Examining Unmet Needs for Patients with Vasomotor Symptoms Due to

MENOPAUSE:

Challenges with Traditional Therapeutic Options and the Rationale for Novel Treatments

FACULTY

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Agenda

I. VMS due to Menopause: An Overview

a. Epidemiology/prevalence/incidence

b. Pathophysiology

c. Symptoms and course

d. Burdens

II. The Treatment Landscape for VMS due to Menopause

a. Traditional pharmacotherapies

b. Risks and benefits based on clinical experience

III. New and Emerging Pharmacotherapeutic Options to Better Manage VMS due to Menopause

a. Clinical trial-based efficacy, safety, and tolerability profiles

b. Real-world evidence

IV. Communication Issues and Challenges Between Women with VMS due to Menopause and Their Healthcare Providers

a. Patient education resources

b. Strategies for effective patient communication with healthcare professionals

V. Conclusions

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PROGRAM OVERVIEW

This enduring activity is designed to assess the pathophysiological mechanism that results in vasomotor symptoms (VMS) due to menopause as well as evaluate both traditional and novel therapeutic options for treatment. Effective communication strategies for patient/physician interactions and possible barriers to communication will also be discussed.

TARGET AUDIENCE

This enduring activity is designed to meet the educational needs of U.S.-based obstetrician-gynecologists, primary care physicians, including internists, family practitioners, nurse practitioners, physician assistants, nurses, and additional healthcare providers who treat menopausal women.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Assess the pathophysiological mechanisms that result in VMS due to menopause
- Evaluate traditional treatment options for patients with VMS due to menopause
- Develop strategies that allow for effective communication with patients on issues and challenges associated with VMS due to menopause

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James A. Simon, MD	Dr. Simon discloses that he has conducted research for AbbVie, Bayer Healthcare, Dare Bioscience, Ipsen, Mylan/Viatris, Myovant Sciences, and Sebela Pharmaceuticals. He holds stock with a direct purchase plan in Sermonix Pharmaceuticals. He is a consultant for Bayer HealthCare Pharmaceuticals, Besins Healthcare, Biote Medical, California Institute of Integral Studies (CIIS), Dare Bioscience, and Femasys. He is on speakers Bureaus for Astellas Pharma, Mayne Pharma, Myovant Sciences, Pfizer, Pharmavite, and Scynexis.

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Examining Unmet Needs for Patients With Vasomotor Symptoms Due to Menopause: Challenges With Traditional Therapeutic Options and the Rationale for Novel Treatments

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Disclosures

- **Dr Pinkerton** discloses that she has conducted research as a principal investigator (PI) for multicenter Bayer nonhormone clinical trial fees to the University of Virginia; she is an *UpToDate* and Merck professional and consumer
- **Dr Simon** discloses that he has conducted research for AbbVie, Bayer Healthcare, Daré Bioscience, Ipsen Bioscience, Mylan/Viatris, Myovant Sciences, and Sebela Pharmaceuticals; he holds stock with a direct purchase plan in Sermonix Pharmaceuticals; he is a consultant for Bayer HealthCare Pharmaceuticals, Besins Healthcare, Biote Medical, California Institute of Integral Studies (CIIS), Daré Bioscience, and Femasys; and he serves on the speakers bureau for Astellas Pharma, Mayne Pharma, Myovant Sciences, Pfizer, Pharmavite, and Scynexis
- During this lecture Dr James Simon and Dr JoAnn Pinkerton may mention the use of medications for both US Food and Drug Administration (FDA)-approved and non-FDA-approved indications

All relevant financial relationships have been mitigated.

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Learning Objectives

- Assess the pathophysiological mechanisms that result in vasomotor symptoms (VMS) due to menopause
- Evaluate traditional treatment options for patients with VMS due to menopause
- Develop strategies that allow for effective communication with patients on issues and challenges associated with VMS due to menopause

VMS Due to Menopause: An Overview

JoAnn V. Pinkerton, MD, MSCP, FACOG

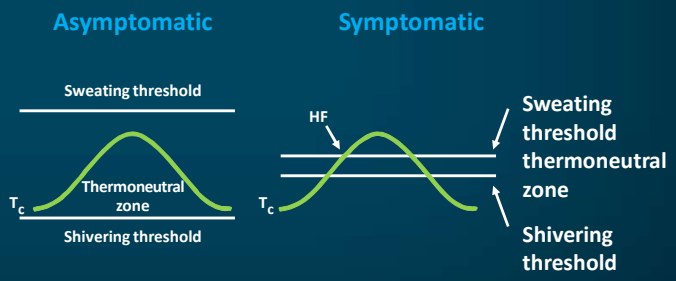
Menopause and Vasomotor Symptoms

- Menopause is defined as 12 months of amenorrhea, due to loss of ovarian follicular activity, occurring at a median age of 51.3 years in the United States
  - It is determined retrospectively
  - It is preceded by the menopause transition, which on average lasts 4 years
- Nearly 80% of women worldwide suffer from VMS, ranging in severity and affecting quality of life and overall health; 25% may require treatment
- VMS persist for a median duration of 7 years and have been associated with significant comorbidities such as cardiovascular disease, osteoporosis, and cognitive complaints
- Women who experience VMS during perimenopause may continue to have symptoms for much longer, with a median duration of almost 12 years
- Race, ethnicity, comorbidities, lifestyle factors, and psychosocial factors affect menopause symptoms

Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287. Richard-Davis G, Wellons M. *Semin Reprod Med.* 2013;31(5):380-386.

