When Personalised Medicine Meets HTA: Are We on Target?

Oliver K

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One of the greatest American novels – *To Kill a Mockingbird* – is set in the Deep South of the United States and is a story of racial injustice and the destruction of innocence. The hero of the novel is a lawyer called Atticus Finch and at one point in the book he turns to his young daughter and offers her this crucial piece of moral advice.

He says: “If you can learn a simple trick, you’ll get along a lot better with all kinds of folks. You never understand a person until you consider things from his point of view, until you climb into his skin and walk around in it” [1].

It is important for all stakeholders in the brain tumour journey to symbolically climb into someone else’s skin, or put on another person’s shoes and walk around in them, so they can look at things from another point of view.

### A Brave New World

These days, the patient’s point of view is often quite well informed based on a much more pro-active role in their treatment decisions. Many are fully aware that we are entering the brave new world of stratified medicine and targeted therapies.

As patients and their advocates, we should consider what the challenges of Health Technology Assessment (HTA) might be in relation to targeted therapies.

The National Cancer Institute’s definition of targeted cancer therapies is: “Drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression” [2].

With targeted therapies comes the necessity for companion diagnostic tests to determine if a particular therapy is relevant to an individual’s biomarkers.

Patients are beginning to recognise that marrying a diagnostic test to a treatment is a new and important approach for developing and implementing innovative neuro-oncology drugs.

Many patients are also acutely aware through popular media reports that the key health policy tool for managing the introduction and use of targeted therapies and companion diagnostics in the community is HTA.

So on the one hand we have the brave new world of targeted therapies but on the other hand the rather blunt tools that HTA currently uses to determine cost effectiveness.

### What Levels of Evidence?

What levels of evidence will HTA use for targeted therapies? HTA likes traditional phase-III randomised controlled trials with thousands of patients providing masses of data on which to base not only clinical effectiveness but cost effectiveness as well.

How will HTA cope with targeted therapies that only produce trial evidence from much smaller patient cohorts? Will the same historic HTA principles and methodology still apply or will a new model of assessment be needed? As patients and their advocates, we believe that evidence developed through qualitative research – which might not have been considered previously – may now need to be incorporated into HTA, particularly for the much smaller brain tumour patient populations which will be the recipients of targeted therapies.

It will be more important than ever for HTA to not only worship more warily on the altar of the randomised controlled trial but to look at new ways of accepting different kinds of evidence.

### Real-World Patient Data

For example, incorporating real-world brain tumour patient data into the HTA process will better reflect the patient’s lived experience and capture dynamic, extended data that is not available by any other means.

Real-world data can also inform pharmacovigilance. As brain tumour patients and caregivers, we are not only interested in whether a drug works or not, although of course it is crucial that a drug is effective. But we also need to know specifically how it impacts on people’s lives in terms of side effects for example.

Obviously, work needs to be done on ways of turning the experiential reports of the patient into the measurable, evidence-based assessments needed for good HTA.

The patient view on side effects, quality of life, and what really represents innovation and value for them should carry just as much weight in an HTA appraisal for a targeted therapy as the scientific data. And there should be tools created to fairly and accurately measure these aspects. Educating patients about how these tools work is also crucial so they better understand how their real-world data is captured and interpreted by HTA.

Speaking of value, any value-based pricing assessment mechanism must fully incorporate the patient perspective.
What Is Really Valued?

These days, we seem to know the cost of everything but not always the value of everything. We need to change that and think about what really matters to patients and caregivers.

My husband and I cared for our son for seven-and-a-half years after he was diagnosed with a brain tumour, and the notion of healthcare delivering value was something which constantly impacted his life and ours.

We highly valued a chemotherapy which could be easily and conveniently taken at home as a capsule.

We put high value on a therapy which allowed our son to return to work for a while and be a contributing member of society rather than a consumer of expensive healthcare resources.

We welcomed the value of a newer epilepsy medication for our son which did not cause him to break out in spots, making him self-conscious in front of his friends, as the older medication he was originally taking did.

What About Companion Diagnostics and HTA?

Will results from companion diagnostics for targeted therapies be reliably replicated and consistently and accurately interpreted from country to country, lab to lab, so that not a single patient who is appropriate to that treatment will mistakenly be denied access?

Even for one targeted therapy there may be different diagnostic tests or varying methods of conducting these tests. Tests may be given in different sequences or have different cut-off points between labs A, B, and C.

What about the supply of a new molecular drug when diagnostics are subject to such variables, or if a diagnostic is not 100% accurate?

With this in mind, how will diagnostics be subject to HTA scrutiny?

How does HTA view stratification? Will there be criteria in place to evaluate the credibility of subgroup analyses? And how will the move towards a more value-based healthcare system affect, and be affected by, stratification?

One of our fears as patient advocates is this: that personalised medicine will become exclusive medicine where, based on genetic profiling, targeted therapies and companion diagnostics create “haves” and “have-nots” in the patient population.

How can we all ensure that academic institutions and industry are incentivised to develop innovative medicines to treat the “have-nots” as well as the “haves”? Does HTA have a role to play in this scenario?

What about patients who defy their genetic profiling and despite scientific belief, do well on a targeted therapy that officially was not meant to work for them? There are always exceptions to the rule. How will HTA grapple with this possibility?

And while HTA is working out the complex methodological issues required to jointly assess a diagnostic and a targeted treatment, what do we do about patient access to therapy in the meantime? We must ensure that any shift in methodology happens as swiftly as possible because there are always patients waiting for treatment.

Patients Are Willing to Share Their Medical Data

Finally, it is important to dispel one of the myths that may be holding back innovative development of new targeted therapies.

Despite belief to the contrary, patients are actually quite willing to share their personal medical data for the advancement of science.

This fact was highlighted by a 6-country survey of patients and the general public carried out by pharmaceutical company Eli Lilly as part of their new global initiative called “Patient Access to Cancer care Excellence” (PACE) [3].

The “PACE Cancer Perceptions Index” found that 89% of the total general population surveyed (nearly 4500 people) would be willing to allow their medical records and test results to be shared with clinicians and scientists who are doing cancer research. However, the survey also highlights the importance of keeping these records secure. Forty-four per cent of those surveyed said security is a worry.

With very small patient subgroups using targeted therapies, the sharing of patient data will be absolutely critical across not only countries but continents. Digitalisation of information will make this easier.

Walking Around in Someone Else’s Shoes

Clearly, we need new HTA processes to meet the challenges of innovative targeted therapies, companion diagnostics, digitalisation, and what constitutes value. We need new relationships, new partnerships, and new understanding.

And maybe what we also all need is someone else’s shoes in which to walk around for a while, and understand other peoples’ perspectives.

Disclosure

KO serves as a patient advocate on the Global Council for the PACE initiative.

References:

Correspondence to:
Kathy Oliver
International Brain Tumour Alliance
PO Box 244, Tadworth, Surrey KT20 5WQ, United Kingdom
e-mail: kathy@theibta.org