

Senolytics

Johnny Adams

www.AgingIntervention.org

JAdams@AgingInterventionFoundation.org

(949) 922-9786

<https://www.aginginterventionfoundation.org/Senolytics.pdf>

Constantly improved. Check for updates. You may not have the current version.

Last updated June 2, 2021

Friendly Disclaimer: These are ideas that I use in my own age management program. It's not my intention to provide specific medical advice, but rather to provide others with information to better understand their health. This is not medical advice including diagnosis and treatment. Always seek the advice of a trained health professional for medical advice, diagnosis or treatment.

Several GRG members have thoughtfully taken the time to send information about dasatinib, sources, and testing.

This is a serious matter. If misused, senolytics can be dangerous.

EDUCATE YOURSELF WITH INFORMATION FROM MULTIPLE SOURCES, AND READ AND UNDERSTAND EVERYTHING BELOW BEFORE YOU PROCEED WITH SENOLYTICS

If you're not going to take the time to read and understand everything below – **and further educate yourself beyond my inadequate information provided for your benefit here**

THEN YOU HAVE NO BUSINESS MESSING WITH SENOLYTICS.

You will benefit from our learning curve, which has been substantial.

Members quotes from submitted messages are attributed to them.

Definition – what we're dealing with

Senescence is a condition or process of deterioration with age. As we age, cells can become senescent. Senescent cells do not work properly – and they release a variety of factors such as pro-inflammatory cytokines and chemokines, which amplifies their impact by contributing to the physical dysfunction of tissues and organs during aging. They change cellular behavior for the worse, and destructively remodel the structure of tissues. Programmed cell death (apoptosis) often doesn't turn on.

Senolytic therapy is an emerging aging intervention therapy. Senolytic drugs and over the counter compounds are intended to specifically target and eliminate senescent cells. It appears senescent cells are necessarily the ONLY targets of senolytics.

For example, dasatinib clears senescent adipocytes (fat cells), fisetin clears senescent endothelial cells (blood-vessel lining), and azithromycin clears senescent fibroblasts (skin & structure cells).

In animal studies eliminating senescent cells improved some physical dysfunctions and increased the healthy life span of mice, even the elderly mice. In mice, senolytic therapies have been shown to slow the progression of numerous age-related diseases.

Research in humans is underway, and results from early human trials have shown some positive effects.

Educate yourself as to the potential risks and benefits before undertaking it.

PLEASE SEND ME your information and results on human studies – informal, pilot or formal studies to JAdams@grg.org or call (949) 922-9786.

Warnings

I suggest these warnings apply not only to dasatinib, which is a cancer drug – but to all senolytics including:

quercetin

fisetin

FOXO4-DRI

Ouabain (a derivative of Digitalis)

theaflavins

piperlongumine

Tocotrienols - alone or with quercetin

L-Carnosine – sometimes taken with ALCAR and/or DMAE

BCL-2 family inhibitors navitoclax / ABT263 and ABT-737

Some other BCL-2 inhibitors like TW-37 are reported not to be senolytic, so it isn't just any old

BCL-2 inhibition that works

BCL-XL inhibitors A1331852 and A1155463

17-DMAG

ABT-737

ABT263

navitoclax

isoquercetin

venetoclax

sulforaphane

BCL-2 protein family inhibitors in general

HSP90 inhibitors

to name a few.

I believe this was true at one time, but may have changed:

Unity Biotechnology is deriving from navitoclax and using in their current studies.

Oisín Biotechnologies (DNA construct) lipid nanoparticle/p16-promoter/caspase DNA "drug"
SIWA Therapeutics (antibody).

Re nilotinib, a GRG member advised:

Interesting positive Alzheimer's study. I remember reading in the past that nilotinib might be a good alternative to dasatinib for senolytic therapy because it readily crosses the blood-brain barrier. They postulate that the improved parameters are due to autophagy, but I wonder about senolysis also. It was safe at the lower dose taken daily for a year.

