Supplementary File S3: Randomisation sequence, allocation and masking

The randomisation numbers were generated using the following procedure to ensure that treatment assignment was unbiased and concealed from patients and masked investigator staff. RETAIN was designed as a single masked study. It was impossible to double-mask the laser treatment because the Treating Investigator could potentially identify laser burns on fundus images, and those patients with previous experience of laser treatment would have been able to differentiate between sham and active laser treatments. Thus, in order to provide a reasonable degree of masking, the study was observer-masked and for fulfilment of the masking requirements each site required a masked 'Evaluating Investigator' and an unmasked 'Treating Investigator'. The evaluating investigator (masked to the treatment assignment) performed BCVA and other study efficacy assessments but did not perform postinjection IOP measurements and judged the presence or absence of BCVA stability and the presence or absence of DME disease activity/recurrence. He/she provided this information to the treating investigator(s). The treating investigator(s) (unmasked to the treatment assignment) received treatment allocation cards and administered study treatment (ranibizumab injections or laser treatment) based on the judgment of the evaluating investigator regarding BCVA stability and DME activity/recurrence and according to treatment schedule (i.e. group) a given patient had been randomised to as per treatment allocation cards. The treating investigator(s) was not involved in any study efficacy evaluations and did not divulge details of the treatment assignment to anyone.

Each patient was uniquely identified in the study by a combination of his/her centre number and patient number. The centre number was assigned by Novartis to the investigative site. Upon signing the informed consent, the patient was assigned a patient number by the BCVA assessing investigator. At Visit 2, the treating investigator randomised patients who fulfilled the inclusion/exclusion criteria using the sealed treatment allocation cards supplied by Novartis. The investigator was required to maintain an accurate record of the shipment and dispensing of study drug in a drug accountability ledger. Monitoring of drug accountability was performed by the field monitor during site visits and at the completion of the trial. Novartis drug supply management provided sufficient supplies of ranibizumab 0.5 mg for treatment to each study site.