Title: Defining the Rate of Pathologic Upstaging in Patients with Clinical T1b Esophageal Cancer: Should we consider Neoadjuvant Therapy?

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### Abstract:

#### Introduction:

Neoadjuvant chemoradiation therapy (NCRT) for cT1b esophageal cancer is not recommended despite risk of pathologic upstaging (PU) with increased depth of penetration. We aimed to (1) define the rate of and factors associated with PU, (2) describe current trends in treatments, and (3) compare overall survival (OS) with and without NCRT for surgically resected cT1b lesions.

# Methods:

We used the 2020 National Cancer Database (NCDB) to identify patients with cT1bN0 esophageal cancer with or without PU who underwent removal of their tumor. We built multivariable logistic regression models to assess for factors associated with PU. Survival was compared using log-rank analysis and modeled using multivariable Cox proportional hazards regressions.

## Results:

Out of 1,106 patients with cT1b esophageal cancer, 17.3% (N=191) had PU. A higher tumor grade (p=0.002), greater tumor size (p<0.001), and presence of lympho-vascular invasion (p<0.001) were associated with PU. 8.0% (N=114) of patients were treated with NCRT. Five-year OS was 49.4% for patients who received NCRT compared to 67.2% for upfront esophagectomy (p<0.05). PU was associated with decreased OS (PU 43.7% vs. NPU 67.7%) [HR 2.12 (95% CI, 1.70-2.65; p<0.001)]. Compared to esophagectomy, LTE was associated with a decreased OS [HR 1.50 (95% CI, 1.19-1.89; p=0.001)]

## Conclusions:

PU of cT1b lesions is associated with decreased OS. NCRT does not increase OS in cT1b lesions compared to upfront esophagectomy. Esophagectomy confers survival benefit over LTE for these lesions and should continue to be standard of care. However, treatment strategies in patients with high-risk tumors should include multidisciplinary management.

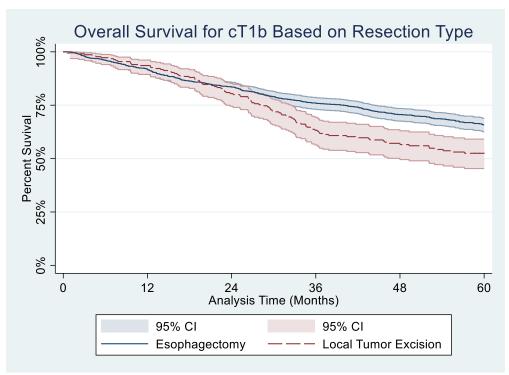


Figure 1.