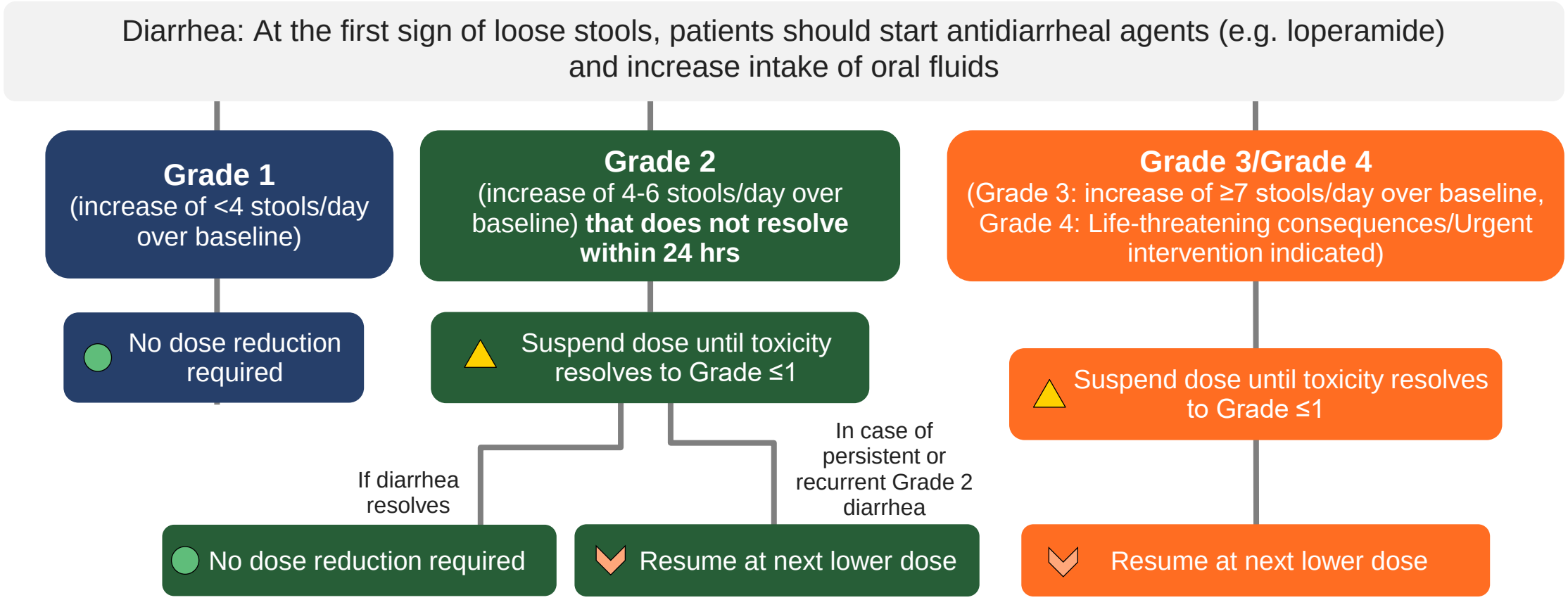


Incidence of diarrhea in MONARCH 3[2]



[a]There were no grade 4 and 1 grade 5 events. [b]No grade ≥4 diarrhea was observed. AE=Adverse Event. Cycles, 28 days. 1. Rugo HS, et al. Abstract presented at: *St. Gallen 2021*. Abstract PO13. 2. Rugo HS, et al. Abstract presented at: *ESMO 2018*. Abstract 339P.

Recommendations for Management of Diarrhea[1-3]



1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Rugo HS, et al. *Oncologist.* 2021;26(1):e53-e65. 3. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009.

Dehydration and Fluid Intake for Patients With Diarrhea

Patients who experience diarrhea should have their hydration status monitored during treatment[1]

- Dizziness, weakness, excessive thirst, and decreased urination are subjective symptoms of dehydration
- Objective assessments of dehydration include orthostatic hypertension, weight loss, skin turgor, and dry mucous membranes

To avoid dehydration and electrolyte imbalance, it is important to maintain fluid intake[1]

Oral intake of 3-4 L of fluid/day, including water, sports drinks, broth, weak decaffeinated teas, caffeine-free soft drinks, clear juices, and gelatin, should be encouraged[2]

If the patient shows an inability to maintain adequate hydration, IV fluid support may be required[2]

This may help minimize the need for hospitalization due to dehydration[2]

IV=Intravenous. 1. ONS:Edge. White paper. 2014. 2. Shaw C. *Clin J Oncol Nurs.* 2012;16:413-417.

