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Study No.: ARI40006
Title: A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer
Rationale: Prostate adenocarcinoma is the most common non-cutaneous cancer, and the second leading cause of cancer death in men worldwide. In most cases, however, it is a slowly progressive disease. Although the aggressive forms of prostate cancer are associated with poor outcomes and decreased survival, the most frequent harm derived from the majority of prostate cancers is not death, but morbidity and complications from treatment. Therefore, any strategy that reduces the risk of biopsy detectable prostate cancer, either by avoiding or slowing its development or delaying its growth, will reduce the overall health burden of the disease. Pooled data from Phase IIIa BPH studies with dutasteride showed that the cumulative incidence of prostate cancer reported as adverse events in a BPH population was significantly lower versus placebo at 24 months. Results from longer-term follow-up indicate a decrease of 50% over 27 months (1.2% dutasteride vs 2.5% placebo, $p=0.002$). Study ARI40006 was developed to determine the efficacy and safety of long-term treatment with dutasteride to reduce the risk of biopsy detectable prostate cancer in a population at increased risk of developing the disease.
Phase: III
Study Period: 06 March 2003 – 11 May 2009
Study Design: International, multicenter, randomized, double-blind, placebo-controlled, parallel group study
Centres: 821 investigators in 42 countries
Indication: Prostate cancer risk reduction
Treatment: Dutasteride 0.5 mg or matched placebo
Objectives: To assess the effect of repeat oral once daily dosing of 0.5 mg dutasteride compared to placebo on the risk of biopsy-detectable carcinoma of the prostate after 2 years and 4 years of treatment
Primary Outcome/Efficacy Variable: The primary efficacy endpoint was biopsy-detectable prostate cancer at Year 2 and at Year 4
Secondary Outcome/Efficacy Variable(s): Gleason score at diagnosis, occurrence and quantity of high grade prostatic intraepithelial neoplasia (HGPIN) at biopsy, percentage of core involved at diagnosis, number of cancer positive cores, treatment alteration score, incidence of intervention (surgical and non-surgical) for treatment of prostate cancer, benign prostate hyperplasia (BPH) symptom scores as assessed by International Prostate Symptom Score (IPSS), prostate volume, Maximum urine flow, use of alpha blockers to control BPH symptoms, acute urinary retention (AUR), urinary tract infections (UTI), post-biopsy macroscopic hematuria/hemospermia, overall survival, levels of serum testosterone and dihydrotestosterone (DHT), health outcome measures: impact on quality of life assessments (i.e., QOL Q8, BII, MOS Sleep-6S, NIH CPSI, and PAS SFI).
Statistical Methods: The comparison between the 0.5 mg dutasteride group and the placebo group for grouped time to biopsy-detectable prostate cancer after 2 years and after 4 years of treatment was the primary comparison of interest. The primary endpoint of the study was time to biopsy-detectable prostate cancer. With S_{dut} and S_{pbo} representing the distribution of time to biopsy-detectable prostate cancer for the two treatment groups, then the null and alternative hypotheses tested were that $S_{dut} = S_{pbo}$ or that $S_{dut} \neq S_{pbo}$, respectively. Enrollment of 4000 subjects per treatment group was planned in order to provide 51% power to detect a treatment difference using a two-sided test at the 0.001 significance level after 2 years of treatment and 94% power to detect a treatment difference using a two-sided test at the 0.01 significance level after 4 years of treatment. The Efficacy Population was the primary efficacy analysis population and consisted of all randomized subjects with a negative entry prostate biopsy as determined by the Central Pathology Laboratory and who received at least one dose of study treatment. The Safety Population consisted of all randomized subjects (subjects who had a treatment number assignment or a double-blind treatment start date). The Biopsied population consisted of all subjects in the Efficacy population who had at least one post-baseline biopsy reviewed by the Central Pathology Laboratory. The primary analysis of the primary endpoint at Year 4 was performed using the Mantel-Cox test (i.e., the life-table extension of the Mantel-Haenszel test) stratified by site cluster and time period (Year 1-2 and Year 3-4). Relative risk (0.5mg dutasteride treatment vs. placebo), relative risk reduction, and 95% confidence intervals for the relative risk reduction were computed based on the Mantel-Haenszel estimate of the relative risk. The primary analysis of the primary endpoint was performed using the crude rate analysis approach for determining

the risk set (including all subjects at risk at the beginning of each time period). To investigate the sensitivity of the results to the method of handling biopsy data, two types of alternative analyses were also conducted: the restricted crude rate analysis approach (including all subjects biopsied in each time period), and the modified crude rate analysis approach (including subjects diagnosed with prostate cancer and subjects having protocol-specified biopsies).		
Study Population: Male subjects only, aged ≥ 50 and ≤ 75 years (≤ 71 years in France) at increased risk of prostate cancer as defined by PSA ≥ 2.5 ng/mL and ≤ 10 ng/mL (men aged 50-60 years) or ≥ 3.0 ng/mL and ≤ 10 ng/mL (men >60 years) with a single, recent negative prostate biopsy of 6 to 12 cores in the preceding 6 calendar months (negative biopsy was confirmed by Central Pathology review). Subjects were excluded from the study if they had: more than one prior negative prostate biopsy, a history of prostate cancer, prior prostate surgery, evidence of HGPIN or ASAP on entry biopsy, history of AUR within the previous 2 years, prostate volume >80 cc, post-void residual volume (PVRV) >200 mL, maximum flow rate (Qmax) <5 mL/sec, or severe prostatism as manifested by an IPSS symptom score (calculated using the first 7 questions only) of ≥ 25 or ≥ 20 if already on alpha blocker therapy for BPH, causes other than BPH which might result in urinary symptoms or changes in flow rate, history of prior malignancies in the past 5 years (other than basal or squamous cell carcinoma), ALT, AST or ALP >2 times the upper limit of normal, or bilirubin or serum creatinine >1.5 times the upper limit of normal, known hypersensitivity to 5ARIs or related drugs, concomitant and/or previous use (within the past 12 months) of drugs with antiandrogenic properties, anabolic steroids or 5ARIs or had serious co-existing unstable medical conditions.		
	Placebo	Dutasteride
Number of Subjects:		
Planned, N	4000	4000
Randomized (Safety Population), N	4126	4105
Completed, n (%)	2915 (71)	2912 (71)
Total Number Subjects Withdrawn, N (%)	1211 (29)	1193 (29)
Withdrawn due to Adverse Events n (%)	282 (23)	364 (31)
Withdrawn due to Lack of Efficacy n (%)	n/a	n/a
Withdrawn for other reasons n (%)	929 (77)	829 (69)
Demographics (Safety Population)		
	Placebo	Dutasteride
Males	4126	4105
Mean Age, years (SD)	62.7 (6.08)	62.8 (6.04)
Median Age, years (min.-max.)	63.0 (48.0 to 77.0)	63.0 (49.0 to 76.0)
White, n (%)	3747 (91)	3744 (91)
Primary Efficacy Results:		
Efficacy Population, N	4073	4049
Incidence of prostate cancer--crude rate approach (Efficacy Population)	Placebo N=4073	Dutasteride N=4049
Years 1-2		
Prostate cancers/subjects at risk, n (%)	578/4073 (14.2)	435/4049(10.7)
Mantel-Cox p-value	<0.0001	
Relative risk estimate for dutasteride (95% confidence interval [CI])	0.76 (0.67, 0.85)	
Relative risk reduction vs placebo, % (95% CI)	24.3 (15.0, 32.6)	
Overall		
Prostate cancers/subjects at risk, n (%)	858/4073 (21.1)	659/4049 (16.3)
Mantel-Cox p-value	<0.0001	
Relative risk estimate (95% CI)	0.77 (0.70, 0.84)	
Relative risk reduction, % (95% CI)	23.3 (15.6, 30.3)	
Incidence of prostate cancer--modified crude rate approach (Efficacy Population)	Placebo N=4073	Dutasteride N=4049
Years 1-2		
Prostate cancers/subjects at risk, n (%)	578/3319 (17.4)	435/3209 (13.6)
Mantel-Cox p-value	<0.0001	
Relative risk estimate for dutasteride (95% Confidence Interval [CI])	0.77 (0.69, 0.87)	
Relative risk reduction vs placebo, % (95% CI)	22.6 (13.2, 30.9)	
Overall		
Prostate cancers/subjects at risk, n (%)	858/2903 (29.6)	659/2869 (23.0)
Mantel-Cox p-value	<0.0001	
Relative risk estimate (95% CI)	0.77 (0.70, 0.84)	

