www.multiplemyeloma.org.nz

5 September 2022

Pharmac
Via email to:
Copy to:

Dear Pharmac

Submission to request funding for daratumumab in relapsed/refractory multiple myeloma

Myeloma New Zealand, a charitable organisation representing New Zealanders living with myeloma, write to request the urgent funding of daratumumab for patients with relapsed/refractory disease.

Myeloma is a relapsing, remitting blood cancer for which currently there is no prevention, screening or cure. Patients therefore rely on drug therapies, and for those with sufficient health status, stem cell transplants. With the exception of expanded access to already funded drugs (lenalidomide maintenance post-transplant and bortezomib unrestricted), there has been no new investment in myeloma treatment since 2014 (Pharmac.govt.nz 2022).

Myeloma New Zealand welcomes Pharmac's expressed intention to improve consumer consultation and input into medicines funding decisions. We provide scientific evidence and rationale for the funding of daratumumab on behalf of our members. Whilst daratumumab in relapsed/refractory disease is the focus of this submission, given ongoing treatment gaps in the management of myeloma we also provide a brief overview of other drugs we believe are critical to fund in New Zealand.

About Myeloma New Zealand

Myeloma New Zealand is a charitable trust established in 2016 by leading New Zealand haematologist Dr Ken Romeril. Our purpose is to focus specifically on myeloma and to improve the quality of life and survival of New Zealanders living with it. We are primarily a patient advocacy organisation, that seeks to empower patients with information, research and support; to advocate with government to allow myeloma patients access to the remarkable treatments that are transforming lives and survival in other comparable countries; and to raise awareness and understanding among the general public of myeloma, the second most common of blood cancers.

Dr Romeril understood that the goal of improving quality of life and survival would require advocating for better treatment options as there was desperate need for better treatments for New Zealand myeloma patients at the time Myeloma New Zealand was established. Since then, no new drugs have been funded. What was a desperate need in 2016 is even more so now, particularly given the number of myeloma treatments approved by Medsafe and appearing on the Pharmac Options for Investment list (Pharmac 2022). Many more options for myeloma patients are also available outside of New Zealand.

In 2019 Myeloma New Zealand appeared before the Health Select Committee with a submission that followed a petition signed by over 2,000 signatories asking for funding for daratumumab, carfilzomib, lenalidomide (for maintenance), pomalidomide, elotuzumab and ixazomib. While lenalidomide was funded for maintenance, these other treatments are still desperately needed.

myeloma new zealand

About Multiple Myeloma

Multiple myeloma (myeloma) is a blood cancer that resides in the bone marrow. It affects multiple sites in the body where bone marrow is normally active in adults, including the spine, skull, pelvis, ribs, shoulders and hips. Sufferers of myeloma experience serious complications including bone and kidney disease, serious infections, and excessive levels of calcium which can lead to confusion, disorientation and weakness (Milne, Boyd et al. 2019).

Each year, approximately 450 New Zealanders are diagnosed with myeloma and the rate is increasing. There is currently an estimated 2500 individuals with myeloma in New Zealand (Milne, Boyd et al. 2019) and approximately 150 a year die from myeloma (Ministry of Health 2016).

Inequity exists in myeloma with Māori and Pasifika reporting a higher rate of diagnosis and a lower rate of survival (Milne, Boyd et al. 2019).

Although myeloma is currently incurable, overseas it is becoming more like a chronic disease for many, and myeloma specialists are now talking about a cure being in sight[1]. We need this to be the case in New Zealand too.

> *More recently, immunotherapy strategies—including the cellular therapies—have allowed us to expand our ability to achieve and maintain measurable residual disease negativity even in the refractory setting. These advances have brought us much closer to a cure for multiple myeloma; clearly, it has become more realistically achievable, challenging the dogma of multiple myeloma as an incurable disease.*[2]

Our goal is for New Zealand patients to live longer, until these newer treatments like CAR T-cell and BiTE are available. Having treatments like daratumumab is essential to achieve this goal.

We note also that a significant focus of Te Aho o Te Kahu (Cancer Control Agency) is to reduce cancer incidence by preventing cancers in the first place. Myeloma is not a cancer that can be knowingly prevented. While we understand that myeloma treatment can be costly, myeloma patients should not be disadvantaged by not having an ability to reduce or avoid their cancer burden.

Significant impact of previous PHARMAC approvals

We would like to draw your attention to a significant improvement in survival that was observed following Pharmac's funding of bortezomib in 2011 and lenalidomide in 2014. Post Pharmac approval of bortezomib and lenalidomide, the five year survival rates increased to 45% from 36% in the previous time period (prior to these two being funded) (Milne, Boyd et al. 2019). We believe that PHARMAC approving funding for daratumumab will also provide life changing benefits for myeloma patients in New Zealand.

Addressing unmet health need in relapsed/refractory myeloma

While we acknowledge that Pharmac operates within a fixed budget, we believe myeloma patients have been substantially let down by a lack of investment over the past eight years. Specifically,

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[1] https://www.ajmc.com/view/is-there-a-possibility-of-a-cure-in-multiple-myeloma-
https://ascopubs.org/doi/full/10.1200/EDBK_349603
https://www.cancertreatmentreviews.com/article/S0305-7372(21)00132-8/fulltext
https://www.lls.org/blog/new-drug-approval-moves-us-closer-long-term-control-multiple-myeloma
https://www.youtube.com/watch?v=kmbWEI2_ILI https://www.youtube.com/watch?v=ujhrqXQgMkw
https://www.youtube.com/watch?v=kmbWEI2_ILI&t=28s

[2] https://ascopubs.org/doi/full/10.1200/EDBK_349603

patients who have relapsed following their initial treatment are currently able to receive funded treatment with thalidomide. Although thalidomide does have its place in myeloma treatment, international myeloma guidelines do not recommend thalidomide (with or without dexamethasone) treatment after first relapse (NCCN 2022). In summary, thalidomide is outdated as a second line treatment. Thalidomide has its place in the myeloma world and we still need it, but in 2022 New Zealanders need much better for a second line treatment.

This submission asks that you fund daratumumab for relapsed/refractory myeloma, to be used in combination with bortezomib and dexamethasone, or in combination with lenalidomide and dexamethasone; or as a monotherapy.

Evidence for daratumumab

The CASTOR trial is the pivotal study for the use of daratumumab in combination with bortezomib and dexamethasone in patients with relapsed/refractory myeloma.

Myeloma New Zealand founder, Dr Ken Romeril, recently reviewed the 3-year update of the CASTOR study (Romeril 2021). The full review is attached below. Key messages from the review include:

- *In the ongoing CASTOR study, after an extended median follow-up of 40 months, triple therapy with daratumumab, bortezomib, and dexamethasone showed improved efficacy outcomes (including PFS, ORR, and MRD-negativity rate) compared with bortezomib and dexamethasone alone.*

- *The most pronounced improvement in response was observed in patients who had one prior line of therapy.*

- *Triple therapy with daratumumab, bortezomib, and dexamethasone showed improved efficacy outcomes compared with bortezomib and dexamethasone alone in patients who were refractory to lenalidomide in any prior line of treatment.*

- *The safety profile remained consistent after a median 40 months of follow-up, emphasising the tolerability and predictability of maintenance therapy with daratumumab alone.*

At a recent European Myeloma Network meeting, Sonneveld et al (2022) reported the final overall survival and updated MRD-negativity and safety results after ~6 years of follow-up of CASTOR (Sonneveld, Chanan Khan et al. 2022). The abstract is attached below. Authors concluded:

- *Treatment with daratumumab plus bortezomib and dexamethasone significantly prolonged overall survival compared with bortezomib plus dexamethasone alone;*

- *The greatest overall survival benefit was observed in patients with 1 prior line of therapy;*

- *These results support early use of daratumumab plus bortezomib and dexamethasone to maximise patient benefit.*

Other treatment considerations impacting myeloma patients

- The absence of publicly funded daratumumab is affecting the ability for myeloma patients in New Zealand to access clinical trials. New Zealand haematologists have reluctantly turned down five trials recently because not enough patients would qualify given prior treatment with daratumumab as a prerequisite. This is extremely concerning because trials have been an essential pathway for patients to access newer treatments. This is also a reflection of how far New Zealand's treatment of myeloma has fallen behind the rest of the developed

world, where daratumumab is the standard of care that newer innovations are measured against.

- One of Pharmac's concerns previously was the lengthy infusion time for daratumumab intravenous treatment. Now that daratumumab is available in a subcutaneous option, this significantly reduces chair time and the burden on hospital day stay clinics.

- Myeloma is a highly individual cancer, with a wide variation in experiences and responses to treatment. Not every drug works for every patient. Patients can have reactions to one drug, or not be able to tolerate another. Together with the relapsing remitting nature of myeloma, this heterogenicity of disease emphasises the urgent need for new treatments, including – but not limited to – daratumumab.

- The increasing ability to understand and predict the likely course of myeloma is already enabling clinicians who have access to funded novel drugs to tailor precise, personalised, combination treatments for an individual patient, rather than a one-size-fits-all approach. This personalised treatment is increasingly seen as the pathway to eventually treating myeloma as a chronic disease, rather than a fatal one.

- With daratumumab, patients benefit for longer, continue working for longer and stay well longer. Patient reported outcomes from the CASTOR trial confirm that health-related quality of life is maintained during the first eight cycles of therapy, with improvements thereafter (Hungria, Beksac et al. 2021).

- Newer treatments like daratumumab, are easier to tolerate than older drugs like thalidomide. Toxicity associated with thalidomide commonly limits its use. Peripheral neuropathy, for example, occurs in one third to one half of patients taking thalidomide for more than three months (Ghobrial and Rajkumar 2003). Furthermore, international guidelines suggest thalidomide only in certain circumstances due to concerns with toxicity (Dimopoulos, Moreau et al. 2021, Moreau, Kumar et al. 2021, NCCN 2022).

- Māori and Pasifika (who are already over-represented in the myeloma population) are less likely to have a stem cell transplant and their overall survival is worse (Milne, Boyd et al. 2019). We need better treatments like daratumumab so these patients are able to live longer on each treatment, with less side effects.

Further treatments needed

We also ask that you consider the serious need to fund:

i. Lenalidomide for frontline induction (as RVD: lenalidomide, bortezomib and dexamethasone);

ii. Pomalidomide, carfilzomib, elotuzumab and ixazomib for relapsed/refractory multiple myeloma.

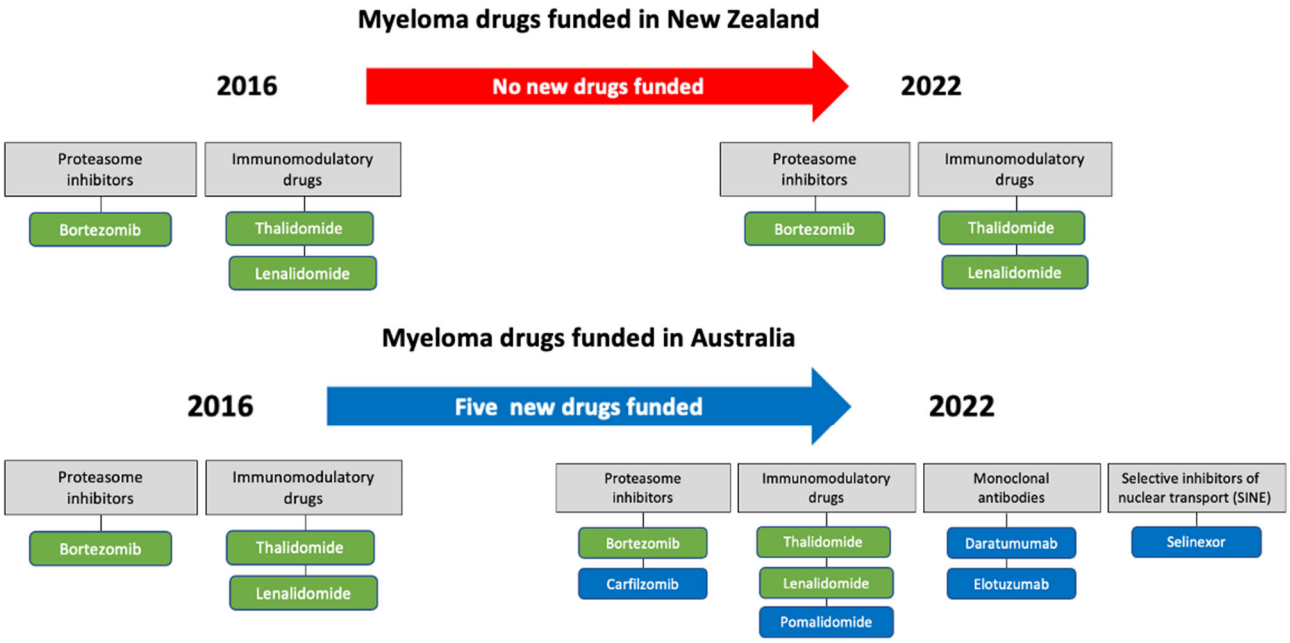
The same reasons as funding daratumumab apply here - we need multiple treatment options, so that clinicians can use the right treatment for each patient and keep patients alive longer.

