Figure 1. Participant Flow

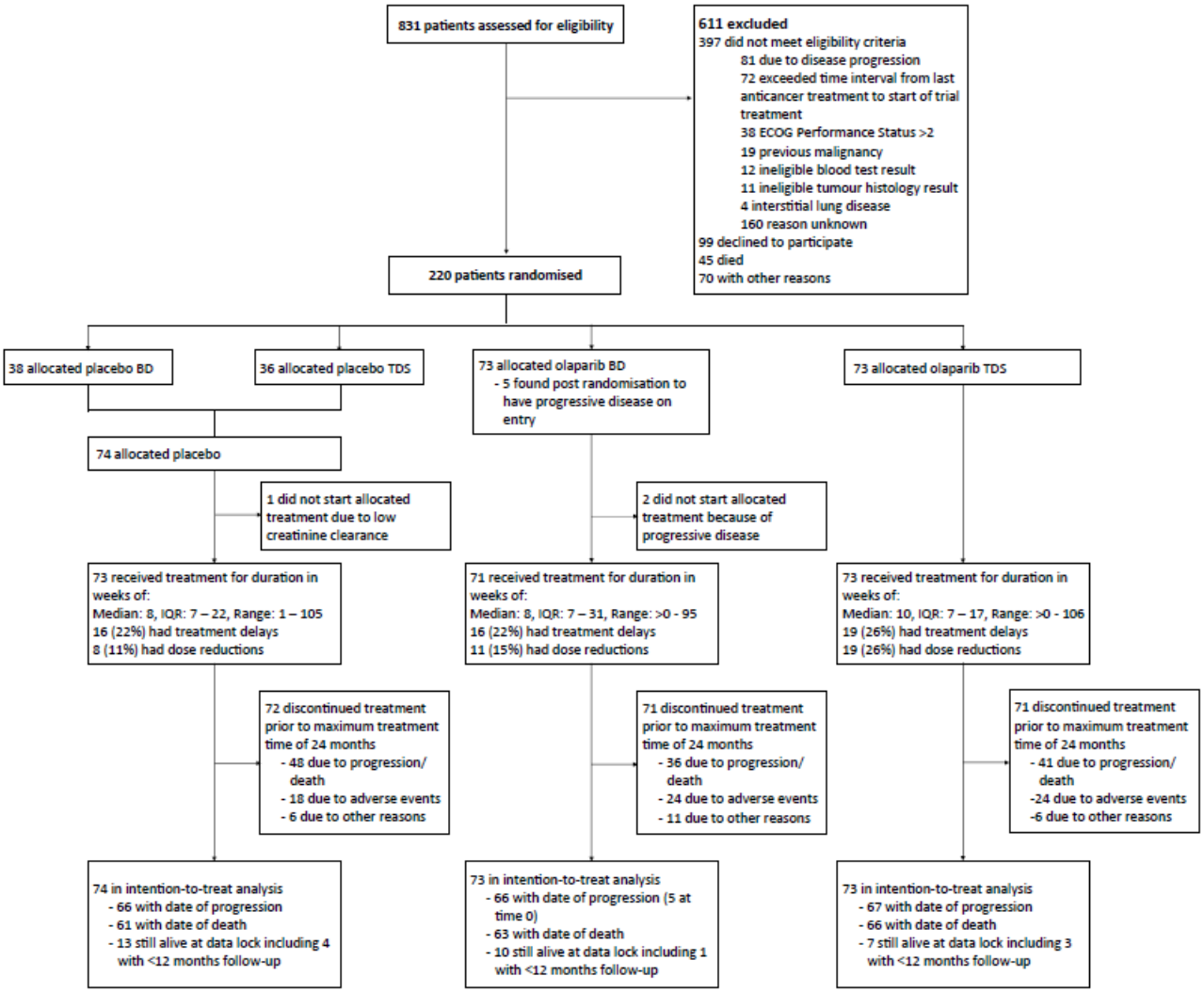

Table 1. Baseline patient characteristics

	Placebo N = 74	**Olaparib BD N = 73**	**Olaparib TDS N = 73**
Age, years			
Median	64	66	63
Inter-quartile range	58 – 68	58 – 70	55 – 69
Range	43 – 86	43 – 89	42 – 82
Sex, number (percent)			
Male	34 (46%)	36 (49%)	31 (42%)
Female	40 (54%)	37 (51%)	42 (58%)
Time from diagnosis to randomisation			
Weeks, median (range)	22 (15, 34)	25 (16, 38)	24 (15, 32)
Disease extent at diagnosis			
M0	21 (28%)	22 (30%)	23 (32%)
M1a	6 (8%)	6 (8%)	5 (7%)
M1b	47 (64%)	45 (62%)	45 (62%)
Chemotherapy regimen			
Carboplatin, etoposide	52 (70%)	56 (77%)	54 (74%)
Cisplatin, etoposide	18 (24%)	16 (22%)	13 (18%)
Cisplatin, carboplatin, etoposide	4 (5%)	1 (1%)	6 (8%)
Chemotherapy, number of cycles			
3	1 (1%)	0	2 (3%)
4	31 (42%)	27 (37%)	23 (32%)
5	5 (7%)	3 (4%)	4 (5%)
6	37 (50%)	43 (59%)	44 (60%)
Radiotherapy schedule			
Concurrent	10 (14%)	6 (8%)	4 (5%)
Sequential	57 (77%)	57 (78%)	61 (84%)
None	7 (9%)	10 (14%)	8 (11%)
Radiotherapy sites			
Thoracic & cranial	40 (54%)	33 (45%)	36 (49%)
Thoracic only	2 (3%)	5 (7%)	5 (7%)
Cranial only	25 (34%)	25 (34%)	24 (33%)
None	7 (9%)	10 (14%)	8 (11%)
Response to primary treatment			
Complete response	5 (7%)	4 (5%)	7 (10%)
Partial response	69 (93%)	64 (88%)	66 (90%)
Progression	0	5 (7%)	0
ECOG performance status			
0	18 (24%)	17 (23%)	25 (34%)
1	48 (65%)	51 (70%)	44 (60%)
2	8 (11%)	5 (7%)	3 (4%)
Not known	0	0	1 (1%)

Outcome Measures

Table 2. Primary outcome measure: Progression-free survival time measured from date of randomisation

