A randomized phase III study to evaluate the value of the omission of prophylactic neck dissection for stage I/II tongue cancer (RESPOND: JCOG1601)


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Background: The standard local treatment for early-stage tongue cancer with no clinical lymph node metastases is partial glossectomy. However, whether or not prophylactic neck dissection (ND) should be performed has been controversial. In 2015, D’Cruz et al. reported that prophylactic ND contributes to the improvement of overall survival (OS) for clinical T1-2N0 tongue cancer regardless of the depth of invasion (DOI). However, considering the occult lymph node metastasis of 30% and disadvantages associated with prophylactic ND such as cosmetic issues and complications including accessory and facial nerve paralysis, partial glossectomy alone can still be regarded as a treatment option for patients (pts) carefully selected by DOI, provided there is appropriate follow-up with full use of computed tomography (CT) and other diagnostic imaging modalities to detect recurrence early enough to conduct salvage surgery.

Trial design: We have commenced a phase III randomized controlled trial to confirm the non-inferiority of glossectomy alone compared to glossectomy with prophylactic ND (standard arm) in terms of OS. Histologically proven stage I/II tongue cancer with DOI 3-10 mm by enhanced magnetic resonance imaging is eligible. The selection based on the DOI is a novel aspect of this study. We set the key inclusion criterion of DOI as 3-10 mm since prophylactic ND is unnecessary for pts with DOI < 3 mm according to the data from D’Cruz et al., and pts with DOI > 10 mm are classified as T3 according to the 8th TNM classification. The primary endpoint is OS. The secondary endpoints include relapse-free survival (RFS), local-RFS, proportion of non-resectable recurrence, proportion of neck lymph node recurrence, and adverse events. We assumed a 5-year OS of 85% in the standard arm and set the non-inferiority margin at 7.5%. The sample size was set at 440 pts, with a one-sided α of 5%, power of 70%, an accrual period of 3 years, and a follow-up period of 5 years. For follow-up observation, CT is essential at 3, 6, 12, 18, and 24 months postoperatively and then annually thereafter. Enrollment launched November 2017 and five pts were enrolled as of April 2018.

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