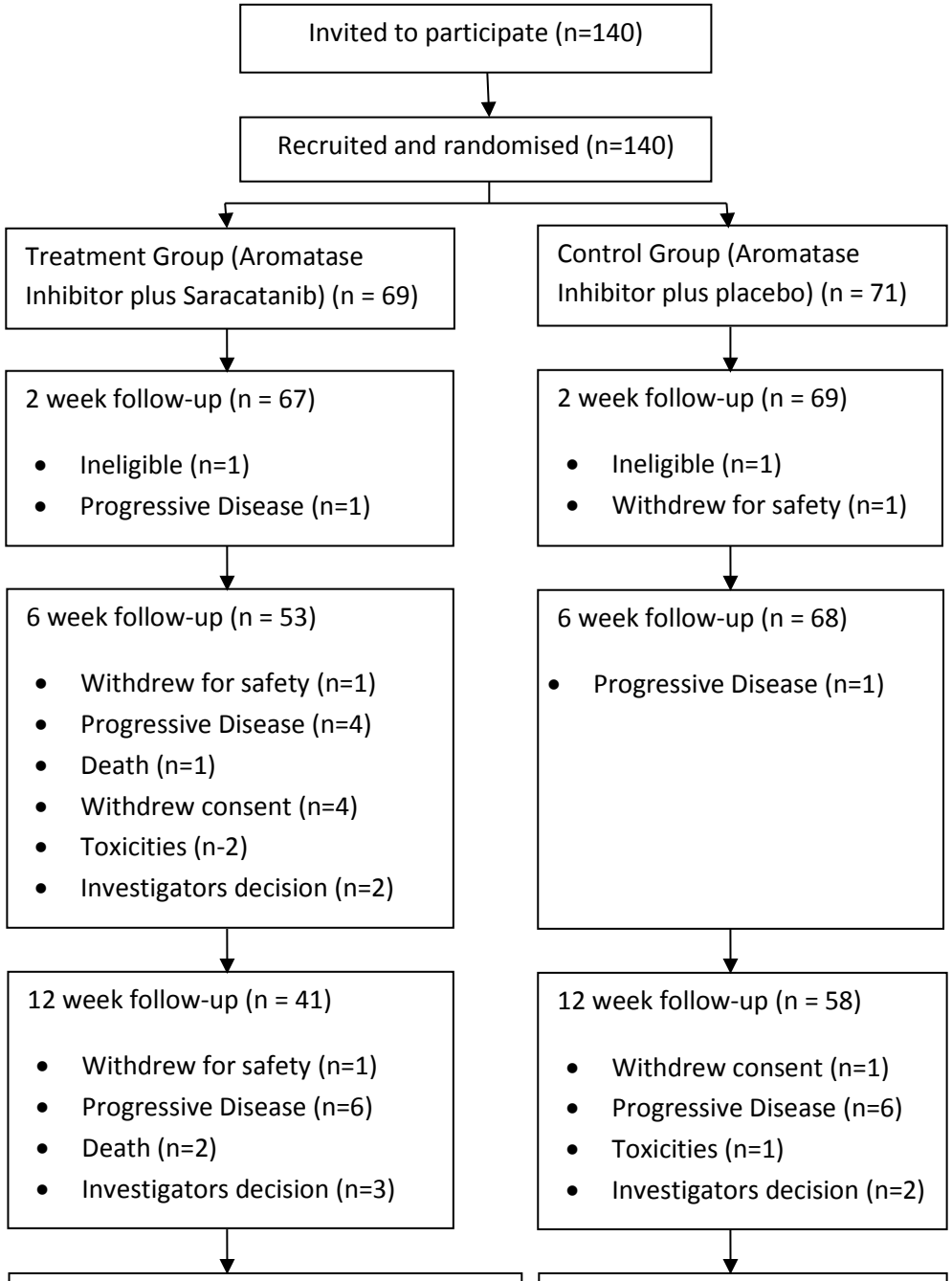
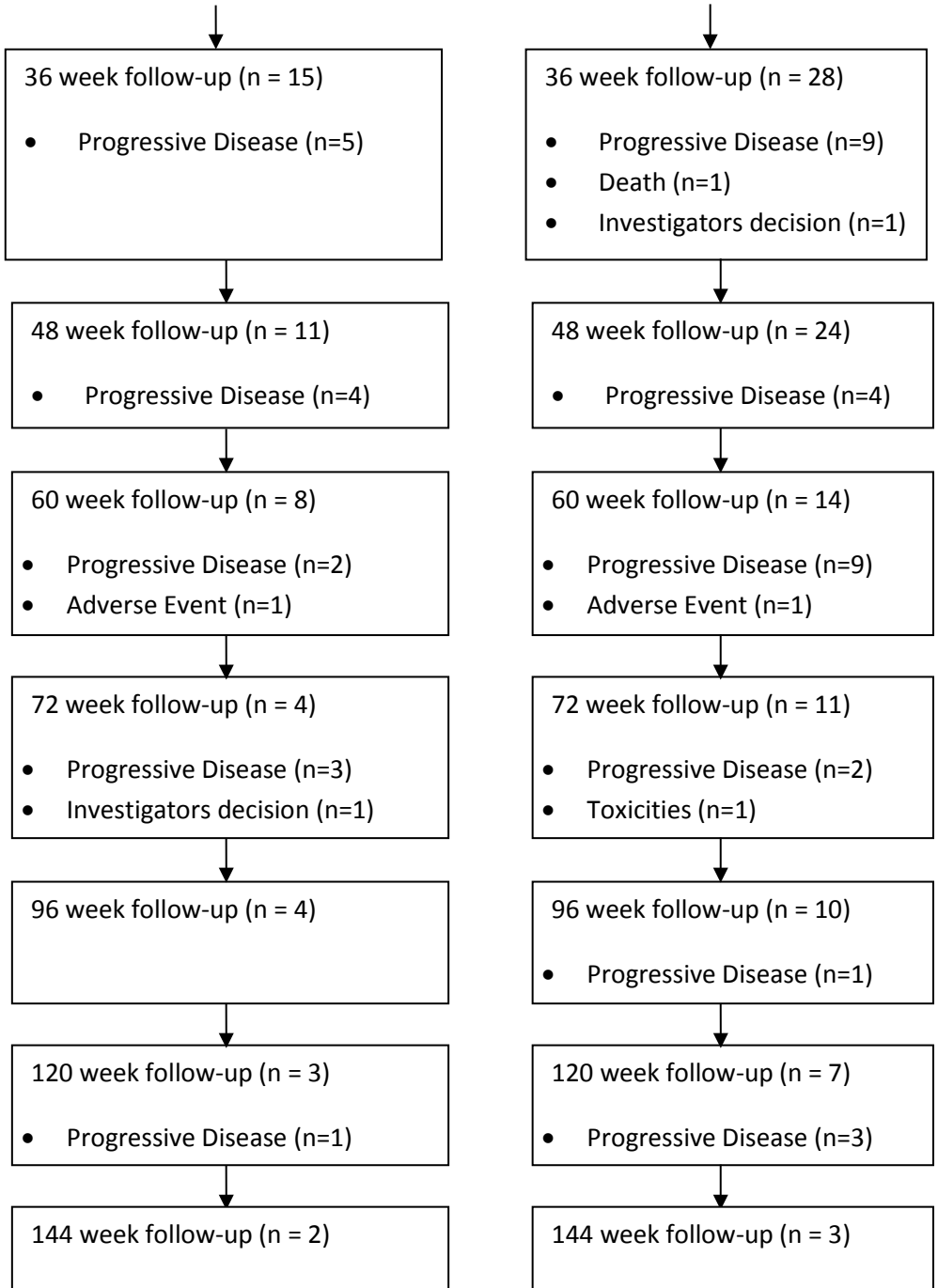
Participant Flow