	Placebo N = 74	**Olaparib BD N = 73**	**Olaparib TDS N = 73**
Progression-free survival time (PFS)			
Median PFS, months (90% CI)	2.5 (1.8, 3.7)	3.7 (3.1, 4.6)	3.6 (2.8, 4.7)
Comparison to placebo			
Hazard Ratio (90% CI)		0.76 (0.57, 1.02)	0.86 (0.64, 1.15)
p-value from stratified log-rank test		0.180	0.164
p-value from adjusted Cox model		0.125	0.402

Table 3. Secondary outcome measures: Progression-free (rate at 4 months), overall and quality-adjusted survival time outcomes measured from date of randomisation

	Placebo N = 74	**Olaparib BD N = 73**	**Olaparib TDS N = 73**
Progression-free survival (PFS)			
PFS rate at 4 months (90% CI)	36% (27, 45)	45% (35, 54)	45% (35, 54)
Overall survival time (OS)			
Median OS, months (90% CI)	9.7 (7.1, 12.2)	11.0 (7.9, 12.9)	9.6 (6.8, 11.8)
OS rate at 6 months (90% CI)	66% (56, 75)	69% (60, 77)	66% (56, 75)
Comparison to placebo			
Hazard ratio (90% CI)		0.85 (0.63, 1.15)	1.03 (0.77, 1.39)
p-value from stratified log-rank test		0.709	0.990
p-value from adjusted Cox model		0.376	0.850
Quality-adjusted life weeks within 6 months of trial entry (QALM6)			
Mean QALM6 (90% CI)	3.2 (2.8, 3.5)	3.0 (2.7, 3.3)	3.2 (2.9, 3.6)

Table 4. Secondary outcome measure: Key adverse events reported in the trial (Note: events are included if their overall incidence in the trial is ≥ 10% and/or there was >1 patient experiencing the event at grade 3 or above). Data are shown as number (percentage) of patients who experienced the event at least once.