Current myeloma funding in New Zealand compared to Australia

The 2019 Myeloma New Zealand Burden of Disease report states that New Zealand had a five year survival of 45%. This is compared to the Cancer Council Australia reporting in 2018 that Australia's five year survival was 51%. A difference of 6% means that amongst the 450 New Zealanders who

will be diagnosed with myeloma this year, an additional 27 of them would still be alive in five years if they were diagnosed and treated in Australia instead of New Zealand.

Today, New Zealand myeloma patients are worse off for treatments compared to Australian myeloma patients in 2016. Since 2016, Australia has added daratumumab, carfilzomib, pomalidomide, elotuzumab and selinexor to the PBS. Additionally, Australia funds lenalidomide in frontline treatment (as RVD) (pbs.gov.au 2022). Australia now has five more funded novel myeloma treatments than New Zealand, plus RVD front line, so it is reasonable to assume the survival gap between New Zealand and our closest neighbours will continue to widen.



Fairness issues

Patients with other chronic disease like diabetes are treated for their entire life. Myeloma patients should be able to continue to access treatments as needed and given the chance to keep living, especially given that myeloma is being considered more of a chronic disease in some countries and that there is talk of a cure in sight. Daratumumab being funded will help with that.

The current lack of funding for daratumumab highlights the 'two tier' effect to medicines access in New Zealand. Daratumumab, pomalidomide and carfilzomib are all available privately in New Zealand. It is heart-breaking, hearing from patients who get in touch with us who have run out of options, that they know daratumumab is available in New Zealand, but not to them if they cannot afford private treatment, which for most is out reach.

We have many myeloma patients who thought they were doing the right thing by having medical insurance, but who didn't realise until diagnosed that they are not able to have their treatment funded. We ran an informal survey in our Myeloma New Zealand Facebook group (of 561 active members) and the results are below. Less than half of respondents had private medical insurance and only 5% had insurance that covered all costs with no patient co-pay.

Insurance status	n (%)
No insurance	33 (54.1%)
Have insurance but doesn't cover cancer or doesn't cover enough, or co-pay too expensive, so treated publicly	18 (29.5%)
Have insurance but only covers Pharmac funded drugs (so same treatment as public but nicer hospital and less patients)	2 (3.3%)
Insurance covers some and I pay the rest	5 (8.2%)
Insurance covers everything with no co-pay	3 (4.9%)

The inability to access clinical trials due to a lack of access to prior treatment with daratumumab highlighted earlier in this paper is a further example of unfairness faced by myeloma patients in New Zealand.

We also wish to highlight the inequitable approach to the value of life across healthcare. With life transforming drugs, cost is being put ahead of the value of life. Delivery of medicines is the only health service in New Zealand where the value of a life is weighed against a budget (compared with hospitals, emergency services, ACC, and the pandemic response for example).

As mentioned earlier, Māori already suffer an inequitable burden of incidence and outcomes in myeloma, a situation that is further compounded the longer access to better therapies in earlier lines of treatment are denied.

We have anecdotally heard of patients considering moving to Australia and the United Kingdom where they are able to access better treatments for their myeloma. New Zealanders shouldn't have to move overseas to access treatment which is standard of care across the OECD.

Patient stories

We have attached patient letters, where in their own words they describe the urgent need for daratumumab. They are attached and follow on from this letter. Key quotes include:

> *"Were subcut Dara funded in New Zealand I'm hopeful it would treat me through first relapse, and allow me to keep working in NZ for years to come. I am hopeful from what I've read it would be compatible with work. I'd also like to see my son through high school here, and continue to enjoy time in NZ with my family."*

> *"I was switched to CTD (cyclophosphamide, thalidomide and dexamethasone). I couldn't continue to sustain my busy job so swapped out of my high pressure role to an alternate job, working less hours. I found thalidomide hard to tolerate – especially needing huge hours of sleep, and ongoing tiredness. I was dropped to a minimal dose by the haematologist as I was finding it so hard to get through the week."*

> *"This constant worry about medications and funding is a stress that is so unnecessary and shouldn't be such a big part of our lives while living with an incurable but very treatable cancer."*

> *"People with cancers and chronic diseases are not waiting to die: we are part of the wider community and we are not invisible."*

"In New Zealand we are far behind the rest of the world in regards to treatment for Multiple Myeloma. Many drugs that are used as first line treatments overseas are not even available here. This is extremely concerning as overseas Multiple Myeloma is now a treatable chronic disease. People return to work, leading practically normal lives and contributing to society."

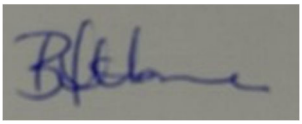
In summary

Myeloma New Zealand have been calling for daratumumab to be funded for a number of years. New Zealand patients are missing out on trials because they have not have access to daratumumab. We are seriously falling behind the rest of the world in myeloma treatment and patients are dying because they lack good treatment options.

We implore you, please fund daratumumab.

If you need further information on our submission, please contact our Trustee, Nichola Oakenfull on or 027 xxxxxx

Yours sincerely



PP 

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Attachments:

- References
- 17 Patient stories (some removed for this public version)
- CASTOR study review
- Sonneveld et al (2022)
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References:

Dimopoulos, M. A., P. Moreau, E. Terpos, M. V. Mateos, S. Zweegman, G. Cook, M. Delforge, R. Hajek, F. Schjesvold, M. Cavo, H. Goldschmidt, T. Facon, H. Einsele, M. Boccadoro, J. San-Miguel, P. Sonneveld, U. Mey, E. H. A. G. C. E. a. guidelines@ehaweb.org and E. G. C. E. a. clinicalguidelines@esmo.org (2021). "Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." Ann Oncol **32**(3): 309-322.

Ghobrial, I. M. and S. V. Rajkumar (2003). "Management of thalidomide toxicity." J Support Oncol **1**(3): 194-205.

Hungria, V., M. Beksac, K. C. Weisel, A. K. Nooka, T. Masszi, I. Spicka, M. Munder, M. V. Mateos, T. M. Mark, M. Qi, X. Qin, J. Fastenau, A. Spencer, P. Sonneveld, W. Garvin, T. Renaud and K. S. Gries (2021). "Health-related quality of life maintained over time in patients with relapsed or refractory multiple myeloma treated with daratumumab in combination with bortezomib and dexamethasone: results from the phase III CASTOR trial." Br J Haematol **193**(3): 561-569.

Milne, R., M. Boyd, H. Chan and e. al (2019). The burden of multiple myeloma: A study of the human and economic costs of myeloma in New Zealand.

Ministry of Health (2016). Cancer: New registrations and deaths 2013.

Moreau, P., S. K. Kumar, J. San Miguel, F. Davies, E. Zamagni, N. Bahlis, H. Ludwig, J. Mikhael, E. Terpos, F. Schjesvold, T. Martin, K. Yong, B. G. M. Durie, T. Facon, A. Jurczyszyn, S. Sidana, N. Raje, N. van de Donk, S. Lonial, M. Cavo, S. Y. Kristinsson, S. Lentzsch, R. Hajek, K. C. Anderson, C. Joao, H. Einsele, P. Sonneveld, M. Engelhardt, R. Fonseca, A. Vangsted, K. Weisel, R. Baz, V. Hungria, J. G. Berdeja, F. Leal da Costa, A. Maiolino, A. Waage, D. H. Vesole, E. M. Ocio, H. Quach, C. Driessen, J. Blade, X. Leleu, E. Riva, P. L. Bergsagel, J. Hou, W. J. Chng, U. H. Mellqvist, D. Dytfeld, J. L. Harousseau, H. Goldschmidt, J. Laubach, N. C. Munshi, F. Gay, M. Beksac, L. J. Costa, M. Kaiser, P. Hari, M. Boccadoro, S. Z. Usmani, S. Zweegman, S. Holstein, O. Sezer, S. Harrison, H. Nahi, G. Cook, M. V. Mateos, S. V. Rajkumar, M. A. Dimopoulos and P. G. Richardson (2021). "Treatment of relapsed and refractory multiple myeloma: recommendations from the International Myeloma Working Group." Lancet Oncol **22**(3): e105-e118.

NCCN. (2022). "NCCN Clinical Practice Guidelines in Onocology: Multipile Myeloma; Version 5.2022, March 9, 2022." Retrieved 16 May 2022, from https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

pbs.gov.au. (2022). "Pharmaceutical Benefits Scheme (PBS) Australia." Retrieved 31 August 2022, from https://www.pbs.gov.au/pbs/home.

Pharmac. (2022). "Priority lists for funding applications - options for investment." Retrieved 1 June 2022, from https://connect.Pharmac.govt.nz/apptracker/s/ranking-lists-for-funding-applications?reportType=OFI.

Pharmac.govt.nz. (2022). "Pharmac Application Tracker." 2022, from https://connect.Pharmac.govt.nz/apptracker/s/.

Romeril, K. (2021). "Research Review Study Preview: Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with previously treated multiple myeloma: three-year follow-up of CASTOR." Researchreview.co.nz.

Sonneveld, P., A. A. Chanan Khan, K. Weisel and e. al (2022). Daratumumab plus bortezomib and dexamethasone versus bortezomib and dexamethasone alone in patients with previously treated multiple myeloma: overall survival results from the phase 3 CASTOR trial. . Poster presented at: European Myeloma Network (EMN) Meeting; April 6-9, 2022; Virtual.

myeloma new zealand

4 September 2022

Dear Pharmac

I was diagnosed with multiple myeloma in June 2020, just after my 41st birthday. This was after three years of many symptoms that had people telling me I was a hypochondriac, including multiple doctors who didn't use those words but who told me to see a psychologist. So I did. I wasted $1000 on a psychologist who tried to help me to get "physical symptoms of stress" to go away. My GP was amazing though and never gave up sending me to specialists and not making me feel bad when I would go to ED in extreme pain. No one could find anything wrong except for telling me my back and shoulder muscles were too tight. My bloods were all at the bottom of normal but ok. Finally I broke my back and that was the last piece of the jigsaw that she needed. I was diagnosed within about two weeks. Unsurprisingly, after starting treatment, these symptoms all went. I wasn't stress, I just had cancer.

My son was six when I was diagnosed. I had a placental abruption when he was born and had to have a GA for his birth. I ended up with post-natal depression and then between 15 months and four years he had nine febrile seizures. You'd think that was bad enough luck but then at almost five he had what appeared to be laughing seizures, three of them. I never thought that three long minutes of laughing could be so terrifying. Having had nine tonic clonic febrile seizures by then we knew what post seizure looked like for him – this was the same with wetting his pants and then the drowsiness. We were told by the consultant (not in ED, through the outpatients consultant paed) that he almost definitely had a hypothalamic hamartoma, they just had to find it. We had five weeks of hell, and they found nothing. We eventually saw a private paediatrician and his view was they were just hypnagogic events, after his first sleep cycle, similar to night terrors.

