Mise à jour sur la ménopause

(et la périménopause)

Journée médicale 2026

Centre Hospitalier du Grand-Portage

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Objectifs de la présentation

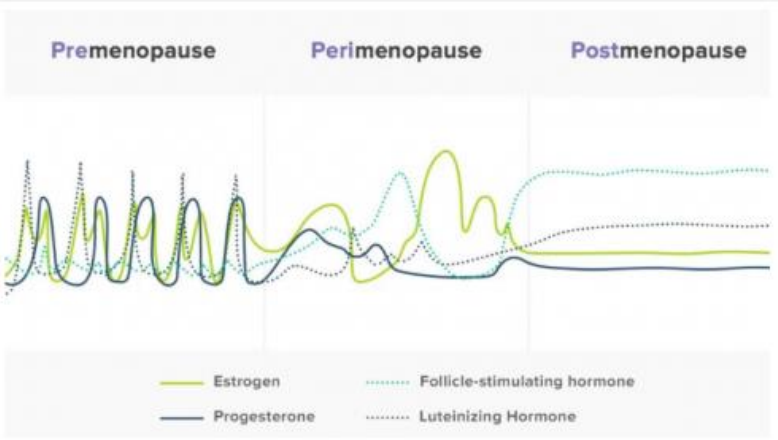
1. Revoir la **physiologie** et les symptômes de la transition vers la ménopause.
2. Résumer les **données récentes** sur le traitement hormonal de la ménopause (HT), **les risques et les contre-indications**.
3. Explorer les alternatives **non-hormonales,** avec un focus sur les options nouvellement disponibles.
4. Optimiser la prise en charge de la patiente en **périménopause**.

* Pas à l'horaire – le traitement du SGUM 

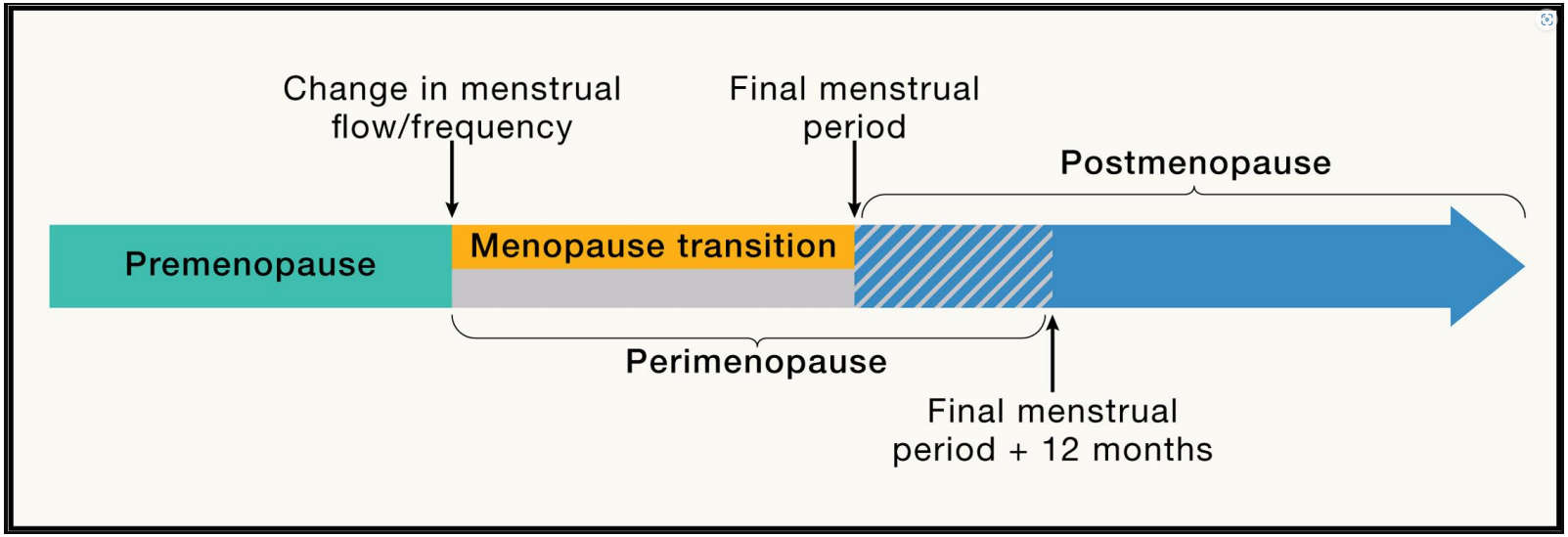
Épidémiologie

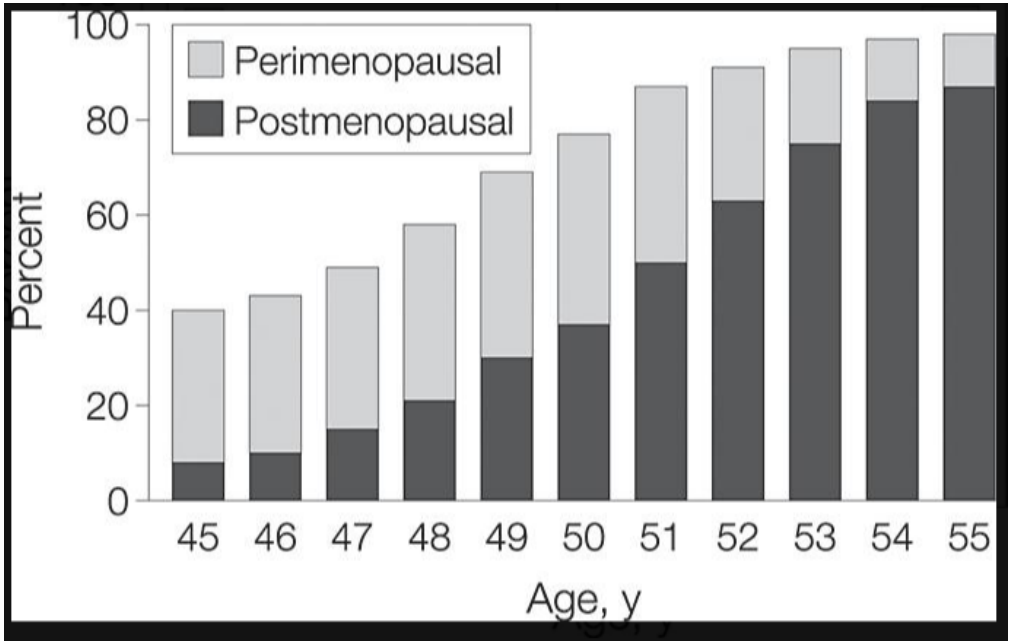
- Ménopause : arrêt définitif des menstruations ≥ 12 mois
- Âge moyen : 51 ans (Canada)
  - 50% des femmes ont une menopause au même âge que leur mère
  - Ménopause précoce (40-45 ans) chez 10% des femmes
    - 6-8x plus élevé chez les patientes avec un historique chez leur mère
    - Augmentation significative de risque de MCAS
  - Insuffisance ovarienne précoce (<40 ans) chez 1-2% des femmes
    - Référer en gynécologie SVP 😊

- Facteurs de risque modifiables sur l'âge de la ménopause:
  - **Tabagisme** (1-2 ans + tôt)
  - IMC (+ tard?)
  - Chirurgies gynécologiques (+ tôt)
  - Parité (+ tard)



Physiologie de la ménopause





Physiologie de la ménopause

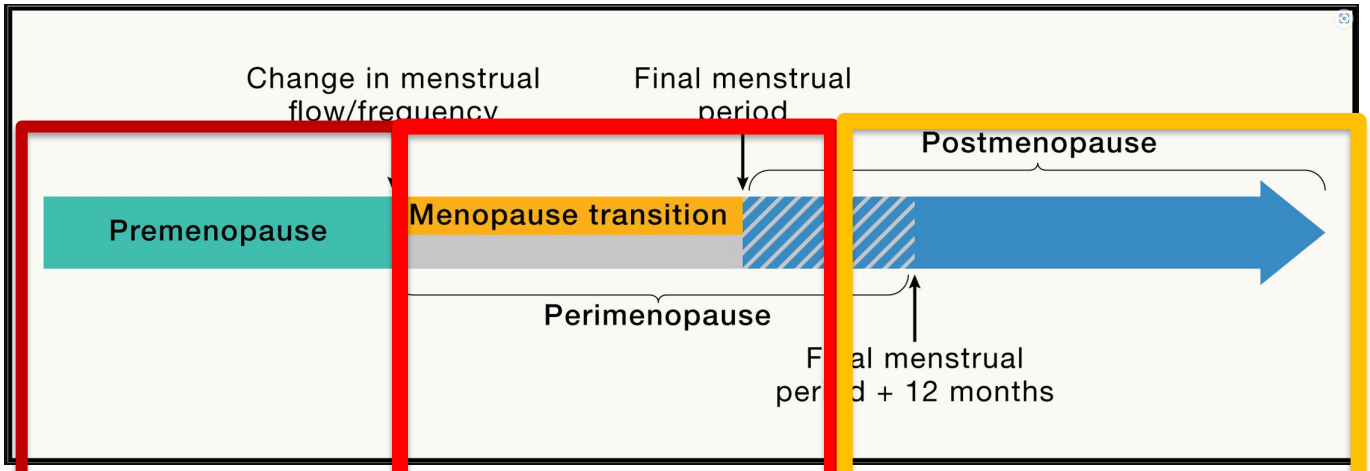
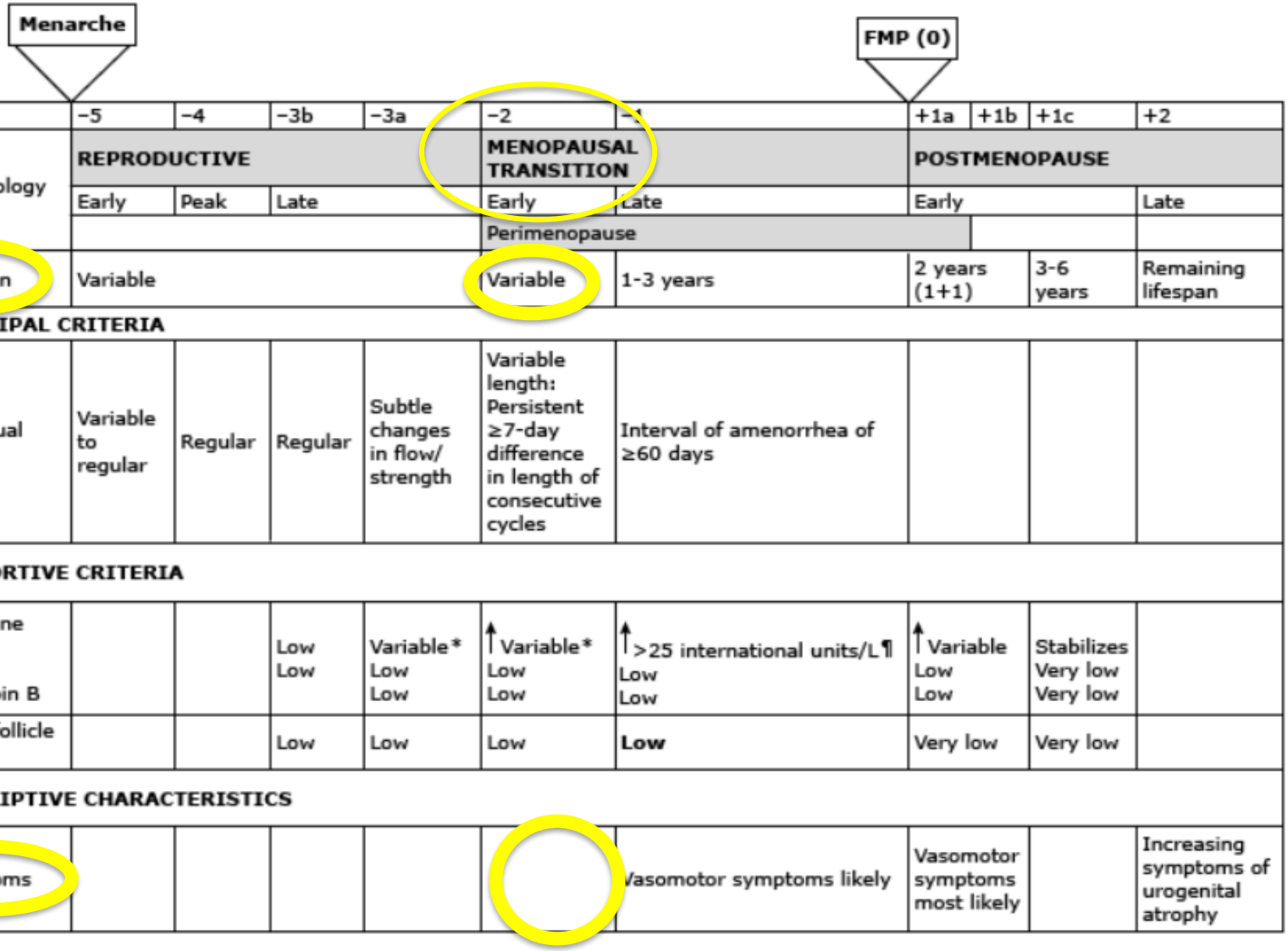


Table 1. Stages of the Menopausal Transition, Ranges of Hormone Levels, and the Prevalence of Hot Flushes.

