

An evaluation of the possible interaction of gastric acid suppressing medication and the EGFR tyrosine kinase inhibitor erlotinib.

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Background: The NCIC CTG BR21 trial demonstrated a 2 month overall survival (OS) benefit from erlotinib (E), when compared to placebo (P), in advanced NSCLC patients after the failure of 1st or 2nd line chemotherapy . Gastric acid suppression (AS), through the use of proton pump inhibitors (PPIs) and H2 receptor antagonists (H2RA), increases gastric pH which may reduce the absorption of E. **Methods:** We retrospectively evaluated the impact of AS use on E drug levels, progression-free survival (PFS) and OS using the BR21 trial database. Patients were allocated to the AS cohort if they received PPIs or H2RAs at baseline or at any time during protocol treatment. PFS and OS comparisons were performed using Cox models with a time-dependent covariate for AS use and adjusting for known covariates. **Results:** Of 731 patients randomized to BR21, 267 received PPIs or H2RAs (AS cohort: 191 randomized to E and 76 to P; non-AS cohort 297 randomized to E and 167 to P). Within the E and P cohorts, no statistically significant differences were found in baseline characteristics between those patients receiving AS and those who did not. In the AS cohort, the mean of median E plasma levels over the study were not significantly lower compared with the non-AS cohort (1551.3 vs. 1655.3 ng/mL, p=0.96). AS was prognostic for inferior OS and PFS compared to the non-AS cohort, regardless of which arm patients were randomized to. Therefore, this finding does not appear to be due to an interaction between AS use and E. **Conclusion:** Based on participants from the BR21 trial, these results suggest that, although the use of H2RAs and PPIs may reduce the absorption of E, the impact on median plasma levels is modest and this does not appear to reduce its efficacy significantly.

Group and Outcome	AS Use Median in months (95% CI)	Non AS Use Median in months (95% CI)	Adjusted HR (95% CI)	p-value
Erlotinib				
- OS	5.52 (4.14 ; 7.52)	7.20 (5.95 ; 8.28)	1.69 (1.37 ; 2.09)	<0.0001
- PFS	2.20 (1.91 ; 3.29)	2.27 (1.91 ; 3.38)	1.77 (1.45 ; 2.16)	<0.0001
Placebo				
- OS	3.33 (3.02 ; 4.67)	5.88 (4.57 ; 7.59)	1.98 (1.45 ; 2.69)	<0.0001
- PFS	1.84 (1.74 ; 1.91)	1.81 (1.77 ; 1.87)	1.53 (1.14 ; 2.07)	0.005
Interaction				
- OS				0.81
- PFS				0.16