36 week follow-up (n = 15)
Progressive Disease (n=5)
36 week follow-up (n = 28)
Progressive Disease (n=9)
Death (n=1)
Investigators decision (n=1)
48 week follow-up (n = 11)
Progressive Disease (n=4)
48 week follow-up (n = 24)
Progressive Disease (n=4)
60 week follow-up (n = 8)
Progressive Disease (n=2)
Adverse Event (n=1)
60 week follow-up (n = 14)
Progressive Disease (n=9)
Adverse Event (n=1)
72 week follow-up (n = 4)
Progressive Disease (n=3)
Investigators decision (n=1)
72 week follow-up (n = 11)
Progressive Disease (n=2)
Toxicities (n=1)
96 week follow-up (n = 4)
96 week follow-up (n = 10)
Progressive Disease (n=1)
120 week follow-up (n = 3)
Progressive Disease (n=1)
120 week follow-up (n = 7)
Progressive Disease (n=3)
144 week follow-up (n = 2)
144 week follow-up (n = 3)

Baseline Characteristics

Table 1: Baseline characteristics of subjects recruited into the study

	All	**Treatment group**	**Control group**
Mean age (min-max)	63 (41-88)	63 (41-88)	64 (41-84)
AI Sensitivity (Sensitive or Naive/Prior AI)	69/71	36/33	33/38
Performance status (0/1/2)	80/53/7	38/29/2	42/24/5
Primary Tumour type (Ductal no specialty type/Lobular/other)	104/28/17	51/15/8	53/13/9
HER2 Status (Negative/Positive/Missing)	134/5/1	66/3/0	68/2/1
Surgery at diagnosis (Breast conserving/Mastectomy/Axillary procedure/None)	51/68/93/27	22/35/46/13	29/33/47/14
Endocrine Therapy(Tamoxifen/Anastrozole/Letrozole/Exemestane)	85/49/44/7	39/22/21/4	46/27/23/3
Disease site (Bone mets only/other)	8/132	2/67	6/65
Current Bisphosphonate use (Yes/No/Missing)	74/65/1	37/32/0	37/33/1
Mean of Sum of longest target lesions (min-max)	47.85 (10-177)	48.46 (10-177)	47.25 (10-147)

Outcome Measures

Primary outcome:

1. Progression Free Survival by treatment arm.

Arm	Total N	N of Events	Censored		Median 95% CI		
			N	Percent	Estimate	Lower bound	Upper bound
AI plus saracatinib	69	61	8	11.6%	3.733	1.419	6.048
AI plus placebo	71	67	4	5.6%	5.600	4.370	6.830
Overall	140	128	12	8.6%	5.433	3.698	7.169

Secondary Outcomes:

