**The REMARK checklist MS 9598**

| **Item to be reported** | Reported on Page Number & Line Number | Reported on Section and Paragraph |
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## Introduction

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| 1 State the marker examined, the study objectives, and any pre-specified hypotheses. | marker: page 4, line 12 to page 5 line 15<br>study objectives: page 5 lines 16-18<br>pre-specific hypothesis: page 5 lines 6-15 | marker, study objectives and pre-specific hypothesis: see "Introduction", main text |

## Materials and Methods

### Patients

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| 2 Describe the characteristics (e.g., disease stage or co-morbidities) of the study patients, including their source and inclusion and exclusion criteria. | page 8 lines 1-10<br>table 1 | see "Study population" in the "Results" section, main text |

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| 3 Describe treatments received and how chosen (e.g., randomized or rule-based). | page 5 lines 23-24 | see „Methods" section, main text |

### Specimen characteristics

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| 4 Describe type of biological material used (including control samples) and methods of preservation and storage. | page 5 line 24 to page 6 line 3 | see "Methods" section, main text |

### Assay methods

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| 5 Specify the assay method used and provide (or reference) a detailed protocol, including specific reagents or kits used, quality control procedures, reproducibility assessments, quantitation methods, and scoring and reporting protocols. Specify whether and how assays were performed blinded to the study endpoint. | page 6 line 11 to page 7 line 5 | see “Syndecan serum expression, ELISA” and “Histopathological work-up and immunohistochemistry (IHC) “ in the “Methods” section, main text |

## Study design

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| 6 State the method of case selection, including whether prospective or retrospective and whether stratification or matching (e.g., by stage of disease or age) was used. Specify the time period from which cases were taken, the end of the follow-up period, and the median follow-up time. | page 5 lines 23-24<br>page 6 lines 7-9<br>page 8 lines 3-7 | see “Methods” section and “Study population” in the “Results” section, main text |

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| 7 Precisely define all clinical endpoints examined. | page 6 lines 5-7 | see “Methods” section, main text |

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| 8 List all candidate variables initially examined or considered for inclusion in models. | table 1 | see table 1 |

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| 9 Give rationale for sample size; if the study was designed to detect a specified effect size, give the target power and effect size.<br>Statistical analysis methods. | page 7 lines 8-20 | see “Statistical analysis” in the “Methods” section, main text |

## Statistical analysis methods

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| 10 Specify all statistical methods, including details of any variable selection procedures and other model-building issues, how model assumptions were verified, and how missing data were handled. | page 7 lines 8-20 | see “Statistical analysis” in the “Methods” section, main text |

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| 11 Clarify how marker values were handled in the analyses; if relevant, describe methods used for cutpoint determination. | page 7 lines 16-20 | see “Statistical analysis” in the “Methods” section, main text |

## Results

### Data

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| 12 Describe the flow of patients through the study, including the number of patients included in each stage of the analysis (a diagram may be helpful) and reasons for dropout. Specifically, both overall and for each subgroup extensively examined report the numbers of patients and the number of events. | page 5 lines 23-24 and page 6 lines 1-3 | “Methods” section, main text |

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| 13 Report distributions of basic demographic characteristics (at least age and sex), standard (disease-specific) prognostic variables, and tumor marker, including numbers of missing values. | page 8 lines 1-18<br>table 1 | see “Study population” and “Histopathological findings” in the “Results” section, main text |

### Analysis and presentation

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| 14 Show the relation of the marker to standard prognostic variables. | page 8 line 21 to page 9 line 16 | see “Correllation of sSDC1 concentration levels with clinicopathological parameters” in the “Results” section, main text |

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| 15 Present univariable analyses showing the relation between the marker and outcome, with the estimated effect (e.g., hazard ratio and survival probability). Preferably provide similar analyses for all other variables being analyzed. For the effect of a tumor marker on a time-to-event outcome, a Kaplan-Meier plot is recommended. | page 9 line 23 to page 10 line 8<br>figure 2 | see “Survival analysis” in the “Results” section, main text and also figure 2 |

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| 16 For key multivariable analyses, report estimated effects (e.g., hazard ratio) with confidence intervals for the marker and, at least for the final model, all other variables in the model. | page 10 lines 9-15 | see “Survival analysis” in the “Results” section, main text |

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| 17 Among reported results, provide estimated effects with confidence intervals from an analysis in which the marker and standard prognostic variables are included, regardless of their statistical significance. | page 10 lines 9-15 and table3 | see “Survival analysis” in the “Results” section, main text and table 3 |

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| 18 If done, report results of further investigations, such as checking assumptions, sensitivity analyses, and internal validation. | not done | not done |

## Discussion

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| 19 Interpret the results in the context of the pre-specified hypotheses and other relevant studies; include a discussion of limitations of the study. | page 10 line 17 to page 13 line 8 | see “Discussion” section, main text |

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| 20 Discuss implications for future research and clinical value. | page 10 line 17 to page 13 line 8 | see “Discussion” section, main text |

From: McShane LM, Altman DG, Sauerbrei W, Taube SE, Gion M, Clark GM: Reporting recommendations for tumor marker prognostic studies (REMARK). J Natl Cancer Inst 2005; 97: 1180-1184.

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*As the checklist was provided upon initial submission, the page number/line number reported may be changed due to copy-editing and may not be referable in the published version. In this case, the section/paragraph may be used as an alternative reference.