	Placebo N = 74		**Olaparib BD N = 73**		**Olaparib TDS N = 73**	
	All	**G3+**	**All**	**G3+**	**All**	**G3+**
At least one AE reported	72 (97%)	33 (45%)	70 (96%)	38 (53%)	72 (99%)	36 (49%)
Haematological						
Anaemia	15 (20%)	0	37 (51%)	4 (5%)	41 (56%)	11 (15%)
Leucopenia	0	0	3 (4%)	3 (4%)	1 (1%)	1 (1%)
Lymphopenia	0	0	8 (11%)	8 (11%)	9 (12%)	9 (12%)
Neutropenia	0	0	5 (7%)	5 (7%)	2 (3%)	2 (3%)
Thrombocytopenia	2 (3%)	2 (3%)	4 (5%)	4 (5%)	5 (7%)	5 (7%)
Non-Haematological						
Constipation	19 (26%)	0	16 (22%)	0	14 (19%)	1 (1%)
Diarrhoea	18 (24%)	3 (4%)	13 (18%)	1 (1%)	12 (16%)	2 (3%)
Dyspepsia	12 (18%)	0	11 (15%)	1 (1%)	6 (8%)	0
Nausea	44 (59%)	2 (3%)	47 (64%)	1 (1%)	51 (70%)	2 (3%)
Vomiting	21 (28%)	3 (4%)	25 (34%)	0	33 (45%)	2 (3%)
Fatigue	55 (74%)	10 (14%)	64 (88%)	16 (22%)	58 (79%)	7 (10%)
Chest Pain	9 (12%)	0	10 (14%)	0	3 (4%)	0
Respiratory infection	15 (20%)	5 (7%)	21 (29%)	2 (3%)	22 (30%)	6 (8%)
Anorexia	30 (41%)	0	34 (47%)	2 (3%)	28 (38%)	2 (3%)
Hypomagnesemia	5 (7%)	2 (3%)	2 (3%)	0	1 (1%)	0
Hyponatraemia	12 (16%)	7 (9%)	7 (10%)	3 (4%)	10 (14%)	4 (5%)
Arthralgia	17 (23%)	0	6 (8%)	0	9 (12%)	0
Back pain	18 (24%)	1 (1%)	13 (18%)	0	14 (19%)	2 (3%)
Dizziness	14 (19%)	0	16 (22%)	0	15 (21%)	0
Dysgeusia	12 (16%)	0	12 (16%)	0	12 (16%)	0
Headache	18 (24%)	0	19 (26%)	1 (1%)	17 (23%)	0
Insomnia	10 (14%)	0	8 (11%)	0	5 (7%)	1 (1%)
Cough	27 (36%)	0	25 (34%)	0	27 (37%)	0
Dyspnoea	21 (28%)	3 (4%)	26 (36%)	1 (1%)	28 (38%)	3 (4%)
Pneumonia	0	0	0	0	4 (5%)	2 (3%)
Alopecia	11 (15%)	0	13 (18%)	0	16 (22%)	0
Hypertension	8 (11%)	3 (4%)	5 (7%)	1 (1%)	4 (5%)	1 (1%)
Thromboembolic Event	3 (4%)	2 (3%)	3 (4%)	1 (1%)	6 (8%)	3 (4%)

Adverse events

Table 5: All adverse events reported in the trial shown at any grade and grade 3 or above. Data shown as number (percentage) of patients who experienced the event at least once.

