# Preferences for treatment in first-line chronic lymphocytic leukemia: a multi-criteria decision analysis in Italy

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**Background:** Chronic lymphocytic leukemia (CLL) is the most common leukemia in the Western world, accounting for 30% of all leukemias. Recent research advancements have led to the development of targeted drugs, with various options recommended by guidelines for the first-line treatment (1L) of CLL.

**Aims:** This study aimed to identify the key criteria used for making decisions in the selection of 1L treatment for CLL for patients (pts) with mutated or unmutated IGHV ($IGHV^{mut}$ or $IGHV^{unmut}$) and to evaluate the relevance of these criteria from a multi-stakeholder perspective in Italy.

**Methods:** A multi-criteria decision analysis (MCDA) was developed following the ISPOR MCDA Emerging Good Practices Task Force. First, a multi-stakeholder group was established, comprised of clinicians, methodologists/payers, and pts. Second, targeted therapies reimbursed in Italy were selected based on ESMO guidelines, including Bruton tyrosine kinase inhibitors (BTKis; acalabrutinib, ibrutinib [I], zanubrutinib), venetoclax (V) + obinutuzumab, and VI. Criteria for 1L CLL treatment were selected through literature review, discussed with the stakeholders, and finalized based on data availability. A performance matrix, which associated a value with each therapeutic option and criterion, was built using data from clinical trials and literature. Preferences between criteria (weighting) and for changes within criteria (scoring) were assessed by 20 stakeholders (9 clinicians, 6 methodologists/payers, 5 pts) via the Measuring Attractiveness by a Categorical-Based Evaluation Technique (MACBETH) method. Mean weights, reported as percentage values, reflect the relative importance of each criterion. Global scores of treatments were calculated by combining the scores of the alternatives for each criterion with the weights assigned to those criteria by respondents. Results were interpreted with the stakeholders' group.

**Results:** The final criteria for selecting 1L treatment for CLL were efficacy (progression-free survival), safety (treatment discontinuation rate due to adverse events), drug cost, quality of life, convenience of administration, and treatment duration (Table). In pts with $IGHV^{mut}$, efficacy was the most relevant criterion for pts and payers, with mean weight of 23% for both, while clinicians prioritized treatment duration (24%). Compared to pts with $IGHV^{mut}$, the mean weight of efficacy in pts with $IGHV^{unmut}$ increased for all stakeholders' groups, emerging as the most important criterion for clinicians (36%) and payers (30%); for pts, the most important criterion was safety (27%), followed by efficacy (26%).

Overall, only efficacy and safety had a mean weight of at least 20% in all groups regardless of IGHV mutation status, while drug cost and convenience of administration did not reach a mean weight of 20%. In terms of mean global scores, the treatment option with the highest score in pts with $IGHV^{mut}$ was zanubrutinib for pts and payers, and for clinicians was VI. In pts with $IGHV^{unmut}$, second-generation BTKis were the treatment option with the highest score.

**Conclusions:** This study suggests that efficacy and safety had higher mean weights than other criteria for Italian stakeholders when deciding on 1L CLL treatment regardless of IGHV mutation status, except for clinicians when treating pts with $IGHV^{mut}$, for whom treatment duration was the most important criterion. Insights from this MCDA contribute significantly to the literature.

*Table: Criteria weights and ranking among stakeholders*

***IGHV mutated patients***

| | Payers | | Patients | | Clinicians | |
|---|---|---|---|---|---|---|
| | Weights | Ranking | Weights | Ranking | Weights | Ranking |
| **Efficacy** [81.0% ► 90.0%] | 23% | 1st | 23% | 1st | 21% | 3rd |
| **Treatment duration** [fixed ► until progression] | 9% | 6th | 14% | 4th | 24% | 1st |
| **QoL** [demonstrated improvement in GHS at 6 months ► not demonstrated improvement] | 15% | 4th | 22% | 2nd | 13% | 4th |
| **Safety** [8.9% ► 16.0%] | 22% | 2nd | 22% | 2nd | 23% | 2nd |
| **Convenience of admin** [oral, home, constant dosage ► IV+oral, hospital+home, variable dosage] | 13% | 5th | 15% | 3rd | 12% | 5th |
| **Drug cost** [17,000 € ► 40,000 €] | 18% | 3rd | 4% | 5th | 7% | 6th |

***IGHV unmutated patients***

| | Payers | | Patients | | Clinicians | |
|---|---|---|---|---|---|---|
| | Weights | Ranking | Weights | Ranking | Weights | Ranking |
| **Efficacy** [69.8% ► 81.9%] | 30% | 1st | 26% | 2nd | 36% | 1st |
| **Treatment duration** [fixed ► until progression] | 9% | 6th | 10% | 5th | 17% | 3rd |
| **QoL** [demonstrated improvement in GHS at 6 months ► not demonstrated improvement] | 14% | 3rd | 22% | 3rd | 10% | 4th |
| **Safety** [8.9% ► 16.0%] | 20% | 2nd | 27% | 1st | 20% | 2nd |
| **Convenience of admin** [oral, home, constant dosage ► IV+oral, hospital+home, variable dosage] | 13% | 5th | 10% | 4th | 10% | 5th |
| **Drug cost** [17,000 € ► 40,000 €] | 14% | 4th | 5% | 6th | 6% | 6th |

Acronyms: BTK=Bruton's tyrosine kinase; GHS = Global Health Status; QoL= Quality of Life; IGHV= immunoglobulin heavy chain variable