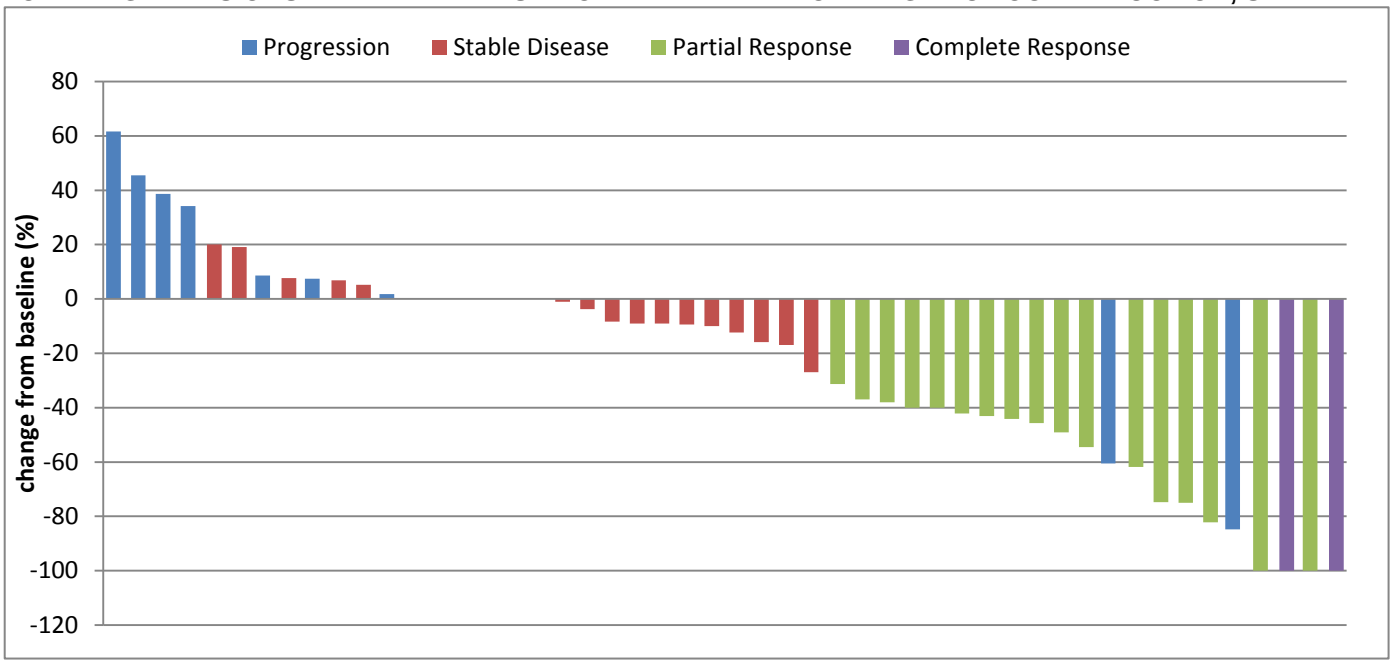
1. TOXICITY

		CTCAE (V4.0) GRADE				Percentage Safety Population							
	Arm	0-1	2	3	4	0-1	2	3	4	Mean Rank	Sum of Ranks	Mann-Whitney U	p value
ANAEMIA	AI plus saracatinib	66				98.51%				68.00	4488.00	2277.00	1.000
	AI plus placebo	69				100.00%				68.00	4692.00		
ALT	AI plus saracatinib	63	2			94.03%	2.99%			66.57	4327.00	2182.00	.729
	AI plus placebo	67	2			97.10%	2.90%			68.38	4718.00		
ALKALINE	AI plus	63	2	1		94.03%	2.99%	1.49%		67.83	4476.50	2265.50	.955

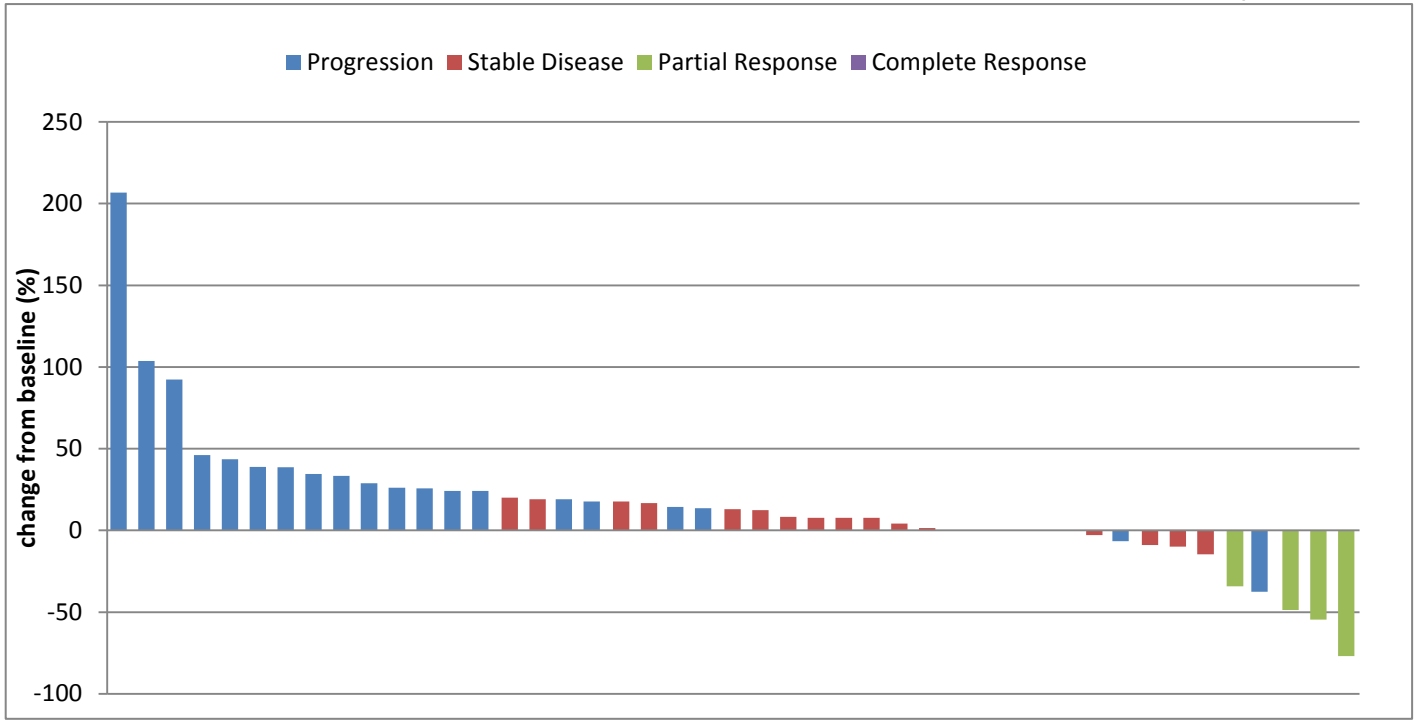
PHOSPHATASE	saracatinib												
	AI plus placebo	58	10	1		84.06%	14.49%	1.45%		68.17	4703.50		
PHOSPHATE	AI plus saracatinib	39	19	8		58.21%	28.36%	11.94%		79.65	5257.00	1442.00	.000
	AI plus placebo	64	4			92.75%	5.80%			55.71	3788.00		
Low SODIUM	AI plus saracatinib	66				98.51%				66.92	4417.00	2206.00	.626
	AI plus placebo	65	0	3	1	94.20%	0.00%	4.35%	1.45%	69.03	4763.00		
High SODIUM	AI plus saracatinib	66				98.51%				68.55	4524.00	2241.00	.535
	AI plus placebo	69				100.00				67.48	4656.00		
Low POTASSIUM	AI plus saracatinib	58	7			86.57%	10.45%			69.66	4528.00	2037.00	.073
	AI plus placebo	66	2			95.65%	2.90%			64.46	4383.00		
High POTASSIUM	AI plus saracatinib	64	0	1		95.52%	0.00%	1.49%		67.52	4389.00	2176.00	.306
	AI plus placebo	68				98.55%				66.50	4522.00		
NEUTROPENIA	AI plus saracatinib	63	2	1		94.03%	2.99%	1.49%		69.25	4570.50	2194.50	.571
	AI plus placebo	66	3			95.65%	4.35%			66.80	4604.50		
THROMBOCYTOPENIA	AI plus saracatinib	66				98.51%				66.55	4392.00	2181.00	.438
	AI plus placebo	67	1	0	1	97.10%	1.45%	0.00%	1.45%	69.39	4788.00		

