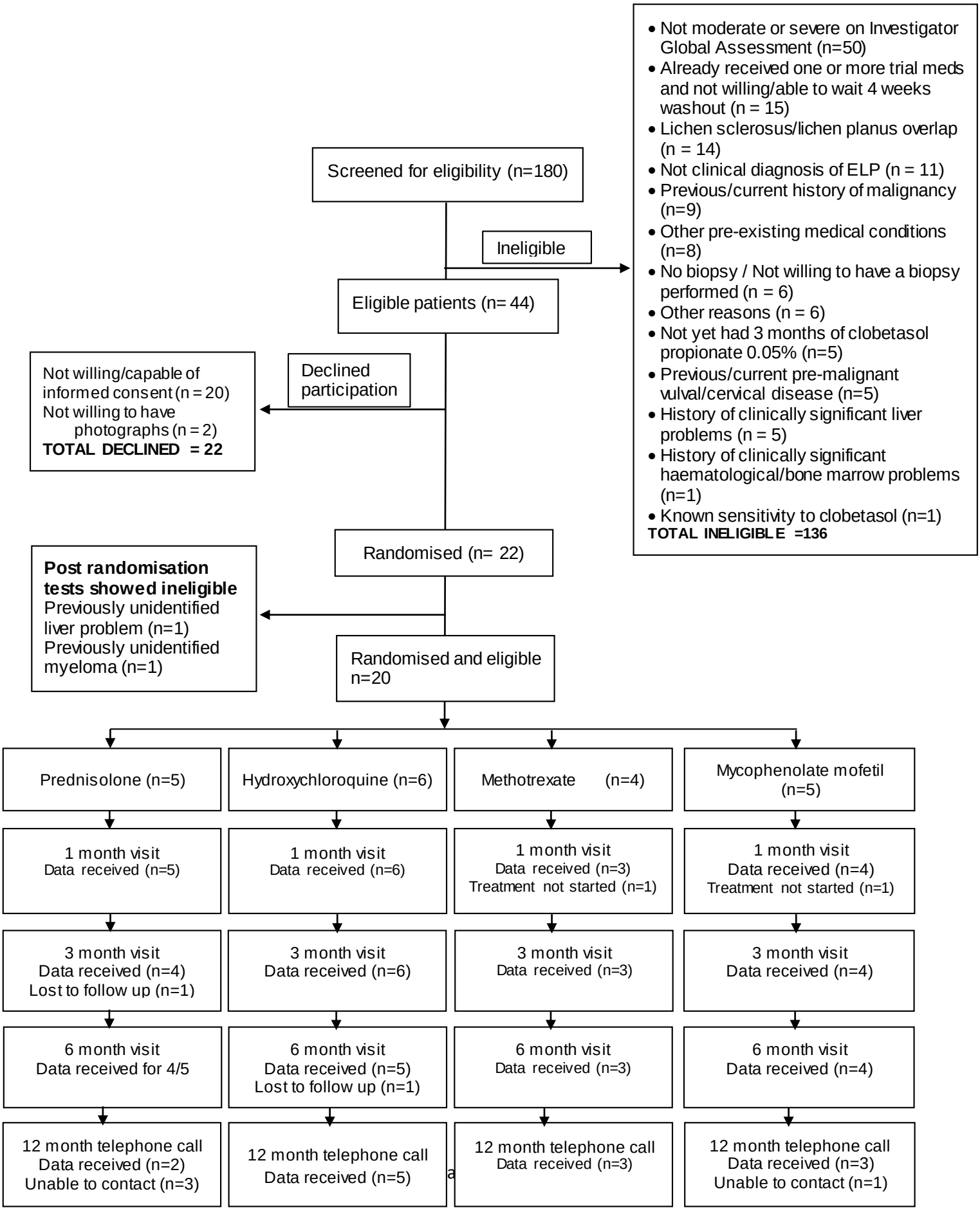
Participant Flow



Baseline Characteristics

Baseline characteristics	Prednisolone group	Hydroxychloroquine group	Methotrexate group	Mycophenolate mofetil group
Number of participants	5	6	4	5
Age range (years)	45-73	51-82	57-70	63-79
Age mean (years), sd	58.4 ± 11.3	66.7 ± 10.4	63.3 ± 6.2	69 ± 6.0
Time since diagnosis (years) Median (IQR)	3.7 (0.9, 5.5) *n=4*	0.6 (0.5, 1.2) *n=4*	0.8 (0.1, 1.5) *n=4*	3.3 (0.9, 5.6) *n=4*
Menopausal status n (%)				
Pre menopausal	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Peri menopausal	0 (0%)	0 (0%)	0 (0%)	1 (25%)
Post menopausal	4 (80%)	6 (100%)	4 (100%)	3 (75%)
Vulvovaginal gingival syndrome n (%)	3 (60%)	0 (0%)	1 (25%)	1 (25%)
Previous use of hELP systemic medications for ELPV ? n (%)				
Hydroxychloroquine	2 (40%)	0 (0%)	0 (0%)	0 (0%)
Methotrexate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mycophenolate mofetil	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Prednisolone	0 (0%)	0 (0%)	1 (25%)	0 (0%)
hELP medications not used before	3 (60%)	6 (100%)	3 (75%)	5 (100%)
Other medications n (%), *n=data present*				
B Blockers	0 (0%) *n=3*	0 (0%) *n=0*	0 (0%) *n=3*	0 (0%) *n=4*
Non-steroidal anti inflammatory drugs	0 (0%) *n=3*	0 (0%) *n=0*	0 (0%) *n=3*	0 (0%) *n=4*
Baseline soreness scale Median (IQR) *n=data present*	7.5 (5.5, 8.0) *n=4*	6 (4.0, 8.0) *n=5*	8.5 (6.5, 9.8) *n=4*	6.5 (4.5, 8.5) *n=4*
Baseline IGA				
Moderate, n (%)	3 (60%)	5 (83.3%)	2 (50%)	4 (100%)
Severe, n (%)	2 (40%)	1 (16.7%)	2 (50%)	0 (0%)
Data present (n)	*n=5*	*n=6*	*n=4*	*n=4*