<https://onlinelibrary.wiley.com/doi/10.1002/ana.25775>

*** SENOLYTICS WARNING -- Caution is advised re. excessive senolytics.**

Note: What's excessive may be different between individuals

Vince Giuliano advises senolytic signaling is critical for cell renewal – you need enough inflammation and senescence to signal for regeneration factors -- so if you go overboard in senolytics therapy it's bad, you will miss out on cell renewal.

www.anti-agingfirewalls.com/2018/09/02/aging-cell-and-tissue-repair-renewal-and-regeneration-inflammation-and-the-sasp

More is often not better. Quote by *Reason in the FightAging blog*: **All senolytics, so far, look like things you would take once every few years at most.** More won't be any more effective than that one dose - it will kill the senescent cells it can kill the first time, and won't be helpful again until more senescent cells turn up in volume.

www.fightaging.org/archives/2018/03/how-to-plan-and-carry-out-a-simple-self-experiment-a-single-person-trial-of-senolytic-peptide-foxo4-dri#caveats-in-more-detail

Reason discusses cancer drugs in general, and navitoclax specifically in the article *An Example to Illustrate Why Navitoclax is Not a Suitable Clinical Senolytic Drug* makes important points like

The earliest discovered senolytic small molecule drugs are chemotherapeutics. It is fair to say that they are selective for senescent cells, but in some cases far from selective enough. They kill a lot of non-senescent cells and, further, cause all sorts of problematic and potentially serious side-effects.

<https://www.fightaging.org/archives/2020/06/an-example-to-illustrate-why-navitoclax-is-not-a-suitable-clinical-senolytic-drug/>

Dave Kekich is a leader in our community. Dave advises: In terms of chronic inflammation, the downstream consequences of inflammation accelerate most of the common age-related conditions and diseases, such as atherosclerosis and neurodegeneration.

However, 'good inflammation' is central to life!

Healing processes, such as regeneration from an injury, depend upon a clear cycle of inflammation that starts, progresses, and ends. The problem emerges when this naturally structured cycle becomes disrupted. This 'disruption' happens when the inflammatory signaling system becomes fused in place in a perpetual call to action which inadvertently assaults the tissues.

Senescent cell researcher ***Dorota Skowronska-Krawczyk PhD*** personally discourages us from having long treatments with senolytic drugs. In fact she suggests they should only be taken for short periods interspaced with longer recovery times.

Stan Goldfarb has decades of applied nutritional supplement and aging intervention experience. He advises: I think even 2.5mg per KG is a higher than I want to take, especially when combining it with EMIQ (which in itself has no bad side effects till very high doses). I weigh 137 and am going to take 100mg once only. You should also be taking at least 10000iu of D3 to complete apoptosis and don't take any blood thinners such as aspirin or omega supplements as it has been proven to go after fat cells for several days before and after. Without doing all of this a person is simply taking an unnecessary risk. When I did my first test of this in 2015, there were some really sharp people to say exactly what to do and when. I don't see that now with the current crop of people and it concerns me. People have died from overdosing this drug! I also remember that several people who did take multiple doses experienced minor problems after the second dose (especially flu like symptoms but not after the first. One group is saying take what you're doing twice one week apart. This is potentially risky. The effect Dasatinib has lasts longer than many people seem to think and that is why I think a second dose just one week later makes no sense.

James Kirkland MD PhD recommends not evaluating senolytics on our own at this early stage.

Similar cautions apply to other aging intervention therapies. There's a lot we don't know about this new frontier.

Everyone is different - some may be harmed from senolytics, some may benefit from more senolytic, others may need very little (and will be harmed by more).

Individuals may respond differently to combinations.

Retreatment interval may vary from individual to individual.

From the Age Reversal Network (formerly Rescue Elders) document presented at RAADfest 2018:

Possible side effects: Mild flu symptoms, diarrhea, headache, fatigue for 12-24 hours.

Note from Johnny: And for some people who knows what else, and for how long.

Read the product information.

**Take in the presence of a qualified medical doctor in case of severe allergic reaction.
Do not engage in strenuous exercise during, or for one week after, the treatment period.**

That said . . .

Dasatinib and Quercetin act on different paths and are often taken together.

Dasatinib

They usually come in tablets. I have heard of 20, 50 and 70 mg.
I get 20 mg because it's easier to measure the exact dose I want to take.

