From Feasibility to Findings: Supporting Indirect Treatment Comparisons with Generative AI

MSR114

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INTRODUCTION

- Indirect treatment comparisons (ITCs) and network meta-analysis (NMAs) are essential in health technology assessments (HTA) when direct head-to-head trials are lacking. They enable evaluation of relative effectiveness through connected evidence networks, but their reliability depends on strong assumptions and study comparability[1]
- A key step in this process is feasibility assessment, which determines whether an ITC is methodologically appropriate. This involves evaluating factors such as similarity of patient populations, consistency in study design, alignment of outcome definitions, and the structure of the evidence network[2]
- These assessments are complex and time-intensive, relying heavily on expert judgment. Generative Artificial Intelligence (GenAI) is transforming this process by enabling efficient analysis of large clinical datasets, improving transparency, and standardizing feasibility assessments while reducing manual effort and variability[3]
- In this study, we explore the application of GenAI to support ITC and NMA by generating a structured, transparent feasibility report for hepatocellular carcinoma (HCC). The proposed approach aims to enhance efficiency, consistency, and interpretability

OBJECTIVE

- To evaluate the use of GenAI in conducting ITCs and NMA and its ability to support transparent, HTA-aligned decision-making in HCC
- To validate AI-generated outputs against expert human assessments

METHODS

STUDY IDENTIFICATION AND DATA EXTRACTION

Published Randomized Controlled Trials (RCTs) in first-line HCC were identified through targeted searches. Eligible studies in treatment-naïve patients were extracted into a structured Excel database for ITC as shown in Figure 2

GENAI-ASSISTED FEASIBILITY AND NMA

GenAI assessed ITC feasibility, generated structured reports, and recommended appropriate analyses. Outputs were reviewed by experienced ITC methodologists for accuracy

ANALYTICAL APPROACH

Where feasible, NMAs were conducted using an in-house metaSLR tool, with models selected based on deviance criteria and relevance. Sensitivity analyses were performed to assess robustness as shown in Figure 1 and Figure 4

GENAI-ASSISTED INTERPRETATION AND REPORTING

GenAI summarized results, highlighted key differences, and generated draft reports aligned with establish guidelines. Outputs were validated by ITC experts as shown in Figure 3

Figure 1: Feasibility Domain Scores of All Four Components

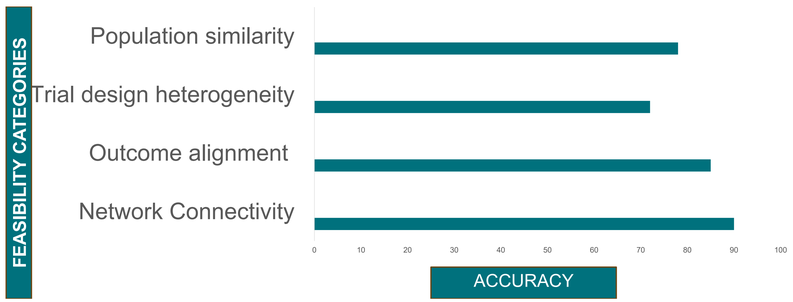
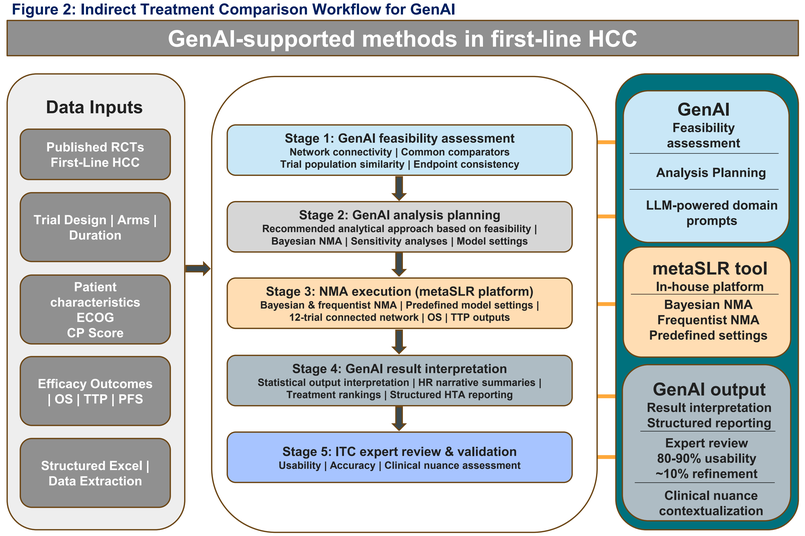


Figure 2: Indirect Treatment Comparison Workflow for GenAI



LLM – Large Language Models, OS – Overall Survival, TTP – Time to Progression, PFS – Progression Free Survival, ECOG - Eastern Cooperative Oncology Group, SLR – Systematic Literature Review, CP - Child-Pugh, HTA – Health Technology Assessment, HCC – Hepatocellular Carcinoma, ITC – Indirect Treatment Comparison, PFS – Progression Free Survival, HR- Hazard Ratio, RCT – Randomized Controlled Trials, GenAI – Generative Artificial Intelligence

Figure 3: Proportion of AI-assisted Output versus Human Intervention

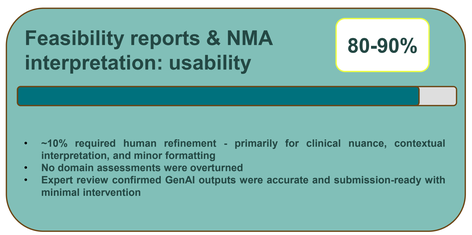


Table 1: Summary of Network Characteristics and Overall Survival Outcomes

Component	Value
RCTs in connected network	12
HR - Best OS sintilimab + bevacizumab	0.38
Regimens with significant OS benefit vs placebo	3

HR – Hazard Ratio, RCT – Randomized Controlled Trials, OS – Overall Survival

Figure 4: Feasibility Domain Scores Components

Network Connectivity
- 12 trials
- Connected star network
- Common comparator (Sorafenib)

Population similarity
- ECOG, Child-Pugh, prior therapy comparable
- Minor variation in aetiology distribution

Trial design heterogeneity
- Dosing schedules
- Blinding consistent
- Minor variation

Outcome alignment
- OS and PFS are consistent
- HRQoL instruments varied
- Mapped for secondary analysis.

