The REMARK checklist

	Item to be reported	Page no.
INTRODUCTION		
1	State the marker examined, the study objectives, and any pre-specified hypotheses.	Page 6, line 94-98
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 7, line 107-113; Page 10, line 183 – Page 11, line 199; Table 1
3	Describe treatments received and how chosen (e.g., randomized or rule-based).	Page 7, line 107-110
Specimen characteristics		
4	Describe type of biological material used (including control samples) and methods of preservation and storage.	Page 7, line 117-121
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.	Page 7, line 123 – Page 9, line 152
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 7, line 107-109; Page 9, line 158-163; Page 10, line 187-192
7	Precisely define all clinical endpoints examined.	Page 9, line 155 – Page 10, line 176
8	List all candidate variables initially examined or considered for inclusion in models.	Page 8, line 134-136; Page 9, line 155 – page 10, line 176
9	Give rationale for sample size; if the study was designed to detect a specified effect size, give the target power and effect size.	Page 10, line 183-186
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 9, line 154 – Page 10, line 179
11	Clarify how marker values were handled in the analyses; if relevant, describe methods used for cutpoint determination.	Page 8, line 134 – Page 9, line 150; Page 9, line 160-163; Page 11, line 195-199; Page 12, line 218-224
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.	Page 10, line 183-192; Figure 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.	Table 1
Analysis and presentation		
14	Show the relation of the marker to standard prognostic variables.	NA
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.	Figure 2; Figure 3; Figure 5; Figure S2; Table S1; Table S3; Table S6

Source: 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.

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 11, line 198-199; Page 12, line 216-218; Page 13, line 255-256; Page 14, line 279 – Page 15, line 281; Table S1
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.	Table S1
18	If done, report results of further investigations, such as checking assumptions, sensitivity analyses, and internal validation.	NA
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.	Page 15, line 296 - Page 18, line 367;
20	Discuss implications for future research and clinical value.	Page 15, line 302 – Page 16, line 304; Page 17, line 333-336; Page 18, line 361-367; Page 189, line 370-375

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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.

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