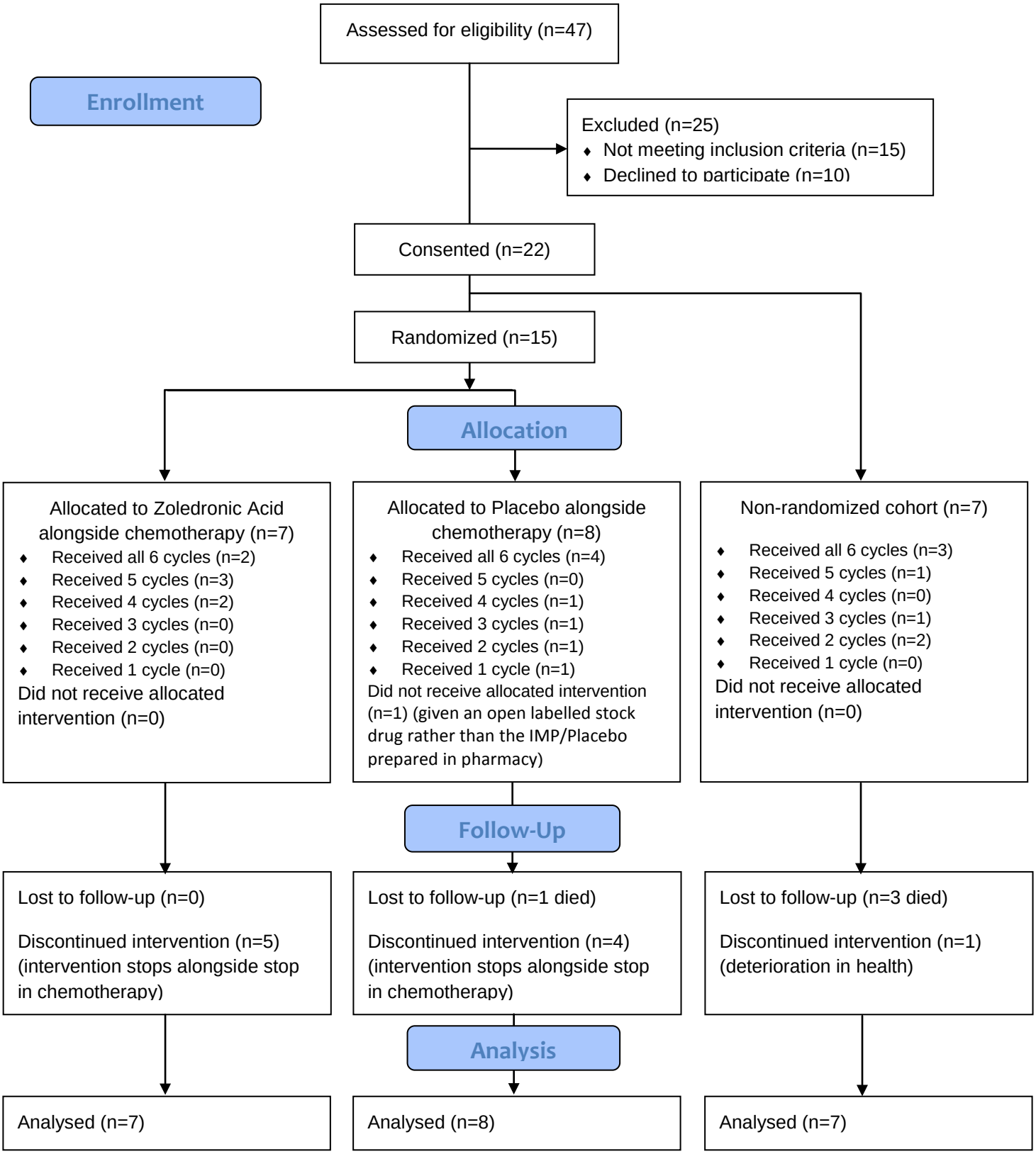
Participant Flow:



Baseline Characteristics:

Table 1 Summary of baseline characteristics and medical history, by trial arm and overall

