Treat-and-Extend Versus As-Needed Regimen in Neovascular Age-Related Macular Degeneration: 1-Year Findings from a Network Meta-Analysis

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Introduction

- In the last decade, the incidence of age-related macular degeneration (AMD) in Asia has gradually increased, and it has become the third leading cause of blindness in China[1]. Neovascular AMD (nAMD) is characterized by choroidal neovascularization (CNV), which affects only 10%-15% of patients with AMD but accounts for 90% of severe vision loss caused by AMD[2].
- Anti-vascular endothelial growth factor (VEGF) treatment for nAMD has been demonstrated to inhibit retinal angiogenesis and avoid associated vision loss[3]; however, outcomes are dependent on consistent injections or monitoring as well[3-5].
- It is a challenge for clinicians to determine the optimal treatment regimen for nAMD given the variety of anti-VEGF regimens available, in particular how to balance vision improvement with the burden of treatment.
- We conducted a network meta-analysis (NMA) to explore differential functional outcomes between treat and extend (T&E) and as-needed (pro re nata [PRN]) regimens and compared their injection burden in routine clinical practice.

Methods

Protocol Registration: PROSPERO CRD42022333024

Data sources and searches

- Data Sources: MEDLINE, Embase, the Cochrane Library, Web of Science, Chinese BioMedical Literature Database, Wanfang, China National Knowledge Infrastructure, and VIP databases
- Data searches: All databases were searched in January 2021.

Criteria for considering studies

- Included studies of randomized controlled trials (RCTs) published in English or Chinese, which met the following criteria:
  - Patients: Adult patients (≥18 years of age) with nAMD (whether treatment-naïve or not)
  - Interventions: Three anti-VEGF drugs (intravitreal ranibizumab [IVR], intravitreal aflibercept [IVT-AFL], and intravitreal conbercept [IVC]) are commonly used in clinical practice in China.
    - ✓ IVT-AFL, IVR, and IVC using a T&E or PRN regimen
    - ✓ Any other regimens which could increase the available indirect information in the network (such as monthly or bimonthly therapies)
- Primary outcomes
  - Mean change from baseline in best-corrected visual acuity (BCVA) at 1 year
  - Mean number of injections at 1 year

Data extraction, quality assessment, and data analysis

- Extracted data
  - Study information: Name of first author, year of publication, trial name/registration number, study design (protocol of randomization or blind), region, multicenter or not, sample size (number of patients and eyes), and inclusion/exclusion criteria
  - Baseline characteristics: Description of interventions (dosage, frequency), gender, age, treatment-naïve or not (number of patients who were treatment-naïve), baseline visual acuity, and baseline central retinal thickness
  - Outcomes and results data: Definition of the outcomes, observed timepoint, results data (mean and standard deviation, number of missing, and total number for analysis)
- Quality assessment
  - Seven domains of the Cochrane Risk of Bias tool[6] were evaluated, including sequence generation, allocation concealment, blinding of patients and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases.
- Data analysis
  - The random-effects NMA with a Bayesian framework was conducted. The pooled estimations were obtained using the Markov chain Monte Carlo method. The model convergence was assessed by trace plots and Brooks-Gelman-Rubin plots[7]. Continuous outcomes were estimated using the standardized mean difference (SMD) or mean difference (MD) and its 95% credible interval (CrI). Evidence inconsistency and clinical similarities in patient characteristics and settings across trials were carefully assessed before analysis.
  - Software: R 3.6.3 (GeMTC package)[8]

Results

Study selection and risk of bias assessment

- A total of 29 RCTs (involving 8,402 patients) were included (Figure 1).
- Risk of bias was assessed for each RCT (Figure 2).