Baseline PGA vulva				
0	0	0	0	0
1	1	2	2	2
2	2	2	1	2
3	2	2	1	0
Data present (n)	*n=5*	*n=6*	*n=4*	*n=4*
Oral site affected n (%)	3 (60%)	3 (50%)	2 (50%)	2 (50%)
Vaginal site affected n (%)	3 (60%)	3 (50%)	1 (25%)	2 (50%)
Comorbidities n (%)	5 (100%)	5 (83.3%)	3 (75%)	5 (100%)

sd=standard deviation, IQR=Interquartile range, IGA=Investigator Global Assessment, Patient global Assessment of vulval erosive lichen planus: 0=no bother at all/not much bother, 1 = a little bother, 2= a lot of bother, 3=very much bother

Outcome measures

Primary outcome measures

PRIMARY CLINICAL OUTCOME				
	Prednisolone group	**Hydroxychloroquine group**	**Methotrexate group**	**Mycophenolate mofetil group**
Number randomised to group (n)	**5**	**6**	**4**	**5**
6 month data available for primary OM (n)	4	5	3	4
Patient global assessment 0 or 1	2	3	1	4
Clinical assessment shows improvement from baseline*	0	2^	0	2
Treatment success (n)	**0**	**2**	**0**	**2**

* Blinded assessment of images. If these were not available, Investigator Global Assessment (unblinded) from clinic visits were used instead

^ ½ of these assessments was taken from Investigator Global Assessment (unblinded) in clinic

Early stopping of trial medications

Treatment group	**Randomised to group (n)**	**Started treatment (n)**	**Stopped treatment early (n)**	**Reason for stopping**		
				Treatment failure (n)	**Adverse event (n)**	**Loss to follow up (n)**
Hydroxychloroquine	6	6	2	0	1	1
Methotrexate	4	3	0	0	0	0
Mycophenolate mofetil	5	4	2	0	2	0
Prednisolone	5	5	2	1	0	1