Relative risk reduction, % (95% CI)	23.1 (15.5,30.0)	
Incidence of prostate cancer--restricted crude rate approach (Efficacy Population)	Placebo N=4073	Dutasteride N=4049
Years 1-2		
Prostate cancers/subjects at risk, n (%)	578/3364 (17.2)	435/3244 (13.4)
Mantel-Cox p-value	<0.0001	
Relative risk estimate (95% CI)	0.78 (0.69, 0.87)	
Relative risk reduction, % (95% CI)	22.4 (13.0, 30.8)	
Overall		
Prostate cancers/subjects at risk, n (%)	858/3424 (25.1)	659/3305 (19.9)
Mantel-Cox p-value	<0.0001	
Relative risk estimate (95% CI)	0.77 (0.70, 0.85)	
Relative risk reduction, % (95% CI)	22.8 (15.2, 29.8)	
Secondary Outcome Variable(s):		
Gleason score at diagnosis (Biopsied population)	Placebo	Dutasteride
Overall	n=3407	n=3299
Gleason score 2 – 6, n (%)	617 (18.1)	437 (13.2)
Gleason score 7 – 10, n (%)	233 (6.8)	220 (6.7)
Gleason score 8 – 10, n (%)	19 (0.6)	29 (0.9)
Overall occurrence of HGPIN at biopsy (Biopsied Population)	Placebo N=3424	Dutasteride N=3305
HGPIN and/or prostate cancer diagnosis, n/N (%)	1126/ 3424 (33)	810/ 3305 (25)
HGPIN and no prostate cancer, n/N (%)	268/ 3424 (8)	151/ 3305 (5)
HGPIN and no ASAP and no prostate cancer, n/N (%)	206/3424 (6)	121/3305 (4)
HGPIN and/or ASAP, n/N (%)	675/3424 (20)	409/3305 (12)
HGPIN and/or ASAP and no prostate cancer, n/N (%)	373/3424 (11)	248/3305 (8)
HGPIN, ASAP and/or prostate cancer diagnosis, n/N (%)	1231/3424 (36)	907/3305 (27)
Volume of HGPIN (ccx10⁻³) at biopsy (Biopsied Population)		
n=number of subjects	3403	3297
Mean (SD)	0.1105 (0.52753)	0.0446 (0.27710)
Percentage of core involved at diagnosis (Prostate Cancer Population)	Placebo N=858	Dutasteride N=659
n=number of subjects with needle biopsies	849	657
Mean percentage (SD) %	13.4 (14.84)	12.2 (13.00)
Number of cancer positive cores (Prostate Cancer Population)	Placebo N=858	Dutasteride N=659
n= number of subjects with needle biopsies	850	656
Mean (SD) %	1.9 (1.31)	1.8 (1.33)

Treatment alteration score (Biopsied Population)	Placebo N=3424	Dutasteride N=3305
Nuclear (Overall n)	3357	3256
Mean (SD)	0.008 (0.1116)	0.019 (0.1734)
Architectural (Overall n)	3357	3258
Mean (SD)	0.009 (0.1289)	0.023 (0.2112)
Total (Overall n)	3357	3256
Mean (SD)	0.017 (0.2336)	0.041 (0.3737)
Overall incidence of intervention (surgical and non-surgical) for prostate cancer treatment (Efficacy Population)	Placebo N=4073	Dutasteride N=4049
Any intervention, n(%)	438 (10.8)	300 (7.4)
Any surgical intervention, n(%)	304 (7)	221 (5)
Any non-surgical intervention, n(%)	172 (4)	95 (2)
IPSS change from baseline (Efficacy Population, LOCF=Last Observation Carried Forward)	Placebo N=4073	Dutasteride N=4049
Month 48, n	3847	3815
Adjusted mean (SE)	1.35 (0.087)	-0.46 (0.087)
Prostate volume percentage change from baseline (Efficacy Population, LOCF)	Placebo N=4073	Dutasteride N=4049
Year 4, n	3289	3194
Adjusted mean % change from baseline (SE)	19.7 (0.77)	-17.5 (0.54)
Maximum urine flow (mL/sec) change from baseline (Efficacy Population, LOCF)	Placebo N=4073	Dutasteride N=4049
Month 48, n	1390	1359
Adjusted Mean (SE)	-0.9 (0.303)	0.41 (0.307)
Percentage of subjects starting alpha blockers to control BPH symptoms (Efficacy Population)	Placebo N=4073	Dutasteride N=4049
Overall, n (%)	770 (18.9)	515 (12.7)
AUR (Efficacy Population)	N=4073	N=4049
Number (%) of subjects with at least one AUR	272 (6.7)	63 (1.6)
UTI (Efficacy Population)	N=4073	N=4049
Number (%) of subjects with at least one UTI	360 (8.8)	214 (5.3)
Post-biopsy macroscopic hematuria (Efficacy Population)	N=4073	N=4049
Subjects with hematuria, n (%)	168 (4.1)	127 (3.1)
Post-biopsy macroscopic hematospermia (Efficacy Population)	N=4073	N=4049
Subjects with hematospermia, n (%)	78 (1.9)	53 (1.3)
Overall survival (Efficacy Population)	N=4073	N=4049
Number of deaths/ subjects at risk (%)	77/4073 (1.9)	70/4049 (1.7)
Deaths due to prostate cancer, n (%)	0	0
Health outcomes measures, change from baseline to Month 48 (Efficacy Population, LOCF)	Placebo N=4073	Dutasteride N=4049
BII, n	3733	3727
Adjusted mean (SE)	0.44 (0.037)	-0.21 (0.037)
MOS Sleep-6S, n	3726	3709
Adjusted mean (SE)	-0.03 (0.211)	0.02 (0.212)
NIH CPSI, n	2576	2590
Adjusted mean (SE)	0.94 (0.123)	-0.37 (0.123)
QOL Q8, n	3853	3821
Adjusted mean (SE)	-0.06 (0.018)	-0.33 (0.018)
PASSFI, n	3413	3329
Adjusted mean (SE)	-0.82 (0.064)	-1.5 (0.065)
Serum DHT concentration (nmol/L) (Efficacy Population, LOCF)	Placebo N=4073	Dutasteride N=4049
Month 48, n	3865	3822
≤0.555, n (%)	493 (13)	3414 (89)