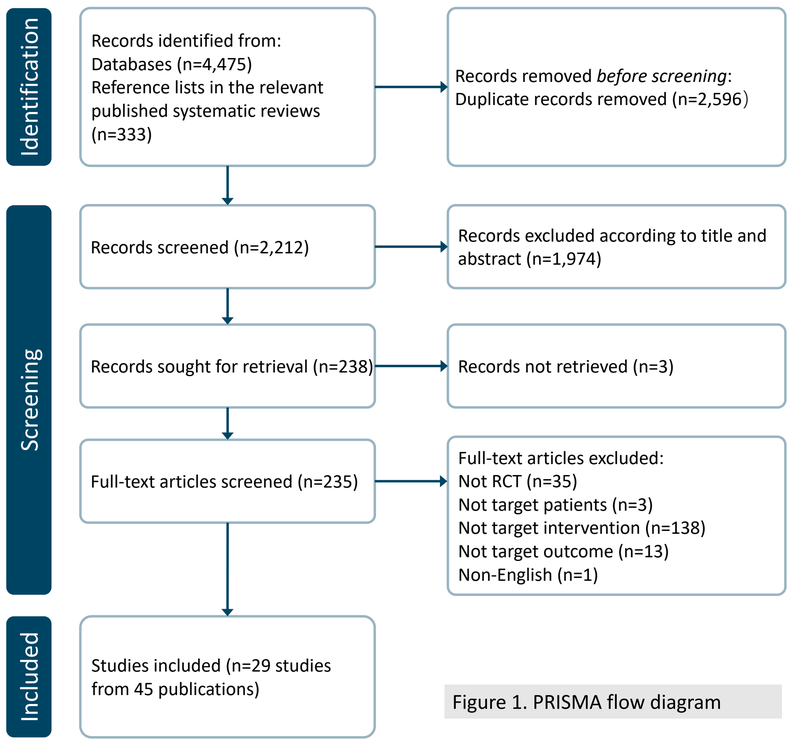


Figure 1. PRISMA flow diagram

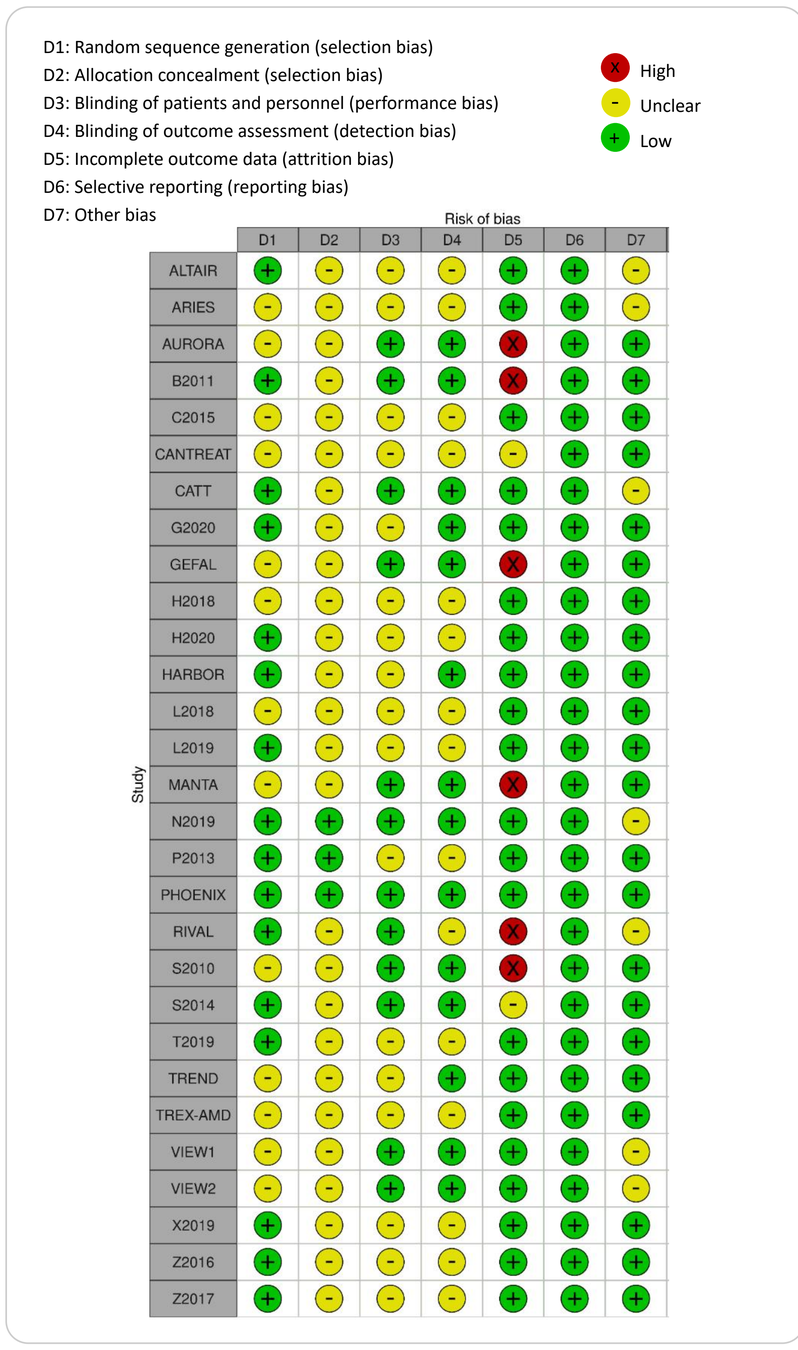
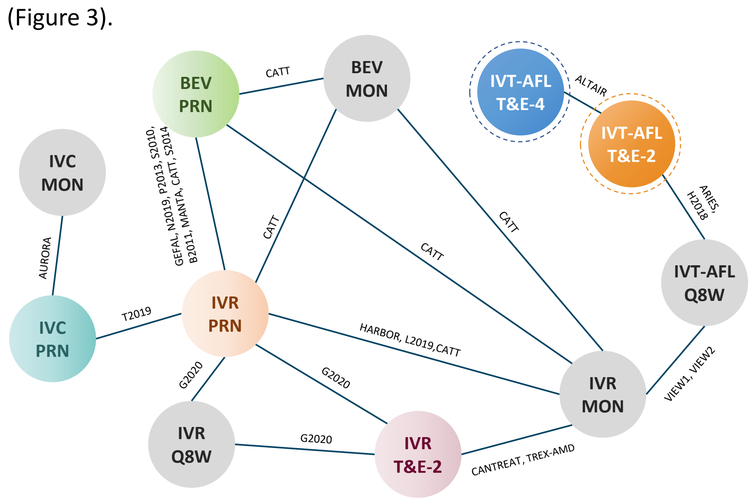


Figure 2. Risk of bias of included RCTs

Network geometry for the two primary outcomes

- 20 RCTs (involving 5,372 patients) reporting the two primary outcomes were included in this NMA.
- A total of 11 interventions were extracted from the 20 included RCTs (Figure 3).



Direct comparisons are represented by the lines connecting the different interventions. BEV, intravitreal bevacizumab; IVC, intravitreal conbercept 0.5 mg; IVT-AFL, intravitreal aflibercept 2 mg; IVR, intravitreal ranibizumab 0.5 mg; MON, monthly; PRN, pro re nata; Q8W, every 8 weeks; T&E-2, treat-and-extend with 2-week adjustment; T&E-4, treat-and-extend with 4-week adjustment.

