<table>
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<th>Guideline Page and Request</th>
<th>Panel Discussion/References</th>
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| **CSLL-D 1 of 6** Internal request Comment to reassess the category 1 recommendation for chlorambucil + obinutuzumab as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for frail patients with significant comorbidity and patients age ≥65 y and younger patients with significant comorbidities based on the data from iLLUMINATE study. | Based on the discussion of the data in the noted reference, the panel consensus supported the continued listing of chlorambucil + obinutuzumab as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for frail patients with significant comorbidity and patients age ≥65 y and younger patients with significant comorbidities with a category 2A recommendation.  
| **CSLL-D 1 of 6** Internal request Comment to change chlorambucil + anti-CD20 monoclonal antibody (obinutuzumab, ofatumumab and rituximab) as first-line therapies for CLL/SLL without del(17p)/TP53 mutation from preferred regimens to other recommended regimens for frail patients with significant comorbidity and patients age ≥65 y and younger patients with significant comorbidities | Based upon the panel discussion, the panel consensus was to change “chlorambucil + anti-CD20 monoclonal antibody (obinutuzumab, ofatumumab and rituximab)” as first-line therapies for CLL/SLL without del(17p)/TP53 mutation from preferred regimens to other recommended regimens for frail patients with significant comorbidity and patients age ≥65 y and younger patients with significant comorbidities. | YES | NO | ABSTAIN | ABSENT |
| **CSLL-D 1 of 6** Internal request Comment to change bendamustine + anti-CD20 monoclonal antibody as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation from a preferred regimen to other recommended regimen for  
- Patients age ≥65 y and younger patients with significant comorbidities  
- Patients Age <65 y without significant comorbidities based on the results of the Alliance North American Intergroup Study (A041202) | Based upon the discussion of the data in the noted reference, the panel consensus was to change “bendamustine + anti-CD20 monoclonal antibody” as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation from a preferred regimen to other recommended regimen for  
- Patients age ≥65 y and younger patients with significant comorbidities  
- Patients Age <65 y without significant comorbidities  
CSLL-D 1 of 6
Internal request
Comment to reassess the category 2A recommendation for ibrutinib as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for patients age <65 y without significant comorbidities based on the results of the ECOG-ACRIN Cancer Research Group (E1912) trial.

Based on the discussion of the data in the noted reference, the panel consensus supported the continued listing of ibrutinib as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for patients age <65 y without significant comorbidities with a category 1 recommendation.


CSLL-D 1 of 6
Internal request
Comment to reassess the category 1 recommendation for FCR (fludarabine, cyclophosphamide, rituximab) as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for patients age <65 y without significant comorbidities based on the results of the ECOG-ACRIN Cancer Research Group (E1912) trial.

Based on the discussion of the data in the noted reference, the panel consensus supported the continued listing of FCR as a first-line therapy for CLL/SLL without del(17p)/TP53 mutation for patients age <65 y without significant comorbidities with a category 2A recommendation. FCR was also changed from a preferred regimen to other recommended regimen with a footnote clarifying that FCR is appropriate first-line treatment for young, fit patients with mutated IGHV.


External request
Submission request from Pharmacyclics LLC and Janssen Biotech, Inc. for first-line therapy for CLL/SLL without del(17p)/TP53 mutation

- Recommend inclusion of IGHV status in clinical decision tree for therapy determination. (Affected pages may include CSLL-3, 4, 5, and updates to)

The panel consensus was to include the recommendation to reevaluate IGHV mutation status in patients with indications for treatment with a footnote “necessary for treatment when considering chemoimmunotherapy” on CSLL-3.
the relevant suggested treatment regimens on CSLL-D):

- For frail patients with significant comorbidity and age ≥65 y and younger patients with significant comorbidities:
  - Ibrutinib: Retain as Category 1, preferred regimen, for patients with unmutated and mutated IGHV.
  - Ibrutinib + CD20 monoclonal antibody: Recommend as Category 1, preferred regimen, for patients with unmutated and mutated IGHV.

The panel consensus was to not include ibrutinib + CD20 monoclonal antibody as a category 1, preferred regimen for frail patients with significant comorbidity and age ≥65 y and younger patients with significant comorbidities with unmutated and mutated IGHV due to the absence of data from a randomized clinical trial that has compared ibrutinib vs ibrutinib + anti-CD20 monoclonal antibody.