MonashHealth

Clinicians, Consumers, Evidence
Centre for Clinical Effectiveness

Evidence Snapshot

The safety and efficacy of Bendamustine in the treatment of patients with relapsed/refractory Marginal Zone Lymphoma

Citation Yap G. 2017. The safety and efficacy of Bendamustine in the treatment of patients with relapsed/refractory Marginal Zone Lymphoma: Evidence Snapshot. Centre for Clinical Effectiveness, Monash Innovation and Quality, Monash Health, Melbourne, Australia.

Background

The Single Patient Use Sub-Committee has requested for a review of evidence on the safety and efficacy of Bendamustine in treating patients with relapsed/refractory Marginal Zone Lymphoma to inform future Committee decision-making.

Question

What is the safety and efficacy of Bendamustine in the treatment of patients with relapsed/refractory Marginal Zone Lymphoma (MZL)?

Search methods

Table 1. Search methodology used

Medication	Bendamustine
Indication	Include: Patients with relapsed/refractory Marginal Zone Lymphoma (MZL) Exclude: Other subtypes of Non-Hodgkins Lymphoma
Outcomes	Safety and clinical effectiveness
Publication details	*Inclusion*: Synthesised data from systematic reviews (SR), meta-analysis (MA), and evidence-based guidelines. *Exclusion*: Non-synthesised literature
Date limitation	No limits; only the most recent and updated evidence will be presented
Databases	NICE guidelines, BMJ Best practice, TRIP database, Cochrane database of systematic reviews.
Search terms	“Bendamustine” AND “Marginal Zone Lymphoma”

Results

Evidence was limited and only two sources met inclusion criteria. One was a moderate quality guideline (2017) from the National Comprehensive Cancer Network (NCCN) which was based on lower-level evidence, but uniform NCCN consensus. The other was a low-moderate quality Horizon Scanning Report (2016) published by the National Institute for Health Research (NIHR) Horizon Scanning Research & Intelligence Centre. A summary of the evidence about suggested treatment regimens is outlined in Table 2.

The National Institute for Health and Care Excellence (NICE) terminated the technology appraisal: Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab in 2010. BMJ Best practice listed treatment options for Bendamustine in combination with Rituximab as a first line of treatment in indolent lymphomas. As the treatment listed was not for relapsed or refractory MZL, this evidence was excluded. Another report

published by NIHR Horizon Scanning Research & Intelligence Centre was excluded as it did not include Bendamustine in the treatment of refractory marginal zone lymphomas.

Summary of findings

Table 2. Sources of evidence that met the inclusion criteria and a summary of evidence included

Source	Quality of Evidence	Indication	Treatment	Description of Evidence
NCCN guidelines Version 3.2017 (Mar 2017)	Moderate	B-cell lymphoma guidelines	+ Bendamustine + Obinutuzumab	The following is based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate: Bendamustine and Obinutuzumab suggested as a second line and subsequent therapy for MZL (in fifth order of preference to other treatment therapies) For patients treated with Obinutuzumab-Bendamustine for recurrent disease, then Obinutuzumab maintenance for rituximab-refractory disease (1 g every 8 weeks for total 12 doses) as a first preference as an optional second line consolidation or extended dosing for MZL. (Ref: MZL-A 2 of 2; MS-58) Link to full guidelines (registration required): https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf
NIHR HSRIC (Feb 2016)	Low	Indolent CD 20+ NH-lymphoma; refractory	+ Idelalisib + Bendamustine + Rituximab	For relapsed disease, second line treatments include rituximab in combination with chemotherapy followed by rituximab maintenance therapy (unless high dose therapy is considered a suitable option). Regimens commonly used include: • R-Benda – appropriate to re-treat patients who have gained a long remission (> 2 years) with previous R-Benda therapy. • R-CHOP. • R-CVP. • Fludarabine. • Fludarabine in combination with rituximab, mitoxantrone and dexamethasone. Link to report: http://www.io.nihr.ac.uk/topics/idelalisib-in-combination-with-bendamustine-and-rituximab-for-indolent-non-hodgkin-lymphoma-second-line/

Conclusion and Limitations

There was limited synthesised evidence for the use of Bendamustine in the treatment of refractory MZL. Evidence of its safety or efficacy in the treatment of refractory MZL was lacking. The NCCN guidelines were based on low levels of evidence, but a uniform expert consensus that the intervention is appropriate. The lack of a systematic approach to the search of its evidence limited the quality of the guideline. The NIHR HSRIC Report lacked clear documentation of its approach to obtaining its evidence, or links to the sources of evidence. There was also no appraisal or categorisation of the evidence included in the report. Therefore the NIHR HSRIC Report was ranked as poor quality.

References

- National Institute for health Research Horizon Scanning Research & Intelligence Centre, University of Birmingham. Idelalisib in combination with bendamustine and rituximab for indolent non-Hodgkin lymphoma – second line. NIHR HSRIC ID: 9052. Download from: www.hsric.nihr.ac.uk

- National Comprehensive Cancer Network. NCCM Clinical Practice Guidelines in Oncology: B Cell Lymphomas. Version 3.2017 – March 2017. Download from https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf