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Economic Evaluation of Bispecific Antibodies in Europe: A Systematic Review

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INTRODUCTION

- Bispecific antibodies (BsAbs) are innovative therapies that simultaneously target two different antigens or epitopes, offering new treatment options for various cancers, especially hematologic malignancies. As their use grows across Europe, questions about their economic value have become increasingly important due to high treatment costs[1]
- The mechanism of action is determined by the BsAbs molecular targets and structure (or format), which can be manipulated to create variable and novel functionalities, including linking immune cells with tumor cells, or dual signaling pathway blockade[1]

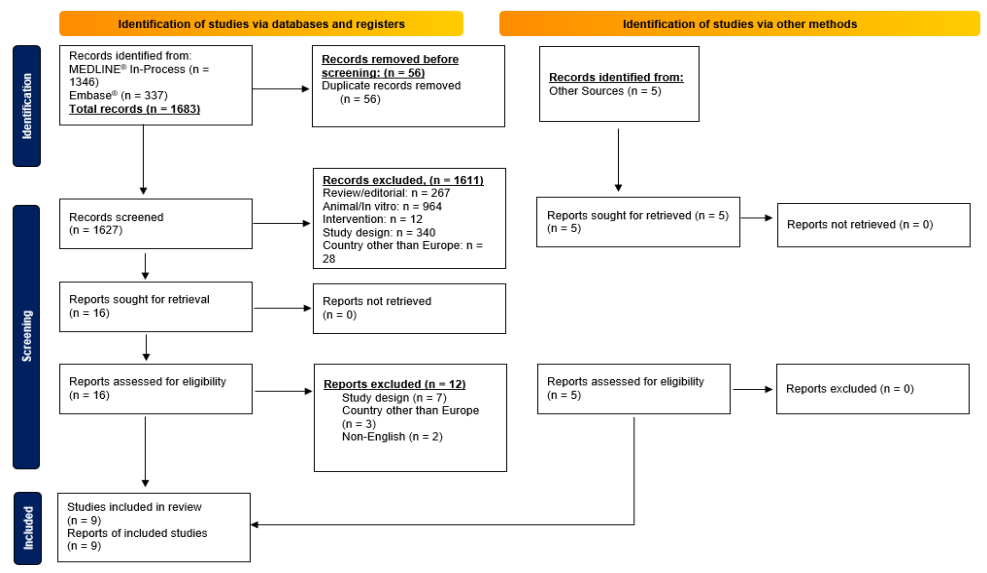
OBJECTIVES

- This systematic literature review assessed model-based economic evaluations of BsAbs in Europe

METHODS

- A systematic search of Embase® and PubMed® was conducted from database inception to June 2025 using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify English-language publications on the economic evaluation of BsAbs in various diseases
- Electronic searches were supplemented by bibliographic and hand searches. Two independent reviewers screened publications, with a third resolving any discrepancies

Figure 1: PRISMA flow diagram



RESULTS

- Among the 1,683 records retrieved from the electronic database search, four met the inclusion criteria and five were added from the hand searches, totaling nine studies. The details for the flow of studies are presented in Figure 1 using a PRISMA flow diagram

