

# Use of Alkylating Chemotherapy in High Grade Neuroendocrine Tumours: Evaluation of Real World Data

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**Background:** High grade neuroendocrine tumours (NETs) are believed to have activity to certain alkylating agents. These regimens include streptozocin (STZ) (used in combination with doxorubicin or 5-fluorouracil) and dacarbazine (DTIC). Current series report variable responses between 6 – 69%. Our objective was to evaluate our real world data to better understand treatment decision-making and clinical outcomes with alkylating agents in advanced high grade NETs.

**Methods:** We reviewed the medical records of 36 patients with metastatic NETs who received alkylating systemic chemotherapy with either a DTIC regimen (n=15) or STZ based regimen (n=21). Patient cases were evaluated for age, time on treatment, time to progression (TTP), overall survival (OS), and reason for discontinuation by two sample t-test.

**Results:** Observed time on treatment was slightly prolonged with DTIC (77.5 days vs STZ: 64.0 days). STZ had a prolonged TTP of 7.0 months with STZ vs. 5.5 months with DTIC (p=0.778). There was no significant difference in OS with a mean of 9.1 months (DTIC) vs. 12.4 months (STZ) (p=0.355). The predominant cause of treatment discontinuation in both groups was progressive disease; DTIC (71%) versus STZ (42%). Toxicity resulted in treatment discontinuation in 19% for STZ vs 7% for DTIC.

Regression analysis based on the Ki67 index revealed a significantly prolonged TTP of 11 months with a Ki67<20 as compared to 2.6 months with a Ki67>20 (p=0.014).

**Conclusion:** STZ containing regimens demonstrated a trend toward prolonged PFS in comparison to DTIC, but there was no difference in OS between the two groups. Despite STZ appearing to have an increased toxicity rate, the rate of cessation between the groups was similar. There was a significant improvement in PFS in tumours with a Ki67<20 regardless of therapy. This real world evaluation suggests similar efficacy with improved tolerability of DTIC based chemotherapy as a potential alternative to other alkylating agents.