Version	1.0
Date	1st August 2025
Brief Title	Match-Adjusted Indirect Comparison (MAIC) of Fruquintinib plus Paclitaxel versus Ramucirumab plus Paclitaxel in Advanced Gastric/GEJ Adenocarcinoma
Acronym	FRUIT-MAIC
Sponsor	
Information provided by	
Brief Summary	This anchored matching-adjusted indirect comparison (MAIC) evaluates the relative efficacy of fruquintinib-paclitaxel (using IPD from the FRUTIGA trial, n=703) versus ramucirumab-paclitaxel (using published AgD from RAINBOW-Asia, n=440) in advanced gastric/GEJ adenocarcinoma. Baseline characteristics are adjusted via entropy balancing weights. Primary endpoint is progression-free survival (PFS) analyzed by Bucher method; secondary endpoints include overall survival (OS) and objective response rate (ORR). Sensitivity analyses comprise restricted mean survival time (RMST) analysis and simulated treatment comparison (STC).
Detailed Description	This retrospective MAIC analysis employs individual patient data (IPD) from the FRUTIGA trial (fruquintinib arm) and published aggregate data (AgD) from RAINBOW-Asia (ramucirumab arm), with placebo as the common anchor. Pseudo individual participant data (Pseudo-IPD) for the RAINBOW-Asia trial were reconstructed from published Kaplan-Meier curves using the Guyot algorithm (2012). • **Weighting Methodology:** o Seven prognostic factors balanced: age <65, male sex, ECOG 0, GEJ primary, peritoneal metastases, metastatic sites, prior doublet chemotherapy o Optimization via BFGS algorithm (convergence tolerance 1e-6) o Effective sample size (ESS) retention: > 50% • **Statistical Analysis:** o Primary: Adjusted PFS hazard ratio (HR) using Bucher method with 95% bootstrap CI (100 iterations) o Secondary: Weighted Cox models for OS; logistic regression for ORR/DCR o Sensitivity: Simulated Treatment Comparison (STC) and covariate threshold analyses • **Sensitivity Analyses:** o RMST analyses were conducted as supportive evidence alongside primary Cox models for time-to-event endpoints violating proportional hazards assumptions. o Restricted mean survival time (RMST) o Simulated Treatment Comparison (STC) o Bootstrap confidence intervals (100 iterations)
Official Title	Adjusted Indirect Treatment Comparison of Fruquintinib-based Therapy Versus Standard Care in Advanced Gastric/Gastroesophageal Junction Adenocarcinoma: A MAIC Analysis.
Conditions	• Advanced Gastric Cancer • Gastroesophageal Junction Adenocarcinoma
Intervention/Treatment	Experimental: Fruquintinib + paclitaxel, Ramucirumab + paclitaxel Common comparator: Placebo + paclitaxel (weighted FRUTIGA and RAINBOW-Asia reference arm)
Inclusion Criteria	1. Histologically confirmed gastric/GEJ adenocarcinoma 2. Advanced or metastatic disease 3. ECOG 0-1 4. Received either fruquintinib + paclitaxel or reference regimen 5. Available baseline characteristics for matching variables
Exclusion Criteria	1. Missing key outcome data 2. Incomplete baseline characteristics for >2 matching variables 3. Prior fruquintinib exposure (control arm only)

Primary Purpose	Treatment Comparison
Allocation	Observational
Interventional Model	Indirect Treatment Comparison
Masking	
Participant Group/Arm	Group 1: Fruquintinib + Paclitaxel (IPD) Group 2: Control Therapy (AgD from RAINBOW-Asia)
Intervention/Treatment	

Primary Outcome Measures		
Outcome Measure	**Measure Description**	**Time Frame**
Progression-Free Survival (PFS)	Time from randomization to progression/death, assessed via weighted Cox model	per FRUTIGA trial data cutoff

Second Outcome Measures		
Outcome Measure	**Measure Description**	**Time Frame**
Objective Response Rate (ORR)	CR+PR per RECIST 1.1, compared via weighted logistic regression	per FRUTIGA trial data cutoff
Disease Control Rate (DCR)	CR+PR+SD≥6 weeks, analyzed via weighted proportions	per FRUTIGA trial data cutoff
Overall Survival (OS)	Time from randomization to death, analyzed using weighted Kaplan-Meier	per FRUTIGA trial data cutoff
Subgroup Analyses	PFS/OS by ECOG, metastasis burden, primary site, etc.	As per primary outcomes

Other Outcome Measures		
Outcome Measure	**Measure Description**	**Time Frame**
Progression-Free Survival (PFS)	Simulated Treatment Comparison (STC), Bootstrap confidence intervals (100 iterations)	per FRUTIGA trial data cutoff