Secondary outcome measures

	Prednisolone				Hydroxychloroquine				Methotrexate				Mycophenolate mofetil			
Number randomised to group (n)	**5**				**6**				**4**				**5**			
SECONDARY CLINICAL OUTCOMES																
Soreness vulva (Visual analogue scale 0-10)																
Baseline (median IQR)	7.5 (5.5, 8.0) n=4				6.0 (4.0, 8.0) n=5				8.5 (6.5, 9.8) n=4				6.5 (4.5, 8.5) n=4			
6 months (median IQR)	4 (1, 9.3) n=4				5.5 (3.3, 7.8) n=4				6 (2, 10) n=3				1.5 (0.3, 2.8) n=4			
Overall change (median IQR)	-2.5 (-5.5, 1.3) n=4				-0.5 (-2.5, 0.8) n=4				-2 (-8.0, -1.0) n=3				-5 (-5.8, -4.3) n=4			
IGA* vulva	**0**	**1**	**2**	**3**	**0**	**1**	**2**	**3**	**0**	**1**	**2**	**3**	**0**	**1**	**2**	**3**
Baseline	0	0	3	2	0	0	5	1	0	0	2	2	0	0	4	0
3 months	0	2	1	1	0	4	2	0	0	1	1	1	1	2	1	0
6 months	1	0	2	1	0	3	2	0	1	0	1	1	1	3	0	0
Improvement at 6 months (n)	1				4				1				4			
PGA^ vulva	0	1	2	3	0	1	2	3	0	1	2	3	0	1	2	3
Baseline	0	1	2	2	0	2	2	2	0	2	1	1	0	2	2	0
3 months	0	1	3	0	2	3	1	0	0	2	1	0	4	0	0	0
6 months	1	1	1	1	0	3	2	0	0	1	1	1	3	1	0	0
Improvement at 6 months (n)	1				1				1				4			
Blinded assessment of clinical images																
Improvement from baseline at 6 months (n)	0				1				0				2			
Assessment of other affected sites																
Patients with oral disease (n)	4				3				4				2			
Overall improvement in oral disease (n)	**2**				**0**				**1**				**2**			
Patients with vaginal disease (n)	1				2				4				2			
Overall improvement in vaginal disease (n)	**0**				**0**				**1**				**3**			
Continuation of treatment																
Continuation past 6 months(n)	1				1				2				2			
Continuation at 12 months(n)	0				1				2				2			
Hospital Anxiety Depression Scale[$]																
HADS-A baseline median (IQR)	7.5 (2.3, 18.8) n=4				9.5 (5.5, 15.3) n=6				12.5 (5.5, 15.8) n=4				10.0 (3.0, 17.0) n=2			