Variable	Reproductive Years			Menopausal Transition (Perimenopause)		Postmenopausal Years	
	Early	Peak	Late	Early	Late	Early	Late
Menstrual cycle	Regular or variable	Regular		Variable cycle length; 1 or 2 missed cycles per yr	3 or more missed cycles per yr	None	
Range of steroid hormones (pg/ml)							
Estradiol	50–200			50–200 or slightly higher		40	0–15
Testosterone	400			400		400	400
Range of pituitary hormones (mU/ml)							
Follicle-stimulating hormone	10 on days 2–4			10 or higher on days 2–4		>100	
Luteinizing hormone	10 on days 2–4			10 or higher on days 2–4		>100	
Prevalence of hot flushes (%)			10	40	65	50	10–15



Stage	−5	−4	−3b	−3a	−2	−1	+1a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	Variable				Variable	1-3 years	2 years (1+1)		3-6 years	Remaining lifespan
PRINCIPAL CRITERIA										
Menstrual cycle	Variable to regular	Regular	Regular	Subtle changes in flow/ strength	Variable length: Persistent ≥7-day difference in length of consecutive cycles	Interval of amenorrhea of ≥60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑ Variable* Low Low	↑ >25 international units/L¶ Low Low	↑ Variable Low Low		Stabilizes Very low Very low	
Antral follicle count			Low	Low	Low	**Low**	Very low		Very low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms likely	Vasomotor symptoms most likely			Increasing symptoms of urogenital atrophy

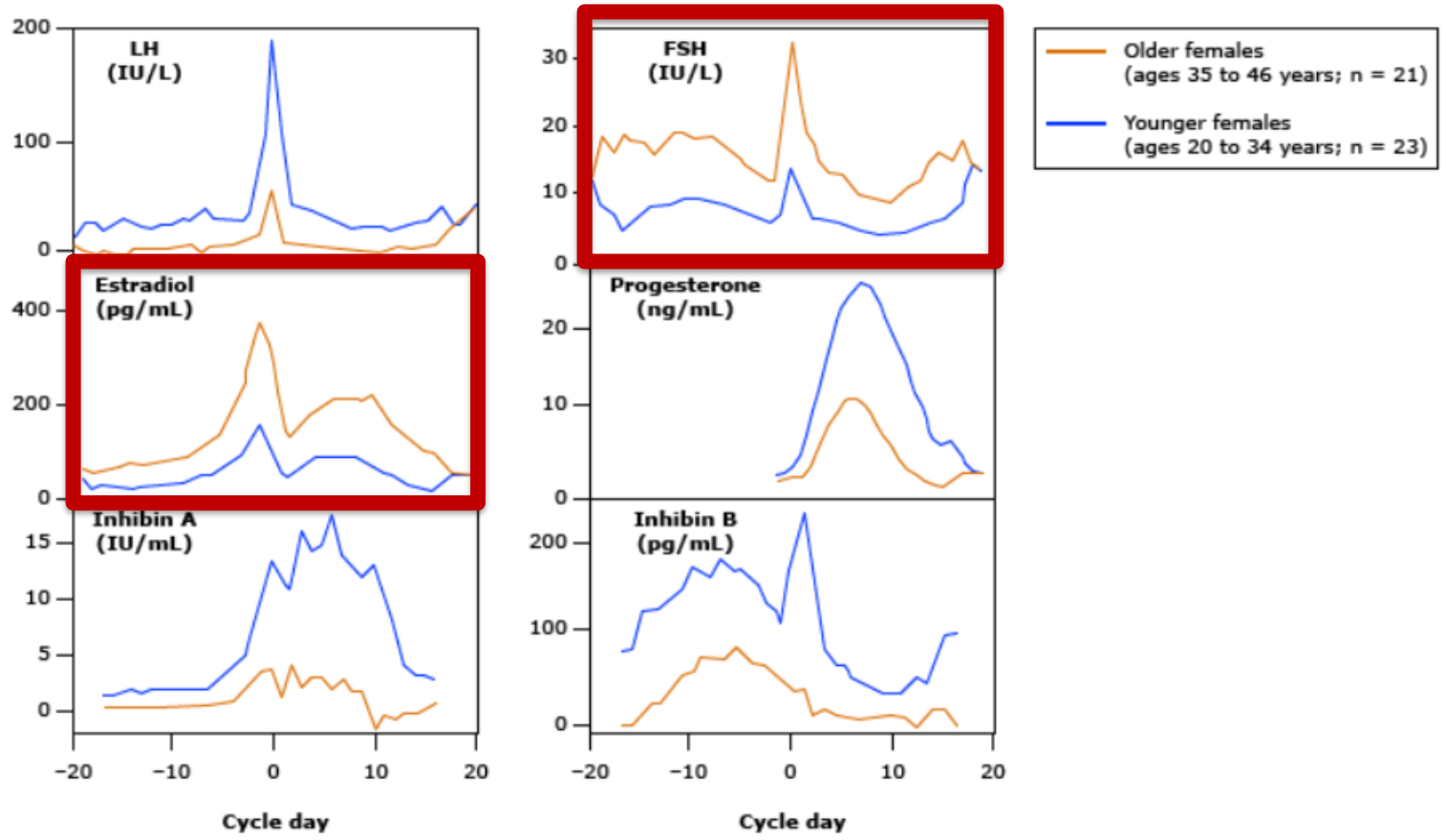
FMP: final menstrual period; FSH: follicle-stimulating hormone; AMH: anti-müllerian hormone; Arrow: elevated.

* Blood draw on cycle days 2 to 5.

¶ Approximate expected level based on assays using current international pituitary standard.

The estimated prevalence of VMS ranges from 46 percent during the early menopausal transition (from the beginning of menstrual irregularities to menopause) to approximately 60–80 percent at any time in the menopausal transition or postmenopause (Avis, Crawford, and Green 2018; Gibson 2018; Randolph et al. 2005; Thurston and Joffe 2011).

In the Study of Women's Health Across the Nation (SWAN), median total duration of symptoms was 7.4 years among women experiencing frequent VMS (occurring on ≥6 days in past 2 weeks) and these persisted for 4.5 years after the final menstrual period (FMP) (Avis et al. 2015). The shortest median VMS duration (3.4 years) was in women who were postmenopausal at VMS onset, whereas those who were premenopausal or early perimenopausal at their first VMS had the longest median VMS duration (≥11.8 years) and post-FMP persistence (9.4 years) (Avis et al. 2015). That study showed that factors associated with longer VMS duration also include race and ethnicity, low educational level, perceived stress, high symptom sensitivity, and depression at first report of VMS (Avis et al. 2015).



Mean daily levels of gonadotropins, sex steroids, and inhibins in older (ages 35 to 46 years; n = 21), shown in orange, and younger females (ages 20 to 34 years; n = 23), shown in blue.

FSH: follicle-stimulating hormone; LH: luteinizing hormone.

Adapted from: Welt CK, McNicholl DJ, Taylor AE, Hall JE. Female reproductive aging is marked by decreased secretion of dimeric inhibin. J Clin Endocrinol Metab 1999; 84:105.

Symptômes de la périménopause

- Symptômes vasomoteurs (bouffées de chaleur, sueurs nocturnes) : 80% (+)
  - Symptômes VM sévères (qui affectent la qualité de vie) : ~ 40%
- Perturbations du sommeil ~ 30-60%
- Changements cognitifs subjectifs et symptômes dépressifs
- Arthralgies ~ 10-15%
- Diminution de la libido
- Symptômes génito-urinaires (SGUM) 45-77%

Évaluation diagnostique

- Basé sur symptômes (changements menstruels, symptômes vasomoteurs) et âge (>45 ans).
- Dosages hormonaux non nécessaires sauf cas particuliers (ex: <40 ans).
- DDx : dysthyroïdie, dépression, anémie, néoplasie, syndrome carcinoïde.

MANIFESTATIONS CLINIQUES LIÉES À LA PÉRIMÉNOPAUSE ET À LA POSTMÉNOPAUSE

Les manifestations cliniques liées à la périménopause et à la postménopause :

→ Peuvent toucher plusieurs systèmes à une intensité variable, ce qui peut avoir un impact défavorable sur la qualité de vie;

→ Débutent généralement à la périménopause et persistent en moyenne de 4 à 7 ans, mais elles peuvent durer jusqu'à 15 ans et même davantage chez certaines femmes. Les manifestations génito-urinaires peuvent persister jusqu'au décès.

Principales manifestations cliniques liées à la périménopause et à la postménopause

La majorité des femmes présenteront au moins une de ces manifestations cliniques[1]	Autres manifestations cliniques possibles[1] *(liste non exhaustive)*
• Altérations du sommeil	• Difficultés cognitives (p. ex. pertes de mémoire, difficultés à se concentrer)
• Manifestations cliniques génito-urinaires	• Douleurs articulaires ou musculaires
• Manifestations cliniques sexuelles (p. ex. diminution de la libido ou du désir, altération de la fonction sexuelle)	• Gain pondéral, surtout au niveau abdominal
• Symptômes vasomoteurs (bouffées de chaleur, sueurs nocturnes ou diurnes)	• Instabilité émotionnelle
	• Symptômes anxieux ou dépressifs Palpitations (15-30%)

1. L'information est présentée en ordre alphabétique. La fréquence des manifestations peut différer selon les caractéristiques des populations.

Qui traiter?

PRINCIPES DE TRAITEMENT

→ **La décision d'amorcer ou non l'hormonothérapie pour soulager les manifestations cliniques liées à la ménopause doit tenir compte :**

Traitement Hormonal de la ménopause

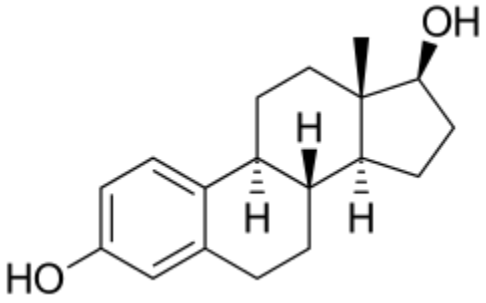
- Symptômes ménopausaux (vasomoteurs) qui **affectent la qualité de vie**
  - **Peu importe si la patiente est ménopausée ou non**

- Estrogène systémique (transdermique* ou oral)
- +/- Progestatif (oral, vaginal, injectable, intra-utérin) si utérus en place*.

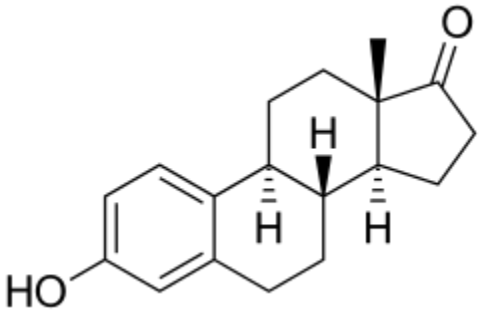
  *Aussi considérer si patiente connue pour endométriose.

- De loin le traitement le plus efficace
  - Diminution de 75% de la fréquence et la sévérité des bouffées de chaleur.
  - Amélioration subjective de la qualité du sommeil – réveils moins fréquents.
  - Amélioration des arthralgies
  - Amélioration de la qualité de vie
  - « Ça a changé ma vie »
  - … effet sur la libido?
  - … effet sur l'humeur?

