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Health equity improvements driven by faricimab in diabetic macular edema using an aggregate distributional cost-effectiveness analysis from an English NHS perspective

Aurelie Meunier[1], Oyin Opeifa[1], Oliver Cox[2], Christian Bührer[2], Simon P. Kelly[3], Richard Gale[4]

1. Putnam PHMR Ltd, London, UK; 2. F. Hoffmann-La Roche Ltd, Grenzacherstrasse, Basel, Switzerland; 3. Beaumont Hospital, Bolton, UK; 4. York Teaching Hospital NHS Foundation Trust, York, UK

Background and Objective

- Diabetic macular edema (DME), caused by swelling of the macula, affects around 7.1% of patients with diabetes in England annually (1). DME is a leading cause of sight loss in working-age people in developed countries (2, 3).
- Socio-economic deprivation is associated with diabetes and DME on the continuum of the disease and treatment pathway. DME is more prevalent in areas of higher deprivation of England, due to the link to diabetes. Patients living in areas of higher deprivation are more likely to present with worse visual acuity at first-time eye screenings. These patients are also more likely to be lost to follow-up (4-7) and have greater diabetes-related physical and mental health comorbidities (8-11).
- Anti-vascular endothelial growth factor (anti-VEGF) intravitreal injections are the first-line therapy in DME; however, they require frequent administrations. Faricimab is a novel therapy which demonstrated sustained efficacy using treat and extend (T&E) dosing intervals of up to 16 weeks compared to aflibercept administered every 8 weeks (12).
- Distributional cost-effectiveness analysis (DCEA) is an extension of cost-effectiveness analysis (CEA) that looks at the equity impact of adopting interventions, evaluating how health outcomes and costs are distributed in the population, and quantifying potential trade-offs between health maximization and health equity. The National Institute of Health and Care Excellence (NICE) in the UK is exploring DCEA to support the development of its Technology Appraisals (TAs).
- We aimed to conduct an aggregate DCEA from an English NHS perspective to determine the equity impact of faricimab T&E for the treatment of DME and capture its value more comprehensively.

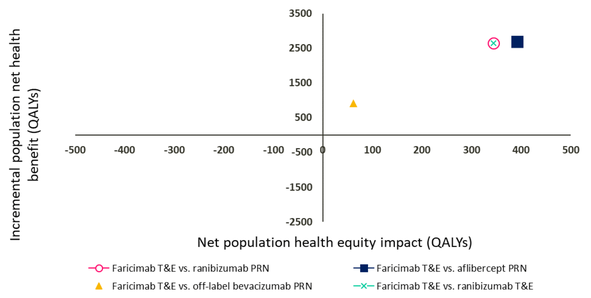
Methods

- The population was divided into quintiles based on the index of multiple deprivation (IMD), an area-level measure of socio-economic deprivation.
- In an aggregate DCEA, average health outcomes and costs from a CEA are used to derive the distributions of the health benefits and health opportunity costs. These are summated to derive the distribution of net health benefit (NHB). Differences from the baseline distribution of health are calculated to assess changes in population health and health equity.
- The patient population was estimated using data on the prevalence of diabetes from the Quality and Outcomes Framework, 2021-22 and the distribution of cases by IMD from the National Diabetes Audit (13, 14). DME prevalence statistics were informed by literature (1). The eligibility criteria for faricimab were taken from the NICE TA (15).
- The baseline distribution of population health was taken from literature (16).
- Data on health benefits and costs were derived from a CEA conducted by Roche comparing faricimab T&E with ranibizumab as required [*pro re nata* (PRN)] and aflibercept PRN which are the main regimens used in NHS clinics in England. Ranibizumab T&E and off-label bevacizumab PRN were included in a scenario analysis. A societal perspective was used in the base-case, including productivity gains and informal care costs. Effectiveness data were informed by the YOSEMITE and RHINE randomized trials and a network meta-analysis (12, 15).
- The opportunity cost threshold, representing the cost per QALY forgone because of displacing resources in the NHS, was set at the lower bound of the standard NICE threshold range, £20,000/QALY. The distribution of health opportunity costs by IMD was informed by literature (17).
- An equity-efficiency impact plane was plotted to display potential trade-offs between health maximization and health equity. Equity impacts were measured using the Atkinson inequality index, which captures societal preferences to forego some of the population health to reduce health inequalities through an inequality aversion parameter (IAP) (18).
- Changes in societal welfare, weighting both health and equity, were assessed using the equally distributed equivalent health (EDEH), which is the mean level of health per person that, if equally distributed across the population, would give the same level of societal welfare as the current unequal distribution (19). Scenario analyses were conducted varying a range of model parameters.