HADS-A 6 months median (IQR)	9.5 (4.3, 16.3) n=4	10.0 (5.5, 13.0) n=4	9.0 (3.0, 15.0) n=3	5.0 (3.0, 7.0) n=4
HADS-A change median (IQR)	**2.0 (-2.5, 2.0) n=4**	**0 (-1.5, 0.8) n=4**	**-1.0 (-7.0, 0) n=3**	**-5.0 (-10.0, 0) n=2**
HADS-D baseline median (IQR)	3.5 (2.0, 14.8) n=4	4.5 (3.8, 8.8) n=6	6.5 (1.5, 10.8) n=4	5.5 (5.0, 6.0) n=2
HADS-D 6 months median (IQR)	7.0 (2.3, 11.8) n=4	7.5 (1.8, 11.8) n=4	9.0 (4.0, 11.0) n=3	2.0 (0.5, 3.5) n=4
HADS-D change median (IQR)	**0.5 (-4.5, 4.8) n=4**	**2.0 (-2.5, 6.5) n=4**	**1.0 (-2.0, 1.0) n=3**	**-4.5 (-5.0, -4.0) n=2**
Overall HADS baseline median (IQR)	11 (4.25, 33.5) n=4	14 (9.25, 23.5) n=6	18.5 (8, 26) n=4	15.5 (9, 22) n=2
Overall HADS 6 months median (IQR)	16.5 (6.5, 28) n=4	17.5 (7.25, 24.75) n=4	20 (7, 24) n=3	6 (5, 10) n=4
Overall HADS Change (median (IQR))	**2.5 (-7, 6.75) n=4**	**2 (-4, 7.25) n=4**	**-2 (-6, 0) n=3**	**-9.5 (-15, -4) n=2**
Sexual function				
Baseline sexually active	0 n=4	0 n=6	0 n=4	0 n=3
6 months sexually active	0 n=4	0 n=4	0 n=3	0 n=4
Improvement in sexual function at 6 months	0 n=4	0 n=4	0 n=3	0 n=3
Skindex-29[%]				
Symptoms:				
Baseline median (IQR)	73.2 (60.71, 83.9) n=4	71.4 (57.1, 82.1) n=5	50 (41.1, 71.4) n=4	32.1 (28.6, 35.7) n=2
6 months median (IQR)	59.4 (42.2, 73.4) n=4	53.1 (40.6, 62.5) n=3	64.2 (59.4, 75) n=3	20.3 (3.1, 37.5) n=2
Change median (IQR)	**-12.06 (-36.83, 7.81) n=4**	**-18.3 (-19.64, -16.54) n=3**	**2.23 (-10.7, 21.43) n=3**	**-11.83 (-32.58, 8.93) n=2**
Function:				
Baseline median (IQR)	53.4 (38.6, 71.6) n=4	34.1 (27.3, 38.6) n=5	59.1 (29.6, 69.3) n=4	29.5 (15.9, 43.2) n=2
6 months median (IQR)	37.5 (18.4, 57.3) n=4	12.5 (6.25, 38.6) n=3	72.9 (52.1, 87.5) n=3	13.5 (12.5, 14.6) n=2
Change median (IQR)	**-19.3 (-21.79, -12.79) n=4**	**1.71 (-14.77, 4.51) n=3**	**9.27 (-2.47, 12.5) n=3**	**-16 (-28.6, -3.41) n=2**
Emotion:				
Baseline median (IQR)	40 (23.8, 73.8) n=4	55 (40, 55) n=5	46.3 (28.8, 71.3) n=4	47.5 (7.5, 87.5) n=2
6 months median (IQR)	41.3 (15, 61.3) n=4	32.5 (22.5, 55) n=3	70 (60, 70) n=3	16.25 (12.5, 20) n=2
Change median (IQR)	**-8.75 (-22.5, 1.25)**	**0 (-22.5, 7.5)**	**12.5 (-15, 25)**	**-31.25 (-67.5, 5)**

	n=4	n=3	n=3	n=2
SF-36[£]				
Physical component summary				
Baseline (median (IQR))	36.8 (32.1, 48.7) n=4	47.4 (45.1, 51.2) n=5	42.5 (33.8, 59.9) n=3	50.9 (48.5, 53.4) n=2
6 months (median (IQR))	44.7 (37.3, 54.4) n=4	47.1 (46.8, 57.1) n=3	32.8 (32.4, 60.8) n=3	43.9 (26.1, 52.4) n=4
Change (median (IQR))	**5.5 (2.6, 10.7) n=4**	**5.6 (-1.3, 12.5) n=2**	**-1.4 (-9.7, 0.9) n=3**	**-7.0 (-9.4, -4.7) n=2**
Mental component summary				
Baseline (median (IQR))	48.9 (19.9, 60.4) n=4	50.5 (38.8, 53.3) n=5	27.1 (22.4, 54.3) n=3	45.2 (31.2, 59.2) n=2
6 months (median (IQR))	48.2 (33.9, 57.9) n=4	40.9 (27.5, 56.5) n=3	30.3 (20.4, 43.8) n=3	54.0 (50.3, 57.9) n=4
Change (median (IQR))	**-2.5 (-6.9, 20.1) n=4**	**-10.9 (-22.9, 0.9) n=2**	**-2.0 (-10.5, 3.2) n=3**	**8.3 (-9.1, 25.8) n=2**
TOPICAL STEROID USE				
Days of topical steroid used during trial period mean (sd)[range]	90 (63.4) [0, 158] n=5	92.2 (51.6) [39, 161] n=6	87 (76.1) [0, 172] n=4	42.2 (31.9) [0, 75] n=5
TREATMENT SATISFACTION AT 6 MONTHS				
Very	2	0	0	3
Somewhat	1	2	1	0
Neutral	0	0	1	1
Not very	1	1	1	0
Not at all	0	0	0	0
Missing	1	3	1	1
COST OF INTERVENTION				
Mean cost (£)of prescriptions issued during trial period in (n)	13.55 (3)	32.72 (5)	20.75 (3)	112.51 (4)

