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#IPD2022

The Newcastle upon Tyne Hospitals NHS Foundation Trust

Homologous Recombination Deficiency (HRD) testing in advanced high grade ovarian cancer – An audit

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1. BACKGROUND

Ovarian cancer carries the worst prognosis of all gynaecological malignancies, the commonest of which is high-grade serious ovarian cancer (HGSOC). The majority of women with HGSOC would have advanced disease at the time of diagnosis[1].

HGSOC is characterised by chromosomal instability due to homologous recombination deficiency (HRD). Mechanisms of HRD include germline mutations in the BRCA 1/2 genes (most common mechanism), germline and somatic mutations in other homologous recombination genes and epigenetic modifications of other genes involved in the HR pathway[1].

In ovarian cancer, patients with homologous recombination deficiencies exhibit specific clinical behaviours and have demonstrated improved sensitivity to treatment such as platinum-based chemotherapy and poly(ADP-ribose) polymerase (PARP) inhibitors, have been observed[2].

2. AIMS

1. To identify the proportion of women with HGSOC who are HRD positive by detecting tBRCA 1/2 variants and assessing genomic instability scores (GIS)
2. To calculate the proportion of tests which are inconclusive, using both the original and the Myriad Plus assay

3. STANDARD

Approximately 50% of women with ovarian cancer are expected to have HRD, thus making them eligible for treatment with PARP inhibitors

4. METHODS

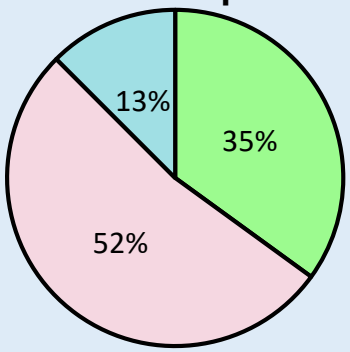
- A retrospective analysis of 40 patients with ovarian cancer who underwent testing for HRD between April 2021 to July 2022
- Patients were identified from a clinical database and histology reports were manually reviewed using APEX
- Patients were identified as HRD positive if they were found to have tBRCA 1/2 gene mutations and/or have a total genomic instability score of ≥42

References:

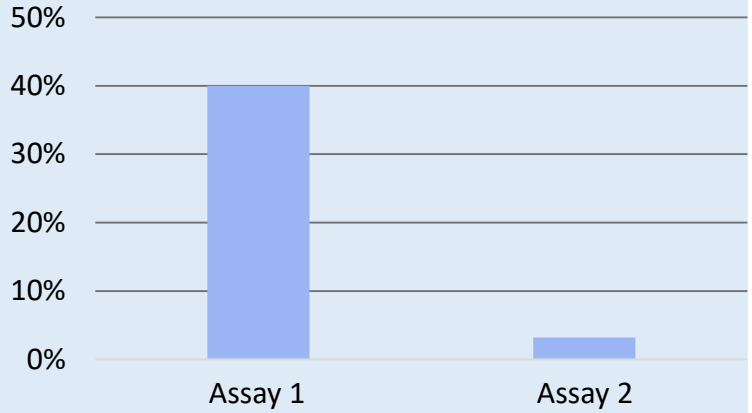
1. Takaya, H. *et al.* Homologous recombination deficiency status-based classification of high-grade serous ovarian carcinoma. *Sci Rep* **10**, 2757 (2020).
2. Frey, K et al. Homologous recombination deficiency (HRD) testing in ovarian cancer clinical practice: a review of the literature. *gynaecol oncol res pract* **4**, 4 (2017).

5. RESULTS

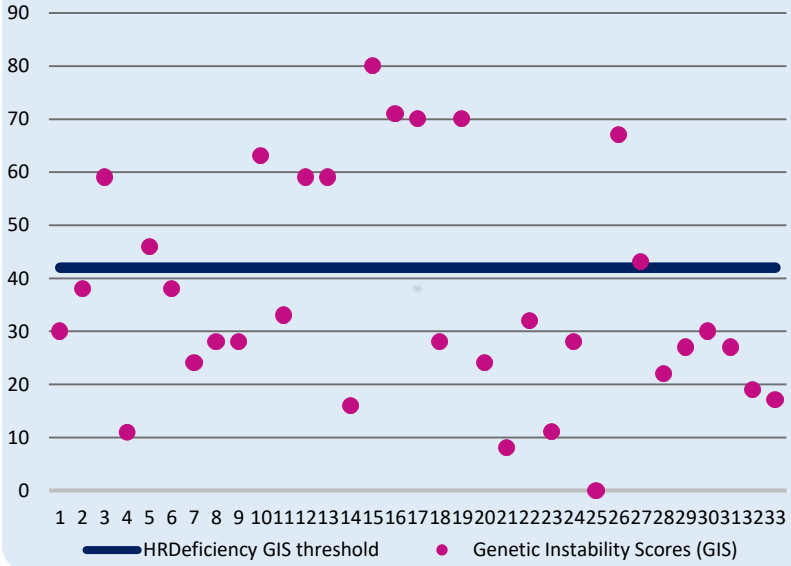
Proportion of HRD positive patients



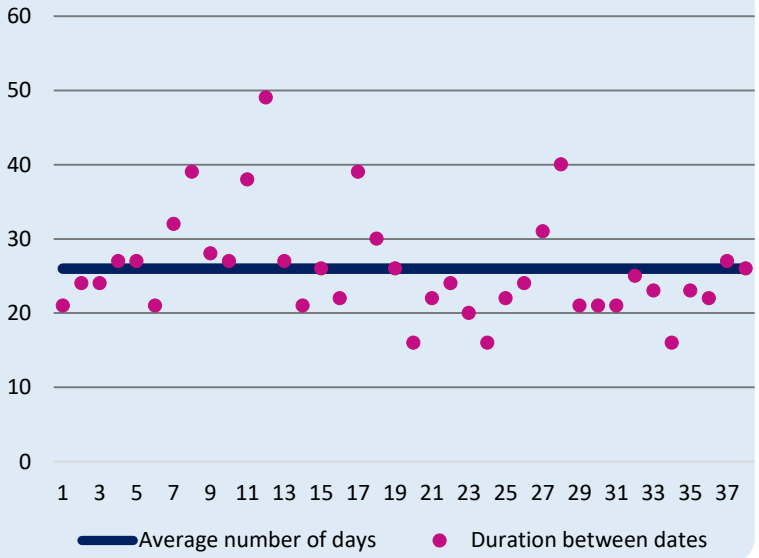
Proportion of Inconclusive tests



GIS SCORES



Turaround Times



6. DISCUSSION AND CONCLUSION

- 5 patients (13%) had inconclusive tests
  - 40% of tests using Assay 1 led to an inconclusive result (4 out of 10)
  - Only 3.2% of tests using Assay 2 led to an inconclusive result (1 out of 30)
- Average turnaround time was 26 days between when the request was first sent to when the result was received
- 35% of patients were identified to be HRD positive
  - This does **NOT** surpass the set standard

Action plan

- Use Assay 2 exclusively to reduce % of inconclusive tests
- Increase sample size
- Reaudit