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L1CAM GENE OVEREXPRESSION IS ASSOCIATED WITH PLATINUM RESISTANCE IN HIGH-RISK ENDOMETRIAL CARCINOMA

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Introduction: L1 cell adhesion molecule (L1CAM) expression has been reported to be associated with high-grade disease and non-endometrioid histology, as well as poor prognosis, in endometrial carcinoma (EC). These high-risk EC types have already spreaded outside the uterus when diagnosed and, after an extensive surgery, are often treated with chemo and radiation therapy. We hypothesized that L1CAM gene expression could discriminate, among poor outcome EC patients, those who do and who do not respond to adjuvant platinum-based chemotherapy.

Experimental Model: Using an efficient multiplex qRT-PCR, we studied L1CAM mRNA expression on 117 EC and 16 normal endometrial (NE) flash-frozen tissues, with HPRT1 and PPIA as reference genes.

Results: L1CAM mRNA was significantly overexpressed in EC compared to NE tissues (p=0.02), significantly upregulated in G3 *vs*. G1-2 ECs (p<0.001) and in non-endometrioid vs. endometrioid ECs (p< 0.001). Our analysis showed no difference in L1CAM expression of stage I-II vs. stage III-IV ECs (p=0.5). Of the initial 117 EC patients, 47 received chemotherapy on adjuvant setting and were classified as platinum-sensitive and platinum-resistant patients, based on PFI>12 months and <6 months, respectively. L1CAM gene was significantly overexpressed in resistant vs. sensitive EC (p=0.001). Moreover, by means of a multivariate logistic regression model, we found L1CAM gene overexpression as an independent indicator of the probability to harbor a platinum-resistant EC (p=0.047, OR=3.5). In addition, univariate and multivariate survival analysis showed L1CAM gene upregulation is associated with poor outcome, in terms of progression-free survival and disease-specific survival.

Conclusions: Our results suggest L1CAM gene expression as a potential prognostic marker and a predictive biomarker of platinum response in high-risk EC patients.

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