Below quantification limit, n (%)	42 (1)	2210 (58)
Percent change from baseline in testosterone (Efficacy Population, LOCF)	Placebo N=4073	Dutasteride N=4049
Month 48, n	3841	3796
Adjusted mean	-6.1	12.7
Adjusted mean difference, (95% CI)	18.8 (17.3, 20.4)	
Safety Results: Treatment emergent on-therapy AEs and SAEs were defined as those with onset on or after study medication start date, through the safety follow-up period.		
	Placebo N=4126	Dutasteride N=4105
Most Frequent Adverse Events – On-Therapy	n (%)	n (%)
Subjects with any AE(s)	2966 (72)	3017 (73)
Erectile dysfunction	363 (9)	494 (12)
Hypertension	330 (8)	355 (9)
Nasopharyngitis	288 (7)	313 (8)
Back pain	247 (6)	265 (6)
Influenza	213 (5)	204 (5)
Arthralgia	159 (4)	176 (4)
Libido decreased	90 (2)	167 (4)
Bronchitis	112 (3)	144 (4)
Headache	127 (3)	142 (3)
Hypercholesterolemia	141 (3)	139 (3)
Upper respiratory tract infection	155 (4)	132 (3)
Prostatitis	150 (4)	102 (2)
	Placebo N=4126	Dutasteride N=4105
	n (%) [related]	n (%) [related]
Subjects with non-fatal SAEs, n (%) [number related]	784 (19) [18]	699 (17) [15]
Osteoarthritis	26 (<1) [0]	39 (<1) [0]
Coronary artery disease	22 (<1) [1]	35 (<1) [1]
Myocardial infarction	30 (<1) [3]	31 (<1) [2]
Inguinal hernia	28 (<1) [0]	31 (<1) [0]
Pneumonia	24 (<1) [1]	21 (<1) [0]
Cerebrovascular accident	14 (<1) [0]	19 (<1) [0]
Atrial fibrillation	21 (<1) [0]	18 (<1) [0]
Cholelithiasis	10 (<1) [1]	16 (<1) [0]
Angina pectoris	35 (<1) [2]	14 (<1) [0]
Calculus ureteric	5 (<1) [0]	11 (<1) [0]
Colon cancer	10 (<1) [0]	10 (<1) [0]
Cardiac failure	3 (<1) [1]	10 (<1) [0]
Angina unstable	7 (<1) [1]	9 (<1) [0]
Syncope	6 (<1) [0]	9 (<1) [0]
Gastritis	4 (<1) [0]	9 (<1) [0]
Transient ischaemic attack	13 (<1) [0]	8 (<1) [1]
Coronary artery stenosis	10 (<1) [0]	8 (<1) [0]
Hypertension	10 (<1) [0]	8 (<1) [1]
Nephrolithiasis	7 (<1) [0]	8 (<1) [0]
Lung neoplasm malignant	8 (<1) [0]	7 (<1) [0]
Cardiac failure congestive	4 (<1) [1]	7 (<1) [0]
Deep vein thrombosis	8 (<1) [0]	6 (<1) [1]
Post procedural haemorrhage	8 (<1) [0]	6 (<1) [0]
Dyspnoea	7 (<1) [1]	6 (<1) [1]
Cholecystitis	6 (<1) [0]	6 (<1) [0]
Intervertebral disc protrusion	6 (<1) [0]	6 (<1) [0]

Myocardial ischaemia	5 (<1) [0]	6 (<1) [0]
Retinal detachment	4 (<1) [1]	6 (<1) [0]
Back pain	4 (<1) [0]	6 (<1) [0]
Epididymitis	4 (<1) [0]	6 (<1) [0]
Arthralgia	2 (<1) [0]	6 (<1) [0]
Colonic polyp	2 (<1) [0]	6 (<1) [0]
Rib fracture	2 (<1) [0]	6 (<1) [0]
Vertigo	2 (<1) [0]	6 (<1) [1]
Malignant melanoma	1 (<1) [0]	6 (<1) [0]
Arrhythmia	16 (<1) [0]	5 (<1) [0]
Benign prostatic hyperplasia	10 (<1) [0]	5 (<1) [0]
Pulmonary embolism	10 (<1) [0]	5 (<1) [1]
Acute myocardial infarction	8 (<1) [0]	5 (<1) [0]
Bladder cancer	7 (<1) [0]	5 (<1) [0]
Cellulitis	3 (<1) [0]	5 (<1) [0]
Cerebral infarction	2 (<1) [0]	5 (<1) [0]
Renal cancer	2 (<1) [0]	5 (<1) [0]
Gastric ulcer	0	5 (<1) [0]
Cholecystitis acute	7 (<1) [0]	4 (<1) [0]
Rectal haemorrhage	6 (<1) [0]	4 (<1) [0]
Urosepsis	6 (<1) [0]	4 (<1) [0]
Aortic aneurysm	4 (<1) [0]	4 (<1) [0]
Coronary artery occlusion	4 (<1) [0]	4 (<1) [0]
Hydrocele	4 (<1) [0]	4 (<1) [0]
Non-cardiac chest pain	4 (<1) [0]	4 (<1) [0]
Post procedural complication	4 (<1) [0]	4 (<1) [0]
Arthritis	3 (<1) [0]	4 (<1) [0]
Chronic obstructive pulmonary disease	3 (<1) [0]	4 (<1) [0]
Hypertensive crisis	3 (<1) [1]	4 (<1) [0]
Meniscus lesion	3 (<1) [0]	4 (<1) [0]
Prostate cancer	3 (<1) [0]	4 (<1) [0]
Pyrexia	3 (<1) [0]	4 (<1) [0]
Rectal cancer	3 (<1) [0]	4 (<1) [0]
Renal colic	3 (<1) [0]	4 (<1) [0]
Carotid artery stenosis	2 (<1) [0]	4 (<1) [0]
Cardiac valve disease	1 (<1) [0]	4 (<1) [0]
Musculoskeletal pain	1 (<1) [0]	4 (<1) [0]
Urinary retention postoperative	1 (<1) [0]	4 (<1) [0]
Haematemesis	0	4 (<1) [0]
Thrombocytopenia	0	4 (<1) [0]
Wound	0	4 (<1) [0]
Urinary retention	17 (<1) [0]	3 (<1) [0]
Haematuria	9 (<1) [0]	3 (<1) [0]
Urinary tract infection	6 (<1) [0]	3 (<1) [0]
Chest pain	6 (<1) [0]	3 (<1) [0]
Gastrointestinal carcinoma	5 (<1) [0]	3 (<1) [0]
Renal cell carcinoma	5 (<1) [0]	3 (<1) [0]
Renal failure	5 (<1) [0]	3 (<1) [0]
Femur fracture	4 (<1) [0]	3 (<1) [0]
Pancreatitis	4 (<1) [0]	3 (<1) [0]
Rotator cuff syndrome	4 (<1) [0]	3 (<1) [0]
Calculus bladder	3 (<1) [0]	3 (<1) [0]
Depression	3 (<1) [0]	3 (<1) [0]

