Devimistat Development Progresses in Relapsed/Refractory Burkitt Lymphoma

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Hoping to expand the armamentarium in relapsed/refractory Burkitt lymphoma and high-grade B-cell lymphoma, investigators are evaluating the activity of the investigational anti-mitochondrial agent devimistat (CPI-613) in an ongoing phase 2 clinical trial (NCT03793140).

"Patients who have relapsed Burkitt lymphoma or relapsed double-hit lymphoma (DHL) or triple-hit lymphoma (THL) have no viable treatment options," said lead study author Ariela Noy, MD. "In fact, the National Comprehensive Cancer Network guidelines specify to give agents that patients have not had before. We know that we have a true unmet need."

Investigators plan to enroll 34 previously treated patients into 2 cohorts—those with Burkitt lymphoma and those with high-grade B-cell lymphoma who harbor MYC and BCL-2 (DHL) and/or BCL-6 (THL) rearrangements. All patients must have measurable disease or isolated bone marrow involvement and undergone stem cell transplant ≥3 months prior to enrollment.

Patients with active central nervous system parenchymal disease are ineligible for the trial. However, patients with leptomeningeal disease are eligible if their cerebral spinal fluid (CSF) is negative for lymphoma for >4 weeks and they are currently receiving intrathecal therapy.

The primary end point of the trial is overall response rate. Key secondary endpoints include duration of response, progression-free survival, and overall survival. Moreover, investigators will evaluate whether the regimen can serve as a bridge to autologous stem cell transplant (ASCT) or allogeneic stem cell transplant (SCT).

After the first 10 patients complete 2 cycles of treatment or discontinue treatment, an interim safety analysis will be conducted.

In June 2018, the FDA granted an orphan drug designation to devimistat for the treatment of patients with Burkitt lymphoma. The FDA has also granted devimistat orphan drug status for the treatment of patients with pancreatic cancer, acute myeloid leukemia, myelodysplastic syndrome, and peripheral T-cell lymphoma.

In an interview with *OncLive*, Noy, a medical oncologist at Memorial Sloan Kettering Cancer Center, discussed the rationale and design of the phase 2 study of devimistat in patients with aggressive lymphoma.

***OncLive*: Could you provide a rationale for this study?**
Noy: In a prior study with devimistat in hematologic malignancies, 1 patient with primary refractory Burkitt lymphoma—secondary after multiple prior regimens—had a partial response lasting 1 year. After the patient had her disease resected, [she] remained disease free for 3 years after that. As such, we had clear rationale to do this study in Burkitt lymphoma.

Could you highlight the trial design?
The study is a very simple, phase II clinical trial. There are 2 cohorts of patients, and we are assessing each of them individually. One cohort is made up of patients with Burkitt lymphoma who have primary relapsed/refractory disease. The other cohort is similar but consists of patients with DHL and THL. Thus far, we have enrolled a few patients.

Pending positive results, what would be the next steps for this research?
In the first 10 patients, we are hoping to show at least 1 response in each cohort. I know that sounds like a very low bar, but [this is a disease in which] we would [otherwise] expect almost no response. [If we see 1 response], that would be a 10% increase [from what we've seen historically].

The next phase of the trial would be to accrue a total of 17 patients to each arm and demonstrate some efficacy. If this works, it is probably enough for an FDA registration in this setting where there are [no alternative treatment regimens] for patients.

In addition, we hope that this could be a bridge for either ASCT or allogeneic SCT, which would give patients a curative option.

Finally, if the drug works, we could consider bringing it into the frontline setting. We know how to define patients who have high-risk features in Burkitt lymphoma, specifically those who have peripheral blood bone marrow or leptomeningeal disease.

Is there anything else regarding this trial you would like to highlight?
We are [enrolling] patients who are very sick. They can have a performance status as low as 40%, which allows [many patients who would otherwise be ineligible to enroll]. We're also enrolling patients who have HIV infection, as well as those who have leptomeningeal disease. For the latter category, we require that the leptomeningeal disease be cleared. [Patients with] CSF [can] continue maintenance therapy. We can't [enroll] patients with active disease at the time of enrollment.

Noy A, Pardee TS, Nikolaenko L, et al. A phase II clinical trial of CPI-613 (devimistat) in patients with relapsed or refractory Burkitt

lymphoma/leukemia or high-grade B-cell lymphoma with rearrangements of MYC and BCL2 and/or BCL6. Blood. 2019;134(suppl 1; abstr 4087). doi:10.1182/blood-2019-131563