

Table 1. Summary of key consensus statements for APLC expert consensus on the management of chronic lymphocytic leukaemia in Asia.

	Statements	Mean	Median	IQR
Diagnosis				
1	Patients with asymptomatic early-stage CLL should not be treated until disease progression occurs, and active surveillance remains the standard for management.	4.94	5	0
2	Current randomised phase III trials evaluating early treatment (including CIT and ibrutinib) in asymptomatic CLL patients show increased toxicity without improved overall survival, thus it is recommended to adhere to iwCLL guidelines 2018 for the initiation of therapy for CLL.	4.65	5	0
3	Genetic testing recommendations for first-line therapy: • Testing for <i>TP53</i> mutations and FISH for 17p deletion is recommended for all patients before initiating first-line therapy.¹² • Assessment of <i>IGHV</i> mutation status is recommended as it informs treatment selection. • Conventional karyotyping may be considered in select cases for additional cytogenetic information.	4.41	4	1
4	Assessment for 17p deletion by FISH is recommended for determining therapeutic approaches. However, if resources and accessibility permit, it is highly recommended that both FISH for 17p deletion and testing for <i>TP53</i> mutation be done simultaneously.	3.47	4	1.5
Treatment				
5	Clinicians should communicate with patients about the chronic nature of CLL, potential treatment relapses and expectations for long-term management.	5	5	0
6	It is recommended to avoid, if possible, BTKis with drugs that have antiplatelet effects, such as non-steroidal anti-inflammatory drugs.	3.76	4	1
7	In patients requiring planned surgery, it is recommended to discontinue BTKis from 3 to 7 days both before and after surgery, with the duration dependent on the type of surgery. Nevertheless, the given risk and benefit of holding BTKi treatment for less urgent procedures should be discussed with the patient depending on their disease control and clinical status.	4.41	4	1
8	In patients requiring antiplatelet agents, it is recommended that while single antiplatelet agent use in association with BTKi may be acceptable, dual antiplatelet agents plus BTKi are to be avoided.	4.24	4	1
9	It is recommended to delay BTKi therapy if dual antiplatelet therapy is considered necessary.	3.82	4	1.5
10	Multiple randomised phase III trials have demonstrated that the use of targeted therapy prolongs progression-free survival, and in some cases, overall survival and have good safety profiles. CIT with FCR may be an acceptable treatment option in fit patients with <i>IGHV</i> -mutated CLL without <i>TP53</i> aberrations if access to BTKi or venetoclax-based regimens are not available. The risk of secondary cancers and MDS/AML approximately 5% after FCR should be conveyed to patients.	4.35	4	1
11	Patients with <i>TP53</i> aberration should be treated with novel agents, BTKi or with BCL2i plus anti-CD20 monoclonal antibodies. While progression-free survival in patients with <i>TP53</i> mutations will be shorter in fixed-duration treatment, given the lack of direct comparison of continuous BTKi and V+O in this population, and taking into account patient preferences and other factors, V+O remains a reasonable option.	3.88	4	0
12	The choice of BTKi is decided depending on the access. Second-generation BTKis are preferable to ibrutinib, if available.	4.18	4	1
13	Targeted therapy agents, either BTKi or BCL2i-based regimens, should be considered the standard of care for patients with <i>TP53</i> dysfunction.	4.53	5	1
14	The mutational status of the <i>IGHV</i> gene, <i>TP53</i> mutations and complex karyotype are the best factors to predict long-term outcomes in patients treated with targeted therapies.	4.41	4	1
15	BCL2i and BTKi are preferred in all patients with R/R CLL after prior CIT. The choice between BCL2i and BTKi is largely based on patient-related factors, for example, comorbidities and desire for finite therapy. The choice among BTKi is dependent on toxicity profile and availability.	4.53	5	1
16	In patients with disease responding to covalent BTKi, treatment should be continued until progression and/or intolerance.	4.59	5	1
17	If treated with fixed-duration venetoclax-based treatment or CIT, observation is recommended until relapse with indications for retreatment.	4.59	5	1

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	Statements	Mean	Median	IQR
18	In patients with BTKi resistance, the following points are to be noted: - Do not abruptly stop BTKi, as this may precipitate rapid progression. - Consider switching to BCL2i with an anti-CD20 monoclonal antibodies. - In patients 2 had two or more prior therapies including a covalent BTKi and venetoclax, BTK-targeted agents (e.g. non-covalent BTKi or BTK degraders) can be considered.	4.24	4	1
19	Second-line treatment after frontline V+O: - Retreat with venetoclax-based therapy if patient has 3-year treatment free interval. - Second generation BTKi	4.24	4	1
20	For patients resistant to covalent BTKi and BCL2i therapies: - Non-covalent BTKi may be considered for patients previously treated with both BTKi and BCL2i, in accordance with current regulatory approvals. - Allo-SCT, CAR-T-cell or bispecific antibody, if available	4.29	4	1
21	Patient preference is very important in deciding between a second-generation covalent BTKi and V+O as initial therapy, given the duration of therapy, oral versus intravenous therapy and intensity of initial clinic monitoring.	4.53	5	0.5
22	Allo-SCT can be considered in patients with double-refractory CLL with available donor and sufficient fitness, if CAR-T cell therapy is not an option.	4.06	4	1
23	Patients undergoing long-term treatment should undergo routine monitoring for cardiac condition and an emphasis on immunisation, infectious prophylaxis and second primary malignancies to manage common comorbidities.	4.65	5	1
Management				
24	The iwCLL guidelines for response criteria should be followed in monitoring treatment response in CLL.	4.59	5	1
25	For monitoring immunochemotherapy and venetoclax-based therapy, the most relevant prognostic parameters are <i>IGHV</i> mutational status, serum β 2-microglobulin, and the presence of del(17p) and/or <i>TP53</i> mutations. Usually, high-risk CLL is defined, at least in part, by a genetic aberration of the <i>TP53</i> gene (i.e. del[17p] or <i>TP53</i> mutation).	4.18	4	1
26	Measurable residual disease (MRD) testing is not part of routine clinical practice and there is no evidence that an MRD-guided approach should be used outside clinical trials.	4.00	4	0
27	Patients on long-term BTKi should be clinically monitored due to the risk of adverse side effects such as atrial fibrillation and bleeding, and future use of BTKi should be avoided in patients in the event of ventricular arrhythmias and cardiac arrest.	4.71	5	1
28	With venetoclax-based therapy, close laboratory monitoring is required at the commencement of therapy to prevent side effects such as tumour lysis syndrome and cytopenia during treatment.	4.76	5	0.5
29	Autoimmune cytopenia should be treated with immunosuppression including corticosteroids and/or anti-CD20 monoclonal antibodies. In patients who have a suboptimal response, CLL-directed therapy is needed, which could include drugs such as ibrutinib or venetoclax.	4.12	4	0.5

allo-SCT: allogeneic stem cell transplantation; AML: acute myeloid leukaemia; BTKi: Bruton's tyrosine kinase inhibitor; BCL2i: B-cell lymphoma-2 inhibitors; CAR-T-cell: chimeric antigen receptor T cell; CIT: chemoimmunotherapy; CLL: chronic lymphocytic leukaemia; FISH: fluorescence in situ hybridisation; FCR: fludarabine, cyclophosphamide, rituximab; *IGHV*: immunoglobulin heavy chain variable region gene; IQR: interquartile range; iwCLL: International Workshop on Chronic Lymphocytic Leukemia; MDS: myelodysplastic syndromes; R/R: relapsed/refractory; V+O: venetoclax+obinutuzumab