Systematic literature review (SLR) of randomized controlled trials (RCTs) of treatments for first-line (1L) gastric cancer/gastroesophageal junction adenocarcinoma (GC/GEJ) in adult patients

Authors: Elizabeth Smyth,[1] Teresa Kangappaden,[2] Sofiya Portuhay,[2] Amrita Debnath,[2] Samantha Craigie,[2] JeanPierre Coaquira Castro,[3] Eugenia Priedane,[4*] Lin Zhan[3]
*Presenting author

Affiliations: [1]Oxford University Hospitals NHS Foundation Trust, Oxford, Oxfordshire, UK; [2]EVERSANA, Burlington, ON, Canada; [3]BeiGene USA, Inc., Emeryville, CA, USA, [4]BeiGene UK, London, UK

ABSTRACT

Objectives: To conduct an SLR of efficacy, safety, and health-related quality of life (HRQoL) outcomes among treatment regimens, with a focus on programmed death receptor-1/programmed death ligand-1 (PD-1/PD-L1) inhibitors, in 1L unresectable, locally advanced, or metastatic GC/GEJ.

Methods: Embase, Ovid MEDLINE®, and Cochrane CENTRAL were searched from inception to February 2024 for English-language RCTs of treatments in 1L HER2- GC/GEJ. Hand searches of bibliographies, health technology assessment agencies, conference proceedings, and trial registries were also conducted. Study selection was performed in duplicate. Study information and outcomes of interest were extracted.

Results: Of 11,756 records identified, 41 RCTs were included. Treatments included immuno-oncology (IO) agents (e.g., PD-1/PD-L1 inhibitors, cytotoxic T-lymphocyte-associated antigen 4 [CLTA-4] inhibitors, etc.), targeted therapies (e.g., kinase inhibitors, CLDN18.2 inhibitors, etc.) and chemotherapy. Among trials of PD-1/PD-L1 inhibitors (tislelizumab, nivolumab, pembrolizumab, sugemalimab, sintilimab), improvements in overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) were observed for PD-1/PD-L1 inhibitors plus chemotherapy versus chemotherapy alone at median follow-up times ranging from 11.6 to 54.3 months, with median OS, median PFS, and ORR ranging from 12.5 to 17.45 months, 6.9 to 10.94 months, and 47.3% to 68.6%, respectively. Survival and response benefits of PD-1/PD-L1 inhibitors varied by levels of PD-L1+ expression and geographic regions. Among other targeted therapies, response and survival benefits compared to chemotherapy were mixed; improvements in response and survival were seen with the CLDN18.2 inhibitor zolbetuximab and the FGFR inhibitor bemarituzumab, while benefits compared to chemotherapy were not seen with cetuximab, ramucirumab, andecaliximab, onartuzumab, rilotumumab, pazopanib, or ipatasertib. HRQoL data were reported by twelve trials using various instruments.

Conclusions: PD-1/PD-L1 inhibitors showed improved efficacy compared to chemotherapy for the treatment of 1L GC/GEJ; while other targeted therapies showed promise in certain biomarker-selected patients. Increasing availability of new agents may provide options to address unmet need.