



VHL UK/Ireland Patient/Carer Belzutifan Survey - Summary

Results Published July 2023 (Data collected June 2023)

This short survey was commissioned by the Trustees of VHL UK/Ireland Charity to aid their submissions to the relevant UK/Ireland healthcare authorities* for the appraisal of belzutifan (Welireg) for VHL in UK/Ireland.

We offer our sincere thanks to all participants, whose insights are vital to understanding patient/carers experience of this new drug and to the VHL Alliance for your unwavering support.

*relevant healthcare authorities include, but is not exclusive to: NICE (England & Wales), SMC (Scotland), EMA (Ireland), additional bodies where relevant (e.g. for Northern Ireland)

Latest details about the appraisal can be found on the VHL UK/Ireland website:

<https://vhl-uk-ireland.org>

!!!!Trigger Warning!!!!

Please note some of these results may be unsettling especially to newly diagnosed patients or their carers or anyone currently having a difficult time with the disease. Please note this data was collected to help understand the impact of this new potential drug on patients and their carers to support improvements in its treatment.

Questions about this report or its data can be directed to teamnice@vhl-uk-ireland.org

EXECUTIVE SUMMARY

Overall, this survey demonstrates that a significant number of patients using belzutifan (Welireg) experience a positive impact on their tumours (stability, growth and reduction) and also on their lives and well-being as a result. Side effects are manageable and the treatment is 91% more desirable than the only other current alternative – surgery. Carers' lives are also significantly impacted for the better when the patient they care for is being treated with belzutifan (Welireg).

- Patients had an average of 2.5 areas of their body affected by VHL tumours when they started using belzutifan (Welireg), with **57%** of patients having 3 or 4 areas affected. **68%** of patients said they started to use the treatment as an alternative to one or more probable surgeries. **64%** had been using the treatment for more than 1 year.
- Significantly, although the number of patients who experienced side effects was high (**75%**), **NO** patients surveyed stopped treatment permanently and 17 patients (**52%**) continued using it regardless. Of those who took some action, the most common response was to reduce dosage, either temporarily or permanently (10 patients/**30%**).
- The effectiveness of the treatment varies by patient but significantly, **ALL** patients experienced some form of stability, slowdown of growth, reduction in size or disappearance of some tumours (where scans had taken place):
 - **61%** of patients reported one or more tumours stabilised (23% at least one tumour)
 - **66%** of patients reported one or more tumours slowed speed of growth (14% at least one tumour)
 - **66%** of patients reported one or more tumours reduced in size (30% at least one tumour)
 - **16%** of patients reported one or more tumours disappeared (**27%** at least one tumour)
- **80%** of patients believe they have avoided an imminent surgery due to use of belzutifan (Welireg). Not knowing the long-term effect of taking belzutifan (Welireg) worries only **34%** of patients. **98%** are grateful for the opportunity to try this treatment and **82%** worry less about their VHL when using belzutifan (Welireg). **68%** of patients say their quality of life has improved since using this treatment and **91%** said using belzutifan (Welireg) is more desirable than surgery.
- Whilst we know VHL affects all areas of a patient's life, the most positive impacts reported from belzutifan (Welireg) patients were:
 - **Mental Health** - 37 patients - (84%) said 'Yes'
 - **Planning for the future** - 36 patients (82%) said 'Yes'
 - **Social/Leisure activities** - 31 patients (70%) said 'Yes'
 - **Independence** - 30 patients (68%) said 'Yes'
 - **Relationships** - 28 patients (64%) said 'Yes'
 - 50% or more also said work/career and travel had been positively impacted.
- We know from previous surveys that sometimes the impact on the carer, especially around their own mental health can sometimes be greater than that of the patient. All respondents of this survey who care for a VHL patient said they were grateful the patient they care for had the opportunity to try this treatment and although **63%** worry about the long-term effects, **75%** worry less about the patient they care for when they are using belzutifan (Welireg). **88%** said it had improved their own quality of life and the treatment was **100%** more desirable than surgery.
- The most positive impacts reported from belzutifan (Welireg) carers were:
 - **Work/Career** - 7 patients (88%) said 'Yes'
 - **Social/Leisure activities** - 7 patients (88%) said 'Yes'
 - **Planning for the future** - 7 patients (88%) said 'Yes'
 - **Mental Health** - 7 patients (88%) said 'Yes'
 - **Independence** - 6 patients (75%) said 'Yes'
 - **Travel** - 6 patients (75%) said 'Yes'

TOTAL RESPONDANTS

- 44 patients who have used belzutifan (Welireg). Notes:
 - Due to an error in the survey, only 28 of these respondents were asked which country they were from. Of these 28, 89% were from the USA, 7% from Canada, 4% from UK.
 - No data regarding respondent age was taken
- 8 carers-of-patients who have used belzutifan (Welireg). Notes:
 - Due to an error in the survey, no carer respondents were asked which country they were from.
 - No data regarding respondent age was taken.

