Drivers and resistors of acceptance of single arm data

ACHIEVING EARLY ACCESS IN ONCOLOGY WITH NON-COMPARATIVE DATA

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Introduction

An increasing number of oncology drug candidates are gaining regulatory approval based on non-comparative phase II trials. This creates a number of hurdles for pricing and reimbursement but in an ever-changing healthcare environment, payers, HTA agencies and manufacturers have adopted increasingly flexible stances to ensure that patients can gain access to promising new oncology drugs.

Market Access Transformation recently met with current and former HTA and payer experts from France, Italy and the UK to discuss early access in oncology based on non-comparative evidence and the associated challenges and opportunities for drug developers.

In Part 2 of this 3-part series, we explore the drivers and barriers to the acceptance of single arm data along with some recent assessments in France, Italy and the UK.

UNMET NEED AND LACK OF RCT FEASIBILITY ARE KEY DRIVERS FOR THE ACCEPTANCE OF SINGLE ARM TRIALS FOR ONCOLOGY MEDICINES

While HTA agencies prefer data gathered through head to head clinical trials, they will accept single arm data in specific circumstances. Where there is a high unmet need, for example because there are limited or no other effective therapeutic options against which to compare a new oncology drug, single arm trials are seen as acceptable as former national and regional payer in Italy, explains “The drivers of acceptability include unmet need, the lack of alternatives the relatively small number of patients meaning a limited budget impact……the main driver is unmet need. We are able to take into consideration relatively weak data because there is [only] a comparison with a relatively weak benchmark”.” Moreover, AIFA appreciates that, for certain diseases the patient population is too small for a robust head-to-head trial to be conducted. “This is the case of orphan drugs where it is difficult to enrol many patients and there are few pragmatic options to construct a head-to-head trial.”

The promise of survival benefit is also key as the French HTA expert, ex member of the Transparency Commission in France, comments “If you achieve a very good response rate, for example compared to standard of care or an overall survival which is above six months improvement compared to real world evidence, there might be more flexibility. If you have two months or less improvement compared to real world evidence with a single arm trial it is likely to be heavily challenged.” The endpoints on which main benefit was demonstrated are also important “There is a hope for cure or at least very long remission if you achieve a very deep response. If you have partial response when there is too much uncertainty and partial response as well as overall response are not well recognized by the committee as meaningful endpoints, they’re supportive for sure, but they don’t drive the process.

OPTIMIZING INDIRECT COMPARISONS IS KEY TO INCREASE THE VALIDITY OF THE SINGLE ARM DATA

In the absence of head to head comparisons some HTA agencies accept indirect comparisons. Ensuring the robustness of the non-comparative clinical data should be an important part of the access strategy. Italian HTA expert advises manufacturers to consider their approach carefully "…another point is how robust the single arm evidence is…we need to find some benchmarks to minimize the biases and the weakness linked to an indirect comparison.

A similar approach has been adopted in the UK, and timely planning to identify data sources to support indirect comparisons is key, as noted by former member and chair of the NICE technology appraisal committee, "With drugs licensed on single arm studies, you have to get a comparative population and try to make the data as robust as possible. Think early about what registries you can tap for data." Gathering early HTA advice is also advised at this stage to inform how to create the most reliable data package possible. As the UK HTA expert further explains "Engage early with NICE and with NHS England about your plans, early engagement usually means that both NICE and the payer can give you very direct and valuable feedback as to how to shape your proposal."

PRICING AGREEMENTS AND FLEXIBILITY CAN OVERCOME HURDLES ASSOCIATED WITH SINGLE ARM DATA

Another approach to overcome the hurdle of single arm data is to offer a more flexible pricing package, as the Italian HTA expert comments " For products developed in a single arm trial, approvals are conditional because and are re-evaluated after two years". A flexible position [is taken in order to account for any upfront errors in assessment and allow for adjustments based on increased experience following an evaluation. "

This flexibility on pricing and reimbursement is something that this encouraged by NICE, with approval via the Cancer Drugs Fund being reviewed after a period of time as the UK HTA expert explains "The Cancer Drug Fund may [give] early access … After a period of such access, maybe two or three years a final decision is made as to whether NICE will approve routine commissioning or not."

Access under routine commissioning by NHS England is also not out of bounds, provided the manufacturer is willing to compromise on price as the UK expert adds "There are examples where you can get into routine commissioning, [for example] blinatumomab for minimal residual disease patients after induction chemotherapy in acute leukemia is in routine commissioning based on a single arm study, nivolumab in Hodgkin's lymphoma. Likewise, lorlatinib for ALK-positive lung cancer. It very much depends on how keen the manufacturers are to get into routine commissioning. The Cancer Drug Fund one could say answers is uncertain place because you may get early access but if the promise isn't borne out, then you'll get a no from NICE later on."

In the face of high unmet need, promising early data and/or limited effective comparators for the trial population, HTA agencies have adapted their approach to ensure that patients can get access to the most promising drugs in a timely fashion. However, while the hurdles may have been lowered, the burden is still on the manufacturer to prove ongoing efficacy and value for money in the longer term or adapt their price accordingly.

About Market Access Transformation (MAT)

Founded by industry veterans, MAT specializes in developing cutting edge technologies that enable the healthcare community to gather and exchange insight that assess the real-world potential of their products. MAT offers an online, information exchange platform, Rapid Payer Response™ (RPR), that is revolutionizing the way to global payer insights.

About Rapid Payer Response™ (RPR)

Rapid Payer Response™ (RPR) is an agile, on-demand platform that allows you to conduct faster, higher quality, more insightful research via direct payer engagement. Through our global payer network, it is possible to gather more accurate, robust feedback by probing further and asking deeper questions at any time, ensuring you always have the exact answers you need in a fraction of the time and cost of a traditional payer research project.

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