

# Lucentis®

## Composition

Active substance: Ranibizumab  
 Excipients: α-trehalose dihydrate, histidine, histidine hydrochloride monohydrate, polysorbate 20, water for injections  
 Information might differ in some countries.

**Pharmaceutical form and quantity of active substance per unit**  
 Vial: 10 mg/ml ranibizumab (vial containing 2.3 mg ranibizumab in 0.23 ml of solution).  
 Pre-filled syringe 10 mg/ml ranibizumab (pre-filled syringe containing 1.65 mg ranibizumab in 0.165 ml of solution).

**Indications/Potential uses**  
 Lucentis is indicated for the treatment of:  
 • wet age-related macular degeneration (wet AMD).  
 • visual impairment due to diabetic macular oedema (DME).  
 • visual impairment due to macular oedema secondary to retinal vein occlusion (branch retinal vein occlusion, BRVO, or central retinal vein occlusion, CRVO).  
 • visual impairment due to choroidal neovascularisation (CNV) secondary to pathological myopia (PM).

**Dosage/Administration**  
 Dosage  
 Lucentis may only be administered by a qualified ophthalmologist with access to the appropriate infrastructure. Lucentis is administered by intravitreal injection. A Lucentis vial contains 0.23 ml and a pre-filled syringe contains 0.165 ml. Both are intended for once-only use in a single patient.  
 The recommended dose of 0.5 mg is given as a single intravitreal injection. This corresponds to an injection volume of 0.05 ml. The interval between two injections may not be shorter than one month. The injection should be monitored monthly.

**Treatment of wet AMD**  
 If it is not possible to give monthly injections in the long term, treatment may be given as follows:  
 Treatment is given monthly and continued until maximum visual acuity is achieved, i.e. when visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.  
 Treatment should be resumed when monitoring indicates renewed disease activity (confirmed by renewed loss of visual acuity, or morphological changes), and should continue until visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.

**Treatment of visual impairment due to DME**  
 Treatment is given monthly and continued until maximum visual acuity is achieved, i.e. when visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.  
 Treatment should be resumed when monitoring indicates renewed disease activity (confirmed by renewed loss of visual acuity, or morphological changes), and should continue until visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.

**Treatment of visual impairment due to macular oedema secondary to RVO**  
 Treatment is given monthly and continued until maximum visual acuity is achieved, i.e. when visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.  
 Treatment should be resumed when monitoring indicates renewed disease activity (confirmed by renewed loss of visual acuity, or morphological changes), and should continue until visual acuity is stable on Lucentis therapy in at least three consecutive monthly assessments.

**Treatment of visual impairment due to CNV secondary to PM**  
 Treatment is initiated with a single injection.  
 If monitoring reveals signs of disease activity, further treatment is recommended. Monitoring for disease activity may include clinical examinations such as measuring visual acuity, optical coherence tomography (OCT) or fluorescein angiography (FA). In the first year of treatment, monthly monitoring is recommended during the first two months of treatment, and subsequently at least every three months. Following the end of the first year of treatment, the frequency of monitoring should be determined by the treating physician. Following initial therapy, the interval between two injections may not be shorter than one month. There is no experience with treatment lasting for more than one year.

**Administration**  
 The patient's medical history should be thoroughly evaluated for possible hypersensitivity reactions prior to intravitreal administration (see "Warnings and precautions").  
 Lucentis must be administered under aseptic conditions (suitable premises, sterile drape, gloves and instruments). Suitable anaesthesia and a topical broad spectrum microbicide to disinfect the skin around the eye, the eyelid and the surface of the eye should be applied before the injection.  
 The entire contents of the vial are withdrawn using a syringe and a 5 µm filter needle. The filter needle is removed prior to intravitreal injection, and the injection needle (30G x 13 mm) is attached to the syringe. The contents should be expelled until the plunger tip is aligned with the line that marks 0.05 ml (50 µl) on the syringe. The contents of one vial are to be used for administration of a single dose. Discard leftover solution.  
 The injection needle should be fully inserted 3.5-4.0 mm posterior to the limbus, avoiding the horizontal meridian and aiming towards the centre of the globe.  
 The injection volume is delivered slowly, and attention should be paid to changing the scleral injection site for subsequent injections.  
 The patient's intraocular pressure must be monitored after the injection. Monitoring should consist of a check for perfusion of the optic nerve disc immediately after the injection, tonometry within 30 minutes, and ophthalmoscopy, slit-lamp examination and funduscopy 2-7 days later. Patients must be instructed to report any signs of endophthalmitis to their doctor immediately (see "Warnings and precautions").