So when I was told I might have cancer, I asked my GP, is this like when the hospital paediatrician told us my son almost definitely had a tumour and it turned out to be nothing? She said no, this is definitely something. And the hell started all over again, but now I live it every day. I've lost 4cms, lost my hair, but gained over 20kgs of weight. A broken back, not being able to run, months of not being able to eat. I am in Facebook international groups where people constantly say "don't worry, myeloma isn't the death sentence it once was, we have so many treatments now days, it's a chronic disease". But not in New Zealand. That's not true in New Zealand.

I have had full medical cover since I was born. I thought I was doing the right thing. But like most medical insurance in New Zealand it doesn't cover my chemo because medical insurance hasn't kept up with the costs of treatment. So that leaves me with the public system. The haematologists and nurses are amazing, but kindness doesn't keep me alive. Better treatments do. My next line of treatment is thalidomide. That's my second line and that is it. The end of the line. It's 2022!!!!

So I looked into moving to Australia, but it that is going to be too expensive. My husband has a business. He employs staff. He is a builder. We can't just move because he has jobs underway. I work full time. Here we are, contributing to New Zealand, paying taxes. We have given everything but who is there for me? Again, the medical staff are so lovely, but my haematologist can't give me the extra five drugs I would be able to get if I was in Australia. It's so frustrating because I remember a few years back hearing of a couple of cancer patients who didn't have insurance. So I looked into mine and thought I had $200,000 a year. I misunderstood that even though I was on the highest

policy, that was only for if you needed surgery, not for things like chemo. I feel like I tried to do everything right – I pretty much gave up alcohol about seven years ago after hearing it contributes to cancer. I didn't use weed killers because I heard they cause cancer. There I was out with my hot water and dishwashing liquid killing my weeds. It seems laughable now. I still got cancer. I feel like I did everything right and now everything has gone wrong.

I thought once my son grew out of his febrile seizures we could start having overseas trips (stopping breathing and flying over the middle of an ocean don't mix well). How can I do that if I am exhausted all the time from thalidomide and have to give up my job like I hear so many others do? We can't afford to live on just what my husband earns. I'm terrified of how we will cope. I feel like we often don't hear how bad the side effects are because the average myeloma patient is retired and they aren't working. With a friend I started an under 50s group and it's really scary hearing how others who are still working have been affected by thalidomide, knowing that is my next and only option.

I'm a mum of an eight year old. I matter. My son matters. I should have the same right to live longer that myeloma patients in other countries have. I understand we are a small country with a small tax intake. But we spend so much less than other countries per person on health care. I know you personally haven't decided Pharmac's budget, but I need you to fight for me, please. For my son. I don't want to die while he is at school. I don't want to mess up his schooling. I want to help him decide what to study at university, or decide what kind of job he might do, or what country he might live in. I want to show him where I lived in Japan and England, and where his family is from in Europe. I want to take him to Disneyland. Being diagnosed right at the beginning of covid has stolen two years of my life – I need an opportunity to show him the world while I am still alive. I need better and multiple treatment options for that – I need daratumumab, pomalidomide, carfilzomib, elotuzumab, selinexor, isatuximab and ixazomib. We need these to be used in the combinations they are used overseas. Yes this is a lot to ask for, but we have had no new treatments funded for eight years so we are so far behind now.

I got a quote for daratumumab privately and it was $230,000 for the first year and $120,000 for each year after that. Plus nurse/chair charges. I can't afford that. I can't use my kiwisaver because my husband needs it to pay the mortgage after I die. My haematologist told me that when I need to change treatment I should pay $24,000 for pomalidomide (if the compassionate access is still there then) because thalidomide was such a horrible drug. I want to take my son overseas but how can I when I need to pay $24,000 when I relapse for pomalidomide? That's more than what I save in a year anyway. I'd have to try a givealittle. There's no way I could do a givealittle for daratumumab for $230,000 for the first year and then $120,000 a year after that. Plus the hospital charge to give it to me. I just feel so hopeless, it's like I'm in a horrible nightmare.

I want my myeloma to be like the myeloma that patients overseas have. I connected with a New Zealander overseas and she was told to expect nine years to her first relapse and to expect to live 20 to 30 years (which because of her age means she would have a normal life expectancy). I was told two years from my stem cell transplant would be good and 10 – 12 years to live (although I'm not sure how that works because it's not like I'm going to get seven years from thalidomide). How can two New Zealanders have the same disease and have such different outcomes?

I've just had the worst luck with my health and my son's health. I didn't even cover how he was born at 34+2 and had two operations (hernia and adenoids/tonsils). That seems so minor in the big scheme of things. I just want to have the chance to keep living. It feels like everything you watch and read overseas about myeloma now is talking about it being a chronic disease and how a cure is in sight. Please fund the treatments that are needed to keep me going until then. If I was a diabetic you wouldn't treat me for just a few years. I understand myeloma treatments are expensive, but unless

insurance is changed like in the US where they have to let people with pre-existing conditions in (so I could get one of the ones with $500k cover) I only have Pharmac funded treatments to keep me alive. I know this letter sounds desperate and probably comes across as whiny, but when you have only thalidomide left if your tool kit, you do get a bit desperate.

I hate when people say I am fighting cancer, I'm not fighting cancer – I couldn't bear to feel like I was in a battle every day. But I'm doing what I can to fight for better treatments to stay alive as long as I can. This submission was my idea. I'm the one who rallied the troops so to speak. With our amazing team we are doing what we can to change this. I haven't given up and I won't give up. Please fund daratumumab, and please consider all the other treatments we need too.

Thank you so much for reading this.

Regards
Anon

8 August 2022

To Pharmac

My name is Paul Crosbie. I was born and raised in New Zealand and have spent over 25 years working as a pilot with Air New Zealand. I'm married and live with my wife and two young sons in Auckland.

In 2014, at the age of 46, I was diagnosed with multiple myeloma – something I had never heard of before this time. I underwent intensive therapy including high dose steroids, radiation therapy, chemotherapy and stem cell transplantation. Although arduous, I came through this with a complete response and returned to work about 2 ½ years after my diagnosis.

Since then, I've continued to work, raise my family and live a full life. There is, however, one aspect of having myeloma that keeps me awake at night: It will relapse, and when it does my next line of treatment is thalidomide, an option that is simply laughable in any country with a modern health system.

There is also a chance I might be re-treated with the chemotherapy that I had when I was first diagnosed. Either way, there is a substantial gap in available funded treatments for New Zealanders with myeloma. Other countries have access to many options that offer substantially better survival and quality of life than thalidomide or retreatment.

One of these treatments is daratumumab. I see from Pharmac's website that daratumumab and has been assessed and recommended to be funded. This needs to happen with urgency so that people like me get the treatment they need and deserve. Without it, our options are bleak and our ability to continue to work and contribute to our families and society will be unjustly limited.

I urge Pharmac to address this critical need for myeloma patients and act to fund daratumumab with urgency.

Regards

Paul Crosbie

Kia ora. My name is Colin MacDonald. I live in Wellington with my wife Paula and we have 3 grown up children and 3 granddaughters. We are a close family and Paula and I are very involved in bringing up the grandchildren. I am a company director on two Crown company boards and one publicly listed company. I also chair several risk and assurance committees across the public sector.

Paula and I with 2 of our 3 children and our 3 granddaughters

In July 2015, the result of a routine annual blood test turned my world upside down. I was 57 years old at the time and had a demanding job as the Chief Executive of the Department of Internal Affairs.

When I saw that I had raised protein levels in my blood and that this was likely to indicate multiple myeloma, I immediately pushed it to the back of my mind, as I had important meetings that day – it's interesting how the brain works sometimes. I knew about multiple myeloma as my mother had died from it when she was 59 and our oldest child was less than a year old (he's now 34), but I wasn't ready to deal with it. However, when my GP called later that day and asked me to arrange a full bone scan to check for damage, I was forced to bring it to the fore and start to confront the road ahead.

Multiple myeloma (MM) is the second-most common blood cancer in New Zealand. It lives in the bone marrow and affects multiple parts of the body. It often causes damage to the spine, skull, pelvis and hips and complications such as kidney disease, serious infections (due to compromised immunity) and excess calcium in the blood, which can impact your heart and your brain. Most patients will die from these complications. It is a relapsing-remitting cancer which means that, while it can't currently be cured, patients can enjoy a period of remission following treatment, but that will inevitably be followed by a relapse. Further (and different) treatment will be required to try to bring it back under control.

In my case, I was lucky that it was detected very early on, before it had caused any damage. Under the care of the excellent haematology team at Wellington Regional Hospital, I was monitored for the next 4 years until the disease progressed to the point that damage was starting. I began the long and arduous process of a stem cell transplant (SCT) in June 2019.

SCT is the 'standard of care' globally for MM so, in that respect, New Zealand is up with the play. However, this is where we fall away rapidly as my story illustrates.

Thanks to my SCT, I achieved a 'very good partial response' and my protein levels reduced from 42g/L to under 1. This looked like a great result, but my numbers started to climb within a few short months of completing the treatment. While I always knew that this would happen, it was a shock when it happened so quickly as I had hoped to get several years without further treatment. My haematologist recommended that I go on to lenalidomide (as we had already used thalidomide to try to get the best response during the SCT), cyclophosphamide and dexamethasone.

While this slowed the progression down for a couple of months, the drug combination likely caused a pulmonary embolism and I came off the regime as a result. It was at this point that it really hit home how badly-off we are in New Zealand, as there were NO MORE FUNDED TREATMENTS available.

Paula and I emigrated here in 1994 and have never regretted the decision. We have built a wonderful life here and our family has benefited from and contributed to this country. Our kids are proud kiwis who have spent time overseas but have come back here to start their own families. If we were still living in the UK, I would have 6 or 7 funded treatments available for the haematology team to consider. This just doesn't seem right.

Once again, I've been lucky. Thanks to my haematologist, I was accepted onto the compassionate access programme for Daratumumab in August 2021. Over the next few months, I received weekly, fortnightly then monthly infusions, and I am now on a monthly sub cut injection. This takes about 2 hours, then I am free to get on with my life.

Daratumamub is not a chemotherapy. It is a targeted therapy that is specifically tuned to recognise and impact myeloma cells. As such, side effects tend to have less of an impact.

While on Daratumumab I've experienced no side effects, my energy levels have improved and my overall blood chemistry is better than it's been for several years. When I compare it to the chemotherapies I've been on, it is much kinder as it only impacts the cells it needs to destroy.

One of the things you learn about chemotherapy is that you can often kill the cancer, but you need to be careful not to kill the patient. My chemo regimes have caused me to be in ICU with my body shutting down, to be so tired that I couldn't walk from one end of the ward to the other, and to have a permanent loss of feeling in my feet and toes. I'm not complaining about this – I might not be here if it wasn't for these treatments – but it is a fact of life that they can have damaging side effects.

Thank you for reading my story. My goal in writing this was to try to bring the impact of MM to life, to show that we need options and alternatives for when treatments no longer work and, with that support, we can continue to contribute to New Zealand society.

My son lost his grandmother to myeloma when he was just a few months old, and my daughters never met her. Thanks to the treatments I've been able to access in New

Zealand, I have lived to see my 3 granddaughters (2½ years, 6 months and 6 weeks) and I am able to be a part of their lives. Daratumumab has been a crucial part of this story, but it should not come down to luck to decide whether its available, as it was in my case.

Ngā mihi nui

Colin MacDonald

myeloma new zealand

To Whom it May Concern,

Before March 2019, my wife and I had worked all our lives, and looked forward to our eventual retirement. We understood that one or both of us would eventually get sick as we aged, as we all do, but that we would receive modern, timely care in Aotearoa New Zealand. My children, who were just leaving home and finding their own paths, also believed, as we did, that the Aotearoa New Zealand health care system was on par with leading OECD nations. They expected that they too, could work in Aotearoa and feel confident that even if blindsided by health issues, Aotearoa's wealth of resources and famous pragmatic culture would also manifest itself as quality, best-practice, life-extending care.