Epilepsy	3 (<1) [2]	3 (<1) [0]
Lower respiratory tract infection	3 (<1) [0]	3 (<1) [0]
Spinal column stenosis	2 (<1) [0]	3 (<1) [0]
Arteriosclerosis	1 (<1) [0]	3 (<1) [0]
Arteriosclerosis coronary artery	1 (<1) [0]	3 (<1) [0]
Bladder transitional cell carcinoma	1 (<1) [0]	3 (<1) [0]
Dehydration	1 (<1) [0]	3 (<1) [0]
Hip fracture	1 (<1) [0]	3 (<1) [0]
Ileus	1 (<1) [0]	3 (<1) [0]
Lymphadenopathy	1 (<1) [0]	3 (<1) [0]
Pleural effusion	1 (<1) [0]	3 (<1) [0]
Post procedural haematuria	1 (<1) [0]	3 (<1) [0]
Thrombophlebitis	1 (<1) [0]	3 (<1) [0]
Acute myeloid leukaemia	0	3 (<1) [0]
Haemorrhagic stroke	0	3 (<1) [0]
Intervertebral disc disorder	0	3 (<1) [0]
Orthostatic hypotension	0	3 (<1) [1]
Thrombosis	0	3 (<1) [0]
Upper gastrointestinal haemorrhage	0	3 (<1) [0]
Sepsis	17 (<1) [0]	2 (<1) [0]
Appendicitis	12 (<1) [0]	2 (<1) [0]
Atrial flutter	7 (<1) [0]	2 (<1) [0]
Tibia fracture	6 (<1) [0]	2 (<1) [0]
Basal cell carcinoma	5 (<1) [0]	2 (<1) [0]
Acute coronary syndrome	4 (<1) [0]	2 (<1) [0]
Small intestinal obstruction	4 (<1) [0]	2 (<1) [0]
Abdominal pain	3 (<1) [0]	2 (<1) [0]
Asthma	3 (<1) [0]	2 (<1) [0]
Bacteraemia	3 (<1) [0]	2 (<1) [0]
Bronchial carcinoma	3 (<1) [0]	2 (<1) [0]
Diverticulitis	3 (<1) [0]	2 (<1) [0]
Iron deficiency anaemia	3 (<1) [0]	2 (<1) [0]
Lumbar spinal stenosis	3 (<1) [0]	2 (<1) [0]
Pericarditis	3 (<1) [0]	2 (<1) [0]
Umbilical hernia	3 (<1) [0]	2 (<1) [0]
Anxiety	2 (<1) [0]	2 (<1) [0]
Diarrhoea	2 (<1) [0]	2 (<1) [0]
Duodenal ulcer	2 (<1) [0]	2 (<1) [0]
Epistaxis	2 (<1) [0]	2 (<1) [0]
Haemorrhoids	2 (<1) [0]	2 (<1) [0]
Lower limb fracture	2 (<1) [0]	2 (<1) [0]
Phimosi	2 (<1) [0]	2 (<1) [0]
Aortic valve disease	1 (<1) [0]	2 (<1) [1]
Brain neoplasm benign	1 (<1) [0]	2 (<1) [0]
Carotid artery occlusion	1 (<1) [0]	2 (<1) [0]
Cartilage injury	1 (<1) [0]	2 (<1) [0]
Chronic sinusitis	1 (<1) [0]	2 (<1) [0]
Emphysema	1 (<1) [0]	2 (<1) [0]
Femoral neck fracture	1 (<1) [0]	2 (<1) [0]
Gastric cancer	1 (<1) [0]	2 (<1) [0]
Gastrooesophageal reflux disease	1 (<1) [0]	2 (<1) [0]
Haematoma	1 (<1) [0]	2 (<1) [0]
Haemothorax	1 (<1) [0]	2 (<1) [0]
Hypokalaemia	1 (<1) [0]	2 (<1) [0]
Incisional hernia	1 (<1) [0]	2 (<1) [0]

Infective exacerbation of chronic obstructive airways disease	1 (<1) [0]	2 (<1) [0]
Intermittent claudication	1 (<1) [0]	2 (<1) [0]
Joint dislocation	1 (<1) [0]	2 (<1) [0]
Mitral valve incompetence	1 (<1) [0]	2 (<1) [0]
Multiple injuries	1 (<1) [0]	2 (<1) [0]
Non-Hodgkin's lymphoma	1 (<1) [0]	2 (<1) [0]
Presyncope	1 (<1) [0]	2 (<1) [0]
Skin cancer	1 (<1) [0]	2 (<1) [0]
Ulna fracture	1 (<1) [0]	2 (<1) [0]
Ventricular extrasystoles	1 (<1) [0]	2 (<1) [0]
Ventricular tachycardia	1 (<1) [0]	2 (<1) [0]
Abdominal pain upper	0	2 (<1) [0]
Anaemia	0	2 (<1) [0]
Bladder transitional cell carcinoma recurrent	0	2 (<1) [0]
Cataract	0	2 (<1) [0]
Chronic lymphocytic leukaemia	0	2 (<1) [0]
General physical health deterioration	0	2 (<1) [0]
Hepatic enzyme increased	0	2 (<1) [1]
Insulin-requiring type 2 diabetes mellitus	0	2 (<1) [0]
Knee deformity	0	2 (<1) [0]
Leukopenia	0	2 (<1) [0]
Mental disorder	0	2 (<1) [0]
Microcytic anaemia	0	2 (<1) [0]
Musculoskeletal chest pain	0	2 (<1) [0]
Myelopathy	0	2 (<1) [0]
Pneumothorax	0	2 (<1) [0]
Post procedural haematoma	0	2 (<1) [0]
Procedural hypotension	0	2 (<1) [0]
Radius fracture	0	2 (<1) [0]
Small intestinal perforation	0	2 (<1) [0]
Spinal osteoarthritis	0	2 (<1) [0]
Splenomegaly	0	2 (<1) [0]
Sternal fracture	0	2 (<1) [0]
Subdural haematoma	0	2 (<1) [0]
Prostatitis	18 (<1)[0]	1 (<1) [0]
Post procedural sepsis	7 (<1) [0]	1 (<1) [0]
Dizziness	6 (<1) [1]	1 (<1) [0]
Postoperative wound infection	4 (<1) [1]	1 (<1) [0]
Road traffic accident	4 (<1) [0]	1 (<1) [0]
Tachycardia	4 (<1) [0]	1 (<1) [0]
Foot deformity	3 (<1) [0]	1 (<1) [0]
Hypotension	3 (<1) [0]	1 (<1) [0]
Renal failure acute	3 (<1) [0]	1 (<1) [0]
Supraventricular tachycardia	3 (<1) [0]	1 (<1) [0]
Type 2 diabetes mellitus	3 (<1) [0]	1 (<1) [0]
Urinary bladder haemorrhage	3 (<1) [0]	1 (<1) [0]
Abdominal hernia	2 (<1) [0]	1 (<1) [0]
Aortic stenosis	2 (<1) [0]	1 (<1) [0]
Aortic valve stenosis	2 (<1) [0]	1 (<1) [0]
Bronchitis	2 (<1) [0]	1 (<1) [0]
Bronchitis chronic	2 (<1) [0]	1 (<1) [0]
Cholangitis	2 (<1) [0]	1 (<1) [0]
Diverticulum	2 (<1) [0]	1 (<1) [0]
Gastroenteritis	2 (<1) [1]	1 (<1) [0]
Headache	2 (<1) [0]	1 (<1) [1]

Head injury	2 (<1) [0]	1 (<1) [0]
Hiatus hernia	2 (<1) [0]	1 (<1) [0]
Hyperthyroidism	2 (<1) [0]	1 (<1) [0]
Lacunar infarction	2 (<1) [0]	1 (<1) [0]
Multiple myeloma	2 (<1) [0]	1 (<1) [0]
Oedema peripheral	2 (<1) [0]	1 (<1) [0]
Post procedural infection	2 (<1) [0]	1 (<1) [0]
Pyelonephritis	2 (<1) [0]	1 (<1) [0]
Scapula fracture	2 (<1) [0]	1 (<1) [0]
Skeletal injury	2 (<1) [0]	1 (<1) [0]
Tendon rupture	2 (<1) [0]	1 (<1) [0]
Tonsillitis	2 (<1) [0]	1 (<1) [0]
Abdominal abscess	1 (<1) [0]	1 (<1) [0]
Amnesia	1 (<1) [0]	1 (<1) [1]
Anal fistula	1 (<1) [0]	1 (<1) [0]
Ankle fracture	1 (<1) [0]	1 (<1) [0]
Aortic valve incompetence	1 (<1) [0]	1 (<1) [0]
Atrioventricular block complete	1 (<1) [0]	1 (<1) [0]
B-cell lymphoma	1 (<1) [0]	1 (<1) [0]
Benign neoplasm of bladder	1 (<1) [0]	1 (<1) [0]
Biliary colic	1 (<1) [0]	1 (<1) [0]
Bradycardia	1 (<1) [0]	1 (<1) [0]
Brain abscess	1 (<1) [0]	1 (<1) [0]
Brain contusion	1 (<1) [0]	1 (<1) [0]
Cardiac failure acute	1 (<1) [0]	1 (<1) [0]
Carpal tunnel syndrome	1 (<1) [0]	1 (<1) [0]
Cerebral ischaemia	1 (<1) [0]	1 (<1) [0]
Cerebral thrombosis	1 (<1) [0]	1 (<1) [0]
Cerebrovascular disorder	1 (<1) [0]	1 (<1) [0]
Chest discomfort	1 (<1) [0]	1 (<1) [0]
Cholangitis suppurative	1 (<1) [0]	1 (<1) [0]
Colon cancer recurrent	1 (<1) [0]	1 (<1) [0]
Colorectal cancer	1 (<1) [0]	1 (<1) [0]
Concussion	1 (<1) [0]	1 (<1) [0]
Empyema	1 (<1) [0]	1 (<1) [0]
Erysipelas	1 (<1) [0]	1 (<1) [0]
Facial bones fracture	1 (<1) [0]	1 (<1) [0]
Febrile neutropenia	1 (<1) [0]	1 (<1) [0]
Gastritis haemorrhagic	1 (<1) [0]	1 (<1) [1]
Gastric ulcer haemorrhage	1 (<1) [0]	1 (<1) [0]
Haemoptysis	1 (<1) [0]	1 (<1) [0]
Hernia obstructive	1 (<1) [0]	1 (<1) [0]
Humerus fracture	1 (<1) [0]	1 (<1) [0]
Hypertrophic cardiomyopathy	1 (<1) [0]	1 (<1) [0]
Hypoaesthesia	1 (<1) [0]	1 (<1) [0]
Ischaemic stroke	1 (<1) [0]	1 (<1) [0]
Laryngeal cancer	1 (<1) [0]	1 (<1) [0]
Laryngitis	1 (<1) [0]	1 (<1) [0]
Lower gastrointestinal haemorrhage	1 (<1) [0]	1 (<1) [0]
Metastases to bone	1 (<1) [0]	1 (<1) [0]
Nausea	1 (<1) [0]	1 (<1) [0]
Oesophageal ulcer	1 (<1) [0]	1 (<1) [0]
Osteoporosis	1 (<1) [1]	1 (<1) [0]
Pain in extremity	1 (<1) [0]	1 (<1) [0]
Peripheral artery aneurysm	1 (<1) [0]	1 (<1) [0]