**Additional information for special patient populations**  
**Renal impairment**  
 No dose adjustment is necessary in patients with renal impairment (see "Pharmacokinetics").  
**Hepatic impairment**  
 No studies are available. No special precautions are considered necessary as systemic exposure is negligible.

**Children and adolescents**  
 Data on safety and efficacy are not available. Lucentis is not recommended for use in children and adolescents.  
**Elderly patients (aged 65 and over)**  
 No dose adjustment is necessary.

**Contraindications**  
 Hypersensitivity to ranibizumab or to any of the excipients. Lucentis is contraindicated in patients with ocular or periorcular infections, and in patients with active intravitreal inflammation.

**Warnings and precautions**  
 Intravitreal injections have been associated with infectious endophthalmitis and retinal detachment. Aseptic injection techniques must be used when administering Lucentis. In addition, patients should be monitored during the days following the injection to permit early detection and treatment of infection (see "Adverse effects").  
 Transient increases in intraocular pressure have been seen within 60 minutes of injection of Lucentis. Persistently elevated intraocular pressure has also been reported. Both intraocular pressure and the perfusion of the central retinal artery must be monitored and managed appropriately (see "Adverse effects").  
 The safety and efficacy of Lucentis treatment administered to both eyes concurrently have not been investigated in experimental studies.  
 The limited data on bilateral Lucentis use (including administration on the same day) does not suggest an increased risk of systemic adverse events compared with unilateral use.  
 There is a potential risk of arterial thromboembolic events following intravitreal use of vascular endothelial growth factor (VEGF) inhibitors. Patients with known risk factors for stroke (e.g. a prior stroke or transient ischaemic attack) may be at higher risk.  
 The pre-treatment incidence of immunoreactivity to Lucentis was 0-3% in all treatment groups. Following monthly administration, low antibody titres were detected in 1-6% of patients after 12-24 months. These immunogenicity data reflect the percentage of patients in whom electrochemoluminescence assay results were positive. The data were highly dependent on the sensitivity and specificity of the assay. The clinical significance of immunoreactivity to Lucentis is unclear at this time. Iritis and vitritis were reported in some patients with the highest levels of immunoreactivity.  
 Lucentis has not yet been studied in patients with active systemic infections or concurrent eye conditions such as retinal detachment or macular hole.  
 There is limited experience in patients with prior episodes of RVO and patients with ischaemic RVO. In patients with RVO presenting with clinical signs of irreversible ischaemic visual function loss, treatment is not recommended.  
 Use of Lucentis in patients who have previously received laser photocoagulation, and co-administration of Lucentis with laser photocoagulation were studied. If Lucentis is to be given on the same day as laser photocoagulation, the injection may not be administered until at least 30 minutes after laser photocoagulation.

**Interactions**  
 No specific interaction studies have been performed.

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 No specific interaction studies have been performed.

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**Effects on the ability to drive and use machines**  
 Treatment with Lucentis may induce temporary visual disturbances, which may affect the ability to drive or use machines (see "Adverse effects"). Patients who experience such effects must not drive or use machines until the temporary visual disturbances subside.