My experience of multiple myeloma from age 65 has taught us that our expectations far exceeded the reality that we had laboured under our whole lives. New Zealand has so many elements of potentially wonderful healthcare: generous, hardworking professionals, a small relatively wealthy population with high levels of education, and strong global reputation to attract expertise. However, at each step of the journey, I feel that too many aspects of the health system let patients and practitioners down. The three issues relating to cancer and particularly myeloma that require urgent attention and intervention are diagnosis and GP care, specialist care and resourcing, and the availability of treatment.

Diagnosis Care: My multiple myeloma diagnosis followed five months of terrible pain and incapacitation from collapsed vertebrae – a broken back – due to tumours in my spine. My GP was unable to recognise the disease himself despite intense sudden onset pain, low platelets and anaemia, but he also wasn't able to order adequate testing, such as MRIs and other imaging. Instead, my GP sent me to osteopathy sessions where my yet-to-be-identified broken bones were physically manipulated, to my complete agony. My diagnosis journey took multiple admissions to A&E, atypical blood results and months waiting for a specialist capable of ordering the right tests. Finding a sports doctor able to order an MRI who had a short-notice cancellation was the lucky break (so to speak) that found shattered bones and cancer. By this time, I was very ill and my family and I were in significant, avoidable, distress. My experience shows GPs are not empowered to take the necessary steps to quickly rule out conditions and get the correct cancer care faster, which also reduces the necessary treatment down the line.

Specialist treatment: Despite the efforts of so many brilliant hospital staff helping me through an autologous stem cell treatment, my experience with the specialists has generally been devastating in its insensibility. While aging is part of life, a cancer diagnosis is confusing, exhausting and scary. From now on, the length *and* quality of my life is in the hands of experts, but to date, expert input has been of patchy comfort, if at all as it appears so under-resourced. Like so many fellow sufferers I have spoken to, we endeavour to follow instructions to the letter but the advice is poorly explained, and concerns or questions are brushed off or avoided in the first instance. I pushed for inclusion in a NZ-run clinical trial, despite this option initially being shrugged off as my base hospital wasn't a participating facility. It surprised me that something as useful as the opportunity to join an existing NZ-lead trial was not readily forthcoming but instead was again the product of luck and my own advocacy. Very few of my fellow sufferers, it transpired, were aware of the trial despite the benefits for the state-of-the-art of myeloma treatment and potential benefits for individual patients.

Once I was diagnosed and partway through the chemotherapy trial, a lost referral when my specialist left for overseas meant that my haematological consultation and stem cell treatment was avoidably delayed by five months, and I needed extra chemotherapy in the interim so as not to lose ground. Stem cell treatment is a big step with its own dangers that had loomed before us for some months, and so the delay and subsequent extra chemo caused a lot of heartache when we were so desperate for help. The mistake was only found after prompting by my family and I, but the atmosphere in consultation was often such that I daren't ask about the way forward, or the outlook of my cancer journey and no specialist bothered to enquire about my overall state. Before my observations are filed away under the banner of the mental health crisis: this is not a matter for more counsellors or specialised mental health support. We simply seek dignified, respectful treatment at appointments where the professional has sufficient time, capacity, and empathy training to engage with us patients as complete, intelligent individuals, who might have questions, and not as burdens on the health system. Cancer, and its treatment, is hard and awful, but I had never expected that speaking to doctors would be similar.

Drug Availability: Finally, more modern drug treatments for common cancers and conditions must be made available. The research and clinical experience for many treatments is well established and unlike the two previous issues, drug availability is not a matter of wholesale systemic change.

I acknowledge that resources are limited but any discussion of cost-benefit seems absurdly premature when it is considered that even funded myeloma treatments that could improve survival and quality of life are so restricted that they cannot be used in the right combination or at the most beneficial time in the disease[1]. Living with myeloma is a race against the clock so it beggars belief that daratumumab as a second-line therapy is still under review for use in NZ since April 2021, when the same treatment has been fully funded in Australia since January 2021[2], and in the UK since 2019[3]. New Zealand's spend on medicines is only 0.3% of GDP, compared to 1.3% in Australia, or 1.2% in Finland (with a similar population and GDP to NZ)[4], where these drugs are funded. Is this strategy of delays and discounts the product of some sort of warped exceptionalism that means that New Zealand's citizens are not worthy of the same medicines that much of the world has established as perfectly reasonable?

My experience and that of my family has shown me that the attitude to health funding in NZ is no longer pragmatic, and the fear of the "aging population" has clouded the determination of benefit. A person can have chronic, incurable, or difficult conditions like multiple myeloma and still deserve modern drugs. The miserly approach to health funding in NZ is sending a message that devalues New Zealand as a whole, because access to quality healthcare when we are sick, even as we age, is part of the "deal" we keep with each other. People with cancers and chronic diseases are not waiting to die: we are part of the wider community and we are not invisible. Why should our young people want to stay in New Zealand and work, if the reward they see at the end of it all is poorer medicine than they

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[1] Milne et al., 2019, *The Burden Of Multiple Myeloma: A Study Of The Human And Economic Costs Of Myeloma In New Zealand*, Myeloma New Zealand, Wellington.

2 https://myeloma.org.au/darzalex-to-be-pbs-funded

3 https://www.myeloma.org.uk/news/daratumumab-combination-approved-england-wales-cancer-drugs-fund/

4 https://data.oecd.org/healthres/pharmaceutical-spending.htm retrieved 2022.09.01, https://www.stats.govt.nz/indicators/gross-domestic-product-gdp/, https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/setting-and-managing-the-combined-pharmaceutical-budget-cpb/ retrieved 2022.09.01.

could receive if they had laboured elsewhere? Why should motivated, conscientious medical professionals wish to work in New Zealand when they will be under-resourced compared to the global standard? The artificial constraints put on medicine funding in New Zealand have outlasted their usefulness as a negotiation ploy and are instead dragging us all backwards.

My myeloma journey has been physically painful. I am in remission and the next step is to wait to find out if relapse will occur before or after the funding of the next most appropriate treatment such as daratumumab is decided upon. Myeloma is increasing in prevalence in New Zealand and it is my hope that diagnostic capabilities at GP-level are improved so that future sufferers will not spend as much time in pain and wasting misspent resources prior to diagnosis, or wondering what might have been had they been diagnosed earlier.

Future sufferers should not have to go through the same anxiety and demoralisation as I did from challenges in administration and communication with experts, and with side effects from ancient drugs like thalidomide. Most importantly, future sufferers of long-term or incurable diseases must not be treated as an accounting problem, and specialists must be afforded the resourcing that they need to provide world-class, equitable care that Aotearoa can be proud of. Healthcare funding must increase across the board, and a more holistic approach to the cost-benefit assessment of healthcare funding must be adopted including that investing in health infrastructure and in life-extending medicines, even where a cure is not an immediate outcome, is an investment in communities, not just in individuals.

Yours faithfully,
David, Auckland, aged 67.

myeloma new zealand

Date 1 September 2022

I am writing as someone who loves someone who has myeloma to ask you to agree to fund daratumumab, carfilzomib and pomalidomide, and lenalidomide for earlier use in induction treatment.

I hope you will take the time to read this letter and that my story will help you understand the urgent need for these treatments, and the power you have in your hands to allow people like my partner to stay alive and well, to continue to contribute to society, and to see his only grandson grow.

My partner Al was diagnosed with myeloma in February 2021. He was 66 at the time, and still working in his painting business, employing others. He was otherwise fit and healthy, with plans to build a retirement home on a section bought for the purpose. Those plans came to an abrupt end.

Having cancelled long-standing private medical insurance due to rising costs, he was put into the public system on diagnosis. The care and attention we received was exemplary and we have no complaints to date. However, the treatment regime was difficult, and we have since discovered that NZ is behind with its toolkit to treat Multiple Myeloma.

The initial drugs included Cyclophosphamide which induced mental anxiety and depression, an inability to cope with his business, and overwhelming fatigue. During the course of 5 months of treatment, Allen was moved to Thalidomide but this also had severe side effects for him including debilitating rashes, bowel problems and insomnia. Al was given a SCT in October 2021, and a subsequent 3 months of chemotherapy, this time including Lenalidomide, which was easier to manage.

Allen is now 68, and 19 months since diagnosis. He is in a ‘good partial remission’ and as such he now works a little in his business, continuing to employ. He is on a maintenance of Lenalidomide, with some side effects including infections. Our section has been sold as we need to live near to healthcare, and our future is uncertain. We recently had a first grandchild who is a delight and the apple of his Grandad’s eye.

Whilst we are grateful for our position, we are aware that options for the future are limited. A second SCT may not be offered if he relapses, as the cut-off is 70, with some exceptions. Our research shows that daratumumab, carfilzomib and pomalidomide may significantly improve his longevity, and yet they are not available as they are for our Australian cousins.

I am constantly amazed at Al’s ability to fight on, to work and complete tasks despite the physical hindrances he now endures. I have confidence that if he can access the latest in drugs and treatments available overseas for Myeloma, he could live out his natural life and not die for lack of funding, continuing to be a valuable member of society.

I therefore ask that you please fund daratumumab, carfilzomib and pomalidomide, and lenalidomide for earlier use in induction treatment.

Sarah MacDonald, partner of Allen Wilkinson
West Auckland

myeloma new zealand

Age 74

Diagnosed June 2020
Thalidomide was a relief after my first round of cyclophosphamide. The side effects were much less. After 26 weeks I went into remission which should have enabled me to have respite. Sadly this was not the case and I'm now on lenalidomide.

My concern is that at my age and weight loss I'm not eligible for stem cell transplant (at great expense) and there are limited options available.

Talking with MM people I know personally in Portland Oregon and Queensland i am disheartened at our limited range of drugs and the opportunities ahead.

Until I was diagnosed I was providing non-stypendary chaplaincy services for up to 20 hours a week as I am a qualified chaplain. Regretfully the drugs I've had have left me with a diminished quality of life.

When comparing what is available here to overseas we are sadly lacking in quality drugs and I believe that should they be available I would have been able to continue to volunteer and be a useful member of the community.

Kind regards

Judith

I am 59 years young, and thanks to my great fortune to be accepted into the DREAMM 7 trial of daratumumab and a more recent derivative called belantamab, I am currently in remission and living a reasonably normal life. It would be more normal if I had not taken thalidomide in 2015-16 following my second stem-cell transplant, as this has resulted in permanent neuropathy in my feet and lower leg, which limits my ability to walk long distances (which I enjoyed) or run anywhere (which I never enjoyed anyway 😉). Life would also be more normal if an alternative to chemotherapy and stem cell transplants had been available back in 2006 when I was first diagnosed, as my digestion system would probably work better, saving embarrassment in public and at work. Its only noise…!

I was (un)lucky enough to be on the newer belantamab arm of the DREAMM7 trial. I was in remission after only 6 doses – but the side-effects of irritable eyes and blurry vision limited by ability to continue full time work for periods of days at a time. I understand that those on the daratumumab arm suffered no such side effects, and their treatment was almost as successful.

I therefore ask that Pharmac conduct a full benefit/cost study, including the counterfactual, for the equation in front of them, when considering myeloma patients. My equation looks like this:

Without monoclonal treatment:

- 2 x stem cell transplants at $..... (do not know the cost – presumably Pharmac do)
- Each required 2-3 months off work and up to 8-12 months before back to normal work function
- All the associated drugs, visits to and stays in hospital, specialist staff etc
- Myeloma reappeared after 10 years the first time, and 3 years the second time
- I believe I would need to reduce or even stop work before I was 60, had I not had access to a newer generation of treatments than lenalidimide (my only funded option left)

With monoclonal treatment (not daratumumab, but newer derivative)

- 3 doses of monoclonal antibody, twice over 12 months, with recovery period in between for eyes to recover vision
- Time off work to go to hospital for a half day every 3 weeks for each IV dose; 6 IV treatments in the year, and some steroid effects, in total amounting to no more than a couple of weeks off work
- Associated drugs to ensure immune system safe (part of the trial)
- A biopsy in June 2022, 15 months after the trial started, showed no myeloma cells present – in remission
- No lasting effects (other than those caused by the old-style treatments), feel I can keep working and fully contributing well beyond 65 at this point.
- A more positive outlook on my career opportunities and continuing back to society as well once I am 65.

