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Amivantamab and Hyaluronidase-lpuj (RYBREVANT FASPRO™) plus Lazertinib (LAZCLUZE®) Patient Management

Description:

- The purpose of this document is to discuss clinical considerations and general management of patients undergoing treatment with subcutaneous amivantamab and hyaluronidase-lpuj (SC amivantamab) plus lazertinib combination therapy.

Background:

- Amivantamab is a bispecific antibody that binds to the extracellular domains of epidermal growth factor receptor (EGFR) and mesenchymal-epithelial transition receptor (MET) blocking ligand binding and promoting degradation of these receptors. It also recruits immune effector cells to kill tumor cells through mechanisms such as antibody-dependent cellular cytotoxicity and trogocytosis. Hyaluronidase temporarily breaks down hyaluronan in the subcutaneous tissue to create space for the agent to spread into surrounding tissues.
- Lazertinib is an irreversible EGFR tyrosine kinase inhibitor that is highly selective for mutant EGFR and is brain penetrant.
- FDA approved indications for the combination of SC amivantamab and lazertinib include:
    - First-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- Adverse Reactions
    - The most common adverse reactions (≥ 20%) were rash, nail toxicity, musculoskeletal pain, fatigue, stomatitis, edema, nausea, diarrhea, vomiting, constipation, decreased appetite, and headache.
    - The most common Grade 3 or 4 laboratory abnormalities (≥ 2%) were decreased lymphocyte count, decreased sodium, decreased potassium, decreased albumin, increased alanine amino transferase, increased aspartate amino transferase, decreased platelet count, increased gamma-glutamyl transferase, and decreased hemoglobin.

PQI Process:

Upon receipt of a new order for treatment with SC amivantamab and lazertinib:

- Review patients' EGFR mutational testing for appropriate positive results including exon 19 deletion or exon 21 L858R substitution.
- Administer SC amivantamab in combination with lazertinib until disease progression or unacceptable toxicity.

Table 1. Recommended Dosage for SC Amivantamab in Combination with Lazertinib (Every 4-Week Dosing)

Body Weight at Baseline*	Recommended Dose	Dosing Schedule
< 80 kg	1,600 mg amivantamab and 20,000 units hyaluronidase	Weekly (total of 4 doses) from Weeks 1 to 4 • Weeks 1 to 4 - Injection on Day 1
	3,520 mg amivantamab and 44,000 units hyaluronidase	Every 4 weeks starting at Week 5 onwards
≥ 80 kg	2,240 mg amivantamab and 28,000 units hyaluronidase	Weekly (total of 4 doses) from Weeks 1 to 4 • Weeks 1 to 4 - Injection on Day 1
	4,640 mg amivantamab and 58,000 units hyaluronidase	Every 4 weeks starting at Week 5 onwards

*Dose adjustments not required for subsequent body weight changes.

Table 2. Recommended Dosage for SC Amivantamab in Combination with Lazertinib (Every 2-Week Dosing)

Body Weight at Baseline*	Recommended Dose	Dosing Schedule
< 80 kg	1,600 mg amivantamab and 20,000 units hyaluronidase	Weekly (total of 4 doses) from Weeks 1 to 4 • Weeks 1 to 4 - Injection on Day 1
		Every 2 weeks starting at Week 5 onwards
≥ 80 kg	2,240 mg amivantamab and 28,000 units hyaluronidase	Weekly (total of 4 doses) from Weeks 1 to 4 • Weeks 1 to 4 - Injection on Day 1
		Every 2 weeks starting at Week 5 onwards

*Dose adjustments not required for subsequent body weight changes.

- Adult patients receiving IV amivantamab at an every 2-week dosing regimen may switch to SC amivantamab at an every 2-week or at an every 4-week dosing regimen at their next scheduled dose on or after Week 5.
- Adult patients currently receiving SC amivantamab at an every 2-week dosing regimen may switch to an every 4-week dosing regimen at their next scheduled dose on or after Week 5.
- Prior to first SC amivantamab injection (Week 1 Day 1), administer premedications as per Table 3 to reduce administration-related reactions. Administer both an antihistamine and antipyretic before all SC amivantamab doses. Glucocorticoid administration is required at the initial dose at Week 1 Day 1 only, and upon re-initiation after prolonged dose interruptions, then as necessary for subsequent injections

Table 3. Premedications

Medication	Dose	Route of Administration	Dosing Window Prior to SC Amivantamab Administration
Antihistamine*	Diphenhydramine (25 mg to 50 mg) or equivalent	Intravenous	15 to 30 minutes
		Oral	30 to 60 minutes
Antipyretic*	Acetaminophen (650 mg to 1,000 mg) or equivalent	Intravenous	15 to 30 minutes
		Oral	30 to 60 minutes
Glucocorticoid±	Dexamethasone (20 mg) or equivalent	Intravenous	45 to 60 minutes
		Oral	At least 60 minutes
Glucocorticoid¥	Dexamethasone (10 mg) or equivalent	Intravenous	45 to 60 minutes
		Oral	60 to 90 minutes

*Required at all doses; ± Required at initial dose [Week 1, Day 1] or at next subsequent dose if administration-related reaction occurs; ¥Optional for subsequent doses

