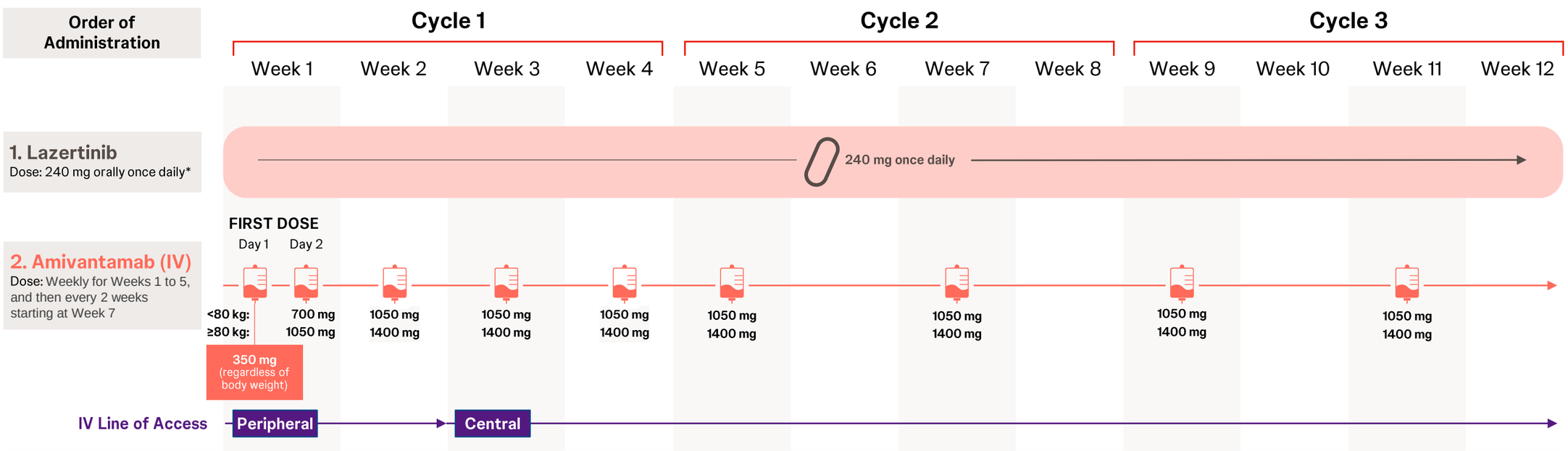
Dosage and Administration of Amivantamab in Combination With Lazertinib: MARIPOSA Study

Amivantamab + Lazertinib Dosing (28-Day Cycles)[1-3]

Amivantamab Infusion and Preparation[1]

- IV infusion set requirements
  - In-line PES filter (0.2 µm)
  - PU, PBD, PVC, PP, or PE ONLY
- Prime administration set with filter with 5% dextrose or 0.9% sodium chloride injection prior to amivantamab infusion
- Do not infuse in the same IV line as other agents



When given in combination with lazertinib, administer amivantamab any time after lazertinib when given on the same day. Refer to the lazertinib prescribing information for recommended lazertinib dosage and administration information.

Premedications and Proactive Therapy Management[1-3]

Medication	Dose	Route of Administration	Recommended Dosing Window	Required at:
Antihistamine	Diphenhydramine 25 mg to 50 mg (or equivalent)	IV	15 to 30 mins	All doses
		Oral	30 to 60 mins	
Antipyretic	Acetaminophen 650 mg to 1000 mg	IV	15 to 30 mins	
		Oral	30 to 60 mins	
Glucocorticoid	Dexamethasone 20 mg or equivalent	IV	45 to 60 mins	Initial dose (Week 1 Day 1)
Glucocorticoid	Dexamethasone 10 mg or equivalent	IV	45 to 60 mins	2nd dose (Week 1 Day 2), then optional

Prophylactic Anticoagulation

Prophylactic anticoagulation is recommended to be used for the first 4 months of treatment

Use of vitamin K antagonists is not recommended

Proactive Therapy Management[4, 5]

