Living Network Meta-Analysis for Up-to-Date Comparative Effectiveness: A Case Study in Multiple Myeloma Maintenance

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HTA145

INTRODUCTION

Background

- The volume and speed of publications reporting new relevant evidence can lead to Health Technology Assessment (HTA) decisions being informed by out-of-date evidence.
- Therefore, payers are beginning to embrace the concept of living HTA, which ensures pre-defined commitment to regular updates. Network meta-analyses (NMAs) are integral to HTAs.
- While the traditional NMA methods for synthesizing comparative clinical evidence are time-consuming, requiring extensive data preparation and knowledge of statistical programming, a living NMA tool presents an opportunity to recreate existing NMAs, monitor new evidence, and quickly update analyses within a few minutes.
- In 2021, 33 abstracts on interventions for multiple myeloma maintenance were presented at major oncology congresses. This reflects the rapidly shifting evidence landscape, which requires a nimble analytic approach that is easier and quicker to update.

Objective

- **In this study, we replicated and updated a previously published NMA using LiveNMA™, a new interactive NMA tool connected with LiveSLR®, an interactive, up-to-date SLR library.**

Methods

- Leveraging an existing living systematic literature review (LiveSLR) platform, which is regularly updated to capture newly published articles and abstracts, we developed an integrated living NMA tool (LiveNMA).
- LiveNMA is an R-based tool that performs Bayesian NMAs for overall survival (OS) and progression-free survival (PFS) using studies identified by LiveSLR.
- To validate this tool, a previously published NMA of PFS among multiple myeloma maintenance regimens by Luchinin et al. [1] was replicated.
- Luchinin et al. conducted their NMA using the frequentist approach, with R software version 3.4.2 (netmeta package).
- The network consisted of 13 trials (**Table 1**).[2-14]
- Included trials involved 10 treatment regimens.
- We updated the analysis using the LiveNMA tool with data from a recently published study (Dytfeld, D et al., 2022[15]) identified through LiveSLR, comparing carfilzomib-lenalidomide-dexamethasone with lenalidomide.

Table 1. Included studies

Reference	Trial Identifier	Interventions
Mateos et al. 2014[2]	GEM2005 trial (NCT00443235)	Bortezomib-Thalidomide vs Bortezomib-Melphalan
McCarthy et al, 2012[3]	CALGB/Alliance (NCT00114101)	Lenalidomide vs Observation
Attal et al, 2012[4]	IFM 2005-02 (NCT00430365)	Lenalidomide vs Observation
Palumbo et al, 2014[5]	NCT00551928	Lenalidomide vs Observation
Gay et al, 2015[6]	RV-MM-EMN-441 (NCT01091831)	Lenalidomide + Prednisone vs Lenalidomide
Morgan et al, 2013[7]	MRC-Myeloma IX	Thalidomide vs Observation
Sonneveld et al, 2012[8]	HOVON-65/GMMG-HD4 (ISRCTN64455289)	Bortezomib vs Thalidomide
Palumbo et al, 2014[9]	NCT01063180	Bortezomib + Thalidomide vs Observation
Mateos et al, 2020[10]	ALCYONE	Daratumumab vs Observation
Bahlis et al, 2019[11]	MAIA	Daratumumab + Lenalidomide + Dexamethasone vs Lenalidomide + Dexamethasone
Graham et al, 2019[12]	Myeloma XI	Lenalidomide vs Observation
Benboubker et al, 2014[13]	NCT00551928	Lenalidomide + Dexamethasone vs Observation
Dimopoulos et al. 2019[14]	TOURMALINE-MM3 (NCT02181415)	Ixazomib vs Observation
Dytfeld et al, 2022[15]	ATLAS (NCT02659293)	Carfilzomib + Lenalidomide + Dexamethasone vs Lenalidomide

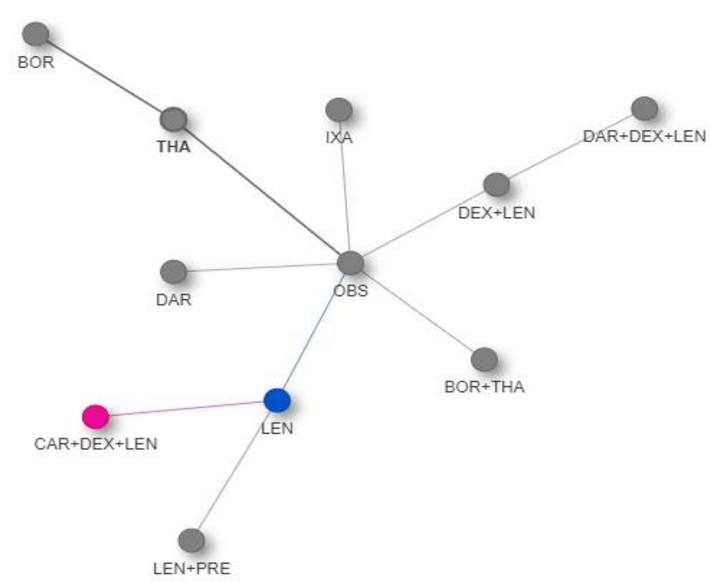
*** All studies are P3 RCTs.**
**** Red text indicates newly added study.**

