



The fight for a life-saving drug: a personal perspective

Mary Lander

A diagnosis of meningioma presents challenges but more so when you discover that mifepristone, which could halt the growth of the tumour, is unapproved in Australia

Medical practitioners often face the difficult challenge of delivering unpleasant news to patients. When my doctor used the words “brain tumour”, like most people who have to deal with that diagnosis, I found it difficult to comprehend anything else for a few moments. However, the word “benign” did bring me some comfort. I had had no pain and just a little hearing loss in my right ear so was stunned by the finding.

Over the next few months, I saw specialists for opinions on treatment options for meningioma. It was important for me to gain a better understanding of what I had to deal with and my treatment options and their associated risks.

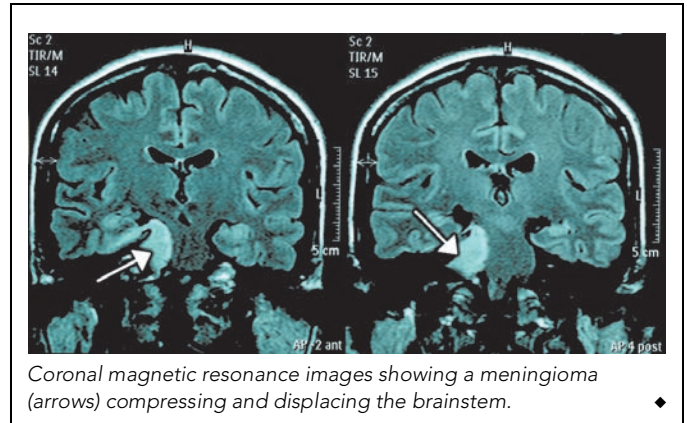
I didn't let family or friends know for some time and needed more information to be equipped to deal with those who might react emotionally, particularly my elderly mother who was convinced my hearing loss was probably caused by ear wax.

It soon became apparent to me that, owing to the tumour's location at the skull base, adjacent to the brainstem (Box), and its involvement with three facial nerves and the carotid artery, removal or treatment was not going to be without considerable risk. While doing some research on the subject, I came across references indicating that a high percentage of meningiomas contained progesterone receptors, and there was mention of a drug that could halt the growth of the tumour. The drug was RU486 (mifepristone), the most effective progesterone antagonist available. In overseas clinical studies, it had been successful in some meningioma patients.¹⁻³ In my view, a trial of the drug was a better option than the 50% risk of irreparable damage to my vision through surgery. The uncertainty of the long-term prognosis after stereotactic radiotherapy was also unappealing.

After doing more research on the drug itself, I found that it had extensive medical uses, such as treatment of meningioma, some breast and ovarian cancers, endometriosis and fibroid tumours and, in higher doses, its action as a glucocorticoid antagonist in Cushing's syndrome.⁴ Research on the drug's myriad medical uses had been plagued by controversy. Why? Well, apparently because progesterone is the hormone necessary to sustain a pregnancy, and not interfering with it is considered to be sacrosanct by the powerful antiabortion lobby groups. As a result, research into and clinical trials on the drug's other uses have been hampered and delayed.

I contacted the Feminist Majority Foundation and the Association of Reproductive Health Professionals in the United States and had several email conversations with their representative. The insights provided were invaluable, and we maintained regular contact for some time. I will always be grateful for the information and support she provided at that time.

When I looked into the drug's availability in Australia, I came across a story on the website of the Australian Broadcasting Corporation titled “No room at the inn for RU486”, posted only a few months earlier in November 2004. It included dialogue with representatives of the Minister for Health and Ageing. In closing, the message to those who were interested in the drug being made available in Australia was “don't hold your breath”.⁵



Coronal magnetic resonance images showing a meningioma (arrows) compressing and displacing the brainstem.

I had a tumour growing in a confined space that threatened to compromise the functioning of vital nerves and life itself. I understand there is about a 1 : 50 000 chance of a diagnosis of meningioma and 20% of these are at the skull base, therefore a 1 : 250 000 chance of diagnosis of a skull-base meningioma. What are the chances of having a diagnosis of meningioma while working in the Department of Health and Ageing, as I was at the time?

There was no point in raising the issue internally. I was acutely aware of the precarious position I was in, but, nonetheless, I had to do something about this issue. After giving the matter some thought, I contacted Senator Lyn Allison, the leader of the Australian Democrats, who made some enquiries in Parliament via Questions on Notice to the Minister for Health. I was later provided with a copy of the response. The government knew the drug could be used for a range of serious medical conditions and advised it could be obtained through the Special Access Scheme of the Therapeutic Goods Administration (TGA). I thought it peculiar that the government knew this, but did not make that information public to ensure patients and doctors were also informed.

I contacted my general practitioner with the details, and she lodged an application with the TGA. On 7 September 2005, Senator Allison gave a speech in Parliament titled “Matters of public importance — mifepristone”.⁶ The campaign to amend the legal status of the drug was subsequently launched. Thankfully, Senator Allison had the courage to take on this enormous challenge and the breadth of vision to do so in the interests of public health.

The day after Senator Allison's speech in Parliament, the TGA issued a permit to my GP to import the drug to treat my tumour. I was elated and spent the next month and a half trying to track down overseas suppliers, with the help of a local pharmacist. When I obtained those contact details, I then saw my GP again so we could get the importation under way. At that point she advised me that she had decided not to proceed, because of medical indemnity insurance issues. I offered to get a lawyer to draw up a personal indemnity. She refused the offer.

