Lomustine

Lomustine (CCNU), marketed under the name CeeNU in U.S.) is an alkylating nitrosourea compound used in chemotherapy. It is in the same family as streptozotocin. This is a highly lipid-soluble drug, and thus crosses the blood-brain barrier. This property makes it ideal for treating brain tumors, and is its primary use. Lomustine has a long time to nadir (the time when white blood cells reach their lowest number).

Lomustine is regarded as 1 common anti-vascular endothelial growth factor agent.

The efficacy of adjuvant lomustine to chemotherapy remains controversial for recurrent glioblastoma. Fu et al. conducted a meta-analysis to explore the influence of adjuvant lomustine on the treatment efficacy of recurrent glioblastoma.

They searched PubMed, EMBASE, Web of Science, EBSCO, and Cochrane library databases through August 2019 and included randomized controlled trials assessing the efficacy and safety of adjuvant lomustine for recurrent glioblastoma.

Four randomized controlled trials are included in the meta-analysis. Overall, compared with the control group for recurrent glioblastoma, adjuvant lomustine has no substantial effect on objective response (risk ratio [RR], 1.32; 95% confidence interval [CI], 0.91 to 1.93; P = 0.15), complete response (RR, 1.76; 95% CI, 0.26-11.90; P = 0.56), progressive response (RR, 1.32; 95% CI, 0.88-1.99; P = 0.18), median progression-free survival (standard mean difference [SMD], 0.73; 95% CI, -0.65 to 2.11; P = 0.30), or median overall survival (SMD, 0.26; 95% CI, -0.30-0.83; P = 0.36), but results in the increase in 6-month progression-free survival (SMD, 1.71; 95% CI, 0.38-3.04; P = 0.01). There is no increase in grade ≥3 adverse events after adjuvant lomustine treatment (RR, 1.55; 95% CI, 0.84-2.89; P = 0.16) compared with the control intervention.

Adjuvant lomustine to other chemotherapy may provide no obvious benefits for the glioblastoma recurrence treatment [1].

In clinical trials, lomustine alone has been increasingly used as a control arm, assigning this drug a standard-of-care position in the setting of Glioblastoma recurrence. Weller et al. reviewed the activity of lomustine in the treatment of diffuse gliomas of adulthood in various settings. The most compelling data for lomustine stem from three randomized trials when lomustine was combined with procarbazine and vincristine as the PCV regimen in the newly diagnosed setting together with radiotherapy; improved survival with PCV was restricted to patients with IDH-mutant tumors. No other agent with the possible exception of regorafenib has shown superior activity to lomustine in Glioblastoma recurrence, but activity is largely restricted to patients with tumors with O6-methylguanine DNA methyltransferase (MGMT) promoter methylation. Hematological toxicity, notably thrombocytopenia often limits adequate exposure. [2].

Despite somewhat prolonged progression-free survival, treatment with lomustine plus bevacizumab did not confer a survival advantage over treatment with lomustine alone in patients with progressive glioblastoma [3)]

Kaloshi et al. measured the evolution of the mean tumor diameter (MTD) in adult patients with low-grade glioma LGG before (n = 28 patients) and after (n = 38 patients) CCNU administration.

Natural (spontaneous) growth of LGG in the present study was 4.3 mm/year (range 2.1-6.6 mm/year). The median MTD decrease after CCNU was 5.1 mm/year (range 1-8.9 mm/year). MTD decrease was noted in 30 patients (late decrease in 4 patients, and ongoing decrease in 24 patients with oligodendroglial tumors and 2 with astrocytic tumors). The median duration it took for the MTD to decrease after initiation of CCNU treatment was 619 days (1038 days for oligodendroglial tumors vs 377 days for astrocytic tumors; p = 0.003).

These results show that CCNU as a single agent has a significant impact on LGG tumor growth. The impact of CCNU seems to be comparable to the previously reported impact of temozolomide therapy and of combined procarbazine, CCNU, and vincristine chemotherapy [4)].

Case series

Kim et al reviewed eight immunocompetent patients (five males/three females, mean age: 56 years) who received salvage PCV chemotherapy (procarbazine 60 mg/m(2), days 8 through 21: CCNU 110 mg/m(2), day 1: vincristine 2 mg, days 8 and 28) for recurrent PCNSL and two patients switched to PCV chemotherapy due to severe adverse effects of HD-MTX chemotherapy. Radiologic responses, survival, and adverse effects were analyzed.

Of the eight recurrent PCNSLs, three patients (37.5%) showed radiologic complete response, one patient (12.5%) showed partial response, and four patients (50%) showed progressive disease after PCV chemotherapy. Median progression free survival (PFS) from the first administration of PCV to relapse or last follow-up was 7 months (range 5-32 months) and median overall survival was 8 months (range 2-41 months). The two patients who switched to PCV chemotherapy showed PFS of 9 and 5 months from the beginning of PCV to relapse. The common side effects were thrombocytopenia, neutropenia, and peripheral neuropathy. There were 4 grade III or IV myelo-suppression, but no fatal complications, including severe hemorrhage or infection, were observed. CONCLUSION: Salvage PCV chemotherapy has a moderate anti-lymphoma activity for recurrent PCNSLs after the HD-MTX-based chemotherapy with tolerable toxicity [5)]

1)
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