Do not cut, crush, or chew the tablets

Brands I have heard of:

Sprycel brand from Bristol-Myers Squib

Others from offshore sources.

Research grade can be good and comes highly recommended by one of our skilled MD associates. But you would need a scale and measuring small amounts can be tricky. I bought a scale and other items needed for this, but decided against it.

I DO NOT recommend research grade. But if you have a lot of experience, here you go
<https://lclabs.com/products/d-3307-dasatinib-free-base>

READ THIS: Useful Sprycel dasatinib info from Bristol-Myers Squib

www.sprycel.com

It says:

- **Do not cut, crush, or chew the tablets**
- **Do not drink grapefruit juice during treatment with SPRYCEL**
- **Do not take St. John's wort during treatment with SPRYCEL**

Grapefruit juice competes for the clearance channel with metformin, probably the same for dasatinib.

Hence it may be bad to take dasatinib with metformin. It appears some more experienced members of our community take grapefruit juice along with therapies – presumably for increased effectiveness and to save money. This sounds really tricky and I do not think I'll try it.

Dosing

I'm kind of sensitive to drugs, also conservative. When initially naïve once I took too much so called “anti aging” therapies and it made me seriously ill.

So first time around I took about 1/3 of the usual. A new and innovative lab test we developed showed positive results. But that's just me.

Stan Goldfarb has decades of applied nutritional supplement and aging intervention experience. He advises: I think even 2.5mg per KG is a higher than I want to take, especially when combining it with EMIQ (which in itself has no bad side effects till very high doses) . I weigh

137 and am going to take 100mg once only . You should also be taking at least 10000iu of D3 to complete apoptosis and don't take any blood thinners such as aspirin for several days before and after. Without doing all of this a person is simply taking an unnecessary risk. When I did my first test of this in 2015, there were some really sharp people to say exactly what to do and when. I don't see that now with the current crop of people and it concerns me. People have died from overdosing this drug!

One group is saying take what you're doing twice one week apart. This is high risk and probably even irrational.

Here's dosing recommendations from the Age Reversal Network (formerly Rescue Elders) document presented at RAADfest 2018. I do not know how this was arrived at:
One quercetin + dasatinib dose once a week for two weeks only (two total doses)

Quercetin

25 mg per kilogram of body weight, which is approx.:
100 pounds = 1125 mg

Dasatinib

2.5 mg per kilogram of body weight is approx.:
100 pounds = 112 mg

Hopefully you can do the math to arrive at your personal dosage.

Example, I weigh 146 lb, so dasatinib would be

112 mg for first 100 lb

Plus $46/100 \times 112 = 51.52$ (or $.46 \times 112$)

= 163.52

REMEMBER Do not cut, crush, or chew the tablets

So round down (or up).

Testing Pharmaceuticals Purchased Offshore and Elsewhere for Safety and Efficacy

I do not trust drugs from sources other than licensed pharmacies (and even licensed pharmacies have been known to get it wrong). I've been burned.

Counterfeit products is a huge international problem. It's not just jeans, Gucci bags, Barbie dolls and GI Joes -- others include counterfeit airplane parts, pharmaceuticals and other mission-critical products. Whatever makes money. A doctor once told me about fake Lasix medicine made seriously ill patients even sicker because it had been mixed in a container that had previously been used to mix pesticide, and had traces of the pesticide in the "Lasix".

Appearance and packaging are VERY convincing. I read that a phoney Apple store was opened in China with real looking "Apple" products.

So I do not automatically trust that offshore suppliers will provide pharmaceuticals that are pure or contain the specified content.

Pete Cooperider replied to John Cramer's post:

John, I see that the Bon Hoa pharmacy has several brands of dasatinib like Lucidas, Dasanix, Dasanat. Kindly tell us which one you used that you refer to as having been tested?

My response

Pete --

I suggest that testing one pill is pretty good evidence the rest in the bottle is OK, and the entire lot or batch is probably OK I guess – but does not necessarily mean that all tablets from that source are OK now, or will be into the future.