Incalculable but real is the impact on me and my families well-being and general outlook and gratitude on life.

Some more information about me:

- Had myeloma for (years/months) – first discovered something wrong in early 2006, diagnosed in March 2007, so that is 15 years and 5 months ago
- How did you find thalidomide? – gave me neuropathy, which I still have and live with constant dull pain.
- Why would you prefer daratumumab to thalidomide? – YES (from what I know of others on DREAMM7)
- How did you find daratumumab? – as above
- Why do you think we need daratumumab funded? – the response is better and should be longer lasting. So the full cost-benefit equation, if it takes into account the effectiveness of the number of treatments, how long they are effective and the continued contribution to society without other impacts on health, could well be positive – recognising that dara is not cheap.
- How does it make you feel knowing we haven't had any new drugs funded for myeloma for eight years? – devalued as a member of society, in the sense that yes, myeloma is a "manageable" cancer. But that belies the impacts that the disease, and particularly the older treatments used to "manage" it, have on the ability to contribute positively to society, rather than being a burden on society.
- What would having daratumumab funded mean to you? – I was very fortunate to have had a trial available. Knowing what I know now, having dara funded would mean that many people just like me would be able to continue to live longer and more complete lives than they possibly could with the currently available treatments.
- Why do you want better drugs funded for myeloma? – because it is a very much more effective and long lasting treatment than those currently available.
- Feel free to add any other comments you would like. –I think some tough calls would still need to be made on who would receive the dara. I also have wondered about the cost of earlier diagnosis – I was diagnosed very early, before any serious impacts on my kidney function or bone strength occurred. But it was only because I was a blood donor and was refused a donation session because of anaemia, which set off a succession of tests until diagnosis a full year later. A simple blood test, at a time when people have tests for other potential ailments, could provide early diagnosis and make the return to NZ from drugs like daratumumab even greater.

Warm regards,

Anon

myeloma new zealand

To Whom It May Concern

My name is Debbie Hayne. I have lived in Upper Hutt, Wellington most of my life.

I live with a condition called Multiple Myeloma. I'd never heard of it until I was diagnosed on 31st October 2019.

Multiple Myeloma is a blood cancer that develops in your plasma cells and they undergo a toxic change. As they multiply, they crowd the bone marrow and prevent it from making normal red and white cells and platelets. This causes many problems such as anaemia, kidney disease, weakened and broken bones to name a few.

I was a fit, healthy 59 year old, working fulltime and going to the gym or pools each morning. I had always looked after myself and led a relatively healthy lifestyle.
The date I was diagnosed sticks very clearly in my mind, as we were to travel to the United States six days later. This was to be the start of our extended overseas ventures, after raising two boys, looking after sick grandparents and parents for the last few years. We (my hubby Greg and I) thought finally it's our time.

For several months I had been treated for sprained ribs, but felt continually unwell, to the stage when I got blood tests returned on the 31st October, I was sent urgently to hospital and started on double chemotherapy the next day. By this stage I was also in renal failure and my prognosis was very poor indeed.

It has been quite a roller-coaster ride, as I had four months of chemotherapy, then stopped responding. I then had a bone marrow (stem cell) transplant in March 2020. This was followed by another 8 months of chemotherapy. I am currently on Lenalidomide until it stops working. I had a Very Good Partial Response (VGPR) to the transplant.
The transplant was pretty tough going but I returned to my normal life.

I'm very grateful for the amazing haematologist I have and the outstanding care of the haematology team at Wellington Blood and Cancer Centre. They have enabled me to return to my near normal life.

What concerns me greatly is the limited access we have to drugs in this country.
As I said I'm currently on Lenalidomide (Revlimid), which is funded for me because I have had a transplant. I was extremely lucky that funding for this drug was extended for people who had had Stem Cell Transplant (SCT), along with extended use of Bortezomib chemotherapy about the time of my transplant.

Sadly, if you have not had a SCT (bone marrow transplant) you do not qualify unless it is used as a last line of treatment. Unbelievable, when it is a first line treatment overseas!

In New Zealand we are far behind the rest of the world in regards to treatment for Multiple Myeloma. Many drugs that are used as first line treatments overseas are not even available here. This is extremely concerning as overseas Multiple Myeloma is now a treatable chronic disease. People return to work, leading practically normal lives and contributing to society.

For me when Lenalidomide stops working (I have had approximately 18 months of remission now), I will be reliant on the availability of a clinical trial, or having to try and purchase something from overseas, or try and seek treatment overseas.

This is very distressing, as I still have a lot of life to live and a lot to contribute to society. I have returned to work part time, where I feel I have a lot to offer. We have three beautiful grandchildren that I want to see grow.

We have always contributed to society, whether it be through Scouts, coaching sports teams, school committees, boards of trustees and many other community fundraising activities. My husband is a volunteer rural firefighter which involves extensive volunteer time. When I was going to lose my hair from chemotherapy it coincided with LBC's Shave for a Cure, so I turned it into a positive and raised over $3000 for LBC.

We are givers not takers and always felt we would be looked after in our own country. Should my husband and I have to sell our house and give up our life's savings to fund treatment, which will leave nothing for our children and grandchildren, and a poor retirement for my husband.

I understand there are limited resources, but surely funding the appropriate drugs keeps us out of hospital, working and paying taxes, while having a good quality of life and contributing to society. Luckily, I am very stubborn and have the will to fight but I feel it is grossly unfair that we are treated as third world citizens and feel like we have to fight for scraps when there are so many other treatments available overseas. No new drugs have been funded for Multiple Myeloma in New Zealand for **eight** years. We are at least eight drugs behind Australia and a long, long way behind Europe, Canada and America.

My immediate future is every four weeks I have blood tests to see if my cancer has become refractory. This is stressful in itself, as I wonder if the cancer is active again what my choices are going to be.

If Pharmac funded other drugs or treatments, such as those readily available overseas, I could continue to lead a pretty normal life without the threat or worry every four weeks. There are many drugs available that put Multiple Myeloma into deep remission for many, many years, but tragically those drugs are not available in New Zealand.

I implore Pharmac on behalf of myself and MM patients, some who do not have any resource, to re-evaluate the Multiple Myeloma drugs and to make life changing drugs available to Multiple Myeloma patients in New Zealand to enable us to have a future that we are entitled to.

At the very least if Pharmac could fund daratumumab (darzalex) subcut, lenalidomide as a first line treatment and pomalidomide (pomalyst) and carfilzomib (kyprolis) for second line onwards.

Car-T Cell therapy is also becoming first line treatment overseas instead of SCT.

This gives MM patients several different options, if one is not suitable. These drugs are extremely successful overseas, putting patients into deep remission for many, many years.

Surely, we (multiple myeloma patients) as taxpayers should be entitled to the best medicine that will ensure the least drain on the health system.

Yours sincerely

Debbie Hayne

myeloma new zealand

03 September 2022

I am writing as someone who is living with myeloma to ask you to agree to fund daratumumab, carfilzomib, pomalidomide and lenalidomide for earlier use in induction treatment.

I hope you will take the time to read this letter and that my story like many others will help you understand the urgent need for these treatments, and the power you have in your hands to allow people like me to stay alive and well for my beautiful daughter Grace. I have always led a productive meaningful life, contributing to my local community, working and paying taxes and hopefully been a good and once valued citizen.

My diagnosis came about by chance, through giving blood in May 2018. Myeloma isn't hereditary, poor lifestyle choices, environmental just random and incurable to date. I was calm even after I was diagnosed with smouldering myeloma at Middlemore with a booklet in my hand I drove back to work and completed my day. I had smouldering for 2 years - the beast was waiting and in June 2020 it came awake and became active. To all I was strong and brave at home alone I was scared.

I went to a support meeting and heard the names of drugs I couldn't pronounce and more alarming was the talk of very few drug treatment options here. The group was hopeful and positive but I sat in the LBC car park and wept.

The stars were aligned almost immediately I became active a clinical drug trial (Kiwi Trial) carfilzomib based induction and post transplant consolidation was open to me. We have so few trials in NZ I was grateful for the opportunity. Carfilzomib was the only newer drug used in my treatment combination unfortunately cyclophosphamide and worse still thalidomide were the part of the treatment. I still have taste issues from thalidomide to this day. Even after my stem cell transplant I didn't get complete remission but with having Lenalidomide as maintenance it has got my paraproteins to <1.

Would Lenalidomide at induction or consolidation given a better prognosis I believe so.

We have so few alternatives and are one of the lowest ranked in the OECD for drug funding. My friends in Australia are appalled when I tell them my options. All the drugs I'm asking for are funded in Australia , our closest neighbours , we haven't seen any new drug treatments for 7 years in the myeloma space in NZ and we are lagging behind. These life extending drugs with substantial clinical, health and cost benefits are desperately needed.

These drugs aren't the newest and brightest but by adding to our arsenal would improve outcomes and progression of disease and extend a pathway to a cure. Overseas

specialists are now saying functional cure instead of incurable so exciting but we need better and targeted drugs. Drugs like thalidomide have higher toxicity and side effects than their newer counterparts. Less money on hospitalisation and keeping a population healthy and productive makes good economic sense.

I want to see my daughters childcare center thrive and for me to be part of that and continue help to develop caring and resourceful citizens of the future. It brings me joy and a deep sense of satisfaction. I need you to help me achieve that. I DESERVE better and our country deserves the benefits of healthy happy citizens.

We in the myeloma community have seen such advances overseas and ask that some hope can be brought to our shores. Our lives have value.

We all understand that you have a finite amount to fund with but please use wisely and look at the need for more effective targeted drugs like daratumumab, carfilzomib, and pomalidomide.

Many Thanks
Megan
Auckland

myeloma new zealand

1 August 2022

Submission for Pharmac regarding the funding of Daratumamab in NZ for multiple myeloma and AL amyloidosis and the impact that will have on future treatment options for patients.

Dear Pharmac,

Please fund the immunotherapy drug Daratumamab for blood cancer patients. I have multiple myeloma and AL amyloidosis that has significantly damaged my heart. I am 56 years old now, working in the field of supportive cancer care and end of life counselling, enrolled at Massey for a PG Diploma in Psychology beginning February 2023 and I am currently living an active and healthy life.

I was diagnosed in January 2017, treated with two months of CyBorD (Cyclophosphamide, Bortezomib and Dexamethasone) chemotherapy and achieved a miraculous complete haematological response (CHR). The normal course of treatment for someone with my disease is six to nine months of CyBorD.

At the time I achieved CHR I was in late-stage heart failure and my prognosis was not good. Only 25-50% of cardiac amyloidosis patients will have a return of organ function after achieving a CHR or VPGR. I was one of the lucky ones. My age and active lifestyle helped me to recover and while my heart still shows damage I can live a normal active life.

I was in CHR for 5 years until 1 June 2022 when my light chains tested above the normal limit. I am now faced with more chemotherapy. My haematologist has offered a more toxic chemotherapy combination and advised me to prepare for a stem cell transplant. These treatments will be a hard-slog and I'll need time off work, school and be faced with a long recovery again.

In the past five years Daratumamab-based treatments are becoming the standard of care around the world for patients like me with myeloma and amyloidosis, as first-line treatment and for use in relapsed patients. Daratumamab with CyBoRD is less toxic and some patient reports that I read suggest that they are able to continue with many aspects of their normal lives while on treatment.

At the time of my first treatment I was in late stage heart failure and a stem cell transplant was not an option. I am so very lucky that I had access to Bortezomib here in New Zealand. That new and revolutionary drug saved my life. Now I need access to Daratumamab, the next revolution in blood cancer treatment. Please help.