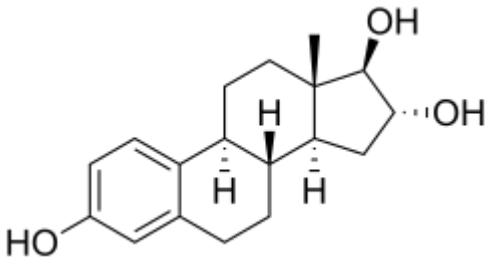
Qu’en est-il de l’hormonothérapie dite «bio-identique»



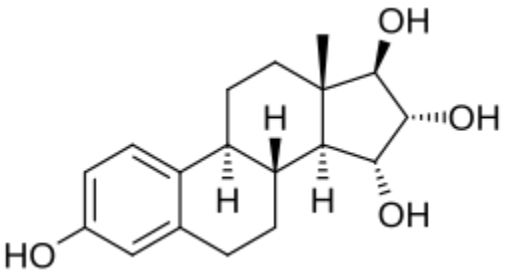
Estradiol
(17B-estradiol)



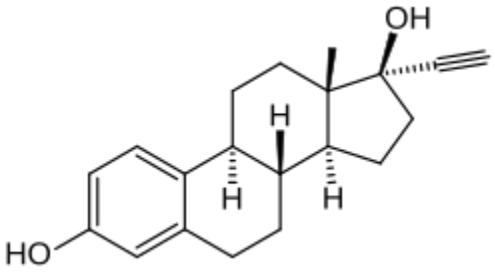
Estrone



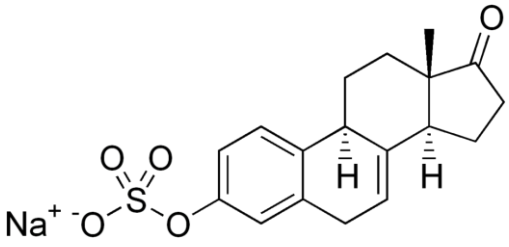
Estriol



Estétrol

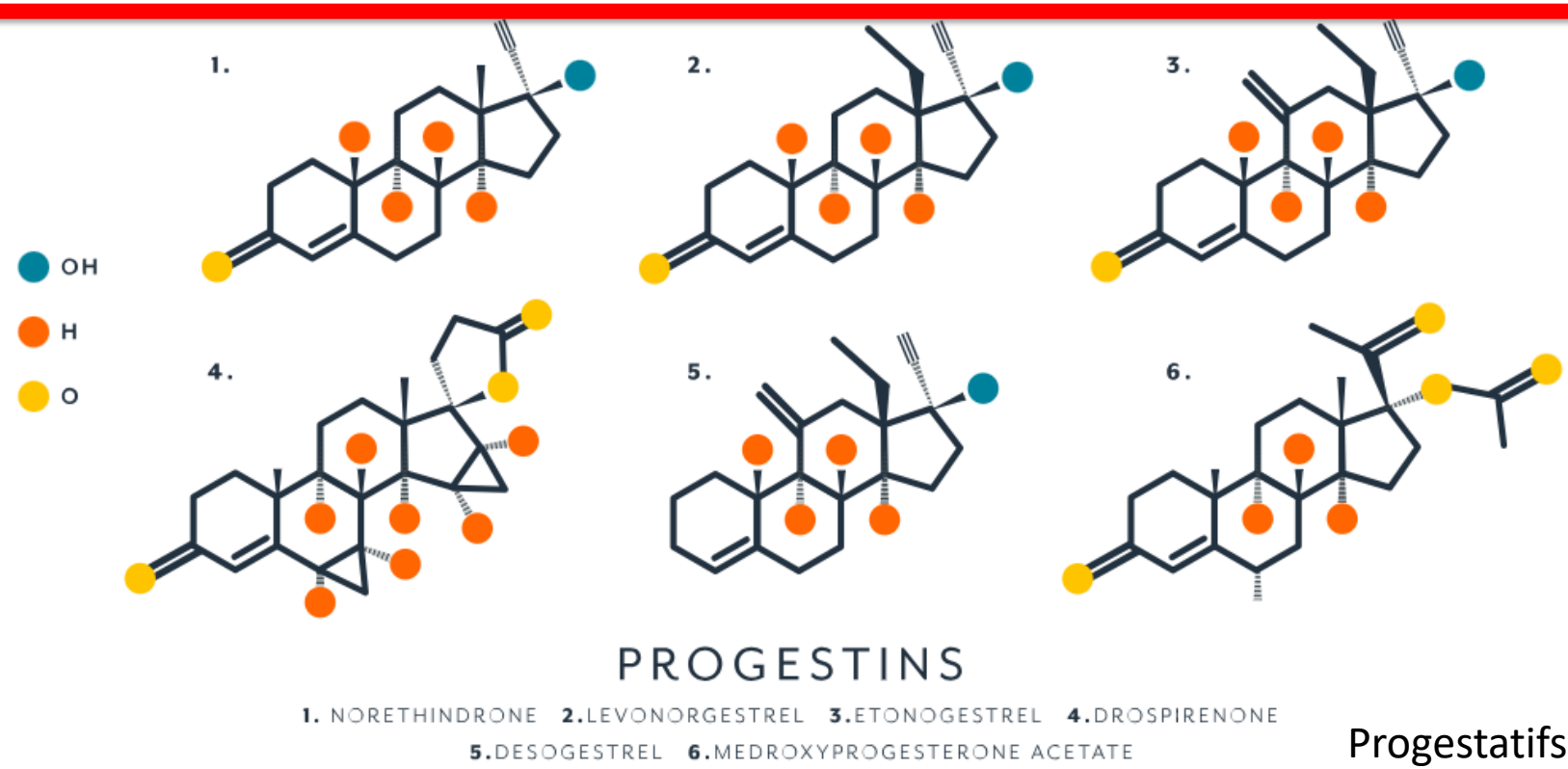


Éthinylestradiol

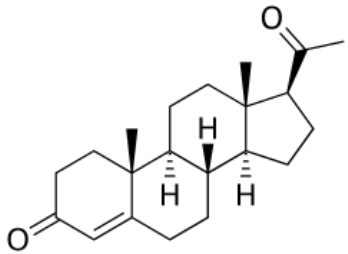


Oestrogènes Conjugués Équins (Prémarin)

Qu'en est-il de l'hormonothérapie dite «bio-identique»



Progestatifs



Progestérone

Progestogènes

Résumé des bénéfices	HT dite bio-identique	HT Classique
SVM	++	++
Douleurs articulaires	?	++
Fonction sexuelle	+ (voie TD)	+ ou =
Sommeil	++	++
Sx anxieux et / ou dépressifs	+ * ou =	=
Poids	= ou -	=
Peau et cheveux	?	?
DM 2	++ (voie TD)	++
Fractures	?	++
Troubles neurocognitifs majeurs	= ou + *	+* ; - si débuté après 65 ans

PAS MAL PAREIL

* : niveau évidence très faible; TD : transdermique; PM: Progestérone Micronisée
+ : effet positif - : effet négatif ?: Aucune donnée disponible

Crédit Dre Sophie Desindes – UdeS

Résumé des risques	HT dite bio-identique	HT Classique
TEV	= (TD) ↑ (PO)	↑
Cancer endomètre	↑	↓
Cancer du sein	↑ (en lien avec la durée); possible ↓ si amorcée à moins de 60 ans *; = si PM *	↑ si ECE + AMP ↓ si ECE seul
AVC	= (TD)* ; ? (PO)	↑ ou = selon âge à l'amorce
Maladie de la vésicule biliaire	= (TD) ; ↑ (PO)	↑ ↑
Mortalité globale	↓ * ou =	=

- : niveau évidence très faible; TD : transdermique; PM: Progestérone Micronisée

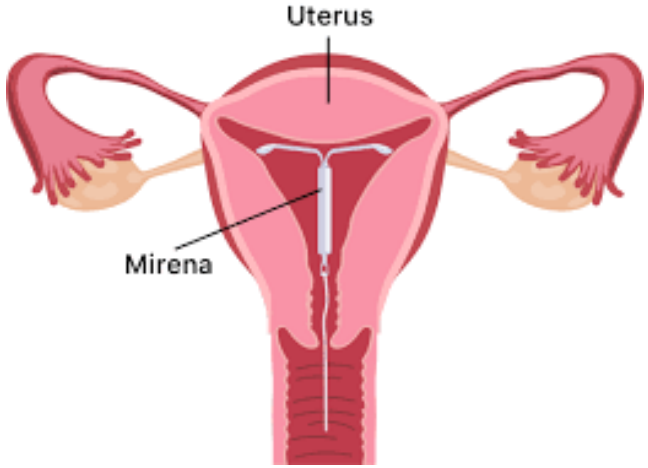
↓: diminution du risque ↑: augmentation du risque = : pas de différence ?: Aucune donnée

Crédit Dre Desindes – UdeS

Quoi donner?

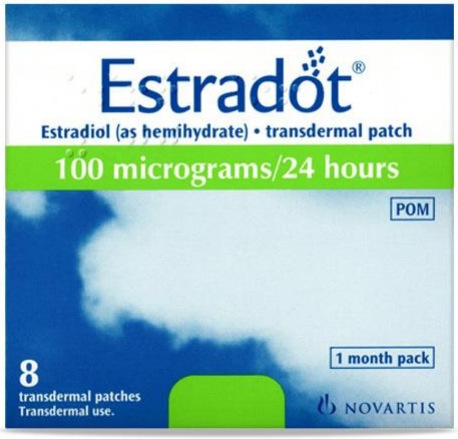
1-2 actuations / jour*

Estrace 1-2 mg PO DIE



100-200mg PO HS

Bijuva
0.5 mg / 100mg
1mg / 100mg



25-50 mcg / timbre
Changer timbre q3-4 jours

Estrogène conjugués (0.45mg)
+
Bazédoxifène (SERM)

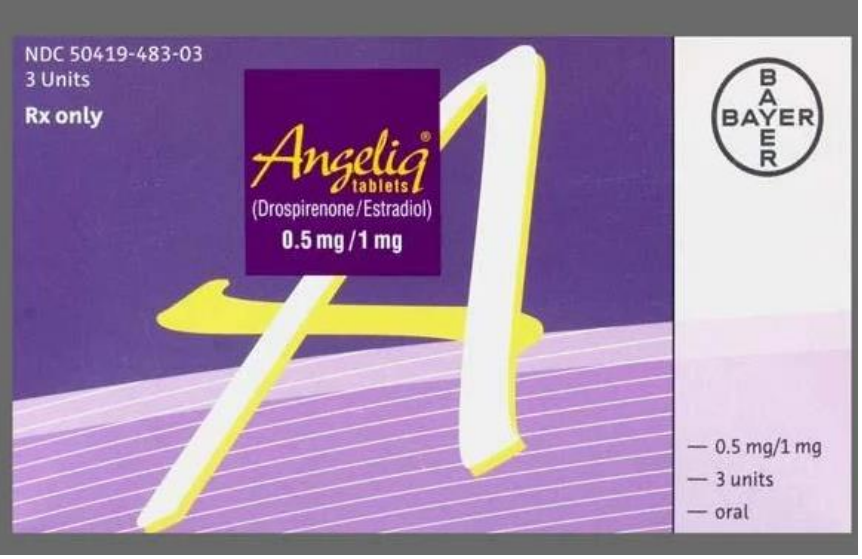
Donc de l'hormonothérapie (CEE)
+
Modulateur du récepteur de progestérone
= TSEC (Tissue Selective Estrogen Complex)

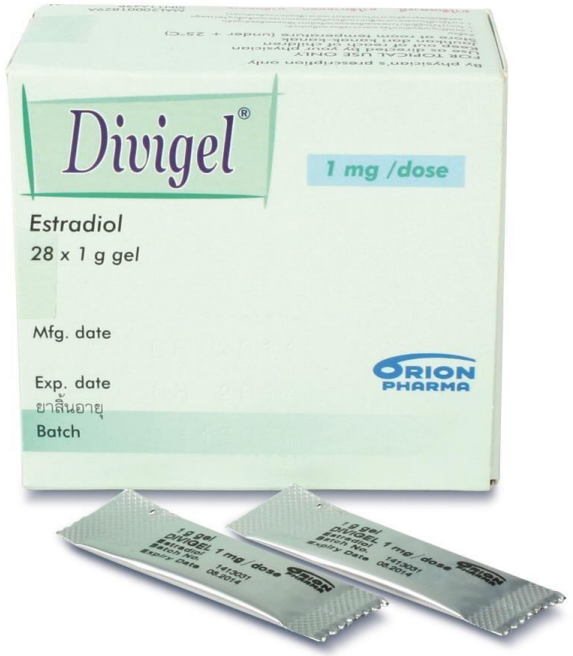
Avantages :

- Désactive l'effet de l'estrogène sur l'endomètre (effet protecteur)
- Ne modifie pas le tissu mammaire (à priori n'augmente pas le risque de cancer)
- Effet bénéfique sur la densité osseuse

Désavantages :

- ~ 100$ / mois … possibilité de médicament d'exception si tout essayé
- Ruptures de stock fréquentes
- Peut-être insuffisant comme dose pour les patientes en périménopause pour traiter les symptômes
- Essentiellement les mêmes contre-indications que l'HT standard


NDC 50419-483-03
3 Units
Rx only
Angeliq
tablets
(Drospirenone/Estradiol)
0.5 mg/1 mg
BAYER
— 0.5 mg/1 mg
— 3 units
— oral


Divigel®
1 mg /dose
Estradiol
28 x 1 g gel
Mfg. date
Exp. date
ยาสิ้นอายุ
Batch
ORION PHARMA


2.5 mg
Tibolone
2.5 mg Tablets
84 Tablets
Oral Use
NORTHSTAR Rx

*


DIN 02522802
PrSlynd®
drospirenone
4 mg
Slynd

Contre-indications à l'hormonothérapie systémique

- Antédécent de maladie cardiovasculaire (STEMI / NSTEMI, MCAS connue)
  - Risque de Framingham peut-être utilisé dans le doute; probablement à éviter avec un risque >10%
- Antédécent de cancer du sein ou cancer hormonodépendant
  - L'histoire familiale n'est pas une contre-indication
  - La prédisposition génétique à un cancer du sein (ex: BRCA) n'est pas non plus une contre-indication
- TEV … oui, mais…
  - Chez une **patiente jeune** qui comprend les risques, qui aurait eu un **évènement provoqué unique** (fracture, infection, postpartum,…) l'utilisation de l'estradiol transdermique + progestérone PO est sécuritaire.

Les avantages de la forme transdermique

- RR de TVE pour HTM orale 1.6-1.9 vs 1.0 pour transdermique.
- **≈ 9 cas supplémentaires de VTE par 10 000 femmes-années** (nombre à faire varier selon âge, formulation ; pour certaines associations comme CEE+MPA l'excès peut être plus élevé).
- NNH: 1076 femmes traitées en 1 an pour une TVE supplémentaire.
- Voie orale: premier passage hépatique et ↑ facteurs de coagulation, ↑ SHBG, ↑ CRP, ↓ protéine S

Mohammed K et al. *Oral vs transdermal estrogen therapy and vascular events* (meta-analysis). **J Clin Endocrinol Metab 2015**

Contre-indications à l'hormonothérapie systémique

- Maladie hépatique grave avec perturbation des enzymes hépatiques
  - Une stéatose hépatique à l'échographie **n'est pas une c-i**

- **Patiente âgée de 60 (?65) ans ou plus OU patiente qui est ménopausée depuis plus de 10 (15?) ans**
  - Augmentation significative de **MCAS, ACV, TEV** et du risque de **TNC** associés lorsque HT **débutée** chez ces patientes.
  - **À priori, toutefois, les patientes déjà traitées peuvent continuer si leur état de santé reste stable et que les symptômes persistent.**

- **Saignement vaginal inexpliqué, thrombophilies**

Traitements non-hormonaux

- Options non pharmacologiques prouvées:
  - Activité physique: **musculation** pourrait être efficace – exercice aérobique ou yoga peu efficace.
  - Psychothérapie (**CBT**) : preuve forte, surtout si composante d'humeur, de stress ou d'anxiété perçue comme comorbide – aide surtout la perception de la sévérité.

- Options non pharmacologiques théoriques / non prouvées:
  - «Ergothérapie» : mesures et stratégies du quotidien qui peuvent faciliter l'épreuve → vaporisateur à portée de main, s'habiller en «pelures d'oignon», ventilateurs, etc.
  - Éviter les déclencheurs: café, alcool, nourriture et boissons chaudes ou épicées.
  - Changements alimentaires (soya, fruits, légumes, …)

Traitements non-hormonaux

Options pharmacologiques recommandées

- Gabapentin – titrer de 900 à 2400mg / jour
  - Effets secondaires: étourdissements, nausées, fatigue/somnolence.
  - À considérer chez les patientes avec prépondérance de symptômes nocturnes.
- ISRS / ISRN
  - Venlafaxine 75 / Desvenlafaxine
  - Paroxetine 10mg*
  - Citalopram / Escitalopram 20

} Effet modéré

- Oxybutynine 2.5 – 5mg BID
  - Effets secondaires: xérostomie, étourdissement, TNC
  - À considérer chez patiente jeune avec symptômes d'urgenturie

Traitements non-hormonaux

Options pharmacologiques non recommandées

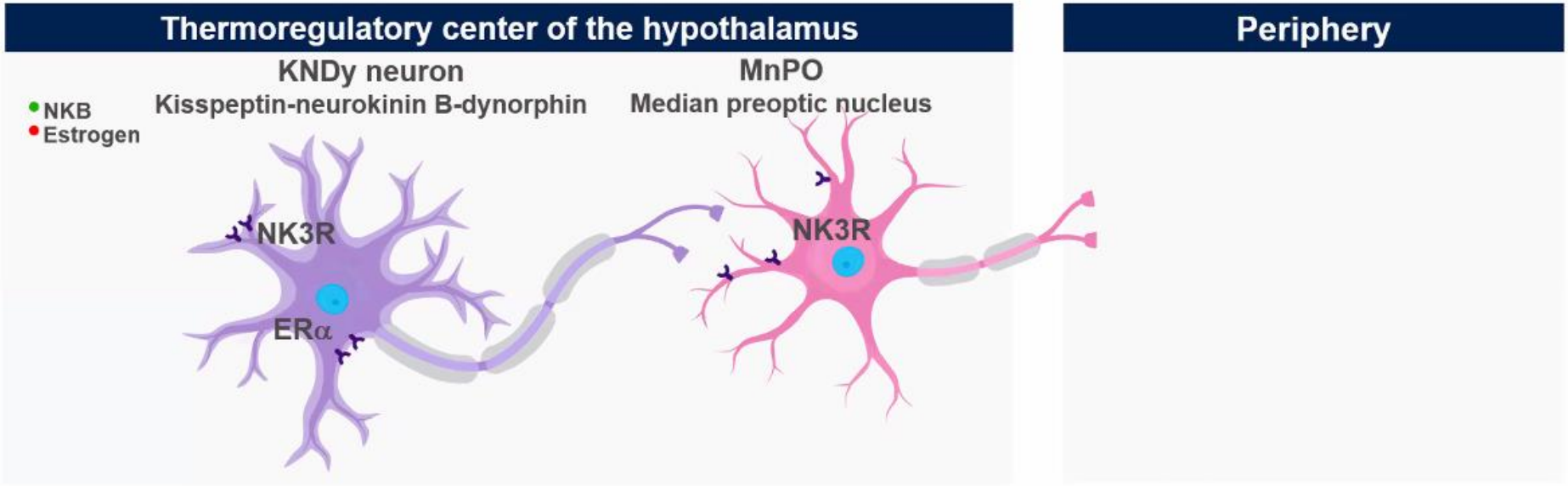
- Pregabalin
- Clonidine
- Suvorexant

The Menopause Society – Non Hormone Therapy position statement 2023

Nouveautés : antagonistes du récepteur NK3

- Mécanisme : Neurones KNDy → régulation hypothalamique.
- Médicament :
  - Fezolinetant « Veozah » (Santé Canada 2024)
  - Elinzanétant « ??? » (Santé Canada 2025)
- Efficacité : réduction ~60 % des bouffées de chaleur après 12 semaines.
- Tolérance : bonne, surveillance hépatique.

Normal thermoregulatory homeostasis



The thermoregulatory center of the hypothalamus is innervated by KNDy neurons that are stimulated ⊕ by NKB via NK3R and inhibited ⊖ by estrogen.

ERα, estrogen receptor alpha; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; NK3R, neurokinin 3 receptors; NKB, neurokinin B.
Figure adapted from Depypere H, et al. Expert Opin Investig Drugs. 2021;30:681-694
Slide and animation courtesy of Dr. Marla Shapiro, presented at the Canadian Menopause Society 4th Biennial National Scientific Conference Nov. 2023

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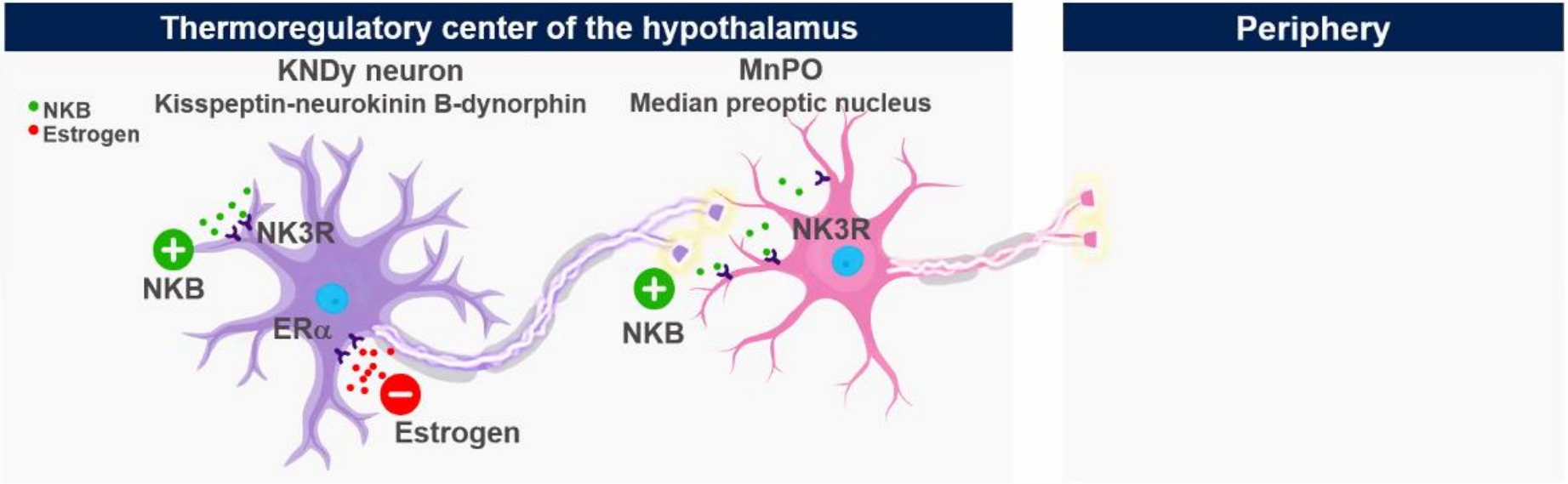

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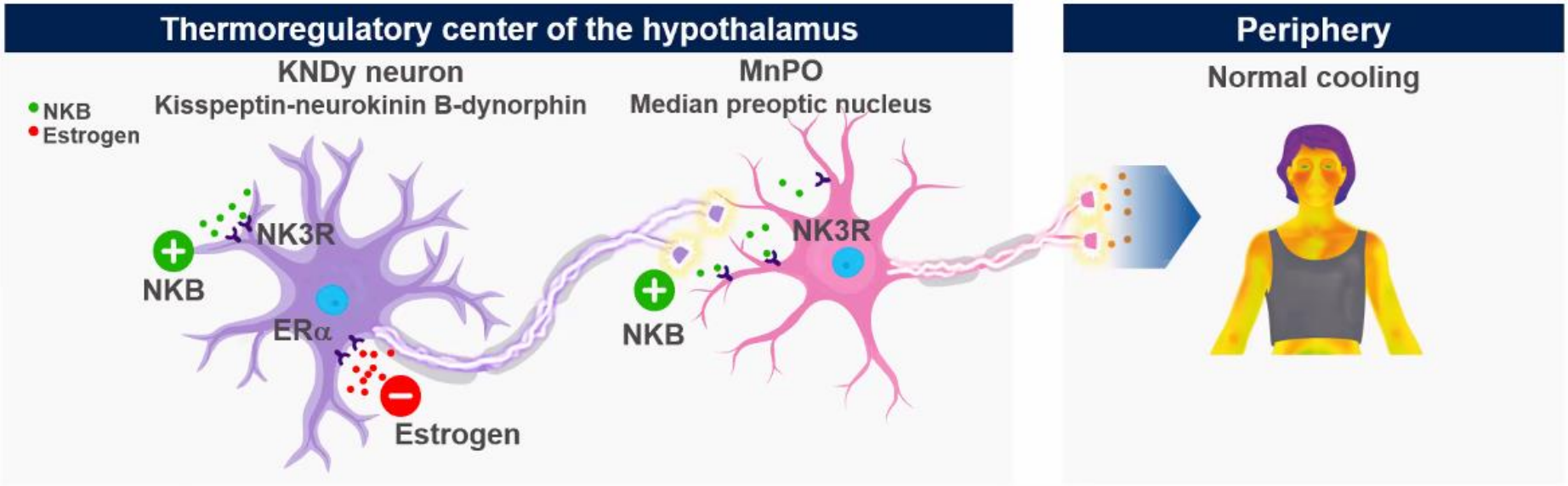