Postoperative ileus	1 (<1) [0]	1 (<1) [0]
Reflux oesophagitis	1 (<1) [1]	1 (<1) [0]
Respiratory tract infection	1 (<1) [0]	1 (<1) [0]
Retinal haemorrhage	1 (<1) [0]	1 (<1) [0]
Sinusitis	1 (<1) [0]	1 (<1) [0]
Splenic rupture	1 (<1) [0]	1 (<1) [0]
Suicide attempt	1 (<1) [0]	1 (<1) [0]
Wound infection	1 (<1) [0]	1 (<1) [0]
Accidental overdose	0	1 (<1) [0]
Adenoidal disorder	0	1 (<1) [0]
Adrenal haematoma	0	1 (<1) [0]
Alcohol abuse	0	1 (<1) [0]
Alcoholic psychosis	0	1 (<1) [0]
Allergy to plants	0	1 (<1) [0]
Anaemia postoperative	0	1 (<1) [0]
Anaphylactic reaction	0	1 (<1) [0]
Anaphylactic shock	0	1 (<1) [0]
Anastomotic leak	0	1 (<1) [0]
Animal bite	0	1 (<1) [0]
Aortic aneurysm rupture	0	1 (<1) [0]
Arterial thrombosis limb	0	1 (<1) [0]
Arthritis bacterial	0	1 (<1) [0]
Asthenia	0	1 (<1) [0]
Autoimmune thrombocytopenia	0	1 (<1) [0]
Back injury	0	1 (<1) [0]
Benign gastric neoplasm	0	1 (<1) [0]
Benign gastrointestinal neoplasm	0	1 (<1) [0]
Benign neoplasm of thyroid gland	0	1 (<1) [0]
Biliary tract disorder	0	1 (<1) [0]
Bladder neck obstruction	0	1 (<1) [0]
Bladder papilloma	0	1 (<1) [0]
Bladder tamponade	0	1 (<1) [0]
Blood disorder	0	1 (<1) [0]
Brain neoplasm malignant	0	1 (<1) [0]
Brain stem glioma	0	1 (<1) [0]
Brain stem infarction	0	1 (<1) [0]
Cardiac enzymes increased	0	1 (<1) [0]
Cardiac failure chronic	0	1 (<1) [0]
Cardiac myxoma	0	1 (<1) [0]
Carotid sinus syndrome	0	1 (<1) [0]
Cerebral artery embolism	0	1 (<1) [0]
Cervical spinal stenosis	0	1 (<1) [0]
Cervical vertebral fracture	0	1 (<1) [0]
Chest injury	0	1 (<1) [0]
Cluster headache	0	1 (<1) [0]
Colitis	0	1 (<1) [0]
Colitis ulcerative	0	1 (<1) [0]
Collapse of lung	0	1 (<1) [0]
Colon cancer stage 0	0	1 (<1) [0]
Contusion	0	1 (<1) [0]
Convulsion	0	1 (<1) [0]
Coronary artery restenosis	0	1 (<1) [0]
Cubital tunnel syndrome	0	1 (<1) [0]
Cushing's syndrome	0	1 (<1) [0]
Deafness unilateral	0	1 (<1) [0]

Delirium	0	1 (<1) [0]
Dementia Alzheimer's type	0	1 (<1) [0]
Dermatitis	0	1 (<1) [0]
Dermatitis allergic	0	1 (<1) [0]
Diabetes mellitus inadequate control	0	1 (<1) [0]
Diabetic foot	0	1 (<1) [0]
Diastolic dysfunction	0	1 (<1) [0]
Diverticulum intestinal	0	1 (<1) [0]
Duodenal ulcer haemorrhage	0	1 (<1) [0]
Duodenal ulcer perforation	0	1 (<1) [0]
Dysphagia	0	1 (<1) [0]
Dysplastic naevus syndrome	0	1 (<1) [0]
Electrolyte imbalance	0	1 (<1) [0]
Endocarditis	0	1 (<1) [0]
Epstein-Barr virus infection	0	1 (<1) [0]
Facial paresis	0	1 (<1) [1]
Fall	0	1 (<1) [0]
Femoral arterial stenosis	0	1 (<1) [0]
Food poisoning	0	1 (<1) [0]
Forearm fracture	0	1 (<1) [0]
Foreign body trauma	0	1 (<1) [0]
Fracture nonunion	0	1 (<1) [0]
Full blood count abnormal	0	1 (<1) [0]
Gait disturbance	0	1 (<1) [0]
Gastric disorder	0	1 (<1) [0]
Gastrointestinal dysplasia	0	1 (<1) [0]
Gastrointestinal injury	0	1 (<1) [0]
Gastrointestinal ulcer haemorrhage	0	1 (<1) [0]
Genital discomfort	0	1 (<1) [0]
Gout	0	1 (<1) [0]
Groin pain	0	1 (<1) [0]
Gynaecomastia	0	1 (<1) [0]
Haemorrhagic cerebral infarction	0	1 (<1) [0]
Helicobacter infection	0	1 (<1) [0]
Hemicephalgia	0	1 (<1) [0]
Hepatic function abnormal	0	1 (<1) [0]
Hepatomegaly	0	1 (<1) [0]
Herpes zoster	0	1 (<1) [0]
Hip dysplasia	0	1 (<1) [0]
Hydronephrosis	0	1 (<1) [0]
Hyperlipidaemia	0	1 (<1) [0]
Hypoglycaemia	0	1 (<1) [0]
Iliac artery stenosis	0	1 (<1) [0]
Iliac artery thrombosis	0	1 (<1) [0]
Infected bites	0	1 (<1) [0]
Infection	0	1 (<1) [0]
Injection site abscess	0	1 (<1) [0]
Intervertebral disc injury	0	1 (<1) [0]
Intervertebral discitis	0	1 (<1) [0]
Intestinal adenocarcinoma	0	1 (<1) [0]
Intracranial pressure increased	0	1 (<1) [0]
Jaundice cholestatic	0	1 (<1) [0]
Jaw fracture	0	1 (<1) [0]
Joint prosthesis user	0	1 (<1) [0]
Labyrinthine fistula	0	1 (<1) [0]

