Current disease status: **second recurrence**

Identifying appropriate patients for Avmapki™ Fakzynja™ Co-Pack

Diagnosis:

***KRAS*-mutated LGSOC (7 years ago)**

- LGSOC confirmed by histopathologic exam of tissue removed during debulking surgery
- *KRAS* mutation confirmed by NGS testing; ER+ confirmed by IHC
- Involvement of omentum detected by CT scan

First recurrence:

Patient reported bloating, fullness when eating, and shortness of breath; tumor marker CA-125 elevated; CT scan, followed by MRI

Second recurrence:

Detected during follow-up; CA-125 elevated, tumor molecular testing; CT scan

CA, cancer antigen; CT, computed tomography; ER+, estrogen receptor-positive; IHC, immunohistochemistry; MRI, magnetic resonance imaging; NGS, next generation sequencing.

Kayla

56 years old
Single
Data Analyst
Enjoys crafting

This is a hypothetical patient profile.

INDICATION

Avmapki Fakzynja Co-Pack is indicated for the treatment of adult patients with *KRAS*-mutated recurrent low-grade serous ovarian cancer (LGSOC) who have received prior systemic therapy.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- **Ocular Toxicities:** Ocular toxicities, including visual impairment and vitreoretinal disorders, occurred. Perform comprehensive ophthalmic evaluation at baseline, prior to cycle 2, every three cycles thereafter, and as clinically indicated. Withhold Avmapki Fakzynja Co-Pack for ocular toxicities until improvement at the same or reduced dose. Permanently discontinue Avmapki Fakzynja Co-Pack for any grade 4 toxicity.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

AVMAPKI™ FAKZYNJA™ CO-PACK
(avutometinib capsules; defactinib tablets) 0.8 mg; 200 mg

Current disease status: **second recurrence**

Kayla's treatment history

Primary debulking surgery

↓

**Chemotherapy*
Maintenance hormone therapy†**

↓

First recurrence

48 months post-chemotherapy

↓

**MEK inhibitor
until disease progression**

While challenging, her side effects were managed by her HCP, so she could stay on therapy.

↓

Second recurrence

at 42 months on MEK-only inhibitor

Not a candidate for secondary debulking surgery,‡ not on warfarin, no active skin disorder, no ocular disorder, not pregnant, not breastfeeding.

*Initiated 4 weeks postsurgery, 6 cycles of paclitaxel/carboplatin for 5 months.

†Letrozole.

‡Patient had a supracervical hysterectomy and is postmenopausal.

IMPORTANT SAFETY INFORMATION (CONT'D)

Warnings and Precautions (cont'd)

- **Serious Skin Toxicities:** Skin toxicities, including photosensitivity and severe cutaneous adverse reactions (SCARs), occurred. Adhere to concomitant medications. Monitor for skin toxicities and interrupt, reduce or permanently discontinue Avmapki Fakzynja Co-Pack based on severity, tolerability, and duration.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

AVMAPKI™ FAKZYNJA™ CO-PACK
(avutometinib capsules; defactinib tablets) 0.8 mg; 200 mg

Current disease status: **second recurrence**

Kayla may be an appropriate candidate for Avmapki Fakzynja Co-Pack

The first treatment specifically approved for women with *KRAS*-mutated recurrent LGSOC who have received prior systemic therapy[1]

Considerations for starting treatment[1]

- A comprehensive ophthalmic exam at baseline, prior to cycle 2 and every 3 cycles thereafter, regardless of baseline exam findings, and as clinically indicated
- Prophylactic medications for skin reactions administered with initiation of and during at least the first 2 cycles*
- Limit unnecessary exposure to sunlight and apply sunscreen with SPF ≥30
- Monitor liver function tests prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated
- Monitor CPK prior to the start of each cycle, on day 15 of the first four cycles, and as clinically indicated
- Verify pregnancy status and advise use of effective contraception

*Topical corticosteroid (applied to the face, scalp, neck, upper chest, and upper back) and systemic oral antibiotics.
CPK, creatine phosphokinase; SPF, sun protection factor.

IMPORTANT SAFETY INFORMATION (CONT'D)

Warnings and Precautions (cont'd)

- **Hepatotoxicity:** Monitor liver function tests prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated. Withhold, reduce or discontinue Avmapki Fakzynja Co-Pack based on severity and persistence of abnormality.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

AVMAPKI™ FAKZYNJA™ CO-PACK
(avutometinib capsules; defactinib tablets) 0.8 mg; 200 mg

IMPORTANT SAFETY INFORMATION (CONT'D)

Warnings and Precautions (cont'd)

- **Rhabdomyolysis:** Monitor creatine phosphokinase prior to the start of each cycle, on day 15 of the first four cycles, and as clinically indicated. If increased CPK occurs, evaluate patients for rhabdomyolysis or other causes. Withhold, reduce or permanently discontinue Avmapki Fakzynja Co-Pack based on severity and duration of the adverse reaction.
- **Embryo-Fetal Toxicity:** Avmapki Fakzynja Co-Pack can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Adverse Reactions

The most common (≥ 25%) adverse reactions, including laboratory abnormalities, were increased creatine phosphokinase, nausea, fatigue, increased aspartate aminotransferase, rash, diarrhea, musculoskeletal pain, edema, decreased hemoglobin, increased alanine aminotransferase, vomiting, increased blood bilirubin, increased triglycerides, decreased lymphocyte count, abdominal pain, dyspepsia, dermatitis acneiform, vitreoretinal disorders, increased alkaline phosphatase, stomatitis, pruritus, visual impairment, decreased platelet count, constipation, dry skin, dyspnea, cough, urinary tract infection, and decreased neutrophil count.

Drug Interactions

- **Strong and moderate CYP3A4 inhibitors:** Avoid concomitant use with Avmapki Fakzynja Co-Pack.
- **Strong and moderate CYP3A4 inducers:** Avoid concomitant use with Avmapki Fakzynja Co-Pack.
- **Warfarin:** Avoid concomitant use of Avmapki Fakzynja Co-Pack with warfarin and use an alternative to warfarin.
- **Gastric acid reducing agents:** Avoid concomitant use of Avmapki Fakzynja Co-Pack with proton pump inhibitors (PPIs) or H2 receptor antagonists. If use of an acid-reducing agent cannot be avoided, administer Fakzynja 2 hours before or 2 hours after the administration of a locally acting antacid.

Use in Specific Populations

- **Lactation:** Advise not to breastfeed.
- **Fertility:** May impair fertility in males and females.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

Reference: 1. Avmapki Fakzynja Co-Pack. Prescribing Information. Verastem, Inc. 2025.

VERASTEM ONCOLOGY

AVMAPKI™ FAKZYNJA™ CO-PACK
(avutometinib capsules; defactinib tablets) 0.8 mg; 200 mg