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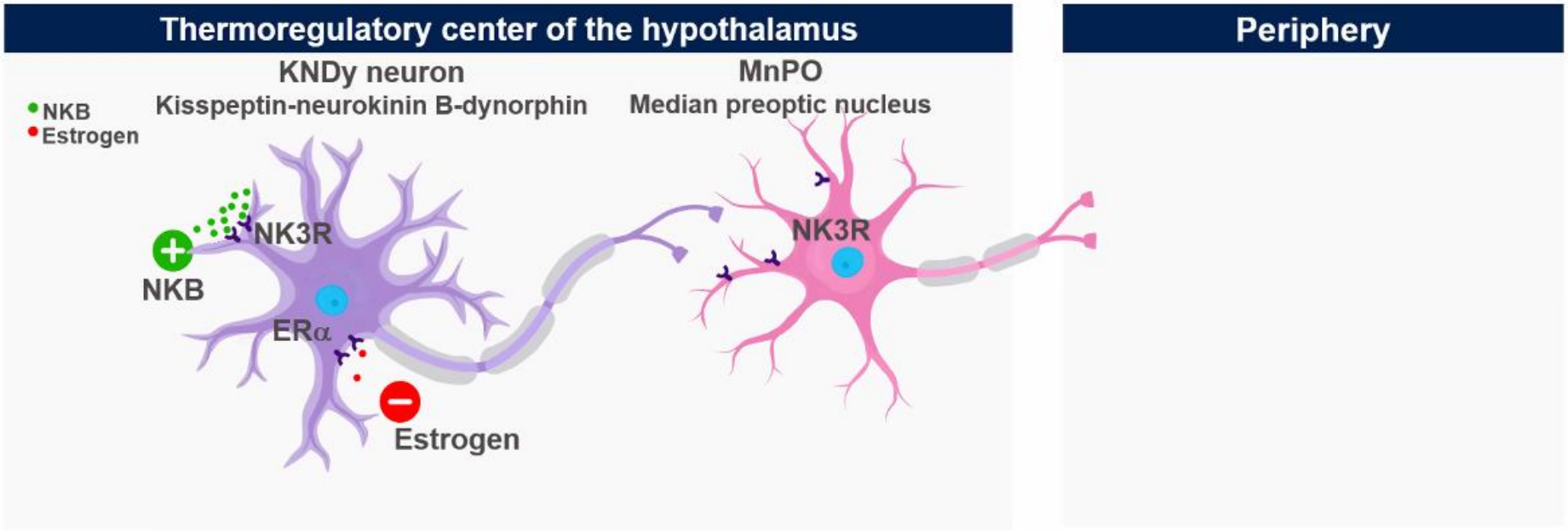
Slide and animation courtesy of Dr. Marla Shapiro, presented at the Canadian Menopause Society 4th Biennial National Scientific Conference Nov. 2023

VMS: Altered thermoregulatory activity



With declining estrogen levels, **NK3R-mediated activation is unopposed**.

ERα, estrogen receptor alpha; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; NK3R, neurokinin 3 receptors; NKB, neurokinin B.
Figure adapted from Depypere H, et al. Expert Opin Investig Drugs. 2021; 30: 681-694
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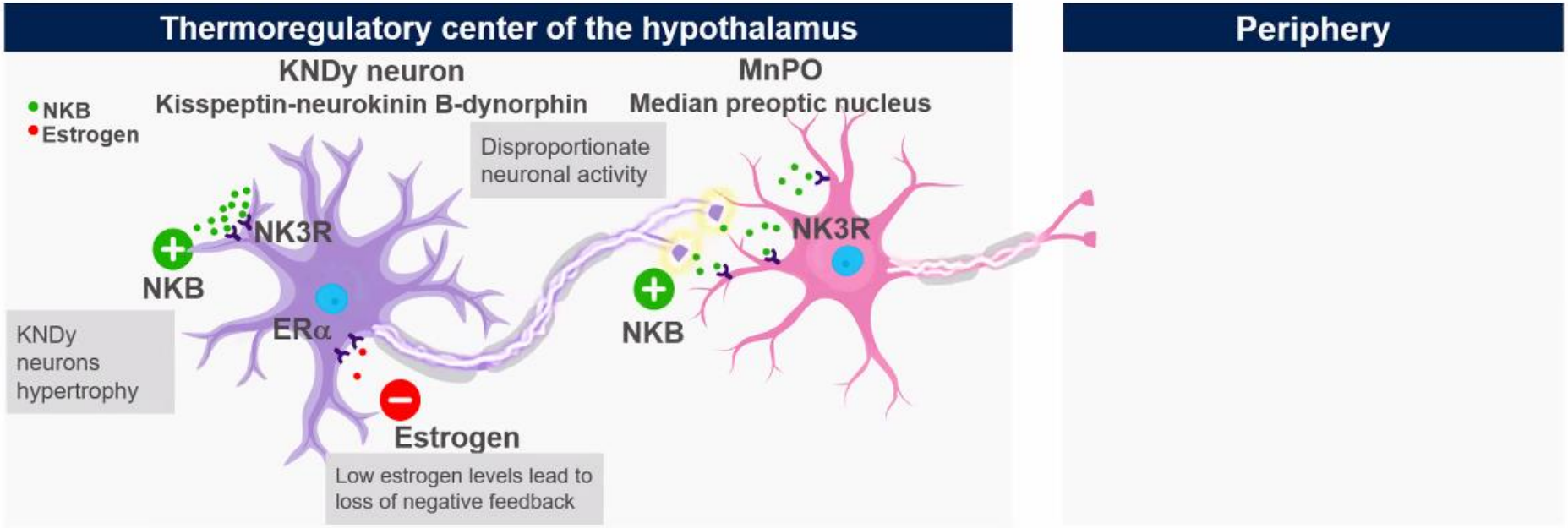
VMS: Altered thermoregulatory activity

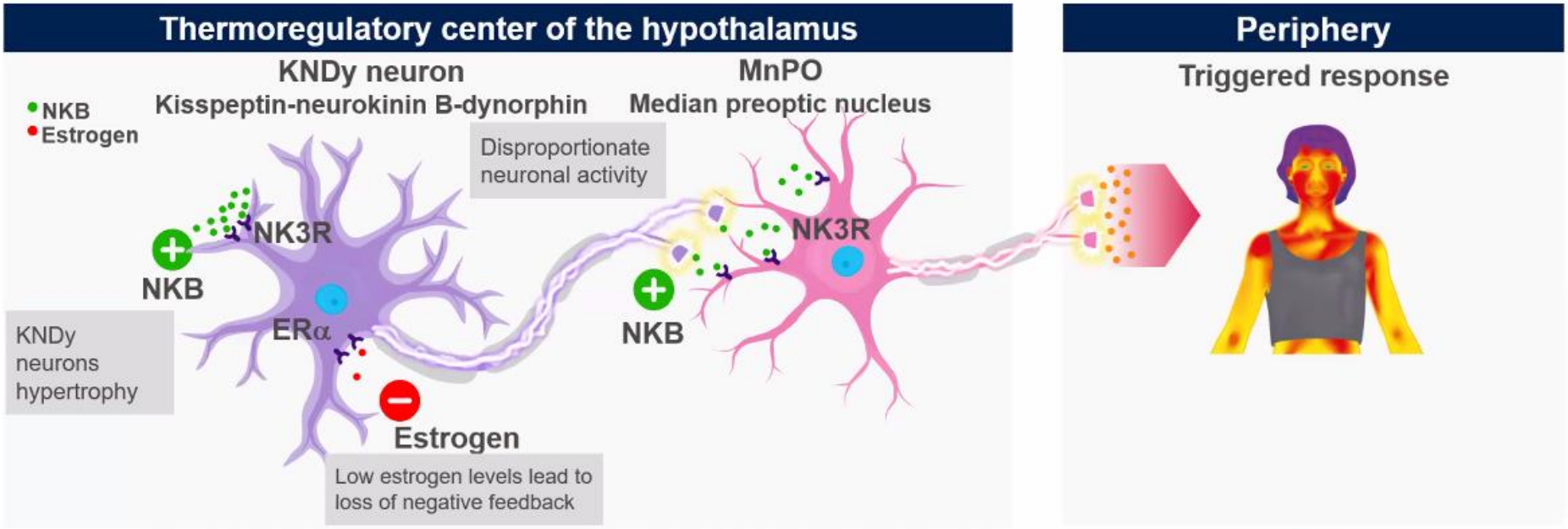


With declining estrogen levels, **NK3R-mediated activation is unopposed**.

Unopposed NKB signalling increases neuronal activity, leading to **hypertrophy of the KNDy neuron**, and alters the activity on the **thermoregulatory center**.

ERα, estrogen receptor alpha; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; NK3R, neurokinin 3 receptors; NKB, neurokinin B.
Figure adapted from Depypere H, et al. Expert Opin Investig Drugs. 2021; 30: 681-694
Slide and animation courtesy of Dr. Marla Shapiro, presented at the Canadian Menopause Society 4th Biennial National Scientific Conference Nov. 2023

VMS: Altered thermoregulatory activity



With declining estrogen levels, **NK3R-mediated activation is unopposed**.

Unopposed NKB signalling increases neuronal activity, leading to **hypertrophy of the KNDy neuron**, and alters the activity on the **thermoregulatory center**.

This triggers **heat dissipation effectors**. Vasodilation in the skin causes heat loss, experienced as **hot flashes, sweating, chills**.

ERα, estrogen receptor alpha; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; NK3R, neurokinin 3 receptors; NKB, neurokinin B.
Figure adapted from Depypere H, et al. Expert Opin Investig Drugs. 2021; 30: 681-694
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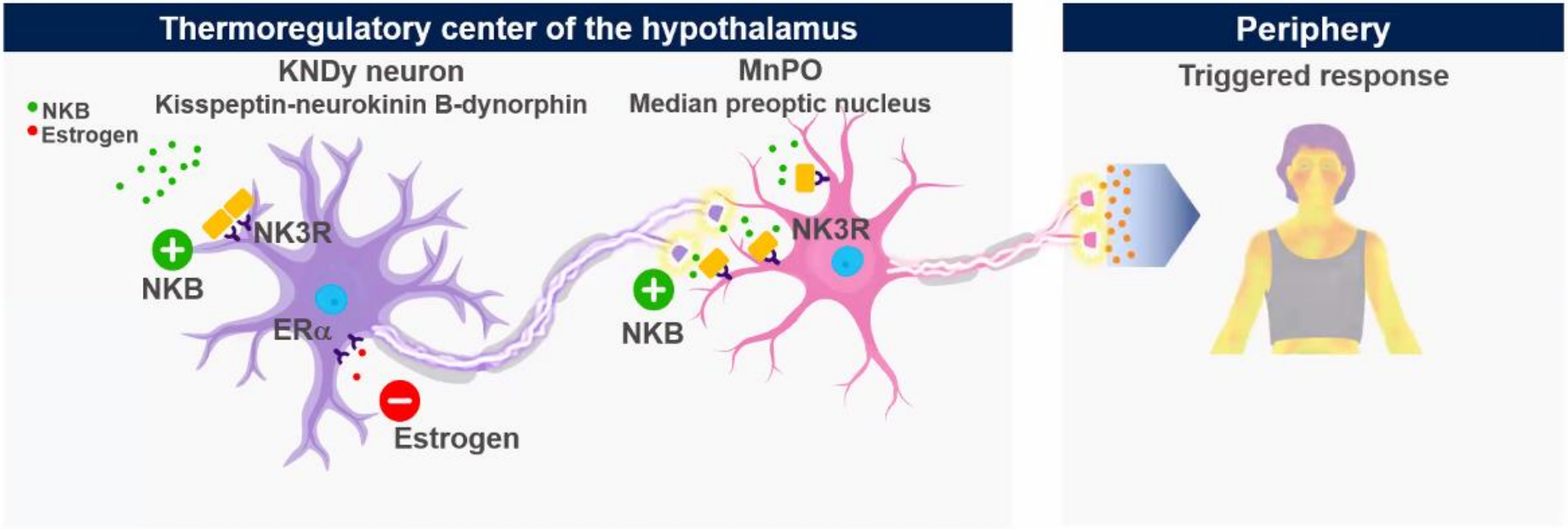
VMS: Altered thermoregulatory activity



But when NK3R is **blocked**,
NK3R-mediated activation is reduced …

… and **homeostasis is restored**.