Summary of evidence

- Among the nine included studies, eight were cost–utility analyses: two were conducted in France[2,3], two in the Netherlands[4,5], two in the UK[6,7], and one each in Spain[8] and Italy.[9] A cost-minimization analysis covered the broader European context (UK, France, Italy, Spain, and Germany)[10]
- Most of the included studies were model-based economic evaluations, with the majority employing Markov[3,4,7,9] or partitioned[2,5,8] survival models, and one using an individual-level simulation model[6]
- Across studies, hemophilia A and hematologic malignancies (such as acute lymphoblastic leukemia and multiple myeloma)[2,4,5,7,9] were the most frequently evaluated conditions, while one study assessed ophthalmic diseases such as wet age-related macular degeneration and diabetic macular oedema[6]
- The studies evaluated innovative therapies including: emicizumab[3,4,7,9,10] (a bispecific monoclonal antibody for hemophilia A); Blinatumomab[2,5] (a bispecific T-cell engager for acute lymphoblastic leukemia); valoctocogene roxaparvovec[4] (a gene therapy for hemophilia A); tisagenlecleucel[5] (a chimeric antigen receptor T-cell [CAR T-cell] therapy for B-cell malignancies); elranatamab[8] (a bispecific antibody targeting B-cell maturation antigen and CD3 for multiple myeloma); and faricimab[6] (a bispecific antibody targeting Ang-2 and VEGF-A for retinal vascular diseases), versus conventional treatment options
- Most evaluations adopted a healthcare payer or national health service[2,5,6, 8-10] perspective; however, some incorporated a societal perspective[2-5] to capture the broader economic impact
- The time horizons ranged from 5 years[3,6,10] to lifetime[2,5,7-9], with discount rates typically between 2.5%[2]–4%[5] per year
- Health states varied by disease area, but generally included stages such as no bleed/bleed/death for hemophilia models[3,4,7,9], and progression-free/post-progression/death for oncology models[2,5,8]
- Costs were presented mainly in Euros (€)[9,3,8,10,2,4,5,6] with British pounds (£)[7] used in UK-based studies; price years spanned 2019[4,9]–2024[8]

KEY TAKEAWAYS

- In France, emicizumab was dominant and a cost-effective treatment for patients with hemophilia A with inhibitors[3], Blinatumomab was dominant and a cost-effective treatment for patients with high-risk, first-relapse B-cell precursor, acute lymphoblastic leukemia[2] (each compared with their relevant alternatives)
- Specifically, Blinatumomab provided 7.16 additional quality-adjusted life years (QALYs) and 8.39 life years over high-risk consolidation chemotherapy, with an incremental cost-effectiveness ratio (ICER) of €7,308/QALY[2]
- In Spain, elranatamab was a cost-effective option compared with physician's choice of treatment (ICER: €24,754/QALY) for relapsed and refractory multiple myeloma, outperforming teclistamab and providing 0.60 additional QALYs and savings of €101,026[8]
- In the UK, faricimab was dominant over aflibercept, resulting in total cost savings of £15,108,609 and 60.06 QALYs gained for patients with wet age-related macular degeneration or diabetic macular oedema[6]
- Compared with the ranibizumab biosimilar, faricimab yielded an additional 105.7 QALYs, with an ICER of £19,574/QALY[6]
- Additionally, in the UK, recombinant factor VIII Fc was found to be a dominant strategy over emicizumab in patients without inhibitors, offering comparable QALYs (15.497 versus 15.483) but lowering total costs by £4.61 million due to reduced prophylaxis and bleed management expenses[7]
- In Europe (including the UK, France, Italy, Spain, and Germany), the cost-minimization analysis showed that using recombinant factor VIII Fc instead of emicizumab resulted in 5-year savings of €89.3–150 million for adolescents/adults and €173.4–253.2 million for children with hemophilia A without inhibitors[10] (Table 2)