*Investigator Global Assessment (IGA) of vulval erosive lichen planus severity:0=clear/almost clear, 1=mild, 2=moderate, 3=severe

^Patient global Assessment of vulval erosive lichen planus: 0=no bother at all/not much bother, 1 = a little bother, 2= a lot of bother, 3=very much bother

[$] Hospital Anxiety and Depression Score (HADS): Scores for each subscale (anxiety and depression) range from 0-21. Scores for the entire scale range from 0-42, with higher scores indicating more distress.

[%] Skindex-29: Range of scores are from 0 (no effect) to 100 (effect experienced all the time). Higher score = higher impact of skin disease

[£] Short form 36 survey: All questions are scored on a scale from 0 to 100, with 100 representing the highest level of functioning possible.

Adverse events

All adverse events experienced in the hELP study, whether related or not

Event	Prednisolone	Hydroxychloroquine	Methotrexate	Mycophenolate mofetil	Total
Central Nervous System adverse events					
Headaches	2			1	3
Cardiovascular system adverse events					
Dizzy	1				1
Irregular heartbeat/ palpitations	1	1			2
Increased BP	1				1
Hypotension				1	1
Dermatological adverse events					
Easy bruising	1				1
Facial hair		1			1
Breast rash		1			1
Rash on neck		1			1
Leg rash		1			1
Rash on arms		1			1
Rash and lupus			1		1
Urticarial rash				1	1
Increased susceptibility to bruising			1		1
Endocrine adverse events					
Weight gain	2				2
Gastrointestinal adverse events					
Upset stomach	1				1
Heartburn	1				1
Abdo pain	1		1	6	8
Hungry	1				1
Thirsty	1				1
Flatulence		1			1
Diarrhoea & vomiting		2			2
Frequent bowel movements (not diarrhoea)		1			1
Diarrhoea		1			1
Vomiting			1		1
Hiatus hernia			1		1
Nausea			2		2
Nausea dyspepsia				1	1
Reduced appetite			1		1
General other adverse events					
Tiredness	1	1			2

Gynaecological adverse events					
Developed secondary Zoon's Vulvitis and vulvodynia			1		1
Fissure to clitoris			1		1
Haematological					
Abnormal blood tests - Hb 104				1	1
Blood results 9/4/15 MCH 32.6 (27-32), LY 1.0 (1.5-4)		1			1
Nose bleeds		1			1
Immunosuppressive effects					
Severe cold	1				1
Sore throat	1				1
Sinusitis	1				1
Headache and URTI				1	1
UTI				1	1
headache/sore throat/temperature				1	1
Viral gastroenteritis				1	1
Flu				1	1
Cough			1		1
Liver effects					
Raised ALT & AST		1			1
Borderline raised Gamma GT to 94			1		1
Borderline raised ALT 49 (7-40)			1		1
Borderline raised ALP to 150			1		1
Musculoskeletal effects					
Muscle ache	1				1
Degeneration of spine				1	1
Neuropsychiatric effects					
Insomnia/ can't sleep	1				1
Paracetamol overdose	1				1
Headaches and facial numbness			1		1
Tingling in fingers & toes		1			1
Fall		2			2

Ocular effects					
Blurred vision		1			1
Urogenital effects					
Increased urinary frequency	1				1
Cystitis		1			1
Abnormal eGFR - 52				1	1
Incontinence			1		1