Pharma Funding for Patient Advocacy: Unethical or a Necessity?

Description

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INTRODUCTION

In three reports starting November 24, 2014[1] Global News questioned the ethics of relationships between patient support groups and pharmaceutical companies making expensive drugs for which Canadian patients want financial coverage through provincial drug plans.

The Global News reports did, however, bring atypical hemolytic uremic syndrome (aHUS) to public attention, along with the serious issue of the frequent lack of access to new expensive drugs for rare diseases that exists in Canada. The drug for which aHUS Canada[2] wants financial coverage is eculizumab, which costs half a million dollars per year for a patient's lifespan.

This commentary addresses some of the difficulties faced by groups supporting patients with rare disorders in trying to convince provincial governments to include new expensive drugs in public drug plans.

THE DISEASE: ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS)

aHUS is an extremely rare, life-threatening, chronic, progressive, genetic disease that can damage vital organs. It affects 1-2 individuals per million,[3] which means that there are less than 100 sufferers in Canada. aHUS can occur at any age, although just over half of those affected are children.

aHUS is caused by mutations to genes that produce proteins that control part of the body's complement system, called the alternative pathway, which is part of the immune system. The pathway is always active to be ready to attack invading diseases. The proteins produced by a normal complement response protect the body, but if one or more of the proteins are defective, the response is also directed against cells of the body, such as the lining of blood vessels. When blood vessels are damaged in this manner, a clotting system is activated. The clotting affects the function of various vital organs including the kidneys, brain, lung, heart, stomach, muscles and bones.

aHUS most often targets the renal system. The clotting prevents proper renal functioning, leading to kidney damage that can result in complete renal failure.

PROGNOSIS

aHUS patients have a poor prognosis, with a mortality rate of up to 25% and progression to end-stage

renal disease in 50%.[4] When the kidneys stop working, dialysis is required to remove waste products from the blood.

Although dialysis is necessary to sustain life, it is also associated with significant morbidities and worsening prognosis.[5] Kidney transplant is not a viable option for aHUS patients without the availability of an effective treatment for the disease because, when it has been performed, aHUS recurred in 60% of the patients and transplant failure occurred in more than 90%.[6]

Not only is the mortality rate high in aHUS patients, their quality of life is also poor. In addition to renal complications, they suffer from fatigue, hypertension, neurological impairme nt, and gastrointestinal disorders.[7]

TREATMENT

No cure exists for aHUS. Plasma exchange has been the traditional therapy. This involves withdrawing blood from the patient, removing the damaged plasma, replacing it with donor plasma, and transfusing the blood back into the patient.

Plasma therapy does not treat the underlying disease and there are no controlled trials of its efficacy or safety in aHUS. In addition, it is associated with significant safety risks including hypotension, infection and thrombosis.[8]

THE MEDICATION: ECULIZUMAB (SOLIRIS)

Eculizumab, which blocks complement activation, has been shown to be efficacious and safe (when appropriate protection against certain infections are used) against aHUS and to improve patient quality of life.[9] Studies have also shown that aHUS patients treated with eculizumab had improved kidney function, reduced blood vessel damage, decreased risk of blood clots, and were able to discontinue plasma therapy and dialysis.[10]

For the first time, eculizumab offers the potential to change the course of the disease and to provide a real opportunity for successful transplantation in aHUS patients on chronic dialysis.

HEALTH CANADA REVIEWS

Eculizumab was originally reviewed by Health Canada as a new active substance for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), another extremely rare life-threatening disease for which no other drug exists. Since the benefits of the drug outweighed its adverse effects, the drug was given a Notice of Compliance (NOC) in January 2009. The approval was based on a randomized placebo-controlled study and interim results from two open-label trials.

In March 2013, the manufacturer of eculizumab received an NOC with Conditions for the treatment of aHUS in response to a Supplement to a New Drug Submission application based on open-label studies of small numbers of patients. The Conditions included the submission of the final results of an ongoing study and appropriate post-market safety monitoring, including the establishment of a Canadian patient registry.

COMMON DRUG REVIEW (CDR) ASSESSMENTS

Eculizumab for PNH was reviewed by the CDR which, in 2010, recommended that the drug "not be listed."[11] The reason for the recommendation was that eculizumab was not considered to be cost-effective without a substantial reduction in its price. Despite the CDR recommendation, eculizumab for PNH is now covered in all provinces and territories.[12]

In January 2013, the manufacturer of eculizumab submitted an application to the CDR for its use in aHUS. The review committee noted that no randomized controlled trials were identified so that its assessment was based on three uncontrolled studies. The CDR decision was again that the drug "not be listed" because "the clinical benefit of eculizumab could not be adequately established."[13] Numerous case reports demonstrating the benefits of eculizumab and expert opinions that the drug represents a breakthrough in aHUS seem to have no role in the CDR evaluation. So far, only Quebec has approved funding for the drug.

Transparency exists around the CDR assessment with information about reviews being posted online. However, the criteria used are rigidly focused on results from randomized trials, which are frequently difficult to undertake in rare diseases due to small potential numbers of study participants and, where there are no effective treatments, an unwillingness to be randomly assigned to what might be a placebo.

