

SUPPLEMENTAL MATERIALS

Impact of demographic and clinical factors on elagolix plus add-back therapy effects on patient-reported nonbleeding symptoms in women with heavy menstrual bleeding and uterine fibroids: a post hoc analysis of data from two clinical trials

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SUPPLEMENTAL TABLE 1

Meaningful improvement^a at month 1 in nonbleeding symptoms and menstrual bleeding across different patient subpopulations as evaluated using the Patient Global Impression of Change scale

Subpopulation ^b	Treatment	Patients with meaningful improvement ^a , n/N (%)					
		Abdominal or pelvic pain	Abdominal or pelvic pressure	Abdominal or pelvic cramping	Back pain	Abdominal bloating	Menstrual bleeding
Overall							
	ELA+AB	153/373 (41.0) ^{***}	142/373 (38.1) ^{***}	151/372 (40.6) ^{***}	98/373 (26.3) ^{***}	104/373 (27.9) ^{***}	186/374 (49.7) ^{***}
	Placebo	25/187 (13.4)	24/187 (12.8)	26/187 (13.9)	19/187 (10.2)	23/187 (12.3)	25/188 (13.3)
BMI, kg/m ²							
< 30	ELA+AB	42/125 (33.6) [*]	36/125 (28.8) ^{**}	42/124 (33.9) ^{***}	26/125 (20.8)	34/125 (27.2)	58/124 (46.8) ^{***}
	Placebo	7/59 (11.9)	5/59 (8.5)	6/59 (10.2)	5/59 (8.5)	9/59 (15.3)	6/60 (10.0)
30 to < 35	ELA+AB	43/106 (40.6) ^{***}	38/106 (35.8) ^{**}	40/106 (37.7) ^{**}	26/106 (24.5) [*]	31/106 (29.2) [*]	55/108 (50.9) ^{***}
	Placebo	7/50 (14.0)	6/50 (12.0)	7/50 (14.0)	4/50 (8.0)	6/50 (12.0)	8/50 (16.0)
≥ 35	ELA+AB	68/141 (48.2) ^{***}	68/141 (48.2) ^{***}	69/141 (48.9) ^{***}	46/141 (32.6) [*]	39/141 (27.7) ^{**}	73/141 (51.8) ^{***}

	Placebo	11/78 (14.1)	13/78 (16.7)	13/78 (16.7)	10/78 (12.8)	8/78 (10.3)	11/78 (14.1)
Primary FIGO fibroid classification							
0–3	ELA+AB	33/75 (44.0)**	27/75 (36.0)**	32/75 (42.7)***	19/75 (25.3)*	24/75 (32.0)*	39/75 (52.0)***
	Placebo	5/35 (14.3)	3/35 (8.6)	2/35 (5.7)	2/35 (5.7)	4/35 (11.4)	3/35 (8.6)
4	ELA+AB	70/177 (39.5)***	68/177 (38.4)***	71/176 (40.3)***	49/177 (27.7)**	49/177 (27.7)*	87/178 (48.9)***
	Placebo	13/91 (14.3)	13/91 (14.3)	15/91 (16.5)	11/91 (12.1)	13/91 (14.3)	17/92 (18.5)
5–8	ELA+AB	47/115 (40.9)***	44/115 (38.3)***	46/115 (40.0)***	30/115 (26.1)**	30/115 (26.1)**	58/115 (50.4)***
	Placebo	5/57 (8.8)	7/57 (12.3)	8/57 (14.0)	5/57 (8.8)	4/57 (7.0)	5/57 (8.8)

ELA + AB = elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg); BMI = body mass index; FIGO = International Federation of Gynecology and Obstetrics; PGIC = Patient Global Impression of Change.

* $P < .05$; ** $P < .01$; *** $P < .001$. P values were descriptive only and no adjustments were made for multiplicity.

^aMeaningful improvement defined by PGIC responses of “very much improved” or “much improved.”

^bSubpopulations based on baseline demographic or clinical characteristics.

SUPPLEMENTAL TABLE 2

Meaningful improvement^a at month 3 in nonbleeding symptoms and menstrual bleeding across different patient subpopulations as evaluated using the Patient Global Impression of Change scale

Subpopulation ^b	Treatment	Patients with meaningful improvement ^a , n/N (%)					
		Abdominal or pelvic pain	Abdominal or pelvic pressure	Abdominal or pelvic cramping	Back pain	Abdominal bloating	Menstrual bleeding
Overall	ELA+AB	236/342 (69.0) ^{***}	239/342 (69.9) ^{***}	237/342 (69.3) ^{***}	182/342 (53.2) ^{***}	172/341 (50.4) ^{***}	286/340 (84.1) ^{***}
	Placebo	28/168 (16.7)	32/168 (19.0)	32/168 (19.0)	27/168 (16.1)	22/168 (13.1)	39/169 (23.1)
BMI, kg/m ²							
< 30	ELA+AB	75/114 (65.8) ^{***}	75/114 (65.8) ^{***}	77/114 (67.5) ^{***}	63/114 (55.3) ^{***}	58/114 (50.9) ^{***}	93/113 (82.3) ^{***}
	Placebo	12/57 (21.1)	13/57 (22.8)	14/57 (24.6)	11/57 (19.3)	10/57 (17.5)	16/58 (27.6)
30 to < 35	ELA+AB	66/96 (68.8) ^{***}	65/96 (67.7) ^{***}	67/96 (69.8) ^{***}	52/96 (54.2) ^{***}	44/96 (45.8) ^{***}	83/96 (86.5) ^{***}
	Placebo	5/41 (12.2)	6/41 (14.6)	7/41 (17.1)	5/41 (12.2)	5/41 (12.2)	9/41 (22.0)
≥ 35	ELA+AB	94/131 (71.8) ^{***}	98/131 (74.8) ^{***}	92/131 (70.2) ^{***}	67/131 (51.1) ^{***}	69/130 (53.1) ^{***}	109/130 (83.8) ^{***}
	Placebo	11/70 (15.7)	13/70 (18.6)	11/70 (15.7)	11/70 (15.7)	7/70 (10.0)	14/70 (20.0)