	Placebo N = 74		**Olaparib BD N = 73**		**Olaparib TDS N = 73**	
	All	**G3+**	**All**	**G3+**	**All**	**G3+**
At least one AE reported	72 (97%)	33 (45%)	70 (96%)	38 (53%)	72 (99%)	36 (49%)
Blood and lymphatic						
Anaemia	15 (20%)	0	37 (51%)	4 (5%)	41 (56%)	11 (15%)
Leucopenia	0	0	3 (4%)	3 (4%)	1 (1%)	1 (1%)
Lymphopenia	0	0	8 (11%)	8 (11%)	9 (12%)	9 (12%)
Neutropenia	0	0	5 (7%)	5 (7%)	2 (3%)	2 (3%)
Neutropenic sepsis	0	0	0	0	1 (1%)	1 (1%)
Thrombocytopenia	2 (3%)	2 (3%)	4 (5%)	4 (5%)	5 (7%)	5 (7%)
Cardiac						
Atrial fibrillation	0	0	2 (3%)	1 (1%)	0	0
Heart failure	0	0	1 (1%)	1 (1%)	0	0
Ear and labyrinth						
Hearing impaired	2 (3%)	0	3 (4%)	0	3 (4%)	1 (1%)
Gastrointestinal						
Abdominal Pain	6 (8%)	0	6 (8%)	0	8 (11%)	0
Constipation	19 (26%)	0	16 (22%)	0	14 (19%)	1 (1%)
Diarrhoea	18 (24%)	3 (4%)	13 (18%)	1 (1%)	12 (16%)	2 (3%)
Dyspepsia	12 (18%)	0	11 (15%)	1 (1%)	6 (8%)	0
Dysphagia	5 (7%)	0	5 (7%)	1 (1%)	3 (4%)	1 (1%)
Melaena	0	0	1 (1%)	0	1 (1%)	1 (1%)
Mucositis	10 (14%)	0	8 (11%)	0	2 (3%)	1 (1%)
Nausea	44 (59%)	2 (3%)	47 (64%)	1 (1%)	51 (70%)	2 (3%)
Oesophageal stenosis	0	0	0	0	1 (1%)	1 (1%)
Rectal haemorrhage	0	0	0	0	1 (1%)	1 (1%)
Vomiting	21 (28%)	3 (4%)	25 (34%)	0	33 (45%)	2 (3%)
General						
Fatigue	55 (74%)	10 (14%)	64 (88%)	16 (22%)	58 (79%)	7 (10%)
Deteriorating condition	0	0	1 (1%)	1 (1%)	0	0
Gait disturbance	1 (1%)	0	1 (1%)	1 (1%)	1 (1%)	0
Chest Pain	9 (12%)	0	10 (14%)	0	3 (4%)	0
Sudden death NOS	1 (1%)	1 (1%)	0	0	0	0
Infections and infestations						
Respiratory infection	15 (20%)	5 (7%)	21 (29%)	2 (3%)	22 (30%)	6 (8%)
Sepsis	1 (1%)	1 (1%)	1 (1%)	1 (1%)	0	0
Urinary tract infection	3 (4%)	1 (1%)	3 (4%)	0	6 (8%)	1 (1%)
Injury, poisoning and procedures						
Injury to right of chest	1 (1%)	1 (1%)	0	0	0	0
Spinal fracture	1 (1%)	1 (1%)	0	0	0	0
Splenic rupture	1 (1%)	1 (1%)	0	0	0	0
Investigations						