Physiologic Mechanisms of VMS

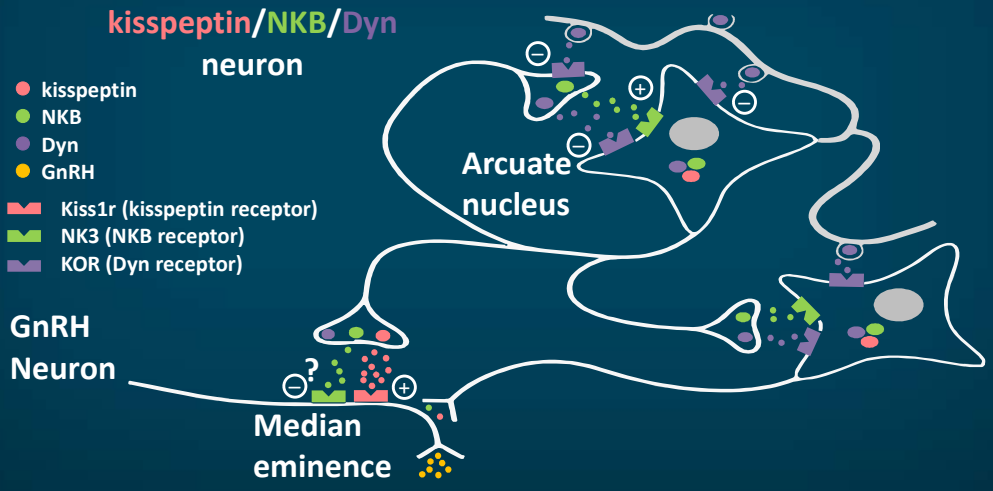
- VMS involve the vasodilation of cutaneous vessels with increased skin temperatures
  - Vasodilation and sweating occur as heat dissipation
- The mechanism is not completely understood; neurokinin receptors are involved
- Related to small fluctuations in core body temperature superimposed on an extremely narrow thermoneutral zone
- Triggered when core body temperature rises above upper (sweating) threshold
- Shivering occurs when core body temperature falls from elevated level to a level below the lower threshold of thermoneutral zonet



Freedman RR, Blacker CM. *Fertil Steril.* 2002;77:487-490. Freedman RR, Subramanian M. *Menopause.* 2005;12:156-159. Freedman RR. *Semin Reproductive Med.* 2005;32:117-125.

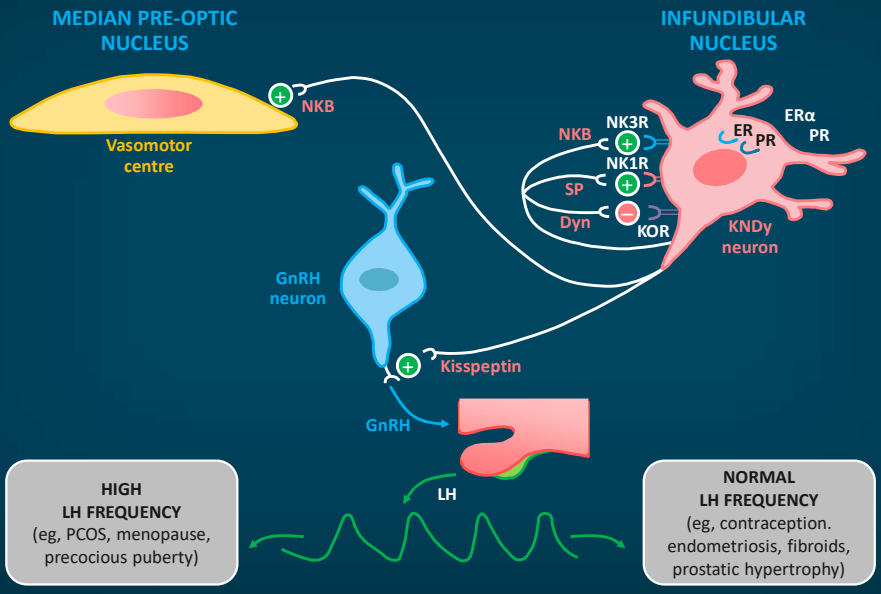
Neurokinin

- NK-3 receptors in hypothalamic KNDy neurons become hyperactivated due to low estrogen levels and stimulate the thermoregulatory pathway–



Wakabayashi Y, et al. *J Neurosci*. 2010;30(8):3124-3132.

Kisspeptin and Neurokinin B Neuroendocrine Pathways in the Control of Human Ovulation



LH = luteinizing hormone; PCOS = polycystic ovary syndrome.

Anderson RA. *J Neuroendocrinol*. 2024;e13371.

Symptoms of VMS

VMS are the most common and bothersome symptoms, with hallmark symptoms of hot flashes and night sweats

Hot flashes are described as episodes of sudden intense sensation of heat, often starting in the upper chest area, that may last 1 to 5 minutes

- May be accompanied by chills, sweating, feelings of dread, or palpitations

Night sweats refer to hot flashes occurring in the night, often awakening a person from sleep

- May be just a sensation of warmth to soaking sweats

FDA definition of VMS

Mild:	The sensation of heat without sweating
Moderate:	The sensation of heat with sweating, able to continue activity
Severe:	The sensation of heat with sweating, causing cessation of activity

FDA = US Food and Drug Administration; VMS = vasomotor symptoms.

FDA. Guidance for industry, 2003 (https://www.fda.gov/media/71359/download). Accessed 5/1/2024.

Menopause and Sleep

- Women transitioning into menopause typically complain of
  - Poor sleep quality
  - Insufficient sleep
  - Nocturnal awakenings
- Sleep deprivation is a known risk factor for
  - Cardiovascular disease
  - Diabetes
  - Obesity (weight gain)
  - Neurobehavioral dysfunction (brain fog, decreased concentration)

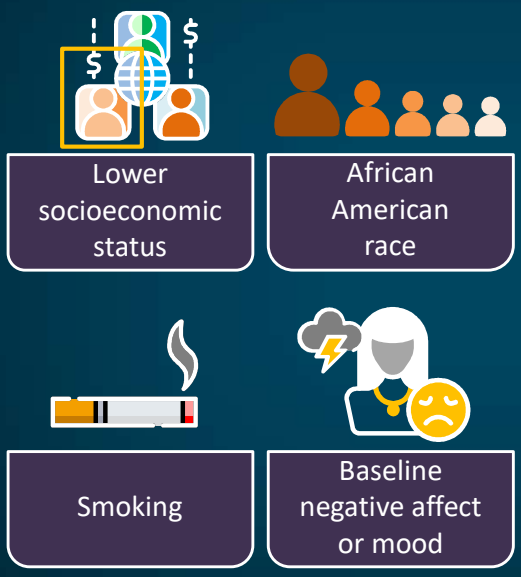
→ Self-reported in 40% to 56% of women compared to premenopausal women

