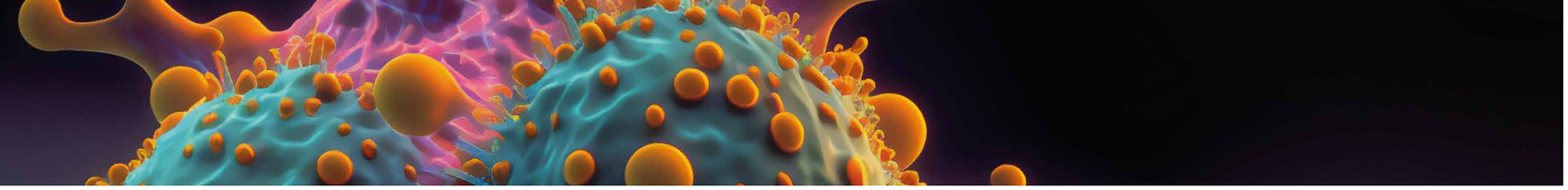

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Updates in Cutaneous T-cell Lymphomas at ASH 2022

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Although the rarity and heterogeneity of cutaneous T-cell lymphomas (CTCL) hamper our efforts to understand the disease pathogenesis and, consequently, to develop effective therapies, substantial progress in this field has been made in recent years.[1,2] Some of these advances, including studies on clinicopathologic determinants of survival and clinical outcomes with current and emerging therapies, were presented at the 64th ASH Annual Meeting and Exposition, which took place in December 2022.

For patients with advanced mycosis fungoides (MF) and Sézary syndrome (SS), two types of CTCL, allogeneic hematopoietic stem cell transplantation (allo-HSCT) is currently the only curative option, while haploidentical (haplo)-HSCT has been increasingly used in this clinical setting.[3-6] At the congress, additional evidence for the efficacy of allo-HSCT was provided, together with encouraging survival data for recipients of haploidentical versus human leukocyte antigen (HLA)-identical sibling transplants.[7]

Important results were also presented for targeted agents indicated for the treatment of patients with CTCL. Favorable clinical outcomes with brentuximab vedotin,[8] a CD30-directed antibody-drug conjugate (ADC), that were reported in the phase III ALCANZA trial[9] were further corroborated in a retrospective chart review study versus other second-line standard therapies.[10] Another approved therapy, mogamulizumab,[11] is an anti-CCR4 monoclonal antibody that demonstrated significant progression-free survival (PFS) benefit compared with vorinostat in adult patients with relapsed or refractory MF or SS in the phase III MAVORIC trial.[12] In this study, one-quarter of patients experienced mogamulizumab-associated rash (MAR), which was more frequent among responders than non-responders. Indeed, several case studies further reported a potential association between the presence of MAR and improved efficacy with mogamulizumab.[13-16] This also includes the retrospective analysis presented at last year's ASH congress, which demonstrated that MAR correlates with increased rates of overall response, as well as complete response, and significantly prolonged PFS and overall survival (OS).[17] These data collectively suggest that rash may be a surrogate marker of favorable clinical outcomes with mogamulizumab.

Various presentations offered novel insights into emerging therapies for CTCL. In the relapsed/refractory setting, the investigational therapy E7777, a fusion protein of interleukin-2 and diphtheria toxin that is produced in an improved manufacturing process, demonstrated clinically meaningful efficacy with manageable toxicity in the single-arm registrational 302 trial.[18,19] Another regimen that might present a potential therapy for SS patients who have failed other treatments is lacutamab, a humanized KIR3DL2 antibody acting via antibody-dependent cell cytotoxicity.[20] Data from a phase II trial showed promising efficacy and safety of lacutamab in heavily pretreated patients, with responses observed in both skin and blood.

The treatment of CTCL with currently available therapies is challenging, with a main focus on preventing disease progression.[21] The treatment landscape of CTCL has expanded over the last years and the emerging therapies are promising for patients with advanced disease. Overall, the ASH 2022 congress showed us that immunotherapy is gaining momentum also in advanced CTCL and provides hope for more effective therapeutic options for patients with a dismal prognosis.

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