INDIRECT TREATMENT COMPARISON OF INTERVENTIONS FOR NEOVASCULAR (WET) AGE-RELATED MACULAR DEGENERATION (nAMD)

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Background and Objectives

Neovascular (wet) age related macular degeneration (nAMD) is a leading cause of vision loss globally (1). In the United Kingdom (UK), the prevalence of nAMD is 284,000 with 39,700 new cases a year (2). In the United States the prevalence of nAMD is 1.2 million with more than 200,000 new cases a year (3). The prevalence of nAMD is also expected to grow with increasing life expectancy and it is forecast that the prevalence of nAMD is likely increase significantly over coming years (3, 4).

There are two main forms of treatment for nAMD: photodynamic therapy (PDT) to destroy the abnormal blood vessels and anti-VEGF injections to prevent the growth of new ones. A number of anti-VEGF treatments are available including ranibizumab (Lucentis®), aflibercept (Eylea®) and pegaptanib (Macugen®).

Here we present a network meta-analysis comparing the relative effectiveness of the four EU licenced treatments / posologies for nAMD: ranibizumab, aflibercept, pegaptanib, and PDT.

Results

A total of 21 trials were included in the network following a full systematic literature review. The results of the analyses for the two key endpoints (12 and 24 months) are presented in tables 1 and 2 respectively. Ranibizumab and aflibercept were found to be clinically superior to PDT and pegaptanib at 12 and 24 months. The mean difference in BVCA estimated between ranibizumab and PDT at 12 months was 18.85 [15.42 to 22.26] and at 24 months was 20.62 [17.25 to 23.96]. The mean difference in BVCA estimated between ranibizumab and pegaptanib at 12 months was 11.16 [2.93, 20.63] and at 24 months was 11.71 [3.31, 25.06]. Results for aflibercept were quantitatively similar. There was minimal difference in the effectiveness of ranibizumab and aflibercept at any time point: mean difference at 12 months was 0.05 [-1.33 to 1.52] and at 24 months was 0.02 [-1.36 to 1.44]. It should be note that results for pegaptanib were based on only short term data from one RCT and are based on extrapolation. Results for pegaptanib are therefore subject to a considerable degree of uncertainty and should be interpreted with caution.

Table 1: Change in BCVA at 12 months

		Comparator		
		PDT	Aflibercept	Pegaptanib
Treatment	Ranibizumab	18.85 [15.42, 22.26]	0.11 [-2.63, 2.80]	11.16 [2.93, 20.63]
	PDT		-18.74 [-22.25, -15.27]	-7.67 [-16.25, 2.21]
	Alfibercept			11.08 [2.66, -20.63]
	Pegaptanib			

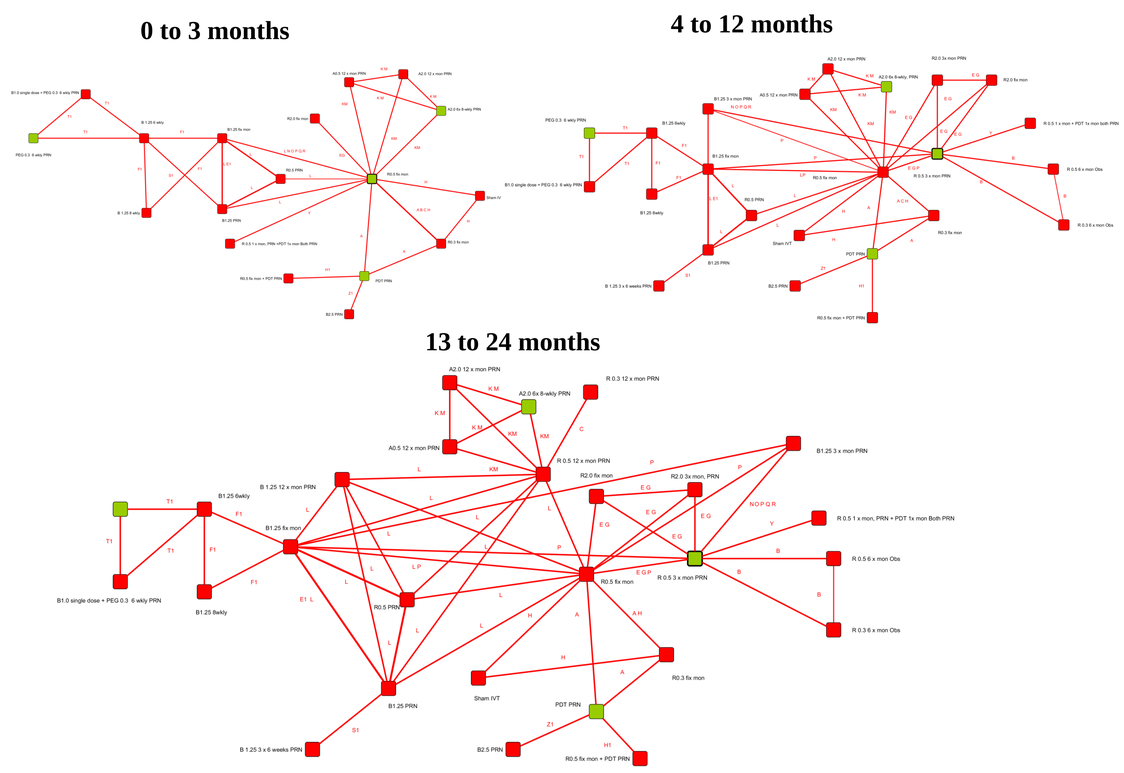
Table 2: Change in BCVA at 24 months

		Comparator		
		PDT	Aflibercept	Pegaptanib
Treatment	Ranibizumab	20.62 [17.25, 23.96]	1.00 [-2.45, 4.53]	11.71 [3.31, 25.06]
	PDT		-19.62 [-23.88, -15.37]	-8.90 [-17.76, 4.46]
	Alfibercept			-10.72 [-24.01, -1.98]
	Pegaptanib			

Methods

A systematic review was undertaken to identify trials comparing any of the interventions to treat nAMD reporting mean change from baseline in best corrected visual acuity (BCVA). A NMA of the studies was carried out using WinBugs. Identified studies often reported results at multiple time points and mean change from baseline in BCVA was modelled at multiple time points. To reflect changes in treatment frequency over time and the equivalence of some posologies at some time points, three difference networks were employed. These are depicted in Figure 1.

Figure 1: Network Diagrams



Green nodes are the EU licensed posologies of interest

To account for the time structure within the data a number of models as proposed by Dakin et al. (5) and Ding and Fu (6) were applied and the deviance information criterion (DIC) was used to select the most appropriate model. Model options included controlling for baseline differences in BCVA and grouping of posologies. The model selected was one proposed by Ding and Fu (6) in which the mean relative treatment effect with time follows a parametric model.

Conclusions

Ranibizumab and aflibercept are effective treatments for nAMD demonstrating a clinically and statistically significant improvement in mean change from baseline BVCA compared to PDT and pegaptanib. There were only very small numerical advantages favouring ranibizumab (non-statistically significant) with respect differences in the relative effectiveness of versus aflibercept 1 and 2 years (0.11 and 1.00 letters respectively).

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