Anaplastic Thyroid Carcinomas (ATC) are aggressive, undifferentiated tumors for which there are currently no curative treatment options available. Although ATC accounts for a mere 1% to 2% of all thyroid cancers in the United States, it is disproportionately responsible for a large fraction of thyroid cancer-related deaths. Patients diagnosed with ATC have grim prognoses, with a median survival rate of 5 months. Although ATC is not limited to the traditional radio and chemotherapeutics, targeted approaches are required. Here, we propose a novel course of treatment that may provide a clinical benefit for patients presenting with ATC.

**Methods:**
SCD1 expression patterns were examined in patient samples of normal thyroid, follicular adenoma (FA), papillary thyroid carcinoma (PTC), high grade follicular thyroid carcinoma (FTC), and ATC via quantitative real-time PCR as well as by immunohistochemistry. Activity of the SCD1 inhibitor A939572 was tested in representative patient derived cell lines.

**Results:**
SCD1 demonstrates high levels of expression in papillary thyroid carcinoma (PTC), high grade follicular thyroid carcinoma (FTC), and ATC. Application of an SCD1 inhibitor (A939572) surprisingly yielded strong anti-tumor proliferation and induction of apoptosis specifically in ATC cell lines, but had little to no activity among the other subtypes of thyroid carcinoma. In addition, A939572 induced the endoplasmic reticulum (ER) stress pathway, leading to endoplasmic reticulum-associated degradation (ERAD) activation - a proteasome-mediated survival response to ER stress. Sequential application of a proteasome inhibitor with A939572 led to synergistic anti-tumor activity in ATC cell lines.

**Conclusions:**
We propose that administration of an SCD1 Inhibitor concomitantly with a proteasome inhibitor is a novel course of treatment that may provide a clinical benefit for patients presenting with ATC.

**REFERENCES**