**Adverse effects**  
 A total of 1,315 patients constituted the safety population in the three phase III clinical studies on the treatment of wet AMD. All the patients were treated with Lucentis for at least 24 months. 440 patients were treated with the recommended dose of 0.5 mg.  
 Serious adverse events related to the injection procedure were: endophthalmitis, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract (see "Warnings and precautions").  
 Intraocular inflammation and increased intraocular pressure were also seen in patients treated with Lucentis (see "Warnings and precautions").  
 In the controlled phase III studies of wet AMD – FV2598g (MARINA), FV2587g (ANCHOR) and FV3192g (PIER) – the adverse events listed below occurred at a higher rate (at least two percentage points higher) in patients with wet AMD receiving treatment with 0.5 mg Lucentis than in patients in the control groups (sham injection (see "Properties/Actions") or verteporfin PDT). They were therefore considered potential adverse drug reactions (ADRs). The safety data provided below also include all adverse events suspected to be at least potentially caused by the injection procedure or the medicinal product in the 440 patients in the combined 0.5 mg Lucentis treatment groups in wet AMD.  
**CNV secondary to PM patient population**  
 The safety of Lucentis was studied in the 12-month clinical study RADIANCE, which included 224 ranibizumab-treated patients with CNV secondary to PM (see "Properties/Actions"). Ocular and non-ocular events in this trial were reported with a frequency and severity similar to those seen in the wet AMD trials.  
**Frequencies: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/100 to < 1/1,000); rare (≥ 1,000 to < 1/10,000); very rare (< 1/10,000).**

**Infections**  
**Very common:** Nasopharyngitis (12.5–16.4%).  
**Common:** Influenza, urinary tract infection.

**Blood and lymphatic system disorders**  
**Common:** Anaemia.  
**Immune system disorders**  
**Common:** Hypersensitivity reactions.

**Psychiatric disorders**  
**Common:** Anxiety.  
**Nervous system disorders**  
**Very common:** Headache (6-15%).  
**Common:** Stroke.

**Very common:** Intraocular inflammation (10-18%), vitritis (2.3-10%), vitreous detachment (18-19%), retinal haemorrhage (25%), visual disturbances (6.6-10.5%), eye pain (27-32%), vitreous floaters (7-25%), conjunctival haemorrhage (5.5-7.2%), eye irritation (12-15%), foreign body sensation in eyes (12-15%), increased lacrimation (10-14%), blepharitis (8-11%), eye pruritus (8-5-10%).  
**Common:** Retinal degeneration, retinal detachment, retinal tear, detachment of retinal pigment epithelium, tear in retinal pigment epithelium, reduced visual acuity, vitreous haemorrhage, vitreous disorders, uveitis, iritis, iridocyclitis, (subcapsular) cataract, posterior capsule opacification, punctate keratitis, corneal abrasion, opacification of aqueous humour, blurred vision, injection site haemorrhage, eye haemorrhage, (allergic) conjunctivitis, eye discharge, photopsia, photophobia, ocular discomfort, eyelid pain, eyelid oedema, conjunctival hyperaemia.  
**Uncommon:** Endophthalmitis, hypopyon, hyphaema, keratoopathy, iris adhesions, corneal melt, corneal oedema, corneal striae, injection site pain and irritation, blindness, eyelid irritation.

**Cardiovascular disorders**  
**Arterial thromboembolic events**, as defined by the Antiproteinase Trials' Collaboration (1994), including vascular deaths, non-fatal myocardial infarctions, non-fatal ischaemic strokes and non-fatal haemorrhagic strokes, have been linked to the systemic availability of highly potent VEGF inhibitors. In the first year, the incidence of thromboembolic events in both of the patient groups treated with Lucentis (0.3 and 0.5 mg) was 2.3%, compared with 1.3% in the control group. In the second year of the MARINA study, it was 3.0% in both treatment groups and 3.2% in the control group.

**Respiratory, thoracic and mediastinal disorders**  
**Common:** Cough.  
**Gastrointestinal disorders**  
**Common:** Nausea.  
**Skin and subcutaneous tissue disorders**  
**Common:** Allergic reactions (rash, urticaria, pruritus, erythema).

**Musculoskeletal disorders**  
**Very common:** Arthralgia (8–12%).  
**Investigations**  
 Increased intraocular pressure.  
**Immunogenicity**  
 As with all therapeutic proteins, there is the potential for an immune response in patients treated with Lucentis. The immunogenicity data reflect the presence of any anti-drug antibodies for antibodies to ranibizumab and immunocasts and were highly dependent on the sensitivity and specificity of the assays. In the AMD studies, the pre-treatment incidence of immunoreactivity to Lucentis was 0-3% in all treatment groups. After monthly administration of Lucentis for 12 to 24 months, antibodies to ranibizumab were detected in approximately 1-8% of patients with neovascular AMD.  
 In the DME studies, the pre-treatment incidence of immunoreactivity to Lucentis was 0-2% in all treatment groups. After monthly administration of Lucentis for 12 months, antibodies to ranibizumab were detected in approximately 2-4% of patients with DME.  
 In the RVO studies, the pre-treatment incidence of immunoreactivity to Lucentis was 2-3% in all treatment groups. After monthly administration of Lucentis for 12 months, antibodies to ranibizumab were detected in approximately 4-5% of patients with RVO.  
 The clinical significance of immunoreactivity to Lucentis is unclear at this time.

