Health Innovation
Oxford & Thames Valley

Office for Life Sciences

NHS

EE347

Early Economic Modelling of Mutant TNF (mutTNF) as a BBB-Permeabilising Adjunct in Breast Cancer Brain Metastases (BCBM): A UK NHS Perspective

Chauhan AS[1], Sibson NR[2], Campbell SJ[2], Lord S[2], Rose J[1], Bajre M[1]

[1] Health Innovation Oxford and Thames Valley, Oxford, UK [2] Department of Oncology, University of Oxford, Oxford, UK

Introduction

Brain metastases affect 20–40% of metastatic breast cancer patients, especially HER2-positive and triple-negative subtypes, with poor prognosis and limited CNS response to systemic therapy due to the blood–brain barrier (BBB).[1,2]

Mutant tumour necrosis factor (mutTNF), a TNFR1-selective biologic, transiently permeabilises the BBB at tumour sites, enhancing intracranial delivery of systemic agents in preclinical models.[3,4]

With GMP production underway and early clinical trials approaching, there is an urgent need for health economic evidence to assess mutTNF's value and inform NHS adoption, pricing, and reimbursement.

Aims

To evaluate the cost-effectiveness of standard treatment and management for breast cancer brain metastases (BCBM), with and without the addition of mutTNF.

Objectives

- Conduct a cost-effectiveness analysis comparing standard care with and without mutTNF, estimating incremental costs, quality-adjusted life-years (QALYs), the incremental cost-effectiveness ratio (ICER), and net monetary benefit (NMB).
- Provide a clinically and mechanistically coherent comparator framework.
- Undertake subgroup analyses.
- Perform scenario and threshold analyses.
- Implement probabilistic sensitivity analysis (PSA) to assess decision uncertainty.
- Generate recommendations to inform NHS integration, reimbursement, and policy.

Methods

Comparators

This evaluation directly compared two strategies:

- Standard care: the established treatment framework for patients with BCBM, including systemic therapy alone or in combination with surgery or radiotherapy.
- Standard care + mutTNF: the same framework, augmented with mutTNF

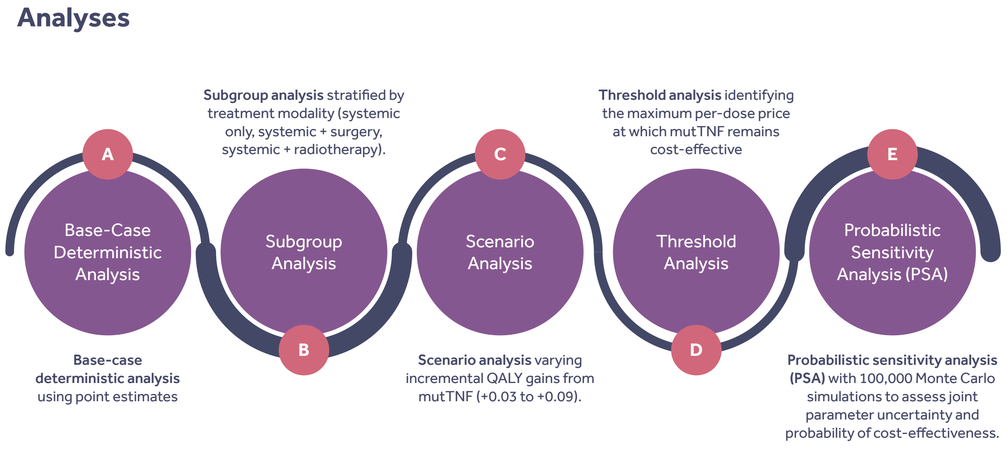
Perspective and Time Horizon

- UK NHS perspective
- 1-year horizon, aligned with BCBM clinical course and NICE early modelling guidance

Model Framework and Outcomes

- Decision-analytic model to estimate total costs and QALYs
- Outcomes: ICER and NMB at £30,000/QALY threshold

Analyses



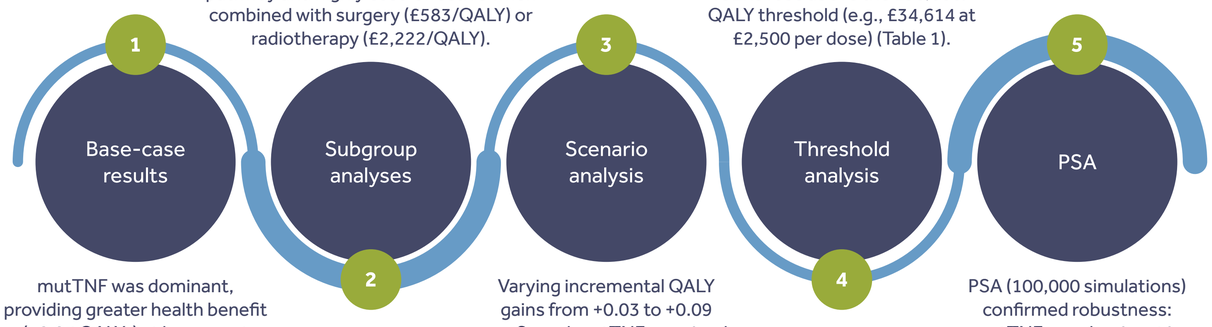
Conclusion

mutTNF is likely to be a cost-effective adjunct to BCBM care, even under conservative assumptions. The findings offer strategic insights to inform value-based pricing, trial design, and early HTA engagement.

Results

Cost-effectiveness was consistent across treatment contexts. mutTNF was dominant in the systemic-only pathway and highly cost-effective when combined with surgery (£583/QALY) or radiotherapy (£2,222/QALY).

mutTNF remained cost-effective up to a unit price of ~£2,194 per dose. Beyond this point, ICERs rose above the £30,000/QALY threshold (e.g., £34,614 at £2,500 per dose) (Table 1).



mutTNF was dominant, providing greater health benefit (+0.07 QALYs) at lower cost (–£171) compared with standard care. This corresponded to an ICER of –£2,587 per QALY and an NMB gain of £2,160 at a £30,000/QALY threshold.