I have been told that my next option for treatment is six months of LenBorD (Lenalidomide, Bortezomib and Dexamethasone). Because of the nature of Lenalidomide I must do a stem cell harvest to be prepared for a stem cell transplant. I have been told that the LenBorD

will be a more toxic chemotherapy for me with more side effects.

Certainly, a stem cell transplant will inhibit my work and ongoing schooling for a considerable time. Whereas patient experiences that I see reported on a global AL Amyloidosis Facebook group suggest that I could maintain a part time work schedule and a more normal life if my next line of treatment included Daratumamab with the CyBorD that already worked a miracle and gave me five good years. Daratumamab has less toxicity for cardiac amyloidosis patients like me.

A review and meta-analysis published 4 July 2022 in Cancer Cell International on the efficacy of Daratumamab-based treatments for AL amyloidosis concludes that Daratumamab may improve survival for relapsed refractory and newly diagnosed AL amyloidosis patients. [Sun, C., Wang, X., Zang, R. et al. Efficacy and safety of intravenous daratumamab-based treatments for AL amyloidosis: a systematic review and meta-analyisis.]

A Google search of Daratumamab + Myeloma + Amyloidosis provides a plethora of positive and encouraging conclusions on the efficacy of Daratumamab-based chemotherapy regimes that are becoming the standard of care around the world. For blood cancer patients here in Aotearoa the addition of Daratumamab to our future treatment options will improve our outcomes and potentially reduce the reliance on stem cell transplants for our disease.
Some of us with damaged hearts and other organs that make a stem cell transplant even more dangerous will benefit greatly. Thank you.

Tove Jensen-Munroe

When were you diagnosed: June 2022

Why would you prefer daratumumab to thalidomide? I have heard Dara has much less severe side effects which would enable me to have better quality of life and spend more time with my family.

How does it make you feel knowing we haven't had any new drugs funded for myeloma for eight years? I understand that New Zealand is a small county but with so many people fighting this disease I feel we are overdue for new treatment options.

What would having daratumumab funded mean to you? It would mean the world to me and my family. It would give us hope and enable me to live a longer and happier life.

Karen, 55, Northland

A RESEARCH REVIEW™
STUDY REVIEW

Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with previously treated multiple myeloma: three-year follow-up of CASTOR

Making Education Easy 2021

About the Expert

Dr Ken Romeril
FRACP, FRCPA

Ken is a haematologist specialising in malignant haematology. He trained in Christchurch, Sydney and Southampton, and is currently at the Bowen Icon Cancer Centre. Ken has a particular interest in translational myeloma research and genetics. He is involved in clinical trials, is the current Chair of Myeloma New Zealand, a former chair of the ALLG Myeloma Sub-Committee, and is the NZ representative on the International Myeloma Working Group, which has around 200 members.

Abbreviations used in this review

ASCT = autologous stem cell transplant
CR = complete remission
ITT = intent-to-treat
MRD = minimal residual disease
ORR = overall response rate
RRMM = relapsed or refractory multiple myeloma
PFS = progression-free survival
PI = proteasome inhibitor

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RESEARCH REVIEW™
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In the primary and follow-up analyses of the phase 3 CASTOR study in patients with relapsed or refractory multiple myeloma (RRMM), a regimen of daratumumab, bortezomib, and dexamethasone significantly prolonged progression-free survival (PFS) and induced higher rates of deeper responses than bortezomib and dexamethasone alone.[1-3] This publication summarises data from an update of the CASTOR study after a median follow-up of 40 months[3] and demonstrated that a regimen of daratumumab, bortezomib, and dexamethasone maintained significant benefits in RRMM patients and with a consistent safety profile.

Introduction

Daratumumab is a human, CD38-targeted, immunoglobulin G1 kappa (IgG1κ) monoclonal antibody with a direct on-tumour and immunomodulatory mechanism of action.[4-6] In phase 3 trials, daratumumab-based regimens reduced either disease progression/death by ≥40%, doubled CR rates, and/or tripled minimal residual disease (MRD) negativity in patients with newly diagnosed multiple myeloma and relapsed or refractory multiple myeloma (RRMM).[1,2, 7-13] In the phase 3 CASTOR study in patients with RRMM, a regimen of daratumumab, bortezomib, and dexamethasone significantly prolonged progression-free survival (PFS) and induced higher rates of deeper responses than bortezomib and dexamethasone alone.[1, 2] In the 2-year, follow-up analysis of the CASTOR study (median follow-up of 19.4 months), median PFS was 16.7 months with daratumumab, bortezomib, and dexamethasone versus 7.1 months with bortezomib and dexamethasone alone (hazard ratio [HR] 0.31; 95% confidence interval [CI] 0.24, 0.39; p<0.0001).[2]

This update of the CASTOR study provides efficacy and safety data from the CASTOR study after a median follow-up of 40.0 months (nearly 3 years after the primary analysis).[3]

Methods

Study design

The study design of the CASTOR study has been previously described (NCT02136134).[1, 2] This phase 3, multicentre, open-label trial enrolled patients with RRMM who had received at least 1 prior line of therapy.

Treatment

Patients were randomised to receive daratumumab, bortezomib, and dexamethasone or bortezomib and dexamethasone alone, with stratification by International Staging System at baseline (I, II, or III), prior lines of therapy (1, 2, or > 3), and prior exposure to bortezomib.[1, 2]

- All patients received eight 21-day cycles of subcutaneous bortezomib 1.3 mg/m^2 (days 1, 4, 8, and 11) and oral dexamethasone 20 mg (days 1, 2, 4, 5, 8, 9, 11, and 12).
- Patients in the daratumumab, bortezomib, and dexamethasone arm received intravenous daratumumab 16 mg/kg:
  - Cycles 1-3: on days 1, 8, and 15 (3-week cycles);
  - Cycles 4 to 8: once every 3 weeks on day 1 (3-week cycles); and
  - Cycle 9 onwards: once every 4 weeks until the patient withdrew consent, the disease progressed, or unacceptable toxic effects developed.

After protocol amendment, patients receiving bortezomib and dexamethasone alone were offered daratumumab monotherapy after disease progression.[3]

Patients

Eligible patients had documented multiple myeloma, had received at least one prior line of therapy (with at least a partial response [PR]), and had disease progression classified per International Myeloma Working Group criteria. Patients were excluded if they had disease refractory to bortezomib or another proteasome inhibitor (prior bortezomib exposure was permitted).

Study endpoints

The primary end point was PFS; secondary end points included, time to disease progression, overall response rate (ORR), MRD negativity, and safety. Efficacy analyses were based on the intent-to-treat (ITT) population unless otherwise specified.[3]

Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with previously treated multiple myeloma: three-year follow-up of CASTOR

Results

Patients

A total of 498 patients had received treatment at the time of clinical cut-off for this analysis (October 2, 2018). The demographics and baseline characteristics were well-balanced between the treatment arms (**Table 1**).[1, 2]

In the daratumumab, bortezomib, and dexamethasone arm, the median age of the patients was 64 years (range, 30–88 years), and patients had received a median of two prior lines of therapy (range, 1-9).[3] Patients in the bortezomib plus dexamethasone arm had similar baseline demographics and clinical characteristics.

Prior therapies received by patients included bortezomib (66% of patients) and thalidomide (49%), and 48% of patients had received both a proteasome inhibitor (PI) and an immunomodulatory agent; 42% of patients had received prior lenalidomide.[3] Forty seven percent of patients had received one prior line of therapy, most frequently including an alkylating agent (89%), an immunomodulatory agent (65%), or a PI (53%).[3]

Disposition and drug exposure

At the time of this analysis, all patients in both treatment arms had completed the protocol-specified 8 cycles of treatment with bortezomib and dexamethasone or had discontinued study treatment.

For the 243 patients treated with daratumumab, bortezomib, and dexamethasone, the median duration of treatment was 13.4 months (range, 0-46.6 months). For the 237 patients treated with bortezomib and dexamethasone alone, the median duration of therapy was 5.2 months (range, 0.2-8.0 months).[3] A total of 297 (62%) patients discontinued treatment, largely due to progressive disease (213 [44%] patients).[3]

Efficacy

After a median follow-up of 40.0 months, PFS was significantly longer with daratumumab, bortezomib, and dexamethasone than with bortezomib and dexamethasone in the ITT population (median: 16.7 vs 7.1 months; HR 0.31; 95% CI 0.25, 0.40, p <0.0001; **Figure 1**).[3] The PFS benefit was maintained across patient subgroups, including patients aged <65 years and ≥65 years and cytogenetic risk status (high and standard).[3] The PFS benefit for daratumumab, bortezomib, and dexamethasone over bortezomib

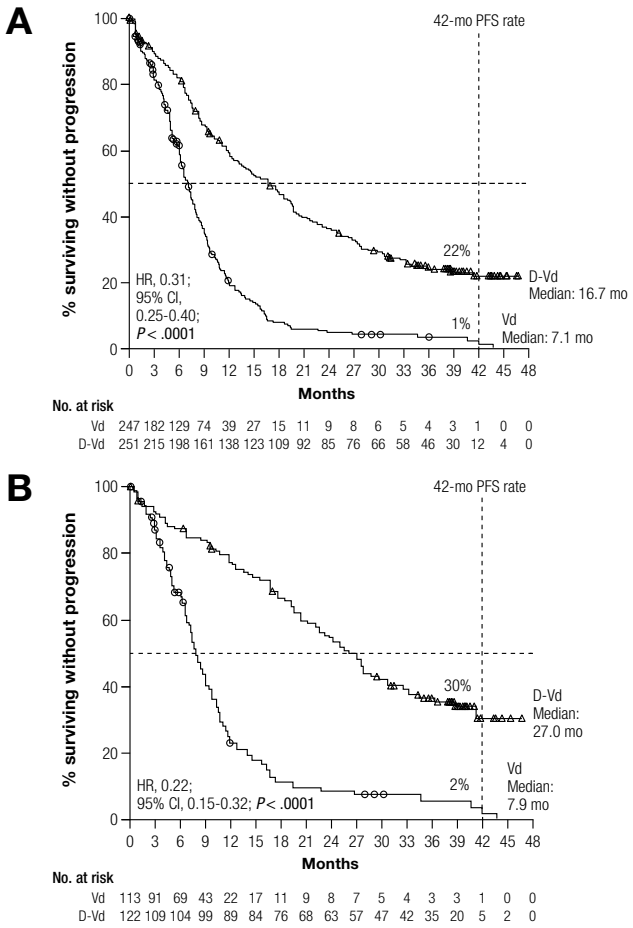

Figure 1. Progression-free survival (PFS) for **A**) the ITT population and **B**) patients who received one prior line of therapy.[3]

D-Vd = daratumumab, bortezomib, and dexamethasone; **HR** = hazard ratio; **mo** = months; **Vd** = bortezomib and dexamethasone.

Table 1. Baseline characteristics

Characteristic (% pts)	ITT population		Patients receiving one prior line of therapy	
	Daratumumab, bortezomib, and dexamethasone (n=251)	Bortezomib and dexamethasone (n=247)	Daratumumab, bortezomib, and dexamethasone (n=122)	Bortezomib and dexamethasone (n=113)
Median age, years (range)	64 (30-88)	64 (33-85)	63 (30-84)	64 (40-85)
Median time from diagnosis, years (range)	3.87 (0.7-20.7)	3.72 (0.6-18.6)	2.81 (0.7-14.9)	2.98 (0.6-18.1)
Prior lines of therapy				
Median, n (range)	2 (1-9)	2 (1-10)	1 (1-1)	1 (1-1)
1, % pts	49	46	100	100
2, % pts	28	30		
3, % pts	15	13		
>3, % pts	9	11		
Prior PI, % pts	67	70	53	52
Prior bortezomib, % pts	65	66	51	50
Prior IMiD, % pts	71	80	59	72
Prior thalidomide, % pts	50	49	48	43
Prior lenalidomide, % pts	36	49	12	29
Prior PI + IMiD, % pts	45	52	24	29
Refractory to lenalidomide, % pts	24	33	5	16

IMiD = immunomodulatory drug; **ITT** = intent-to-treat; **PI** = proteasome inhibitor.