ERα, estrogen receptor alpha; KNDy, kisspeptin-neurokinin B-dynorphin; MnPO, median preoptic nucleus; NK3R, neurokinin 3 receptors; NKB, neurokinin B.
Figure adapted from Depypere H, et al. Expert Opin Investig Drugs. 2021; 30: 681-694
Slide and animation courtesy of Dr. Marla Shapiro, presented at the Canadian Menopause Society 4th Biennial National Scientific Conference Nov, 2023

SKYLIGHT 1 and 2: Identical, phase 3, randomized, double-blind, placebo-controlled studies of fezolinetant 30 mg and 45 mg in women for whom MHT was unsuitable

Pooled data:

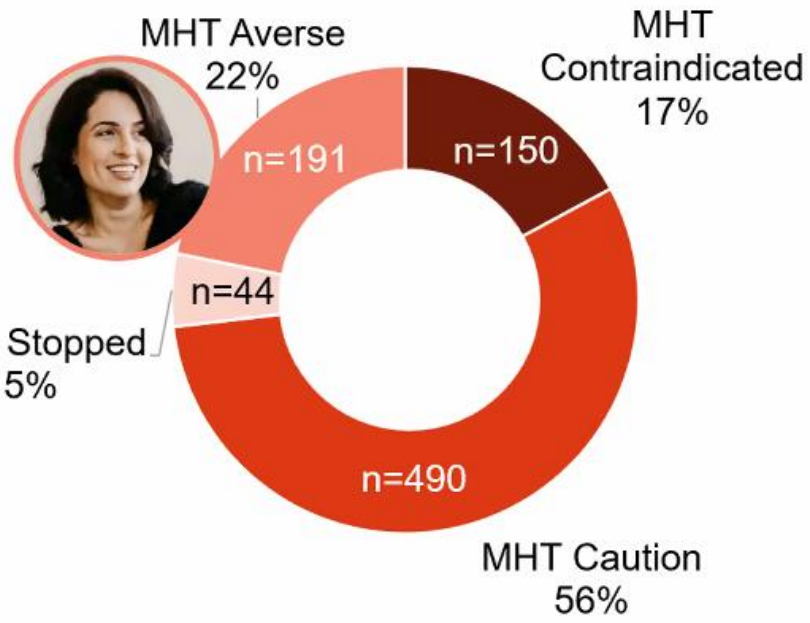
875 participants with moderate-to-severe VMS in whom MHT was unsuitable

Average age: **54 years** (range 40–65 years)

Average of **≥7** hot flashes a day

Conducted in **8 countries** in North America and Europe, including Canada

Reason MHT was unsuitable:

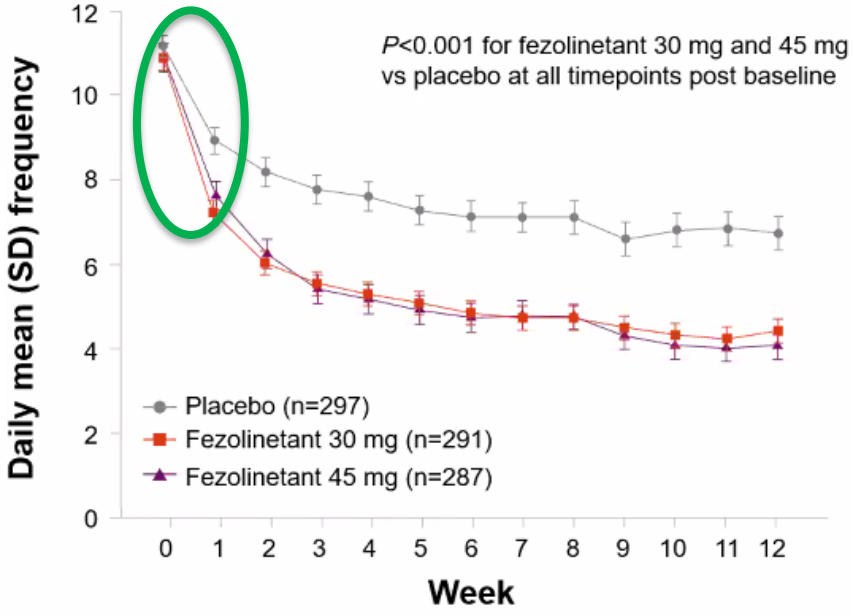


MHT, menopause hormone therapy; VMS, vasomotor symptoms.
Adapted from Santoro N, et al. Curr Med Res Opin. 2025;41(2):375-384

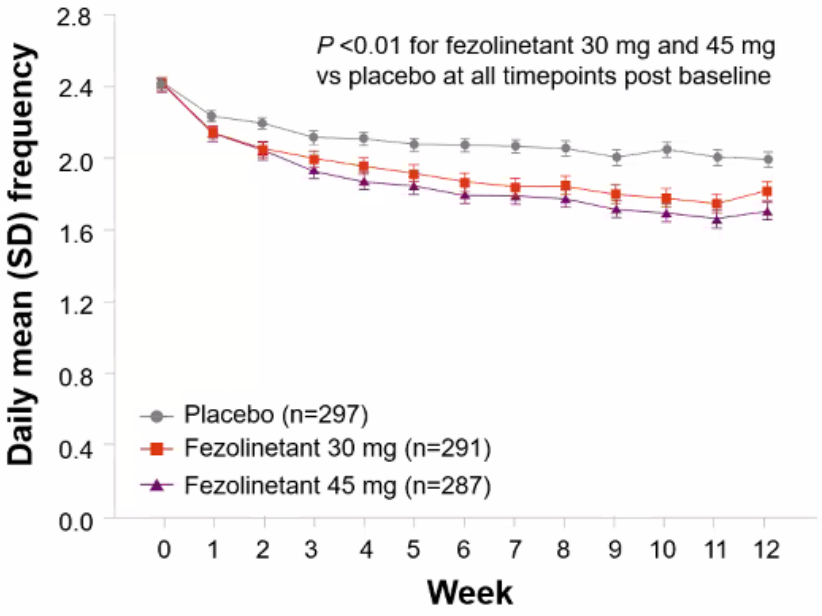
Fezolinetant 45 mg/d significantly reduced VMS frequency and severity as of Week 1

Pooled analysis of SKYLIGHT 1 and 2 (Phase 3, randomized, double-blind, placebo-controlled studies)

Mean frequency of VMS per 24 hours



Mean severity of VMS per 24 hours



SD, standard deviation; VMS, vasomotor symptoms.
Adapted from Santoro N, et al. Curr Med Res Opin. 2025;41(2):375-384

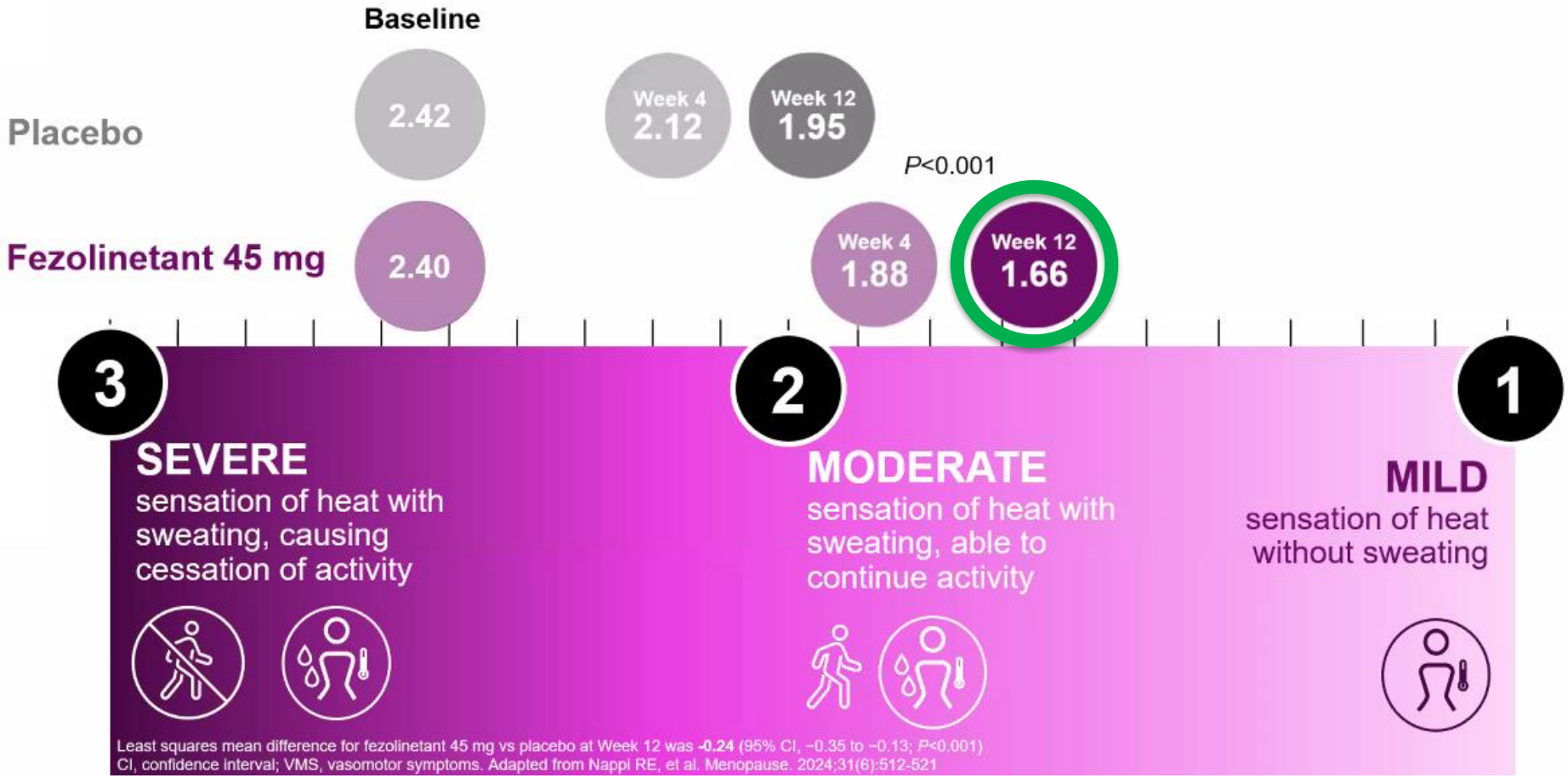
Fezolinetant 45 mg/d reduced VMS frequency by 61% at Week 12

Pooled analysis of SKYLIGHT 1 and 2 (Phase 3, randomized, double-blind, placebo-controlled studies)

Least squares mean difference for fezolinetant 45 mg vs placebo at Week 12 was -2.5 (95% CI, -3.20 to -1.82) *P*<0.001.
CI, confidence interval; VMS, vasomotor symptoms.
Adapted from Nappi RE, et al. Menopause. 2024;31(6):512-521

Pooled analysis of SKYLIGHT 1 and 2
(Phase 3, randomized, double-blind, placebo-controlled studies)

Fezolinetant 45 mg/d significantly reduced VMS severity

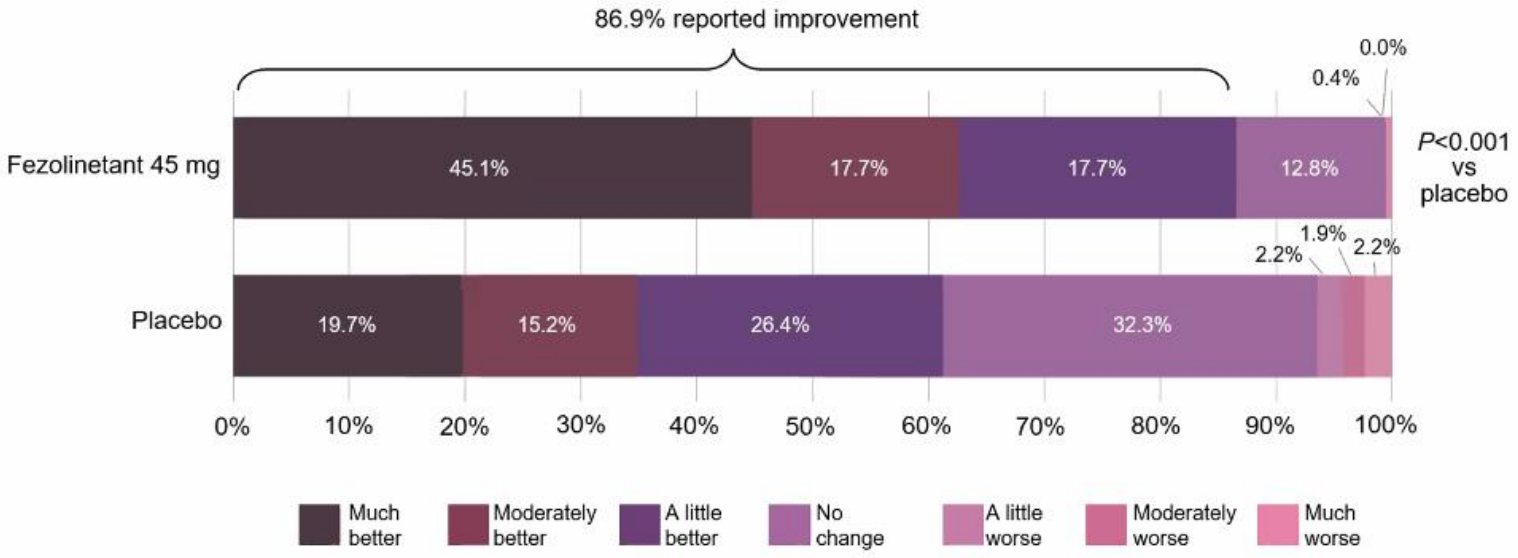


Least squares mean difference for fezolinetant 45 mg vs placebo at Week 12 was **-0.24** (95% CI, −0.35 to −0.13; *P*<0.001)
CI, confidence interval; VMS, vasomotor symptoms. Adapted from Nappi RE, et al. Menopause. 2024;31(6):512-521

Pooled analysis of SKYLIGHT 1 and 2 (Phase 3, randomized, double-blind, placebo-controlled studies)

45% of participants receiving fezolinetant 45 mg/d reported VMS were “much better” by Week 4

Week 4: PGI-C VSM (Patient Global Impression of Change in Vasomotor Symptoms)



By Week 12, 49% were “much better” and 93.4% reported improvement.