Click to learn more about proactive therapy management for AEs

Proactive therapy management for AEs

Infusion Rates for Amivantamab + Lazertinib[1]

Week	Dose (per 250 mL bag)		Initial Infusion Rate (mL/hr)		Subsequent Infusion Rate† (mL/hr)	
	<80 kg	≥80 kg	<80 kg	≥80 kg	<80 kg	≥80 kg
Week 1 (split dose infusion)						
Week 1 Day 1	350 mg	350 mg	50	50	75	75
Week 1 Day 2	700 mg	1050 mg	50	35	75	50
Week 2	1050 mg	1400 mg	85	65	85	65
Week 3	1050 mg	1400 mg	125	85	125	85
Week 4	1050 mg	1400 mg	125	125	125	125
Week 5	1050 mg	1400 mg	125	125	125	125
Week 6	No dose					
Week 7 and every 2 weeks thereafter	1050 mg	1400 mg	125	125	125	125

Concomitant Measures

When initiating treatment with amivantamab in combination with lazertinib, reduce the risk of dermatologic adverse reactions by:

- Administering alcohol-free (eg, isopropanol-free, ethanol-free) emollient cream
- Encouraging patients to:
  - Limit sun exposure during and for 2 months after treatment
  - Wear protective clothing
  - Use broad-spectrum UVA/UVB sunscreen

Consider prophylactic measures (eg, use of oral antibiotics) to reduce the risk of dermatologic adverse reactions. Refer to the lazertinib prescribing information for information about concomitant medications

hr, hour; IV, intravenous; min, minute; PBD, polybutadiene; PE, polyethylene; PES, polyethersulfone; PP, polypropylene; PU, polyurethane; PVC, polyvinyl chloride; Q2W, every 2 weeks.
*The recommended dosage of lazertinib is 240 mg orally once daily administered in combination with amivantamab with or without food. Lazertinib tablets should be swallowed whole and not crushed, split, or chewed. If a patient misses a dose of lazertinib within 12 hours, patients are instructed to take the missed dose. If more than 12 hours has passed since the dose was to be given, patients are instructed to take the next dose at its scheduled time. If vomiting occurs any time after taking lazertinib, patients are instructed to take the next dose at its next regularly scheduled time.[6] †In the absence of infusion-related reactions, increase the initial infusion rate to the subsequent infusion rate after 2 hours based on patient tolerance. Total infusion time is ~4-6 hours for Day 1 and 6-8 hours for Day 2. Subsequent infusion time is ~2 hours.[1]

1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Cho BC, et al. *N Engl J Med.* 2024 (suppl). doi:10.1056/NEJMoa2403614. 3. Yang JCH, et al. Presented at the European Lung Cancer congress (ELCC); March 26-29, 2025; Paris, France. 4. Spira AI, et al. *J Thorac Oncol.* 2025. doi:10.1016/j.jtho.2025.01.018. 5. Girard N, et al. Presented at the European Lung Cancer Congress (ELCC); March 26-29, 2025; Paris, France. 6. LAZCLUZE™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.

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Dosage and Administration of Amivantamab in Combination With Lazertinib: MARIPOSA Study

Proactive Therapy Management for AEs[1-4]

Begin Amivantamab + Lazertinib

IRR Prophylactic Regimen (SKIPPirr)[1]	VTE Prophylactic Regimen (PALOMA-2, PALOMA-3)[2,3]
2 days–1 hour before start Oral 8-mg dexamethasone BID 2 days and 1 day prior and 8 mg 1 hour before first infusion[a]	**First 4 months** Oral anticoagulants as per NCCN or local guidelines

Dermatologic Prophylactic Regimen (COCOON)[4,b]

Antibiotic prophylaxis	**Weeks 1–12** 100-mg BID doxycycline or minocycline	**Weeks 13+** 1% topical clindamycin lotion on the scalp daily
Nail cleaning agent	**Weeks 1+** 4% chlorhexidine on the fingernails and toenails daily for 12 months	
Long-acting skin hydration	**Weeks 1+** Ceramide-based moisturizer at least daily for 12 months[c]	

[a]Includes standard premedication (antihistamines, antipyretics, and glucocorticoids). [b]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID; topical clindamycin lotion 1% on scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization: La Roche-Posay Lipikar AP+M moisturizer on the body and face at least daily. [c]La Roche-Posay Lipikar AP+M moisturizer was used in COCOON.

