

MERLOT TRIAL

EudraCT - 2009-012509-20

Study eye adverse events

Eye disorders	Epimacular brachytherapy N=244		Ranibizumab monotherapy N=119	
	Events	%	Events	%
Anterior chamber cell	1	0.4		
Anterior chamber flare	3	1.2		
Asthenopia	1	0.4		
Blepharitis	5	2.0	4	3.4
Blindness transient			1	0.8
Cataract	162	66.4	29	24.4
Cataract nuclear	3	1.2		
Cataract operation	44	18.0	10	8.4
Charles Bonnet syndrome			1	0.8
Choroidal effusion	1	0.4		
Choroidal hemorrhage	2	0.8		
Choroidal neovascularization	1	0.4		
Conjunctival granuloma	1	0.4		
Conjunctival hemorrhage	21	8.6	3	2.5
Conjunctival hyperemia	2	0.8		
Conjunctival irritation			1	0.8
Conjunctivitis	9	3.7	2	1.7
Conjunctivitis allergic	1	0.4		
Corneal abrasion	6	2.5	1	0.8
Corneal erosion	1	0.4		
Corneal infection	1	0.4		
Corneal edema	2	0.8		
Cyst drainage	1	0.4		
Cystoid macular edema	3	1.2		

Dacryoadenitis acquired	1	0.4		
Detachment of retinal pigment epithelium	2	0.8	1	0.8
Device malfunction	1	0.4		
Diplopia	1	0.4		
Drug hypersensitivity	1	0.4		
Dry eye	3	1.2		
Episcleritis	1	0.4		
Eye contusion	3	1.2	1	0.8
Eye discharge	2	0.8		
Eye hemorrhage	1	0.4		
Eye infection	1	0.4		
Eye inflammation	5	2.0		
Eye irritation	5	2.0	1	0.8
Eye laser scar	1	0.4		
Eye operation complication	6	2.5	1	0.8
Eye pain	21	8.6	5	4.2
Eye pruritus	2	0.8		
Eyelid ptosis	1	0.4		
Foreign body sensation in eyes	3	1.2	1	0.8
Glaucoma	2	0.8	2	1.7
Intraocular pressure increased	12	4.9	8	6.7
Iodine allergy			1	0.8
Iridocyclitis	2	0.8		
Iritis	1	0.4		
Lacrimation increased	5	2.0	1	0.8
Laser therapy	1	0.4		
Lenticular opacities	2	0.8		
Macular fibrosis	2	0.8		
Macular hole	1	0.4		
Macular scar	1	0.4		

Meibomianitis	1	0.4		
Metamorphopsia			1	0.8
Neovascular age-related macular degeneration	1	0.4		
Ocular discomfort	5	2.0		
Ocular hyperemia	2	0.8	2	1.7
Open angle glaucoma	3	1.2		
Ophthalmic herpes simplex	1	0.4		
Paracentesis eye	1	0.4	2	1.7
Photopsia	3	1.2	2	1.7
Polypoidal choroidal vasculopathy	1	0.4		
Posterior capsule opacification	9	3.7	3	2.5
Posterior capsule rupture	2	0.8		
Primary open angle glaucoma			1	0.8
Radiation retinopathy	3	1.2		
Retinal aneurysm	1	0.4		
Retinal artery embolism	1	0.4		
Retinal cyst	2	0.8		
Retinal degeneration	1	0.4		
Retinal exudates	1	0.4		
Retinal fibrosis	1	0.4		
Retinal hemorrhage	19	7.8	3	2.5
Retinal ischemia	1	0.4		
Retinal pigment epithelial tear	5	2.0	2	1.7
Retinal tear	19	7.8		
Retinal telangiectasia	1	0.4		
Retinal vein occlusion	2	0.8		
Retinoschisis	2	0.8		
Skin abrasion	1	0.4		
Subretinal fluid	2	0.8		

Suture related complication	1	0.4		
Ulcerative keratitis	1	0.4		
Uveitis	2	0.8		
Vision blurred	4	1.6		
Visual acuity reduced	32	13.1	7	5.9
Visual field defect			1	0.8
Visual impairment	4	1.6	1	0.8
Vitreous detachment			1	0.8
Vitreous floaters	4	1.6	2	1.7
Vitreous hemorrhage	3	1.2	1	0.8
Vitreous opacities			1	0.8
Total	503		104	