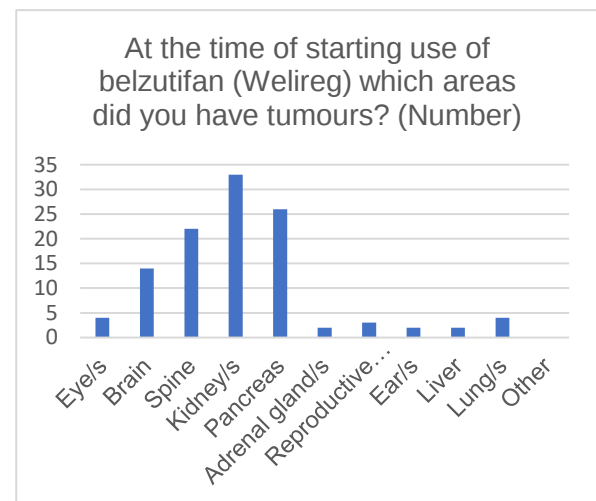
VHL PATIENT RESPONDENT DATA:

Patients' response data were collected from 44 participants in the survey.

Question 1: At the time of starting use of belzutifan (Welireg) which areas did you have tumours?

- At the time of starting use of belzutifan (Welireg) 44 patients had 112 tumours between them (an average of 2.5)
- The most areas of the body affected by any one patient were 5 (9 patients/20%), 4 areas (12 patients/27%), 3 areas (13 patients/30%), 2 areas (9 patients/20%), 1 area (1 patient/2%)
- Most commonly affected areas were, Kidney/s (29%), Pancreas 23%, Spine (20%), Brain (13%)

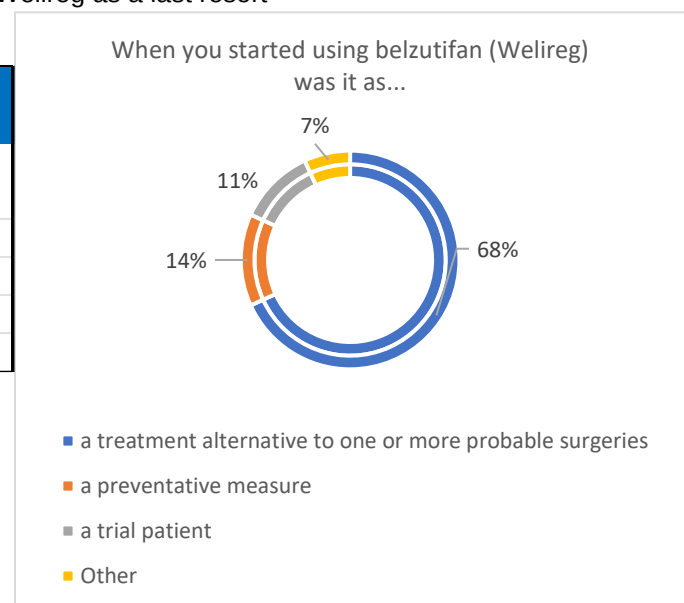
	Number	%
Kidney/s	33	29%
Pancreas	26	23%
Spine	22	20%
Brain	14	13%
Eye/s	4	4%
Lung/s	4	4%
Reproductive Organs	3	3%
Adrenal gland/s	2	2%
Ear/s	2	2%
Liver	2	2%
Other	0	0%
	112	100%



Question 2: When you started using belzutifan (Welireg) was it as...

- A treatment to avoid probable surgery (30 patients/68%), a preventative measure (6 patients/14%), a trial patient (5 patients/11%)
- 3 patients who reported using belzutifan (Welireg) for 'Other' reasons listed:
 - To save what is left of my pancreas (head) and my kidneys after 3 partial nephrectomies & 2 RFAs
 - Surgical intervention no longer possible, Welireg as a last resort
 - Kidney cancer treatment

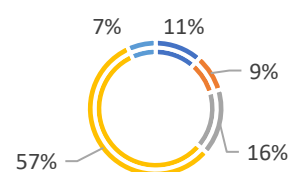
When you started using belzutifan (Welireg) was it as...	Number	%
a treatment alternative to one or more probable surgeries	30	68%
a preventative measure	6	14%
a trial patient	5	11%
Other	3	7%
	44	100%



Question 3: How long have you been using/did you use belzutifan (Welireg) for?