Alanine Aminotransferase increased	1 (1%)	1 (1%)	0	0	1 (1%)	1 (1%)
Aspartate aminotransferase increased	1 (1%)	1 (1%)	0	0	0	0
GGT Increased	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)
C-reactive protein increased	0	0	0	0	1 (1%)	1 (1%)
Metabolism and nutrition						
Anorexia	30 (41%)	0	34 (47%)	2 (3%)	28 (38%)	2 (3%)
Dehydration	1 (1%)	1 (1%)	3 (4%)	1 (1%)	2 (3%)	1 (1%)
Hypocalcaemia	2 (3%)	0	9 (12%)	0	3 (4%)	0
Hypokalaemia	4 (5%)	0	4 (5%)	0	4 (5%)	1 (1%)
Hypomagnesemia	5 (7%)	2 (3%)	2 (3%)	0	1 (1%)	0
Hyponatraemia	12 (16%)	7 (9%)	7 (10%)	3 (4%)	10 (14%)	4 (5%)
Hypophosphatemia	1 (1%)	1 (1%)	3 (4%)	0	2 (3%)	0
Musculoskeletal and connective tissue						
Arthralgia	17 (23%)	0	6 (8%)	0	9 (12%)	0
Back pain	18 (24%)	1 (1%)	13 (18%)	0	14 (19%)	2 (3%)
Flank pain	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)
General muscle weakness	2 (3%)	1 (1%)	0	0	1 (1%)	0
Muscle Weakness Lower Limb	2 (3%)	0	3 (4%)	1 (1%)	3 (4%)	1 (1%)
Muscle Weakness right side	0	0	0	0	1 (1%)	1 (1%)
Pain in extremity	2 (3%)	0	13 (18%)	0	5 (7%)	0
Spinal cord compression	1 (1%)	1 (1%)	0	0	0	0
Nervous system						
Dizziness	14 (19%)	0	16 (22%)	0	15 (21%)	0
Dysarthria	0	0	0	0	2 (3%)	1 (1%)
Dysgeusia	12 (16%)	0	12 (16%)	0	12 (16%)	0
Headache	18 (24%)	0	19 (26%)	1 (1%)	17 (23%)	0
Neuralgia	1 (1%)	1 (1%)	0	0	0	0
Paraesthesia	5 (7%)	0	2 (3%)	0	7 (10%)	1 (1%)
Peripheral sensory neuropathy	2 (3%)	0	3 (4%)	1 (1%)	4 (5%)	0
Seizure	1 (1%)	0	1 (1%)	0	2 (3%)	1 (1%)
Stroke	1 (1%)	1 (1%)	0	0	1 (1%)	1 (1%)
Psychiatric						
Anxiety	8 (11%)	0	2 (3%)	0	4 (5%)	0
Confusion	3 (4%)	1 (1%)	1 (1%)	1 (1%)	5 (7%)	0
Insomnia	10 (14%)	0	8 (11%)	0	5 (7%)	1 (1%)
Renal and urinary						
Urinary incontinence	2 (3%)	1 (1%)	1 (1%)	0	1 (1%)	0
Respiratory, thoracic and mediastinal						
Cough	27 (36%)	0	25 (34%)	0	27 (37%)	0
Dyspnoea	21 (28%)	3 (4%)	26 (36%)	1 (1%)	28 (38%)	3 (4%)
Hypoxia	0	0	0	0	1 (1%)	1 (1%)
Pleural effusion	1 (1%)	1 (1%)	0	0	0	0

Pneumonia	0	0	0	0	4 (5%)	2 (3%)
Pneumonitis	0	0	1 (1%)	0	3 (4%)	1 (1%)
Respiratory failure	1 (1%)	1 (1%)	0	0	0	0
Skin and subcutaneous tissue						
Alopecia	11 (15%)	0	13 (18%)	0	16 (22%)	0
Dry skin	5 (7%)	0	6 (8%)	1 (1%)	4 (5%)	0
Pruritis	7 (9%)	1 (1%)	4 (5%)	0	4 (5%)	0
Rash	8 (11%)	0	5 (7%)	0	5 (7%)	0
Vascular						
Hypertension	8 (11%)	3 (4%)	5 (7%)	1 (1%)	4 (5%)	1 (1%)
Hypotension	1 (1%)	0	1 (1%)	0	4 (5%)	1 (1%)
Superior vena cava syndrome	1 (1%)	1 (1%)	0	0	0	0
Thromboembolic Event	3 (4%)	2 (3%)	3 (4%)	1 (1%)	6 (8%)	3 (4%)

Table 5. Serious Adverse Events in the Placebo subgroup

Category	Toxicity	Affected	Exposed	Occurrences	Related	Fatal	Related & Fatal	Percentage Affected
Cardiac disorders	Left ventricular systolic dysfunction	1	73	1	1	0	0	1
Gastrointestinal disorders	Nausea	1	73	1	1	0	0	1
	Vomiting	3	73	3	3	0	0	4
General disorders and administration site conditions	Chills	1	73	1	0	0	0	1
Infections and infestations	Lung infection	4	73	4	0	0	0	5
	Urinary tract infection	1	73	1	1	0	0	1
Injury, poisoning and procedural complications	Splenic Rupture	1	73	1	0	0	0	1
Metabolism and nutrition disorders	Hyponatremia	2	73	2	0	1	0	3
Musculoskeletal and connective tissue disorders	Back pain	1	73	1	0	0	0	1
	Bone pain	1	73	1	0	0	0	1
	Generalized muscle weakness	1	73	1	0	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Neoplasms Benign, Malignant And Unspecified	1	73	1	0	0	0	1
	New Primary Tumour	1	73	1	0	0	0	1
Nervous system disorders	Ischemia cerebrovascular	1	73	1	0	0	0	1
	Peripheral motor neuropathy	1	73	1	0	0	0	1
	Seizure	1	73	1	0	0	0	1
Psychiatric disorders	Confusion	1	73	1	0	0	0	1
Respiratory, thoracic and mediastinal disorders	Dyspnea	4	73	4	0	0	0	5
Vascular disorders	Superior vena cava syndrome	1	73	1	0	0	0	1
	Thromboembolic event	1	73	1	0	0	0	1