My GP gave me a copy of the letter which accompanied the permit. It was signed by a “delegate of the Secretary” and dated 8 September 2005. It stated “All parties involved need to recognise the practice may carry medico-legal risk, and there may be implications regarding indemnity”. Why did the TGA wait until they issued a permit before providing that advice? Clearly, no consideration was given to the impact on the patient who had the rug pulled out from under her feet in an instant. I contacted Senator Allison to inform her of this problem and she raised it at the public hearings in the Senate in December. Senator Allison asked the following question of the Secretary of the Department of Health and Ageing and the head of the TGA: “Could you outline the issues to do with medical indemnity, which I gather are a problem in some of these cases?”. They both replied, “not that we are aware of”. When asked whether the Department had done any studies of the drug, the Secretary advised that they had not. She also advised that the Department was responsible for administering the legislation and believed it did so with “due diligence”.⁷ She claimed there were no barriers for anyone wanting to do research here into the drug’s non-abortifacient uses, but the experiences of some have been to the contrary.⁸

Unknown to most people is the fact that the supplier succumbed to pressures via threats of boycotts by the powerful antiabortion lobby groups some years ago and decided that “... the company would not sanction exports unless ranking government officials in the country urged them to do so ... there must be an actual wish for the licensing of mifepristone in a particular country ... the letter indicated such a wish could come in the form of a written request from a representative, competent body such as the government or health authorities”.⁹

Lobbying during the campaign to change the legislation to allow the TGA to regulate RU486 was intense, and to help raise awareness of the drug’s use as a treatment for meningioma, I participated in some broadcasts, with the help of the Australian Broadcasting Corporation.¹⁰

My contact in the US kindly did a submission for the Senate Inquiry,¹¹ and I later found one from Professor Healy,¹² who wrote the first clinical review of the drug in 1985.¹³ Because of the hard work of many, the parliamentary conscience vote to repeal ministerial responsibility for approval of RU486 in early 2006 was won by a resounding majority. The vote was an important milestone, but there is still a long way to go before the drug will be readily available. The amendment changed the legal status of the drug and allowed a drug company to lodge an application with the TGA for approval of mifepristone for use as an abortifacient. Easier access to the drug will facilitate research and clinical trials into the drug’s uses in Australia, depending on the necessary funding approvals by government. Access to the drug for individual patients and for non-abortifacient uses is, at this stage, only available via the TGA’s Special Access Scheme.

It was over a year after I found out about mifepristone, and nine months after the TGA issued its first permit, before I was finally able to start my treatment, with the assistance of an oncologist who heard of my predicament. He was willing to import the drug and required only my written agreement to be treated with an unapproved drug.

I have now been taking mifepristone for just over a year at 200 mg per day and can say from personal experience that it has very little in the way of side effects, and I am happy to continue with my treatment. It will be another year or so before any

meaningful responses can be measured via magnetic resonance imaging.

A few months ago, I was contacted by another patient with meningioma (diagnosed several years earlier and treated by monitoring of the progress of the tumour). She would have liked to have had a trial of mifepristone, but like most people, thought it was unavailable here. Unfortunately, her vision had deteriorated since her initial diagnosis. I provided her with information, and as a result, she has recently commenced treatment on the drug as well. Why don’t GPs refer patients to oncologists when they refer them to specialists for opinions, especially when standard treatment options carry such substantial risks?

If the Australian Government is serious about “better health outcomes for all Australians”, including those who would benefit from the drug’s non-abortifacient uses, some thought should be given to the people who could be helped by this drug.

Interestingly, in addition to the medical uses mentioned earlier, recent developments in overseas research indicate that mifepristone has potential use in some gastric cancers as well,^{14,15} and it also has viability for use as a helper-dependent adenovirus vector in gene therapy for cancer treatments.¹⁶

The more research I did, the more fascinated by this drug I became. The anti-glucocorticoid effects are dose-dependent, but on the basis of animal trials it has been shown to be neuroprotective¹⁷ and can minimise the adverse effects of ischaemic stroke.¹⁸ Mifepristone can prevent retrograde amnesia induced by electroconvulsive therapy¹⁹ and is currently being trialled for that purpose (ClinicalTrials.gov identifier NCT00285818). In animal studies the drug has been shown to help ameliorate the symptoms of diabetes.²⁰ The drug’s potential use in overcoming the adverse effects of elevated cortisol due to a dysfunctional hypothalamic–pituitary–adrenal axis means it is a potential treatment for Alzheimer’s disease, in which higher cortisol levels are associated with a higher level of impairment.²¹

The US Food and Drug Administration has just approved mifepristone for the purposes of reversing the side effects of corticosteroids and for use in patients with Cushing’s disease.^{22,23} If only a drug sponsor in Australia would consider sponsoring the drug for the TGA’s Orphan Drug Program. This would see it subsidised via a special appropriation until such time as it is made available on the Pharmaceutical Benefits Scheme, which may take up to 10 years for some non-abortifacient uses pending further clinical trials. It saddens me to think that those on low incomes or age or disability pensions would not be able to afford the drug via the TGA’s Special Access Scheme, even if other treatment options are not suitable.

Although the Senate amendment was an important campaign to be part of, and I feel honoured to have contributed, given my personal circumstances, it was a challenge I really could have done without. The next is to be able to continue to pay the cost of this currently unsubsidised drug.

Competing interests

None identified.

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