Health technology assessments for personalised medicines: Are current methodologies suitable for the assessment of personalised therapies?

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Objective
An increased drive towards personalised healthcare and medicine by policy-makers, alongside technological advances in medicines and diagnostics, is leading to more personalised medicines being developed.

Given that personalised medicines differ from traditional medicines in their development, use and cost, it is believed that current health technology assessments (HTA) methodologies are not designed to appropriately evaluate these technologies. This research was conducted to provide insights on methods for evaluating personalised medicines and what modifications to current HTA processes would be needed to ensure robust and timely assessment.

Methods
Qualitative interviews were conducted with six experts in personalised medicine and market access across the UK, US and Germany:

- Professor, IGES Institute, Germany
- Vice President, Consulting, Quintiles, Germany
- Past Chairman, Scottish Medicines Commission, UK
- Professor Health Economics, NICE Committee Member, UK
- Health Economist, Scottish Medicines Commission, UK
- Practice Lead, Consulting, Quintiles, US

Discussions covered the movement towards personalised medicines as well as the process by which they should be evaluated by reimbursement authorities. Insights into data collection and presentation as well as diagnostics, were supported with secondary research and used to provide suggestions on how the structure and methodology of personalised medicine assessments would need to be altered.

Results

Companion or post-hoc diagnostics

It was evident from the interviews that there is differentiation in how products are assessed depending on whether a) the diagnostic techniques used to stratify patient populations were embedded in clinical trials for the drug from the outset (true companion diagnostics) or b) diagnosis were developed to support sub-group analysis (post-hoc diagnostics).

The assessment of diagnostics was considered in two dimensions, technical accuracy and clinical benefit. The parameters for assessing a diagnostic test itself for its technical accuracy are well established, relating to accuracy, specificity, false positives etc.

In terms of clinical benefit, the consensus was that companion diagnostics which were integral to the trial were usually sufficiently supported by evidence and therefore can be assessed alongside the drug through the established HTA process.

However respondents agreed that post-hoc diagnostics presented a greater challenge. A number of reasons were given for this, including insufficient power of sub-populations for robust assessment because of the lack of statistically significant efficacy and tolerability data and no evidence of biologic plausibility to show that the response in the subgroup population was not simply a chance association.

This has given rise to a perception amongst payers that the introduction of post-hoc diagnostic tests is an attempt to gain a premium price for a product that otherwise would not be able to achieve it. (It was however recognised that defining a population using a diagnostic test created a target population that was more robust than other segmentation methods.)

Cost of tests and impact on budgets

Another consideration is how to assess the cost to the health system as a whole of conducting relevant diagnostic tests. With increasing numbers of tests being conducted, there is an incremental cost to the health economy, which may or may not be accounted for in the cost benefit analysis of the product it is supporting.

The direct costs of such tests was considered clear, in that the total number of tests undertaken to uncover a suitable patient would be included in the total cost of the test. Less clear were the costs associated with widespread administration of the test.

Opinion was divided as to whether overall costs for diagnosing and treating a particular condition would rise (due to the increased volume and frequency of tests) or decrease (due to more effective treatment, improved outcomes leading to efficiencies in delivery and streamlining of processes). This is starting to be addressed by reimbursement authorities although not consistently.

In Scotland, where the Scottish Medicines Consortium only accesses medicines, a separate organisation is being established to assess companion diagnostics. The group would act as an advisory panel, so those with budgetary responsibility would ultimately make the decision on whether a test is offered. The process itself would be initiated either through a request by SMC as they assess the drug itself or receiving a request from physicians who wish to use the test at specific centres.

In these assessments, the cost of the test will be included in the net cost of the treatment package and the cost of the test would follow the direct cost method mentioned above. Germany has recently started classifying stratification tests as part of the diagnostic process rather than the treatment for assessment purposes. This has the potential to benefit the manufacturer because the budget impact and cost-effectiveness is reduced if the test is no longer a factor in the cost of the treatment. It would not however change the economic burden of testing on the whole health economy.

Type of analysis

Where intention to treat analysis is used for example in Germany, there are also issues of unaccounted bias due to patient crossover (when patients in the comparator treatment experience disease progression and therefore are moved into the experimental treatment arm). This occurs often within oncology trials and can lead to clinical benefit being under-represented.

Therapy areas

It was observed that personalised medicine is predominantly occurring in oncology due to more advanced diagnostics in this area as compared to, for example, mental health. It is likely that this is driven by the emotive nature of cancer and the high cost of treatment in this area. There is however an expectation that personalised medicine would move from the oncology space as techniques develop and budget pressures continue. Interviewees agreed that uptake of diagnostic tests to stratify patient populations is likely to be driven by clinicians.

Conclusions

The increasing number of personalised medicines reaching the market has created new demands on HTA bodies. Whilst some are adapting in response to the challenge, others are still trying to catch up.

For pharmaceutical companies bringing a product to market, we would advise the following steps:

- Ensure any subgroup analysis is sufficiently robust to support the proposition of clinical benefit
- Make a realistic appraisal of the burden of testing on the health economy as a whole
- Engage with clinicians to establish that a new marker is positioned appropriately and that the advice to payers is consistent

References