

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Cummings SR, Ensrud K, Delmas PD, et al. Lasofoxifene in postmenopausal women with osteoporosis. *N Engl J Med* 2010;362:686-96.

**Table A. Rates of adverse events in the PEARL Trial that occurred with less than 10 cases per 1000 person-year difference between placebo and either dose of lasofoxifene and P<0.05 for the comparison for either dose of lasofoxifene with placebo**

Adverse event*	Placebo		Lasofoxifene 0.25 mg/d			Lasofoxifene 0.5 mg/d		
	No. of Events	No. of Cases per 1000 Person-Yr	No. of Events	No. of Cases per 1000 Person-Yr	P Value	No. of Events	No. of Cases per 1000 Person-Yr	P Value
Back pain	741	57.8	662	51.4	0.015	704	54.8	0.260
Hypertension <sup>†</sup>	652	50.9	542	42.1	0.005	558	43.4	0.018
Gastritis	248	19.3	216	16.8	0.06	200	15.6	0.008
Headache	208	16.2	164	12.7	0.018	181	14.1	0.156
Insomnia	157	12.2	113	8.8	0.011	99	7.7	0.001
Atrophic vulvovaginitis	130	12.6	102	9.9	0.060	98	9.5	0.031
Anaemia	140	10.9	198	15.4	0.004	167	13.0	0.11
Hyperlipidemia	127	9.9	60	4.7	<0.001	65	5.1	<0.001
Hypercholesterolemia	93	7.3	24	1.9	<0.001	31	2.4	<0.001
Herpes zoster	83	6.5	58	4.5	0.039	51	4.0	0.005
Vaginal bleeding <sup>‡</sup>	36	2.8	70	5.4	0.011	90	7.0	<0.001
Vaginal disorder	27	2.6	94	9.1	<0.001	99	9.6	<0.001
Vaginal discharge	23	2.2	70	6.8	<0.001	68	6.6	<0.001
Uterine leiomyoma	35	3.4	42	4.1	0.42	63	6.1	0.004
Lung cancer <sup>‡</sup>	4	0.3	15	1.2	0.012	13	1.0	0.029

\* Based on subjects with one or more events.

† Although there were fewer reports of hypertension in the lasofoxifene groups, there were no differences between groups for changes in diastolic or systolic blood pressure (-2.8/-3.8 for placebo, -2.6/-4.0 for 0.5 mg/d, and -2.8/-3.5 for 0.25 mg/d) at 3 years.

‡ Based on a composite of MedDRA preferred terms including squamous cell, adenocarcinoma, and small cell cancers. p-values based on number of subjects with preferred term.

**Table B. Adverse events by MedDRA preferred terms in the PEARL Trial for the combination of lasofoxifene 0.25 and 0.5 mg groups versus placebo that differed with a P-value < 0.05.**

MedDRA preferred term	Pooled lasofoxifene incidence (per 1000 subjects)	Placebo incidence (per 1000 subjects)	P-value
Abdominal bruit	1.8	0.0	0.04
Anaemia	57.3	44.2	0.01
Arthritis reactive	1.4	3.9	0.03
Aspartate aminotransferase increased	17.7	10.2	0.007
Back pain	239.5	259.8	0.04
Blood alkaline phosphatase increased	2.6	10.5	<0.001
Blood bilirubin increased	0.2	2.8	0.001
Blood calcium increased	1.8	8.1	<0.001
Blood cholesterol increased	1.4	6.3	<0.001
Blood TSH increased	1.9	0.0	0.02
Bone pain	24.7	17.2	0.03
Carpal tunnel syndrome	5.6	9.8	0.04
Cervical cyst	3.2	0.7	0.03
Cervicitis	10.9	16.8	0.02
Colpocele	8.8	3.9	0.009
Conjunctival haemorrhage	1.9	4.9	0.02
Cystocele	44.5	35.1	0.04
Dolichocolon	0.0	2.1	0.001
Dyslipidaemia	7.7	13.3	0.02
Eczema asteatotic	1.8	0.0	0.04
Epistaxis	5.1	9.1	0.03
Eyelids pruritus	0.4	1.8	0.05
Facial pain	0.9	2.8	0.04
Foreign body trauma	0.2	1.8	0.02
Gastritis	54.7	69.1	0.009
Headache	60.5	72.9	0.03
Hemicephalalgia	0.4	1.8	0.05
Herpes zoster	18.6	28.4	0.005
Hydrometra	8.9	3.9	<0.001
Hypercholesterolaemia	9.5	30.9	<0.001
Hyperhidrosis	15.6	8.4	0.006
Hyperlipidaemia	21.2	43.8	<0.001
Hypertension	161.1	187.2	0.003
Hypoesthesia	12.6	18.2	0.04
Insomnia	34.2	50.1	<0.001
Localised infection	6.8	1.8	0.001
Malaise	2.3	5.3	0.03

Nodule on extremity	0.4	1.8	0.05
Pharyngotonsillitis	1.8	0.0	0.04
Phlebitis	4.7	1.1	0.006
Platelet count decreased	2.6	0.4	0.03
Psoriasis	1.8	4.6	0.03
Reflux oesophagitis	6.0	2.1	0.01
Sensation of heaviness	4.2	1.1	0.01
Somatisation disorder	0.5	2.5	0.02
Tenosynovitis	1.4	4.9	0.005
Tinnitus	12.4	18.6	0.03
Transaminases increased	2.3	0.4	0.04
Trigger finger	1.9	5.6	0.007
Uterine cervical erosion	7.0	3.5	0.05
Uterine leiomyoma	18.4	12.3	0.04
Vaginal discharge	66.4	28.4	<0.001
Vaginal disorder	22.8	8.1	<0.001
Vitreous detachment	2.3	0.4	0.05
Vulvovaginitis	12.3	3.9	<0.001