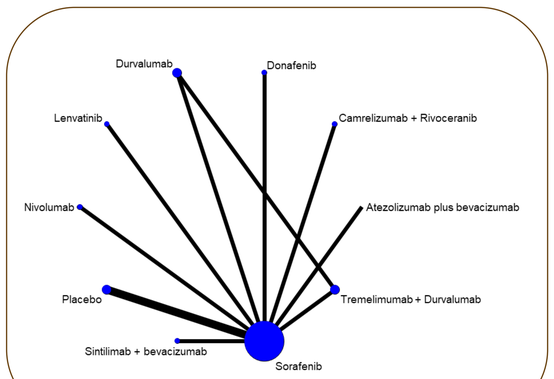
OS – Overall Survival, TTP – Time to Progression, PFS – Progression Free Survival, ECOG - Eastern Cooperative Oncology, HRQoL – Health Related Quality of Life,

Table 2: Hazard Ratio Results

Treatment	HR vs. placebo	95% CrI	Significant
Sintilimab + bevacizumab	0.38	0.21 – 0.79	✓ Yes
Camrelizumab + rivoceranib	0.42	0.21 – 0.82	✓ Yes
Atezolizumab + bevacizumab	0.45	0.23 – 0.87	✓ Yes

HR – Hazard Ratio

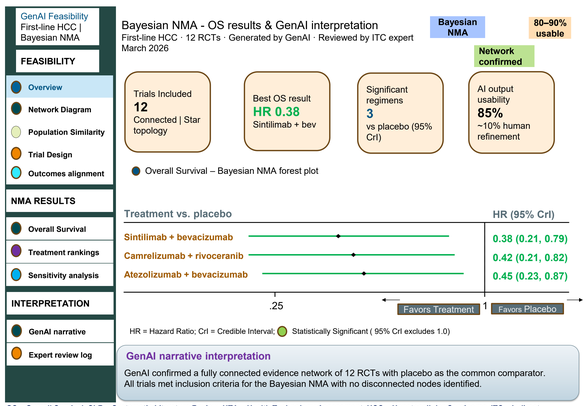
Figure 5: Sample Network diagram Generated through GenAI



RESULTS

- GenAI identified a connected evidence network of 12 trials and confirmed the feasibility for the Bayesian NMA as shown in Figure 5
- Bayesian NMA results showed significant overall survival benefits for sintilimab plus bevacizumab (HR 0.38; 95% Credible Interval CrI 0.21-0.79), camrelizumab plus rivoceranib (HR 0.42; 95% CrI 0.21-0.82), and atezolizumab plus bevacizumab (HR 0.45; 95% CrI 0.23-0.87) compared with placebo as shown in Table 1 and Table 2
- GenAI produced clear, reproducible reports summarizing treatment effects, rankings, and clinical implications as shown in Figure 6
- Treatment rankings favored combination immunotherapy-antiangiogenic regimens. Expert review indicated that GenAI-generated feasibility assessments and reports were 80-90% usable, with approximately 10% requiring human refinement, mainly for clinical nuance and contextual interpretation

Figure 6: Sample Interface of GenAI Report



OS – Overall Survival, SLR – Systematic Literature Review, HTA – Health Technology Assessment, HCC – Hepatocellular Carcinoma, ITC – Indirect Treatment Comparison, HR- Hazard Ratio, RCT – Randomized Controlled Trials, GenAI- Generative Artificial Intelligence

LIMITATIONS

- Indirect comparisons only: The study relies entirely on ITCs and NMA due to the absence of direct head-to-head trials, which inherently introduces uncertainty compared to randomized controlled evidence
- Dependency on structured inputs: GenAI performance likely depends heavily on the quality and completeness of the structured Excel database used for data extraction
- Lack of transparency in reasoning: Large Language Models (LLM) generated assessments may not always provide an auditable or fully interpretable rationale for HTA submissions
- Small network: Only 12 RCTs were included, which may limit the robustness of network estimates
- No blinding of expert reviewers to GenAI outputs is mentioned, introducing potential confirmation bias in the validation step

CONCLUSIONS

- This study demonstrates the significant potential of GenAI to transform the end-to-end ITC workflow in HTA submissions using first-line HCC as a proof-of-concept application
- GenAI, when integrated with established NMA platforms and subject to structured expert validation, represents a reliable, efficient, and scalable augmentation tool for HTA-grade ITC analyses, formatting, and clinical contextualization
- GenAI-generated feasibility assessments and structured reports demonstrated 80-90% usability, with only ~10% requiring human refinement for clinical nuance and contextual interpretation
- Expert reviewers confirmed that GenAI outputs were accurate, submission-ready, and minimally intervention-dependent
- While human oversight remains essential - particularly for clinical interpretation and regulatory nuance - this study establishes a robust framework for AI-assisted evidence synthesis that can meaningfully improve the quality, transparency, and timeliness of health technology assessments across therapeutic areas

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Disclosure: AS, RK, and BS, the authors declare that they have no conflict of interest

ISPOR, May 17-20, 2026, Philadelphia, PA, United States