

CLL and Lymphoma Studies at EHA2021 and 16-ICML



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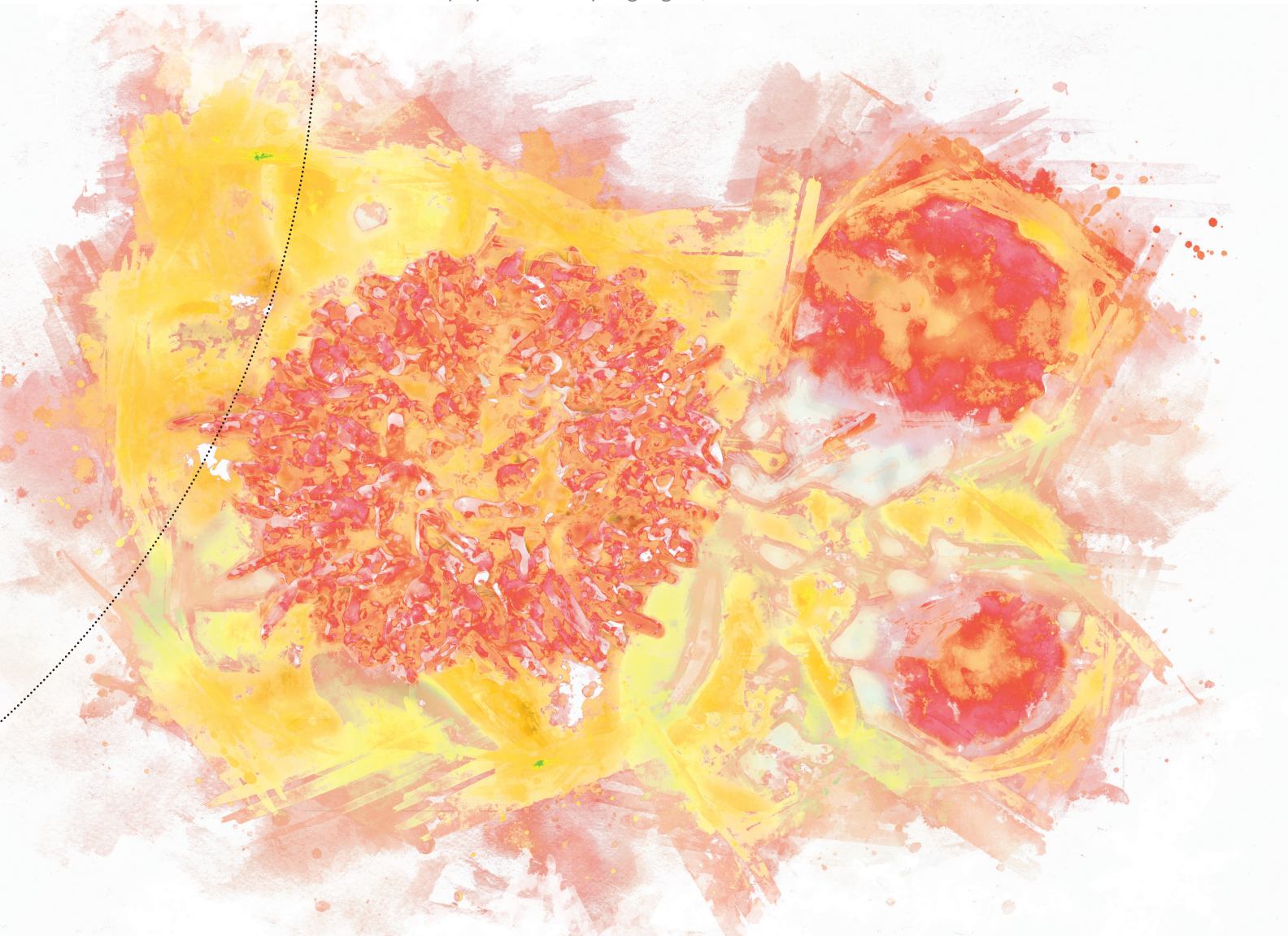
Rossi D. Personal highlights: CLL and lymphoma studies at EHA2021 and 16-ICML. *healthbook TIMES Onco Hema.* 2021;(9):50-51.

At EHA2021 and 16-ICML, there were several relevant presentations in the field of chronic lymphocytic leukemia (CLL) and lymphoma. The first reported on the primary analysis of GLOW, a randomized, phase III trial comparing the time-limited treatment with ibrutinib plus venetoclax, a novel oral combination, versus chlorambucil plus obinutuzumab in treatment-naïve, frail CLL patients.¹ The trial was positive, with a significant improvement in progression-free survival (PFS) with ibrutinib plus venetoclax (median, not reached [NR] vs 21.0 months; HR: 0.216 [95% CI: 0.131–0.357]; $p < 0.0001$), despite a relatively short follow-up. The treatment was deemed to be tolerated in this population of older and unfit CLL patients.

