Cost-effectiveness of systemic treatments in the second-line setting of advanced and metastatic gastric cancer in the Irish healthcare setting

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INTRODUCTION

Globally, gastric cancer is the 5th most frequently diagnosed cancer.

Over recent years there have been rapid changes in the treatment landscape for advanced and metastatic Gastric Cancer in the second- line setting. Notably, in the developments of immunotherapies and targeted therapies. The cost effectiveness of these novel treatments versus more established chemotherapy is uncertain.

Treatments of interest were those recommended by the National Comprehensive Cancer Network (NCCN) and the European Society for Medical Oncology (ESMO) that could be compared within both overall survival and progression-free survival network meta-analyses. Treatments of interest here were paclitaxel alone, irinotecan alone, FOLFIRI, ramucirumab + paclitaxel and pembrolizumab alone. Given its widespread use in clinical practice, paclitaxel was prespecified as the benchmark comparator.

AIMS

To investigate the cost-effectiveness of systemic treatments for second-line advanced/metastatic gastric cancer, informed by network meta-analyses (NMA) and aligned with Irish National HTA guidelines.

METHODS

- A bespoke partitioned-survival model was developed in R.
- Relative efficacy inputs for overall survival and progression-free survival were derived from NMA implemented by the authors (Sharma S, et al. 2026).
- Survival data was extrapolated to a lifetime horizon (10 years).
- Analyses were undertaken from the perspective of the Irish health payer.
- Irish cost data was used where available.
- Utility data were sourced via a targeted literature search.
- A 4% discount rate on outcomes and costs was applied.

NMA Results

OS (HR vs Paclitaxel)

Intervention	HR (95% CrI)
FOLFIRI	0.66 (0.27–1.62)
Ramucirumab + Paclitaxel	0.81 (0.44–1.47)
Irinotecan	0.82 (0.51–1.27)
Pembrolizumab*	0.86 (0.56–1.40)

PFS (HR vs Paclitaxel)

Intervention	HR (95% CrI)
Ramucirumab + Paclitaxel	0.64 (0.33–1.20)
FOLFIRI	0.70 (0.28–1.72)
Irinotecan	0.84 (0.39–1.82)
Pembrolizumab*	1.34 (0.87–2.26)

Grade ≥3 TRAEs (RR vs Paclitaxel)

- Network was not feasible for all five interventions of interest.
- Pembrolizumab: significant decreased risk (RR 0.32 (0.12–0.73))
- No other significant differences.

Partitioned Survival Analysis Framework

- **Digitise KM Curves**
  OS & PFS curves digitised from Wilke et al using WebPlotDigitizer.
- **Reconstruct Pseudo-IPD**
  Wilke et al
- **Fit & Select Distributions**
  Standard extrapolation distributions (n=6).
  Choice informed by statistical fit & clinical plausibility.
- **Derive Health State Durations**
  At each monthly cycle:
  - PFS = S_pfs(t)
  - PPS = S_os(t) − S_pfs(t)
  - Dead = 1 − S_os(t).

  PFS constrained ≤ OS.
- **Apply Efficacy, Utilities & Costs**
  - Efficacy: NMA (PFS & OS)
  - Utility: targeted literature search (PFS 0.68,
  - PPS 0.42)
  - Publicly available drug costs

Cost-effectiveness Analysis Outputs (vs Paclitaxel)

Intervention	Costs (€)	QALYs	ICER (€/QALY)	Probability cost effective
Paclitaxel	6,992	0.487		
Irinotecan	11,055	0.557	58,152	25%
FOLFIRI	28,691	0.644	137,852	0%
Ramucirumab + Paclitaxel	62,528	0.571	654,985	0%
Pembrolizumab*	40,744	0.509	1,496,776	0%

* Limitation

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- Pembrolizumab is recommended in the settings of MSI-H/dMMR tumours (ESMO & NCCN) & TMB-high tumours (NCCN).
- KEYNOTE-061 & KEYNOTE-063 recruited mainly participants with PD-L1-positive disease regardless of MSI-H/dMMR & TMB status.
- It was not possible to consider pembrolizumab in the settings of MSI-H/dMMR tumours & TMB-high tumours in the NMAs/cost-effectiveness analysis.

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R Packages Used in the Analysis

Full analysis conducted in R · All plots (CE plane, CEAC, tornado) produced using base R graphics · No additional plotting packages required

IPDfromKM: Pseudo-IPD Reconstruction

preprocess() and getIPD() used to reconstruct individual patient data from digitised KM curves and numbers at risk from Wilke et al.

Flexsurv: Parametric Survival Fitting

Fitted all 6 distributions to each curve. AIC/BIC extracted for model selection. summary() used to generate survival vectors for the model.

Survival: KM Estimation & Surv() Objects

Surv() objects created for parametric fitting. survreport() used for visual checking of reconstructed KM curves.

MASS: PSA Parameter Sampling

mvrnorm() used to sample correlated survival model parameters from the multivariate normal distribution across 1,000 PSA iterations.

Dplyr: Data Manipulation

pull() function used to extract time and numbers-at-risk columns from the digitised data frames for IPD reconstruction.

```
install.packages(c("IPDfromKM", "flexsurv", "survival", "MASS", "dplyr"))
```

CONCLUSION

Network Meta-Analyses

- There were no statistically significant differences, in OS or PFS, for any of the interventions under consideration vs paclitaxel.
- The NMA can be considered living and could be populated with future eligible RCTs.

Cost-effectiveness Analysis

- None of the interventions are cost effective, vs paclitaxel, at the Irish-payer threshold (€45,000/QALY).
- The CEA could be populated with updated NMA outputs.

Uncertainty

- Utility values are the key drivers of cost-effectiveness

Implications

There remains a need for novel systematic treatments, in this setting, that are effective and cost effective versus more established treatments. The HEALED Consortium overall objective is to enable novel targeted immunotherapies.

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