This concept also applies to nutritional supplements. Some suppliers use cheap ingredients that do not contain the specified amounts, and may even contain toxins.

According to some of my sources: So-called “Canadian” pharmacies are usually not in Canada – they're usually in Asia, India or somewhere else. It is illegal for a Canadian pharmacy to ship to the US, with or without a prescription. Unless the web address has a “.pharmacy” extension it is not legitimate. The legitimate way to get a Canadian pharmaceutical is to go to Canada and get it from a Canadian doctor, then go to the pharmacy.

We recently had dasatinib and rapamycin tested at Echelon Biosciences. I was very satisfied with the service and value.

They now have the qualitative test data and reports for dasatinib and rapamycin. Our foundation covered the initial cost of development, and you will be able to send your tablets to them for testing at a much lower cost.

For dasatinib, they have data for samples tested against a sample from a US pharmacy. For rapamycin they have data for samples tested against a generic (known) sample AND a sample from a US pharmacy.

However, the topic of quantitative versus qualitative has arisen. Qualitative testing evaluates for purity, and that it contains the indicated pharmaceutical. Quantitative evaluates for the amount of the pharmaceutical.

Qualitative analysis (like Echelon did) is easier than quantitative, or active pharmaceutical ingredient (API) analysis.

Quantitative involves building a calibration curve. That may take 1 day, then the test may take 1 day

Total cost quoted from a quantitative testing lab for one instance: \$5K. Others may vary.

I will send you a contact the quantitative testing lab upon request.

Upon further investigation a knowledgeable scientist advised that qualitative comparative analysis (the kind Echelon did) – is all that’s really needed and will tell if there’s the same response in height and peak area – so will tell if pretty much the same amount.

All is beyond my pay grade so I have yet to completely understand it.

We are seeking further details and a conclusive answer as to whether qualitative or quantitative testing are required for our purposes.

Who will take on the task of getting a definitive answer?

Other testing labs can be found on Science Exchange www.scienceexchange.com .

Qualitative uses high-performance liquid chromatography (HPLC) and other methods.

The generic (known) sample of dasatinib, was acquired through Sigma-Aldrich: CAS: 302962-49-8.

www.sigmaaldrich.com/catalog/buildingblock/product/matrixscientific/mat370173661?lang=en®ion=US

Qualitative testing:

Echelon Biosciences now has testing data for dasatinib and rapamycin. They are available to test samples from other members of our community. My group has covered the initial cost, which is greater than the cost of testing additional samples.

➔ **Contact me if you plan to utilize Echelon’s services. Inefficiency and confusion may be eliminated if you have me in the loop.**

Johnny Adams JAdams@grg.org (949) 922-9786

Echelon Biosciences Inc.

Mark Nelson, PhD

675 Arapeen Drive Suite 302

Salt Lake City, UT 84108

mnelson@frontiersci.com

801-588-0455 ex 308

Quantitative testing

Emory Pharma

<https://emorypharma.com/>

Neeku (Niki) Mahdavian

Business Development Manager

Tel: (510) 899-8825

neeku@emorypharma.com

Biomarkers and objective measures to evaluate senolytic therapy effectiveness in subjects/patients

Some useful ones are in part 3:

<https://www.aginginterventionfoundation.org/AgingInterventionProgram.pdf>

Everyone is different - some may be harmed from senolytics, some may benefit from more senolytic, others may need very little (and will be harmed by more).

Retreatment interval may vary from individual to individual.

How do you know whether it's working, and how much to take, and how often?

Current lab tests for this are entirely inadequate. Beta Galactosidase is not practical in humans.

Who has information on effective lab tests to evaluate dose, interval, etc.?
Please send it to JAdams@grg.org or call 949 922 9786.

I have found in testing my own DNA methylation (DNAm) age from blood before and after dasatinib plus quercetin that the DNAm increased (goes in the wrong direction) a little over 1/2 year after dasatinib plus quercetin. This was taken by averaging two replicate tests each time. Another individual communicated a similar result to me. It's uncertain whether this undesirable effect is random, or is on one part of the system that accompanies the supposedly positive effects on others, or some kind of artifact, or what. This needs further study.