The failings of the CDR approach when evaluating the cost-effectiveness of drugs for rare diseases has been criticized for several years and proposals to take a broader perspective in the assessment have been ignored.[14] [15] The National Institute for Health and Care Excellence in the United Kingdom, which tends to take a more comprehensive view than the CDR, has recently recommended funding for eculizumab for aHUS due to the drug having a cost-effective benefit of "a magnitude rarely seen for any new drug."[16]

PAN-CANADIAN PHARMACEUTICAL ALLIANCE NEGOTIATION AND PROVINCIAL REVIEWS

Once a drug has received a recommendation from the CDR, it may go through a price negotiation phase under the pan-Canadian Pharmaceutical Alliance (pCPA), which is a non-transparent process[17] established by the provincial and territorial Ministries of Health that fund and oversee it. The pCPA's principal objective is to capitalize on the combined buying power of all provinces and territories[18] to achieve lower pricing of drugs. Its other aims include improving the consistency of drug listing decisions across Canada and reducing duplication in provincial negotiations.

However, each province is not mandated to list a drug that has been successfully negotiated through the pCPA, so a listing agreement in all provinces is not guaranteed. Each jurisdiction is free to negotiate further price or other concessions from the manufacturer before an agreement is signed, which appears to thwart the objective of consistency in listing decisions. There is also no formal process to prioritize important, potentially life-saving drugs.

Once a drug has gone through the pCPA, provinces perform their own reviews of the product. These reviews are also generally non-transparent and are contrary to the pCPA aim of reducing duplication.

The absence of transparency in the pCPA negotiations and provincial reviews raises questions as to what considerations are taken into account when reviewing a highly expensive drug, like eculizumab, for a rare disease, such as aHUS. For example, does the lack of randomized placebo-controlled trials

negate all other evidence?

In today's healthcare environment in Canada, patient support groups are essential. Patient groups provide education, support and encouragement to their members. When required, they also perform advocacy activities to ensure better access to care and treatment that patients need but the healthcare system is not adequately providing. Without appropriate policies to provide fair access to new drugs for rare disorders and under circumstances where provinces use every reason not to fund expensive drugs, we should not be surprised that advocacy has become a major endeavour.

Has account been taken of the facts that the current plasma therapy for aHUS has limited effectiveness and that its benefits and risks have also not been established with controlled trials? Is cost the only factor of importance?

PATIENT SUPPORT GROUPS

In today's healthcare environment in Canada, patient support groups are essential. They vary from those that consist of a few committed patients and caregivers with little knowledge of how to make an impact to groups with fully staffed national and regional offices, a fund raising program and a defined strategic plan.

Patient groups provide education, support and encouragement to their members. When required, they also perform advocacy activities to ensure better access to care and treatment that patients need but the healthcare system is not adequately providing. Patients with rare diseases likely have a greater need for support due to their isolation.

NEED FOR ADVOCACY FOR DRUG ACCESS

Canada's provinces do not have comprehensive strategies for making drugs for rare disorders available and affordable.[19] However, as greater numbers of these drugs are approved and with more in the pipeline,[20] the provinces need to rapidly develop processes to make them available to patients in a nondiscriminatory and transparent way.

At present, coverage approval seems frequently to be based on the squeaky wheel gets the grease approach in which those who shout loudest and longest gain government attention. Large groups of patients represent a lot of voters and may find it easier to get attention, but less than 100 aHUS patients spread across the country have more difficulty.

Without appropriate policies to provide fair access to new drugs for rare disorders and under circumstances where provinces use every reason not to fund expensive drugs, we should not be surprised that advocacy has become a major endeavour. For example, the Ontario Public Drug Program currently accepts submissions of patient evidence fr om 84 advocacy groups.[21]

All patient groups need funding in order to be able to provide the support, education, encouragement and advocacy required by their members. No matter how large a group is, to expect its members to contribute more than a fraction of the amount needed for its programs is folly. Therefore, patient groups must look for other sources of funding and they turn to the manufacturers of the drugs that they want governments to cover.

Forty-three of the 84 advocacy groups recognized by the Ontario drug plan report accepting company funding.[22] These relationships are, of course, symbiotic since manufacturers also want governments to provide coverage for their products.

Should the ethics of the receipt of funds from a pharmaceutical company by a patient support group lobbying for coverage of the company's drug be questioned, as suggested by Global News? Not when the use of the money is unrestricted and the relationship is transparent, which is the case for aHUS Canada.

In fact, given the desire by governments to not pay for expensive new drugs, industry funding is a necessity because other sources do not exist. Without funding, patient groups could not offer support and services to their members or mount the strong lobbying strategies for drug coverage that are so frequently needed.

CONCLUSION

What the media should be asking when examining issues around provincial drug coverage is:

- Why do CDR's cost-effectiveness evaluations not take a broader perspective for drugs for rare diseases?
- Why is there such a lack of transparency in the pCPA negotiations and provincial reviews?
- Why is there no public information regarding the budgets of the CDR, the pan-Canadian Oncology Drug Review, or the pCPA? How can taxpayers assess whether these organizations, which are funded and overseen by the provinces, provide value for money?
- Why, in a wealthy country like Canada, is there such a need for patient support group advocacy to obtain financial coverage for drugs that could significantly improve the quality and quantity of life for patients with rare diseases for which there are no real alternative treatments?
- When will the provinces introduce fair and transparent processes to make new drugs for rare disorders available without the need for patient support group advocacy?
- Why do billions of taxpayers' dollars continue to be squandered by provincial governments supporting activities that have poor financial oversight leading to wasteful spending,[23] or that are politically motivated,[24] while patients in need of life-changing drugs go untreated?

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