The efficacy of the addition of TRAStuzumab and Pertuzumab to neoadjuvant chemoradiation: a randomized phase III multi-center study in resectable HER2 overexpressing esophageal or gastroesophageal junction (TRAP-2)


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Background
- Despite implementation of neoadjuvant chemoradiotherapy, the introduction of adjuvant nivolumab and demonstrated promising activity in EAC patients.
- HER2 receptor signaling can be blocked with trastuzumab and pertuzumab in combination with ISH positivity.
- Studies suggest that dual HER2 targeting prevents resistance to HER2 blockade.
- The TRAP study showed that addition of trastuzumab and pertuzumab to neoadjuvant chemoradiotherapy was feasible and demonstrated promising activity in EAC patients.

Inclusion Criteria
- Patients with surgically resectable adenocarcinoma (T1-4a, N0-3, M0) of the esophagus or gastroesophageal junction
- HER2 positivity determined by IHC (and ISH): IHC 3+ or IHC 2+ in combination with ISH positivity
- Adequate left ventricular ejection fraction of ≥55%
- ECOG performance status 0 or 1

Study Design
- Stratification based on:
  1. Lymph node status
  2. Radiotherapy yes/no
  3. Proton radiation yes/no

Treatment Sites
- 388 patients will enroll in 6 years
- Multi-center study
  - 26 treatment sites
  - 1 screening only site

Treatments
- TRAStuzumab and Pertuzumab
- Chemoradiation
- HER2 positive esophageal adenocarcinoma

Treatment and Sampling Schedule

Objectives
- Primary: Overall survival
- Secondary: Quality-adjusted life years, Progression free survival, Pathological response, R0 resection rate, Toxicity (CTCAE 5.0), Post-operative complications (Clavien-Dindo), Feasibility, Quality of life (PROMs)
- Tertiary: Overall survival and progression free survival of nivolumab-treated patients in both arms

Potential biomarkers to predict treatment response, clinical outcome and safety:
- In blood (ctDNA and PBMCs)
- In tumor tissue (Nanostring sequencing and HER2 status)

Currenty 4 out of 388 patients are enrolled

References:
1. Van Hagen et al., NEJM, 2012
2. Rolly et al., NEJM, 2021
4. Schnee et al., Cancer Res, 2009
5. Zeeuwen et al., JCO, 2019

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