HER2 testing in advanced gastric cancer – understanding and reducing variation in current practice to improve equity in patient outcomes

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BACKGROUND

Although patients with gastric cancer have a dismal prognosis, (1) there is evidence that tumours that overexpress HER2 (the human epidermal growth receptor 2) as a result of gene amplification are associated with more aggressive disease and a poorer prognosis. (2)

In recent years, therapy targeting HER2 has substantially improved the outcomes for patients with advanced gastric cancer that overexpress HER2 (i.e. are HER2-positive).

PRIMARY AIMS

This study aims to determine the nature and accuracy of testing for HER2 in patients with advanced gastric cancers. Primarily:

1. To determine the extent to which tumours from patients with advanced or recurrent gastric cancer across major centres in Victoria are being adequately assessed for overexpression and/or amplification of HER2; and
2. To determine the extent that standardised testing algorithms are being used to test for HER2 status.

SECONDARY AIMS

1. To determine the percentage of patients who are HER-2 positive (whether based on IHC or ISH testing).
2. To investigate whether there are variations in assessment and testing patterns across different settings, including interobserver variability; and
3. To determine the percentage of HER2-positive patients who were offered HER2 targeted therapy.
4. To determine if and why HER2-positive patients were not offered HER2-targeted treatment.

PHASE I: DATA EXTRACTION

Phase I and II will include patients: participating in the UGICR; diagnosed with metastatic gastric cancer either at the time of diagnosis or on recurrence; diagnosed and/or treated for gastric cancer at any of the **twelve participating sites**.

Ethics approval is being sought from the Monash Health, under the National Mutual Acceptance Scheme. Site governance approval will be sought from participating sites.

The upper-gastrointestinal cancer registry (UGICR) will review medical records of patients with gastric cancer between 2016 to 2023.

Patients with early-stage disease who have since died will be followed-up to check for disease recurrence, via review of electronic medical records.

PHASE II: PATHOLOGY REVIEW

Approximately 200 patients meeting the above criteria will be randomly selected for pathology review. This will be supported by the Royal College of Pathologists Australia Quality Assurance Program (RCPAQAP).

1. **Review IHC and H&E slides**; no DISH.
2. 4-week **washout period.**
3. **Review DISH slides;** IHC & H&E provided.

PHASE III: QUALITATIVE SUB-STUDY

Phase II will involve semi-structured interviews with key stakeholders, to explore barriers and enablers to achieving compliance with standardised testing algorithms.

Thematic analysis of the qualitative data will be guided by the Theoretical Domains Framework.

The results of this phase will be used to identify common barriers and develop evidence-based, cost-effective strategies that can be translated into clinical practice.

Ethics approval is being sought from Monash University.

PROJECT GOVERNANCE

The HER2 Project advisory working group is responsible for overseeing the overall project and to meet at least every three to six months.

The primary objective of this working group, comprised of study investigators, consumer advisor(s) and project staff, is to advise on the recruitment strategy, site communications, research methodology, data set, and methods of data collection.

SIGNIFICANCE

This mixed methods approach incorporating clinical quality registry data may provide us with insight into current HER2 testing practices in Australia, and how to improve testing standards.

Failure to correctly diagnose HER2 positive tumours is that these patients may miss the opportunity to receive targeted drug therapy, which is known to improve response to treatment as well as prolong overall survival.

DISSEMINATION OF FINDINGS

Results will be disseminated in peer-reviewed publications and conference presentations. De-identified site-specific reports will be provided to participating sites.

ACKNOWLEDGEMENTS

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REFERENCES

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