Appendix 1. Primary investigators for the TREND study

List of principal investigators (except for authors) who participated in this study (country):

P Paul Schauwvlieghe (Belguim), E Van Aken (Belguim), B Mazur (Belguim), T Jukic (Croatia), Z Vatavuk (Croatia), D Bosnar (Croatia), I Munch (Denmark), M Mahgoub (Egypt), N Eter (Germany), N Feltgen (Germany), H Berk (Germany), P Szurman (Germany), P Wiedemann (Germany), K Schoepfer (Germany), S Biester (Germany), K Engelmann (Germany), K Heinz Emmerich (Germany), F Gekeler (Germany), L Olof Hattenbach (Germany), D Pauleikhoff (Germany), U Kellner (Germany), A Pielen (Germany), S Schmickler (Germany), A Mueller (Germany), H Thieme (Germany), J Nemeth (Hungary), Z Biro (Hungary), A Seres (Hungary), A Kerenyi (Hungary), T Milibak (Hungary), P Vamosi (Hungary), M Ferencz (Hungary), L Szalczer (Hungary), M Bhende (India), G Devi Paramoo Sreedevi (India), R Erlich (Israel), A Pollack (Israel), M Goldstein (Israel), Y Barak (Israel), I Chowers (Israel), F Bandello (Italy), G Virgili (Italy), U Menchini (Italy), F Boscia (Italy), E Midena (Italy), M Nardi (Italy), M Varano (Italy), P Lanzetta (Italy), G Staurenghi (Italy), H Gon Yu (South Korea), W Ki Lee (South Korea), J Eun Lee (South Korea), K Hyung Park (South Korea), A Meireles (Portugal), J Figueira (Portugal), M Amaro (Portugal), R Flores (Portugal), V Erichev (Russia), E Abdulaeva (Russia), E Milyudin (Russia), E Smirnov (Russia), A Doga (Russia), M Ondrejkova (Slovakia), J Stefanickova (Slovakia), L Branikova (Slovakia), M Alexik (Slovakia), L Javorska (Slovakia), P Jaki Mekjavic (Slovakia), J Escobar (Slovakia), L Sararols Ramsay (Spain), M Lopez Galvez (Spain), A Fernandez-Vega (Spain), P Calvo (Spain), J Garweg (Switzerland), M Zinkernagel (Switzerland), S Michels (Switzerland), I Mantel (Switzerland), B Eldem (Turkey), G Yilmaz (Turkey), G Menon (United Kingdom), A Ross (United Kingdom), R Hamilton (United Kingdom), S George (United Kingdom), S Mahmood (United Kingdom), U Chakravarthy (United Kingdom), D Varma (United Kingdom), and S Taylor (United Kingdom)

Appendix 2. Patient enrollment by country

Country	Total number of patients enrolled
Belgium	15
Croatia	34
Denmark	22
Egypt	10
Germany	68
Hungary	105
India	11
Israel	50
Italy	44
Korea	28
Portugal	38
Russia	40
Slovakia	49
Slovenia	2
Spain	56
Switzerland	26
Turkey	12
UK	40
Total	**650**

Appendix 3. Patient inclusion and exclusion criteria

Inclusion criteria

1. Patient must have given written informed consent
2. Patient (male or female) must have been ≥50 years of age

Inclusion criteria for the study eye at screening:

3. Visual impairment predominantly due to neovascular age-related macular degeneration (nAMD)
4. Active choroidal neovascularization (CNV) secondary to AMD confirmed by presence of active leakage from CNV detected by fluorescein angiography (FA) and/or color fundus photography
5. Presence of intra- or sub-retinal fluid/hemorrhage detected by spectral domain optical coherence tomography (SD-OCT)
6. CNV or sequelae of the CNV (i.e., pigment epithelium detachment; sub-retinal or sub-retinal pigment epithelium (RPE) hemorrhage; blocked fluorescence; macular edema; or sub-retinal, sub-RPE, or intra-retinal fluid) involving the center of the fovea
7. The total area of fibrosis comprising less than 50% of the lesion area
8. Best-corrected visual acuity (BCVA) score must be ≤78 and ≥23 letters at 4 meters starting distance using Early Treatment Diabetic Retinopathy Study (ETDRS)-like visual acuity (VA) charts (approximate Snellen equivalent of 20/32 and 20/320)

Exclusion criteria

Exclusion criteria for systemic medical history and conditions at screening:

1. Any type of advanced, severe, or unstable disease, including any medical condition (controlled or uncontrolled) that could be expected to progress, recur, or change to such an extent that it may bias the assessment of the clinical status of the patient to a significant degree or put the patient at special risk
2. Stroke or myocardial infarction within 3 months before screening
3. Presence of uncontrolled systolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg
4. Known hypersensitivity to the investigational drug (ranibizumab or any component of the ranibizumab formulation) or to drugs of similar chemical class or to fluorescein or any other component of fluorescein formulation

Exclusion criteria for ocular medical history and conditions at screening:

5. Any active periocular or ocular infection or inflammation in both eyes
6. Uncontrolled glaucoma (intraocular pressure [IOP] ≥30 mmHg on medication or according to investigator's judgment) in the study eye
7. Atrophy or fibrosis involving the center of the fovea in the study eye
8. History of focal/grid laser photocoagulation with involvement of the macular area at any time in the study eye
9. Ocular disorders in the study eye (i.e., retinal detachment, pre-retinal membrane of the macula, or cataract with significant impact on VA) at the time of enrollment that may confound interpretation of study results and compromise VA
10. Presence of amblyopia or ocular disorders with final best-corrected vision <20/200 or amaurosis in the fellow eye

Exclusion criteria for prior or current ocular treatment at screening:

11. History of treatment with any anti-angiogenic drugs (including any anti-vascular endothelial growth factor [VEGF] agents; e.g., bevacizumab [Avastin®] and aflibercept [Eylea®]) or verteporfin photodynamic therapy in the study eye
12. History of intravitreal treatment with corticosteroids within 6 months before screening in the study eye
13. History of intraocular surgery within 3 months in the study eye before screening

Exclusion criteria for prior or current systemic medication at screening:

14. Use of other investigational drugs (excluding vitamins and minerals) within 30 days or 5 half-lives from screening, whichever longer
15. Use of any systemic anti-VEGF drugs within 3 months before screening (e.g., bevacizumab [Avastin®] and ziv-aflibercept [Zaltrap®])
16. Current or planned use of systemic medications known to be toxic to the lens, retina, or optic nerve, including deferoxamine, chloroquine/hydroxychloroquine (Plaquenil®), tamoxifen, phenothiazines, and ethambutol

Exclusion criteria for patients at screening:

17. Pregnant or nursing (lactating) women, where pregnancy was defined as the state of a female after contraception and until the termination of gestation, confirmed by a positive human chorionic gonadotropin (hCG) laboratory test
18. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they are using effective methods of contraception during dosing of study treatment