Gastric Cancer
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ORIGINAL ARTICLE

Response to neoadjuvant chemotherapy and survival in molecular subtypes of resectable gastric cancer: a post hoc analysis of the D1/D2 and CRITICS trials

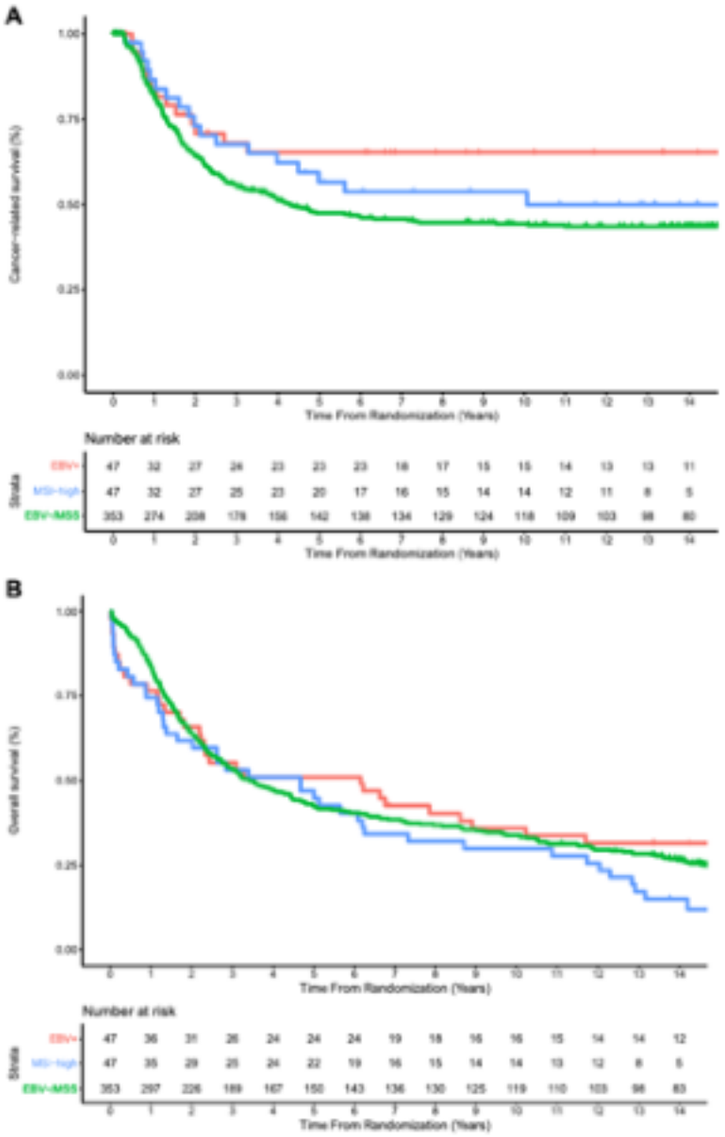

Fig. 2 **a** Cancer-related and **b** overall survival since randomization in 447 patients of the Dutch D1/D2 trial. **a** The hazard ratio was 0.57 (95% CI 0.31–0.99, $P = 0.047$) for EBV+ vs EBV−/MSS, and 0.78 (95% CI 0.48–1.27, $P = 0.32$) for MSI-high vs EBV−/MSS. **b** The hazard ratio was 0.90 (95% CI 0.63–1.30, $P = 0.59$) for EBV+ vs EBV−/MSS, and 1.31 (95% CI 0.92–1.82, $P = 0.10$) for MSI-high vs EBV−/MSS. *EBV+* Epstein–Barr virus positive, *MSI-high* microsatellite instable, *EBV−/MSS* Epstein–Barr virus negative and microsatellite stable

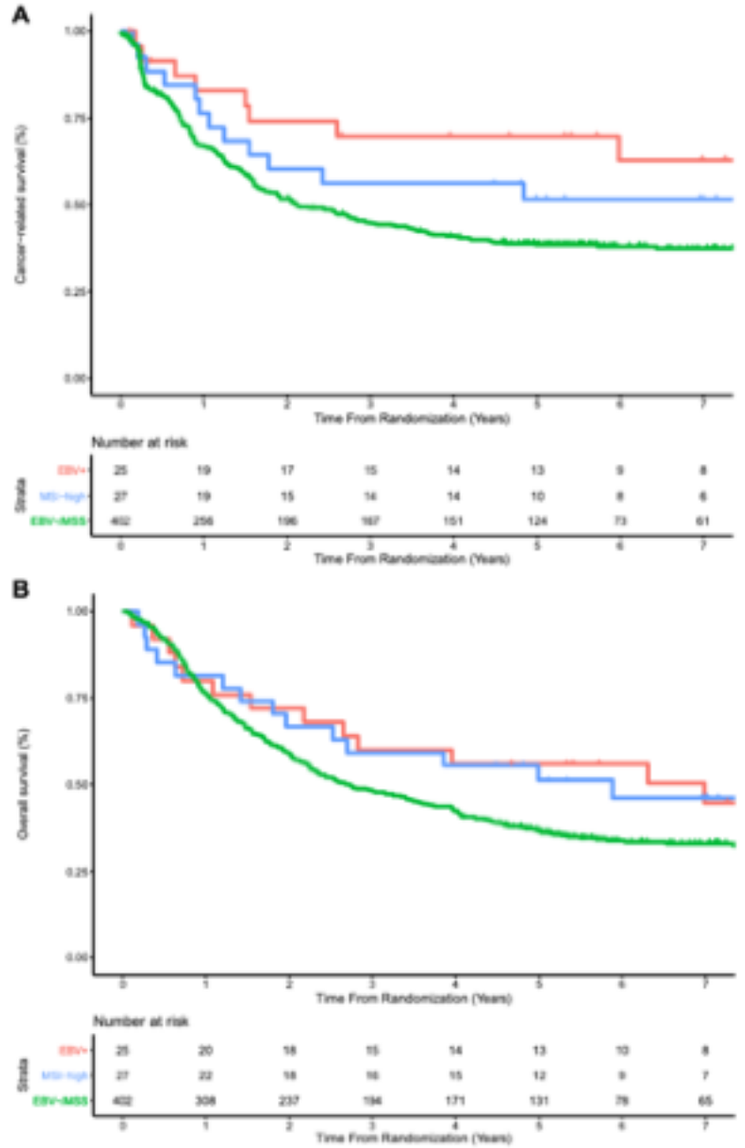

Fig. 3 **a** Cancer-related and **b** overall survival since randomization in 454 patients of the CRITICS trial. **a** The hazard ratio was 0.44 (95% CI 0.22–0.88, $P = 0.02$) for EBV+ vs EBV-/MSS, and 0.67 (95% CI 0.37–1.19, $P = 0.17$) for MSI-high vs EBV−/MSS. **b** The hazard ratio was 0.64 (95% CI 0.36–1.11, $P = 0.11$) for EBV+ vs EBV−/MSS, and 0.67 (95% CI 0.39–1.14, $P = 0.14$) for MSI-high vs EBV−/MSS. *EBV+* Epstein–Barr virus positive, *MSI-high* microsatellite instable, *EBV−/MSS* Epstein–Barr virus negative and microsatellite stable

In conclusion, among molecular subgroups of GCs **EBV+** tumors showed the highest histopathological response rate and favorable outcome compared to EBV–/MSS. We found substantial histopathological response after neoadjuvant chemotherapy in MSI-high GC, **but only in those with a mucinous phenotype.**

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Review Article

Novel Biomarkers for Prediction of Response to Preoperative Systemic Therapies in Gastric Cancer

Table 1. Potential novel biomarkers for the prediction of response to preoperative systemic therapies

Therapeutic agents	Predictive biomarkers		Predictive role
Chemotherapeutic agents	MSI status	MSI-H [14-17]	Resistance to platinum-based chemotherapy
	BIRC3	High BRIC3 expression [27]	Resistance to chemoradiotherapy
Anti-HER2 agents	PTEN	PTEN loss [46-48]	Resistance to trastuzumab and/or lapatinib
	AMNESIA panel	EGFR/MET/KRAS/PI3K/PTEN mutations and EGFR/MET/KRAS amplifications [49]	
	NRF2	High NRF2 expression [54]	
	MET	MET amplification [55]	
	FGFR3	High FGFR3 expression [58]	
Anti-VEGF(R) agents	HOXB9	HOXB9-positive [74]	Resistance to bevacizumab (in CRC)
Immune checkpoint inhibitors	PD-L1	High PD-L1 expression [90,91]	Response to anti-PD-1
	MSI-status	MSI-H [84,90]	
	EBV	EBV-positive [90]	
	Epigenomic promoter	Epigenomic promoter alterations [93]	Resistance to anti-PD-1

MSI = microsatellite instability; MSI-H = microsatellite instability-high; BIRC = baculoviral inhibitor of apoptosis repeat containing; PTEN = phosphatase and tensin homolog; EGFR = epidermal growth factor receptor; PI3K = phosphoinositide 3-kinases; NRF2 = nuclear factor erythroid 2-related factor 2; FGFR = fibroblast growth factor receptor; HOXB9 = homeobox B9; VEGF(R) = vascular endothelial growth factor (receptor); CRC = colorectal cancer; PD-L1 = programmed death-ligand 1; EBV = Epstein–Barr virus; PD-1 = programmed death-1.

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