I worked with some top scientists at a major university research lab to develop an innovative biomarker test that was initially developed to measure cell senescence for before and after senolytic therapy.

It also applies to:
virtually any aging intervention therapy
and gene therapy.

We are now bringing it from the research lab to production mode. I will let you know when it's ready for use in our community.

Finally: now that you are a little more educated about the hazards and how complicated senolytic therapy is, on to sources.

But FIRST - to show you how much I care about you and really don't want you to hurt yourself –

and I took a lot of time out of MY OWN aging intervention program to write all this. So you better read and understand it.

So another friendly reminder:

READ AND UNDERSTAND EVERYTHING ABOVE BEFORE YOU PROCEED WITH SENOLYTICS

If you're not going to take the time to read and understand everything below – **and further educate yourself beyond my inadequate information provided for your benefit here**

THEN YOU HAVE NO BUSINESS MESSING WITH SENOLYTICS.

Sources

US Pharmacy

Sure it costs more money. But you can save yourself the concern over what you're getting and the hassle of testing.

Although they may be reluctant, with a doctors' prescription pharmacies will break open packages or containers and provide smaller quantities than usual.

University pharmacies may be easier to deal with than commercial ones.

CVS specialty pharmacy 800 498 5601 or 800 308 1977

Enrollment dept – must enroll first 800 237 2767

Each 20mg tablet is about \$125.

MedLab: At one time this pharmacy filled compounded dasatinib and quercetin specifically for your body weight. Unfortunately the owner died abruptly. I do not know whether they are continuing this.

On Feb 11 2020 I called to find out and was transferred to an answering machine. I sent them an email and will update this document ASAP.

PLEASE CONTACT ME if you know whether they are still providing it.

They offered 2 customized doses (a one-year supply for most people) for \$225. However, this required a prescription, and the pharmacy could only ship to Florida addresses.

Contact info: the pharmacy at 954-400-0560 or email the pharmacist at rxmailbox(at)gmail(dot)com.

Diagnosis code

Some pharmacies require a diagnosis code.

You may find this useful for dasatinib, and virtually any aging intervention therapy.

2019 ICD-10-CM Diagnosis Code R54 -- Age-related physical debility -- as close to getting aging classified as a disease as we'll get – at least for now.

<https://www.icd10data.com/ICD10CM/Codes/R00-R99/R50-R69/R54-/R54>

The above reference begins with:

ICD-10-CM Coding Rules

- R54 is applicable to adult patients aged 15 - 124 years inclusive.

Applicable To

- Frailty
- Old age
- Senescence

- Senile asthenia
- Senile debility

Type 1 Excludes

- age-related cognitive decline ([R41.81](#))
- sarcopenia ([M62.84](#))
- senile psychosis ([F03](#))
- senility NOS ([R41.81](#))

Most of us have some of the above.
It continues and you can read more for yourself

Offshore if you must:

International Antiaging Systems

<https://www.antiaging-systems.com>

Oreet advises they offer

Sprycel, the Bristol Myers Squibb brand of 60 20mg pills for \$999. They also sell Dasapro, a bottle of 12 30mg pills of dasatinib (manufactured in a EU country and also confirmed in testing) for \$89.99.

Bonhoa

www.bonhoa.com

One of our associates tried buying from them twice. Their web site and payment system was broken. Last time they sent a confirming email that was supposed to have a link, but no link.

Vea Impex

Manthan Shah

sales@veaimpex.co.in

www.veaimpex.co.in

Sprycel dasatinib, Bristol-Myers Squibb

Price for 70 mg tablets, qty 60, was \$753.00 plus shipping, possibly less for 50 mg tablets.

U.S. pharmacy cost is around \$125 per tablet, so \$7,500

One of our associates said Vea Impex representative Manthan Shah can be difficult to understand over the phone

At the time they had only 2 sizes: 50mg and 70 mg.

They may offer other medications.

Payment was by bank wire transfer.

It was extremely difficult getting payment through to them.

However - to their credit - when there was trouble getting payment through, they went ahead and sent the Dasatinib anyway because Shah thought he might need it.

It took several email exchanges with Shah and the bank to get them paid.