2. Change in tumour size analysed using a Waterfall plot in the two strata separately

BEST RESPONSE FOR TARGET LESIONS BY PATIENT BASED ON MAXIMAL PERCENTAGE TUMOUR REDUCTION, STRATA= AI-Sensitive/naive



BEST RESPONSE FOR TARGET LESIONS BY PATIENT BASED ON MAXIMAL PERCENTAGE TUMOUR REDUCTION, STRATA=Prior AI



3. Overall Survival by treatment arm.

Arm	Total N	N of Events	Censored		Median 95% CI		
			N	Percent	Estimate	Lower bound	Upper bound
AI plus saracatinib	69	39	30	43.5%	24.067	16.990	31.143
AI plus placebo	71	41	30	42.3%	22.933	19.532	26.335
Overall	140	80	60	42.9%	22.933	18.178	27.688

Adverse Events

Frequency of Anticipated Adverse Event (non-life threatening) by treatment arm

	CTCAE (V4.0) GRADE							% Safety Population					
	Arm	0	1	2	3	4	Not Assessed	0	1	2	3	4	Not Assessed
FATIGUE	**AI plus saracatinib**	11	20	26	4		6	16.42%	29.85%	38.81%	5.97%		8.96%
	AI plus placebo	14	25	19	1		10	20.29%	36.23%	27.54%	1.45%		14.49%
NAUSEA	**AI plus saracatinib**	30	14	15	2		6	44.78%	20.90%	22.39%	2.99%		8.96%
	AI plus placebo	25	27	8	0		9	36.23%	39.13%	11.59%	0.00%		13.04%
VOMITING	**AI plus saracatinib**	40	16	3	3		5	59.70%	23.88%	4.48%	4.48%		7.46%
	AI plus placebo	49	9	1			10	71.01%	13.04%	1.45%			14.49%
ALOPECIA	**AI plus saracatinib**	44	15	2			6	65.67%	22.39%	2.99%			8.96%
	AI plus placebo	55	4				10	79.71%	5.80%				14.49%
NEUROPATHY	**AI plus saracatinib**	51	8	2			6	76.12%	11.94%	2.99%			8.96%
	AI plus placebo	50	9				10	72.46%	13.04%				14.49%
MUCOSITIS/ STOMATITIS	**AI plus saracatinib**	50	11	0	1		5	74.63%	16.42%	0.00%	1.49%		7.46%
	AI plus placebo	50	8	1			10	72.46%	11.59%	1.45%			14.49%
RASH/ DESQUAMATION	**AI plus saracatinib**	41	17	5	1		3	61.19%	25.37%	7.46%	1.49%		4.48%
	AI plus placebo	51	7	1			10	73.91%	10.14%	1.45%			14.49%
HYPERSENSITIVITY	**AI plus saracatinib**	58	3				6	86.57%	4.48%				8.96%
	AI plus placebo	58	1				10	84.06%	1.45%				14.49%
ANOREXIA	**AI plus saracatinib**	33	21	8			5	49.25%	31.34%	11.94%			7.46%
	AI plus placebo	46	10	3			10	66.67%	14.49%	4.35%			14.49%
DIARRHOEA	**AI plus saracatinib**	42	11	9	1		4	62.69%	16.42%	13.43%	1.49%		5.97%
	AI plus placebo	48	8	3			10	69.57%	11.59%	4.35%			14.49%
CONSTIPATION	**AI plus saracatinib**	44	12	6			5	65.67%	17.91%	8.96%			7.46%