The other two studies compared two second-generation Bruton's tyrosine kinase (BTK) inhibitors, zanubrutinib² and acalabrutinib^{3,4}, respectively, with ibrutinib in patients with relapsed CLL. The main takeaway message from these trials is that

second-generation BTK inhibitors are better tolerated than ibrutinib, especially in terms of lower rates of cardiac events, which may occur in a fraction of patients treated with ibrutinib. Furthermore, the biomarker analyses of the CLL14 trial have started defining high-risk patients who might not benefit from the combination treatment of venetoclax plus obinutuzumab.^{5,6} Although results indicated that this time-limited treatment might not be as advantageous for CLL patients with *TP53* abnormalities compared with those without these aberrations (median PFS, 49.0 months vs NR), data to draw final conclusions are awaited from the longer follow-up from this trial, as well as from head-to-head studies like CLL17⁷.

Furthermore, various interesting trials presented at the congresses assessed immunotherapy in lymphomas. Of these, ZUMA-5⁸ and ELARA^{9,10} investigated chimeric antigen receptor (CAR) T-cell therapies, axicabtagene ciloleucel and tisagenlecleucel, respectively,



in patients with follicular lymphoma (FL). There is currently a great unmet medical need in the treatment of this disease as most of the FL patients cannot reach the life expectancy observed in the general population. Indeed, these patients have impaired survival outcomes because of their underlying recurrently progressing and refractory disease. Although the two trials employed two different CAR T-cell products, they both showed that the therapy is well-tolerated and effective in this patient population.⁸⁻¹⁰ Finally, naratuximab emtansine, an antibody-drug conjugate targeting CD37, in combination with rituximab demonstrated clinical activity in patients with relapsed diffuse large B-cell lymphoma (DLBCL), with an overall response rate of 44.7%, including a complete response rate of 31.6%.¹¹ This is an important signal from the initial results of the trial on this patient population, also with an unmet medical need.

1. Kater A, Owen C, Moreno C, et al. Fixed-duration ibrutinib and venetoclax (I+V) versus chlorambucil plus obinutuzumab (Clb+O) for first-line (1L) chronic lymphocytic leukemia (CLL): Primary analysis of phase 3 GLOW study. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation LB1902.

2. Hillmen P, Eichhorst B, Brown J et al. First interim analysis of ALPINE study: results of a phase 3 randomized study of zanubrutinib vs ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation LBA1900.

3. Hillmen P, Byrd J, Ghia P et al. First results of a head-to-head trial of acalabrutinib versus ibrutinib in previously treated chronic lymphocytic leukemia. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation S145.

4. Hillmen P, Byrd J, Ghia P et al. First Results of a Head-to-Head Trial of Acalabrutinib versus Ibrutinib in Previously Treated Chronic Lymphocytic Leukemia. Presented at the: 16-ICML; 13-17 June 2021. Abstract 033.

5. Al-Sawaf O, Zhang C, Robrecht S et al. Venetoclax-

obinutuzumab for previously untreated chronic lymphocytic leukemia: 4-year follow-up analysis of the randomized CLL14 study. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation S146.

6. Tausch E, Schneider C, Yosifov D et al. Genetic markers and outcome with front line obinutuzumab plus either chlorambucil or venetoclax - updated analysis of the CLL14 trial. Presented at the: 16-ICML; 13-17 June 2021. Abstract 030.

7. A phase 3 multicentre, randomized, prospective, open-label trial of ibrutinib monotherapy versus fixed-duration venetoclax plus obinutuzumab versus fixed-duration ibrutinib plus venetoclax in patients with previously untreated chronic lymphocytic leukaemia (CLL). Available from: <https://www.dcllsg.de/en/trial/ccl17/index.php>.

8. Jacobson CA, Chavez J, Sehgal A et al. Outcomes In ZUMA-5 With Axicabtagene Ciloleucel (Axi-Cel) In Patients With Relapsed/Refractory Indolent Non-Hodgkin Lymphoma Who Had The High-Risk Feature Of Progression Within 24 Months From Initiation Of First Anti-CD20-Containing Chemoimmunotherapy (POD24). Presented at the: EHA2021 Virtual Congress; 9-17 June

2021. Oral presentation S213.

9. Schuster SJ, Dickinson M, Dreyling M et al. Efficacy and safety of tisagenlecleucel in adult patients with relapsed/refractory follicular lymphoma: primary analysis of the phase 2 ELARA trial. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation S210.

10. Fowler NH, Schuster SJ, Dickinson M, et al. Efficacy and Safety of Tisagenlecleucel (Tisa-cel) in Adult Patients (Pts) With Relapsed/Refractory Follicular Lymphoma (r/r FL): Primary Analysis of the Phase 2 ELARA Trial. Presented at the: 16-ICML; 13-17 June 2021. Abstract 085.

11. Levy MY, Grudeva-Popova Z, Treneny M et al. Safety and efficacy of CD37-targeting naratuximab emtansine plus rituximab in diffuse large B-cell lymphoma and other non-Hodgkin's B-cell lymphomas - a phase 2 study. Presented at the: EHA2021 Virtual Congress; 9-17 June 2021. Oral presentation LB1903.