



Reported Impact of the Different Generic Imatinib Brands

Summary

A survey of GCUK members was undertaken to explore the effects of the introduction of branded versions of imatinib via an online questionnaire. 83 responses were received.

The following findings emerged from this study:

1. Respondents confirmed their experiences of all of the major and well-known side-effects of imatinib.
2. Fatigue, Cramps, Muscle pain and Diarrhoea were the most significant in terms of impact on day-to-day lives.
3. Side-effects vary significantly from person to person.
4. There is evidence that some brands have more severe side-effects than others (but the sample size is relatively small).
5. There is no evidence from this study that some brands are more/less effective than others in reducing tumour size or the risk of re-occurrence (although the period of use of some of the brands is, as yet, relatively short).
6. Participants felt that they were prescribed the cheapest version of the drug and that although some pharmacists would respond to requests for different versions where significant side-effects were experienced, this was not always the case or they didn't now they could request a change.

Preamble

Imatinib is the most common drug prescribed to those with a GIST either to reduce the size of tumours or as a preventative treatment to stop re-occurrence post-surgery. Following the introduction of a range of generic imatinib brands in 2017 there has been a concern that some have more serious side-effects or are less effective at preventing re-occurrence. The aim of this study was to explore, with the GCUK community, the impact of the various brands and compare their reported effectiveness against the original branded version Glivec (Gleevec in the US). Specifically, it aimed to:

- Compare the side-effects of Glivec with other branded versions.
- Explore whether there were any additional side-effects or other factors associated with taking the generic versions.
- Identify any emerging differences in the effectiveness of different brands.
- Allow the GIST community in the UK to share their experiences of taking imatinib in all its variations.

Methodology

A survey of members of GCUK's online noticeboard (Listserve) was undertaken. The survey opened on 19th November and closed at midnight on 30th November. In total 83 responses were received. On behalf of the GCUK community we express our appreciation for those who took the time to complete the survey.

The branded variations listed below had been identified and their effects were explored in the survey together with the number and the percentage of respondents reporting taking each brand. Numbers do not sum to 83 (100%) because some respondents have been on more than one brand:

Accord (37, 48%)	Amarox (23, 32%)	Aurobindo (0, 0%)
Dr Reddy (1, 1%)	Glivec (61, 75%)	Mylan (1, 1%)
Pliva (0, 0%)	Sandoz (17, 23%)	Teva (30, 41%)

The low numbers of respondents taking Aurobindo, Dr Reddy, Mylan and Pliva mean that no further consideration is given to these brands in this report. Respondents were largely UK based but some may have been outside of the UK perhaps giving rise to the responses for Dr Reddy and Mylan.

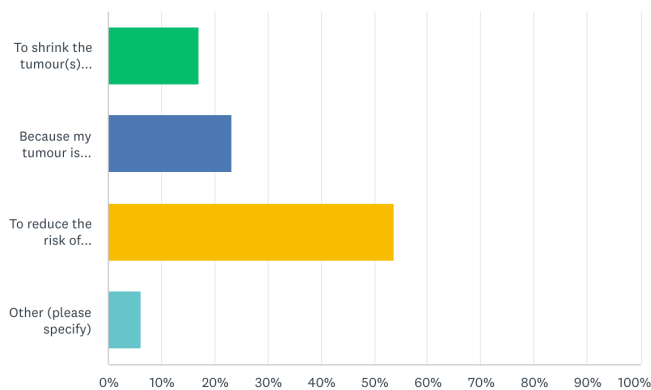
Findings

Reason for taking Imatinib

As background to the research, we were interested in the reasons that participants were taking the drug. The findings are shown in the following figure.

First of all, can you explain why are you taking the drug?