How long have you been using/did you use belzutifan (Welireg) for?	Number	%
Less than 3 months	5	11%
3-6 months	4	9%
6-12 months	7	16%
1-2 years	25	57%
2 years +	3	7%
	44	100%

How long have you been using/did you use belzutifan (Welireg) for?

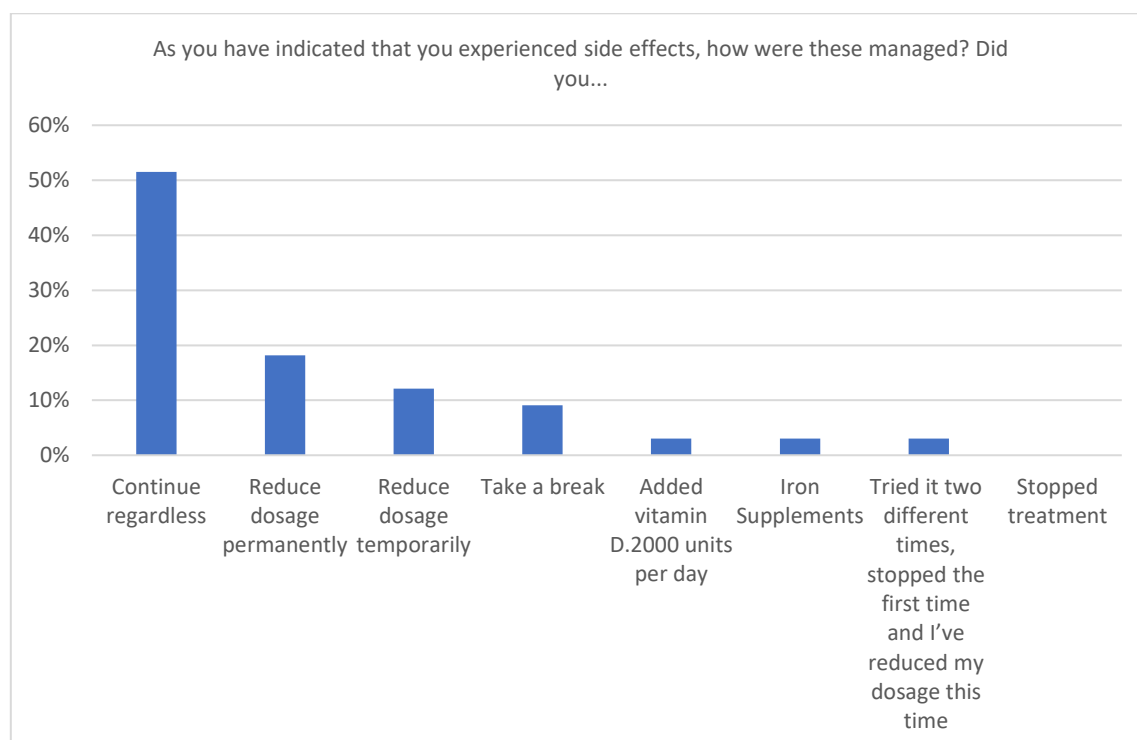


■ Less than 3 months ■ 3-6 months
 ■ 6-12 months ■ 1-2 years
 ■ 2 years +

Question 4 & 5: Side Effects.

- 33 patients (75%) answered 'Yes' to Have you ever experienced side effects from using belzutifan (Welireg)?
- 7 patients (16%) answered 'No', 4 (9%) were 'unsure'
- No patients surveyed stopped treatment permanently and 17 patients 52% continued using it regardless. Of those who took action, the most common response was to reduce dosage, either temporarily or permanently (10 patients/30%).
- One carer reported his wife decided to withdraw from the original trial due to the side effects she experienced but she had stable disease at the time and he indicates she would be willing to use it again in future if the need arises.