Table 6. Serious Adverse Events in the olaparib BD subgroup

Category	Toxicity	Affected	Exposed	Occurrences	Related	Fatal	Related & Fatal	Percentage Affected
Blood and lymphatic system disorders	Anemia	5	71	5	5	0	0	7
	Pancytopenia	1	71	1	1	0	0	1
Cardiac disorders	Atrial fibrillation	1	71	1	1	0	0	1
Eye disorders	Double Vision	1	71	1	0	0	0	1
Gastrointestinal disorders	Nausea	1	71	1	1	0	0	1
General disorders and administration site conditions	Fatigue	2	71	2	2	0	0	3
	Fever	1	71	1	0	0	0	1
	Deteriorating Condition	1	71	1	0	0	0	1
Infections and infestations	Lung infection	1	71	1	0	0	0	1
	Sepsis	1	71	1	0	0	0	1
	Upper respiratory infection	1	71	1	0	0	0	1
Investigations	Platelet count decreased	1	71	1	1	0	0	1
Metabolism and nutrition disorders	Anorexia	1	71	1	1	0	0	1
Musculoskeletal and connective tissue disorders	Back pain	1	71	2	0	0	0	1
	Flank pain	1	71	1	1	0	0	1
	Pain in extremity	1	71	1	0	0	0	1
Nervous system disorders	Headache	1	71	1	0	0	0	1
Respiratory, thoracic and mediastinal disorders	Dyspnea	1	71	1	0	0	0	1
	Pneumonitis	1	71	1	0	0	0	1
Vascular disorders	Thromboembolic event	1	71	1	1	0	0	1

Table 7. Serious Adverse Events in the olaparib TDS subgroup

Category	Toxicity	Affected	Exposed	Occurrences	Related	Fatal	Related & Fatal	Percentage Affected
Blood and lymphatic system disorders	Anemia	5	73	5	5	0	0	7
	Neutropenic Sepsis	1	73	1	1	0	0	1
Gastrointestinal disorders	Constipation	1	73	1	0	1	0	1
	Diarrhea	2	73	2	1	0	0	3
	Mucositis oral	1	73	1	1	0	0	1
	Nausea	2	73	2	1	0	0	3
	Vomiting	1	73	1	1	0	0	1
	Melaena	1	73	1	0	0	0	1
General disorders and administration site conditions	Fever	1	73	1	1	0	0	1
Infections and infestations	Conjunctivitis infective	1	73	1	0	0	0	1
	Lung infection	5	73	6	1	0	0	7
	Sepsis	1	73	1	0	1	0	1
	Urinary tract infection	1	73	1	0	0	0	1
Investigations	Neutrophil count decreased	1	73	1	1	0	0	1
Metabolism and nutrition disorders	Dehydration	1	73	1	0	0	0	1
Musculoskeletal and connective tissue disorders	Flank pain	1	73	1	1	0	0	1
	Muscle weakness lower limb	1	73	1	0	0	0	1
	Muscle weakness right-sided	1	73	1	0	0	0	1
Nervous system disorders	Intracranial hemorrhage	1	73	1	0	0	0	1
	Ischemia cerebrovascular	1	73	1	0	1	0	1
	Seizure	2	73	2	0	1	0	3
Psychiatric disorders	Confusion	1	73	1	0	0	0	1
Respiratory, thoracic and mediastinal disorders	Dyspnea	3	73	4	0	0	0	4
	Pneumonitis	1	73	1	1	0	0	1
	Acute Exacerbation Of Copd	1	73	1	0	0	0	1
	Pneumonia	2	73	2	1	2	1	3
Vascular disorders	Thromboembolic event	1	73	1	0	0	0	1