Abstract: There is a ~~tremendous~~ considerable need for the development of~~ing~~ new ~~useful~~ prognostic factors in ovarian cancer. Galectins are ~~a family of~~ carbohydrate~~-~~ binding proteins ~~which~~ that have been suggested to serve as prognostic factors for various cancer types. In this study, the ~~presence~~ expression of g~~G~~alectin (Gal)-1, -3, and -7 was investigated in 156 ovarian cancer specimens ~~by~~ using immunohistochemical staining~~. Staining was evaluated in the cytoplasm and nucleus of cancer cells as well as the peritumoral stroma using a semi quantitative score (Remmele (IR) score)~~. ~~Patients' o~~Overall patient survival was compared ~~between~~ among ~~different~~ groups ~~of~~ stratified by~~G~~ galectin expression. ~~Galectin (~~Gal~~)~~-1 and -3 staining was observed in the peritumoural stroma as well as the nucleus and cytoplasm of tumour cells, while Gal-7 was only present in the cytoplasm~~ of tumor cells~~. Patients with Gal-1 expression in the cytoplasm or high Gal-1 expression in the peritumoural stroma showed reduced overall survival. Nuclear Gal-3 staining correlated with ~~a~~ better clinical outcomes. ~~We observed a significantly reduced overall survival for c~~Cases with high Gal-7 expression exhibited significantly reduced overall survival, while ~~and a better survival for~~ Gal-7~~-~~ negative cases exhibited improved survival~~, when compared to cases with low expression of Gal-7~~. ~~We were able to show that b~~Our results indicate that ~~oth~~ tumour and stromal staining of Gal-1 and cytoplasmic staining of Gal-7 ~~could~~ serve as negative prognostic factor~~s~~ for ovarian cancer, while nuclear ~~. We were able to confirm cytoplasmic Gal-7 as a negative prognostic factor.~~ Gal-3 staining ~~in the nucleus could~~ may represent~~be~~ a new positive prognosticator for ovarian cancer. These findings suggest that galectins may represent promising new targets for ovarian cancer treatment.

~~**Keywords:**~~
~~Galectin-1; Galectin-3; Galectin-7; ovarian cancer; overall survival~~

Commented [A1]: I have edited this section to ensure that it complies with the journal's limit of 200 words. Specifically, less relevant information has been removed and the presentation of the results has been worded more concisely. A good abstract also concludes with 1-2 sentences describing the broader implications of the results. I have therefore added a sentence serving this purpose.

Text justification has been turned off, as requested by the journal.

Commented [A2]: As the term "immunoreactive" is not used elsewhere in the abstract, the abbreviation "IR" is not needed and has been removed.

Commented [A3]: While protein symbols are capitalized, protein names are only capitalized if they appear at the beginning of a sentence.

Commented [A4]: I have provided a concluding statement for your Abstract here.

Commented [A5]: Please note that keywords are not requested in the manuscript file by the journal.

~~1.~~ Introduction

Ovarian cancer is the most lethal gynecological malignancy, ranking fifth in estimated cancer deaths among women in the USA[1] ~~[1]~~. First-line treatment consists of primary debulking surgery followed by platinum and paclitaxel chemotherapy[2] ~~[2]~~. ~~Still~~Despite these treatments, the 5-year relative survival rate for epithelial ovarian cancer patients ~~is~~ remains below~~less than~~ 50%[3] ~~[3]~~. A lack of screening methods and ~~the~~ frequent presentation with advanced stage disease are considered ~~as~~ the main reasons for the poor outcomes of ovarian cancer patients.

Prognosticators in ovarian cancer include ~~D~~disease stage at diagnosis, extent of residual disease after surgery, histological subtype, and ~~a high~~the volume of ascites[4] ~~can be used as prognosticators in ovarian cancer [4]~~. Numerous studies have aimed to ~~introduce~~ identify new biological prognostic factors in ovarian cancer. Recently, the carbohydrate stem cell marker TF1 has been proposed as a negative prognostic marker in ovarian cancer displaying wild-type p53, while estrogen receptor promoter methylation ~~could~~ predicts overall survival in low-grade ovarian carcinoma patients[5,6] ~~[5,6]~~. Although ~~for these and various other molecules~~ the prognostic value independent~~ly~~ of clinical parameters has been ~~proven~~demonstrated for these and various other molecules, ~~until today~~to date, with the exception ~~of for~~ breast cancer gene (*BRCA*) status, no biological marker is commonly accepted[4] ~~[4]~~. Further specification of anti-cancer therapies~~y~~ necessitate~~sarily requires~~ an improvement ~~of~~ in the biological prognostic markers ~~in~~ for ovarian cancer.

Galectins ~~have been defined as~~belong to a family of proteins sharing two main characteristics: ~~a~~ binding affinity for β-galactosides and ~~a~~ significant similarity in the carbohydrate-recognition domain (CRD)[7] ~~[7]~~. The first member of this family to be described was g~~G~~alectin (Gal)-1, which ~~is~~ can be isolated as a homodimer~~s~~ ~~composed of~~comprising two identical CRD subunits[8] ~~[8]~~. Since then, a growing number of ~~the~~ g~~G~~alectin family members ha~~ve~~s ~~had a growing number of members~~been identified, but ~~only Galectin (~~Gal~~)~~-1–4, Gal-7–10, Gal-12, and Gal-13 are known to be present in humans[9] ~~[9]~~. Similar to Gal-1, Gal-7 typically occurs ~~in~~ as a homodimer~~s~~, while Gal-3 is the only g~~G~~alectin characterized as a chimeric protein that is known to form higher order oligomers[10,11] ~~[10,11]~~. In several types of cancer ~~types~~, g~~G~~alectins are known to affect tumour growth, metastasis, angiogenesis, cell migration, ~~as well as tumor~~ invasiveness, and progression, and they are therefore ~~very likely~~good candidates for proteins with ~~to show a~~ prognostic value for patient~~s'~~ survival[9,12] ~~[9,12]~~.

The role of ~~Galectin~~Gal-1 in cancer has been studied by various groups~~, and several papers already exist on this topic~~. ~~For~~ In patient~~s'~~ sera and ovarian cancer tissues, it has been shown that a combination of CA-125 and Gal~~ectin~~-1 serves as a possible two-marker combination for the preoperative discrimination of benign and malignant ovarian masses ~~[13]~~[13]. ~~Also~~In addition, patients suffering from metastatic epithelial ovarian cancer were observed to ~~show~~ exhibit higher serum Gal-1 levels than those with non-metastatic ~~type~~cancer. Elevated Gal-1 staining of the peritumoural stroma ~~staining of Gal-1~~ was shown

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Commented [A7]: Section numbers are not used in this journal and have been removed.

Commented [A8]: In-text citations have been formatted per the journal's guidelines.

Commented [A9]: This is implied by the beginning of the sentence and has been removed to reduce redundancy.