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Editorial
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Highlights from the 2017 American Society of Hematology (ASH) Meeting: Therapy of Chronic Lymphocytic Leukemia

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Editorial

The treatment of Chronic Lymphocytic Leukemia (CLL) has undergone significant changes based on patients' genetic status, mutation status and with the introduction of the B-cell receptor inhibitors. Algorithms for treatment based on age, mutational and genetic status and co-morbidities are continually evolving. Several abstracts detailing novel therapies of CLL from the 2017 ASH Meeting are highlighted here.

A multicenter Phase II study of ibrutinib plus fludarabine, cyclophosphamide and rituximab (iFCR) was studies as frontline therapy for younger patients. The study was headed by Dr. Matthew S. Davids. Ibrutinib monotherapy was given for 7 days followed by up to six cycles of FCR with responders continuing on maintenance ibrutinib for at least two years. Of the 49 patients accrued, the median age was 55, 26% had del(11q), 9% had del(17p), 57% had un mutated IGHV, 59% were positive for ZAP-70, 6% had the TP53 mutation without del(17p) and 6% had the NOTCH1 mutation. In the 35 patients evaluable for efficacy, the Overall Response Rate (ORR) was 100% with 63% achieving a complete response rate (CR/CRi). Also the rate of CR with bone marrow Minimal Residual Disease (MRD)-negativity at 2 months which increased to 57% after ibrutinib maintenance. Overall, 83% achieved bone marrow MRD-negativity which is significantly higher than that observed in the past with FCR alone. Low rates of hematologic and infectious toxicities were noted with mandatory growth factor and antibiotic prophylaxis. This appears to be an effective therapy in a relatively high risk group of young, fit CLL patients.

Dr. John C. Byrd led a multi-institutional study of acalabrutinib in patients with relapsed/refractory CLL. Acalabrutinib is a highly selective, potent, covalent Bruton tyrosine kinase inhibitor which demonstrated a promising safety and efficacy profile in s prior study. In this trial, 134 patients with relapsed/refractory CLL were enrolled and treated with acalabrutinib in 28-day cycles with a dose escalation phase until progressive disease or unacceptable toxicity. Of these, 39% had bulky lymph nodes greater than or equal to 5 cm, 735 had unmutated IGHV, 23% had del (17p) and 18% had del (11). The overall response rate was 85% with 83% being partial responders. The median time to response was 4.7 months and the duration of response at 18 months was 85%. The safety profile was tolerable. It appears that acalabrutinib continues to be associated with high response rates and durable remissions.

A group from the United Kingdom headed by Dr. Peter Hillman reported on the results of therapy with ibrutinib and venetoclax in relapsed, refractory CLL. Ibrutinib is a Bruton tyrosine kinase inhibitor while venetoclax is a potent, highly selective orally bioavailable Bcl-2 inhibitor. Because ibrutinib causes the reduction of anti-apoptotic molecules, it was thought that this could potentiate the effect of venetoclax. Fifty patients who had relapsed within 3 years of being treated with ibrutinib or FCR or had the 17p deletion and had failed at least one line of therapy were treated with ibrutinib for 8 weeks and then venetoclax was added in escalating doses. In this report, 41 patients had completed the dose escalations. Of these, 25 patients had reached their 8th month and the ORR was 100% with 60% achieving a CR or CRi. After 6 months of therapy, 28% had achieved a MRD-negative remission. Serious adverse events resolved with appropriate management. These abstracts highlight the encouraging approaches to treating CLL in novel ways and offer promise especially to those patients with relapsed and refractory disease.

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