Laceration	0	1 (<1) [0]
Laryngeal papilloma	0	1 (<1) [0]
Left ventricular dysfunction	0	1 (<1) [0]
Leiomyosarcoma	0	1 (<1) [0]
Ligament rupture	0	1 (<1) [0]
Lung cancer metastatic	0	1 (<1) [0]
Lymphocytic lymphoma	0	1 (<1) [0]
Maculopathy	0	1 (<1) [0]
Malaria	0	1 (<1) [0]
Malnutrition	0	1 (<1) [0]
Mechanical ileus	0	1 (<1) [0]
Melanocytic naevus	0	1 (<1) [0]
Meningitis borrelia	0	1 (<1) [0]
Metastases to lung	0	1 (<1) [0]
Metastatic salivary gland cancer	0	1 (<1) [0]
Migraine	0	1 (<1) [0]
Migraine with aura	0	1 (<1) [0]
Mitral valve prolapse	0	1 (<1) [0]
Muscular weakness	0	1 (<1) [0]
Myalgia	0	1 (<1) [0]
Nasopharyngeal cancer	0	1 (<1) [0]
Necrosis ischaemic	0	1 (<1) [0]
Neoplasm	0	1 (<1) [0]
Nervous system disorder	0	1 (<1) [0]
Neuropathy peripheral	0	1 (<1) [1]
Non-Hodgkin's lymphoma recurrent	0	1 (<1) [0]
Nosocomial infection	0	1 (<1) [0]
Oesophageal pain	0	1 (<1) [0]
Oesophageal stenosis	0	1 (<1) [0]
Osteochondrosis	0	1 (<1) [0]
Osteonecrosis	0	1 (<1) [0]
Pancreatitis acute	0	1 (<1) [0]
Paraganglion neoplasm	0	1 (<1) [0]
Paraplegia	0	1 (<1) [0]
Paresis	0	1 (<1) [0]
Pelvic abscess	0	1 (<1) [0]
Penis carcinoma	0	1 (<1) [0]
Peripheral ischaemia	0	1 (<1) [0]
Peripheral vascular disorder	0	1 (<1) [0]
Peyronie's disease	0	1 (<1) [0]
Pharyngeal cancer stage unspecified	0	1 (<1) [0]
Pneumonia primary atypical	0	1 (<1) [0]
Pneumonitis	0	1 (<1) [0]
Poisoning	0	1 (<1) [0]
Polymyalgia rheumatica	0	1 (<1) [1]
Polyp	0	1 (<1) [0]
Procedural site reaction	0	1 (<1) [0]
Pruritus generalised	0	1 (<1) [1]
Renal disorder	0	1 (<1) [0]
Renal neoplasm	0	1 (<1) [0]
Renal oncocytoma	0	1 (<1) [0]
Respiratory acidosis	0	1 (<1) [0]
Respiratory failure	0	1 (<1) [0]
Retinal ischaemia	0	1 (<1) [1]
Retinal vein occlusion	0	1 (<1) [1]

Retrograde ejaculation	0	1 (<1) [1]
Retinal tear	0	1 (<1) [0]
Retroperitoneal haemorrhage	0	1 (<1) [0]
Rhinitis	0	1 (<1) [0]
Salivary gland cancer	0	1 (<1) [0]
Sciatica	0	1 (<1) [0]
Sinoatrial block	0	1 (<1) [0]
Sinus bradycardia	0	1 (<1) [0]
Skin necrosis	0	1 (<1) [0]
Skin ulcer	0	1 (<1) [0]
Small intestinal haemorrhage	0	1 (<1) [0]
Spinal claudication	0	1 (<1) [0]
Spinal cord injury	0	1 (<1) [0]
Splenic haemorrhage	0	1 (<1) [0]
Subdiaphragmatic abscess	0	1 (<1) [0]
Tachyarrhythmia	0	1 (<1) [0]
Testis cancer	0	1 (<1) [0]
Thalamic infarction	0	1 (<1) [0]
Thoracic vertebral fracture	0	1 (<1) [0]
Throat cancer	0	1 (<1) [0]
Thyroid cancer	0	1 (<1) [0]
Upper respiratory tract infection	0	1 (<1) [0]
Ureteric cancer	0	1 (<1) [0]
Urinary tract disorder	0	1 (<1) [0]
Urinoma	0	1 (<1) [0]
Vascular encephalopathy	0	1 (<1) [0]
Vascular graft occlusion	0	1 (<1) [0]
Vasculitic rash	0	1 (<1) [0]
Venous occlusion	0	1 (<1) [0]
Venous thrombosis limb	0	1 (<1) [0]
Fibula fracture	5 (<1) [0]	0
Constipation	4 (<1) [0]	0
Orchitis	4 (<1) [0]	0
Atrioventricular block	3 (<1) [0]	0
Bone pain	3 (<1) [0]	0
Cardiomyopathy	3 (<1) [0]	0
Cystitis	3 (<1) [0]	0
Dupuytren's contracture	3 (<1) [0]	0
Glaucoma	3 (<1) [0]	0
Goitre	3 (<1) [0]	0
Intestinal obstruction	3 (<1) [0]	0
Labyrinthitis	3 (<1) [0]	0
Loss of consciousness	3 (<1) [0]	0
Lumbar vertebral fracture	3 (<1) [0]	0
Nasal polyps	3 (<1) [0]	0
Oesophageal carcinoma	3 (<1) [0]	0
Pulmonary hypertension	3 (<1) [0]	0
Urethral stenosis	3 (<1) [0]	0
Varicose vein	3 (<1) [0]	0
Vomiting	3 (<1) [0]	0
Acquired immunodeficiency syndrome	2 (<1) [0]	0
Atrial tachycardia	2 (<1) [0]	0
Atrioventricular block second degree	2 (<1) [0]	0
Bile duct stone	2 (<1) [0]	0
Cardiac disorder	2 (<1) [0]	0

Comminuted fracture	2 (<1) [0]	0
Confusional state	2 (<1) [0]	0
Escherichia urinary tract infection	2 (<1) [0]	0
Foot fracture	2 (<1) [0]	0
Hepatic neoplasm malignant	2 (<1) [0]	0
Hypoxia	2 (<1) [0]	0
Injury	2 (<1) [0]	0
Joint injury	2 (<1) [0]	0
Limb traumatic amputation	2 (<1) [0]	0
Localised infection	2 (<1) [0]	0
Lymphoma	2 (<1) [0]	0
Mental status changes	2 (<1) [0]	0
Metastases to liver	2 (<1) [0]	0
Multiple fractures	2 (<1) [0]	0
Myasthenia gravis	2 (<1) [0]	0
Neuroendocrine carcinoma	2 (<1) [0]	0
Pancreatic carcinoma	2 (<1) [0]	0
Parkinson's disease	1 (<1) [1]	0
Patella fracture	2 (<1) [0]	0
Peripheral arterial occlusive disease	2 (<1) [0]	0
Pleurisy	2 (<1) [0]	0
Prostatism	2 (<1) [0]	0
Prostatomegaly	2 (<1) [0]	0
Retinal vein thrombosis	2 (<1) [0]	0
Squamous cell carcinoma	2 (<1) [0]	0
Subarachnoid haemorrhage	2 (<1) [0]	0
Testicular abscess	2 (<1) [0]	0
Venous thrombosis	2 (<1) [0]	0
Vestibular neuronitis	2 (<1) [0]	0
Viral infection	2 (<1) [0]	0
Vocal cord polyp	2 (<1) [0]	0
Abdominal injury	1 (<1) [0]	0
Abdominal strangulated hernia	1 (<1) [0]	0
Abdominal wound dehiscence	1 (<1) [0]	0
Abscess	1 (<1) [0]	0
Abscess limb	1 (<1) [0]	0
Acoustic neuroma	1 (<1) [0]	0
Adenoma benign	1 (<1) [0]	0
Alanine aminotransferase increased	1 (<1) [0]	0
Alcoholism	1 (<1) [0]	0
Anal abscess	1 (<1) [0]	0
Aneurysm	1 (<1) [0]	0
Aortic dissection	1 (<1) [0]	0
Aortic elongation	1 (<1) [0]	0
Arachnoid cyst	1 (<1) [0]	0
Arthropathy	1 (<1) [0]	0
Ascites	1 (<1) [0]	0
Aspartate aminotransferase increased	1 (<1) [0]	0
Ataxia	1 (<1) [0]	0
Benign colonic neoplasm	1 (<1) [0]	0
Benign renal neoplasm	1 (<1) [0]	0
Bile duct obstruction	1 (<1) [0]	0
Bipolar I disorder	1 (<1) [0]	0
Bladder cancer recurrent	1 (<1) [0]	0
Blast injury	1 (<1) [0]	0