Of the patients who indicated they experienced side effects, they said they took the following action:

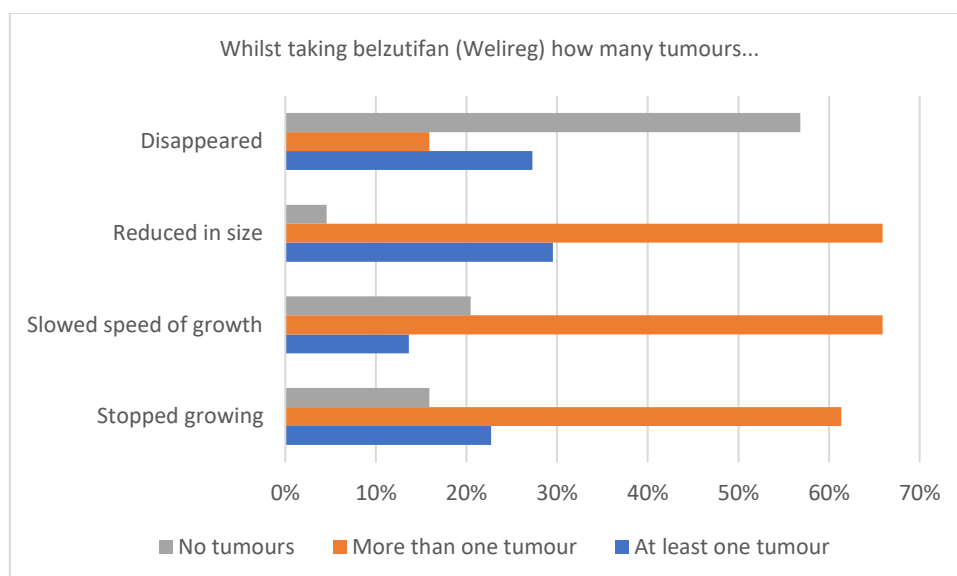


As you have indicated that you experienced side effects, how were these managed? Did you...	Number	%
Continue regardless	17	52%
Reduce dosage permanently	6	18%
Reduce dosage temporarily	4	12%
Take a break	3	9%
Added vitamin D.2000 units per day	1	3%
Iron Supplements	1	3%
Tried it two different times, stopped the first time and I've reduced my dosage this time	1	3%
Stopped treatment	0	0%
	33	100%

Question 6: Impact on tumours

- STOP GROWING: 27 patients (61%) saw 'more than one tumour', 10 patients (23%) in 'at least one tumour', 7 patients (16%) 'No tumours'.
- SLOW SPEED OF GROWTH: 29 patients (66%) saw 'more than one tumour', 6 patients (14%) in 'at least one tumour', 9 patients (20%) 'No tumours'
- REDUCE IN SIZE: 29 patients (66%) saw 'more than one tumour', 13 patients (30%) in 'at least one tumour', 2 patients (5%) 'No tumours'
- DISSAPPEAR: 7 patients (16%) saw 'more than one tumour', 12 patients (27%) in 'at least one tumour', 25 patients (57%) 'No tumours'
- Note one respondent, who had been on belzutifan (Welireg) for 3 months or less had not yet had scans to see the impact.

Whilst taking belzutifan (Welireg) how many tumours...	At least one tumour	More than one tumour	No tumours	TOTAL	At least one tumour	More than one tumour	No tumours
Stopped growing	10	27	7	44	23%	61%	16%
Slowed speed of growth	6	29	9	44	14%	66%	20%
Reduced in size	13	29	2	44	30%	66%	5%
Disappeared	12	7	25	44	27%	16%	57%



Some patient respondents chose to give more detail, in their own words:

