HEM/ONC News

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Duvelisib Approved in Relapsed/Refractory CLL, SLL, and FL

The US Food and Drug Administration (FDA) approved duvelisib (Copiktra, Verastem) on September 24 for adults with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least 2 prior therapies. Duvelisib, an intravenous inhibitor of phosphoinositide 3-kinase delta and gamma, also received accelerated approval for adults with relapsed or refractory follicular lymphoma (FL) after at least 2 prior systemic therapies.

The CLL/SLL indication was based on an open-label trial (NCT02004522) that randomly assigned patients with relapsed or refractory CLL or SLL to receive duvelisib or ofatumumab (Arzerra, Novartis). The estimated median progression-free survival among the 196 patients who had received at least 2 prior therapies was 16.4 months with duvelisib and 9.1 months with ofatumumab.

The FL indication was based on a single-arm trial (NCT02204982) in which 83 patients with FL that was refractory to rituximab and to either chemotherapy or radioimmunotherapy received duvelisib. The overall response rate was 42%.

The prescribing information contains boxed warnings for fatal and/or serious infections, diarrhea or colitis, cutaneous reactions, and pneumonitis, and warnings for neutropenia and hepatotoxicity. Of 442 patients with hematologic malignancies treated with duvelisib at the approved dose, 65% had serious adverse reactions, including infection, diarrhea or colitis, and pneumonia.

FDA Approves Dacomitinib in Metastatic Non–Small Cell Lung Cancer

The FDA approved dacomitinib (Vizimpro, Pfizer) on September 27 for the first-line treatment of patients with metastatic non–small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations. Dacomitinib is an oral pan-EGFR tyrosine kinase inhibitor.

Approval was based on ARCHER 1050, an open-label trial in which 452 patients with unresectable, metastatic NSCLC were randomly assigned to either dacomitinib or gefitinib.

The median progression-free survival was significantly higher with dacomitinib than with gefitinib (14.7 vs 9.2 months, respectively; hazard ratio [HR], 0.59; 95% CI, 0.47-0.74; $P<.0001$). No improvement in overall response rate or overall survival was demonstrated.

The prescribing information for dacomitinib contains warnings and precautions for interstitial lung disease, diarrhea, and dermatologic adverse reactions. Of 394 patients who received dacomitinib, serious adverse reactions occurred in 27%. The most common adverse reactions resulting in discontinuation of dacomitinib were diarrhea and interstitial lung disease. The most common adverse reactions with dacomitinib were diarrhea, rash, paronychia, stomatitis, decreased appetite, dry skin, decreased weight, alopecia, cough, and pruritus.

Cemiplimab-rwlc Approved in Advanced Cutaneous Squamous Cell Carcinoma

The FDA approved cemiplimab-rwlc (Libtayo, Regeneron) on September 28 for patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation. Cemiplimab-rwlc is an intravenous anti–programmed death 1 agent.

Approval was based on the results of 2 open-label clinical trials: R2810-ONC-1423, a dose-finding trial with expansion cohorts in patients with various solid tumors; and R2810-ONC-1540, a multicohort trial in patients with metastatic or locally advanced CSCC regardless of prior treatment, for whom surgery or radiation was not recommended.

The overall response rate to cemiplimab-rwlc was 47% (95% CI, 38%-57%) among 108 patients with advanced CSCC. The median response duration was not reached, and 61% of responses lasted for at least 6 months. Response rates and durability results were consistent across the advanced CSCC subtypes.

Safety data were evaluated in 534 patients who received cemiplimab-rwlc in both trials. Serious adverse reactions consisted of immune-mediated adverse reactions and infusion reactions. The most common adverse reactions were fatigue, rash, and diarrhea.

Additional Approvals

- On October 4, the FDA approved emicizumab-kxwh injection (Hemlibra, Genentech) to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A with or without factor VIII inhibitors. The agent was first approved in 2017 for hemophilia A patients with factor VIII inhibitors.
- On October 16, the FDA approved the oral poly(ADP-ribose) polymerase inhibitor talazoparib (Talzenna, Pfizer) for patients with advanced *BRCA*-positive breast cancer.