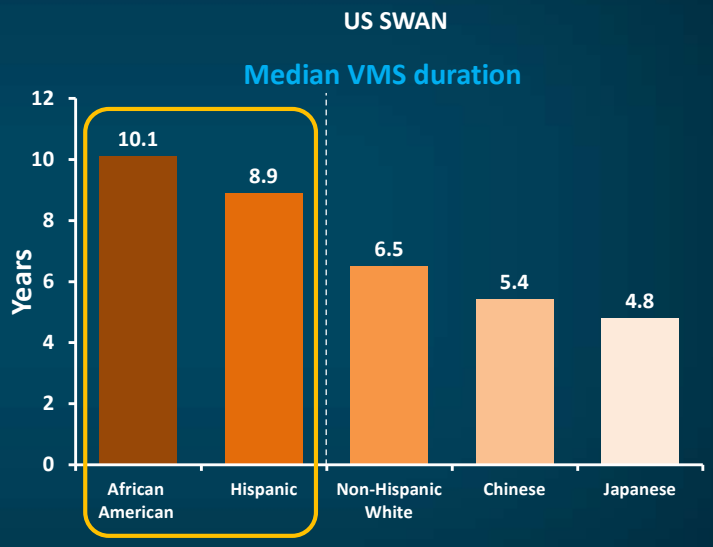
Gava G, et al. *Medicina*. 2019;55(10):688.

We will now watch a short animation describing the pathophysiology of VMS.

Whiteboard on Pathophysiology of VMS

Risk Factors for Developing and Duration of VMS





SWAN = Study of Women's Health Across the Nation; VMS = vasomotor symptoms.
Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287.

Negative Impacts of VMS

VMS can have a significantly negative impact on overall health and well-being

Women who experience frequent VMS (>6 days in the previous 2 weeks) also experience higher rates of anxiety, depression, difficulty sleeping, and overall impaired quality of life

- Almost 3 out of 4 postmenopausal women in a multinational survey suffered from fatigue, and 2 out of 3 had difficulty sleeping

Healthcare utilization and associated costs are significantly higher for women with VMS

Despite these profound impacts, a survey of 1039 women ages 40 to 65 years across the US showed that 73% of women had not received treatment for their VMS

VMS = vasomotor symptoms.
Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287.

Question

Neurokinin receptors have a thermoregulatory affect on which of the following?

a) Ovaries
b) KNDy neurons in the brain
c) Estrogen binding
d) Muscle movement

Amanda Case Study

- Amanda is in her late 40s
- She is experiencing amenorrhea, hot flashes, fatigue, irritability, frequent and severe hot flashes day and night, and weight gain
  - Hot flashes occur 6 to 8 times per day, moderate to severe intensity
  - Last menstrual period was 6 months ago
- Sleep is disrupted 3 to 4 times per night—sometimes just "covers on and off," sometimes soaking sweats
- She has mood swings and irritability that affect her partner, work, and family
- She has tried black cohosh, ashwagandha, soy supplements, and magnesium without improvement
- She is miserable and comes to you for help
- Her sister had breast cancer at age 60 years; she does not want hormone therapy

The Treatment Landscape for VMS Due to Menopause

JoAnn V. Pinkerton, MD, MSCP, FACOG

Self-Management Techniques

- Exercise and yoga
- Cooling techniques
- Dietary modification
- Weight loss
- Trigger avoidance
- Supplements
- Acupuncture

Limitations

- There is no strong evidence that lifestyle changes such as cooling techniques and avoiding triggers improve VMS
- There is insufficient or poor evidence to consider exercise or yoga as a treatment for VMS
- A healthy diet is important for health promotion and chronic disease prevention; limited evidence supports dietary modifications as a tool for improving VMS
- Weight loss may be considered for improving VMS

North American Menopause Society (NAMS). *Menopause*. 2023;30(6):573-590.

Nonhormone Pharmacologic Therapies Used for VMS

Medication name	Drug class	Suggested dosing	Side effects	Additional considerations
Fezolinetant	NK3 receptor antagonist	45 mg daily	Nausea, headache	Monitor liver tests
Gabapentin*	Gamma-aminobutyric acid (GABA) analogue	100–300 mg 3x/day	Dizziness, fatigue	Consider in concomitant migraine or sleep disorders
Paroxetine	SSRI	Paroxetine mesylate: 7.5 mg/day Paroxetine HCl*: 10–20 mg/day	Nausea, dizziness	First US FDA-approved nonhormone option; some data in sleep (7.5mg). CYP2D6 inhibition; avoid in tamoxifen users. Consider higher doses higher in concomitant mood disorders (off-label).
Escitalopram*	SSRI	10-20 mg	Nausea, dizziness	As effective as low-dose estradiol
Venlafaxine*	SNRI	37.5–150 mg/day	Nausea, dizziness	May be safe in tamoxifen users
Oxybutynin*	Anticholinergic, antimuscarinic	2.5 mg–5 mg/2x daily up to 15 mg/day	Dry mouth, urinary difficulties	Avoid in elderly; may benefit concomitant overactive bladder with VMS; side effects appear dose-dependent
Clonidine*	Antihypertensive; α-2 adrenergic agonist	0.05–0.1 5 mg/day	Blood pressure, drowsiness, dry mouth	Inconsistent data; less effective than SSRIs/SNRIs and gabapentinoids; significant side effects

Notes: Data from David et al and Sahni et al.
SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.
Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287.

Used off-label.

The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society

Recommended

- Cognitive-behavioral therapy
- Clinical hypnosis
- SSRIs/SNRIs/gabapentin*
- Fezolinetant (Level I)
- Oxybutynin (Levels I–II)*
- Weight loss
- Stellate ganglion block (Levels II–III)*

Not recommended due to lack of quality information

- Paced respiration; supplements/herbal remedies, cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation, suvorexant, soy foods and soy extracts, soy metabolite equol, cannabinoids, acupuncture, calibration of neural oscillations; chiropractic interventions, clonidine; dietary modification and pregabalin

NAMS. *Menopause*. 2023;30(6):573-590.