Ocular serious adverse events in study eye, and relatedness to treatment

Eye disorders	Events	%	Intensity	Epimacular brachytherapy	Vitrectomy	Ranibizumab	Intravitreal injection
Epimacular brachytherapy n=244							
Retinal detachment	5	2.0	Severe	Unlikely	Likely	Possibly	Possibly
			Moderate	Not Related	Likely	Not Related	Not Related
			Moderate	Not Related	Definitely	Not Related	Not Related
			Severe	Possibly	Possibly	Possibly	Possibly
			Severe	Unlikely	Possibly	Not Related	Likely
Retinal hemorrhage	4	1.6	Severe	Unlikely	Unlikely	Unlikely	Unlikely
			Severe	Unlikely	Not Related	Not Related	Not Related
			Severe	Unlikely	Unlikely	Unlikely	Unlikely
			Severe	Unlikely	Unlikely	Unlikely	Unlikely
			Severe	Unlikely	Unlikely	Unlikely	Unlikely
Retinal tear	1	0.4	Moderate	Not Related	Likely	Not Related	Not Related
Vision blurred	1	0.4	Severe	Possibly	Possibly	Possibly	Possibly
Blindness	2	0.8	Severe	Unlikely	Not Related	Not Related	Not Related
			Severe	Unlikely	Not Related	Not Related	Not Related
Corneal perforation	1	0.4	Severe	Not Related	Possibly	Not Related	Not Related
Endophthalmitis	1	0.4	Severe	Possibly	Possibly	Unlikely	Possibly
Hallucination, visual	1	0.4	Mild	Not Related	Likely	Not Related	Not Related
Hypopyon	1	0.4	Severe	Possibly	Likely	Unlikely	Unlikely
Uveitis	2	0.8	Severe	Possibly	Likely	Unlikely	Unlikely
			Severe	Not Related	Possibly	Not Related	Not Related
Visual acuity reduced	4	1.6	Severe	Unlikely	Possibly	Not Related	Likely
			Severe	Possibly	Possibly	Unlikely	Possibly
			Severe	Possibly	Likely	Unlikely	Unlikely
			Severe	NA	NA	NA	NA
Vitreous floaters	1	0.4	Severe	Possibly	Possibly	Unlikely	Possibly

Vitreous hemorrhage	1	0.4	Moderate	Not Related	Not Related	Possibly	Likely
Choroidal hemorrhage	1	0.4	Severe	Unlikely	Not Related	Not Related	Not Related
Eye pain	1	0.4	Severe	Unlikely	Not Related	Not Related	Not Related
Angle closure glaucoma	1	0.4	Severe	Unlikely	Not Related	Not Related	Not Related
Ranibizumab monotherapy N=119							
Retinal detachment	1	0.8	N/A	N/A	N/A	NA	NA
Blindness	1	0.8	Moderate	N/A	N/A	Unlikely	Unlikely
Retinal hemorrhage	1	0.8	Moderate	N/A	N/A	Unlikely	Unlikely
Visual field defect	1	0.8	Moderate	N/A	N/A	Unlikely	Unlikely

NA - not available, N/A - not applicable

Adverse events, excluding those in the study eye

System Organ Class	Epimacular brachytherapy (EMB) N=244		Ranibizumab monotherapy (Control) N=119	
	Events	%	Events	%
Blood and lymphatic system disorders	2	0.8		0.0
Cardiac disorders	21	8.6	1	0.8
Ear and labyrinth disorders	15	6.1	5	4.2
Endocrine disorders	4	1.6	1	0.8
Eye disorders	99	40.6	35	29.4
Gastrointestinal disorders	57	23.4	31	26.1
General disorders and administration site conditions	29	11.9	15	12.6
Hepatobiliary disorders	2	0.8		
Immune system disorders	6	2.5		
Infections and infestations	184	75.4	75	63.0
Injury, poisoning and procedural complications	95	38.9	31	26.1
Investigations	23	9.4	13	10.9
Metabolism and nutrition disorders	12	4.9	7	5.9
Musculoskeletal and connective tissue disorders	45	18.4	34	28.6
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	5	2.0	2	1.7
Nervous system disorders	39	16.0	24	20.2
Product issues	1	0.4		
Psychiatric disorders	8	3.3	3	2.5
Renal and urinary disorders	12	4.9	2	1.7
Reproductive system and breast disorders	3	1.2	4	3.4
Respiratory, thoracic and mediastinal disorders	44	18.0	16	13.4
Skin and subcutaneous tissue disorders	38	15.6	9	7.6
Social circumstances	2	0.8		
Surgical and medical procedures	34	13.9	15	12.6
Vascular disorders	14	5.7	7	5.9
Total	794		330	