

Online Resource

Treatment selection and influencing factors for chronic lymphocytic leukemia: a physician survey in Japan

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Online Resource 1 Questionnaire

1.

We would like to ask you about selection between BTK^a inhibitors and chemotherapy for first-line treatment. For primary treatment of CLL,^b which treatment do you consider first? (Please check one.)

☐ I will primarily select BTK inhibitors

☐ I will primarily select chemotherapy

^a Bruton's tyrosine kinase

^b Chronic lymphocytic leukemia

2. (If “I will primarily select BTK inhibitors” is checked)

Please tell us the reasons why you would consider BTK inhibitors as the primary treatment option for first-line CLL treatment. (Please select all that apply.)

- ☐ They are recommended in the guidelines
- ☐ I am accustomed to using them (for other diseases as well as CLL)
- ☐ They are backed by evidence
- ☐ They are well tolerated by patients
- ☐ They are highly effective
- ☐ They are very safe
- ☐ There are few restrictions/precautions (e.g., by tumor size) for the patients in which they can be used
- ☐ They can be used in outpatient treatment
- ☐ They are an oral drug
- ☐ They are easy to take
- ☐ They are more affordable for patients
- ☐ Other

3. (If "I will primarily select BTK inhibitors" is not checked)

Please tell us the reasons behind not consider BTK inhibitors as the primary treatment option for first-line CLL treatment. (Please select all that apply.)

- ☐ They have not been adopted at my facility
- ☐ I have no experience using them
- ☐ There is still little evidence
- ☐ They are not very effective
- ☐ Safety concerns
- ☐ Restrictions/precautions (e.g., by tumor size) for the patients in which they can be used
- ☐ The need for patients to continue taking them
- ☐ They are difficult to take
- ☐ They are very expensive for patients
- ☐ Chemotherapy is more effective
- ☐ I have more experience with chemotherapy
- ☐ Other

4.

We would like to ask you about selection between BTK inhibitors and chemotherapy for first-line CLL treatment. Please tell us the degree of impact each of the factors below has on selecting between BTK inhibitors and chemotherapy. (Please check one per row.)

	On your treatment selection between BTK inhibitors and chemotherapy for first-line treatment				
	No influence at all	←	Cannot say either	→	A great influence
17p deletion	☐	☐	☐	☐	☐
<i>TP53</i> mutation	☐	☐	☐	☐	☐
Fit/Unfit (whether indicated for multi-agent chemotherapy)	☐	☐	☐	☐	☐
Age	☐	☐	☐	☐	☐
PS ^a	☐	☐	☐	☐	☐
Speed of disease progression	☐	☐	☐	☐	☐
Cardiovascular comorbidities	☐	☐	☐	☐	☐
Serious comorbidities other than cardiovascular ones	☐	☐	☐	☐	☐
QOL ^b status	☐	☐	☐	☐	☐
Patient's financial situation	☐	☐	☐	☐	☐
Difficulty for patient to make regular visits (i.e., work, childcare, distance, etc.)	☐	☐	☐	☐	☐

^a Performance status

^b Quality of life

5.

Please tell us what you evaluate highly or are satisfied with for the regimens used for first-line CLL treatment. (Please select all that apply for each column.)

	Ibrutinib	Acalabrutinib ± obinutuzumab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Mechanism of action	☐	☐	☐	☐
OS ^a extension effect	☐	☐	☐	☐
PFS ^b extension effect	☐	☐	☐	☐
Overall response rate (ORR)	☐	☐	☐	☐
Complete response (CR) rate	☐	☐	☐	☐
Minimal residual disease (MRD) negative rate	☐	☐	☐	☐
Speed of onset of effect	☐	☐	☐	☐
Effectiveness in maintaining/improving QOL	☐	☐	☐	☐
Few serious adverse events	☐	☐	☐	☐
Few adverse events actually sensed by patients	☐	☐	☐	☐
How easy it is to take (e.g., administration method/tablet size)	☐	☐	☐	☐
How easy it is to introduce on an outpatient basis	☐	☐	☐	☐
How easy it is to explain to/obtain agreement from patients	☐	☐	☐	☐
Simple dosage and administration	☐	☐	☐	☐
Can be used as a single agent	☐	☐	☐	☐

	Ibrutinib	Acalabrutinib ± obinutuzumab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Can continue treatment for a long time	☐	☐	☐	☐
Fixed duration of treatment	☐	☐	☐	☐
Lower out-of-pocket cost for patients	☐	☐	☐	☐
There are no factors that I evaluate highly/am satisfied with	☐	☐	☐	☐
Do not know/Cannot say	☐	☐	☐	☐

^a Overall survival

^b Progression-free survival

6.

Please tell us what you are dissatisfied with or would like to see improved for the regimens used for first-line CLL treatment. (Please select all that apply for each column.)