Used off-label.

Hormone Replacement Therapy

Menopausal hormone therapy remains the most effective treatment for VMS

Current professional guidelines conclude that the benefits of treatment typically outweigh the risks for healthy, symptomatic women under age 60 years and those within 10 years from their FMP

For women with medical comorbidities, an individualized approach to treatment is recommended

For women who cannot use or choose not to use menopausal hormone therapy, there are many evidence-based nonhormonal options available including pharmacologic therapies of which only 2 are FDA-approved

FMP = final menstrual period; FDA = US Food and Drug Administration; VMS = vasomotor symptoms.
Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287.

Who Should Not Take Hormone Therapy

Contraindications for oral and transdermal hormone therapy

- Unexplained vaginal bleeding
- Liver disease
- Prior estrogen-sensitive cancer (including breast cancer)
- Prior coronary heart disease, stroke, myocardial infarction, or VTE
- Personal history or high risk of thromboembolic disease

Potential risks of hormone therapy for women <60 years include

- Rare risk of breast cancer with EPT
- Endometrial hyperplasia/endometrial cancer—inadequately opposed estrogen
- Venous thrombosis and gallbladder disease

Adverse events
Nausea, bloating, weight gain, fluid retention, mood swings (progestogen related), breakthrough bleeding, headaches, and breast tenderness

EPT = estrogen-progestin therapy; VTE = venous thromboembolism.
NAMS. *Menopause*. 2022;29(7):767-794.

Who Should Take Hormone Therapy?

- Hormone therapy remains very effective for relief of hot flashes and nights sweats, as well as improves quality of life and rapid eye movement (REM) sleep; improvements in bone density and reduction of fracture are also seen
- For women who are overweight, have migraine without aura, or to minimize risk of VTE, **transdermal estradiol** can be given in combination with micronized progesterone for women with a uterus, estrogen alone if a woman has had a hysterectomy

Who Should NOT Take Hormone Therapy?

- However, for women who have risk factors or want to avoid hormone therapy or those with estrogen sensitive breast or uterine cancers or significant risk of VTE, stroke, or who have migraine with aura or extensive history of endometriosis, alternative effective nonhormone therapies are needed
- Until the recent approval of the first neurokinin (NK3) receptor antagonist, with the exception of paroxetine 7.5mg, there have not been effective nonhormone therapy options for those who are not good candidates for hormone therapy

Questions?

New and Emerging Pharmacotherapeutic Options to Better Manage VMS Due to Menopause

James A. Simon, MD, CCD, MSCP, IF, FACOG

NK1 and NK3 Antagonists

NKB antagonism (NK3R antagonists)

Specialized hypothalamic KNDy neurons utilize NKB signaling on NK3R; this signaling pathway appears influential in the development of hot flashes within the hypothalamic thermoregulatory neutral zone. Through NK3R antagonism, the signaling pathway can be disrupted and potentially attenuate VMS

Several NK3R antagonists are in phase 3 and 4 trials

- Fezolinetant – FDA approval in May 2023
- Elinzanetant

FDA = US Food and Drug Administration; NK1 = neurokinin 1; NK3R = neurokinin 3 receptor; NKB = neurokinin B; VMS = vasomotor symptoms.

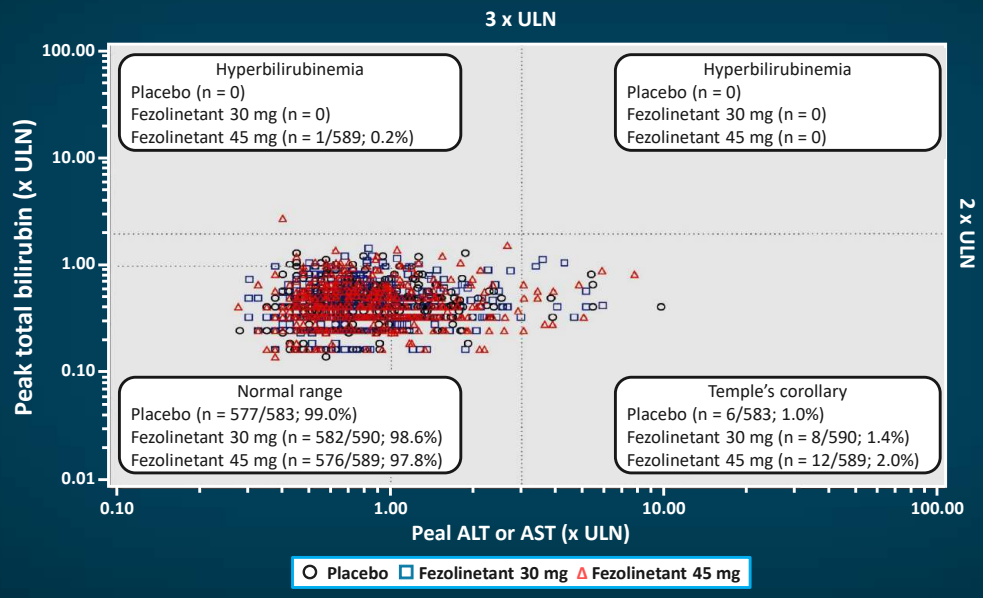
Khan SJ, et al. *Int J Womens Health*. 2023;15:273-287.

Neurokinin Receptor Antagonists

- Effective, nonhormonal treatment for moderate to severe vasomotor symptoms
- Fezolinetant NK3R 45 mg oral daily is the first neurokinin receptor antagonist to receive FDA approval for VMS due to menopause
  - Reduced frequency of VMS about 65%, significantly > placebo; similar to the 75% reduction seen with hormone therapy
  - Efficacy evident within 1 week
  - Demonstrated a very good safety profile including endometrial safety
  - Label recommends baseline liver function tests (LFTs) and every 3 months for 9 months
- NK3R antagonists data (fezolinetant), and dual NK1R/NK3R antagonist (elinzanetant), indicate partial gonadotropin suppression does not reduce estrogen secretion to menopausal levels, thus making deficiency symptoms or effects (bone loss) unlikely

Skorupskaite K, Anderson RA. *Pharmacol Ther*. 2022;230:107960.