patients received an average of 22 out of a possible 24 treatments. The results of the MARINA study after 12 months of treatment were also essentially confirmed after 24 months of treatment (once per month) in 90% of the patients.  
 A total of 423 patients with predominantly classic CNV lesions were enrolled in the ANCHOR study. They received monthly intravitreal injections of either 0.3 mg Lucentis and sham PDT (N = 143), intravitreal injections of 0.5 mg Lucentis and sham PDT (N = 140), or sham intravitreal injections and active verteporfin PDT (N = 143). The initial sham or active verteporfin PDT was given with the initial Lucentis injection. Treatment was given every three months thereafter. If fluorescein angiography showed persistence or recurrence of vascular leakage in the study eye. For the ANCHOR study, data are available up to the end of Month 12. During this time, patients received an average of 12 out of a possible 13 treatments.

The results are summarised in the following tables:  
**Table 0-1 MARINA study: Results at Months 12 and 24**  
**Change in visual acuity (in letters)**  

Month	Sham (N = 238)	Ranibizumab 0.5 mg (N = 240)	Difference (95% CI) <sup>a</sup>
Loss of < 15 letters in visual acuity (%)	62%	35%	27% (26%, 39%)
Gain of ≥ 15 letters in visual acuity (%)	53%	90%	37% (29%, 44%)
Month 24	5%	34%	29% (22%, 35%)
Month 12	+10.5 (16.6)	+7.2 (14.4)	17.5 (14.8, 20.2)
Month 24	-14.9 (18.7)	+6.6 (16.5)	21.1 (18.1, 24.2)

  
<sup>a</sup> after stratification  
<sup>b</sup> p < 0.01

**Table 0-2 ANCHOR study: Results at Months 12 and 24**  
**Change in visual acuity**  

Month	Verteporfin PDT (N = 143)	Ranibizumab 0.5 mg (N = 140)	Difference (95% CI) <sup>a</sup>
Loss of < 15 letters in visual acuity (%)	64%	9%	55% (25%, 41%)
Gain of ≥ 15 letters in visual acuity (%)	24%	66%	42% (16%, 34%)
Month 24	6%	40%	35% (26%, 44%)
Month 12	6%	41%	36% (26%, 44%)
Month 24	6%	41%	36% (26%, 44%)
Month 12	-9.5 (16.4)	+11.3 (14.6)	21.1 (17.5, 24.6)
Month 24	-9.8 (16.4)	+10.7 (16.5)	20.7 (16.8, 24.7)

  
<sup>a</sup> after stratification  
<sup>b</sup> p < 0.01

The improvement in vision reported at Month 12 in both the MARINA and ANCHOR study on treatment with 0.5 mg Lucentis resulted in a benefit for patients, as measured by the three subscales of the National Eye Institute Visual Function Questionnaire (VFQ-25), which had been established previously as secondary end-points for efficacy (activities related to near vision and distance vision, as well as other vision-dependent activities). All differences between 0.5 mg Lucentis and the two control groups were statistically significant and clinically relevant, with p-values between 0.009 and < 0.0001.

The PIER study included 184 patients with CNV lesions (with and without classic components). They received an intravitreal injection of 0.3 mg or 0.5 mg Lucentis, or a sham intravitreal injection, once a month for the first three months. Additional injections of Lucentis were administered once every three months. From Month 14, patients who received a sham injection were also able to be treated with Lucentis, and from Month 19 more frequent injections of Lucentis were possible. Patients treated with Lucentis in PIER received an average of 10 treatments over 24 months.  
 The primary efficacy endpoint was mean change in visual acuity over the 12 months. After an initial increase during the monthly injection phase, patients' visual acuity declined during the quarterly injection phase, returning to baseline after 12 months. This effect was maintained in most patients (82%) treated with Lucentis at Month 24. Data from a limited number of patients who switched over to treatment with Lucentis after more than a year of sham treatment suggest that early initiation of treatment is associated with better preservation of visual acuity.

