Comprehensive Genomic Profiling Approaches in Europe and the US: A Review of Guidelines and Recommendations for Solid Tumours

Poster # HPR68

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Background

- Personalized cancer therapies are available in multiple indications, offering innovative and potentially life-extending treatments compared with traditional chemotherapy.
- Histology-independent therapies (HITs) are those that are based on the genetic and molecular alterations of a cancer, rather than its site of origin.[1]
- HITs are a relatively new innovation in cancer treatment, the first being approved in 1998 for trastuzumab and its associated companion diagnostic for HER2+ breast cancer.[2] Most pipeline HITs currently in development are for solid tumour indications.[1]
- Since the approval of trastuzumab, many more targeted treatments have been developed and are available across the US and Europe, with testing capabilities also improving. Tests that are now available to patients range from single gene tests to comprehensive genomic profiling (CGP), which allows testing for multiple biomarkers simultaneously.
- CGP offers the promise of a personalized approach to treatment, potentially improving clinical outcomes for many patients with different cancer types.
- Despite these advancements in testing and treatment, not all patients have access to CGP; barriers to testing vary by indication and geography.

Objectives

- A rapid literature review was conducted to explore the similarities and differences between geographic regions (US, UK, France, and Germany) in CGP testing guidance and recommendations for solid tumours.

Methods

- A rapid literature review was conducted to identify and compare literature from key national health sources across the US (American Society of Clinical Oncology [ASCO], FDA), Europe (European Society for Medical Oncology [ESMO]), France (Haute Autorité de Santé [HAS]), Germany (Gemeinsamer Bundesausschuss [G-BA], Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [IQWiG]), and the UK (National Institute for Health and Care Excellence [NICE]).
- The sources were assessed to identify similarities and differences between the recommended approaches to CGP use for solid tumours across geographies.
- The rapid review focused on identifying relevant literature pertaining to the following solid tumour conditions: breast cancer, non-small cell lung cancer (NSCLC), lung cancer, colorectal cancer, pancreatic cancer, prostate cancer, gastric cancer, and ovarian cancer.

Results

Search Results

- In total, 16 documents from 7 HTAs and national health authorities were identified and included in this rapid review (**Table 1**).
  - Guidelines were available for the US and Europe (general), France, Germany, and the UK.
  - The number of documents available by disease was highest for breast cancer (n = 7) and lowest for both pancreatic (n = 1) and gastroesophageal cancer (n = 1).
  - France and Germany had the least amount of guidance available (HAS, G-BA, and IQWiG; n = 1 each), and Europe (general) had the most (n = 8), followed by the US (n = 7) and UK (n = 5).

Table 1. Literature Sources Identified by Disease and Geographic Region

Source	Breast cancer	Lung cancer (including NSCLC)	Colorectal cancer	Pancreatic cancer	Prostate cancer	Ovarian cancer	Gastro-esophageal cancer	General/ Others
US								
ASCO	✓3	✓4	×	×	✓5	✓6	×	✓7
FDA	✓8	✓8	✓8	×	✓8	✓8	×	✓9
Europe (General)								
ESMO	✓10	✓10	✓10	✓10	✓10	✓10	✓10	✓10
France								
HAS	✓11	×	×	×	×	×	×	×
Germany								
G-BA	✓12	×	×	×	×	×	×	×
IQWiG	✓13	×	×	×	×	×	×	×
UK								
NICE	✓14	✓15	×	×	✓16	✓17	×	✓18

Key: ✓– documents were identified; × – documents were not identified; **Green** – multiple gene sequencing/testing is recommended if result is likely to impact patient's management; **Orange** – multiple gene sequencing/testing is recommended for specific biomarkers/mutations; **Red** – multiple gene sequencing/testing is not recommended, or evidence is insufficient for a recommendation; **Blue** – open consultation/under review.

CGP Guidance and Recommendations

- **ASCO** stated that multigene testing could be of potential benefit to a patient in cases where there are no genotype-based approved treatments for the patient's disease and recommended that molecular biomarkers may be assessed in situations where the assay result is likely to affect the patient. In cases where the biomarkers were not considered clinically actionable, or treatments were not commercially available, it was recommended that multigene testing should not be offered.
- **ESMO** recommended large multigene panels if the extra cost was acceptable compared with small panels, in NSCLC, prostate cancer, ovarian cancer, and cholangiocarcinoma.
- In the US, guidelines from **ASCO** (n = 5) and documents from the **FDA** (n = 2) indicated that testing for multiple biomarkers was recommended if the results were likely to affect patient management.
  - This was the case for all cancers assessed, except pancreatic cancer and gastroesophageal cancer, for which no evidence was identified.