VMS, vasomotor symptoms.
Adapted from Santoro N, et al. Curr Med Res Opin. 2025;41(2):375-384

Pooled analysis of SKYLIGHT 1 and 2 (Phase 3, randomized, double-blind, placebo-controlled studies)

Most frequent TEAE with fezolinetant 45 mg/d was headache

Overview of treatment-emergent adverse events (TEAEs)

Parameter	Placebo (*n*=293)	Fezolinetant 30 mg (*n*=289)	Fezolinetant 45 mg (*n*=284)	Fezolinetant total (*N*=573)
TEAE, n (%)	121 (41.3)	118 (40.8)	112 (39.4)	230 (40.1)
Drug-related TEAE	31 (10.6)	38 (13.1)	32 (11.3)	70 (12.2)
Serious TEAE	1 (0.3)	3 (1.0)	3 (1.1)	6 (1.0)
Drug-related serious TEAE	0	1 (0.3)	0	1 (0.2)
TEAE leading to withdrawal of treatment	10 (3.4)	9 (3.1)	6 (2.1)	15 (2.6)
Drug-related TEAE leading to withdrawal of treatment	7 (2.4)	5 (1.7)	6 (2.1)	11 (1.9)
Death	0	0	0	0
TEAEs in ≥2.0% of participants*				
Preferred term, *n* (%)				
Headache	16 (5.5)	12 (4.2)	16 (5.6)	28 (4.9)
Dry mouth	1 (0.3)	6 (2.1)	6 (2.1)	12 (2.1)
Nausea	4 (1.4)	4 (1.4)	6 (2.1)	10 (1.7)
Diarrhea	7 (2.4)	1 (0.3)	5 (1.8)	6 (1.0)
Upper respiratory tract infection	10 (3.4)	6 (2.1)	4 (1.4)	10 (1.7)
Arthralgia	1 (0.3)	6 (2.1)	2 (0.7)	8 (1.4)
Nasopharyngitis	5 (1.7)	6 (2.1)	1 (0.4)	7 (1.2)

Serious drug-related TEAEs:

One in the 30-mg arm: transaminases increased.

None in the 45-mg arm.

*>2.0% in any individual treatment arm.
TEAE, treatment-emergent adverse event.
Adapted from Santoro N, et al. Curr Med Res Opin. 2025;41(2):375-384

The DAYLIGHT trial added to our understanding of fezolinetant

DAYLIGHT: Phase 3b, randomized, double-blind, placebo-controlled studies of fezolinetant 45 mg in women for whom MHT was unsuitable

453 participants with moderate-to-severe VMS in whom MHT was unsuitable

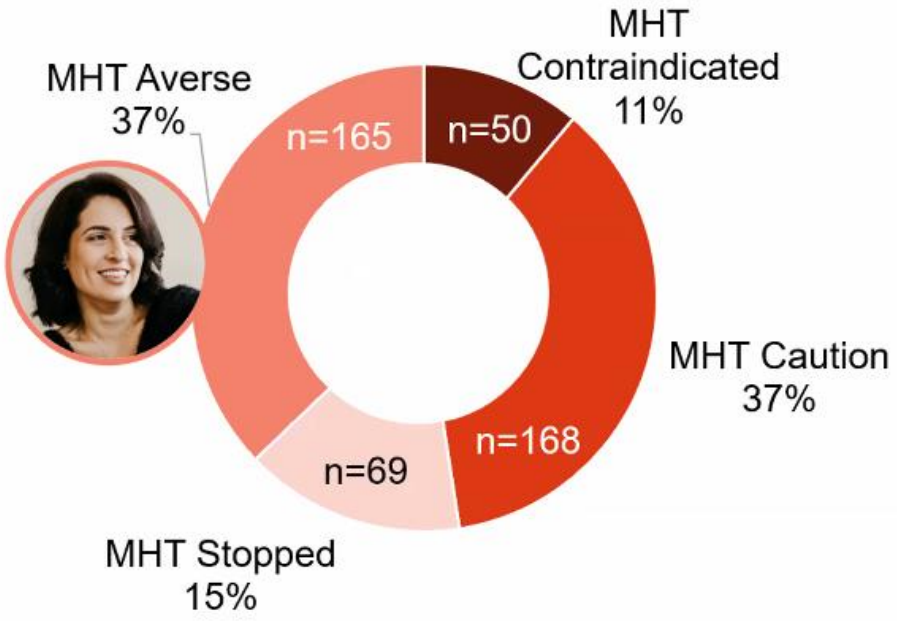
Average age: **54 years** (range 40–65 years)

Average of **≥10** hot flashes a day

Conducted in **16 countries** in North America and Europe, including Canada

Key secondary outcome: Change in patient-reported sleep disturbance

Reason MHT was unsuitable:

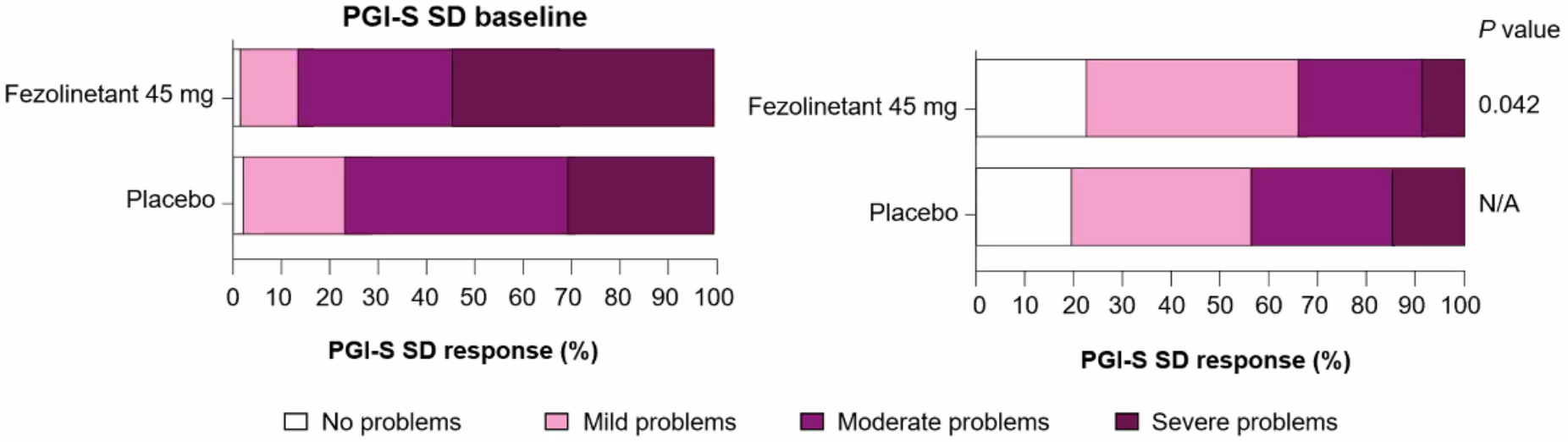


MHT, menopause hormone therapy; VMS, vasomotor symptoms.
Adapted from Schaudig K, et al. BMJ. 2024;387:e079525

In the DAYLIGHT multinational, randomized, placebo-controlled, phase 3b study

More women reported zero/mild sleep problems at Week 24 with fezolinetant 45 mg/d

Exploratory endpoint: Greater proportions of participants reported reductions in sleep disturbance severity with fezolinetant (*P*=0.042 at Week 24)



PGI-S SD, Patient Global Impression-Severity Sleep Disturbance.
Adapted from Schaudig K, et al. BMJ. 2024;387:e079525

Effet bénéfique sur le sommeil modéré

Analysis of pooled data from Phase 3 placebo-controlled DAYLIGHT and SKYLIGHT studies

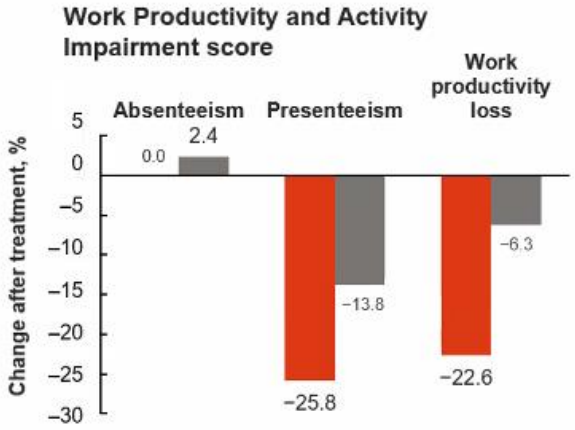
Fezolinetant improved work productivity and reduced indirect costs

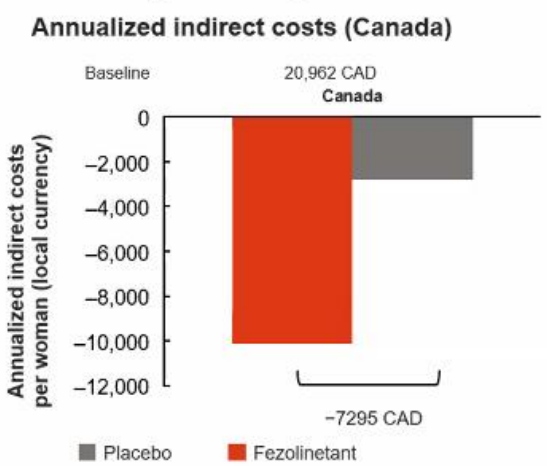
Analysis sets included all participants on placebo, fezolinetant 30 mg, or fezolinetant 45 mg, from the phase 3 SKYLIGHT and DAYLIGHT studies and those considered MHT-unsuitable.

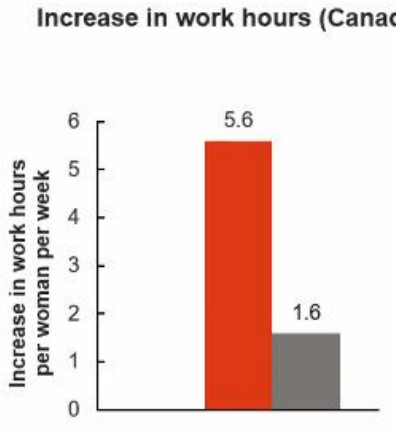
VMS-related work productivity and activity was evaluated using 7 items of the Work Productivity and Activity Impairment (WPAI)-VMS.

Indirect costs were estimated from Work Productivity and Activity Impairment score, employment, and salaries.

Work productivity after 1 year of treatment







MHT, menopause hormone therapy; VMS, vasomotor symptoms; WPAI-VMS, Work Productivity and Activity Impairment questionnaire specific to VMS.

