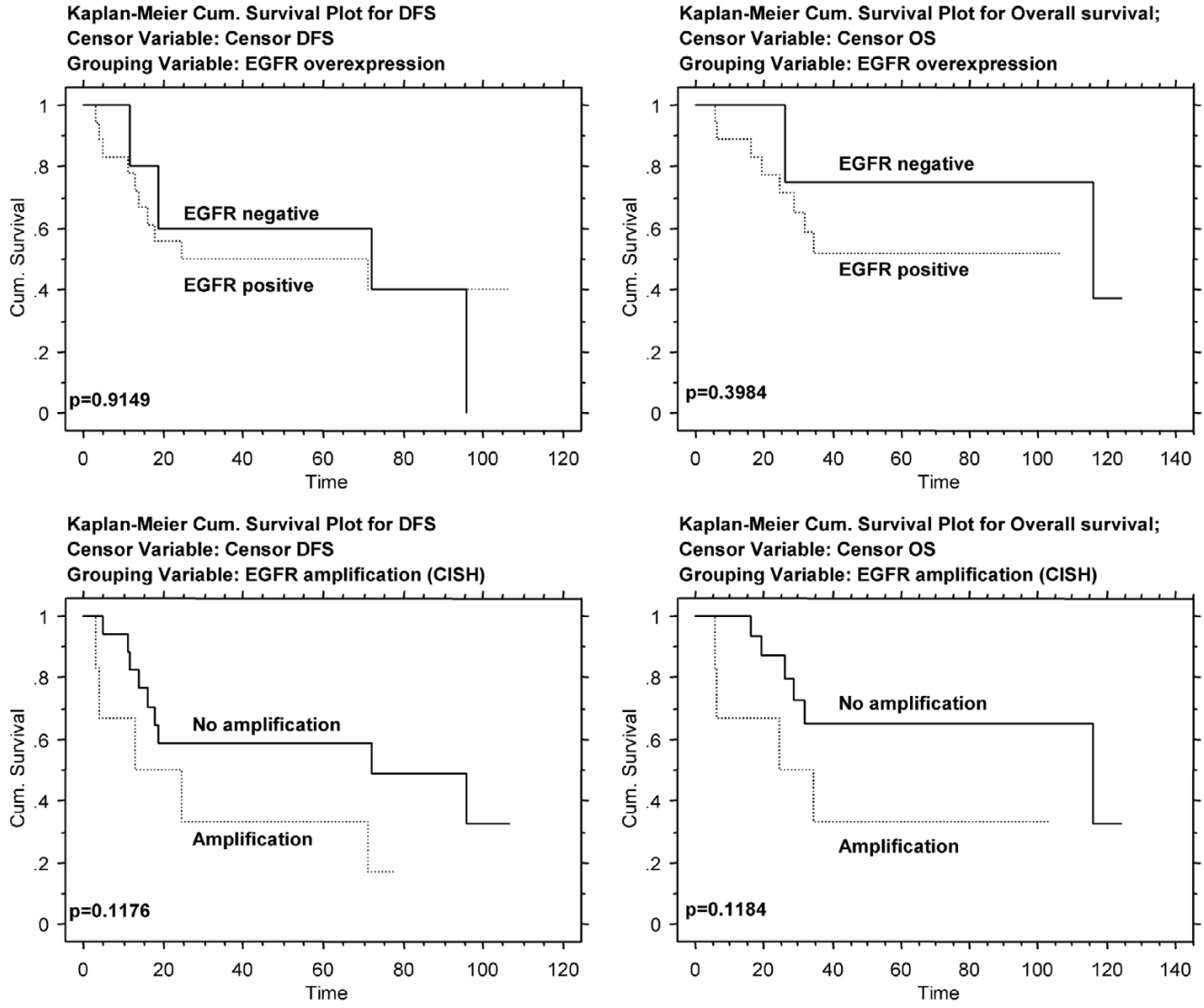
Figure 3



EGFR overexpression and amplification: prognostic impact on DFS and OS. CISH, chromogenic *in situ* hybridization; DFS, disease-free survival; EGFR, epidermal growth factor receptor; OS, overall survival.

showed no amplification. EGFR activating mutations have been described in lung cancer and in brain tumours, but these mutations have proven extremely rare in other types of cancer, including breast carcinomas [8,37]. However, Weber and coworkers [38] recently described EGFR missense mutations in sporadic and familial (*BRCA1*/*BRCA2* related) breast cancer and demonstrated that these mutations are significantly more frequent in the latter. Therefore, further analysis of *EGFR* gene sequence in MBCs may explain the overexpression of EGFR in those cases lacking *EGFR* amplification.

An alternative mechanism for EGFR expression in MBC may be maintenance of a myoepithelial/basal phenotype. In fact, expression of EGFR is part of the definition of 'basal-like' tumours proposed by Nielsen and coworkers [39]. EGFR is consistently expressed in myoepithelial cells of the breast [40]. We [26,41,42] and others [30,31,43-45] have demonstrated that the vast majority of MBCs consistently express basal/myoepithelial markers. Furthermore, indirect evidence from a study using murine cell lines suggests that transformed myoepithelial cells may give rise to tumours with sarcomatous and carcinosarcomatous patterns, similar to those observed in spindle cell carcinomas and carcinomas with heterologous elements [46]. Therefore, one could speculate that overexpression of EGFR, without gene amplification, could simply reflect maintenance of the basal-like/myoepithelial phenotype of these lesions. Conversely, one cannot rule out that *EGFR* gene amplification is one of the genetic mechanisms whereby basal/myoepithelial differentiation pathways are activated in transformed luminal epithelial cells.