AE, adverse event; BID, twice daily; IRR, infusion-related reaction; NCCN, National Comprehensive Cancer Network; VTE, venous thromboembolism.

1. Spira AI, et al. *J Thorac Oncol.* 2025 Jan 24:S1556-0864(25)00051-6. 2. Scott SC, et al. Presented at: American Society for Clinical Oncology (ASCO) Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA. 3. Leighl NB, et al. *J Clin Oncol.* 2024 Oct 20;42(30):3593-3605. 4. Girard N, et al. Presented at: European Lung Cancer Congress (ELCC); March 26–29, 2025; Paris, France.

Dosage and Administration of Amivantamab in Combination With Carboplatin and Pemetrexed

Amivantamab + Carboplatin/Pemetrexed Dosing (21-Day Cycles)[1-4]

Amivantamab Infusion and Preparation[1]

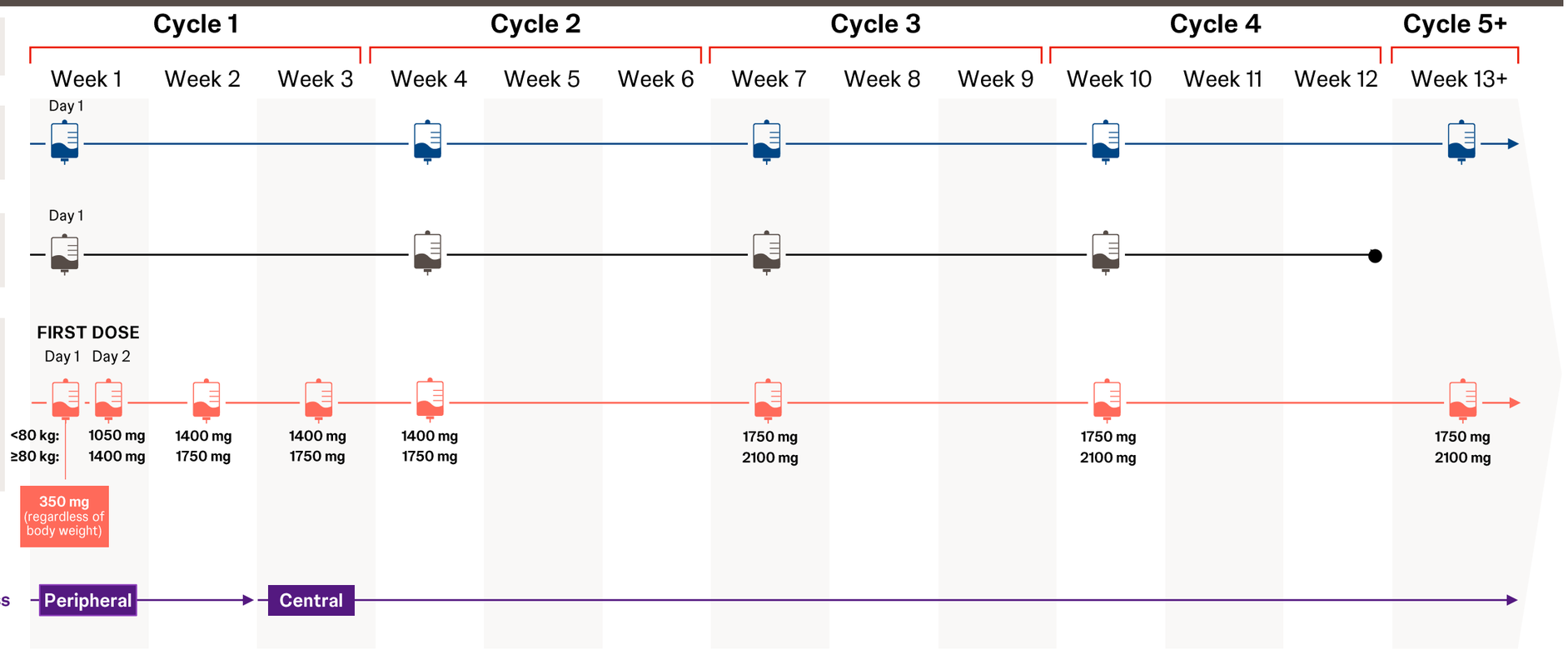
- IV infusion set requirements
  - In-line PES filter (0.2 µm)
  - PU, PBD, PVC, PP, or PE ONLY
- Prime administration set with filter with 5% dextrose or 0.9% sodium chloride injection prior to amivantamab infusion
- Do not infuse in the same IV line as other agents