Morga A, et al. Impact of fezolinetant vs placebo on work productivity and indirect costs among women experiencing VMS associated with menopause. International Society for Pharmacoeconomics and Outcomes Research 2025

Newly approved by Health Canada (July 2025):

Elinzanetant: An NK1 and 3 receptor antagonist

Key trials: Multinational OASIS 1 and 2 randomized, placebo-controlled, double-blind Phase 3 trials

Trial populations: Postmenopausal women aged 40 to 65 experiencing moderate-to-severe VMS

Improvements seen at Week 12 with elinzanetant 120 mg/d:

- **Significantly reduced frequency of VMS:** Least squares mean -3.2 vs placebo, *P*<0.001
  - Significant reductions vs placebo from baseline to week 1 (*P*<0.001)
- **Significantly reduced severity of VMS:** Least squares mean -0.4 or -0.3 vs placebo, *P*<0.001)
- **Improved Sleep:** Significant improvement on the Patient-Reported Outcomes Measurement Information System Sleep Disturbance 8-item short form (*P*<0.001)

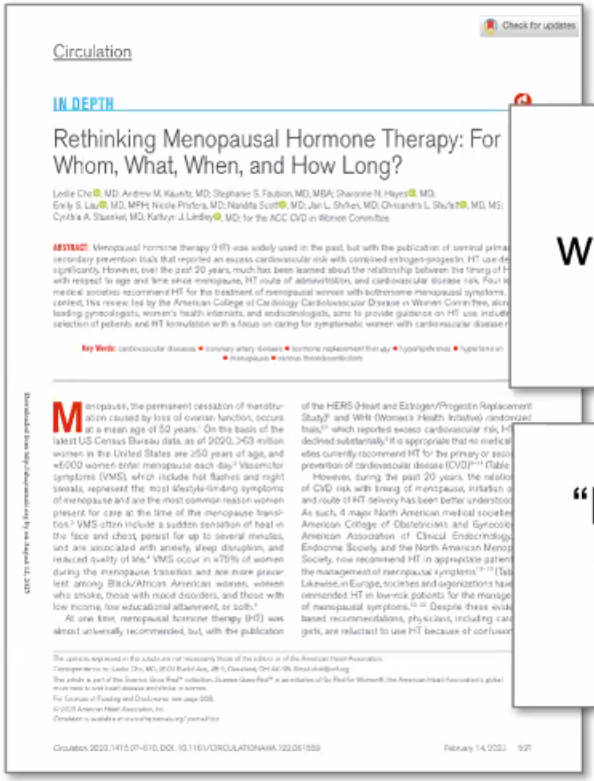
Most frequent TEAE at Week 12 was headache

- No cases of liver enzyme elevations meeting criteria for liver injury
- No clinically relevant changes in vital signs or laboratory parameters throughout the study

NK, neurokinin; TEAE, treatment-emergent adverse events; VMS, vasomotor symptoms.
Adapted from Pinkerton JV, et al. *JAMA*. 2024;332(16):1343-1354

Guidance from the American College of Cardiology CVD in Women Committee

MHT Recommendation by Patient Risk



Circulation

IN DEPTH

Rethinking Menopausal Hormone Therapy: For Whom, What, When, and How Long?

"In general, HT is contraindicated in women with known CHD, including history of MI or peripheral artery disease."

"Estrogen may have plaque-destabilizing and other adverse effects in the setting of advanced atherosclerosis…"

CAD, coronary artery disease; CHD, coronary heart disease; CVD, cardiovascular disease; HT, hormone therapy; MHT, menopause hormone therapy; MI, myocardial infarction.
Cho L, et al. Circulation 2023;147:597-610

Guidance from the American College of Cardiology CVD in Women Committee

MHT Recommendation by Patient Risk

Low Risk MHT
- Recent menopause
- Normal weight
- Normal blood pressure
- Physically active
- 10-year ASCVD risk <5%
- Low risk for breast cancer

Intermediate Risk MHT
- Diabetes
- Smoking
- HTN
- Obesity
- Sedentary/Limited mobility
- Autoimmune disease
- Hyperlipidemia
- Metabolic syndrome
- 10 years ASCVD risk ≥5%–10%
- High breast cancer risk

High Risk MHT *
- Congenital heart disease
- ASCVD/CAD/PAD
- Venous thrombosis or pulmonary embolism
- Stroke/TIA or MI
- Breast cancer
- 10-year ASCVD risk ≥10%

*In general, it is advised to avoid systemic hormone therapy. Consider alternative therapy, and if severe vasomotor symptoms persist, individualized, shared decision-making is recommended.
ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CVD, cardiovascular disease; HTN, hypertension; MI, myocardial infarction; MHT, menopause hormone therapy; PAD, peripheral artery disease; TIA, transient ischemic attack.
Adapted from Cho L, et al. Circulation 2023;147:597-610

Of the nonhormonal therapies recommended in the 2023 NAMS Position Statement, only NK3 receptor antagonists are indicated for VMS in Canada

NAMS 2023 recognized treatments for VMS:

On-label indication for VMS in Canada

- Fezolinetant → NK3 receptor antagonist (first in class, approved in Canada in 2024)

Off-label for VMS in Canada

- SSRIs and SNRIs → "Mild-to-moderate improvements in VMS"
- Gabapentin → "Improvements in frequency and severity of VMS"
- Oxybutynin → "Reduces moderate-to-severe VMS"
  - "In older adults, long-term use may be associated with cognitive decline"

Treatments not recommended by NAMS 2023 for VMS: pregabalin, clonidine, suvorexant

NAMS, North American Menopause Society; NK, neurokinin; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; VMS, vasomotor symptoms.
Adapted from NAMS 2023 Position Statement. Menopause. 2023;30:573-590

- 5% des gens avec fezolinetant ont vu une augmentation transitoire de leur enzymes hépatiques
- Aucun dommage permanent ou irréversible suite à la cessation.
- A tendance à arriver dans les 2 premiers mois du traitement
- **Surveillance obligatoire des enzymes hépatiques** avant de commencer puis aux mois 1-2-3-6-9

Ne pas initier si enzymes au dessus de **2x la limite** supérieure.

Cesser si **5x au dessus de la normale** ou si >2x et **bilirubine élevée**.

+ Estrogène vaginal supplémentaire : OK PRN

+ Estrogene systémique : pas étudié jusqu'à maintenant (ne pas essayer à la maison!)

3 Set treatment expectations.

Health Canada requires lab monitoring for the first 9 months of fezolinetant treatment.*

- Prior to starting and at month 1, 2, 3, 6, 9

Provide standing lab requisitions for liver function tests (to be reviewed in aggregate at the next appointment).

“We do this with many commonly used medications (eg, statins); this tells us if your body is tolerating the treatment. It’s rare to have liver enzyme elevations, and there has not been a case of long-term permanent damage.”

* See notes for referencing.

- Coût: 150$ / mois, couvert par quelques assurances privées mais pas par la RAMQ pour l'instant.

- Durée maximale : indéterminée pour l'instant

- Age maximal (selon études actuelles) 65 ans puisque pas étudié au delà – mais pas une contre-indication formelle.

Key points

- Estrogen therapy appears to have beneficial effects on skin thickness and elasticity and collagen when given at menopause. (Level II)
- Changes in hair density and female pattern hair loss worsen after menopause, but research is lacking regarding a role for hormone therapy in mitigating these changes. (Level II)
- Hormone therapy appears to decrease the risk of neovascular and soft drusen age-related macular degeneration but not early or late-stage macular degeneration. (Level II)
- Estrogen therapy appears to reduce intraocular pressure and mitigate the risk for open-angle glaucoma in Black women. (Level II)
- Evidence of hormone therapy effects on cataracts, optic nerve disease, dry-eye disease, and hearing loss is mixed. (Level II)

Références bibliographiques

- NAMS Position Statement 2023
- NICE NG23 (mise à jour 2024)
- Santoro N. N Engl J Med 2023;389:249–261
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- Fraser GL et al., Lancet 2023;401:255–266
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- INESSS 2024
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- Giri R. Prevalence and Risk Factors of Premature Ovarian Insufficiency/Early Menopause. Semin Reprod Med. 2020
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SOCIÉTÉ CANADIENNE DE MÉNOPAUSE
POCKET GUIDE
MENOPAUSE
MANAGEMENT
A practical tool for
healthcare professionals
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AI Mode
All
Images
Short videos
Forums
Videos
Shopping
Canadian Menopause Society
https://www.canadianmenopausesociety.org › pdf
PDF
POCKET GUIDE MENOPAUSE MANAGEMENT
All four guidelines advise that hormone therapy (estro- gen plus progestogen i
estrogen alone in women without a uterus) is the most ...

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Systemic Menopause Hormone Therapy (MHT) Equivalency Table

Trade Name (Active Ingredient)	Ultra Low	Low	Standard Dose	Moderate-High	High (POI/Early Menopause)
ORAL Estrogen					
Estrace (estradiol), tablet	-	0.5 mg	1 mg	2 mg	3-4 mg
Premarin (conjugated estrogen), tablet	-	0.3 mg	0.625 mg	-	1.25 mg
TRANSDERMAL Estrogen					
Estrogel (0.06% estradiol), gel 1 pump = 0.75 mg		1 pump	1 - 2 pumps	2 - 3 pumps	4 pumps
Divigel (0.1% estradiol), gel	0.25 mg sachet	0.5 mg sachet	1.0 mg sachet	1.0 mg + 0.5 mg sachet	1.0 mg sachet x 2
Estradot (estradiol), patch *Change twice a week*	-	25 - 37.5 mcg	50 mcg	75 mcg	100 mcg
Climara (estradiol), patch *Change once a week*	-	25 mcg	50 mcg	75 mcg	100 mcg
COMBINATION THERAPIES (Estrogen with the Recommended Dose of Progestogen for Endometrial Protection)					
Bijuva (1 mg estradiol with 100 mg micronized progesterone), capsule	-	-	1 capsule	-	-
Activelle LD (0.5 mg estradiol with 0.1 mg norethindrone), tablet	-	m1 tablet	-	-	-
Activelle (1 mg estradiol with 0.5 mg norethindrone), tablet	-	-	1 tablet	-	-
Angeliq (1 mg estradiol with 1 mg drospirenone), tablet	-	-	1 tablet	-	-
Estalis (50 mcg estradiol/ 250 mcg norethindrone), patch *Change twice a week*	-	-	1 patch	-	-
Estalis (50 mcg estradiol /140 mcg norethindrone), patch *Change twice a week*	-	-	1 patch	-	-

Progestogen Doses Recommended for Endometrial Protection					
Prometrium (Micronized Progesterone), capsule *Continuous (daily)*	100 mg	100 mg	100 mg - 200 mg	200 mg	≥ 200 mg
Prometrium (Micronized Progesterone), capsule *Cyclical (sequential)*	200 mg x 12-14 days each month	200 mg x 12-14 days each month	200 mg x 12-14 days each month	≥ 200 mg x 12-14 days each month	≥ 200 mg x 12-14 days each month
Provera (Medroxy Progesterone Acetate), tablet *Continuous (daily)*	2.5 mg	2.5 mg	2.5 - 5 mg	5 mg	5 mg
Provera (Medroxy Progesterone Acetate), tablet *Cyclical (sequential)*	5 mg x 10-12 days each month	5 mg x 10-12 days each month	10 mg x 10-12 days each month	10 mg x 10-12 days each month	10 mg x 10-12 days each month
Norlutate (norethindrone acetate), tablet			5 mg		
Mirena IUS (levonogestrel 52 mg/IUS, up to 5 years)	Yes	Yes	Yes	Yes	Yes
MHT Products Which Do Not Require A Progestogen (Estrogenic effects but formulation also protects endometrial lining)					
Duavive (0.45 mg conjugated estrogen with 20 mg bazedoxifene), tablet			1 tablet		
Tibella (2.5 mg tibolone), tablet			1 tablet		

2021 CMS/SOGC Clinical Guidelines:

"Not desiring" MHT is reason enough to consider nonhormonal prescription therapies for VMS

Recommendations	Grading of Evidence
1. Health care providers should offer MHT as the most effective option for managing VMS.	Strong, high
2. MHT can be safely initiated in women without contraindications who are younger than 60 years of age or less than 10 years postmenopause.	Strong, high
3. MHT should be individualized after careful consideration of symptoms, medical conditions, health risks, family history, treatment goals, patient preferences, and timing of last menstrual period.	Strong, high
4. Duration of MHT should be individualized to the patient, based on ongoing symptoms, benefits, and personal risks. Periodic re-evaluation of MHT is recommended.	Strong, high
5. Women who have experienced loss of ovarian function or with decreased ovarian function before the age of 45 years should consider replacement HT until the average age of menopause.	Strong, high
6. Estrogen-progestogen regimens can be continuous (ie, estrogen-progestogen taken every day) or follow a cyclic regimen, with estrogen taken every day and progestogen taken for 12−14 days every month. In women with hysterectomy, estrogen alone can be taken every day.	Strong, high
7. Options for perimenopausal women include progestogen alone, low-dose combined hormonal contraceptives, MHT, or estrogen in combination with a levonorgestrel-releasing intrauterine system.	Strong, moderate
8. Nonhormonal prescription therapies can be considered when MHT is contraindicated or not desired.	Strong, moderate
9. For cultural traditional therapies, women should be offered the opportunity to work with a cultural leader; health care providers can discuss this option in partnership with women, in order to ensure cultural humility and cultural safety.	Strong, moderate

CMS, Canadian Menopause Society; HT, hormone therapy; MHT, menopause hormone therapy; SOGC, Society of Obstetricians and Gynecologists of Canada; VMS, vasomotor symptoms.

Yuksel N, et al. J Obst Gynaecol Can. 2021;43(10):1188-1204