Blindness	1 (<1) [0]	0
Bone neoplasm malignant	1 (<1) [0]	0
Bronchial hyperreactivity	1 (<1) [0]	0
Bronchiectasis	1 (<1) [0]	0
Bunion	1 (<1) [0]	0
Burnout syndrome	1 (<1) [0]	0
Bursitis	1 (<1) [0]	0
Calculus urinary	1 (<1) [0]	0
Cardiac arrest	1 (<1) [0]	0
Cardiac valve replacement complication	1 (<1) [0]	0
Carotid artery disease	1 (<1) [0]	0
Catheter site infection	1 (<1) [0]	0
Cerebral haemorrhage	1 (<1) [0]	0
Cholecystitis infective	1 (<1) [0]	0
Chronic myelomonocytic leukaemia	1 (<1) [0]	0
Circulatory collapse	1 (<1) [0]	0
Cirrhosis alcoholic	1 (<1) [0]	0
Clavicle fracture	1 (<1) [0]	0
Congestive cardiomyopathy	1 (<1) [0]	0
Corneal opacity	1 (<1) [0]	0
Dacryostenosis aquired	1 (<1) [0]	0
Dementia	1 (<1) [0]	0
Dermatitis bullous	1 (<1) [0]	0
Diabetes mellitus	1 (<1) [0]	0
Diverticular perforation	1 (<1) [0]	0
Dry skin	1 (<1) [0]	0
Dysuria	1 (<1) [0]	0
Endocarditis bacterial	1 (<1) [0]	0
Endophthalmitis	1 (<1) [0]	0
Epididymal cyst	1 (<1) [0]	0
Erythema	1 (<1) [0]	0
Escherichia infection	1 (<1) [0]	0
Escherichia sepsis	1 (<1) [0]	0
Excoriation	1 (<1) [0]	0
Extrasketal ossification	1 (<1) [0]	0
Extravasation of urine	1 (<1) [0]	0
Eye injury	1 (<1) [0]	0
Fatigue	1 (<1) [0]	0
Fibromatosis	1 (<1) [0]	0
Gallbladder pain	1 (<1) [0]	0
Gastric adenoma	1 (<1) [0]	0
Gastric haemorrhage	1 (<1) [0]	0
Gastrointestinal haemorrhage	1 (<1) [0]	0
Gastrointestinal neoplasm	1 (<1) [0]	0
Generalised anxiety disorder	1 (<1) [0]	0
Global amnesia	1 (<1) [0]	0
Head and neck cancer	1 (<1) [0]	0
Heart rate increased	1 (<1) [0]	0
Hemiparesis	1 (<1) [0]	0
Hepatic enzyme abnormal	1 (<1) [0]	0
Hepatitis	1 (<1) [0]	0
Hepatitis alcoholic	1 (<1) [0]	0
Hepatitis E	1 (<1) [0]	0
Hypercalcaemia	1 (<1) [0]	0
Hypercholesterolaemia	1 (<1) [0]	0

Hyperparathyroidism primary	1 (<1) [0]	0
Hypertonia	1 (<1) [0]	0
Hyperuricosuria	1 (<1) [0]	0
Ileus paralytic	1 (<1) [0]	0
Impaired self-care	1 (<1) [0]	0
Infected lymphocele	1 (<1) [0]	0
Infective tenosynovitis	1 (<1) [0]	0
Influenza	1 (<1) [0]	0
Inguinal hernia strangulated	1 (<1) [0]	0
Inguinal hernia, obstructive	1 (<1) [0]	0
Intentional overdose	1 (<1) [0]	0
Intervertebral disc degeneration	1 (<1) [0]	0
Intestinal perforation	1 (<1) [0]	0
Intra-abdominal haemorrhage	1 (<1) [0]	0
Intracranial aneurysm	1 (<1) [0]	0
Ischaemic cardiomyopathy	1 (<1) [0]	0
Jaundice	1 (<1) [0]	0
Labile blood pressure	1 (<1) [0]	0
Large intestinal haemorrhage	1 (<1) [0]	0
Laryngeal neoplasm	1 (<1) [0]	0
Left ventricular failure	1 (<1) [0]	0
Leukocytosis	1 (<1) [0]	0
Limb injury	1 (<1) [0]	0
Lobar pneumonia	1 (<1) [0]	0
Lung adenocarcinoma	1 (<1) [0]	0
Lung disorder	1 (<1) [0]	0
Lung infiltration	1 (<1) [0]	0
Lung squamous cell carcinoma stage unspecified	1 (<1) [0]	0
Lymphocele	1 (<1) [0]	0
Major depression	1 (<1) [0]	0
Melaena	1 (<1) [0]	0
Meningeal neoplasm	1 (<1) [0]	0
Metastases to lymph nodes	1 (<1) [0]	0
Metastases to peritoneum	1 (<1) [0]	0
Metastatic malignant melanoma	1 (<1) [0]	0
Muscle haemorrhage	1 (<1) [0]	0
Muscle injury	1 (<1) [0]	0
Muscle strain	1 (<1) [0]	0
Musculoskeletal disorder	1 (<1) [0]	0
Myopia	1 (<1) [0]	0
Nasal congestion	1 (<1) [0]	0
Neck pain	1 (<1) [0]	0
Neoplasm malignant	1 (<1) [0]	0
Nerve compression	1 (<1) [0]	0
Neuroendocrine tumour	1 (<1) [0]	0
Neurosensory hypoacusia	1 (<1) [0]	0
Non-small cell lung cancer	1 (<1) [0]	0
Obstructive uropathy	1 (<1) [0]	0
Oesophageal varices haemorrhage	1 (<1) [0]	0
Oesophagitis	1 (<1) [0]	0
Optic ischaemic neuropathy	1 (<1) [0]	0
Pancreatic disorder	1 (<1) [0]	0
Panic disorder	1 (<1) [0]	0
Patellofemoral pain syndrome	1 (<1) [0]	0
Pelvic fracture	1 (<1) [0]	0