Order of Administration

1. Pemetrexed (IV)
Dose: 500 mg/m²

2. Carboplatin (IV)
Dose AUC 5 up to 4 cycles

3. Amivantamab (IV)
Doses: Weekly for first 4 weeks (first dose split), then every 3 weeks thereafter



The tables below include the suggested order of study treatments and concomitant therapies in the PAPILLON study protocol. If recommendations were different or absent in the MARIPOSA-2 study protocol, disclaimers are listed under the respective tables. Interventions should be based on specific patient presentation and the treating physician's clinical judgment.

Day 1 of Cycles 1 to 4: Order of Administration When Amivantamab is Given With Carboplatin and Pemetrexed[3,4]*

Medication	Dose	Route of Administration	Recommended Dosing Window
Antiemetic for chemotherapy	Ondansetron 8 mg to 16 mg or equivalent†	IV	Start 60-90 mins before amivantamab infusion; administer in the order indicated
	Fosaprepitant/Aprepitant†	IV	
Antihistamine for chemotherapy	Diphenhydramine 25 mg or equivalent†	Oral	
Antipyretic for chemotherapy	Paracetamol (acetaminophen) 325 mg to 500 mg (or equivalent)†	Oral	
Glucocorticoid	Day 1 of Cycle 1: Dexamethasone 20 mg‡ Day 1 of Cycles 2, 3, 4: Dexamethasone 10 mg to 12 mg as per local practice and guidelines for chemotherapy†	IV	
Chemotherapy	Pemetrexed	IV	–
Chemotherapy	Carboplatin	IV	–
Antipyretic for amivantamab	Paracetamol (acetaminophen) 325 mg to 500 mg (or equivalent)‡	IV or oral	Start 15-30 mins before amivantamab infusion
Antihistamine for amivantamab	Diphenhydramine 25 mg to 50 mg or equivalent‡	IV	
EGFR/MET antibody	Amivantamab	IV	

Dosing order and information listed above are specific to PAPILLON study protocol. In MARIPOSA-2 study protocol, the recommended dosing window for antihistamine administration was 15-30 mins (IV) or 30-60 mins (oral) before amivantamab infusion., and chemotherapy premedication recommendations were not provided.[4]

Days 2, 8, and 15 of Cycle 1: Order of Administration When Amivantamab is Given Without Chemotherapy[3,4]*

Medication	Dose	Route of Administration	Recommended Dosing Window
Glucocorticoid§	Dexamethasone 10 mg or Methylprednisolone 40 mg	IV	Start 15-30 mins before amivantamab infusion
Antipyretic	Paracetamol (acetaminophen) 650 mg to 1000 mg (or equivalent)	IV or oral	
Antihistamine	Diphenhydramine 25 mg to 50 mg (or equivalent)	IV	
EGFR/MET antibody	Amivantamab	IV	–

In MARIPOSA-2 study, the recommended dosing window was 45-60 mins for glucocorticoid and was 15-30 mins (IV) or 30-60 mins (oral) for antipyretic and antihistamine administration before amivantamab infusion.[4]