Answered: 82 Skipped: 1

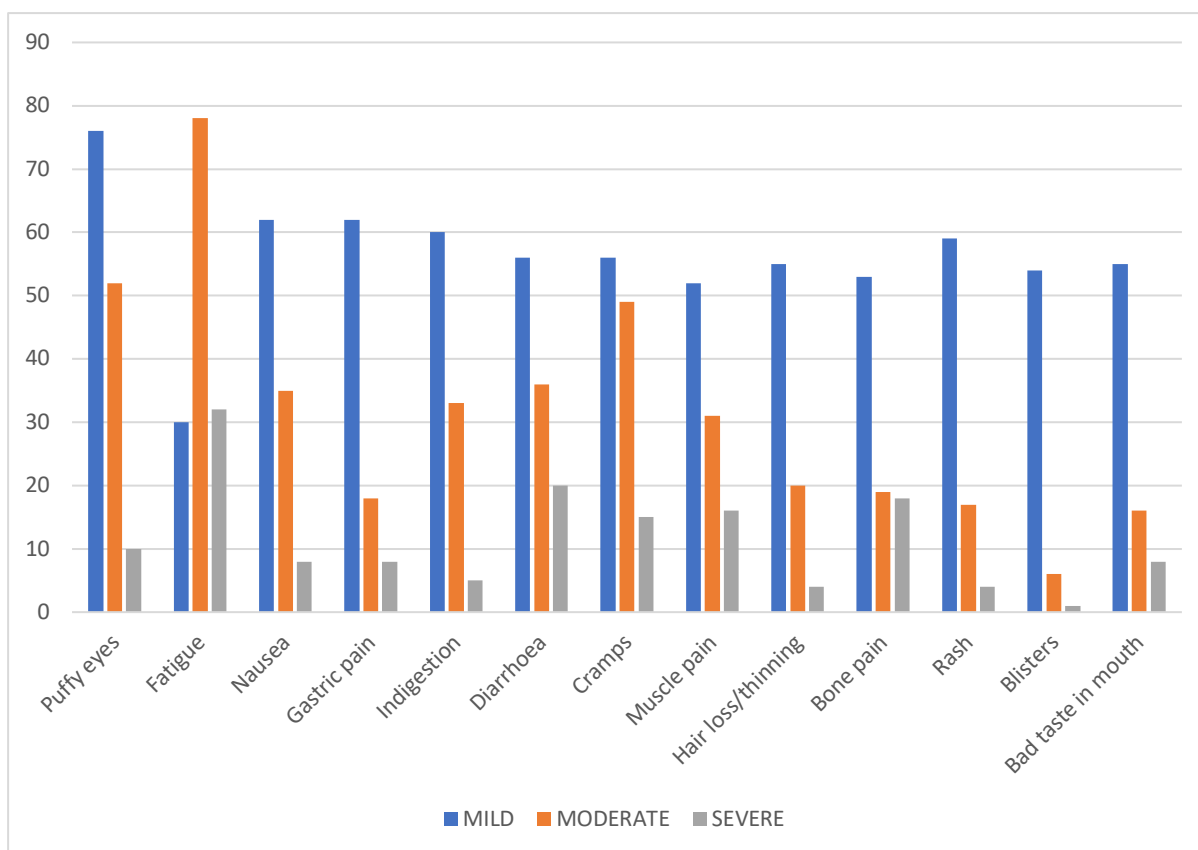


The reduction of the chance for reoccurrence was the main reason according to over 50% of respondents. The 'other reasons' cited were mainly due to the prevention of growth after the partial removal of a tumour following surgery.

Reported side-effects

The main reported side-effects across all imatinib brands are shown in the following figure together with participants' assessment of their impact. All the well-known side-effects were reported although respondents often commented it was sometimes difficult to assess the impact of imatinib separately from other health issues they were suffering.

Fatigue was the most significant side-effect together with Cramps, Muscle pain, Bone pain and Diarrhoea. Puffy eyes, whilst common, was generally assessed as having less of an impact. Some respondents reported no significant side-effects.



