



## **GD2 and GD3 tumor gangliosides as diagnostic markers for all subtypes and stages of ovarian cancer (OC) in liquid biopsies**

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**Objective:** OC is the deadliest gynecological cancer. Detection of OC at early-stages has a 5-year survival rate of >90% and <30% at advanced disease. A major contributor to this poor survival is the lack of early diagnostic tools. Up to 95% of women with OC even in early stages have symptoms for many months and 84% consult a doctor, but the average diagnosis takes 9 months. To alleviate this unmet diagnostic need, we evaluated tumor gangliosides GD2 and GD3, not previously investigated for diagnostic liquid biopsies purposes in OC.

**Methods:** A quantitative ELISA with proprietary antibodies measuring GD2 and GD3 in serum was developed (n=379). To evaluate whether GD2 or GD3, either alone or in combination, could be used as biomarkers of OC, linear models were fit to an independent powered retrospective cohort (n=200). Cross-validation was used to protect against over-fitting.

**Results:** ELISA achieved significant detection GD2 and GD3 in all subtypes (high grade serous, clear cell, endometrioid, and mucinous) and all stages of OC including the hard-to-diagnose early-stage I/II, and the low-CA125 OC cohort. Diagnostic model showed that a novel panel using proprietary algorithm, AKRIVIS GD (AUC 0.983 overall and 0.969 early-stage) is significantly superior to the standard of care CA125 (AUC 0.855 overall and 0.700 early-stage). AKRIVIS GD demonstrated superior sensitivity (97.6% overall and 100% early stage) with specificity of 91.2%. In comparison, CA125, at the clinically validated cut-off of 35 U/mL, sensitivity was 63.4% overall and 53.8% early-stage with specificity of 91.8%.

**Conclusion:** GD2, GD3 and age are high value candidates for building a diagnostic panel, AKRIVIS GD. This diagnostic panel used in symptomatic patients early-on for accurate determination of malignancy will expedite their workup and treatment with an oncologist. Validation of such a panel could alleviate costs and increase survival rates. Future work will aim to validate these biomarkers in independent prospective studies.