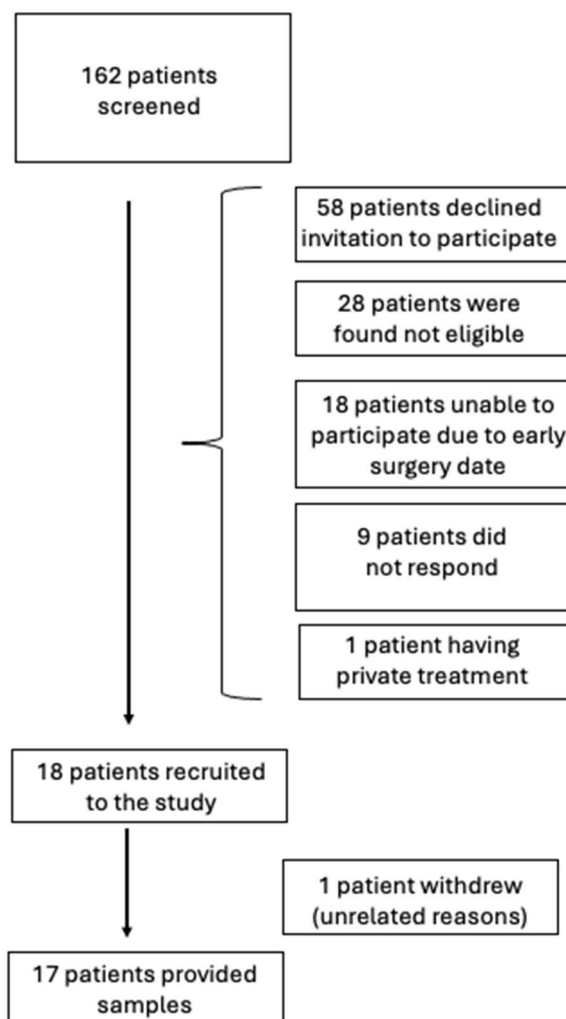


ZOLMENO- The role of ZOLedronic acid and MENOpausal status on the tumour and bone microenvironment in patients with early breast cancer: a single centre, randomised, proof of concept clinical study

Participant flow



Baseline characteristics

			Patients who had blood samples					Bone Aspirates	Bone Trephines
		Patients recruited	Day-7	Day0 Surgery	Day21	Day28	Day49		
Premenopausal	Group A	2	2	2	2	2	X	2	1
	Group B	2	2	2	2	2	2	1	1
Postmenopausal	Group A	6	6	6	6	6	X	5	4
	Group B	8	8	8	8	8	8	4	4

Results

FOLLISTATIN

GROUP A ZOL administered day -7 pre-surgery (day 0)

FOLLISTATIN pg/ml	PRE-meno Group A (n=2)			POST-meno Group A (n=5)			Unpaired	2-way anova
Serum timepoint	mean	median	SD	mean	median	SD	T-Test	PRE v POST-meno all
D-7 (Zol)	2410.7	2410.7	199.1	1431.9	1582.5	327.9	*P=0.012	* P<0.05
D0 (surgery)	1147.2	1147.2	60.2	1455.5	1281.4	566.0	P=0.5	
D21 *	1425.4	1425.4	0.0	1384.8	1654.5	557.6	P=0.95	
D28	1369.7	1369.7	402.7	1951.7	2053.9	674.2	P=0.32	

GROUP B ZOL administered day 21 post-surgery (day 0)

FOLLISTATIN pg/ml	PRE-meno Group B (n=2)			POST-meno Group B			Unpaired	2-way anova
Serum timepoint	mean	median	SD	mean	median	SD	T-Test	PRE v POST-meno all
D-7	1831.3	1831.3	296.3	1269.8	1247.5	217.3	*P=0.036	n.s
D0 (surgery)	1268.3	1268.3	740.7	1559.0	1372.3	604.3	P=0.61	
D21 (Zol)	1166.8	1166.8	513.8	1517.0	1227.7	430.9	P=0.39	
D28	1808.4	1808.4	199.1	1247.5	1240.9	387.8	P=0.12	

ACTIVIN A

GROUP A ZOL administered day -7 pre-surgery (day 0)

ACTIVIN A pg/ml	PRE-meno Group A (n=2)			POST-meno Group A			Unpaired	2-way anova
Serum timepoint	mean	median	SD	mean	median	SD	T-Test	PRE v POST-meno all
D-7 (Zol)	265.4	265.4	92.1	192.5	196.8	54.4	P=0.23	*P<0.01
D0 (surgery)	215.8	215.8	20.7	175.1	171.0	24.5	P=0.1	
D21 *	307.2	307.2	0.0	192.0	191.6	39.3	P=0.06	
D28	252.9	252.9	25.6	185.4	210.6	39.4	P=0.08	

GROUP B ZOL administered day 21 post-surgery (day 0)

ACTIVIN A pg/ml	PRE-meno Group B			POST-meno Group B			Unpaired	2-way anova
Serum timepoint	mean	median	SD	mean	median	SD	T-Test	PRE v POST-meno all
D-7	230.4	230.4	113.4	296.9	306.2	118.8	P=0.53	n.s
D0 (surgery)	252.0	252.0	134.1	184.2	185.0	21.5	P=0.25	
D21 (Zol)	241.7	241.7	52.4	244.2	235.0	63.5	P=0.96	
D28	291.2	291.2	46.9	226.6	206.2	105.6	P=0.80	

*Pre-meno Group A day 21, n=1

Two-sample T-Test performed to compare PRE v POST-menopausal data within same treatment group for same time point

2-way ANOVA performed to compare differences between different time points, and difference between PRE-menopausal & POST-menopausal

Adverse events

The study did not report any serious adverse events related to ZOL and no serious complications due to bone marrow biopsies were recorded.

Non serious adverse events:**Events assessed as having a possible or probable relationship to study drug**

Event	Number of participants
Flu like symptoms	8
Fatigue	3
Aches and pains	2
Headache	1
Low calcium	1
Abdominal pain	1
Rash	1

Events assessed as unrelated to study drug

Event	Number of participants
Breast / surgical wound infection	3
Breast haematoma / breast pain	3
Bone marrow site pain	2
Dizziness	1
Vomiting	1
Back pain	1
Thigh pain	1
Broken tooth	1