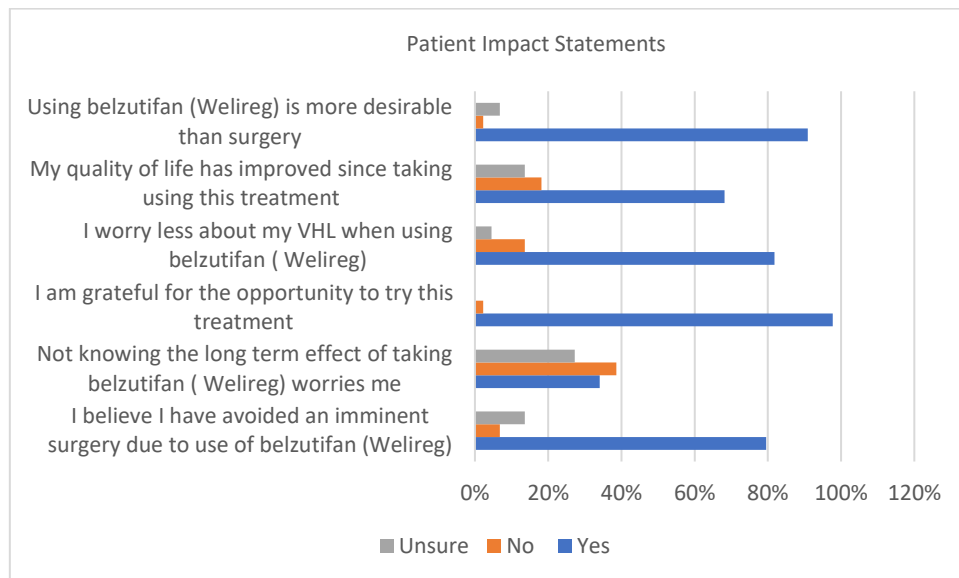
- 1 brain tumor shrank & one disappeared. Pancreas & kidney tumors have stabilized
- Brain and spine shrunk right away. Kidney has 4 tumors and they did not grow
- My RCC growth slowed down (only .2 cm in five years on Welireg) most spinal cord and brain hemangiomas disappear
- Brain tumors and one near optic nerve decreased by about 50% in 6 months, then at a year, they were both "still visible, but not measurable".
- Had 9 brain tumors before taking, now only 4 can be found and those are all smaller. 2 Kidney tumors over 2 cm but are now under 2cm.r
- I had mRCC with over 40 metastatic sites, in addition to 3 cerebellar hemangioma, a spinal hemangioma, a pancreatic pNet, and several lesions on my retinas. ALL HAVE STABILISED, REDUCED, OR DISAPPEARED. I had been told my life was at an end at age 42. On the trial, in the Netherlands, I was randomised to receive the highest dose, 200mg per day. I have had only minor side effects, none required treatment.
- Adrenal - no change. Pancreatic and kidney - tumors reduced in size
- Innumerable spinal lesions showed shrinkage or stagnation
- After 9 months, it stopped working for me
- Tumors shrinking in brain, eyes, kidney
- My two brain tumors reduced in size by 70%. Most pancreas tumors reduced in size. Out of my 4 main cancer tumors on my kidneys 1 shrunk, 2 stayed the same size and 1 grew despite the Welireg.
- 4 pancreatic tumors have completely disappeared
- Cerebellum tumor shrank by 30%
- The tumors in my kidneys, spine and brain have all showed shrinkage or them being slowed down to almost a halt.
- Brain, Spine
- I have a scan in July, not sure what it's done to the tumors yet
- Overall reduction in size, nothing has disappeared, but I've been on for about 3 months.
- Don't know yet! I have not been on Welireg long enough to find out if tumors have responded. Looking forward to getting those scans.
- My kidney did not grow my brain tumors reduced size
- I grew immune to the Welireg and the tumors grew back quick. Had to be taken off of it. And it spread to my lungs and lymph nodes.
- All tumors stopped growing or have been reduced in size. I had 10 tumors in 5 different spots.
- Brain tumors and pancreatic tumors significantly reduced, kidney tumors have been more stubborn.

- Practically all tumors shrink pressure in head went down retinal specialist said my optic nerve and retina looked better/ less red
- Brain and spine tumors have decreased in size. Kidney tumor growth is slower.

Question 7: Impact on patient life

In response to the following statements patients said: (most common result highlighted in yellow)

- **I believe I have avoided an imminent surgery due to use of belzutifan (Welireg)** - 35 patients (80%) said 'Yes', 3 patients (7%) said 'No', 6 patients (14%) were 'Unsure'.
- **Not knowing the long-term effect of taking belzutifan (Welireg) worries me** - 15 patients (34%) said 'Yes', 17 patients (39%) said 'No', 12 patients (27%) were 'Unsure'.
- **I am grateful for the opportunity to try this treatment** - 43 patients (98%) said 'Yes', 1 patients (2%) said 'No', 0 patients (0%) were 'Unsure'.
- **I worry less about my VHL when using belzutifan (Welireg)** - 36 patients (82%) said 'Yes', 6 patients (14%) said 'No', 2 patients (5%) were 'Unsure'.
- **My quality of life has improved since taking using this treatment** - 30 patients (68%) said 'Yes', 8 patients (18%) said 'No', 6 patients (14%) were 'Unsure'.
- **Using belzutifan (Welireg) is more desirable than surgery** - 40 patients (91%) said 'Yes', 1 patients (2%) said 'No', 3 patients (7%) were 'Unsure'.



Belzutifan has had a positive impact on... (most common result highlighted in yellow)

Education - 12 patients (27%) said 'Yes', 18 patients (41%) said 'No', 14 patients (32%) were 'Unsure'.

Work/Career - 24 patients (55%) said 'Yes', 10 patients (23%) said 'No', 10 patients (23%) were 'Unsure'.

Social/Leisure activities - 31 patients (70%) said 'Yes', 9 patients (20%) said 'No', 4 patients (9%) were 'Unsure'.

Relationships - 28 patients (64%) said 'Yes', 9 patients (20%) said 'No', 7 patients (16%) were 'Unsure'.