Figure 3. The direct comparison network of main analysis

Network analysis results for mean change from baseline in BCVA at 1 year

Figure 4a. SMD of BCVA of IVT-AFL T&E-2 to other anti-VEGF regimens

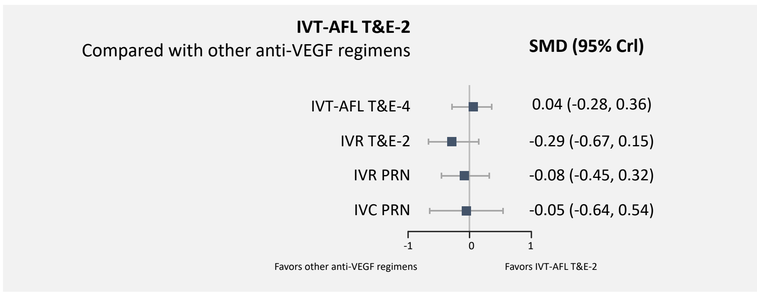
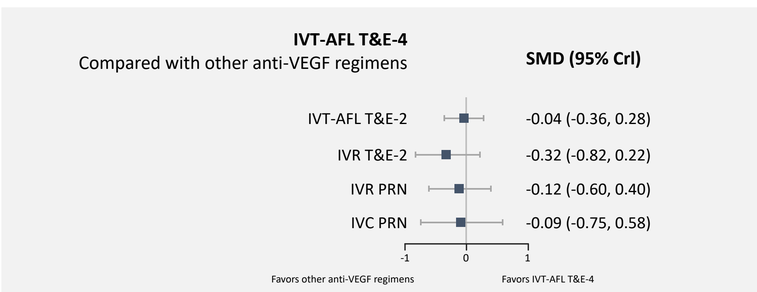


Figure 4b. SMD of BCVA of IVT-AFL T&E-4 to other anti-VEGF regimens



Network analysis results for mean injections at 1 year

Figure 4c. MD of number of injections of IVT-AFL T&E-2 to other anti-VEGF regimens

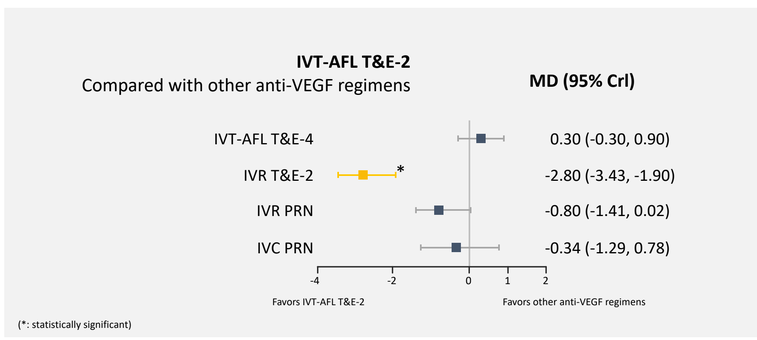
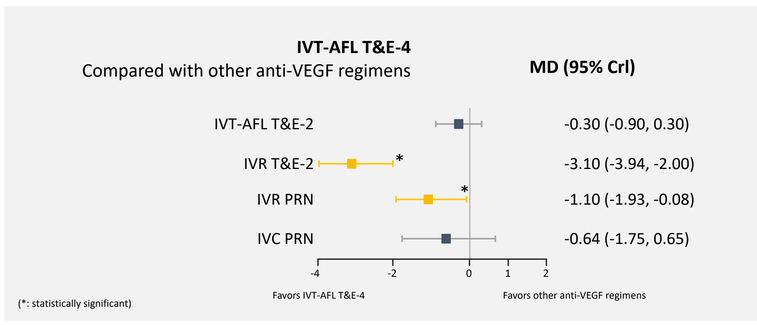


Figure 4d. MD of number of injections of IVT-AFL T&E-4 to other anti-VEGF regimens



Summary of Results

- At a 1-year follow-up, results indicated that there were no clear differences in BCVA improvements between the included anti-VEGF regimens.
- The mean number of injections for IVT-AFL T&E was less than that for T&E and PRN ranibizumab regimens. Although the mean number of injections was less for IVT-AFL T&E extended by 4 weeks than for IVC PRN, statistical significance was not reached.

Conclusions

- Different anti-VEGF regimens may provide similar visual benefits following 1 year of treatment.
- IVT-AFL T&E (with either 2- or 4-week adjustments) may reduce injection burden for patients with nAMD.

References

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Disclosures

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