Current treatment patterns and associated outcomes in Waldenström macroglobulinemia (WM) and related hematologic malignancies: A systematic literature review (SLR).

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Background:
The objectives are to review published literature and identify unmet needs for WM-related treatment and outcomes.

Methods:
A SLR using PubMed was performed to identify WM-related studies published Jan. 2013-Sept. 2018. Inclusion criteria included interventional or observational clinical studies with N > 40, non-case reports or editorial review, English abstracts available.

Results:
Of 1146 evaluable publications, 59 were included (40 real-world data [RWD], 4 clinical trials, 15 guidelines). Specific guideline recommendations varied due to limited comparative Phase III trials. RWD on safety and efficacy of WM treatment primarily included retrospective, single-center chart reviews or database analyses in mainly US and European populations. RWD showed heterogeneous WM treatment patterns and outcomes: (1) first-line chemoimmunotherapy use often did not follow guidelines; and (2) overall and progression-free survival (OS; PFS) with front-line regimens were lower than reported in trials. Reduced adherence, discontinuations (DC), and extended holds (> 8-14 days) with kinase inhibitors (KI; ibrutinib or idelalisib) were common and associated with poorer outcomes (e.g. reduced OS or PFS) (*Table*). Common reasons for KI DC/hold included toxicity, procedure/surgery, patient-request, and low/no disease activity.

Conclusions:
This SLR identified potential unmet needs in current WM treatment associated with poorer clinical outcomes, including KI DC, holds, and reduced adherence. Deviations from treatment guidelines were also reported. Future comparative clinical and RWE studies are needed.

KI Adherence, DC, and Holds.

Endpoint	Finding
Low adherence (ie, dose intensity < 97%)	30% Associated with 3-fold higher progression risk
DC, range	25-54%
Hold, range	24-79%
Median time to DC	7-9 mo
Outcomes associated with KI DC	Median OS after DC: 3-8 mo Shorter OS due to progression vs other reasons:3-17 mo IgM rebound (≥25% increase in serum IgM) 73% Withdrawal symptoms (new-onset symptoms after holds or DC) 19%
Outcomes associated with extended KI holds	4-fold increased progression risk Reduced 1-year OS: 69% vs 84% (no holds)