**Table 0-3 PIER study: Results at Month 12**  
**Change in visual acuity**  

Month	Sham (N = 63)	Ranibizumab 0.5 mg (N = 61)	Difference (95% CI) <sup>a</sup>
Loss of < 15 letters in visual acuity (%)	49	90	41% (23, 52)
Gain of ≥ 15 letters in visual acuity (%)	10	13	3% (5, 12)
Mean change in visual acuity <sup>b</sup>	-16.3 (22.3)	-0.2 (13.1)	14.7 (8.2, 21.2)

  
<sup>a</sup> after stratification  
<sup>b</sup> p < 0.0001

The phase IIIb SAILOR study was carried out in treatment-naïve and previously treated patients with CNV secondary to AMD. SAILOR was a one-year multicentre study. The primary study objective was to estimate the incidence of ocular and non-ocular adverse effects during 12 months of treatment. 2,378 patients, randomised to two groups, were given one 0.3 mg or 0.5 mg dose of Lucentis every month for three months. Depending on the findings, this was followed by further treatment at intervals of not less than one month.  
 There was no imbalance between the two groups with regard either to the overall incidence of ocular and non-ocular adverse effects or to the incidence of stroke in particular, which occurred in 8 of 1,169 patients given 0.3 mg doses (0.7%; 95% CI: 0.3% to 1.3%). 15 of 1,209 patients given 0.5 mg doses (1.2%; 95% CI: 0.7% - 2%). Patients with known risk factors (e.g. a prior stroke or transient ischaemic attack) are presumably at greater risk for stroke during treatment with Lucentis.  
**Treatment of visual impairment due to DME**  
 The clinical efficacy and safety of Lucentis in patients with visual impairment due to diabetic macular oedema (DME) were assessed in the RESTORE study involving a total of 345 patients with visual impairment due to DME. The study had three arms: Patients in arm 1 (N = 116) initially received intravitreal injections of 0.5 mg ranibizumab as monotherapy and sham laser photocoagulation. Patients in arm 2 (N = 118) initially received intravitreal injections of 0.5 mg ranibizumab and laser photocoagulation. Patients in arm 3 (N = 111) initially received laser photocoagulation monotherapy and a sham injection.  
 Treatment with ranibizumab continued with monthly intravitreal injections and was suspended when visual acuity on Lucentis had stabilised at three consecutive visits. Treatment was reinitiated when there was a reduction in visual acuity due to DME progression. Repeat treatment with laser photocoagulation was carried out on the same day, at least 30 minutes before injection of ranibizumab, according to ETRS criteria.

The results are summarised in the following tables:  
**Table 0-4 RESTORE study: Results at Month 12**  
**Change in best-corrected visual acuity (BCVA)**  

Month	Ranibizumab 0.5 mg (n=115)	Ranibizumab 0.5 mg + laser (n=118)	Laser (n=110)
Mean change in BCVA (in letters) from Month 1 to Month 12	6.1 (6.4)	5.9 (7.9)	0.8 (8.6)
Mean change in BCVA (in letters) at Month 12 compared to baseline (standard deviation) <sup>a</sup>	6.8 (8.3) <sup>b</sup>	6.4 (11.8) <sup>b</sup>	0.9 (11.4)
Gain of ≥ 15 letters in BCVA (% of patients)	37.4 <sup>c</sup>	43.2	15.5
Gain of ≥ 15 letters in BCVA (% of patients)	22.6 <sup>d</sup>	22.9 <sup>d</sup>	8.2

  
<sup>a</sup> p < 0.0001, <sup>b</sup> p = 0.0004, <sup>c</sup> p = 0.0001, <sup>d</sup> p = 0.0032, <sup>e</sup> p = 0.0021  
 Treatment of visual impairment due to macular oedema secondary to RVO  
 The clinical safety and efficacy of Lucentis in patients with visual impairment due to macular oedema secondary to retinal vein occlusion (RVO) have been assessed in two randomised, double-masked, controlled studies: BRAVO (N = 397) and CRUISE (N = 392). In both studies, patients received either 0.3 mg or 0.5 mg ranibizumab, or sham treatment. In BRAVO, laser photocoagulation was allowed as rescue treatment at any time in the study from Month 3 in all study arms. The results of BRAVO and CRUISE are summarised in the following tables:  
**Table 0-5 BRAVO study: Results at Months 6 and 12**  
**Change in visual acuity**  

Month	Sham (n=132)	Ranibizumab 0.5 mg (n=131)
Mean change in BCVA (in letters) at Month 6 compared to baseline <sup>a</sup>	+7.3	+18.3
Mean change in BCVA (in letters) at Month 12 compared to baseline <sup>a</sup>	+12.1	+18.3
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 6	28.8%	61.1%
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 12	43.9%	60.3%
Proportion of patients with laser rescue over 12 months	61.4%	34.4%

  
<sup>a</sup> p < 0.0001  
**Table 0-6 CRUISE study: Results at Months 6 and 12**  
**Change in visual acuity**  

Month	Sham (n=132)	Ranibizumab 0.5 mg (n=131)
Mean change in BCVA (in letters) at Month 6 compared to baseline <sup>a</sup>	+0.8	+14.9
Mean change in BCVA (in letters) at Month 12 compared to baseline <sup>a</sup>	+7.3	+13.9
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 6	16.9%	47.7%
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 12	33.1%	50.8%

  
<sup>a</sup> p < 0.0001  
 Patients treated with ranibizumab showed a continuous reduction in central retinal thickness (CRT) in both the BRAVO and CRUISE studies.  
 Apart from improvement in visual acuity after treatment with ranibizumab at Month 6 and 12, the patients' quality of life was also evaluated using the National Eye Institute Visual Function Questionnaire (VFQ-25). The differences between the 0.5 mg ranibizumab group and the control group were assessed at Month 6 with p-values between 0.02 and 0.0002.  
 The 12-month results of the HORIZON extension study for BRAVO and CRUISE (i.e. 24 months from BRAVO/CRUISE baseline) showed the following:  
 The reduced frequency of treatment in the HORIZON trial had little impact on BRVO (branch retinal vein occlusion) patients, who maintained their initial visual acuity improvement observed in the BRAVO study (+17.5 letters at 24 months with a dose of 0.5 mg and an average of 2.4 injections in the second year).  
 In contrast, in CRVO (central retinal vein occlusion) patients, the reduced frequency of treatment was associated with a reduction in the visual acuity gained in the CRUISE study (+12 letters at 24 months with a dose of 0.5 mg and an average of 3.8 injections in the second year).  
**Treatment of visual impairment due to CNV secondary to PM**  
 The clinical safety and efficacy of Lucentis in patients with visual impairment due to CNV secondary to PM were assessed based on the 12-month data of the randomised, double-masked controlled pivotal study RADIANCE, which was designed to evaluate two different dosing regimens of 0.5 mg ranibizumab given as an intravitreal injection in comparison to verteporfin PDT (vPDT, Vesdymne photodynamic therapy).  
 The 277 patients were randomised to one of the following arms:  
 Group I (ranibizumab 0.5 mg, dosing regimen driven by stability criteria defined as no change in BCVA compared to two preceding monthly evaluations)  
 Group II (ranibizumab 0.5 mg, dosing regimen driven by disease activity criteria defined as visual impairment attributable to intra- or subretinal fluid or active leakage due to the CNV lesion as assessed by OCT and/or FA).  
 Group III (vPDT - patients were allowed to receive ranibizumab treatment as of Month three)  
 Over the 12 months of the study, patients received an average 4.6 injections (range 1-11) in Group I and 3.5 injections (range 1-12) in Group II. In Group II (in which patients received the recommended treatment regimen based on disease activity, see "Dosage/Administration"), 50.9% of patients required one or two injections, 34.5% required three to five injections and 14.7% required six to twelve injections over the 12-month study period. In Group II, 62.9% of patients did not require injections in the last six months of the study.  
 Key outcomes from RADIANCE are summarised in Table 0-7 and Figure 0-1.

**Table 0-7 Outcomes at Month 3 and Month 12 (RADIANCE)**  

	Group I 0.5 mg Ranibizumab Visual acuity (n=105)	Group II 0.5 mg Ranibizumab Disease activity (n=116)	Group III vPDT* (n=55)
<b>Month 3</b>			
Mean average BCVA change from Month 1 to Month 3 compared to baseline <sup>a</sup> (letters)	+10.5	+10.6	+2.2
Proportion of patients who gained ≥ 10 letters, or reached ≥ 84 letters in BCVA	61.9%	65.5%	27.3%
Proportion of patients who gained ≥ 15 letters, or reached ≥ 84 letters in BCVA	38.1%	43.1%	14.5%
Number of injections up to Month 12:			
Mean	4.6	3.5	N/A
Median	4.0	2.0	N/A
Mean average BCVA change from Month 1 to Month 12 compared to baseline (letters)	+12.8	12.5	N/A
Proportion of patients who gained ≥ 10 letters, or reached ≥ 84 letters in BCVA	69.5%	69.0%	N/A
Proportion of patients who gained ≥ 15 letters, or reached ≥ 84 letters in BCVA	53.3%	51.7%	N/A

The results are summarized in the following tables:  
**Table 0-4 RESTORE study: Results at Month 12**  
**Change in best-corrected visual acuity (BCVA)**  

Month	Ranibizumab 0.5 mg (n=115)	Ranibizumab 0.5 mg + laser (n=118)	Laser (n=110)
Mean change in BCVA (in letters) from Month 1 to Month 12	6.1 (6.4)	5.9 (7.9)	0.8 (8.6)
Mean change in BCVA (in letters) at Month 12 compared to baseline (standard deviation) <sup>a</sup>	6.8 (8.3) <sup>b</sup>	6.4 (11.8) <sup>b</sup>	0.9 (11.4)
Gain of ≥ 15 letters in BCVA (% of patients)	37.4 <sup>c</sup>	43.2	15.5
Gain of ≥ 15 letters in BCVA (% of patients)	22.6 <sup>d</sup>	22.9 <sup>d</sup>	8.2

  
<sup>a</sup> p < 0.0001, <sup>b</sup> p = 0.0004, <sup>c</sup> p = 0.0001, <sup>d</sup> p = 0.0032, <sup>e</sup> p = 0.0021  
 Treatment of visual impairment due to macular oedema secondary to RVO  
 The clinical safety and efficacy of Lucentis in patients with visual impairment due to macular oedema secondary to retinal vein occlusion (RVO) have been assessed in two randomised, double-masked, controlled studies: BRAVO (N = 397) and CRUISE (N = 392). In both studies, patients received either 0.3 mg or 0.5 mg ranibizumab, or sham treatment. In BRAVO, laser photocoagulation was allowed as rescue treatment at any time in the study from Month 3 in all study arms. The results of BRAVO and CRUISE are summarised in the following tables:  
**Table 0-5 BRAVO study: Results at Months 6 and 12**  
**Change in visual acuity**  

Month	Sham (n=132)	Ranibizumab 0.5 mg (n=131)
Mean change in BCVA (in letters) at Month 6 compared to baseline <sup>a</sup>	+7.3	+18.3
Mean change in BCVA (in letters) at Month 12 compared to baseline <sup>a</sup>	+12.1	+18.3
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 6	28.8%	61.1%
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 12	43.9%	60.3%
Proportion of patients with laser rescue over 12 months	61.4%	34.4%

  
<sup>a</sup> p < 0.0001  
**Table 0-6 CRUISE study: Results at Months 6 and 12**  
**Change in visual acuity**  

Month	Sham (n=132)	Ranibizumab 0.5 mg (n=131)
Mean change in BCVA (in letters) at Month 6 compared to baseline <sup>a</sup>	+0.8	+14.9
Mean change in BCVA (in letters) at Month 12 compared to baseline <sup>a</sup>	+7.3	+13.9
Proportion of patients with gain of ≥ 15 letters in visual acuity (%) at Month 6	16.9%	47.7%
Proportion of patients with gain of ≥ 15 letters		