Day 1 of Cycles 5+: When Amivantamab is Given With Pemetrexed[3,4]*

Medication	Dose	Route of Administration	Recommended Dosing Window
Antiemetic for chemotherapy	Ondansetron 8 mg to 16 mg or equivalent	IV or oral	Start 30-45 mins before amivantamab infusion; administer in the order indicated
Glucocorticoid§‖	Dexamethasone 10 mg or Methylprednisolone 40 mg (optional)	IV	
Antipyretic‡	Paracetamol (acetaminophen) 650 mg to 1000 mg (or equivalent)	IV or oral	
Antihistamine‡	Diphenhydramine 25 mg to 50 mg (or equivalent)	IV	
Chemotherapy	Pemetrexed	IV	–
EGFR/MET antibody	Amivantamab	IV	–

Dosing order and information listed above are specific to PAPILLON study. In MARIPOSA-2 study, the recommended dosing window was 45-60 mins (IV) or 60-90 mins (oral) for glucocorticoid, and was 15-30 mins (IV) or 30-60 mins (oral) for antipyretic and antihistamine administration before amivantamab infusion. In the MARIPOSA-2 study, chemotherapy premedication recommendations were not provided.[4]

Please refer to the Prescribing Information of pemetrexed and carboplatin for complete information on Dosage and Administration, Adverse Reactions, and Boxed Warnings.

AUC, area under curve; EGFR, epidermal growth factor receptor; hr, hour; IV, intravenous; MET, mesenchymal-epithelial transition; min, minute; PBD, polybutadiene; PE, polyethylene; PES, polyethersulfone; PP, polypropylene; PU, polyurethane; PVC, polyvinylchloride.

*From *The New England Journal of Medicine*, Zhou et al., Amivantamab plus Chemotherapy in NSCLC with EGFR Exon 20 Insertions, Volume 389., 2039 – 2051, Copyright © 2023 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society. †Other agents/dosing can be considered/substituted as per local guidelines for chemotherapy prophylaxis. ‡Required pre-medication for amivantamab.[3] §Pre-dose steroids are mandatory for Cycle 1 Day 2 and optional for Cycle 1 Day 8 and Cycle 1 Day 15. Beginning with Cycle 1 Day 8, optional pre-dose steroids may be administered prior to amivantamab if clinically indicated for participants who experienced an infusion-related reaction on Cycle 1 Day 1 or Cycle 1 Day 2.[3] ‖Pre-dose steroids for pemetrexed can be used as per local practice and guidelines.[3]

1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039-2051. 3. Zhou C, et al. *N Engl J Med.* 2023;389(22)(suppl):2039-2051. 4. Passaro A, et al. *Ann Oncol.* 2023;S0923-7534(23)04281-3(suppl). doi:10.1016/j.annonc.2023.10.117

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Dosage and Administration of Amivantamab in Combination With Carboplatin and Pemetrexed

Infusion Rates for Amivantamab + Carboplatin and Pemetrexed[1]

Week	Dose (per 250 mL bag)		Initial Infusion Rate (mL/hr)		Subsequent Infusion Rate (mL/hr)	
	<80 kg	≥80 kg	<80 kg	≥80 kg	<80 kg*	≥80 kg
Week 1 (split dose infusion)						
Week 1 Day 1	350 mg	350 mg	50	50	75	75
Week 1 Day 2	1050 mg	1400 mg	33	25	50	50
Week 2	1400 mg	1750 mg	65	65	65	65
Week 3	1400 mg	1750 mg	85	85	85	85
Week 4	1400 mg	1750 mg	125	125	125	125
Weeks 5 and 6	No dose					
Week 7 and every 3 weeks thereafter	1750 mg	2100 mg	125	125	125	125

*In the absence of infusion-related reactions, increase the initial infusion rate to the subsequent infusion rate after 2 hours based on patient tolerance. Total infusion time is ~4-6 hours for Day 1 and ~6-8 hours for Day 2. Subsequent infusion time is approximately 2 hours.[1]

Amivantamab Dose Reductions and Modifications[1,2†]

Dose Reductions

Dose‡	1st Reduction	2nd Reduction	3rd Reduction
1050 mg	700 mg	350 mg	
1400 mg	1050 mg	700 mg	
1750 mg	1400 mg	1050 mg	
2100 mg	1750 mg	1400 mg	

