The impact of gastric acid suppression therapy on tyrosine kinase inhibitors in advanced cancer patients

Background
Oral tyrosine kinase inhibitors (TKIs) are used across tumor subtypes. Oral drug absorption is dependent on numerous factors including gastric acidity. Few studies have examined effects of gastric acid suppressants such as proton pump inhibitors (PPIs) on TKI outcomes. This study aims to determine if concurrent PPIs and TKIs impair progression free (PFS) and overall survival (OS) in patients (pts).

Methods
Advanced/metastatic non-small cell lung cancer (NSCLC) patients receiving erlotinib from 2007 to 2012 and renal cell cancer (RCC) patients receiving sunitinib from 2007 to 2013 were retrospectively reviewed. The review included the Alberta outpatient/retail pharmacy databases. Pts with ≤ 1 week of therapy were excluded. Aside from demographics, pts were identified as concurrently receiving acid suppression if their pharmacy records included a PPI with prescription dates that overlapped by ≥ 20% of TKI treatment duration. PFS and OS were primary endpoints.

Results
Of 545 NSCLC and 383 RCC pts, 507 and 231 were included, respectively. PPIs given concomitantly with erlotinib was detrimental to both PFS (hazard ratio [HR] 1.71, 95% CI: 1.39-2.11, p<0.0001) and OS (HR 1.29, 95% CI: 1.05-1.59, p=0.016). PPIs also affected sunitinib PFS (HR 1.42, 95% CI: 1.00-2.01, p=0.050) and OS (HR 1.27, 95% CI: 0.88-1.82, p=0.202). In pooled analysis, PPIs negatively impacted TKI PFS (HR 1.60, 95% CI: 1.34-1.91, p<0.0001) and OS (HR 1.34, 95% CI: 1.09-1.57, p=0.003). Considering performance status, acid suppression impaired PFS (HR 1.56, 95% CI: 1.31-1.87, p<0.0001) and OS (HR 1.24, 95% CI: 1.04-1.49, p=0.019) in both RCC and NSCLC.

Conclusion
Despite limitations of a retrospective study, this large cohort study shows PPIs negatively interact with oral TKIs in NSCLC and RCC pts. Our results lend support that PPIs impair TKI absorption leading to poorer survival. This interaction is not found in electronic drug interaction sources and patients embarking on TKI therapy should be made aware that gastric acid suppressants may limit TKI efficacy. Further investigation as to whether this effect is seen in other TKIs is underway.