Peptic ulcer haemorrhage	1 (<1) [0]	0
Pericardial effusion	1 (<1) [0]	0
Peripheral embolism	1 (<1) [1]	0
Peripheral sensory neuropathy	1 (<1) [0]	0
Peritonitis	1 (<1) [0]	0
Pharyngitis	1 (<1) [0]	0
Pharyngoesophageal diverticulum	1 (<1) [0]	0
Phlebitis	1 (<1) [0]	0
Pleuritic pain	1 (<1) [0]	0
Pneumocystis jiroveci pneumonia	1 (<1) [0]	0
Pneumothorax traumatic	1 (<1) [0]	0
Polyp colorectal	1 (<1) [0]	0
Postoperative abscess	1 (<1) [0]	0
Proctocolitis	1 (<1) [0]	0
Prostate infection	1 (<1) [0]	0
Prostatic haemorrhage	1 (<1) [0]	0
Pulmonary fibrosis	1 (<1) [0]	0
Pulmonary oedema	1 (<1) [0]	0
Pulmonary valve stenosis	1 (<1) [0]	0
Pyelonephritis acute	1 (<1) [0]	0
Radicular syndrome	1 (<1) [0]	0
Rectal neoplasm	1 (<1) [0]	0
Renal cyst	1 (<1) [0]	0
Renal failure chronic	1 (<1) [0]	0
Renal injury	1 (<1) [0]	0
Retinoschisis	1 (<1) [0]	0
Sarcoidosis	1 (<1) [0]	0
Scrotal abscess	1 (<1) [0]	0
Septic shock	1 (<1) [0]	0
Sigmoiditis	1 (<1) [1]	0
Skin laceration	1 (<1) [0]	0
Skull fracture	1 (<1) [0]	0
Skull fractured base	1 (<1) [0]	0
Small intestine carcinoma	1 (<1) [0]	0
Soft tissue infection	1 (<1) [0]	0
Streptococcal infection	1 (<1) [0]	0
Subdural haemorrhage	1 (<1) [0]	0
Sudden hearing loss	1 (<1) [0]	0
Temporal lobe epilepsy	1 (<1) [0]	0
Tendon pain	1 (<1) [0]	0
Tendonitis	1 (<1) [0]	0
Testicular cyst	1 (<1) [0]	0
Thyroid adenoma	1 (<1) [0]	0
Tongue neoplasm malignant stage unspecified	1 (<1) [0]	0
Tonsil cancer	1 (<1) [0]	0
Transitional cell cancer of the renal pelvis and ureter	1 (<1) [0]	0
Transitional cell carcinoma	1 (<1) [0]	0
Traumatic brain injury	1 (<1) [0]	0
Traumatic coma	1 (<1) [0]	0
Traumatic haematoma	1 (<1) [0]	0
Tuberculosis	1 (<1) [0]	0
Umbilical hernia, obstructive	1 (<1) [0]	0
Urethral disorder	1 (<1) [0]	0
Urethral injury	1 (<1) [0]	0
Urethral obstruction	1 (<1) [0]	0

Urinary tract infection bacterial	1 (<1) [0]	0
Vascular insufficiency	1 (<1) [0]	0
Ventricular arrhythmia	1 (<1) [0]	0
Ventricular fibrillation	1 (<1) [0]	0
Vestibular ataxia	1 (<1) [0]	0
Viral labyrinthitis	1 (<1) [0]	0
Wound haemorrhage	1 (<1) [0]	0
	Placebo N=4126	Dutasteride N=4105
	n (%) [related]	n (%) [related]
Subjects with fatal SAEs	74 (2) [2]	70 (2) [0]
Myocardial infarction	13 (<1) [2]	7 (<1) [0]
Lung neoplasm malignant	5 (<1) [0]	5 (<1) [0]
Acute myocardial infarction	1 (<1) [0]	4 (<1) [0]
Cerebrovascular accident	5 (<1) [0]	3 (<1) [0]
Pneumonia	1 (<1) [0]	3 (<1) [0]
Cardiac failure acute	0	3 (<1) [0]
Metastases to central nervous system	0	3 (<1) [0]
Cardiac failure	1 (<1) [0]	2 (<1) [0]
Road traffic accident	1 (<1) [0]	2 (<1) [0]
Bladder cancer	0	2 (<1) [0]
Metastatic malignant melanoma	0	2 (<1) [0]
Multi-organ failure	0	2 (<1) [0]
Cardiac arrest	5 (<1) [0]	1 (<1) [0]
Metastases to liver	3 (<1) [0]	1 (<1) [0]
Colon cancer	2 (<1) [0]	1 (<1) [0]
Death	2 (<1) [0]	1 (<1) [0]
Gastric cancer	2 (<1) [0]	1 (<1) [0]
Pancreatic carcinoma	2 (<1) [0]	1 (<1) [0]
Aortic aneurysm	1 (<1) [0]	1 (<1) [0]
Aortic rupture	1 (<1) [0]	1 (<1) [0]
Cardio-respiratory arrest	1 (<1) [0]	1 (<1) [0]
Coronary artery disease	1 (<1) [0]	1 (<1) [0]
Pancreatic carcinoma metastatic	1 (<1) [0]	1 (<1) [0]
Pulmonary embolism	1 (<1) [0]	1 (<1) [0]
Septic shock	1 (<1) [0]	1 (<1) [0]
Acute pulmonary oedema	0	1 (<1) [0]
Adenocarcinoma	0	1 (<1) [0]
Arrhythmia	0	1 (<1) [0]
Benign neoplasm	0	1 (<1) [0]
Blood pressure decreased	0	1 (<1) [0]
Brain neoplasm malignant	0	1 (<1) [0]
Candida sepsis	0	1 (<1) [0]
Cardiac tamponade	0	1 (<1) [0]
Cardiogenic shock	0	1 (<1) [0]
Cardiopulmonary failure	0	1 (<1) [0]
Cholecystitis acute	0	1 (<1) [0]
Crush injury	0	1 (<1) [0]
Dementia	0	1 (<1) [0]
Injury	0	1 (<1) [0]
Lung squamous cell carcinoma stage unspecified	0	1 (<1) [0]
Metastases to pleura	0	1 (<1) [0]
Metastatic neoplasm	0	1 (<1) [0]
Motor neurone disease	0	1 (<1) [0]
Myocardial ischaemia	0	1 (<1) [0]

Non-Hodgkin's lymphoma	0	1 (<1) [0]
Non-small cell lung cancer metastatic	0	1 (<1) [0]
Oesophageal carcinoma	0	1 (<1) [0]
Oesophageal neoplasm	0	1 (<1) [0]
Peritonitis	0	1 (<1) [0]
Polyarteritis nodosa	0	1 (<1) [0]
Post procedural haemorrhage	0	1 (<1) [0]
Postinfarction angina	0	1 (<1) [0]
Pulmonary congestion	0	1 (<1) [0]
Rectal cancer	0	1 (<1) [0]
Renal cancer metastatic	0	1 (<1) [0]
Sepsis	0	1 (<1) [0]
Sleep apnoea syndrome	0	1 (<1) [0]
Subdural haemorrhage	0	1 (<1) [0]
Sudden death	0	1 (<1) [0]
Urinary tract infection	0	1 (<1) [0]
Ventricle rupture	0	1 (<1) [0]
Aneurysm ruptured	2 (<1) [0]	0
Chronic obstructive pulmonary disease	2 (<1) [0]	0
Hepatic neoplasm malignant	2 (<1) [0]	0
Amyotrophic lateral sclerosis	1 (<1) [0]	0
Aortic aneurysm rupture	1 (<1) [0]	0
Arteriosclerosis coronary artery	1 (<1) [0]	0
Bone neoplasm malignant	1 (<1) [0]	0
Bronchial carcinoma	1 (<1) [0]	0
Bronchitis chronic	1 (<1) [0]	0
Cardiac disorder	1 (<1) [0]	0
Cerebrovascular disorder	1 (<1) [0]	0
Colon cancer metastatic	1 (<1) [0]	0
Convulsion	1 (<1) [0]	0
Coronary artery occlusion	1 (<1) [0]	0
Coronary artery thrombosis	1 (<1) [0]	0
Endocarditis	1 (<1) [0]	0
Gastric ulcer	1 (<1) [0]	0
Haemorrhage	1 (<1) [0]	0
Head injury	1 (<1) [0]	0
Hypertension	1 (<1) [0]	0
Intestinal ischaemia	1 (<1) [0]	0
Leukaemia	1 (<1) [0]	0
Lung adenocarcinoma	1 (<1) [0]	0
Lung cancer metastatic	1 (<1) [0]	0
Lymphoma	1 (<1) [0]	0
Lymphoproliferative disorder	1 (<1) [0]	0
Metastases to lung	1 (<1) [0]	0
Overdose	1 (<1) [0]	0
Syringomyelia	1 (<1) [0]	0

Conclusion:**Publications:** N Engl J Med 2010;362:1192-202