Family planning - 16 patients (36%) said 'Yes', 19 patients (43%) said 'No', 9 patients (20%) were 'Unsure'.

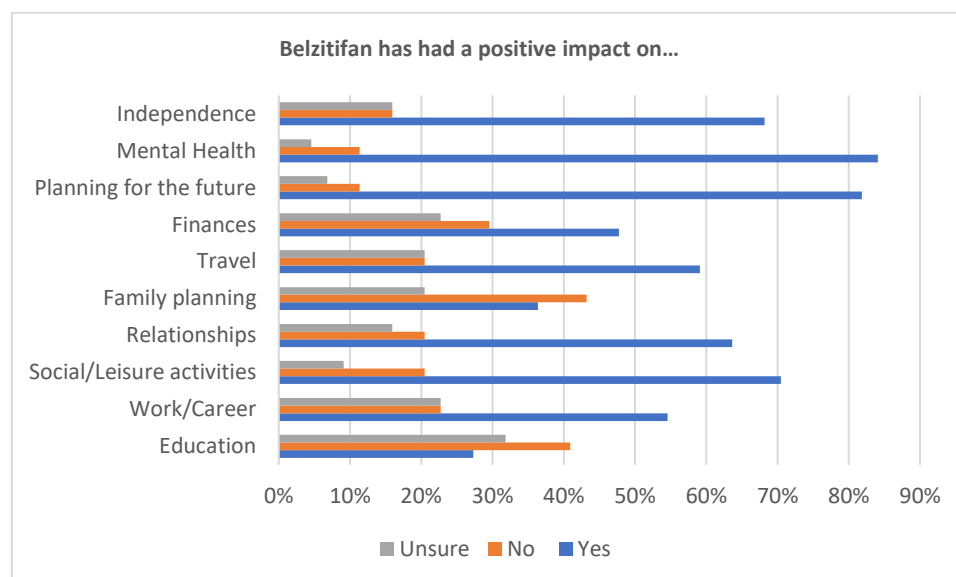
Travel - 26 patients (59%) said 'Yes', 9 patients (20%) said 'No', 9 patients (20%) were 'Unsure'.

Finances - 21 patients (48%) said 'Yes', 13 patients (30%) said 'No', 10 patients (23%) were 'Unsure'.

Planning for the future - 36 patients (82%) said 'Yes', 5 patients (11%) said 'No', 3 patients (7%) were 'Unsure'.

Mental Health - 37 patients (84%) said 'Yes', 5 patients (11%) said 'No', 2 patients (5%) were 'Unsure'.

Independence - 30 patients (68%) said 'Yes', 7 patients (16%) said 'No', 7 patients (16%) were 'Unsure'.



Some patient respondents chose to give more detail, in their own words:

- Side effects have me using home oxygen 24/7 & 1 blood transfusion so far, but so much better than surgery. I am trying this out as I have passed on VHL to my 2 daughters & grandson, so I am willing to be a guinea pig in Canada to see the benefits & problems for my family. My brother died at 18, my sister at 55 & my Dad at 61. I am 70 & surpassed the age I thought I would have died by, so I hope & pray that this works. I have had to drop to 80 mg after 1 year or so to help my pulse ox.
- Godsend!
- feel it is keeping me from dialysis since I only have one kidney and the growth on 4 tumors is stable
- I am one of the original Phase II Clinical trial patients on PT2977 (now Welireg). It delayed for 5 years an imminent surgery on my right kidney. I am going to have the tumor removed surgically soon. I have been approved to continue on the trial!!!!
- Avoiding surgery and/or radiation is amazing!! My only side effect has been low haemoglobin, which has made me a little extra tired at times, but overall not bad.
- Gift from God worth every side effect so grateful.
- I'm so much more comfortable enjoying life and not worrying about my next surgery.
- I feel like i am effectively (not literally) cured of VHL
- I am grateful for the opportunity to take this medication to ward off surgery. This has helped my mental health greatly and left me feeling like I have options and an active way to treat my disease as opposed to waiting for my next surgery.
- It has allowed me to continue life as normal. I suffered in the first few months from fatigue and higher sensitivity to heat but both have subsided and are not noticeable now that my body has adjusted. My first follow up scan resulted in 1 tumor shrinking by 30% which has remained stable since. All other have remained stable as well.
- Honestly the largest impact Welireg has had on my life was that it gave me hope in an area where I had none. I had always just accepted the fact that I was going to die from VHL and