Table 1: Results of included studies

Study name	Intervention/ comparator	QALY	Total cost	ICER
Cortesi 2025 (Italy)[9]	Emicizumab Ppx aPCC Ppx rFVIIa Ppx	Emicizumab Ppx: 24.49 aPCC Ppx: 23.55 rFVIIa Ppx: 23.55	Emicizumab Ppx: 12,156,904€ aPCC Ppx: 32,141,369€ rFVIIa Ppx: 37,429,094€	aPCC Ppx: cost-saving rFVIIa Ppx: cost-saving
Polack 2021 (France)[3]	Emicizumab Ppx BPA	Emicizumab Ppx: 3.3154 BPA: 2.4343	Emicizumab Ppx: 2,293,969€ BPA: 2,528,160€	Emicizumab Ppx treatment is dominant
Encinas 2025 (Spain)[8]	Elranatamab PCT Teclistamab	Elranatamab: 1.64 PCT: 0.92 Teclistamab: 1.05	Elranatamab: 150,504€ PCT: 132,643€ Teclistamab: 251,530€	PCT: ICER per QALY – 24,754€ Teclistamab: ICER per QALY – dominant
Caillon 2023 (France)[2]	Blinatumomab HC3	Blinatumomab: 19.77 HC3: 12.62	Blinatumomab: 154,326€ HC3: 102,028€	ICER per QALY: 7,308€
Ten Ham 2022 (the Netherlands)[4]	Emicizumab Valrox FVIII Ppx	Emicizumab: 6.90 Valrox: 7.03 FVIII Ppx: 6.38	Emicizumab: 4,252,167€ (range: 408,737€–4,853,421€) Valrox: 2,839,210€ (range: 487,449€–10,545,521€) FVIII Ppx: 3,284,690€ (range: 282,686€–10,444,562€)	Emicizumab ICER: dominated Valrox ICER: ref FVIII Ppx ICER: dominated
Thielen 2020 (the Netherlands)[5]	Blinatumomab Tisa-cel Clo-M Clo-C	Blinatumomab: 2.25 Tisa-cel: 11.26 Clo-M: 0.49 Clo-C: 1.70	Total discounted: Blinatumomab: 267,259€ Tisa-cel: 552,679€ Clo-M: 160,803€ Clo-C: 193,920€	ICER (€/QALY)[a] Blinatumomab: 31,682 Clo-M: 36,378 Clo-C: 37,531
Li 2024 (UK)[6]	Faricimab Aflibercept Ranibizumab biosimilar	Faricimab vs aflibercept: 60.06[b] Faricimab vs ranibizumab: 105.7[b]	Faricimab vs aflibercept: -£15,108,609 (cost saving) Faricimab vs ranibizumab: +£2,069,088	Aflibercept: dominant Ranibizumab: £19,574
Kragh 2022 (UK)[7]	Emicizumab rFVIIIFc	Emicizumab: 15.483 rFVIIIFc: 15.497	Emicizumab: £10,593,306 rFVIIIFc: £5,978,424	ICER (cost/QALY): rFVIIIFc: dominant

Key: aPCC, activated prothrombin complex concentrate; Blinatumomab, BPA, bypassing agents; Clo-C, clofarabine combination therapy; Clo-M, clofarabine monotherapy; HC3, high-risk consolidation chemotherapy; ICER, incremental cost-effectiveness ratio; PCT, physician's choice of treatment; Ppx, prophylaxis; QALY, quality-adjusted life year; ref, reference; FVII, factor VIII; rFVIIa, recombinant activated factor VII; rFVIIIFc, recombinant factor VIII Fc; Tisa-cel, tisagenlecleucel; Valrox, valoctocogene roxaparvovec.
Notes: [a] All ICERs are well below the Dutch willingness-to-pay threshold of €80,000/QALY so Tisa-cel is cost-effective against all comparators; [b] QALYs gained.

Table 2: Cost of emicizumab by age group and country

Country	Total cost (€) for adolescents/adults		Total cost (€) for children	
	Emicizumab (≥ 12 years)	rFVIIIFc (≥ 12 years)	Emicizumab (< 12 years)	rFVIIIFc (< 12 years)
UK	253,240,465	149,990,408	109,712,238	52,568,571
France	242,072,812	109,543,556	104,924,016	38,392,777
Italy	173,417,486	109,543,556	75,111,853	38,392,777
Spain	240,430,724	99,431,843	104,239,605	34,848,828
Germany	204,808,819	89,320,131	88,598,450	31,304,879

Key: rFVIIIFc, recombinant factor VIII Fc.

CONCLUSIONS

- The systematic literature review showed that most BsAbs demonstrated high clinical effectiveness across a range of disease areas, particularly in oncology and hematology
- Many of these treatments were found to be cost-effective in model-based economic evaluations conducted across Europe
- Their implementation has the potential to improve patient outcomes while offering economic advantages to healthcare systems

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