Other side-effects

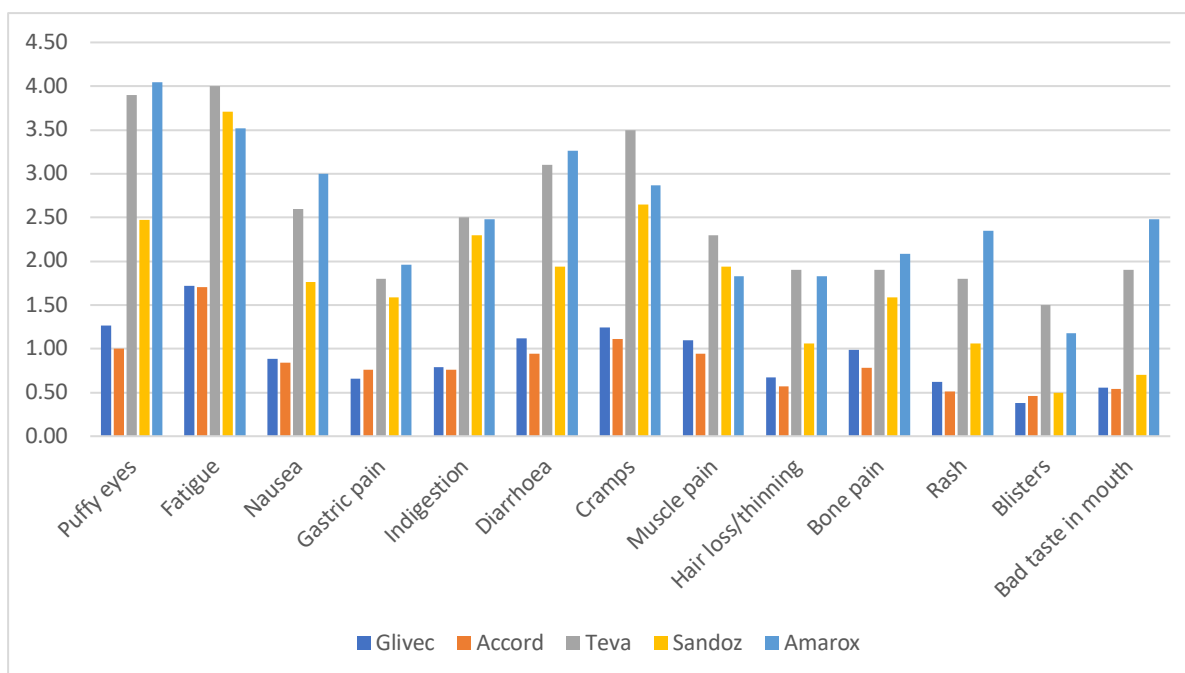
Respondents reported some other side-effects that they associated with taking the drug. The most notable of these was 'migraines':

The migraines, when they occur, are almost intolerable. The sharply deteriorating eyesight, cataracts, and blurred vision (forgot to mention cataracts earlier when completing 'Accord' section) are a real worry. I have now had three new pairs of vari-focals (and three eye tests) in the last 14 months, as I try to keep up with the changes in my eyes.

Effects associated with different brands

One of the main reasons for the study was to identify if there were any significant differences in the side-effects associated with individual brands. The outcomes are shown in the following figure¹.

¹ The relative values are determined by ascribing values of 1 to mild, 2 to moderate and 3 to serious and calculating the resultant value for each drug given the differing number of those reporting taking each. Whilst serious does not necessarily have three times more of an impact than mild, it provides a general means of recording the impact of each drug which makes an allowance for the relative difference of the reported effects. No adjustment is made for the dosage of active ingredient or other factors such as length of time on drug or size of tumour.



The small numbers in some cases and the methodology employed to determine the relative values mean that the results should be approached with caution. However, across all of the reported side-effects, those associated with Teva, Sandoz and AmaroX are all higher than for Glivec and Accord. Quality control should mean the standard of active ingredient (imatinib) is identical in each but the associated packing materials will vary. Whilst there may be a psychological factor associated with taking a variety other than the original, Glivec, this would not explain why the reported effects associated with Glivec and Accord are so similar across all reported categories. The reported outcomes for AmaroX are generally the most negative although there were some reported negative effects of other brands including Glivec and Accord. Having noted the general trends its important to recognise that individuals respond in different ways to each of the brands.

I started on 400mg but my joint pain was very bad so they reduced my dosage to 300mg (Glivec)

Took it for 1 month only in Feb 2022 (as bad rash from Teva.) Migraines returned so went back to Teva. Bad timing as coincided with dermatologist prescribed steroids, and possible Covid bout - so who knows? (Glivec)

I started on 400mg but my joint was very bad so they reduced my dosage to 300mg. The pain everywhere, especially in my knees and my back, was intolerable. (Accord)

I had heard there were awful side effects from this brand but aside from the blood shot eye have perversely found I have the least side effects of the 3 types I have been prescribed. (Accord)

I only lasted a week in this brand, because I was so unwell. (Teva)

Find Teva similar to glivec, eye issues and eye bleeds more common on this though. (Teva)

I belong a group of gist patients and most think Sandox has the least side effects. (Sandoz)

My life is much easier now that I am not sick / feeling nauseous as I was regularly with Accord. (Sandoz)

Requested to be taken off this drug as I was unable to cope. I have been put back on Teva within the last fortnight. (Amarox)

Of all the 3 brands I have taken this is the one I would least like to be issued with again. Primarily because of the permanent bitter taste it leaves on your tongue. My tumour shrank 4mm in 3 months whilst on this brand. (Amarox)

I switched from Accord to Sandoz and the side effects have been much more tolerable. I felt that Accord behaved like a toxin as soon as I swallowed it and it made me violently sick very regularly making my life a misery. I also had more severe side effects e.g. joint pain. Since switching to Sandoz I have been able to tolerate the drug really well, - don't feel as though I am being poisoned, and have fewer, milder side effects.