Primary FIGO fibroid classification

0–3	ELA+AB	50/72 (69.4) ^{***}	53/72 (73.6) ^{***}	53/72 (73.6) ^{***}	35/72 (48.6) ^{***}	37/72 (51.4) ^{***}	61/72 (84.7) ^{***}
	Placebo	2/31 (6.5)	2/31 (6.5)	1/31 (3.2)	2/31 (6.5)	2/31 (6.5)	2/31 (6.5)
4	ELA+AB	111/163 (68.1) ^{***}	113/163 (69.3) ^{***}	112/163 (68.7) ^{***}	92/163 (56.4) ^{***}	82/162 (50.6) ^{***}	134/161 (83.2) ^{***}
	Placebo	16/81 (19.8)	19/81 (23.5)	17/81 (21.0)	12/81 (14.8)	14/81 (17.3)	22/82 (26.8)
5–8	ELA+AB	72/101 (71.3) ^{***}	71/101 (70.3) ^{***}	69/101 (68.3) ^{***}	54/101 (53.5) ^{***}	51/101 (50.5) ^{***}	88/101 (87.1) ^{***}
	Placebo	9/52 (17.3)	10/52 (19.2)	13/52 (25.0)	11/52 (21.2)	5/52 (9.6)	14/52 (26.9)

ELA + AB, elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg); BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; PGIC = Patient Global Impression of Change.

^{**} $P < .01$; ^{***} $P < .001$. P values were descriptive only and no adjustments were made for multiplicity.

^aMeaningful improvement defined by PGIC responses of “very much improved” or “much improved.”

^bSubpopulations based on baseline demographic or clinical characteristics.

SUPPLEMENTAL TABLE 3

Meaningful improvement^a at months 1, 3, and 6 in nonbleeding symptoms and menstrual bleeding across the lowest and highest FIGO fibroid classification subpopulations as evaluated using the Patient Global Impression of Change scale

Subpopulation ^b	Treatment	Patients with meaningful improvement ^a , n/N (%)					
		Abdominal or pelvic pain	Abdominal or pelvic pressure	Abdominal or pelvic cramping	Back pain	Abdominal bloating	Menstrual bleeding
Month 1							
Lowest FIGO fibroid classification							
0–3	ELA+AB	37/92 (40.2)*	31/92 (33.7)**	35/92 (38.0)***	20/92 (21.7)*	24/92 (26.1)	44/92 (47.8)***
	Placebo	6/42 (14.3)	4/42 (9.5)	3/42 (7.1)	3/42 (7.1)	5/42 (11.9)	5/42 (11.9)
4	ELA+AB	81/209 (38.8)***	78/209 (37.3)***	83/208 (39.9)***	58/209 (27.8)***	60/209 (28.7)***	102/210 (48.6)***
	Placebo	14/104 (13.5)	14/104 (13.5)	17/104 (16.3)	12/104 (11.5)	12/104 (11.5)	17/105 (16.2)
5–8	ELA+AB	32/66 (48.5)***	30/66 (45.5)**	31/66 (47.0)***	20/66 (30.3)*	19/66 (28.8)*	38/66 (57.6)***
	Placebo	3/37 (8.1)	5/37 (13.5)	5/37 (13.5)	3/37 (8.1)	4/37 (10.8)	3/37 (8.1)
Highest FIGO fibroid classification							
0–3	ELA+AB	21/45 (46.7)*	16/45 (35.6)*	20/45 (44.4)***	12/45 (26.7)*	12/45 (26.7)	24/45 (53.3)***

	Placebo	4/22 (18.2)	2/22 (9.1)	1/22 (4.5)	1/22 (4.5)	2/22 (9.1)	0/22 (0.0)
4	ELA+AB	64/162 (39.5) ^{***}	60/162 (37.0) ^{***}	63/161 (39.1) ^{***}	44/162 (27.2) ^{**}	46/162 (28.4) ^{**}	79/163 (48.5) ^{***}
	Placebo	9/81 (11.1)	12/81 (14.8)	13/81 (16.0)	9/81 (11.1)	9/81 (11.1)	12/81 (14.8)
5-8	ELA+AB	65/160 (40.6) ^{***}	63/160 (39.4) ^{***}	66/160 (41.3) ^{***}	42/160 (26.3) ^{**}	45/160 (28.1) ^{**}	81/160 (50.6) ^{***}
	Placebo	10/80 (12.5)	9/80 (11.3)	11/80 (13.8)	8/80 (10.0)	10/80 (12.5)	13/81 (16.0)

Month 3

Lowest FIGO fibroid classification

0-3	ELA+AB	58/86 (67.4) ^{***}	58/86 (67.4) ^{***}	60/86 (69.8) ^{***}	41/86 (47.7) ^{***}	40/86 (46.5) ^{***}	72/86 (83.7) ^{***}
	Placebo	2/36 (5.6)	2/36 (5.6)	1/36 (2.8)	2/36 (5.6)	2/36 (5.6)	3/36 (8.3)
4	ELA+AB	128/189 (67.7) ^{***}	131/189 (69.3) ^{***}	130/189 (68.8) ^{***}	103/189 (54.5) ^{***}	96/188 (51.1) ^{***}	157/187 (84.0) ^{***}
	Placebo	17/93 (18.3)	21/93 (22.6)	21/93 (22.6)	15/93 (16.1)	14/93 (15.1)	25/94 (26.6)
5-8	ELA+AB	47/61 (77.0) ^{***}	48/61 (78.7) ^{***}	44/61 (72.1) ^{***}	37/61 (60.7) ^{***}	34/61 (55.7) ^{***}	54/61 (88.5) ^{***}
	Placebo	8/35 (22.9)	8/35 (22.9)	9/35 (25.7)	8/35 (22.9)	5/35 (14.3)	10/35 (28.6)

Highest FIGO fibroid classification

0-3	ELA+AB	29/44 (65.9)***	31/44 (70.5)***	31/44 (70.5)***	21/44 (47.7)**	24/44 (54.5)***	36/44 (81.8)***
	Placebo	2/19 (10.5)	2/19 (10.5)	1/19 (5.3)	2/19 (10.5)	1/19 (5.3)	2/19 (10.5)
4	ELA+AB	102/147 (69.4)***	105/147 (71.4)***	102/147 (69.4)***	78/147 (53.1)***	74/146 (50.7)***	120/145 (82.8)***
	Placebo	12/73 (16.4)	15/73 (20.5)	13/73 (17.8)	8/73 (11.0)	10/73 (13.7)	16/73 (21.9)
5-8	ELA+AB	102/145 (70.3)***	101/145 (69.7)***	101/145 (69.7)***	82/145 (56.6)***	72/145 (49.7)***	127/145 (87.6)***
	Placebo	13/72 (18.1)	14/72 (19.4)	17/72 (23.6)	15/72 (20.8)	10/72 (13.9)	20/73 (27.4)

Month 6

Lowest FIGO fibroid classification

0-3	ELA+AB	53/79 (67.1)***	55/79 (69.6)***	52/79 (65.8)***	37/79 (46.8)***	46/79 (58.2)***	66/79 (83.5)***
	Placebo	2/32 (6.3)	2/32 (6.3)	3/32 (9.4)	3/32 (9.4)	2/32 (6.3)	3/32 (9.4)
4	ELA+AB	118/163 (72.4)***	109/163 (66.9)***	120/163 (73.6)***	101/163 (62.0)***	95/163 (58.3)***	145/164 (88.4)***
	Placebo	23/83 (27.7)	17/83 (20.5)	26/83 (31.3)	21/83 (25.3)	16/83 (19.3)	22/83 (26.5)
5-8	ELA+AB	48/57 (84.2)	45/57 (78.9)	47/57 (82.5)	35/57 (61.4)	32/57 (56.1)	51/57 (89.5)

	Placebo	6/34 (17.6) ^{***}	6/34 (17.6) ^{***}	7/34 (20.6) ^{***}	6/34 (17.6) ^{***}	4/34 (11.8) ^{***}	8/34 (23.5) ^{***}
Highest FIGO fibroid classification							
0–3	ELA+AB	27/39 (69.2) ^{***}	30/39 (76.9) ^{***}	27/39 (69.2) ^{***}	19/39 (48.7) ^{**}	25/39 (64.1) ^{***}	32/39 (82.1) ^{***}
	Placebo	1/18 (5.6)	1/18 (5.6)	2/18 (11.1)	2/18 (11.1)	2/18 (11.1)	2/18 (11.1)
4	ELA+AB	95/129 (73.6) ^{***}	88/129 (68.2) ^{***}	91/129 (70.5) ^{***}	77/129 (59.7) ^{***}	75/129 (58.1) ^{***}	112/130 (86.2) ^{***}
	Placebo	14/63 (22.2)	13/63 (20.6)	15/63 (23.8)	12/63 (19.0)	12/63 (19.0)	12/63 (19.0)
5–8	ELA+AB	97/131 (74.0) ^{***}	91/131 (69.5) ^{***}	101/131 (77.1) ^{***}	77/131 (58.8) ^{***}	73/131 (55.7) ^{***}	118/131 (90.1) ^{***}
	Placebo	16/68 (23.5)	11/68 (16.2)	19/68 (27.9)	16/68 (23.5)	8/68 (11.8)	19/68 (27.9)

ELA + AB = elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg); FIGO = International Federation of Gynecology and Obstetrics; PGIC = Patient Global Impression of Change.

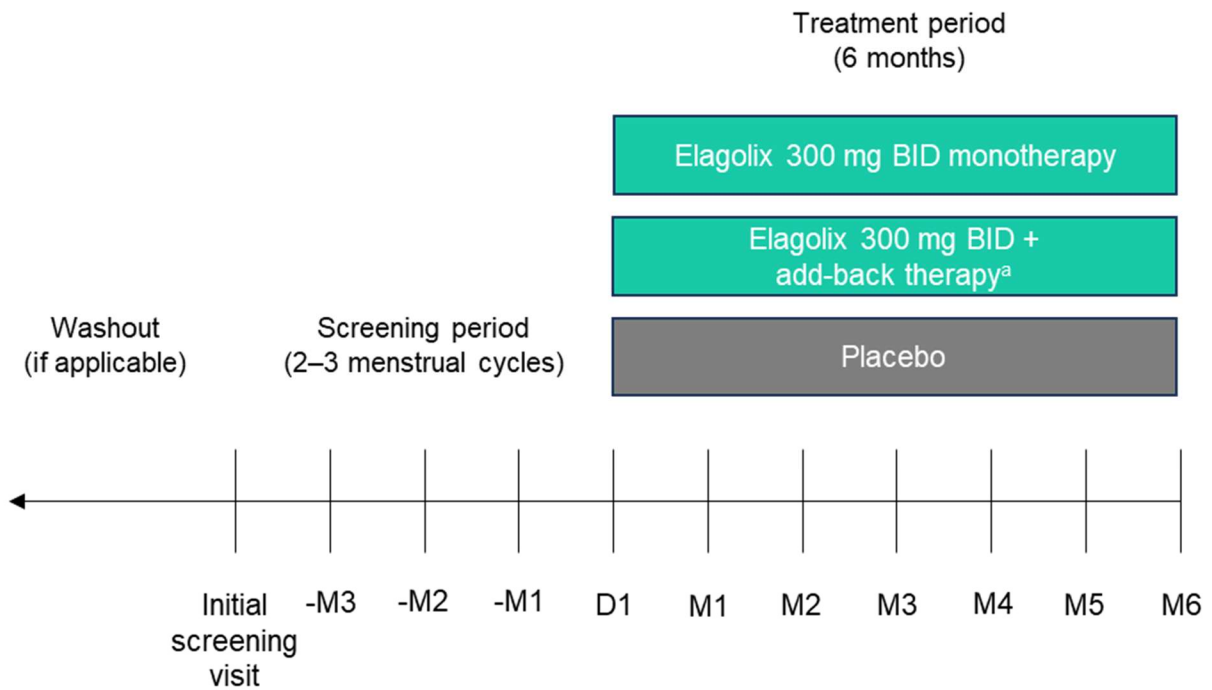
* $P < .05$; ** $P < .01$; *** $P < .001$. P values were descriptive only and no adjustments were made for multiplicity.

^aMeaningful improvement defined by PGIC responses of “very much improved” or “much improved.”

^bSubpopulations based on baseline demographic or clinical characteristics.

SUPPLEMENTAL FIGURE 1

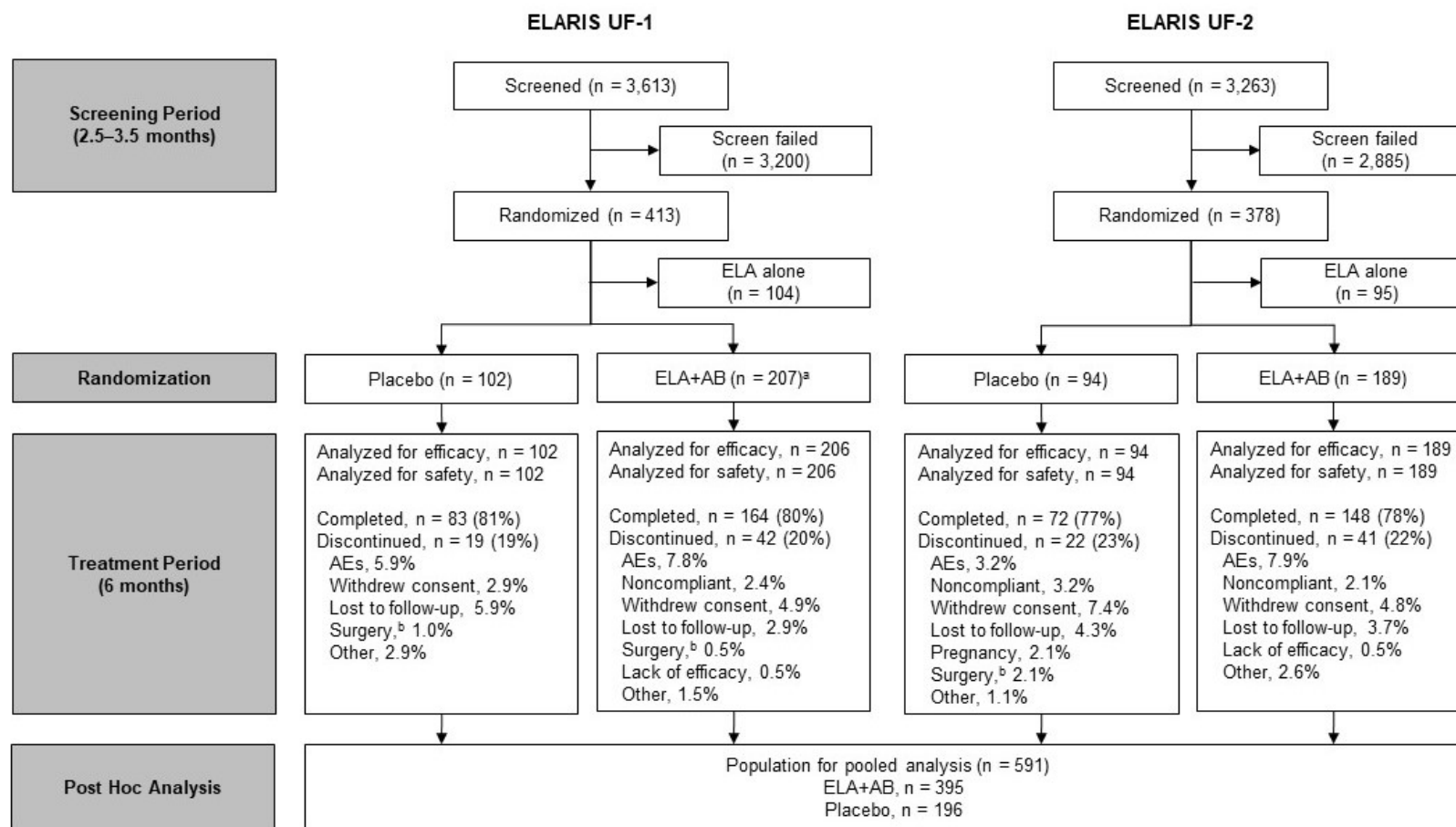
Study design.



^aAdd-back therapy consisted of estradiol 1 mg and norethindrone acetate 0.5 mg.
BID = twice a day; D = day; M = month.

SUPPLEMENTAL FIGURE 2

CONSORT diagram describing study pooling and post hoc analysis in relation to original studies.



^aOne woman in ELARIS UF-1 was randomized but not treated.

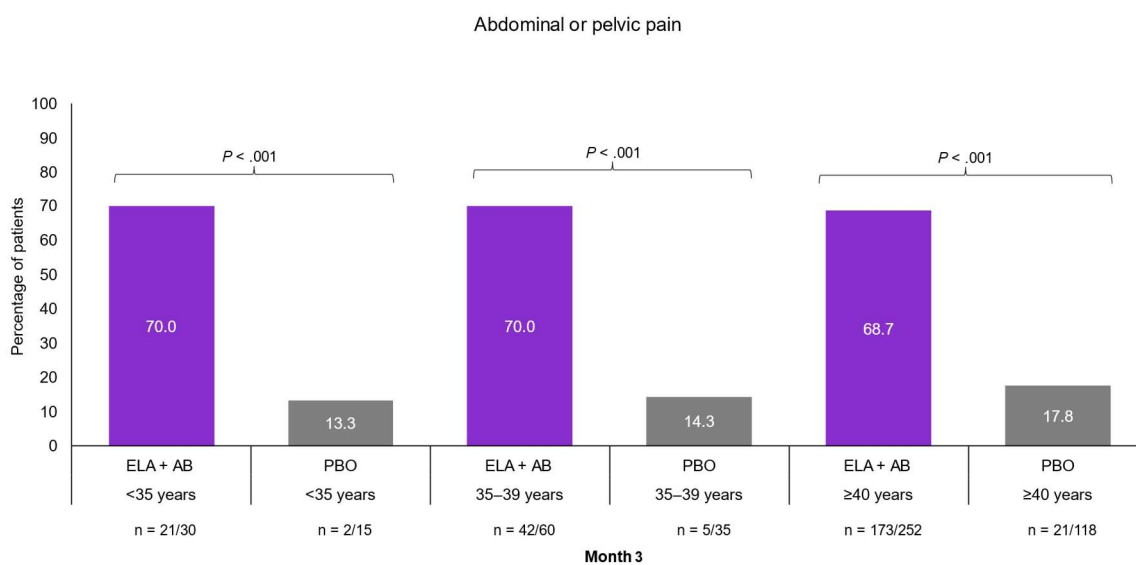
^bWomen require surgery or invasive intervention for treatment of uterine fibroids.