	AI plus placebo	46	9	4			10	66.67%	13.04%	5.80%			14.49%
FEBRILE NEUTROPENIA	**AI plus saracatinib**	60	2				5	89.55%	2.99%				7.46%
	AI plus placebo	58	1				10	84.06%	1.45%				14.49%
INFECTION	**AI plus saracatinib**	44	4	13	5		1	65.67%	5.97%	19.40%	7.46%		1.49%
	AI plus placebo	36	11	16	4		2	52.17%	15.94%	23.19%	5.80%		2.90%

Frequency of Unanticipated Adverse Events (non-life threatening) by treatment arm

		CTCAE (V4.0) GRADE				**Percentage Safety Population**			
	Arm	**0-1**	**2**	**3**	**4**	**0-1**	**2**	**3**	**4**
ANAEMIA	**AI plus saracatinib**	66				98.51%			
	AI plus placebo	69				100.00%			
ALT	**AI plus saracatinib**	63	2			94.03%	2.99%		
	AI plus placebo	67	2			97.10%	2.90%		
ALKALINE PHOSPHATASE	**AI plus saracatinib**	63	2	1		94.03%	2.99%	1.49%	
	AI plus placebo	58	10	1		84.06%	14.49%	1.45%	
PHOSPHATE	**AI plus saracatinib**	39	19	8		58.21%	28.36%	11.94%	
	AI plus placebo	64	4			92.75%	5.80%		
Low SODIUM	**AI plus saracatinib**	66				98.51%			
	AI plus placebo	65	0	3	1	94.20%	0.00%	4.35%	1.45%
High SODIUM	**AI plus saracatinib**	66				98.51%			
	AI plus placebo	69				100.00			
Low POTASSIUM	**AI plus saracatinib**	58	7			86.57%	10.45%		
	AI plus placebo	66	2			95.65%	2.90%		
High POTASSIUM	**AI plus saracatinib**	64	0	1		95.52%	0.00%	1.49%	
	AI plus placebo	68				98.55%			
NEUTROPENIA	**AI plus saracatinib**	63	2	1		94.03%	2.99%	1.49%	
	AI plus placebo	66	3			95.65%	4.35%		
THROMBOCYTOPENIA	**AI plus saracatinib**	66				98.51%			
	AI plus placebo	67	1	0	1	97.10%	1.45%	0.00%	1.45%

Anticipated and Unanticipated Serious Adverse Events/SUSARs (Life Threatening)

Pt No	SAE Description	CTC Grade V4.0	SAE Type	Suspect drug	Aromatase Inhibitor	Causality Assessment of Site Investigator	Causality Assessment of CI	Expectedness Assessment of CI	SUSAR	SAE Outcome
9002	Creatinine increased	3	Death	Saracatinib	Exemestane	Probable	Probable	Unexpected	Y	Death
9004	Pain	3	Death	Saracatinib	Anastrozole	Unlikely	Unrelated	Unexpected	N	Death
9005	Sepsis	4	Life Threatening	Saracatinib	Exemestane	Possible	Possible	Unexpected	Y	Completely recovered
13010	Dyspnoea	2	Death	Saracatinib	Exemestane	Related	Related	Expected	N	Death