RESULTS

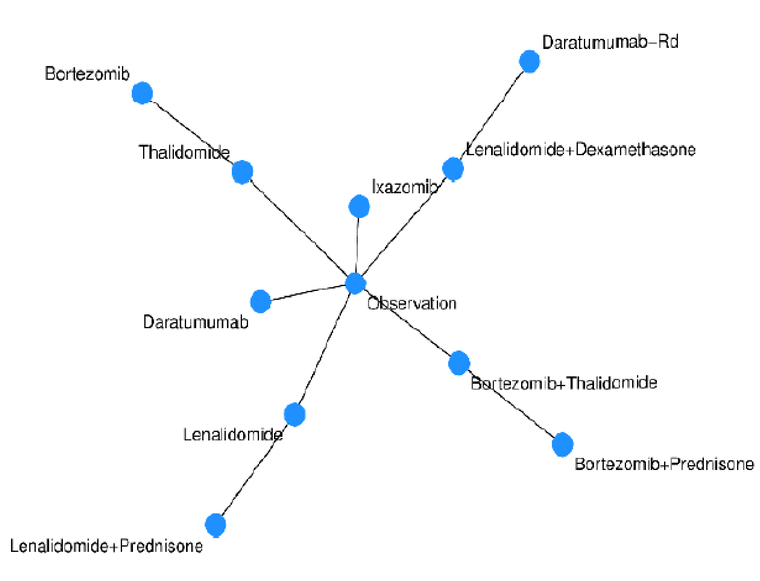
- By combining the LiveSLR platform with the LiveNMA software tool, we replicated the reference network diagram (**Figure 1A**) and treatment hierarchy (**Figure 2A**) within minutes.
- Maintenance PFS data were not published in the GEM2005 trial[2].
- Both networks were structurally similar and treatment ranking was comparable.
- Indirect comparisons between daratumumab-lenalidomide-dexamethasone, lenalidomide-prednisolone and bortezomib, respectively, versus observation were successfully implemented.
- The NMA update was easy and rapid. It showed carfilzomib-lenalidomide-dexamethasone to have the best improvement in PFS compared with the other regimens in the model.

Figure 1. Network Diagram

A. LiveNMA replicate



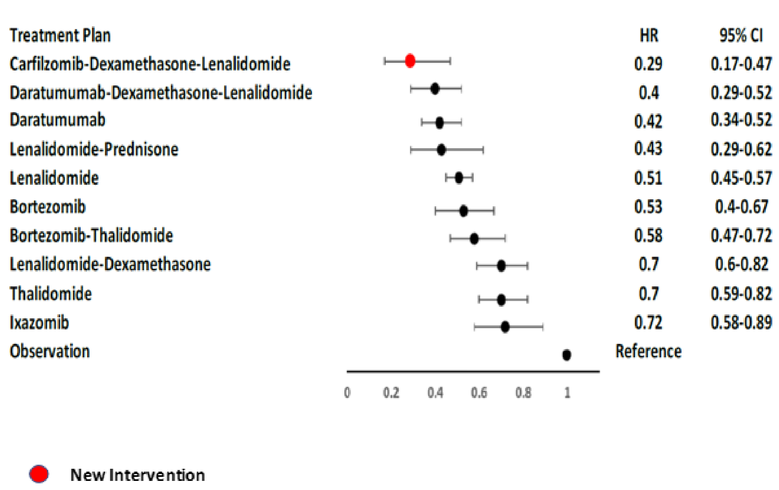
B. Original network diagram (Luchinin et al[1])



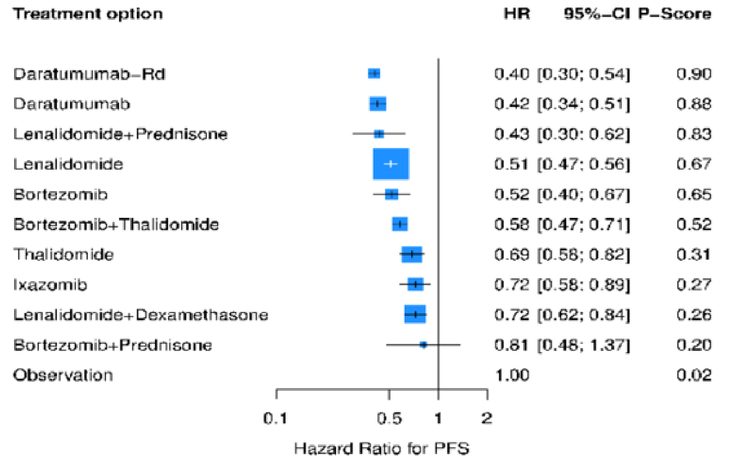
Abbreviations: BOR, Bortezomib; CAR, Carfilzomib; DAR, Daratumumab; DEX, Dexamethasone; IXA, Ixazomib; LEN, Lenalidomide; OBS, Observation; PRE, Prednisone; THA, Thalidomide

Figure 2: Forest plots of PFS Hazard Ratios

A. Replicated Forest Plot



B. Original Forest plot (Luchinin et al.)



Limitations

- The results should be interpreted with caution because the tool is not currently equipped to assess heterogeneity in baseline characteristics and trial designs.
- While treatment comparison against a reference intervention is possible, comparison between treatments in a matrix (pairwise) format cannot yet be implemented.

CONCLUSIONS

- **This study demonstrated the utility of an interactive LiveNMA tool, which replicated and updated an existing NMA analysis in just a few minutes.**
- **This easy and reliable tool can help decision makers stay current with the comparative effectiveness of new and existing treatments.**

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Abbreviations: BOR, Bortezomib; CAR, Carfilzomib; DAR, Daratumumab; DEX, Dexamethasone; HTA, Health Technology Assessment; IXA, Ixazomib; LEN, Lenalidomide; NMA, Network meta-analysis; OBS, Observation; OS, overall survival; PFS, progression-free survival; PRE, Prednisone; THA, Thalidomide;

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