	Ibrutinib	Acalabrutinib ± obinutuzumab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Mechanism of action	☐	☐	☐	☐
OS extension effect	☐	☐	☐	☐
PFS extension effect	☐	☐	☐	☐
Overall response rate (ORR)	☐	☐	☐	☐
Complete response (CR) rate	☐	☐	☐	☐
Minimal residual disease (MRD) negative rate	☐	☐	☐	☐
Speed of onset of effect	☐	☐	☐	☐
Effectiveness in maintaining/improving QOL	☐	☐	☐	☐
Many serious adverse events	☐	☐	☐	☐
Many adverse events actually sensed by patients	☐	☐	☐	☐
How difficult it is to take (e.g., administration method/tablet size)	☐	☐	☐	☐
Cannot be introduced on an outpatient basis	☐	☐	☐	☐
How difficult it is to explain to/obtain agreement from patients	☐	☐	☐	☐
Dosage and administration are not simple	☐	☐	☐	☐

	Ibrutinib	Acalabrutinib ± obinutuzumab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Cannot be used as a single agent	☐	☐	☐	☐
Cannot continue treatment for a long time	☐	☐	☐	☐
Duration of treatment is not fixed	☐	☐	☐	☐
High out-of-pocket cost for patients	☐	☐	☐	☐
There are no factors that I am dissatisfied with/want to see improved	☐	☐	☐	☐
Do not know/Cannot say	☐	☐	☐	☐

7.

We would like to ask about treatment selection for second-line treatment. In the secondary treatment of CLL, which treatment do you consider first? Please tell us for each first-line treatment.

<First-line treatment>

	Ibrutinib- resistance	Acalabrutinib- resistance	Ibrutinib -intolerance	Acalabrutinib -intolerance	Refractory with chemotherapy (primary resistance)	Recurrence after response to chemotherapy (recurrence)	Chemotherapy- intolerance
(Select one for each column)	↓	↓	↓	↓	↓	↓	↓
I will primarily select a BTK inhibitor (ibrutinib)	☐	☐	☐	☐	☐	☐	☐
I will primarily select a BTK inhibitor (acalabrutinib ± obinutuzumab)	☐	☐	☐	☐	☐	☐	☐
I will primarily select BCL2 inhibitors (venetoclax ± rituximab)	☐	☐	☐	☐	☐	☐	☐
I will primarily select chemotherapy	☐	☐	☐	☐	☐	☐	☐

8.

Please tell us what you evaluate highly or are satisfied with for the regimens used for second-line CLL treatment. (Please select all that apply for each column.)

	Ibrutinib	Acalabrutinib ± obinutuzumab	Venetoclax ± rituximab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Mechanism of action	☐	☐	☐	☐	☐
OS extension effect	☐	☐	☐	☐	☐
PFS extension effect	☐	☐	☐	☐	☐
Overall response rate (ORR)	☐	☐	☐	☐	☐
Complete response (CR) rate	☐	☐	☐	☐	☐
Minimal residual disease (MRD) negative rate	☐	☐	☐	☐	☐
Speed of onset of effect	☐	☐	☐	☐	☐
Effectiveness in maintaining/improving QOL	☐	☐	☐	☐	☐
Few serious adverse events	☐	☐	☐	☐	☐
Few adverse events actually sensed by patients	☐	☐	☐	☐	☐
How easy it is to take (e.g., administration method/tablet size)	☐	☐	☐	☐	☐
How easy it is to introduce on an outpatient basis	☐	☐	☐	☐	☐
How easy it is to explain to/obtain agreement from patients	☐	☐	☐	☐	☐
Simple dosage and administration	☐	☐	☐	☐	☐
Can be used as a single agent	☐	☐	☐	☐	☐

	Ibrutinib	Acalabrutinib ± obinutuzumab	Venetoclax ± rituximab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Can continue treatment for a long time	☐	☐	☐	☐	☐
Fixed duration of treatment	☐	☐	☐	☐	☐
Lower out-of-pocket cost for patients	☐	☐	☐	☐	☐
There are no factors that I evaluate highly/am satisfied with	☐	☐	☐	☐	☐
Do not know/Cannot say	☐	☐	☐	☐	☐

9.

Please tell us what you are dissatisfied with or would like to see improved for the regimens used for second-line CLL treatment. (Please select all that apply for each column.)

	Ibrutinib	Acalabrutinib ± obinutuzumab	Venetoclax ± rituximab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Mechanism of action	☐	☐	☐	☐	☐
OS extension effect	☐	☐	☐	☐	☐
PFS extension effect	☐	☐	☐	☐	☐
Overall response rate (ORR)	☐	☐	☐	☐	☐
Complete response (CR) rate	☐	☐	☐	☐	☐
Minimal residual disease (MRD) negative rate	☐	☐	☐	☐	☐
Speed of onset of effect	☐	☐	☐	☐	☐
Effectiveness in maintaining/improving QOL	☐	☐	☐	☐	☐
Many serious adverse events	☐	☐	☐	☐	☐
Many adverse events actually sensed by patients	☐	☐	☐	☐	☐
How difficult it is to take (e.g., administration method/tablet size)	☐	☐	☐	☐	☐
Cannot be introduced on an outpatient basis	☐	☐	☐	☐	☐
How difficult it is to explain to/obtain agreement from patients	☐	☐	☐	☐	☐
Dosage and administration are not simple	☐	☐	☐	☐	☐

	Ibrutinib	Acalabrutinib ± obinutuzumab	Venetoclax ± rituximab	BR (bendamustine + rituximab)	FCR (fludarabine + cyclophosphamide + rituximab)
Cannot be used as a single agent	☐	☐	☐	☐	☐
Cannot continue treatment for a long time	☐	☐	☐	☐	☐
Duration of treatment is not fixed	☐	☐	☐	☐	☐
High out-of-pocket cost for patients	☐	☐	☐	☐	☐
There are no factors that I am dissatisfied with/want to see improved	☐	☐	☐	☐	☐
Do not know/Cannot say	☐	☐	☐	☐	☐