

## Summary

This thesis is focused on the correlation of immunohistochemical, molecular genetic, and clinical features of salivary duct carcinomas. Clinicopathological and follow-up information of 29 patients originally diagnosed as SDC who were treated at Faculty Hospital in Plzeň from 1987 to 2018, were collected.

**Clinical findings:** The patient group comprised 22 males and 4 females, aged between 24-95 years with a mean age at diagnosis of 66 years and median of 64 years. At stage IV, 54% of patients were diagnosed at cervical metastasis and 58% had tumor T3 or T4. The five-year survival rate was 33%.

**Immunohistochemical and molecular findings:** After analysis of immunohistochemical results, the SDC cases were classified according to the revised classification into five subtypes: Apocrine A (AR+/HER2-/MIB1-low); Apocrine B (AR+/HER2-/MIB1-high); Apocrine HER2 (AR+/HER2+); HER2-enriched (AR-/HER2+); and double negative (AR-/HER2-). Apocrine HER2 and HER2-enriched subtypes were significantly associated with lower OS ( $p < 0.05$ ). NGS analysis revealed one case harboring an *ETV6-NTRK3* fusion, therefore it was reclassified as a high-grade secretory carcinoma. Five likely pathogenic mutations were detected in 5 SDC cases (*HRAS*: c.182A>G p.Gln61Arg, 2x *HRAS*: c.37G>C p.Gly13Arg, *AKT1*: c.49G>A p.Glu17Lys, *PTEN* c.1003C>T p.Arg335Ter). Homozygous deletion of locus 9p21 (*CDKN2A*) was detected in one case harboring a *HRAS* mutation. *MDM2* was amplified in one case harboring a *PTEN* mutation.

**Conclusion:** Herein we demonstrated that AR and GATA3 are potential biomarkers of poor outcome in SDC. Also, SDC apocrine HER2 and HER2-enriched subtypes were related to decreased survival, which indicates that the revised classification system might be a useful predictor of prognosis for some subtypes of SDC. Furthermore, NGS analysis in a small subset of SDC cases revealed mutations in *HRAS*, *AKT1*, and *PTEN* genes in five cases. The significance of radical surgical therapy associated with radiotherapy has been confirmed.