Table 2. Response and MRD-negativity rates in the ITT population[3]

Characteristic (% pts)	ITT population		Patients receiving one prior line of therapy	
	Daratumumab, bortezomib, and dexamethasone (n=240)	Bortezomib and dexamethasone (n=234)	Daratumumab, bortezomib, and dexamethasone (n=119)	Bortezomib and dexamethasone (n=109)
ORR	85**	63	92*	74
≥CR	30**	10	43**	15
PR	22	34	15	32
MRD-negative (10^{-5})	14**	2	20**	3

*p<0.001, **p<0.0001 vs bortezomib and dexamethasone. **CR** = complete response; **ORR** = overall response rate; **PR** = partial response.

and dexamethasone alone was evident in patients treated with one prior line of therapy (median PFS 27.0 vs 7.9 months; HR 0.22; 95% CI 0.15, 0.32; p<0.0001; **Figure 1**), including those whose first-line regimen included bortezomib (median 20.4 vs 8.0 months; HR 0.22; 95% CI 0.13, 0.37; p<0.0001) or lenalidomide (median 21.2 vs 7.0 months; HR 0.30; 95% CI 0.11, 0.82; p=0.0140). In patients who were refractory to lenalidomide in any prior line of therapy, median PFS with daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone alone was relatively short but still superior in patients that received daratumumab, bortezomib and dexamethasone at 7.8 vs 4.9 months (HR 0.44; 95% CI 0.28, 0.68; p<0.0002).[3]

ORR were significantly higher with daratumumab-based triple therapy than with bortezomib and dexamethasone alone in the ITT population (85% vs 63%; p<0.0001; **Table 2**), as were CR or better (30% vs 10%; p< 0.0001).[3] These deep responses correlated with longer PFS, with patients with ≥CR achieving 42-month PFS rates of 53% and 10%, respectively. Similarly in patients who had received one prior line of therapy, ORR were higher with daratumumab-based triple therapy than with bortezomib and dexamethasone alone (92% vs 74%; p<0.0001), as were CR or better (43% vs 15%, p<0.001; **Table 2**).[3]

MRD negativity rates (10^{-5}, assessed via next-generation sequencing on bone marrow aspirate samples) were greater with daratumumab, bortezomib, and dexamethasone than with bortezomib and dexamethasone alone in the ITT population (14% vs 2%; p<0.0001), as well as in patients who had one prior line of therapy (20% vs 3%; p<0.0001; **Table 2**).[3] Median overall survival had not been reached.[3]

Safety

The safety profile remained consistent after a median 40 months of follow-up, with no new safety concerns identified.[3] The most commonly reported (>5%) grade 3 or 4 treatment-emergent adverse events (TEAEs) in the daratumumab, bortezomib, and dexamethasone arm compared with the bortezomib and dexamethasone arm were thrombocytopenia (46% vs 33%), anaemia (16% vs 16%), and pneumonia (10% vs 10%).[3] Grade 3-4 infections were more common with the triple therapy regimen than with bortezomib and dexamethasone alone (29% vs 19%); however, after adjusting for exposure, grade 3-4 infection events per patient-year were lower with daratumumab, bortezomib, and dexamethasone than with bortezomib and dexamethasone alone (0.26 vs 0.68). Rates of discontinuation due to TEAE were similar for both treatment arms (10% vs 9%).[3]

Second primary malignancies (cutaneous, invasive, and haematologic) were reported in 6% of patients in the daratumumab, bortezomib, and dexamethasone arm (4 new cases since the previous analysis) and 2% of the patients in the bortezomib, and dexamethasone arm (4 new cases since the previous analysis).

Expert comment

This study summarises data from an extended follow up of the phase 3 CASTOR study in patients with RRMM. On an ITT basis it clearly demonstrates the superiority of the triplet combination of daratumab, bortezomib and dexamethasone over bortezomib and dexamethasone alone. The CR rate of 30% vs 10% and a MRD negativity rate of 14% vs 2% (p<0.001) is much superior with the triplet regimen. The patients in the triple therapy arm who achieved a >CR had an excellent PFS rate of 53%. This compares with only 10% in the doublet treated patients who achieved >CR being progression free at 42 months. It is now well established that patients who go on to achieve MRD negativity tend to have better PFS figures and this was 14% vs 2% in the ITT population.

In the triplet treated patient group the patients had received a median of two prior lines of therapy (range of 1-9). The doublet treated population had similar baseline demographics. It was clear from the study that patients who had only received one line of therapy and got triplet therapy did better both in terms of the ORR and also achieving a CR or better (43% vs 15%). This then translates into a marked improvement in PFS benefit for patients with the triplet and one prior line of therapy. This came out at a median of 27.0 months vs 7.9 months for bortezomib and dexamethasone alone. This benefit was observed independently of whether the patient was exposed to bortezomib in their first-line regimen (median PFS 20.4 vs 8.0 months) or lenalidomide (median PFS 21.2 vs 7.0 months).

The safety profile was consistent after a median follow-up of 40 months and no new safety concerns were identified. It was apparent that grade 3-4 infections were more common in the triplet therapy arm but this was not significant when adjusted for exposure. Also second primary malignancies were quite low and may have been related to prior lenalidomide exposure.

It was of interest that only 8 cycles of bortezomib were used in this study for reasons that were not clear. If we extrapolate to the New Zealand scene, the recent switch to generic lenalidomide and increased access would mean that if this triplet approach were adopted then a longer exposure to a PI in conjuction with daratumumab could confer even better results. Other studies such as POLLUX and CANDOR did not discontinue the daratumab partner which was lenalidomide and carfilzomib, respectively.

The increasing use of lenalidomide as maintenance post ASCT in the New Zealand setting may impact on the response to daratumumab when these particular patients relapse. It does appear that the group of lenalidomide refractory patients do not fare as well on the triplet therapy but still do better than the doublet group (7.8 months vs 4.9 months).

In summary, the triplet therapy approach incorporating daratumumab was shown in this study to confer significant benefit to patients with myeloma relapsing after one line of therapy.

Interpretation

In the ongoing CASTOR study, a triple regimen that included daratumumab, bortezomib, and dexamethasone maintained significant PFS, ORR, and MRD-negativity rates compared with bortezomib, and dexamethasone alone in patients with RRMM.[3] The safety profile remained consistent after a median 40 months of follow-up, emphasising the tolerability and predictability of maintenance therapy with daratumumab alone following 8 cycles of bortezomib, and dexamethasone.

The benefit of triple therapy with daratumumab, bortezomib, and dexamethasone was more pronounced in patients who had received one prior line of treatment, and this benefit occurred regardless of whether the first-line regimen included bortezomib or lenalidomide.[3] Daratumumab, bortezomib, and dexamethasone also improved outcomes compared with bortezomib, and dexamethasone alone for the clinically important group of patients who were refractory to lenalidomide in any prior line of treatment.

EXPERT'S CONCLUDING COMMENTS

The original CASTOR study was published in 2016 and presented solid evidence for the value of adding daratumamab to bortezomib and dexamethasone. This follow-up study 40 months later confirms the initial concept and clearly shows that the triplet regimen:

- confers better defined outcomes in terms of ORR, CR or better and PFS
- tells us that the optimal benefit is obtained if the regimen is utilised following the failure of first line therapy
- the deep responses as measured by MRD analysis translate into prolonged PFS

In New Zealand we currently do not have an effective regime to offer our relapsed patients. This unmet clinical need would be met if we were able to introduce this effective triplet regime into clinical practice.

TAKE-HOME MESSAGES

- In the ongoing CASTOR study, after an extended median follow-up of 40 months, triple therapy with daratumumab, bortezomib, and dexamethasone showed improved efficacy outcomes (including PFS, ORR, and MRD-negativity rate) compared with bortezomib and dexamethasone alone.
- The most pronounced improvement in response was observed in patients who had one prior line of therapy.
- Triple therapy with daratumumab, bortezomib, and dexamethasone showed improved efficacy outcomes compared with bortezomib and dexamethasone alone in patients who were refractory to lenalidomide in any prior line of treatment.
- The safety profile remained consistent after a median 40 months of follow-up, emphasising the tolerability and predictability of maintenance therapy with daratumumab alone.

REFERENCES:

1. Palumbo A, Chanan-Khan A, Weisel K, et al. Daratumumab, bortezomib, and dexamethasone for multiple myeloma. N Engl J Med. 2016;375:754-66.
2. Spencer A, Lentzsch S, Weisel K, et al. Daratumumab plus bortezomib and dexamethasone versus bortezomib and dexamethasone in relapsed or refractory multiple myeloma: updated analysis of CASTOR. Haematologica. 2018;103:2079-87.
3. Mateos MV, Sonneveld P, Hungria V, et al. Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with previously treated multiple myeloma: three-year follow-up of CASTOR. Clin Lymphoma Myeloma Leuk. 2020;20:509-18.
4. de Weers M, Tai YT, van der Veer MS, et al. Daratumumab, a novel therapeutic human CD38 monoclonal antibody, induces killing of multiple myeloma and other hematological tumors. J Immunol. 2011;186:1840-8.
5. Krejcik J, Casneuf T, Nijhof IS, et al. Daratumumab depletes CD38+ immune regulatory cells, promotes T-cell expansion, and skews T-cell repertoire in multiple myeloma. Blood. 2016;128:384-94.
6. Overdijk MB, Jansen JH, Nederend M, et al. The therapeutic CD38 monoclonal antibody daratumumab induces programmed cell death via fcγ receptor-mediated cross-linking. J Immunol. 2016;197:807-13.
7. Mateos MV, Dimopoulos MA, Cavo M, et al. Daratumumab plus bortezomib, melphalan, and prednisone for untreated myeloma. N Engl J Med. 2018;378:518-28.
8. Dimopoulos MA, San-Miguel J, Belch A, et al. Daratumumab plus lenalidomide and dexamethasone versus lenalidomide and dexamethasone in relapsed or refractory multiple myeloma: updated analysis of POLLUX. Haematologica. 2018;103:2088-96.
9. Facon T, Kumar S, Plesner T, et al. Daratumumab plus lenalidomide and dexamethasone for untreated myeloma. N Engl J Med. 2019;380:2104-15.
10. Mateos MV, Cavo M, Blade J, et al. Overall survival with daratumumab, bortezomib, melphalan, and prednisone in newly diagnosed multiple myeloma (ALCYONE): a randomised, open-label, phase 3 trial. Lancet. 2020;11;395(10218):132-41.
11. Dimopoulos MA, Oriol A, Nahi H, et al. Daratumumab, lenalidomide, and dexamethasone for multiple myeloma. N Engl J Med. 2016;375:1319-31.
12. Dimopoulos M, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): results from a randomised, multicentre, open-label, phase 3 study. Lancet. 2020;396:186-97.
13. Moreau P, Attal M, Hulin C, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. Lancet. 2019;394(10192):29-38.

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P03 RATIONALE AND DEVELOPMENT OF AN E-HEALTH APPLICATION TO DELIVER PATIENT CENTERED CARE DURING TREATMENT FOR MULTIPLE MYELOMA IN THE NETHERLANDS.

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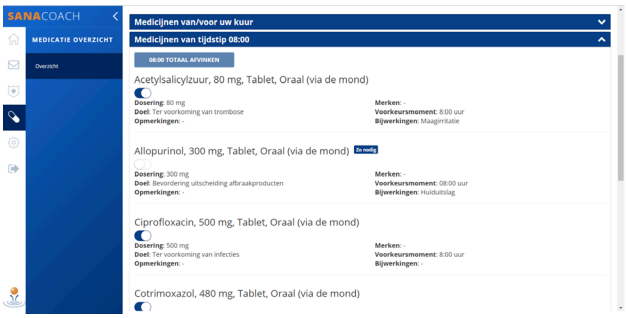
Patients with newly diagnosed Multiple Myeloma (NDMM) face increasingly complicated treatment regimens, including many medications. E-health may support patients and health care providers during treatment, enhancing patient centered care delivery. Therefore, we aimed to develop a multi-modality e-health application. Furthermore, we aimed to assess the application for usability and end-user experiences and to formulate additional requirements for improvement.