		ZA (n=7)		Placebo (n=8)		Non-randomised ZA (n=7)		Overall (randomised) (n=15)		Overall (n=22)	
		n	%	n	%	n	%	n	%	n	%
Baseline Characteristics											
Age	Mean (s.d)	70.0	6.2	74.2	4.6	82.3	5.2	72.2	5.7	75.4	7.2
Sex	Female	1	14.3	0	0.0	1	14.3	1	6.7	2	9.1
	Male	6	85.7	8	100.0	6	85.7	14	93.3	20	90.9
Height (m)	Mean (s.d)	1.78	0.08	1.71	0.05	1.68	0.08	1.74	0.07	1.73	0.08
Weight (kg)	Mean (s.d)	80.4	11.3	73.4	11.4	64.5	6.8	76.6	11.5	72.8	11.6
Body mass index	Mean (s.d)	25.2	2.1	25.0	3.5	22.8	2.4	25.1	2.8	24.4	2.8
WHO performance status	0	2	28.6	4	50.0	0	0.0	6	40.0	6	27.3
	1	5	71.4	4	50.0	7	100.0	9	60.0	16	72.7
Medical History											
Previous 5-year significant history		6	85.7	4	50.0	5	71.4	10	66.7	15	68.18
Hypocalcaemia		0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ischaemic heart disease		0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Dental caries		0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Diabetes mellitus		1	14.3	1	12.5	0	0.0	2	13.3	2	9.1
Other medical history		6	85.7	4	50.0	5	71.4	10	66.7	15	68.2
Current medications		5	71.4	7	87.5	7	100.0	12	80.0	19	86.4
Current drug adverse reactions		2	28.6	0	0.0	3	42.9	2	13.3	5	22.7
Length of symptoms	<1 month	1	14.3	2	25.0	0	0.0	3	20.0	3	13.6
	1-2 months	1	14.3	2	25.0	0	0.0	3	20.0	3	13.6

		ZA (n=7)		Placebo (n=8)		Non-randomised ZA (n=7)		Overall (randomised) (n=15)		Overall (n=22)	
		n	%	n	%	n	%	n	%	n	%
	>2 months	5	71.4	4	50.0	7	100.0	9	60.0	16	72.7
Laterality	Left	5	71.4	3	37.5	2	28.6	8	53.3	10	45.5
	Right	2	28.6	5	62.5	5	71.4	7	46.7	12	54.5
Mode of diagnosis	LA thoracoscopy	3	42.9	3	37.5	5	71.4	6	40.0	11	50.0
	Image guided	3	42.9	2	25.0	1	14.3	5	33.3	6	27.3
	VATS	1	14.2	3	37.5	1	14.3	4	26.7	5	22.7
Cell type	Epithelioid	6	85.7	5	62.5	5	71.4	11	73.3	16	72.7
	Sarcomatoid	1	14.3	1	12.5	1	14.3	2	13.3	3	13.6
	Biphasic	0	0.0	1	12.5	1	14.3	1	6.7	2	9.1
	Mesothelioma NOS	0	0.0	1	12.5	0	0.0	1	6.7	1	4.6
Previous pleurodesis		2	28.6	2	25.0	1	14.3	4	26.7	5	22.7
Intracystic papillary carcinoma in situ		4	57.1	2	25.0	1	14.3	6	40.0	7	31.8

Table 1 Summary of baseline mesothelin blood test, by trial arm and overall

	ZA			Placebo			Non-randomised ZA			Overall (randomised)			Overall		
	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n
Mesothelin test (IU/L)[1]	5.69	5.86	7	5.90	4.15	8	6.03	5.64	6	5.80	4.83	15	5.87	4.93	21

[1] 1 value not detectable (non-randomised ZA arm)

Table 2 Baseline TNM and stage measured via CT scan by randomised group and overall

	ZA	Placebo	Non-randomised ZA	Overall (randomised)	Overall
	n (%)	n (%)	n (%)	n (%)	n (%)
TNM					
000	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
100	1 (14.3%)	3 (42.9%)	5 (71.4%)	4 (28.6%)	9 (42.9%)
110	1 (14.3%)	1 (14.3%)	0 (0.0%)	2 (14.3%)	2 (9.5%)
121	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
210	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
300	1 (14.3%)	1 (14.3%)	0 (0.0%)	2 (14.3%)	2 (9.5%)
320	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
321	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
400	1 (14.3%)	0 (0.0%)	1 (14.3%)	1 (7.1%)	2 (9.5%)
410	0 (0.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (4.8%)
Total	**7 (100%)**	**7 (100%)**	**7 (100%)**	**14 (100%)**	**21 (100%)**
Stage					
0	0 (0.0%)	1 (14.3%)	0 (0.0%)	1 (7.1%)	1 (4.8%)
1A	1 (14.3%)	3 (42.9%)	5 (71.4%)	4 (28.6%)	9 (42.9%)
1B	1 (14.3%)	1 (14.3%)	0 (0.0%)	2 (14.3%)	2 (9.5%)
2	2 (28.6%)	1 (14.3%)	0 (0.0%)	3 (21.4%)	3 (14.3%)
3B	2 (28.6%)	0 (0.0%)	2 (28.6%)	2 (14.3%)	4 (19.1%)
4	1 (14.3%)	1 (14.3%)	0 (0.0%)	2 (14.3%)	2 (9.5%)
Total	**7 (100%)**	**7 (100%)**	**7 (100%)**	**14 (100%)**	**21 (100%)**

Outcome Measures:

Table 3 Summary of response for mid-cycle and 6-month CT scans by trial arm and overall

	ZA	Placebo	Non-randomised ZA	Overall (randomised)	Overall
	n (%)	n (%)	n (%)	n (%)	n (%)
Scan					
Mid-cycle					
Complete response	1 (14.3%)	2 (28.6%)	2 (20.0%)	3 (21.4%)	5 (26.3%)
Partial response	2 (28.6%)	1 (14.3%)	0 (0.0%)	3 (21.4%)	3 (15.8%)
Stable disease	3 (42.9%)	0 (0.0%)	0 (0.0%)	3 (21.4%)	3 (15.8%)
Progressive disease	1 (14.3%)	4 (57.1%)	3 (60.0%)	5 (35.7%)	8 (42.1%)
Total	**7 (100%)**	**7 (100%)**	**5 (100%)**	**14 (100%)**	**19 (100%)**
6-month					
Complete response	2 (28.6%)	2 (40.0%)	1 (33.3%)	4 (33.3%)	5 (33.3%)
Partial response	1 (14.3%)	0 (0.0%)	0 (0.0%)	1 (8.3%)	1 (6.7%)
Stable disease	2 (28.6%)	0 (0.0%)	0 (0.0%)	2 (16.7%)	2 (13.3%)
Progressive disease	2 (28.6%)	3 (60.0%)	2 (66.6%)	5 (41.7%)	7 (46.7%)
Total	**7 (100%)**	**5 (100%)**	**3 (100%)**	**12 (100%)**	**15 (100%)**

Table 4 Summary of TGV assessed via PET-CT scan by randomised group and scan

	ZA			Placebo			Non-randomised ZA			Overall (randomised)			Overall		
	Geo. mean	(Var)	n	Geo. mean	(Var)	n	Geo. mean	(Var)	n	Geo. mean	(Var)	n	Geo. mean	(Var)	n
Scan															
Baseline	579.5	3.4	7	1062.0	2.1	8	588.7	1.1	7	800.4	2.6	15	725.9	2.1	22
Mid-cycle	80.4	5.8	7	253.5	6.1	6	446.7	0.3	4	136.6	5.8	13	180.5	4.7	17

Table 5 Summary of mesothelin blood test results (IU/L), by trial arm and overall

	ZA			Placebo			Non-randomised ZA			Overall (randomised)			Overall		
	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n	Mean	(s.d.)	n
pre-cycle 2	3.08	1.54	6	5.28	3.35	6	9.29	9.38	6	4.18	2.74	12	6.06	6.35	19
pre-cycle 3	2.84	2.11	7	2.88	1.72	4	5.22	4.03	5	2.85	1.88	11	3.59	2.83	16
pre-cycle 4	2.47	2.02	6	5.75	6.83	4	4.65	2.24	4	3.78	4.55	10	4.03	3.96	14
pre-cycle 5	3.03	2.05	4	2.63	2.03	3	6.00	3.38	4	2.86	1.87	7	4.00	2.82	11
pre-cycle 6	3.33	1.99	4	1.60	0.52	3	8.57	5.34	3	2.59	1.71	7	4.38	4.08	10
6-month follow-up[2]	3.76	1.50	5	6.75	4.03	2	9.87	4.38	3	4.61	2.52	7	6.19	3.86	10

[2] 1 value not detectable (ZA arm)

Adverse Events:

Serious Adverse Events	ZA (n = 8)	Placebo (n = 7)	Open label ZA (n = 7)	Overall (n = 22)
Definitely or probably related to the IMP	**0**	**0**	**0**	**0**
Possibly related to the IMP TOTAL	**1**	**0**	**0**	**1**
anticipated electrolyte disturbance	1	0	0	1
Unlikely to be related/ not related TOTAL	**6**	**5**	**4**	**15**
Respiratory, thoracic and mediastinal disorders				
cough	1	0	0	1
pleural infection	2	0	0	2
infection	1	1	1	3
pulmonary embolism	1	0	0	1
rash	0	1	0	1
General disorders				
death	0	0	2	2
pain	0	1	1	2
Blood and lymphatic system disorders				
neutrophil count decreased	1	0	0	1

Non-serious Adverse Events (5% reporting threshold for number of participants affected)	ZA (n = 8)	Placebo (n = 7)	Open label ZA (n = 7)	Overall (n = 22)
Respiratory, thoracic and mediastinal disorders				
pain (unexpected, unrelated)	0	1	2	3
breathlessness (unexpected, unrelated)	0	2	1	3
infection (unexpected, unrelated)	1	3	3	7
Blood and lymphatic system disorders				
anaemia (unexpected, unrelated)	0	2	0	2
General disorders and administration site conditions				
nausea (expected, unrelated)	2	2	1	5
poor appetite (expected, 2 possibly related)	1	1	1	3
fatigue (expected, 2 possibly related)	3	4	2	9
dizziness (unexpected, unrelated)	2	0	1	3
significant weight loss (unexpected, unrelated)	0	0	2	2
Gastrointestinal disorders				
constipation (unexpected, 3 possibly related)	4	2	2	8
vomiting (expected, 1 possibly related)	2	2	1	5
Skin and subcutaneous tissue disorders				
rash (expected, unrelated)	2	3	0	5