- Administration
  - Administer each injection of SC amivantamab in the abdomen over approximately 5 minutes to minimize injection site irritation. Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard, not intact or within 2 inches (5 cm) around the periumbilical area.
  - Divide doses requiring greater than 15 mL into approximately equal volumes in two syringes and administer at separate injection sites, and administer each injection consecutively in separate quadrants of the abdomen. Do NOT exceed 15 mL in each syringe.
  - Lazertinib dosing: one 240 mg tablet orally once daily (taken before SC amivantamab if given on the same day)
- Monitoring
  - SC amivantamab can cause hypersensitivity and administration-related reactions (ARR; e.g., dyspnea, fever, chest discomfort flushing, chills, hypotension, vomiting, etc.). The median time to ARR onset is approximately 2 hours.
  - Monitor patients for new or worsening symptoms of ILD/pneumonitis (e.g., dyspnea, cough, fever). Immediately withhold SC amivantamab in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.
  - SC amivantamab with lazertinib can cause serious and fatal venous thromboembolic (VTE) events. Since most of these events occur within the first four months of therapy without prophylaxis, administer prophylactic anticoagulation during this initial period (vitamin K antagonists not recommended). Monitor for signs and symptoms of VTE and treat as medically appropriate. Withhold SC amivantamab and lazertinib based on severity.
  - SC amivantamab can cause severe rash including toxic epidermal necrolysis, dermatitis acneiform, pruritus, and dry skin. When initiating SC amivantamab, concomitant use of various oral and topical products is recommended to reduce the

risk and severity of dermatologic adverse reactions. See NCODA PQI: The COCOON Protocol.
    - Instruct patients to limit sun exposure during and for 2 months after treatment with SC amivantamab. Advise patients to wear protective clothing and use broad-spectrum UVA/UVB sunscreen.
    - SC amivantamab can cause ocular toxicity including blepharitis, dry eye symptoms, conjunctival redness, blurred vision, visual impairment, ocular itching, eye pruritus and uveitis. Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist.
    - SC amivantamab can cause fetal harm when administered to a pregnant woman. Advise female patients of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of SC amivantamab.
- Dose Modifications for Adverse Events
    - Many dose modifications and recommendations for management of adverse reactions exist. See package insert Table 8 for full dose modifications.
- Drug Interactions
    - Lazertinib is a CYP3A4 substrate and a weak CYP3A4 inhibitor. Avoid concomitant use with strong and moderate CYP3A inducers.

Patient-Centered Activities:

- Provide patient with Patient Education Sheet and review
- A blood thinner will be prescribed for the first 4 months, monitor for any leg swelling/pain, chest pain, or shortness of breath
- Monitor skin at baseline, administer prophylactic COCOON regimen, refer to dermatologist if needed
- Monitor any new/worsening shortness of breath, cough, or fever immediately, these may indicate serious and potentially fatal lung inflammation requiring treatment to be stopped
- Monitor eye pain, redness, blurred vision, or sensitivity to light promptly, refer to ophthalmologist if needed
- Counsel on reproductive risks and confirm pregnancy status
- Check for potential drug interactions with any CYP3A4 medications

References:

1. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2026.
2. LAZCLUZE® (lazertinib) [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2025.

Supplemental Information:

Table 4. Dose Reductions for Adverse Reaction for SC amivantamab (with lazertinib)

Dose at which the adverse reaction occurred	1st Dose Reduction	2nd Dose Reduction	3rd Dose Reduction
1,600 mg amivantamab and 20,000 units hyaluronidase	1,050 mg amivantamab and 13,200 units hyaluronidase	700 mg amivantamab and 8,800 units hyaluronidase	Discontinue SC amivantamab
2,240 mg amivantamab and 28,000 units hyaluronidase	1,600 mg amivantamab and 20,000 units hyaluronidase	1,050 mg amivantamab and 13,200 units hyaluronidase	
3,520 mg amivantamab and 44,000 units hyaluronidase	2,400 mg amivantamab and 30,000 units hyaluronidase	1,600 mg amivantamab and 20,000 units hyaluronidase	
4,640 mg amivantamab and 58,000 units hyaluronidase	3,360 mg amivantamab and 42,000 units hyaluronidase	2,240 mg amivantamab and 28,000 units hyaluronidase	

Table 5. Dosing Volumes for SC amivantamab

SC amivantamab Total Dose	Total Dose Volume
700 mg amivantamab and 8,800 units hyaluronidase	4.4 mL
1,050 mg amivantamab and 13,200 units hyaluronidase	6.6 mL
1,600 mg amivantamab and 20,000 units hyaluronidase	10 mL
2,240 mg amivantamab and 28,000 units hyaluronidase	14 mL
2,400 mg amivantamab and 30,000 units hyaluronidase	15 mL
3,360 mg amivantamab and 42,000 units hyaluronidase	21 mL
3,520 mg amivantamab and 44,000 units hyaluronidase	22 mL
4,640 mg amivantamab and 58,000 units hyaluronidase	29 mL

*Note the following vial sizes:

- For the 21 mL dose volume, the entire contents of the 3,520 mg amivantamab and 44,000 units hyaluronidase/22 mL vial will not be needed. Discard unused portion.
- For the 29 mL dose volume, use one 2,240 mg amivantamab and 28,000 units hyaluronidase/14 mL vial and one 2,400 mg amivantamab and 30,000 units hyaluronidase/15 mL vial to minimize waste. If a different combination of vials is used, discard unused portion

Storage:

- If immediate administration is not possible, store the prepared syringes of SC amivantamab refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for up to 24 hours followed by at room temperature of 15 °C to 30 °C (59 °F to 86 °F) for up to 24 hours.
- Discard the prepared syringe(s) if stored for more than 24 hours refrigerated or more than 24 hours at room temperature. If stored in the refrigerator, allow the solution to come to room temperature before administration.