Dietary Considerations for Patients With Diarrhea

Instruct your patients to contact their HCP right away and to start antidiarrheal medication as soon as possible at the first sign of loose stools

Recommendations for eating and drinking:

- ✓ At least 8 glasses of clear fluids/day
- ✓ Small, more frequent meals
- ✓ Foods that are easy to digest
- ✓ Soft, bland foods (skinless chicken, eggs, toast, plain pasta)
- ✓ Sodium and potassium rich foods and drinks (potatoes, bananas, applesauce, fruits such as apricots or peaches)

Avoid food and drinks that can irritate you or cause gas, such as:

- X Milk and milk products
- X Caffeine or alcohol
- X Fatty or spicy food
- X Sorbitol (sweetener)
- X Very hot or cold food or drinks
- X Fiber-rich foods (wholegrain, bran products, high-fiber fruit and vegetables, nuts and popcorn)

HCP=Healthcare Provider. Lilly USA. Diarrhea Action Plan. 2021.

Common Abemaciclib-Associated AEs: Neutropenia

	Neutropenia Reported by Grade[1-3] Grades 3 and 4 (%) Any Grade (%)	Time to Onset (Grade ≥3, median)[3,4]	Dose Reduction[3,5]	Dose Omission[3,5]	Treatment Discontinuation[3,5]
monarchE (N=2791)	20% 46%	30 days	7.8%	15.3%	0.9%
MONARCH 1 (N=132)	24% 37%	29 days	10.6%	15.9%	0
MONARCH 2 (N=441)	27% 46%	29 days	10.0%	16.3%	1.6%
MONARCH 3 (N=327)	22% 44%	36.5 days	12.8%	17.4%	2.8%

CTCAE Grade: Neutropenia[6]

Grade 1
(<LLN - 1.5x10^9/L)

Grade 2
(<1.5 to 1.0x10^9/L)

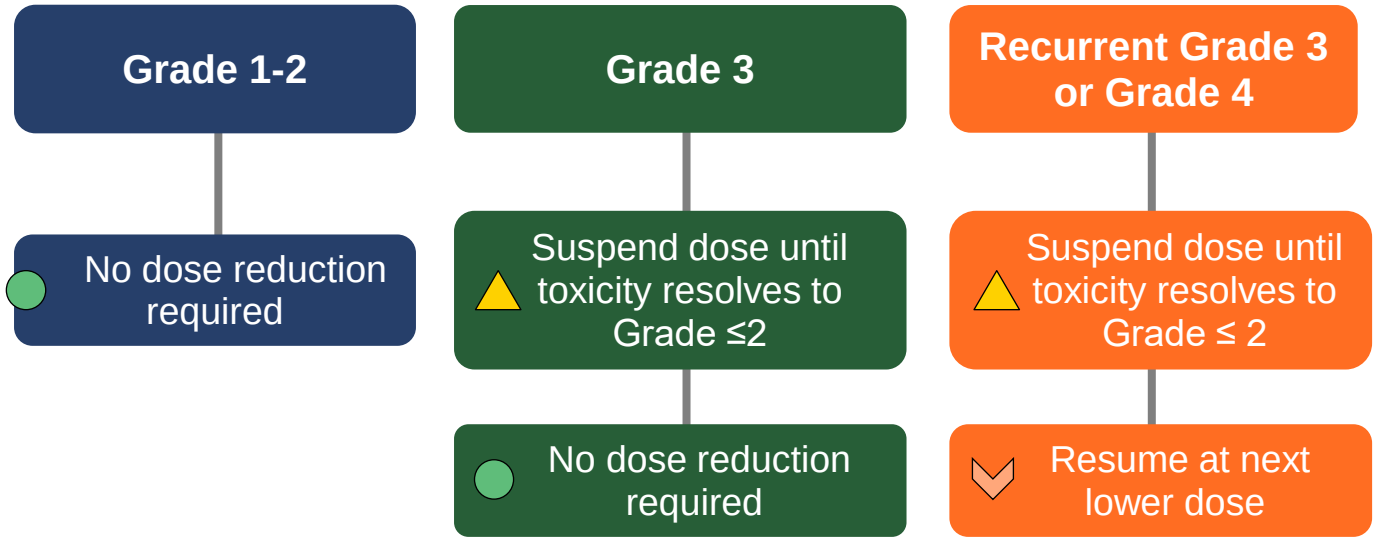
Grade 3
(<1.0 to 0.5x10^9/L)

Grade 4
(<0.5x10^9/L)

AE=Adverse Event; CTCAE=Common Terminology Criteria for Adverse Events; LLN=Lower Limits of Normal. 1. Hardbeck N, et al. *Annals Oncol*. 2021;32(12):1571-1581. 2. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 3. Rugo HS, et al. Abstract presented at: *ESMO 2018*. Abstract 339P. 4. Data on file, Eli Lilly and Company. 5. Rastogi P, et al. Abstract presented at: *SABCS 2020*. Abstract GS1-01. 6. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009.

Recommendations for Management of Hematologic Toxicities[1-2]

Hematological Toxicity: Complete blood counts should be monitored prior to the start of abemaciclib therapy, every 2 weeks for the first 2 months, monthly for months 3 and 4, and then as clinically indicated



- Before the start of each cycle, hematologic toxicity must resolve to grade ≤2
- If blood cell growth factors are administered, abemaciclib treatment must be suspended for at least 48 h after the last administration of cell growth factors and until toxicity resolves to grade ≤2 and reduce the dose of abemaciclib unless already performed for the toxicity that led to the use of growth factor

1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009.

Common Abemaciclib-Associated AEs: Fatigue

	Fatigue Reported by Grade[1] (Grade 3 (%) / Any Grade (%))	Dose Reduction[2]	Treatment Discontinuation[2,3]
monarchE (N=2791)	3% / 38%	4.4%	1.9%
MONARCH 1 (N=132)	13% / 65%	-	0.8%
MONARCH 2 (N=441)	3% / 46%	-	0.2%
MONARCH 3 (N=327)	2% / 40%	-	0.3%

CTCAE Grade: Fatigue[4]

Grade 1
Fatigue relieved by rest

Grade 2
Fatigue not relieved by rest, limiting instrumental ADL

Grade 3
Fatigue not relieved by rest, limiting self-care ADL

ADL=Activities of Daily Living; AE=Adverse Event; CTCAE=Common Terminology Criteria for Adverse Events.1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Rastogi P, et al. Abstract presented at: *SABCS 2020*. Abstract GS1-01. 3. Data on file, Eli Lilly and Company. 4. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009.

Additional Abemaciclib-Associated AEs: Increase in Serum Creatinine

- Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function[1]

monarchE[1]

- Serum creatinine increase was the most common laboratory abnormality
- **99% of patients reported having a grade 1 or 2 event[a]**

Other clinical studies

Increases in serum creatinine[1b]:

- **Occurred within the first 28-day cycle of dosing**
- Remained elevated but nonprogressive throughout the treatment period and was reversible when treatment was discontinued

Other measures of renal function, such as BUN, cystatin C, or calculated GFR, should be used as an alternative to either serum creatinine or creatinine-based calculated estimates of GFR if[2,3]:

- Serum creatinine rise is progressive after the first cycle
- There are other indications of renal injury
- A patient has a need for precise GFR assessment[2,3]

Creatinine may not be an accurate method to assess renal function in these patients[2-4]

[a]0.5% of patients reported having a grade 3 event [b]Mean increase 0.2-0.3 mg/dL. AE=Adverse Event; BUN=Blood Urea Nitrogen; GFR=Glomerular Filtration Rate. 1.Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Milburn J, et al. *Nephrol Dial Transplant*. 2017;32:434-439. 3. Shlipak MG, et al. *N Engl J Med.* 2013;369:932-943. 4. Chappell JC, et al. *Clin Pharmacol Ther.* 2019;105:1187-1195.

Additional Abemaciclib-Associated AEs: Gastrointestinal AEs

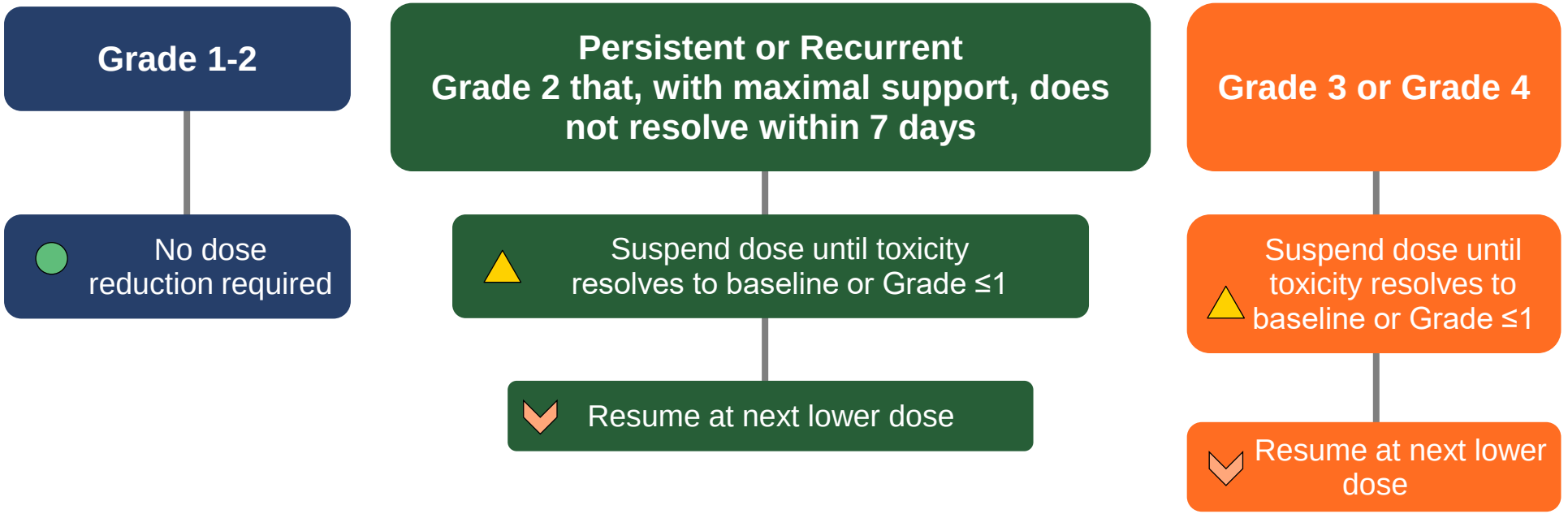
Gastrointestinal AEs	Nausea[1,2]			Decreased Appetite[1,2]			Abdominal Pain[2-5]
	Any Grade	Dose Reduction	Treatment Discontinuation	Any Grade	Dose Reduction	Treatment Discontinuation	Any Grade
monarchE (N=2791)	29.5%	-	-	11.8%	-	-	35.5%
MONARCH 1 (N=132)	64.4%	1.5%	0%	45.5%	0%	0%	38.6%
MONARCH 2 (N=441)	45.1%	3.2%	0.5%	26.5%	0%	0.2%	35.4%
MONARCH 3 (N=327)	41.3%	1.5%	1.5%	26.3%	1.8%	0%	29.1%

Patients who experience gastrointestinal AEs should follow the general guidance outlined in the recommendations for nonhematologic toxicity except diarrhea[1]

AE=Adverse Event. 1 . Hardbeck N, et al. *Annals Oncol*. 2021; [available online]. 2. Johnston SRD, et al. *J Clin Oncol*. 2020;38:3987-3998. 3. Dickler MN, et al. *Clin Care Res* 2017;23(17):5218-5224. 4. Sledge GW, et al. *J Clin Oncol.* 2017;35(25):2875-2884. 5. Goetz MP, et al. *J Clin Oncol.* 2017;35:3638-3646.

Recommendations for Management of Nonhematological Toxicities[1-2]

Nonhematological toxicity, excluding diarrhea, hepatotoxicity, and ILD/pneumonitis



ILD=Interstitial Lung Disease. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Rugo HS, et al. *Oncologist.* 2021;26(1):e53-e65.

Additional Abemaciclib-Associated AEs: VTE

- In clinical trials, VTE included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis[1]
- Across the clinical development program, deaths due to venous thromboembolism have been reported[1]

Incidence of VTE in monarchE[1,2]:
Abemaciclib + ET: 3%
ET alone: 0.6%

Incidence of VTE in MONARCH 3[1]:
Abemaciclib + AI: 5%
Placebo + AI: 0.6%

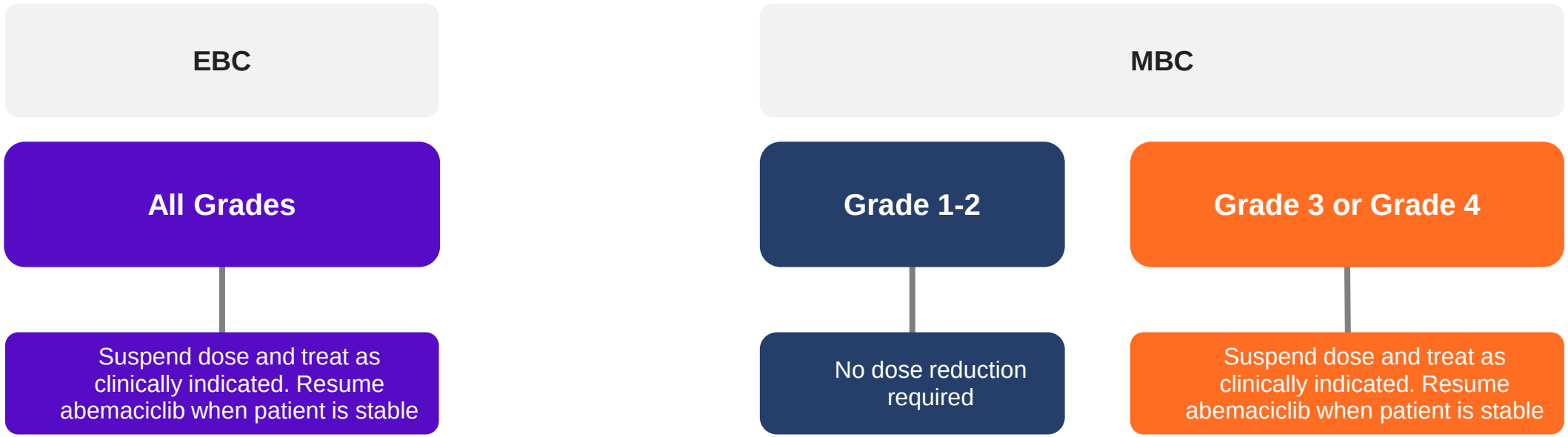
Incidence of VTE in MONARCH 2[1]:
Abemaciclib + Fulvestrant: 5%
Placebo + Fulvestrant: 0.9%

Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.[1]

AE=Adverse Event; AI=Aromatase Inhibitor; ET=Endocrine Therapy; VTE=Venous Thromboembolism. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Harbeck N, et al. *Annals Oncol*. 2021;32(12):1571-1581. .

Additional Abemaciclib-Associated AEs: VTE

VTE: Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate[1-3]



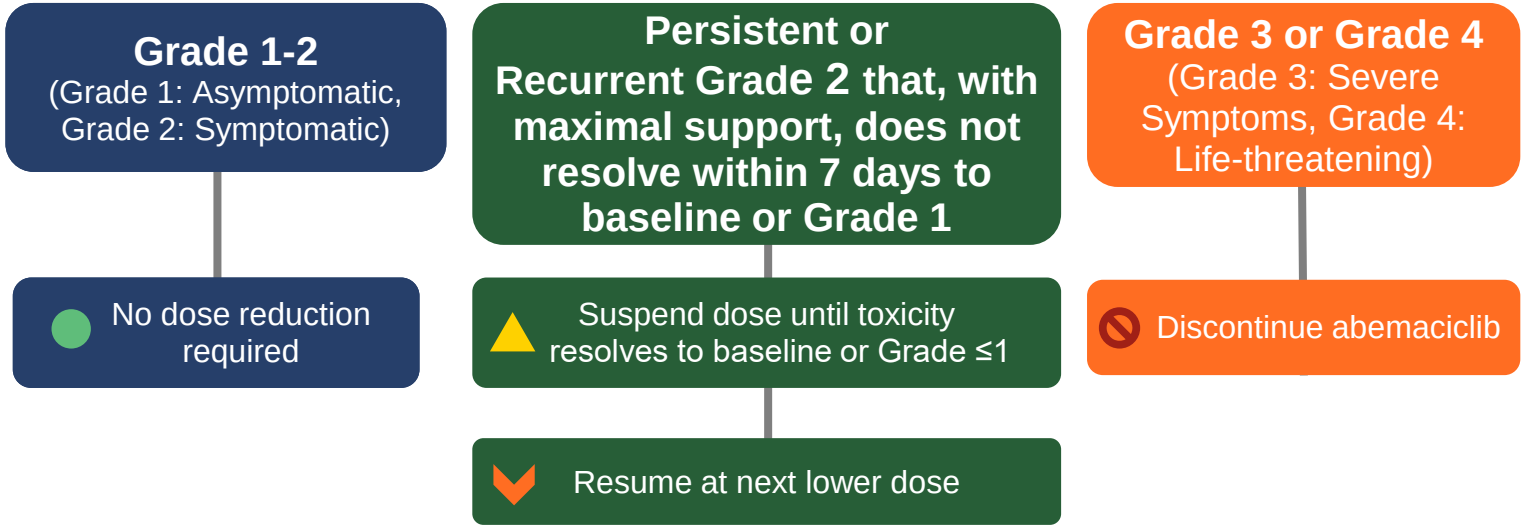
AE=Adverse Event; EBC=Early Breast Cancer; MBC=Metastatic Breast Cancer; VTE=Venous Thromboembolism. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009. 3. Rugo HS, et al. *Oncologist.* 2021;26(1):e53-e65.

Additional Abemaciclib-Associated AEs: ILD/Pneumonitis

Across abemaciclib-treated patients in MONARCH 1, MONARCH 2, and MONARCH 3, ILD/pneumonitis occurred in[1]:

- 3.3% any grade
- 0.6% grade 3 or 4
- 0.4% had fatal outcomes

Interstitial Lung Disease/Pneumonitis: Monitor for clinical symptoms or radiological changes indicative of ILD/pneumonitis. Ask patients to report any new or worsening pulmonary symptoms such as dyspnea, cough, and fever[1-3]



Pulmonary symptoms indicative of ILD/pneumonitis may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic examinations[1]

AE=Adverse Event; ILD=Interstitial Lung Disease. 1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021. 2. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009. 3. Rugo HS, et al. *Oncologist.* 2021;26(1):e53-e65.

Additional Abemaciclib-Associated AEs: Hepatotoxicity

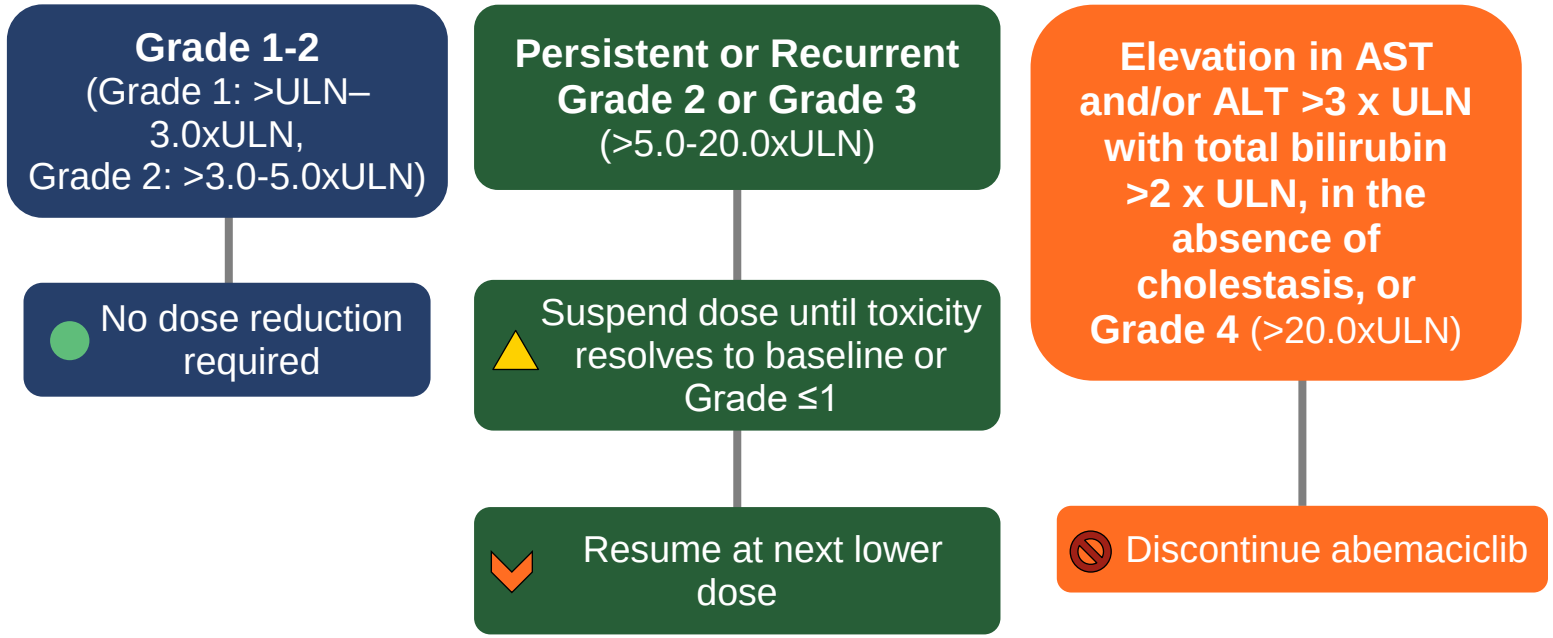
MONARCH 3[1]