The application was developed following an iterative action-based methodology, the Design Thinking approach. Key end-users, including patients, hematologists, pharmacists and nurse specialists, were actively involved. Additional stakeholders, including information technology specialists, secretaries and managers, were consulted during an iterative development process. Before developing the application, the care pathway was evaluated and the ideal care pathway was defined, including integrating an e-health application. Second, the focus of development was determined and a solution ideated during recurring multidisciplinary meetings. Third, mockup display sketches of the intended application modules were recurrently discussed and optimized. Fourth, prototypes were tested and improved. Finally, a final prototype was tested during a pilot study with 18 patients and 7 healthcare professionals, evaluating usability, usage and qualitative experiences.

The application, 'MM E-coach', consisted of a newly developed medication module (Figure 1), patient reported outcomes (PROs) and experiences questionnaire assessments, a messaging service, threshold-based alerts, information provision and a personal care plan. Following 8 weeks of use, the median system usability scale score was 60. Patients appreciated the medication overview and the healthcare professionals the outpatient clinic preparation module. Both appreciated the messaging service. Several recommendations for improvement were made, for example adding new or more flexible functionalities and improving the application view at a glance.

The MM E-coach has the potential to provide patient-centered care by supporting patients and caregivers during Multiple Myeloma treatment and is a promising application to be implemented in the Multiple Myeloma care pathway. Following the recommended improvements, a randomized clinical trial is being conducted to evaluate the clinical effectiveness in hospital practice.



3. Relapsed/Refractory Multiple Myeloma

P04 DARATUMUMAB PLUS BORTEZOMIB AND DEXAMETHASONE VERSUS BORTEZOMIB AND DEXAMETHASONE ALONE IN PATIENTS WITH PREVIOUSLY TREATED MULTIPLE MYELOMA: OVERALL SURVIVAL RESULTS FROM THE PHASE 3 CASTOR TRIAL

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Daratumumab (DARA) is a human IgGκ monoclonal antibody targeting CD38 approved in combination with standard-of-care regimens for pts with newly diagnosed multiple myeloma (NDMM) and as monotherapy and in combination with standard-of-care regimens for pts with relapsed/refractory multiple myeloma (RRMM). In the primary analysis of the phase 3 CASTOR study (median follow-up, 7.4 months), DARA plus bortezomib and dexamethasone (D-Vd) significantly prolonged progression-free survival (PFS) versus bortezomib and dexamethasone (Vd) alone in pts with RRMM, and key secondary endpoints (including time to disease progression, rate of very good partial response or better, overall response rate, and minimal residual disease [MRD]–negativity rate) showed a statistically significant benefit favoring D-Vd. Here, we report final overall survival (OS) and updated MRD-negativity and safety results after ~6 years of follow-up.

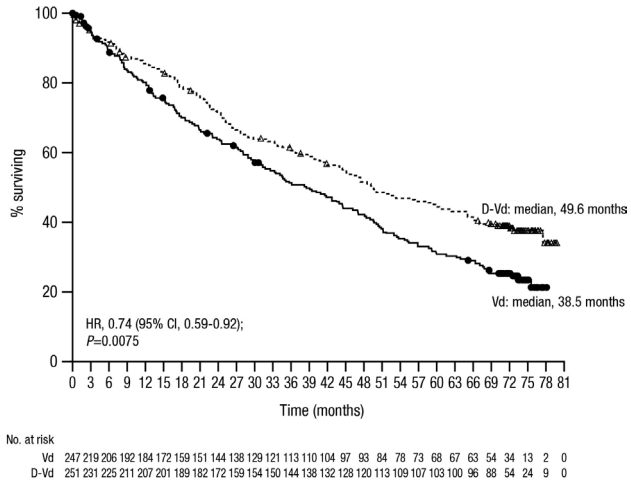
Methods: Pts with RRMM and ≥1 prior line of therapy were randomized 1:1 to receive D-Vd or Vd. All pts received up to 8 (21-day) cycles of Vd (V 1.3 mg/m^2 SC on Days 1, 4, 8, and 11; d 20 mg PO or IV on Days 1, 2, 4, 5, 8, 9, 11, and 12). Pts in the D-Vd group also received DARA (16 mg/kg IV QW in Cycles 1-3, Q3W in Cycles 4-8, and Q4W thereafter until disease progression or unacceptable toxicity). The primary endpoint was PFS; OS was a secondary endpoint.

Results: In total, 498 pts were randomized (D-Vd, n=251; Vd, n=247). Median (range) age was 64 (30-88) years; pts had received a median (range) of 2 (1-10) prior lines of therapy. At a median (range) follow-up of 72.6 (0.0-79.8) months, the CASTOR study showed a statistically significant and clinically meaningful improvement in OS with D-Vd versus Vd (hazard ratio [HR], 0.74; 95% confidence interval [CI], 0.59-0.92; P=0.0075 [crossing the prespecified stopping boundary of P=0.0323]), representing a 26% reduction in the risk of death with D-Vd (Figure). Median OS was 49.6 (95% CI, 42.2-62.3) months with D-Vd versus 38.5 (95% CI, 31.2-46.2) months with Vd. Prespecified subgroup analyses showed an OS improvement with D-Vd versus Vd across most subgroups, including pts aged ≥65 years; pts who had received 1 or 2 prior lines of therapy; pts with International Staging System stage III disease, high-risk cytogenetic abnormalities, or prior bortezomib treatment; and pts who were refractory to their last prior line of therapy. The most

pronounced OS benefit of D-Vd was seen in pts with 1 prior line of therapy (HR, 0.56; 95% CI, 0.39-0.80). D-Vd achieved significantly higher rates of MRD negativity (10^{-5}) versus Vd (15.1% vs 1.6%; $P<0.0001$). The most common (≥10%) grade 3/4 treatment-emergent adverse events (TEAEs; D-Vd/Vd) were thrombocytopenia (46.1%/32.9%), anemia (16.0%/16.0%), neutropenia (13.6%/4.6%), lymphopenia (10.3%/2.5%), and pneumonia (10.7%/10.1%). Rates of discontinuation due to TEAEs were low and similar between treatment groups (D-Vd, 10.7%; Vd, 9.3%). No new safety concerns were identified with extended follow-up.

Conclusion: Treatment with D-Vd significantly prolonged OS compared with Vd alone. These results, together with the OS results observed with DARA in combination with lenalidomide and dexamethasone in the phase 3 POLLUX study, demonstrate for the first time an OS benefit with DARA-containing regimens in RRMM. The greatest OS benefit of D-Vd was observed in pts with 1 prior line of therapy. Our results support early use of D-Vd to maximize pt benefit.

Figure: OS in the ITT population.



OS, overall survival; ITT, intent-to-treat; D-Vd, daratumumab plus bortezomib/dexamethasone; Vd, bortezomib/dexamethasone; HR, hazard ratio; CI, confidence interval.

P05 DARATUMUMAB PLUS LENALIDOMIDE AND DEXAMETHASONE VERSUS LENALIDOMIDE AND DEXAMETHASONE ALONE IN PATIENTS WITH PREVIOUSLY TREATED MULTIPLE MYELOMA: OVERALL SURVIVAL RESULTS FROM THE PHASE 3 POLLUX TRIAL

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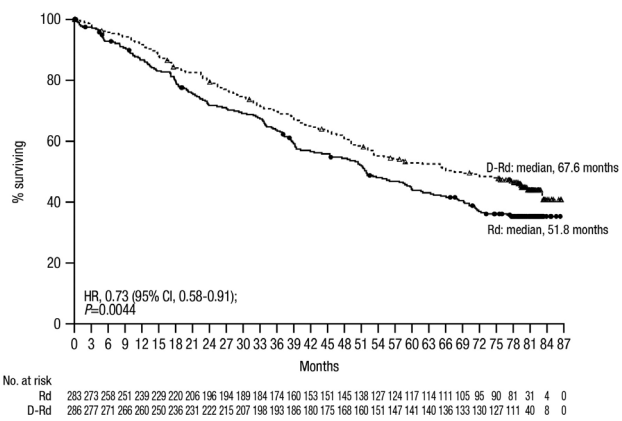
Introduction: Daratumumab (DARA) is a human IgGκ monoclonal antibody targeting CD38 that is approved in combination with standard-of-care regimens for pts with newly diagnosed multiple myeloma (NDMM) and as monotherapy and in combination with standard-of-care regimens for pts with relapsed/refractory multiple myeloma (RRMM). In the primary analysis of the phase 3 POLLUX study (median follow-up, 13.5 months), DARA plus lenalidomide and dexamethasone (D-Rd) provided a significant progression-free survival (PFS) benefit versus lenalidomide and dexamethasone (Rd) alone, and key secondary endpoints (including time to disease progression, rate of very good partial response or better, overall response rate, and minimal residual disease [MRD]–negativity rate) showed a statistically significant benefit favoring D-Rd. Here, we report final overall survival (OS) and updated MRD-negativity and safety results after >6 years of follow-up.

Methods: Pts with RRMM and ≥1 prior line of therapy were randomized 1:1 to receive D-Rd or Rd. All pts received 28-day cycles of Rd (R 25 mg PO on Days 1-21; d 40 mg QW). Pts in the D-Rd group also received DARA (16 mg/kg IV QW in Cycles 1-2, Q2W in Cycles 3-6, and Q4W thereafter). In both groups, pts were treated until disease progression or unacceptable toxicity. The primary endpoint was PFS; OS was a secondary endpoint.

Results: In total, 569 pts were randomized (D-Rd, n=286; Rd, n=283). The median (range) age was 65 (34-89) years; pts had received a median (range) of 1 (1-11) prior lines of therapy. At a median (range) follow-up of 79.7 (0.0-86.5) months, the POLLUX study showed a statistically significant and clinically meaningful improvement in OS with D-Rd versus Rd (hazard ratio, 0.73; 95% confidence interval [CI], 0.58-0.91; $P=0.0044$ [crossing the prespecified stopping boundary of $P<0.0331$]), representing a 27% reduction in the risk of death in the D-Rd group (Figure). The median OS was 67.6 (95% CI, 53.1-80.5) months in the D-Rd group versus 51.8 (95% CI, 44.0-60.0) months in the Rd group. Prespecified subgroup analyses showed an OS improvement with D-Rd versus Rd in most subgroups, including pts aged ≥65 years; pts who had received 1, 2, or 3 prior lines of therapy; pts with International Staging System stage III disease; and pts who were refractory to a proteasome inhibitor or to their last prior line of therapy. D-Rd achieved significantly higher rates of MRD negativity (10^{-5}) versus Rd (33.2% vs 6.7%; $P<0.0001$). The most common (≥10%) grade 3/4 treatment-emergent adverse events (TEAEs; D-Rd/Rd) were neutropenia (57.6%/41.6%), anemia (19.8%/22.4%), pneumonia (17.3%/11.0%), thrombocytopenia (15.5%/15.7%), and diarrhea (10.2%/3.9%). Rates of discontinuation due to TEAEs were comparable between treatment groups (D-Rd, 19.1%; Rd, 16.0 %). There were no new safety concerns identified with extended follow-up.

Conclusion: Treatment with D-Rd significantly prolonged OS compared with Rd alone. These results, together with the OS results observed with DARA in combination with bortezomib and dexamethasone in the phase 3 CASTOR study, demonstrate for the first time an OS benefit with DARA-containing regimens in RRMM. Our results support the use of DARA in pts with RRMM.

Figure: OS in the ITT population.



OS, overall survival; ITT, intent-to-treat; D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval.