

Supplementary Table S1. Comparison of recommendations for first-line treatment with NCCN (ver 3.2024), ESMO CPG interim update (2024) and BSH (2022) guidelines.

Patient population	British Society of Haematology (BSH), 2022 ⁷⁹	ESMO CPG interim update, 2024 ¹⁵	NCCN version 3.2024 ¹⁶
With TP53 mutation or del(17p)	<p>Recommendations (NICE-approved)</p> <ul style="list-style-type: none"> - Fit patients: acalabrutinib, ibrutinib, or venetoclax monotherapy if BTKi contraindicated - V+O or acalabrutinib for patients unsuitable for CIT, irrespective of TP53 status 	<p>BTKis:</p> <ul style="list-style-type: none"> - Acalabrutinib - Zanubrutinib - Ibrutinib <p>Other options:</p> <ul style="list-style-type: none"> - Venetoclax (continuous) - I+V (particularly in younger patients) - V+O 	<p>Preferred regimens:</p> <ul style="list-style-type: none"> - A ± O - V + O - Zanubrutinib <p>Other recommended regimens:</p> <ul style="list-style-type: none"> - Ibrutinib - I + O - I + R - I + V <p>CIT (FCR) may be useful in certain circumstances.</p>
Without TP53 mutation or del(17p)	<p>CIT</p> <ul style="list-style-type: none"> - For fit patients with mutated IGHV, FCR is an acceptable option - Bendamustine-based or chlorambucil-based CIT are no longer recommended 	<p>Time-limited therapies are preferred over continuous therapies if efficacy is similar.</p> <p>Fit/younger patients with mutated IGHV:</p> <ul style="list-style-type: none"> - V+O - I+V - Ibrutinib - Acalabrutinib (±O) - Zanubrutinib - CIT: FCR <p>Unfit/older patients with mutated IGHV:</p> <ul style="list-style-type: none"> - V+O - Acalabrutinib (±O) - Zanubrutinib - Ibrutinib (after cardiovascular work-up) - I + V (after cardiovascular work-up) 	<p>Preferred regimens:</p> <ul style="list-style-type: none"> - A ± O - V + O - Zanubrutinib <p>Other recommended regimens:</p> <ul style="list-style-type: none"> - Ibrutinib - I + V

Patient population	British Society of Haematology (BSH), 2022 ⁷⁹	ESMO CPG interim update, 2024 ¹⁵	NCCN version 3.2024 ¹⁶
		<p>Fit/younger patients with unmutated IGHV:</p> <ul style="list-style-type: none"> - I + V - Ibrutinib - Acalabrutinib (±O) - Zanubrutinib - V + O (as alternative to ibrutinib) <p>Unfit/older patients with unmutated IGHV:</p> <ul style="list-style-type: none"> - V + O - Acalabrutinib (±O) - Zanubrutinib - Ibrutinib (after cardiovascular work-up) - I + V (after cardiovascular work-up) 	