AEs = adverse events; ELA = elagolix; ELA + AB = elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg).

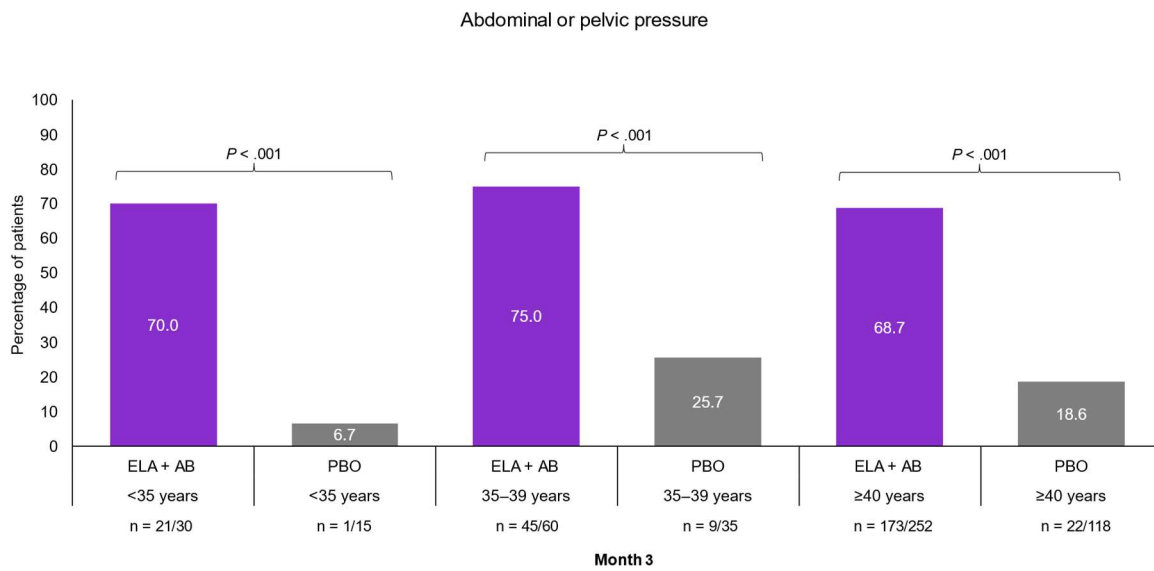
SUPPLEMENTAL FIGURE 3

Meaningful improvements^a in nonbleeding symptoms and menstrual bleeding across age groups as evaluated using the Patient Global Impression of Change scale at month 3.

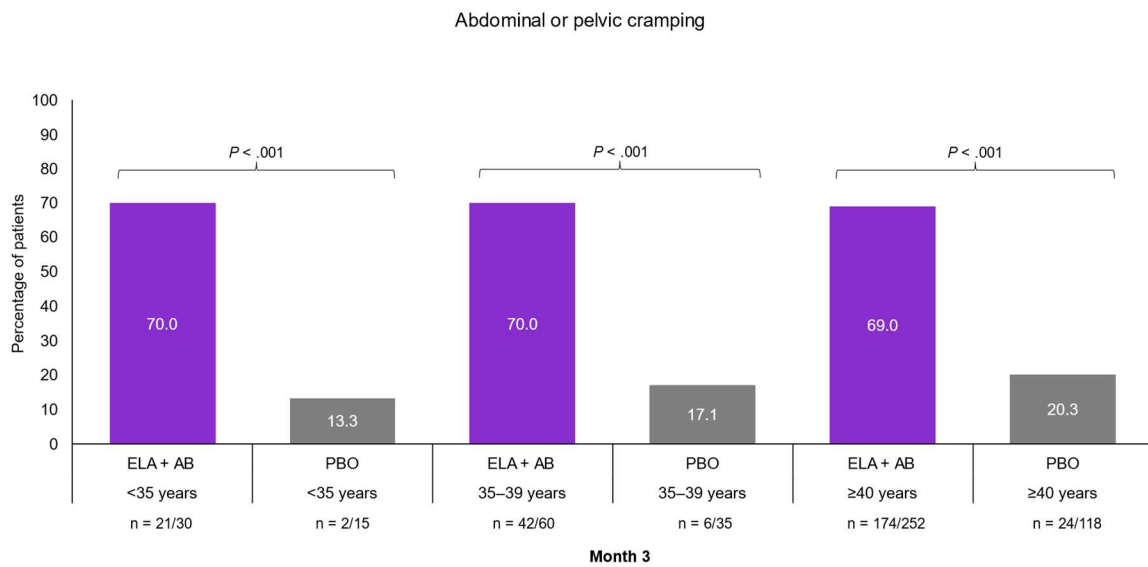
Abdominal or pelvic pain **(A)**, abdominal or pelvic pressure **(B)**, abdominal or pelvic cramping **(C)**, back pain **(D)**, abdominal bloating **(E)**, menstrual bleeding **(F)**.

(A)

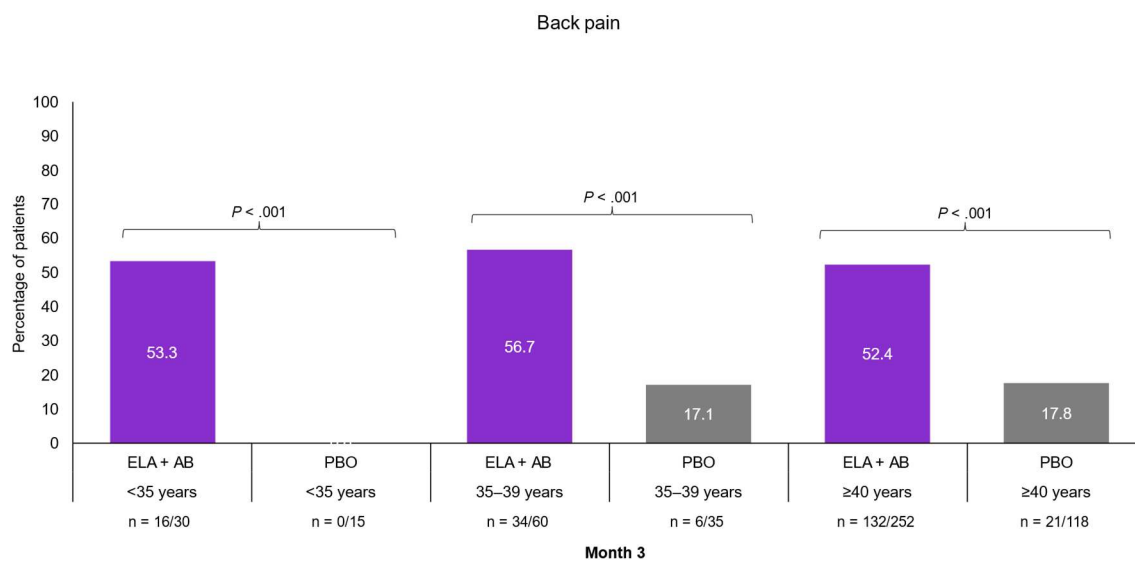
(B)



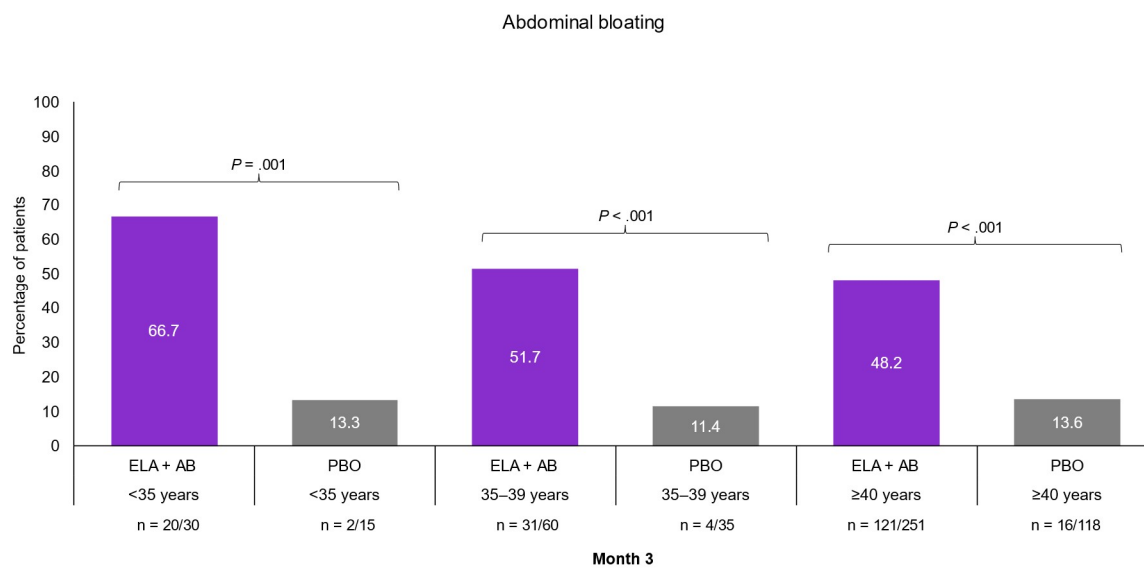
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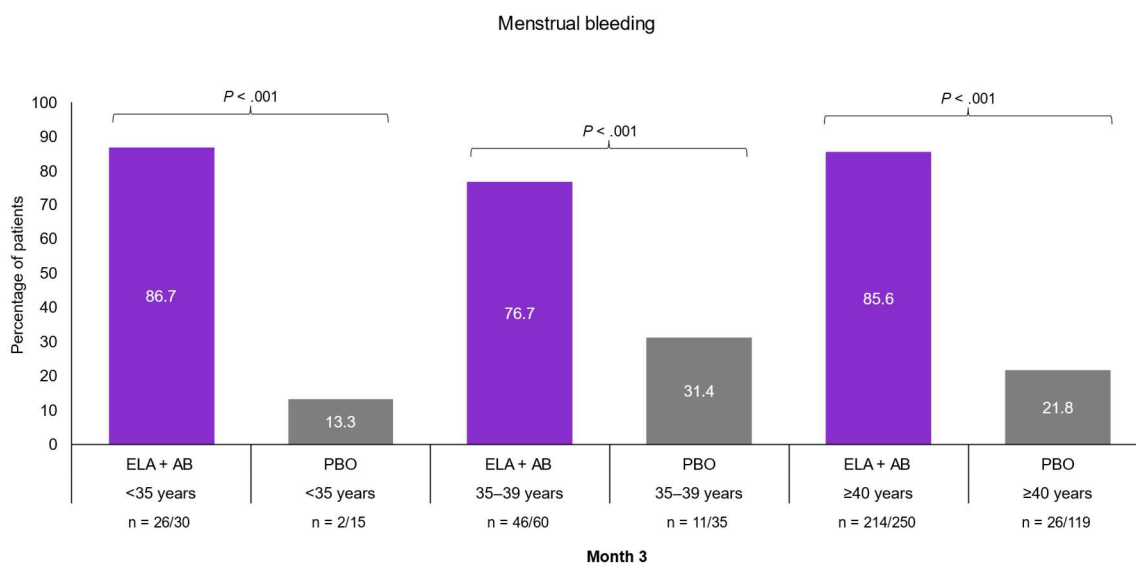
(D)



(E)



(F)



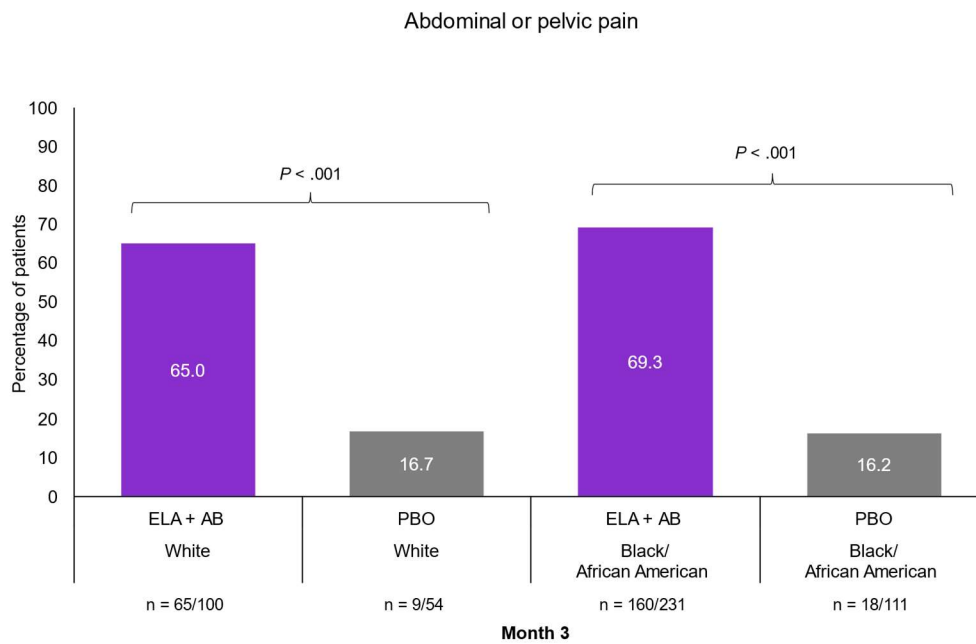
^aMeaningful improvement defined by PGIC responses of “very much improved” or “much improved.”

P values were descriptive only and no adjustments were made for multiplicity.

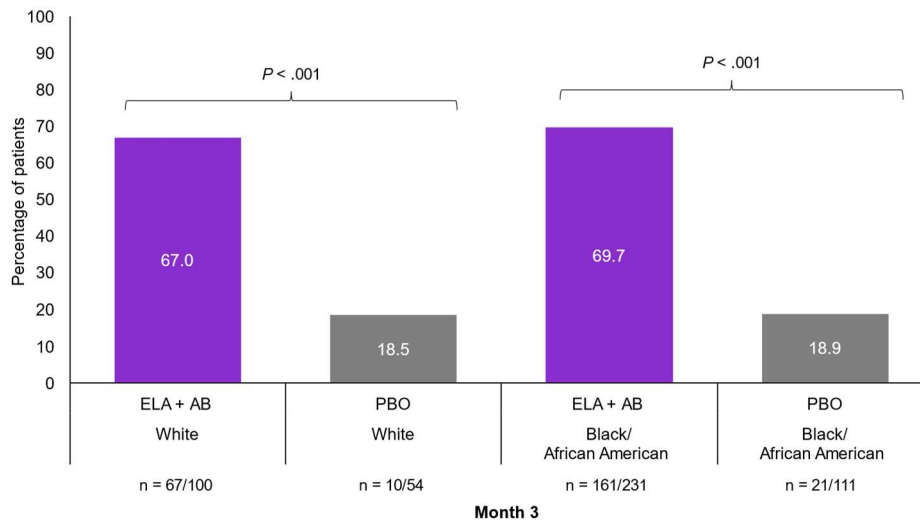
ELA + AB = elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg); PBO = placebo; PGIC = Patient Global Impression of Change.

SUPPLEMENTAL FIGURE 4

Meaningful improvements^a in nonbleeding symptoms and menstrual bleeding by race,^b evaluated using the Patient Global Impression of Change scale at month 3. Abdominal or pelvic pain **(A)**, abdominal or pelvic pressure **(B)**, abdominal or pelvic cramping **(C)**, back pain **(D)**, abdominal bloating **(E)**, menstrual bleeding **(F)**.

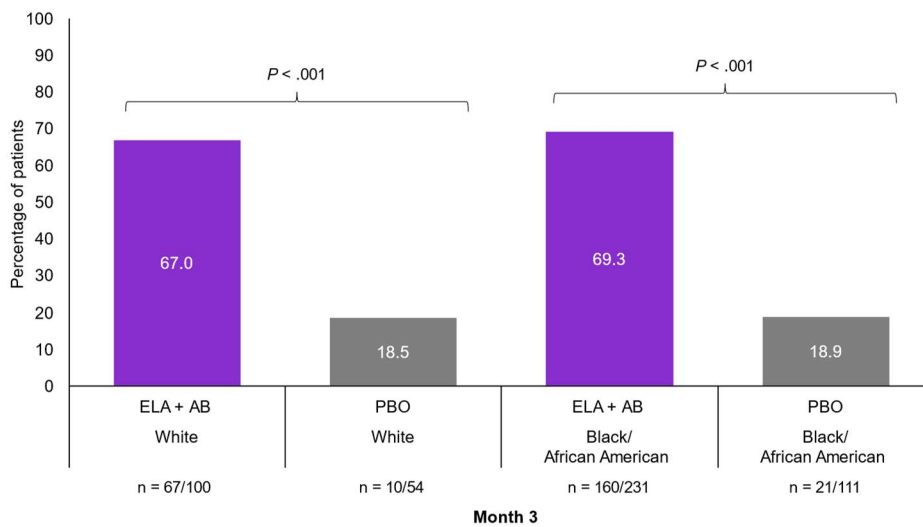
(A)**(B)**

Abdominal or pelvic pressure

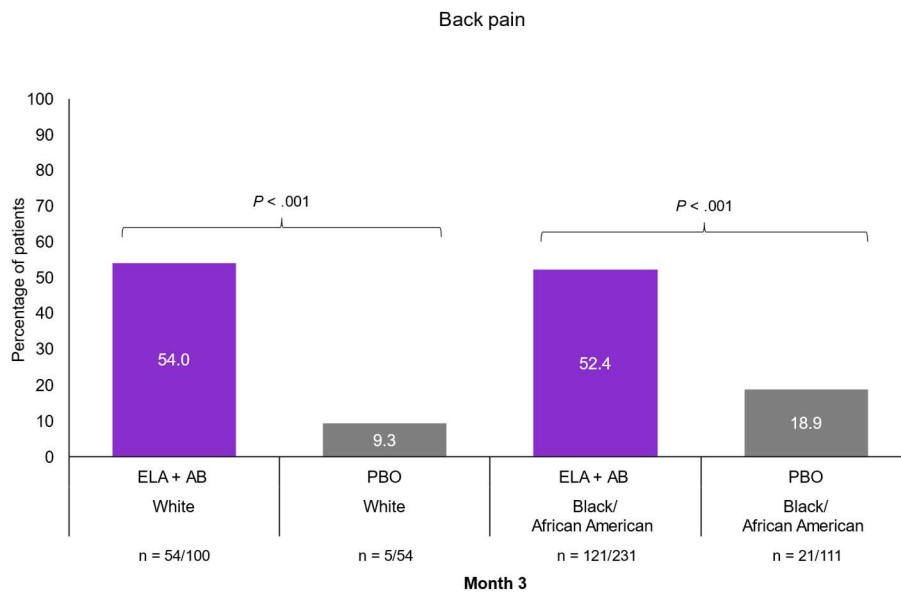


(C)

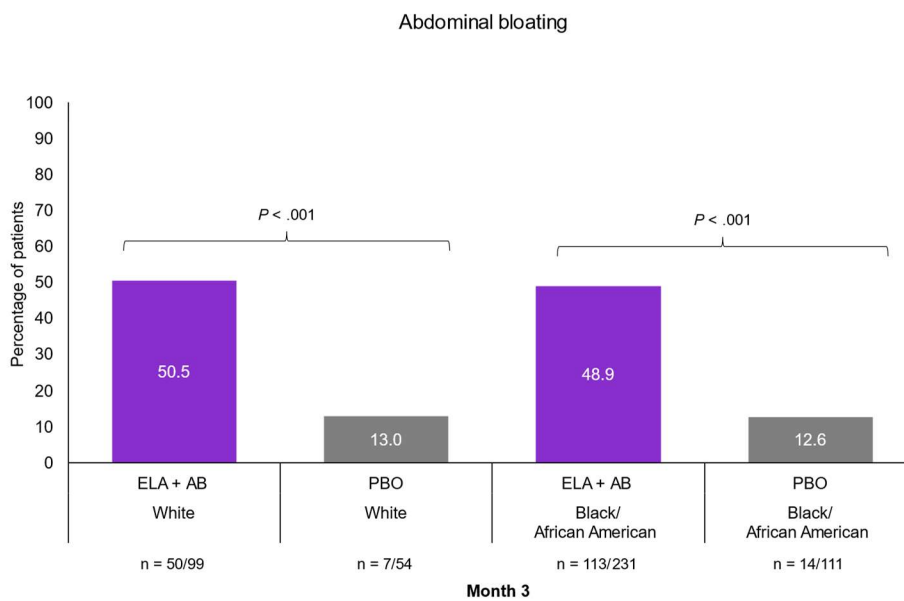
Abdominal or pelvic cramping



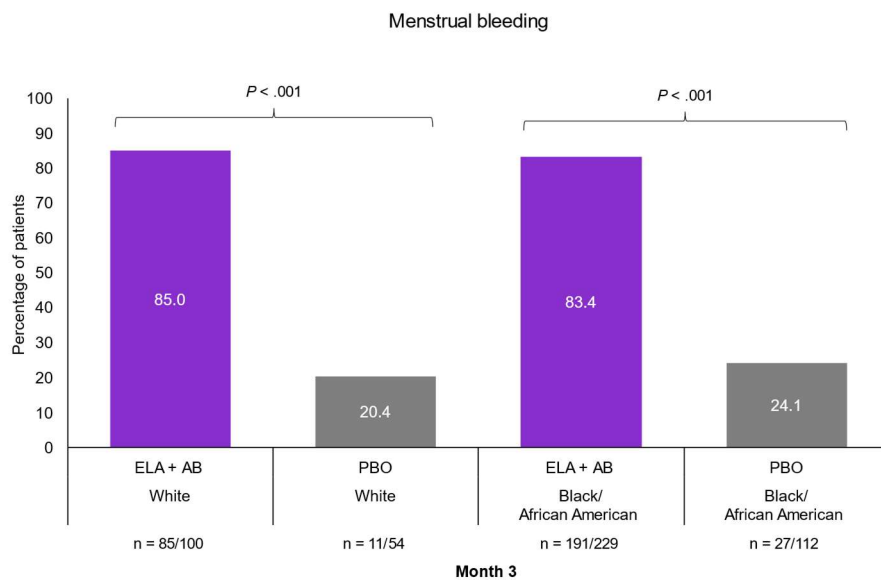
(D)



(E)



(F)



^aMeaningful improvement defined by PGIC responses of “very much improved” or “much improved.”

^bOnly White and Black/African American races were included in this analysis due to small patient numbers of other races.

P values were descriptive only and no adjustments were made for multiplicity.

ELA + AB = elagolix plus add-back therapy (estradiol 1 mg and norethindrone acetate 0.5 mg); PBO = placebo; PGIC = Patient Global Impression of Change.