Bruton's Tyrosine Kinase (BTK) Inhibitors For Patients With Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia (CLL/SLL)

Continuing Medical Education (CME) Summary Gap Analysis

- Despite improved outcomes of modern therapies, the most common reasons for discontinuation of treatment are drug resistance and intolerance. Patients with CLL/SLL represent a new and rapidly growing frontier of unmet medical need.[1]
- Clinicians and other healthcare providers (HCP) who treat patients with CLL/SLL, require more education and understanding of the true efficacy of newer targeted therapies.
    - In a study quantifying knowledge gaps among oncology HCPs, 47% of HCPs (n=270) failed to select the preferred first-line therapy per expert recommendations for a patient with CLL, high tumor burden, and renal insufficiency.[2]
- Obstacles for optimal management of patients with relapsed or refractory (R/R) CLL/SLL that must be addressed
    - The best approach to treat patients who are receiving multiple new treatments simultaneously in the setting of R/R CLL/SLL remains unexplored and, therefore, presents an opportunity for further study in the future.[3]
    - HCPs treating patients with R/R CLL/SLL must find ways to improve patient knowledge and understanding of new therapies available to them.
        - Substantial gaps remain in the awareness of new treatments among patients with CLL.[4]
    - Nonadherence due to adverse events and financial burden seen with BTK inhibitors and particularly ibrutinib have become barriers that must be overcome.
        - Clinical pharmacists are uniquely positioned in addressing issues of nonadherence by creating oral chemotherapy management plans that tackle issues such as avoiding drug-drug interactions and assisting with self-management techniques, and addressing financial issues such as insurance.[5]
    - Comprehensive prognostic measures and workup in the community setting where the majority of patients with CLL/SLL are treated is difficult to achieve.
        - Data from in-form CLL registry indicated a knowledge gap in terms of prognostic marker testing and selection of therapies for patients with high-risk disease, especially those in community-based settings where oncologists are less likely to have known prognostic factors measured, in reference to del(17p)/TP53 and immunoglobulin heavy-chain variable region gene mutational status and fluorescence in situ hybridization testing.[6]
- A growing number of patients are now in need of new therapeutic options with proven efficacy and safety following treatment with a BTK inhibitors and venetoclax, and as such, constitute the vanguard of contemporary unmet need for this disease.[1]

Introduction

CLL and SLL are identified by a progressive accumulation of leukemic cells in the peripheral blood, bone marrow, and lymphoid tissues.[7] The major difference with CLL lies in a significant number of the abnormal lymphocytes found in the peripheral blood, bone marrow and lymphoid tissue.[7] SLL primarily affects lymph nodes, bone marrow, and other lymphoid tissues with a limited presence of abnormal lymphocytes in the peripheral blood.[7]

Treatment Guidelines

B cell receptor signaling drives CLL cell survival, and as a result, various targeted treatments have been developed to alter this signaling. These targeted treatment options include oral BTK inhibitors (e.g., ibrutinib, acalabrutinib, zanubrutinib), oral B cell lymphoma 2 inhibitor (venetoclax), and injectable anti-CD20 monoclonal antibodies (e.g., rituximab, obinutuzumab).[8] First-line CLL treatment has shifted away from cellular immune therapy-based approaches which combine chemotherapy and anti-CD20 agents to oral targeted therapy due to survival advantages and fewer short- and long-term adverse events.[8]

Emerging Role of BTK Inhibitors in (CLL/SLL)

Development of second generation BTK inhibitors such as (acalabrutinib, zanubrutinib and others), which have so far demonstrated comparable efficacy, are expected to have fewer adverse events and better tolerability than ibrutinib.[9] As they receive FDA approval, it is expected that the use of second generation BTK inhibitors will alter the treatment landscape and become more prevalent in clinical practice.[9]

Outlook and Other Therapies

CLL still remains an incurable disease despite the advancements that have been made.[9] Current clinical studies aim to find the most effective combination of BTK inhibitors with the objective of discovering time-efficient, chemotherapy-free regimens.[9]

Venetoclax-based combination regimens also have higher rates of undetectable minimal residual disease like BTK inhibitors,[10] but differ from them in having a fixed treatment duration and not continuously administered until disease progression occurs.[10]

Conclusion

The introduction of newer agents in treating CLL/SLL has increased the complexity of selecting targeted therapies based on individual patient characteristics and profile. As a result, improvements in the prognostic workup and incorporation of new information into treatment guidelines are vital to ensuring that clinicians and patients have the tools for shared treatment decision making. As new studies look to establish evidence-based treatment particularly with BTK inhibitors and other combination regimens, it is crucial that HCPs are kept up to date on these emerging treatment possibilities.

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