Evaluation of Study Drug-Induced Serious Hepatotoxicity

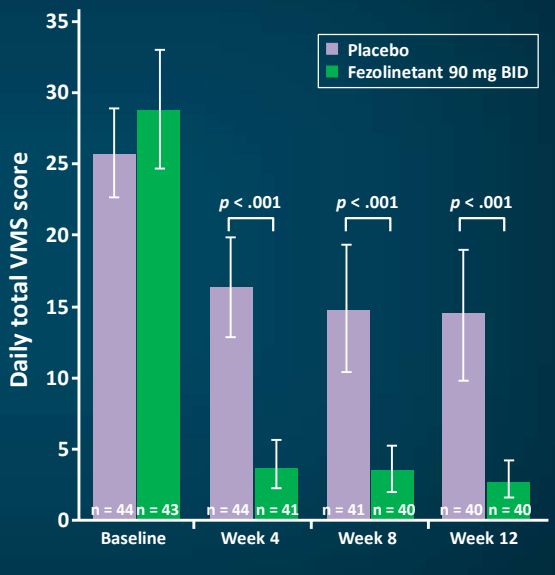


ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit normal.

Neal-Perry G, et al. *Obset Gynecol*. 2023;141(4):737-747.

Fezolinetant

- First studies in 2016, phase 2 trials in 2019
- Results
  - Significant reduction in VMS score (frequency and severity)
    - Decrease by 93% in the 12-week study
    - Effect seen as early as first day of treatment
    - Improvement in sleep quality and decrease in daily interference symptoms
- Adverse events
  - Most common were GI related (NK3 receptors in gut)
  - 12% of patients had transient, mild LFT elevations
  - Baseline and ongoing hepatic function monitoring are recommended

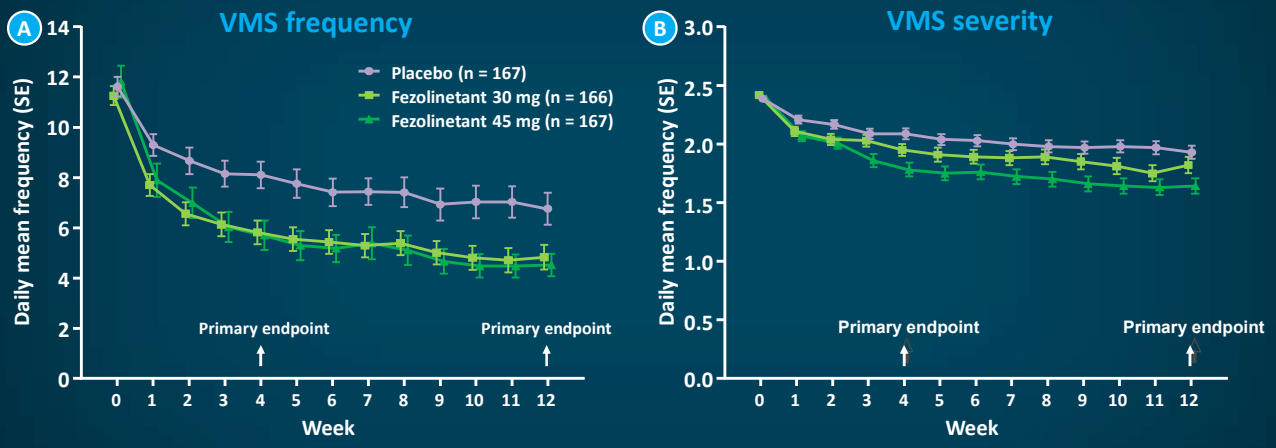


GI = gastrointestinal.

Depypere H, et al. *Expert Opin Investigat Drugs*. 2021;30:7:681-694.

Fezolinetant Reduced VMS Frequency and Severity Across the 12-Week Period (Skylight 2) NK3 to 52 Weeks

Percentage reduction in frequency of moderate and severe VMS per 24 hours by week (FAS)



Mean (A) frequency and (B) severity of moderate and severe VMS during the 52-week treatment period (FAS and FAS-fezolinetant exposure). Genevieve Neal-Perry. Both fezolinetant doses statistically significantly reduced VMS frequency and severity at Weeks 4 and 12 vs placebo.

FAS = full analysis set; SE = standard error; VMS = vasomotor symptoms.

Johnson KA, et al. *J Clin Endocrinol Metab*. 2023;108(8):1981-1997.