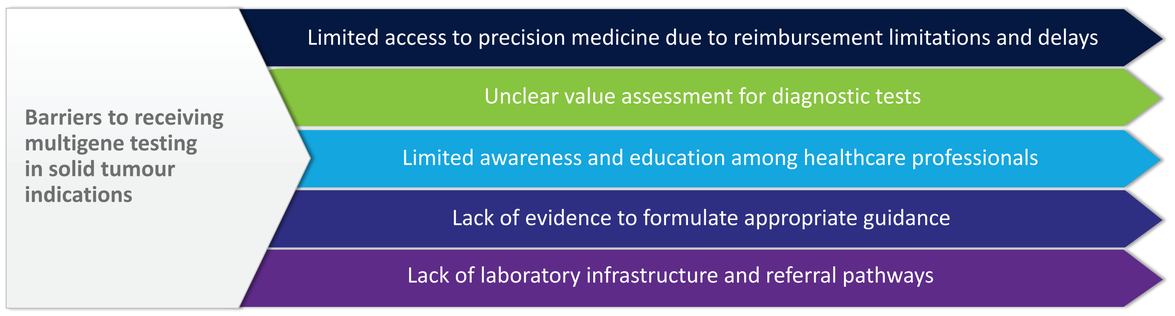
Results (cont'd)

- With respect to Europe, guidelines from **ESMO** (n = 1) were more conservative:
  - Testing for multiple biomarkers was recommended in NSCLC, colorectal, prostate, and ovarian cancer, when the cost of undertaking a test was deemed acceptable. Testing was not recommended in breast, colorectal, pancreatic, or gastroesophageal cancer.
- In France (n = 1), Germany (n = 2), and the UK (n = 5), guidelines were generally even more conservative:
  - **HAS** did not recommend multigene testing for breast cancer.
  - The **G-BA** announced in 2023 that they would review multigene testing in breast cancer, to update **IQWiG's** guidance in 2016, which did not recommend testing for breast cancer.
  - Guidelines were not identified for **HAS**, the **G-BA**, or **IQWiG** for any of the other solid tumours assessed.
  - **NICE** had published guidance recommending multigene sequencing for breast cancer but did not recommend multigene testing for lung or prostate cancer. Multigene testing was under review for ovarian cancer, and no guidelines were identified that were specific to colorectal, pancreatic, or gastroesophageal cancer.
  - In cases where multigene testing was not recommended, this was generally due to alternative methods being available.

Discussion

- Although multigene testing has the potential to provide patients with improved clinical outcomes, this review showed that published guidance does not always support its use.
- Reasons for patients not receiving multigene testing are numerous (**Figure 1**).[19]
  - At a national level, patient access to testing is often dependent on cost, and the actionability of testing (i.e., whether a treatment or access to a clinical trial is available for a specific biomarker result).
  - Other barriers may include infrastructure not always being available to support widespread multigene testing, as well as limited awareness and education among healthcare professionals.[19,20,21]
- This review focused on published guidelines; however, an additional review, assessing whether large-scale observational research can confirm this finding, is required. Furthermore, the clinical and economic implications of differing CGP testing practices between geographies should be investigated to understand whether patients truly benefit from multigene testing in geographies where it is more available.

Figure 1. Potential Barriers to Receiving Multigene Testing[19]



Conclusions

- A more conservative approach to multigene testing appears to be taken in Europe than in the US.
- Although general European guidance provided by ESMO is in favour of testing, this is only in cases where the cost and clinical benefit to the patient is deemed acceptable and is often dependent on indication.
- HTAs and National health authorities were even more conservative in their recommendations than ESMO, with most not recommending multigene testing because other well-established and less-expensive methods are available.
- Subsequent literature reviews are needed to confirm (1) whether large-scale observational studies can confirm that multigene testing is more available to US patients than European patients, and (2) whether this has an impact on real-world clinical and economic outcomes in different locations.

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