Varying incremental QALY gains from +0.03 to +0.09 confirmed mutTNF remained dominant, with ICERs ranging from –£1,781 to –£4,729 per QALY.

PSA (100,000 simulations) confirmed robustness: mutTNF was dominant in ~75–80% of cases, cost-effective in >90% at £30,000/QALY, with minimal risk of health loss (Figure 1).

Table 1: Threshold Analysis: Cost-Effectiveness of mutTNF at Varying Unit Prices

Cost input - mutTNF (£)	Total Cost (£)	Incr. Cost (£)	Effectiveness (QALYs)	Incr. Effectiveness (QALYs)	ICER (£/QALY)	NMB (£)	C/E (£/QALY)
50	28333	-156	0.72	0.07	-2361	-6853	39571
100	28383	-106	0.72	0.07	-1607	-6903	39641
200	28483	-6	0.72	0.07	-97	-7003	39781
400	28683	194	0.72	0.07	2921	-7203	40060
600	28883	394	0.72	0.07	5939	-7403	40339
800	29083	594	0.72	0.07	8958	-7603	40619
1000	29283	794	0.72	0.07	11976	-7803	40898
1500	29783	1294	0.72	0.07	19522	-8303	41596
1532	**29814**	**1325**	**0.72**	**0.07**	**20000**	**-8335**	**41640**
1700	29983	1494	0.72	0.07	22541	-8503	41876
2000	30283	1794	0.72	0.07	27068	-8803	42295
2100	30383	1894	0.72	0.07	28578	-8903	42434
2194	**30477**	**1988**	**0.72**	**0.07**	**30000**	**-8997**	**42566**
2200	30483	1994	0.72	0.07	30087	-9003	42574
2500	30783	2294	0.72	0.07	34614	-9303	42993
3500	31783	3294	0.72	0.07	49707	-10303	44390
5000	33283	4794	0.72	0.07	72345	-11803	46485

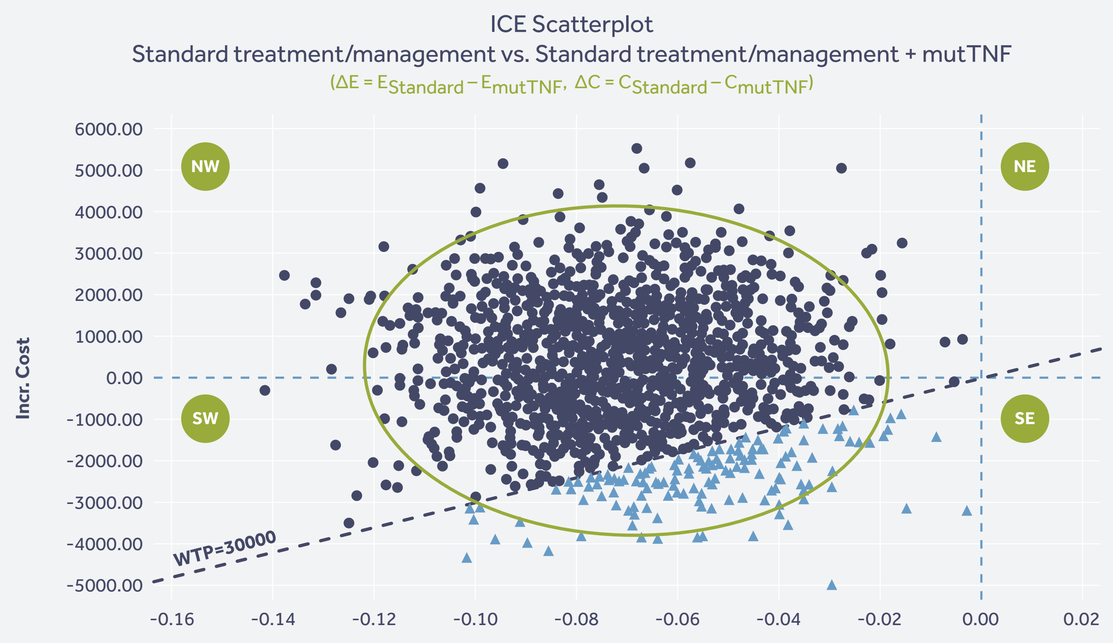


Figure 1: Incremental-cost-effectiveness (ICE) scatterplot

References

1. Lin NU, Amiri-Kordestani L, Palmieri D, Liewehr DJ, Steeg PS. CNS metastases in breast cancer: old challenge, new frontiers. Clin Cancer Res. 2013;19(23):6404–6418.
2. Niwińska A, Murawska M, Pogoda K. Breast cancer brain metastases: differences in survival depending on biological subtype, RPA RTOG prognostic class, and systemic treatment after whole-brain radiotherapy. Ann Oncol. 2010;21(5):942–948.
3. Connell JJ, Chatain G, Cornelissen B, Vallis KA, Hamilton A, Seymour L, et al. Selective permeabilization of the blood–brain barrier at sites of metastasis. J Natl Cancer Inst. 2013;105(21):1634–1643.
4. Muñoz Pinto MF, Campbell SJ, Simoglou Karali C, Johanssen VA, Bristow C, Cheng VWT, et al. Selective blood–brain barrier permeabilization of brain metastases by a type 1 receptor-selective tumor necrosis factor mutein. Neuro Oncol. 2022;24(1):52–63.

Ankur Singh Chauhan
ankur.chauhan@healthinnovationoxford.org

View this poster