Summary of Treatment-Emergent Adverse Events

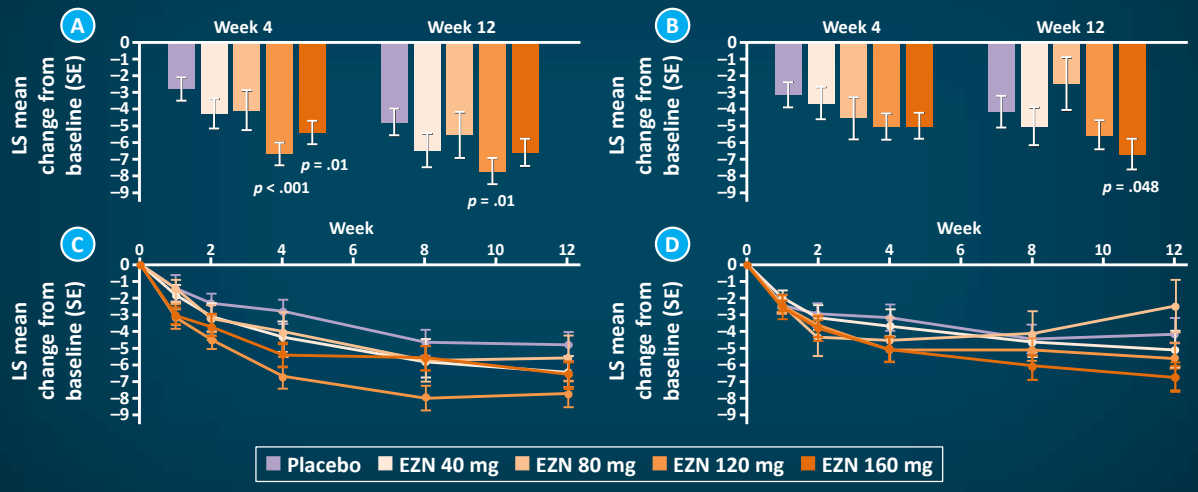
	Placebo (n = 610)	Fezolinetant 30 mg (n = 611)	Fezolinetant 45 mg (n = 609)	Fezolinetant total (n = 1220)
TEAEs*	**391 (64.1)**	**415 (67.9)**	**389 (63.9)**	**804 (65.9)**
Study drug-related TEAEs	106 (17.4)	94 (15.4)	110 (18.1)	204 (16.7)
Serious TEAEs	14 (2.3)	20 (3.3)	23 (3.8)	43 (3.5)
Study drug-related serious TEAEs	1 (0.2)	0	3 (0.5)	3 (0.2)
TEAEs leading to withdrawal of treatment	26 (4.3)	34 (5.6)	28 (4.6)	62 (5.1)
Study drug-related TEAEs leading to withdrawal of treatment	16 (2.6)	16 (2.6)	17 (2.8)	33 (2.7)
Death†	0	1 (0.2)	0	1 (0.1)
TEAEs occurring in 5% or more of participants (by PT)				
Headache	56 (9.2)	52 (8.5)	55 (9.0)	107 (8.8)
COVID-19	38 (6.2)	38 (6.2)	32 (5.3)	70 (5.7)
TEAEs by severity‡				
Mild	180 (29.5)	215 (35.2)	195 (32.0)	410 (33.6)
Moderate	191 (31.3)	185 (30.3)	171 (28.1)	356 (29.2)
Severe	20 (3.3)	15 (2.5)	23 (3.8)	38 (3.1)

COVID-19 = coronavirus disease 2019; PT = preferred term; TEAE = treatment-emergent adverse event.
Data are n (%).
* Defined as an adverse event observed after administration of study intervention was started and up to 21 days after the last dose of study intervention.
† 1 death reported in the fezolinetant 30 mg group was considered unrelated to study drug. Because all TEAEs are listed, death is noted, as well as the TEAE of cardiac arrest and anoxic brain injury that led to treatment withdrawal.
‡ Mild: No disruption of normal daily activities; moderate: Affects normal daily activities; severe: Inability to perform daily activities.

Neal-Perry G, et al. *Obset Gynecol*. 2023;141(4):737-747.

SWITCH-1: Efficacy and Safety of Elinzanetant, a selective Neurokinin-1,3 Receptor Antagonist for Vasomotor Symptoms

A Dose-Finding Clinical Trial

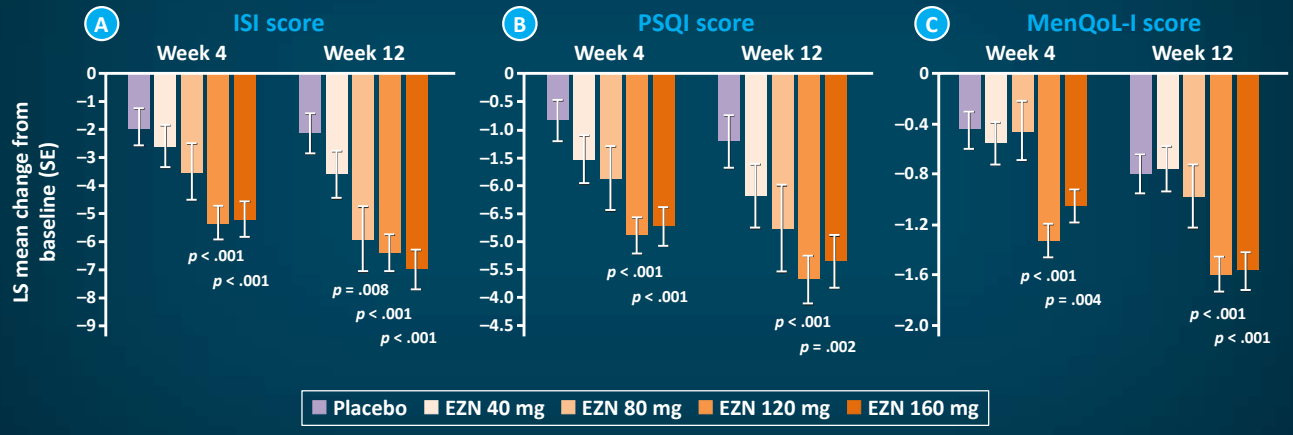


Change from baseline in mean daily frequency (A, C) and weekly severity (B, D) of moderate and severe VMS by treatment group.
EZN = elinzanetant; LS = least squares.

Simon JA, et al. *Menopause*. 2023;30(3):239-246.

SWITCH-1: Efficacy and Safety of Elinzanetant, a selective Neurokinin-1,3 Receptor Antagonist for Vasomotor Symptoms

A Dose-Finding Clinical Trial (cont)



Change from baseline in ISI (A), PSQI (B), and MenQoL-I (C) score by treatment group at Weeks 4 and 12.
EZN = elinzanetant; ISI = Insomnia Severity Index questionnaire; LS = least squares; MenQoL-I = Menopause-specific Quality-of-Life questionnaire intervention version; PSQI = Pittsburgh Sleep Quality Index.

Simon JA, at al. *Menopause*. 2023;30(3):239-246.

Elinzanetant (NK1,3) Met Primary and Key Secondary Endpoints in Pivotal OASIS 1 and 2 Phase 3 Studies TopLine Data

- Efficacy and safety of elinzanetant in postmenopausal women
  - First dual neurokinin-1, 3 (NK-1,3) receptor antagonist
  - Nonhormonal treatment of moderate to severe VMS
- Statistically significant reduction in frequency and severity of moderate to severe VMS vs placebo in postmenopausal women
- Both studies statistically significant over placebo in
  - Reduction in frequency of VMS at Week 1
  - Improvement of sleep disturbances (PROMIS)
  - Menopause-related quality of life (MENQOL)
- The safety profile in both studies consistent with previously published data

Bayer. News release 3/19.2024 (https://www.bayer.com/media/en-us/positive-topline-results-from-phase-iii-long-term-study-oasis-3-support-submissions-for-marketing-authorization-for-bayers-elinzanetant). Accessed 5/1/2024.

Amanda: Case Study (cont)

Nonhormone options discussed include the following

- Low-dose antidepressants: SSRI, SNRI
  - She does not want to take antidepressants even at low doses for relief of hot flashes
- Gabapentin
  - She tried this in the past but had significant drowsiness
- Oxybutynin
  - She has dry eyes so does not want to try this route
- She has normal liver function tests
- She is not taking any CYP1A2 inhibitors including cimetidine
- NK3 receptor antagonist was shown effective in diverse populations, White or Black race, body mass index (BMI) of 30 kg/m^2 or higher, younger or older than age 55 years, smokers, former smokers, and never smokers, in US as well as in Europe

Question

Based on the case study, which of the following would be a suggested pharmaceutical treatment option?

a) Fezolinetant
b) Gabapentin
c) Cognitive behavioral therapy
d) Oxybutynin

Amanda: Case Study (Cont)

- Amanda is given a neurokinin receptor antagonist
- Within 1 to 2 weeks her hot flashes have decreased from 8 to 10 per day to 1 to 2 per day, and they are less severe
- Her night sweats have almost completely resolved
- Her quality of life has increased, although she still has some mild depressed mood

Communication Issues and Challenges Between Women With VMS Due to Menopause and Their Healthcare Providers

JoAnn V. Pinkerton, MD, MSCP, FACOG

We will now watch a short animation on VMS communication.

Whiteboard on VMS Communication

Patient Education Resources

These society and educational web pages have information on hot flashes, hormone therapy, bone loss, and vaginal symptoms.

The Menopause Society™
Leading the Conversation

healthywomen

ENDOCRINE SOCIETY
Hormone Science to Health

ACOG
The American College of Obstetricians and Gynecologists

REDHOTMAMAS
outsmarting menopause™

let's talk menopause!

Society for Women's Health Research

Question

Which of the following is an opportune way to provide enhance patient communication?

a) Build a trusting relationship
b) Create an open dialogue
c) Provide evidence-based information about hormone and nonhormone options
d) Engage in shared decision-making
e) All the above

Strategies for Effective Communication

- Patient-centered communication
  - Varies depending on age, ethnicity, background, fears
  - Be culturally aware
  - Include how menopause is affecting work, life, and sleep difficulties
- Build a trusting relationship
- Create an open dialogue
- Provide evidence-based information about hormone and nonhormone options
- Engage in shared decision-making
- Recognize that providers may need to be flexible about the menopause transition management plan
- Identify helpful technologies to track behaviors, moods or feelings, and experiences
  - Recognize concerns about usability, accessibility, security, and privacy

Let's Revisit Amanda and Her Hot Flashes

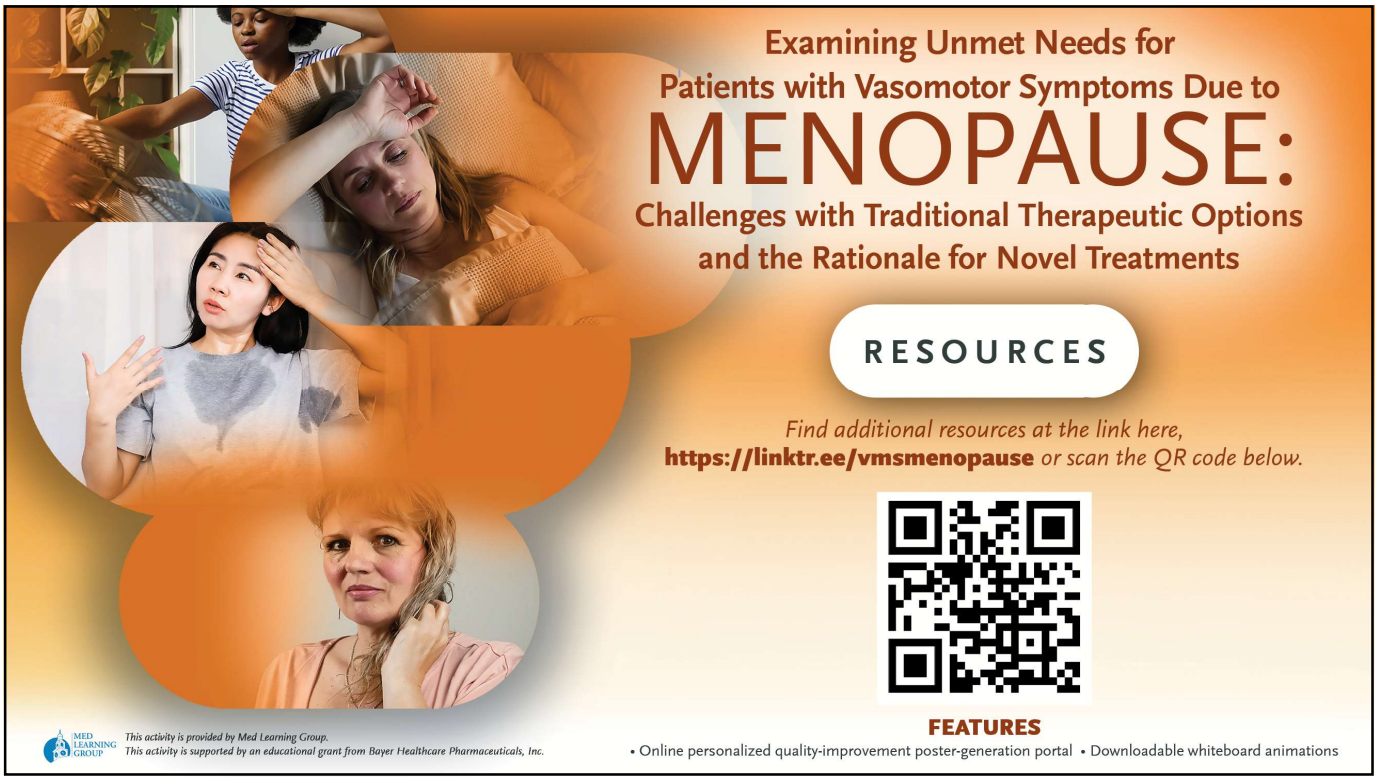
- Although Amanda had clearly bothersome hot flashes and hormone therapy would be the most effective therapeutic option, however, her fear of estrogen and of breast cancer were driving her choices
- Race and ethnicity often play a role in whether patients trust providers recommendations and often on where they are obtaining their information
- Providing written or pictorial information can improve education and build trust
- Recognizing what lifestyle and supplements she had tried and what she was looking for were important to build trust
- Although a good candidate for low-dose hormone therapy as well as nonhormone therapy options such as SSRIs, SNRIs, and gabapentin, she was not willing to take them
- After explaining how the neurokinin receptor antagonists worked, Amanda was very excited to try one, and fezolinetant was discussed

