

INPLASY

Inhibition of Bromodomain and Extra-terminal motif (BET) proteins in pediatric sarcoma: a systematic review of in vitro and in vivo studies

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ADMINISTRATIVE INFORMATION**Support** - Italian Ministry of Health Ricerca Finalizzata.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202570083**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 July 2025 and was last updated on 21 July 2025.**INTRODUCTION**

Review question / Objective This systematic review aims to provide a comprehensive overview of the current landscape of BETi applications in pediatric sarcomas.

Rationale BET inhibitors (BETi), especially those targeting BRD4, show promising preclinical activity against pediatric sarcomas by disrupting oncogenic transcription. However, applying these findings in clinical practice remains difficult due to resistance, toxicity, and inconsistent responses. Future approaches include using biomarkers for patient selection, developing isoform-specific BETi, and designing rational combination therapies to enhance treatment for these aggressive, fusion-driven cancers.

Condition being studied Pediatric Sarcoma.**METHODS**

Search strategy Experimental articles, published until 10 June 2025, were searched on PubMed/MEDLINE, Embase, Scopus, and Web of Science databases using the following query: [(BET OR bromodomain) AND (inhibitor OR inhibition) AND (pediatric OR children OR young) AND sarcoma].

Participant or population Cell lines of Pediatric sarcoma rated in vitro and / or in vivo.

Intervention BET inhibitor.**Comparator** NA.

Study designs to be included Original research articles written in English.

Eligibility criteria Original research articles written in English that reported findings from in vitro and in

vivo studies involving pediatric sarcoma cell lines treated with BETi.

Information sources PubMed/MEDLINE, Embase, Scopus, and Web of Science databases.

Main outcome(s) Title, author(s), publication year, publication, type of tumors, cell lines, used BETi and dosage.

Quality assessment / Risk of bias analysis Quality assessment was conducted independently by two reviewers (S.P. and M.C.), with any disagreements among all authors resolved through discussion.

Strategy of data synthesis Rayyan (<https://www.rayyan.ai/>), a free software, was then used to screen the articles, eliminate duplicates, and record the results.

Subgroup analysis Type of tumor, in vitro and in vivo studies.

Sensitivity analysis NA.

Country(ies) involved Italy.

Keywords BET inhibitors; BRD4; Bromodomain and Extra-terminal motif; Pediatric sarcoma; Fusion-driven cancers.

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