

## Supplementary Online Content

Lee CC, Wang CY, Yen HK, et al. Zoledronate sequential therapy after denosumab discontinuation to prevent bone mineral density reduction: a randomized clinical trial. *JAMA Netw Open*. 2024;7(11):e2443899. doi:10.1001/jamanetworkopen.2024.43899

**eFigure.** Flow Chart of the 2-Year Study

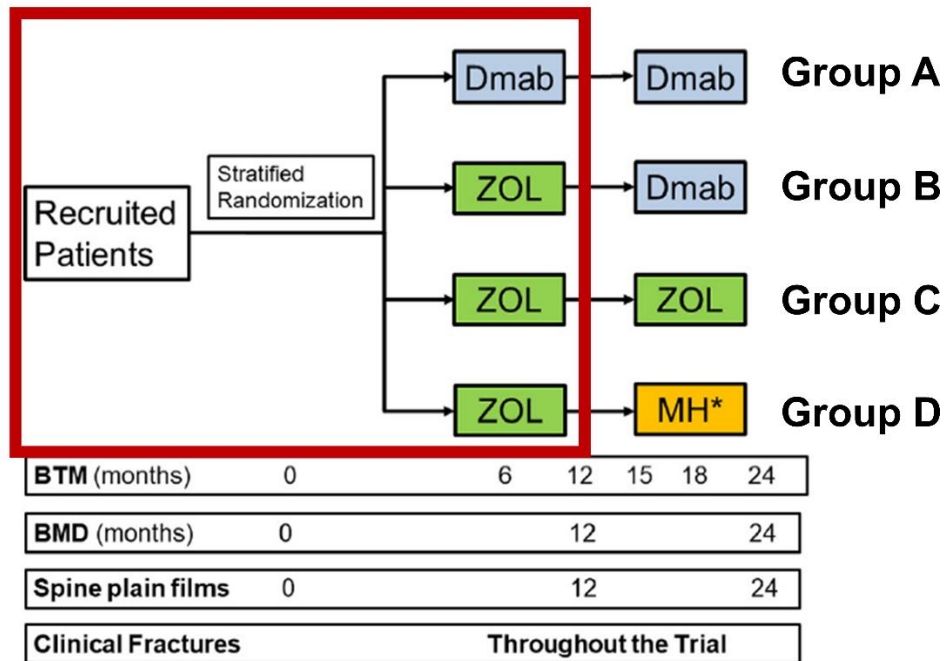
**eTable 1.** Results of Stratified Randomization

**eTable 2.** Bone Mineral Density (BMD) Loss in the Lumbar Spine, Total Hip, and Femoral Neck Exceeding the Least Significant Change in the Zoledronate (ZOL) Group

**eTable 3.** Bone Mineral Density (BMD) Changes in Women Who Had Ever Suffered Vertebral Fractures in the Zoledronate (ZOL) Group (n = 63)

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

**eFigure.** Flow Chart of the 2-Year Study



The red frame highlights the first year of the trial.

**Abbreviations:** Dmab, denosumab; ZOL, zoledronate; MH, monitored drug holiday;

BTM, bone turnover markers; BMD, bone mineral density.

\* An extra ZOL injection will be given once the C-terminal telopeptide levels raise above the pre-specified threshold, 0.573 ng/mL in post-menopausal women and 0.584 ng/mL in men, respectively.

**eTable 1.** Results of Stratified Randomization

Stratification	Stratification	Group	Group	Group	Group	Case number in
by sex	by T-score	A	B	C	D	each stratum
<b>Female</b>	T-score > -2.5	10	10	11	10	41
	T-score ≤ -2.5	13	13	14	14	54
<b>Male</b>	T-score > -2.5	1	1	0	1	3
	T-score ≤ -2.5	1	1	0	1	3
	Case number	25	25	25	26	Total number = 101

**eTable 2.** Bone Mineral Density (BMD) Loss in the Lumbar Spine, Total Hip, and Femoral Neck Exceeding the Least Significant Change in the Zoledronate (ZOL) Group

Least significant change: Lumbar spine >5%, total hip>4%, femoral neck>4%

	Age (median[IQR])	Weight (median[IQR])	BMD change (median[IQR])
<b>ALL (n=73)</b>			
LS(n=11)	73.00[65.00, 75.50]	50.00[44.50, 53.35]	-7.35 [-9.99, -6.69]
TH(n=6)	67.00[63.75, 70.25]	51.25[44.13, 56.50]	-5.09 [-6.11, -4.31]
FN(n=12)	73.00[67.75, 78.00]	56.00[47.00, 58.50]	-5.17 [-6.93, -4.99]
<b>Denosumab use for ≤ 2.5 years (n=58)</b>			
LS(n=5)	71.00[67.00, 74.00]	53.00[52.00, 53.70]	-7.12 [-7.35, -6.99]
TH(n=4)	67.00[63.25, 68.75]	51.25[46.13, 59.25]	-5.99 [-6.28, -5.38]
FN(n=9)	72.00[68.00, 78.00]	55.00[47.00, 58.00]	-5.03 [-8.64, -4.98]
<b>Denosumab use for ≤ 3 years (n=61)</b>			
LS(n=6)	72.50[68.00, 77.75]	52.50[48.25, 53.53]	-7.06 [-7.29, -6.45]
TH(n=4)	67.00[63.25, 68.75]	51.25[46.13, 59.25]	-5.99 [-6.28, -5.38]
FN(n=9)	72.00[68.00, 78.00]	55.00[47.00, 58.00]	-5.03[-8.64, -4.98]
<b>Denosumab use for ≥ 3 years (n=15)</b>			
LS(n=6)	73.35[65.50, 76.25]	44.50[43.25, 48.75]	-8.67 [-10.45, -6.76]
TH(n=2)	68.50[65.75, 71.25]	50.00[46.50, 53.50]	-4.32 [-4.38, -4.26]
FN(n=3)	74.00[68.50, 76.00]	57.00[50.00, 65.50]	-5.31 [-5.84, -5.17]

LS: Lumbar spine; TH: Total hip; FN: Femoral neck

**eTable 3.** Bone Mineral Density (BMD) Changes in Women Who Had Ever Suffered Vertebral Fractures in the Zoledronate (ZOL) Group (n = 63)

	<b>Median [IQR]</b>
<b>Age (years)</b>	71.00 [65.50, 75.50]
<b>Weight (kg)</b>	57.00 [49.00, 64.00]
<b>BMD change (%)</b>	
<b>LS</b>	-0.65 [-3.58, 2.68]
<b>TH</b>	0.48[-1.43, 2.39]
<b>FN</b>	0.81 [-2.53, 3.79]

LS: Lumbar spine; TH: Total hip; FN: Femoral neck