Conclusions

- VMS can be extremely distressing and disruptive
- There are now 2 FDA-approved non-hormonal treatments for hot flashes (paroxetine 7.5mg and fezolinetant 45mg) and others used off-label
- Topline data from OASIS 1 and 2 suggest that elinzanetant working through dual NK1 and NK3 receptor antagonism improves VMS, as well as sleep and menopause-related quality of life
- Effective treatment of VMS can improve not only symptoms but quality of life, workplace productivity and relationships (at home and at work)
- Patient-centered communication is KEY!

Questions?

Thank you!


Examining Unmet Needs for
Patients with Vasomotor Symptoms Due to
MENOPAUSE:
Challenges with Traditional Therapeutic Options
and the Rationale for Novel Treatments
RESOURCES
Find additional resources at the link here,
https://linktr.ee/vmsmenopause or scan the QR code below.
FEATURES
• Online personalized quality-improvement poster-generation portal • Downloadable whiteboard animations
MED LEARNING GROUP
This activity is provided by Med Learning Group.
This activity is supported by an educational grant from Bayer Healthcare Pharmaceuticals, Inc.

Examining Unmet Needs for Patients with Vasomotor Symptoms Due to Menopause: Challenges with Traditional Therapeutic Options and the Rationale for Novel Treatments

Resource	Address
Anderson RA. Kisspeptin and neurokinin B neuroendocrine pathways in the control of human ovulation [published online ahead of print, 2024 Feb 25]. *J Neuroendocrinol*. 2024;e13371.	https://onlinelibrary.wiley.com/doi/10.1111/jne.13371
Faubion SS, Crandall CJ, Davis L, et al. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022;29:767-794.	https://journals.lww.com/menopausejournal/fulltext/2022/07000/the_2022_hormone_therapy_position_statement_of_the.4.aspx
Freedman RR, Blacker CM. Estrogen raises the sweating threshold in postmenopausal women with hot flashes. *Fertil Steril.* 2002;77:487-490.	https://www.fertstert.org/article/S0015-0282(01)03009-6/fulltext
Johnson KA, Martin N, Nappi RE et al. Efficacy and safety of fezolinetant in moderate to severe vasomotor symptoms associated with menopause: A phase 3 RCT. *J Clin Endocrinol Metab*. 2023;108:1981-1997.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10348473/
Khan SJ, Kapoor E, Faubion SS, Kling JM. Vasomotor symptoms during menopause: A practical guide on current treatments and future perspectives. *Int J Womens Health*. 2023;15:273-287.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9938702/
Khan SJ, Kapoor E, Faubion SS, Kling JM. Vasomotor symptoms during menopause: A practical guide on current treatments and future perspectives. *Int J Womens Health*. 2023;15:273-287.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9938702/
Neal-Perry G, Cano A, Lederman S, et al. Safety of fezolinetant for vasomotor symptoms associated with menopause: A randomized controlled trial. *Obstet Gynecol*. 2023;141:737-747.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10026946/pdf/ong-141-737.pdf
Positive topline results from phase III long-term study OASIS 3 support submissions for marketing authorization for Bayer's elinzanetant. Bayer. Published March 19, 2024.	https://www.bayer.com/media/en-us/positive-topline-results-from-phase-iii-long-term-study-oasis-3-support-submissions-for-marketing-authorization-for-bayers-elinzanetant
Richard-Davis G, Wellons M. Racial and ethnic differences in the physiology and clinical symptoms of menopause. *Semin Reprod Med*. 2013;31:380-386.	https://www.thieme-connect.de/products/ejournals/abstract/10.1055/s-0033-1348897
Shufelt CL, Brown V, Carpenter JS, et al. The 2023 nonhormone therapy position statement of The North American Menopause Society. *Menopause*. 2023;30:573-590.	https://journals.lww.com/menopausejournal/abstract/2023/06000/the_2023_nonhormone_therapy_position_statement_of.4.aspx
Simon JA, Anderson RA, Ballantyne E, at al. Efficacy and safety of elinzanetant, a selective neurokinin-1,3 receptor antagonist for vasomotor symptoms: a dose-finding clinical trial (SWITCH-1). *Menopause*. 2023;30:239-246.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9970022/pdf/meno-30-239.pdf

Skorupskaite K, Anderson RA. Hypothalamic neurokinin signalling and its application in reproductive medicine. *Pharmacol Ther*. 2022;230:107960.	https://www.sciencedirect.com/science/article/abs/pii/S0163725821001625
US. Food and Drug Administration Guidance for Industry. Estrogen and Estrogen/Progestin Drug Products to Treat Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms — Recommendations for Clinical Evaluation. January 2003.	https://www.fda.gov/media/71359/download
Wakabayashi Y, Nakada T, Murata K, et al. Neurokinin B and dynorphin A in kisspeptin neurons of the arcuate nucleus participate in generation of periodic oscillation of neural activity driving pulsatile gonadotropin-releasing hormone secretion in the goat. *J Neurosci*. 2010;30:3124-3132.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6633939/

All URLs accessed May 2, 2024