Effectiveness

One of the purposes of the survey was to determine if there were any reported differences in the effectiveness of the different versions of imatinib. The outcomes are shown in the following table in response to the question: 'Did your tumour respond to this drug?'

	Accord	Amarox	Glivec	Sandoz	Teva
YES	50.00%	47.83%	69.49%	50.00%	62.07%
No	0.00%	4.35%	3.39%	6.25%	3.45%
Don't know	32.35%	34.78%	15.25%	37.50%	27.59%
Too early to say	17.65%	13.04%	11.86%	6.25%	6.90%

There is no discernible difference in the percentage of takers reporting each drug was effective. The percentage of respondents reporting that there was no effect was very small and, given the small sample size at the level of the individual brand, apparently significant differences may only represent one single response. There were few comments on their relative effectiveness.

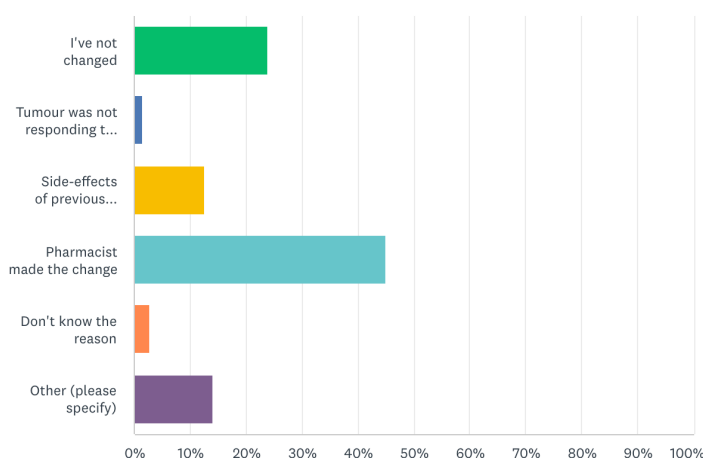
Seemed to reduce tumour size more than Gleevec (Teva)

Reasons for change in brand

Where respondents had changed brands we were interested in the reasons behind this change. The outcomes are shown in the following figure.

Please indicate the reason for any change in brand

Answered: 71 Skipped: 12



Few replied that they had changed as a result of the tumour not responding to their previous drug and most responded that the pharmacist had made the change presumably because of cost and often without explaining the reason for the change. Participants reported that, where there had been significant side-effects with previous versions, pharmacists and/or oncologists were generally willing to change to alternative brands although this was not always the case (or respondees were not aware that they might be able to request such a change).

The Oncologist changed it after surgery, would imagine COST main factor.

Was manageable on the original version now I'm suffering because of cost it's not on.

Hospitals must not regularly swap brands, because of a cheaper contract, this is not like taking aspirin, our bodies can't cope with these changes of brands.

Wanted to try another brand as fatigue was getting to be a problem whilst taking Accord. Switched to Glivec 2 months ago.

The change to Accord was down to the Pharmacy, the change to Sandoz was done in agreement with my Oncologist and the pharmacy due to my reaction to Accord.

I have only had Glevec or AmaroX. I presume I got AmaroX when every one else got it. I was not told It would be changing.

I have been on Imatinib for 5 months. I noticed an increase in side effects for the month when prescribed AmaroX. Returned back to Accord the next month.

Unaware if another type would have fewer side effects. Accord side effects are manageable at the moment.

Symptoms worse on Accord. Oncologist asked for Glivec but not supplied by pharmacist.

Other reported outcomes

There were a few additional comments about related matters.

It seems that the time of day that I take it makes a difference in reducing puffy eyes. I used to take it at night so I wouldn't feel the tiredness but would wake puffy. Now I take it at 3pm ish and it seems to make a difference (less puffiness). (Teva)

Only noticeable difference was in the size of the tablets. When I expressed a preference with the Oncologist for the smaller tablets, I was told it was up to the Hospital Pharmacy which tablets were dispensed.

Use of Findings

This report represents the outcomes of a relatively small-scale study of those taking imatinib in its various formulations. Individual responses will remain confidential. The report will be shared with the GCUK community and with health care practitioners through the GCUK's Medical Advisory Board.

Whilst undertaking the study we became aware of a related study undertaken in the Netherlands which found similar results. We will continue to work with the Netherlands group and others to explore the wider impact of generic versions.

And Finally

We would like to thank all of those members of the GCUK community who shared their experiences of taking imatinib and responded to the questionnaire so promptly.

Mark Atlay, Judith Robinson.

On behalf of GCUK www.gistcancer.org.uk

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