Abstract

Background: Proliferative diabetic retinopathy (PDR) is the most common cause of severe sight impairment in diabetes mellitus. PDR has been managed by pan-retinal laser photocoagulation (PRP) for the past 40 years. Here we report the 1-year safety and efficacy of intravitreal aflibercept.

Methods:
Adults with treatment-naïve or laser-treated active PDR recruited from 22 UK centres were randomly allocated (1:1) to either intravitreal aflibercept or PRP standard care, and managed for 52 weeks according to pre-defined re-treatment criteria. The primary outcome was defined as a change in best-corrected visual acuity (BCVA) at 52 weeks using a linear mixed-effects model that estimated adjusted treatment effects at both 12 and 52 weeks, having excluded fluctuations in BCVA owing to vitreous haemorrhage. This modified intention-to-treat analysis was re-applied to the per protocol participants. Masked optometrists measured BCVA; participants and treating ophthalmologists were unmasked. The non-inferiority margin was pre-specified as -5 letters. Safety was assessed in all participants. Trial registration: ISRCTN32207582.

Findings.
We recruited 232 participants (116 per arm) between August 2014 and November 2015. 221 participants (n=112 aflibercept arm, n=109 PRP arm) contributed to the modified intention-to-treat model, and 211 participants (n=104 aflibercept arm and n=107 PRP arm) within per protocol. Aflibercept was non-inferior and superior to PRP in both the modified intention-to-treat population (mean BCVA difference 3.9 letters; 95% CI 2.3-5.6 letters; $p<0.001$) and the per protocol population (difference 4.0 letters; 95% CI 2.3 -5.6 letters, $p<0.001$).

Interpretation.
Intravitreal aflibercept in PDR results in improved outcome at 1 year compared to PRP standard care.

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