**Impact of Hypoalbuminemia on Toxicity Associated with Etoposide Administration**

**Authors:** Matthew Peery, PharmD; Mandy Gatesman, PharmD, BCOP

**Practice Site:** Virginia Commonwealth University Health System, Richmond, VA

**Background:** Etoposide is a conventional chemotherapy agent that is utilized in multiple different chemotherapy regimens to manage various cancer types. Pharmacokinetic data has revealed that it is highly protein bound medication (94% - 97%), and that low albumin may increase the fraction of free etoposide, subsequently increases the risk of toxicity (i.e., neutropenia). Patients with cancer are commonly cachectic due to numerous factors including chemotherapy induce nausea and vomiting, location of malignancy, lending this patient population to commonly have low serum albumin. Thus, generating the hypothesis that patients with low albumin may require dose reductions to improve tolerability of etoposide.

**Objectives:** The primary objective of this study was to assess the impact of low serum albumin (< 3.5 g/dL) on the incidence of chemotherapy regimen disruption, due to toxicity associated with intravenous (IV) etoposide administration. The primary outcome was the composite of dose reduction after cycle one, delay in cycle schedule and discontinuation of therapy due to toxicity. Secondary outcomes include the addition of granulocyte-colony stimulating factor (GCSF) as secondary prophylaxis, the individual components of the primary endpoint, and inpatient admission due to toxicity (i.e., neutropenic fever, mucositis). The primary composite outcome and the secondary outcome of addition of GSCF were assessed per patient. The remaining outcomes were assessed at each cycle.

**Methods:** This was a retrospective, single-center, cohort study. Patients were allocated to one of the two serum albumin groups based on their baseline serum albumin, with the low serum albumin group being defined as < 3.5 g/dL and high serum albumin group being defined as ≥ 3.5 g/dL. Patients were collected and analyzed if they had received IV etoposide between January 1st, 2018 and December 31st, 2020. Patients who were included were those 18 years of age or older and those who received a chemotherapy regimen containing carboplatin and IV etoposide. This regimen was chosen to maximize the patient’s eligible for inclusion in this trial. Patients were excluded from analysis if they were prisoners or did not meet the inclusion criteria. Via chart review, patient’s baseline characteristics were collected, which included baseline organ function, concurrent treatments (i.e. immunotherapy and radiation), type and stage of malignancy and empiric dose reduction. Patients were then screened during their time receiving the chemotherapy regimen to determine which outcomes were met, if applicable, as well as their organ function and serum albumin at each cycle.

**Results:** There were a total of 68 patients included in this study, with 19 in the low serum albumin group and 49 in the high serum albumin group at baseline. For the primary composite outcome, 78.95% vs. 75.51% was not statistically significant different. For the secondary outcome of addition of GCSF as secondary prophylaxis, 15.78% vs. 14.29%. The remaining secondary outcomes were assessed at each cycle. With the individual components of the composite primary outcome, dose reduction after cycle one, cycle two 10.53% vs. 4.08%, cycle three 0.0% vs. 0.0%, cycle four 9.09% vs. 10.00%; delay in cycle schedule cycle two 21.05% vs. 24.49, cycle three 7.69% vs. 13.64%, cycle four 27.27% vs. 7.50%; treatment discontinuation due to toxicity after cycle one 31.58% vs. 8.16% (P= 0.0233), cycle two 15.38% vs. 9.09%, cycle three 18.18% vs. 12.50%. The final secondary outcome of inpatient admission due to toxicity cycle two 26.32% vs. 8.16%, cycle three 7.69% vs. 9.09%, cycle four 0.00% vs. 15.00%. If the patients were allocated to low vs. high serum albumin groups based on their serum albumin prior to each cycle, then inpatient admission due to toxicity revealed statistical significance, cycle two 26.32% vs. 8.16%, cycle three 37.50% vs. 4.08% (P= 0.0045), cycle four 37.50% vs. 6.98% (P= 0.0394).

**Conclusion:** Based on the results presented, there was no statistically significant difference in meeting the primary composite outcome, based on baseline serum albumin. However, low serum albumin may increase the incidence of early treatment discontinuation and inpatient admission due to toxicity. Suggesting that patients with low serum albumin may be at increased risk of experiencing toxicity with administration of IV etoposide and may warrant a dose reduction to improve tolerability.