Results

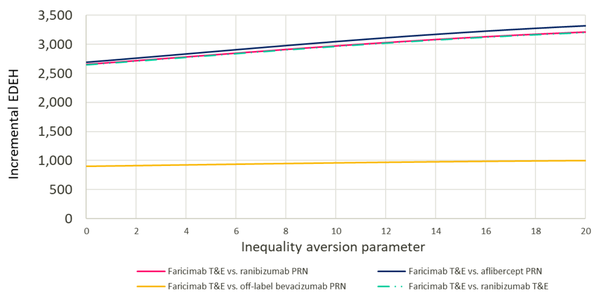
- In England it was estimated 4,179 patients would be eligible for treatment with faricimab T&E each year, 22% living in the most deprived areas compared to 17% in the most affluent ones.
- The equity-efficiency impact plane (Figure 1) shows that faricimab T&E was both health and equity improving against all comparators under a societal perspective at an opportunity cost threshold of £20,000/QALY. Faricimab T&E compared to aflibercept PRN improved population health (2,686 QALYs) and decreased health inequities (north-east quadrant) equivalent to 391 QALYs, improving societal welfare (3,077 QALYs). Results of a scenario analysis against off-label bevacizumab PRN, which is available at low costs and infrequently used in NHS care despite not being licensed for the treatment of DME, resulted in a positive NHB (903 QALYs), equity impact (62 QALYs) and societal welfare impact (965 QALYs) although reduced in size (Table 1).
- The equity impact of faricimab T&E increased with the Atkinson IAP, i.e., greater weight put on health gains in the most deprived quintiles (Figure 2).
- At £15,000/QALY, the opportunity cost threshold value used by the English Department for Health and Social Care, the equity impact was increased against ranibizumab PRN, aflibercept PRN and ranibizumab T&E, against which faricimab T&E resulted in cost-savings. Compared with off-label bevacizumab PRN, against which faricimab T&E resulted in positive incremental costs, the equity impact was decreased. Under a healthcare perspective, faricimab T&E was health and equity improving against ranibizumab PRN, aflibercept PRN and ranibizumab T&E. Compared with off-label bevacizumab PRN, faricimab T&E involved a trade-off between health maximization and reduction of health inequalities

Figure 1. Equity-efficiency impact plane of faricimab against comparator treatments



Abbreviations: PRN, pro re nata; QALY, quality-adjusted life-year; T&E, treat and extend
Analysis settings: societal perspective, £20,000/QALY opportunity cost threshold, Atkinson inequality aversion parameter = 10.95

Figure 2. Equity weighted population health impact with increasing inequality aversion parameter



Abbreviations: EDEH, equally distributed equivalent health; PRN, pro re nata; T&E, treat and extend
Note: Greater value of the inequality aversion parameter reflect a higher willingness to trade some of the population health to reduce health inequalities. Analysis settings: societal perspective, £20,000/QALY opportunity cost threshold

Table 3. Population health, societal welfare and equity impacts

	Base-case		Scenario	
	Faricimab T&E vs. ranibizumab PRN	Faricimab T&E vs. aflibercept PRN	Faricimab T&E vs. bevacizumab PRN	Faricimab T&E vs. ranibizumab T&E
Incremental net health benefit per patient*	0.63	0.64	0.22	0.63
Evaluating changes in population health (change in equity not included)				
Incremental population QALE (ΔQALE*N) (1)	2,650 QALYs	2,686 QALYs	903 QALYs	2,649 QALYs
Evaluating changes in equity-weighted health (changes in health and health equity both included)				
Incremental population EDEH (ΔEDEH*N) (2)	2,994 QALYs	3,077 QALYs	965 QALYs	2,993 QALYs
Health equity impact				
Population equity impact (incremental equity-weighted QALE – incremental QALE) (2-1)	344 QALYs	391 QALYs	62 QALYs	344 QALYs

Abbreviations: QALE, quality-adjusted life-expectancy; ΔQALE, difference in QALE between post-decision and baseline; EDEH, equally distributed equivalent health; ΔEDEH, difference in EDEH between post-decision and baseline; N, England population; PRN, pro re nata; T&E, treat and extend; QALY, quality-adjusted life-year.
Notes: Analysis settings: societal perspective, £20,000/QALY opportunity cost threshold, Atkinson inequality aversion parameter = 10.95.
*Data derived from a cost-effectiveness analysis conducted by Roche

Conclusions

- Faricimab T&E was both cost-effective and health equity improving under the base-case assumptions. The positive equity impact was driven by faricimab T&E having a positive incremental net health benefit, and the patient distribution being skewed towards the most deprived quintiles.
- Faricimab T&E, thanks to a less burdensome schedule of administrations in comparison to conventional treatment for diabetic macular edema, may help to relieve capacity constraints within ophthalmology services, which are the busiest outpatient specialty within NHS England (20), reducing costs and improving patient outcomes and health equity.
- Quantifying equity impacts enables a more comprehensive valuation of interventions. Detailed methodology to construct DCEAs, criteria leading to DCEAs being a requirement, and how the results would be interpreted and integrated into decision-making by health technology assessment bodies such as NICE would be valuable to analysts, manufacturers, and researchers.

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Contact: Aurelie Meunier
Email: aurelie.meunier@phmr.com

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Financial Disclosures
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