honestly it didn't bother me. What bothered me is I had to try and accept that fate for my children.. now it's starting to honestly look like my children may not even have to deal with major surgeries in the future with this being an option. For the first time since I have ever heard the abbreviation "VHL" I have hope that my kids will make it through all of this without all the issues and drama that all of us have had to. I have hope that I myself might actually pull through all of this and come out laughing on the other side because I finally over came the one demon I thought was unbeatable in my life. I am the hugest advocate for this medication in my family. I am constantly begging them all to get on this medication because it truly does make a difference. I've witnessed the results with my own body. Yes it does have some side affects, but honestly it just makes you extra sleepy or sometimes an increase in headache or something like that. Honestly people let that chemo word scare them but this is nothing like chemo in the regards of it doesn't destroy us and make us ungodly sick. I think anyone who has a need for this medication should have access to it and hope you all bring it to the UK and Ireland and anywhere else it is needed very soon.

- Right now, I struggle with fatigue. That factors into everything I do, but I'm hoping it'll get better soon.
- There are fewer and milder side effects than the treatment I was previously receiving for cancer. I have more energy and less pain.
- Anaemia (side effect of Welireg) has slowed me down considerably.
- "If I need surgery for my current tumors, it will be EXTREMELY dangerous. Counting on Welireg to turn my tumor growth around before I get symptoms. So grateful to have this. It's saving my sanity. I'm only 49 and at a high point in my career. "
- I was facing a challenging pancreatic tumor surgery. Taking belzutifan has reduced the size of those tumors. I will gladly trade the fatigue and headaches for keeping my pancreas.
- I cannot prove it but I cannot disprove it either but I believe I had a pericardial effusion due to welireg. I am thankful for the possibility that Welireg offers but I have aflutter now, on blood thinner and other meds due to heart issues I believe Welireg is responsible for the heart issues. I am on 2 pills instead of 3 now. It also raises my blood sugar, weight gain. I will have scans next month to see how it is doing on my kidneys.
- It's good for me biggest issues are random tiredness and I get a lot of bruises, but one thing not a big deal I don't smoke very much weed but when I did the few times a did while on Welireg it made me super unbalanced so now I don't smoke weed at all I don't know if they as everyone or just me

VHL CARER RESPONDENT DATA:

Carer's response data was collected from 8 participants in the survey.

Question 1: Impact on carer-of-VHL-patient life

In response to the following statements, carers said: (most common result highlighted in yellow)

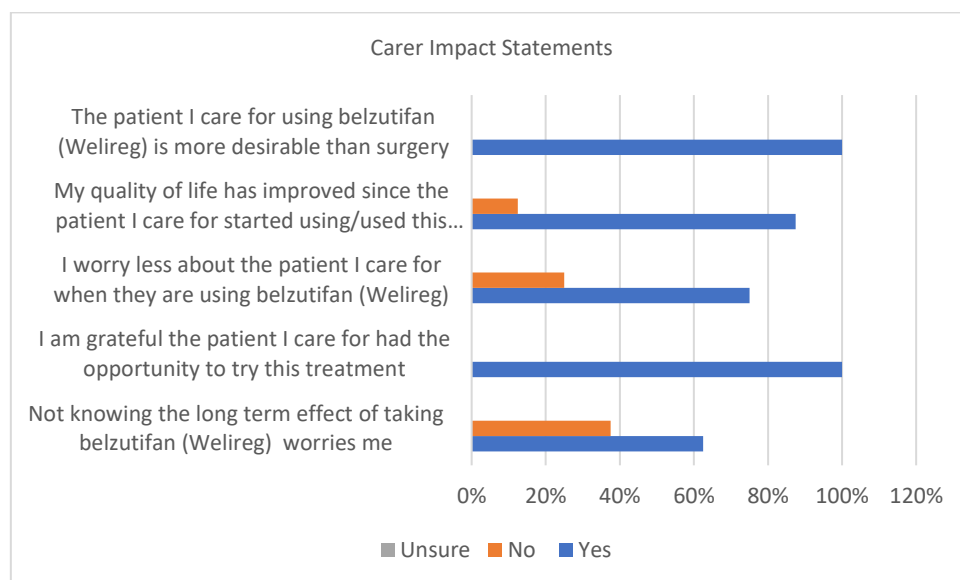
Not knowing the long-term effect of taking belzutifan (Welireg) worries me - 5 carers (63%) said 'Yes', 3 carers (38%) said 'No', 0 carers (0%) were 'Unsure'.

I am grateful the patient I care for had the opportunity to try this treatment - 8 carers (100%) said 'Yes', 0 carers (0%) said 'No', 0 carers (0%) were 'Unsure'.

I worry less about the patient I care for when they are using belzutifan (Welireg) - 6 carers (75%) said 'Yes', 2 carers (25%) said 'No', 0 carers (0%) were 'Unsure'.

My quality of life has improved since the patient I care for started using/used this treatment - 7 carers (88%) said 'Yes', 1 carer (13%) said 'No', 0 carers (0%) were 'Unsure'.

The patient I care for using belzutifan (Welireg) is more desirable than surgery - 8 carers (100%) said 'Yes', 0 carers (0%) said 'No', 0 carers (0%) were 'Unsure'.



Belzutifan has had a positive impact on the carer's own... (most common result highlighted in yellow)

Education - 3 carers (38%) said 'Yes', 3 carers (38%) said 'No', 2 carers (25%) were 'Unsure'.

Work/Career - 7 carers (88%) said 'Yes', 1 carer (13%) said 'No', 0 carers (0%) were 'Unsure'.

Social/Leisure activities - 7 carers (88%) said 'Yes', 1 carer (13%) said 'No', 0 carers (0%) were 'Unsure'.

Relationships - 4 carers (50%) said 'Yes', 1 carer (13%) said 'No', 3 carers (38%) were 'Unsure'.

Family planning - 4 carers (50%) said 'Yes', 1 carer (13%) said 'No', 3 carers (38%) were 'Unsure'.

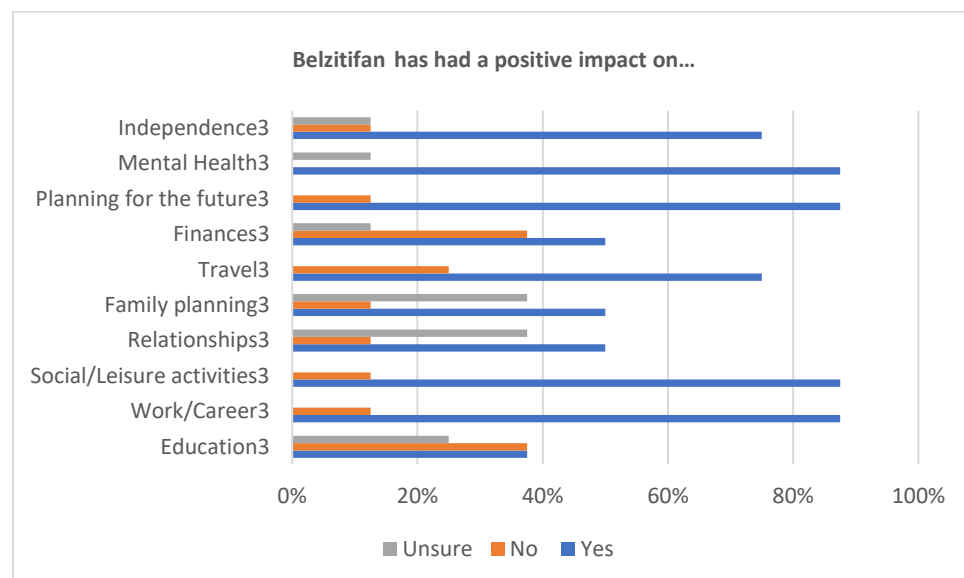
Travel - 6 carers (75%) said 'Yes', 2 carers (25%) said 'No', 0 carers (0%) were 'Unsure'.

Finances - 4 carers (50%) said 'Yes', 3 carers (38%) said 'No', 1 carer (13%) were 'Unsure'.

Planning for the future - 7 carers (88%) said 'Yes', 1 carer (13%) said 'No', 0 carers (0%) were 'Unsure'.

Mental Health - 7 carers (88%) said 'Yes', 0 carers (0%) said 'No', 1 carer (13%) was 'Unsure'.

Independence - 6 carers (75%) said 'Yes', 1 carer (13%) said 'No', 1 carer (13%) was 'Unsure'.



Some carer respondents chose to give more detail, in their own words:

- My wife was in the original trial and had to take a full dose, and it hit her pretty hard. She/NIH had to get permission from the drug company to reduce the dosage. She was happy with the results, but as she was not in a compromised position regarding kidney function, she decided to leave the trial after 18 months due to daily fatigue. A year later a tumor had to be removed by surgery. In the future, she would likely decide to take Belzutifan to shrink tumors to avoid surgery.
- While we are grateful that our daughter is able to take this med and are thrilled with the disappearance of tumors; we still struggle with the strain on her mental health. She also struggles quite a bit with iron deficiency since taking the med. We are trying a new iron supplement that, so far, seems to be working well. Exhaustion is the biggest side effect which may be caused by the low iron.