DISCONTINUE amivantamab

Dose Modifications for Infusion-Related Reactions (IRR)§

Grades 1-2

- **INTERRUPT** amivantamab if IRR suspected + monitor until reaction symptoms resolve
- **RESUME** at 50% of the infusion rate at which the reaction occurred
- **ESCALATE** infusion rate if no additional symptoms after 30 min
- **PREMEDICATE** with corticosteroid for subsequent dose

Grade 4 or any grade anaphylaxis/anaphylactic reactions

- **PERMANENTLY DISCONTINUE** amivantamab

Grade 3

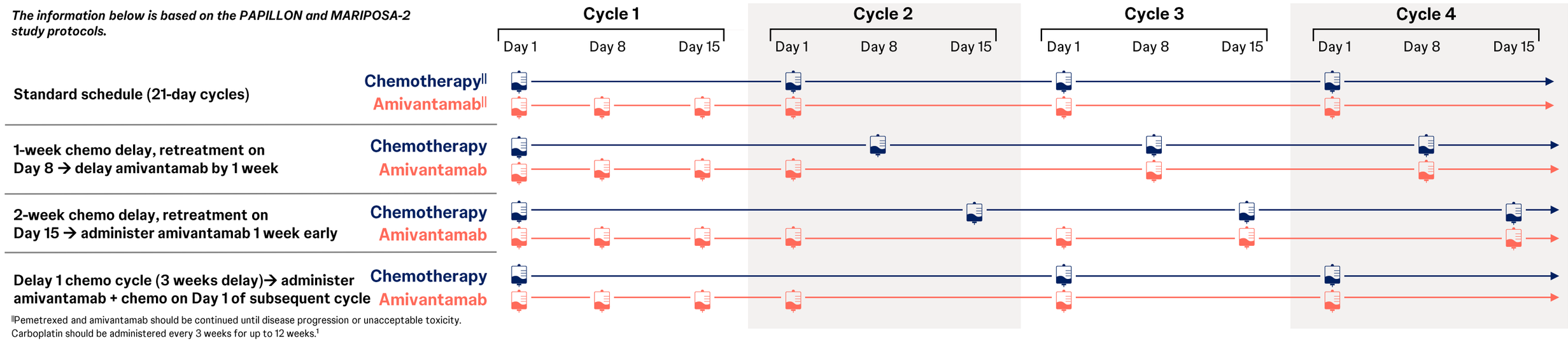
- **INTERRUPT** amivantamab
- **ADMINISTER** supportive care medications
- **MONITOR** continuously until reaction symptoms resolution
- **FOLLOW** additional steps outlined for Grades 1-2
- **PERMANENTLY DISCONTINUE** amivantamab for recurrent Grade 3 IRRs

†Monitor patients for any signs and symptoms of infusion reactions during amivantamab infusion in a setting where cardiopulmonary resuscitation medication and equipment are available.[1] ‡Dose at which the adverse reaction occurred.[1] When administering amivantamab in combination with lazertinib, if there is an adverse reaction requiring dose reduction after withholding treatment and resolution, reduce the dose of amivantamab first. Refer to the lazertinib prescribing information for information about dosage modifications for lazertinib.

§For dose modifications and management of interstitial lung disease, dermatological adverse reactions, and other adverse reactions, please refer to the full amivantamab prescribing information.[1]

Dose Delays + Retreatment Schedule[2,3]

The information below is based on the PAPILLON and MARIPOSA-2 study protocols.



‖Pemetrexed and amivantamab should be continued until disease progression or unacceptable toxicity. Carboplatin should be administered every 3 weeks for up to 12 weeks.[1]

Chemo, chemotherapy; hr, hour; min, minute.

1. RYBREVANT® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Passaro A, et al. *Ann Oncol.* 2023;S0923-7534(23)04281-3(suppl). doi:10.1016/j.annonc.2023.10.117 3. Zhou C, et al. *N Engl J Med.* 2023;389(22)(suppl):2039-2051.