

The REMARK checklist

Item to be reported		Reported on Page Number/Line Number	Reported on Section/Paragraph
INTRODUCTION			
1	a) State the marker examined b) The study objectives c) Pre-specified hypotheses.	Page 5/Line 93-100 Page 5/Line 100-104 Page 4/Line 79-90	Background/Paragraph1
MATERIALS AND METHODS			
Patients			
2	Describe the characteristics (e.g., disease stage or co-morbidities) of the study patients, including their source and inclusion and exclusion criteria.	Page 6/Line 114-127 Page 6-7/Line 129-138	Methods/Paragaph2.2/Paragraph 2.3
3	Describe treatments received and how chosen (e.g., randomized or rule-based).	Page 6/Line 115 (Standard chemotherapy schedules chosen by clinicians)	Methods/Paragraph 2.2
Specimen characteristics			
4	Describe type of biological material used (including control samples) and methods of preservation and storage.	Page 7/Line 140 (blood samples)	Methods/Paragraph 2.4
Assay methods			
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.	N/A (we collected ordinary blood samples before start of chemotherapy)	N/A
Study design			
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 6/Line 114-115 Page 9/Line 185	Methods/Paragraph 2.2
7	Precisely define all clinical endpoints examined.	Page 7/Line 136-138	Methods/Paragraph2.3
8	List all candidate variables initially examined or considered for inclusion in models.	Page 6-7/Line 129-136 Page 7/ Line 140-150	Methods/Paragraph 2.3/2.4
9	Give rationale for sample size; if the study was designed to detect a specified effect size, give the target power and effect size.	N/A (since the retrospective analysis we conducted)	N/A
Statistical analysis methods			

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 7-8/Line 152-165	Methods/Paragraph2.5
11	Clarify how marker values were handled in the analyses; if relevant, describe methods used for cutpoint determination.	Page 8/Line 161-163	Methods/Paragraph2.5

RESULTS			
Data			
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.	Page8-9/Line 168-183	Results/Paragraph3.1
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.	Table1	Table1
Analysis and presentation			
14	Show the relation of the marker to standard prognostic variables.	Page10/Line 219-221	Results/Paragraph3.3
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.	Page9-10/Line192-197/Line 201-205 Figure1-2 Table2	Results/Paragraph3.2 Figure1-2 Table2
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.	Page9-10/Line 197-201/Line 206-207 Table2	Results/Paragraph3.2 Table2
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.	See above (point 14) for the statistical relation between the marker and standard prognostic clinical variables.	Results/Paragraph3.3
18	If done, report results of further investigations, such as checking assumptions, sensitivity analyses, and internal validation.	N/A (investigation not done)	N/A
DISCUSSION			
19	Interpret the results in the context of the pre-specified hypotheses and other relevant studies; include a discussion of limitations of the study.	Page13-14/Line 284-290/Line 303-304/Line 313-319	Conclusions/Paragraph4
20	Discuss implications for future research and clinical value.	Page14/Line 304-309/Line 311-313	Conclusions/Paragraph4

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