Efficacy of Pharmacological and Radiotherapy Interventions in Primary CNS Lymphoma: A Network Meta-analysis of Randomized Controlled Trials

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Introduction

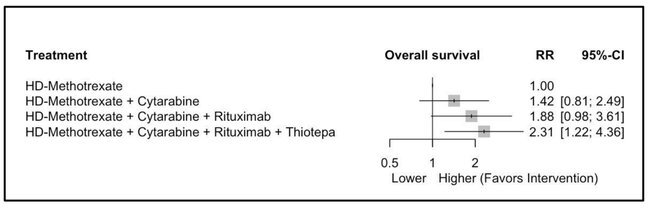
- Primary central nervous system lymphoma (PCNSL) is a rare and aggressive form of non-Hodgkin lymphoma confined to the CNS and Its incidence increases in individuals over 60 years old.
- The unique molecular and biological architecture of PCNSL complicates the identification of new therapeutic targets.
- High-dose (HD) methotrexate-based chemotherapy is the standard treatment, and combined chemoradiotherapy has demonstrated improved outcomes in clinical trials.

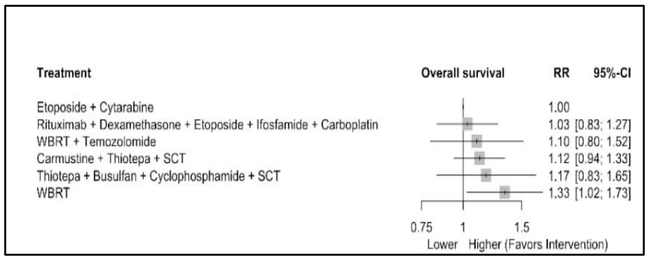
Aim & Objectives

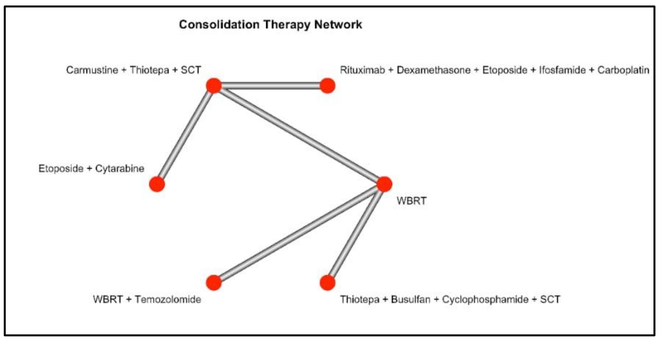
- Through this **Network Meta Analysis**(NMA) we aim to investigate the clinical benefits of various treatment combinations in PCNSL patients

Methods

- We conducted a systematic search PubMed/MEDLINE, Cochrane, EMBASE, Scopus, and ClinicalTrials.gov identified RCTs on PCNSL interventions up to April 2025.
- A frequentist approach was employed, with risk ratios (RRs) for **overall survival** (OS) and their 95% confidence intervals as the outcome.
- Component-based additive modeling was utilized when feasible and for induction therapies, disconnected sub-networks were excluded to ensure a connected network for analysis.
- Data was extracted across a uniform time point of 2-3 years for consolidation(2) and induction regimens(3).

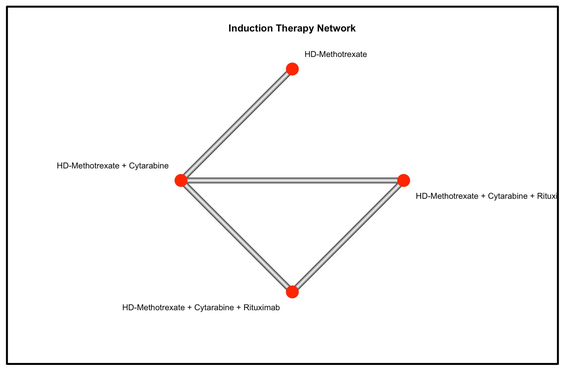






Results

- Our NMA comprised 2 studies involving 298 patients for induction regimens and 5 studies with 709 patients for consolidation regimens.
- The network was connected for induction regimens with 4 pairwise comparisons and 298 observations.
- The reference treatment in the connected network was **HD-Methotrexate. HD-Methotrexate + Cytarabine + Rituximab + Thiotepa** (2.31, 1.22–4.36) showed the greatest improvement compared to HD-Methotrexate alone, while HD-Methotrexate + Cytarabine (1.42, 0.81–2.49) and HD-Methotrexate + Cytarabine + Rituximab (1.88, 0.98–3.61) showed non-significant improvements.
- Heterogeneity was minimal (I^2=0%). The network was connected for consolidation regimens, comprising 5 pairwise comparisons and 709 observations, with Etoposide + Cytarabine as the reference treatment.
- For consolidation therapies, **whole-brain radiotherapy** (WBRT) (1.33, 1.02–1.73) improved OS. Incremental effects revealed that **Temozolomide** (0.82, 0.68–0.99) and **Etoposide** (0.91, 0.84–0.99) reduced survival.



Summary

- This meta-analysis found that **HD-methotrexate combined with cytarabine, rituximab, and thiotepa** provided the greatest survival benefit in primary CNS lymphoma, while other methotrexate-based combinations showed smaller effects. For consolidation, **whole-brain radiotherapy** improved survival, whereas temozolomide and etoposide were linked to reduced survival

Discussion

- The refernece regimen (**HD-Methotrexate + Cytarabine + Rituximab + Thiotepa**) produced the greatest OS benefit compared with HD-Methotrexate alone. These results mirror IELSG32[1], which showed rituximab improved PFS.
- **WBRT** significantly improved survival compared which outperformed etoposide + cytarabine, consistent with prior data on its CNS-wide efficacy.
- **Temozolomide and etoposide** were linked to reduced OS, consistent with prior reports[2-3] of limited CNS activity.

References

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