- Grade ≥3 increases in ALT (6% vs 2%) and AST (3% vs 1%) were reported in the abemaciclib and placebo arms, respectively

MONARCH 2[1]

- Grade ≥3 increases in ALT (4% vs 2%) and AST (2% vs 3%) were reported in the abemaciclib and placebo arms, respectively

Hepatotoxicity: ALT, AST and serum bilirubin should be monitored prior to the start of abemaciclib therapy, every 2 weeks for the first 2 months, monthly for months 3 and 4, and then as clinically indicated[2,3]



AE=Adverse Event; ALT=Alanine Transaminase; AST=Aspartate Aminotransferase; ULN=Upper Limit of Normal.1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2023. 2. Common Terminology Criteria for Adverse Events (CTCAE). U.S Department of Health and Human Services, National Cancer Institute; 2009. 3. Rugo HS, et al. *Oncologist.* 2021;26(1):e53-e65.

Additional Abemaciclib-Associated AEs: Embryo-Fetal Toxicity

- Abemaciclib can cause fetal harm when administered to a pregnant woman
- In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight

Advise pregnant women of the potential risk to a fetus

Advise women of reproductive potential to use effective contraception during treatment with abemaciclib and for at least 3 weeks after the last dose

AE=Adverse Event. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021.

Abemaciclib AE Monitoring

Assessment	At Baseline	Month-1				Month-2				Month-3	Month-4	Month-5 and Beyond
		Week-1	Week-2	Week-3	Week-4	Week-1	Week-2	Week-3	Week-4			
CBC	X		X		X		X		X	Monthly	Monthly	As clinically indicated
LFTs[a]	X		X		X		X		X	Monthly	Monthly	As clinically indicated
Diarrhea	Instruct patients at the first sign of loose stools to initiate antidiarrheal therapy, increase oral fluids, and notify their healthcare provider.											
ILD/ pneumonitis	Monitor for clinical symptoms or radiological changes indicative of ILD/pneumonitis. Permanently discontinue abemaciclib in all patients with grade 3 or 4 ILD or pneumonitis.											
VTE	Monitor patients for signs and symptoms of thrombosis and pulmonary embolism and treat as medically appropriate.											
Embryo-fetal toxicity	Can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.											

[a]ALT, AST, and serum bilirubin. AE= Adverse Event; ALT=Alanine Aminotransferase; AST=Aspartate Aminotransferase; CBC=Complete Blood Count; ILD=Interstitial Lung Disease; LFT=Liver Function Test; VTE=Venous Thromboembolism. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021.

Summary

- Abemaciclib is indicated for treatment of patients with HR+, HER2- advanced or MBC and can be used alone or in combination with an AI or fulvestrant[1]
- Abemaciclib is indicated in combination with endocrine therapy for treatment of patients with HR+, HER2- node-positive, early breast cancer at high risk of recurrence[1]
- Common abemaciclib-associated AEs observed across clinical trials include diarrhea, neutropenia, nausea, abdominal pain, infections, fatigue, anemia, leukopenia, decreased appetite, vomiting, headache, alopecia, and thrombocytopenia[1]
- Appropriate monitoring of adverse events, symptom management strategies, and patient counseling should be utilized to prevent early discontinuation of abemaciclib therapy

AE=Adverse Event; AI=Aromatase Inhibitor; HER2=Human Epidermal Growth Factor Receptor 2; HR=Hormone Receptor; MBC=Metastatic Breast Cancer.1. Verzenio [patient information]. Indianapolis, IN: Eli Lilly and Company; 2023.

Resources

- INFOGRAPHIC: Abemaciclib AE Management Guide