

## The sharp end

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The first fusion inhibitor, T-20, available in Australia through clinical trials since 2001, has been a godsend for people with few other treatment options. But while T-20 holds out the tantalising prospect of a whole new class of anti-HIV drugs, taking this treatment is far from easy, as BERNIE SLAGTMAN explains.

Early in 2001, my doctor suggested that I consider the latest development in managing my HIV — the fusion inhibitor T-20 (enfuvirtide). I was given a Plain Language Statement for the T-20 trial. It all seemed a little foreign to me and scary in the sense of self-injecting as well as being the so-called 'guinea pig'.

My re-salvaged salvage therapy had not delivered any real gains in either T-cells or [viral load](#) [1]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma. reduction. In the background, I had the fear of possibly becoming ill due to some opportunistic infection. So there was the dilemma: what to do about this trial? The Alfred Hospital's Access Centre in Melbourne provided great assistance in obtaining the little available information about this new treatment.

### What is T-20?

T-20 is an HIV fusion inhibitor that seeks to prevent new [virus](#) [2]A small infective organism which is incapable of reproducing outside a host cell. from getting into healthy cells. This differs from the current drugs, which are designed to stop the reproduction of the virus once it is already in the cells.

The treatment requires you to self inject twice daily — as T-20 is protein-based, it cannot be taken orally. With training, this eventually isn't as freaky as it sounds, but initially I never imagined that I could actually inject myself. It does get easier to cope with psychologically over time.

The trial used phenotype testing to scientifically assess the best combination of drugs to be taken in addition to the T-20 injections. This test appears useful when modified to take your medical history into account.

Being an [experimental](#) [3](Of a drug) Not licensed for use in humans, or as a treatment for a particular condition. Experimental drugs are studied in clinical trials to determine their safety and efficacy, and are sometimes made available via Special Access Schemes prior to their approval. drug, the medical evidence on T-20 was limited, although it suggested there was a reasonably good chance of at least a one log viral load reduction.

There appeared to be a high number of drop-outs from the initial stage one trials. Was this due to self-injecting problems, compliance or were there unacceptable side effects? I began to wonder whether they were still alive? Nobody could tell me!

There were no details on the numbers of people affected by side effects or whether they were caused by the introduction of changed antiretroviral drugs. The main issue reported seemed to be the tenderness of injection sites.

### Issues of concern

One issue that still concerns me is whether [resistance](#) [4]HIV which has mutated and is less susceptible to the effects of one or more anti-HIV drugs is said to be resistant. is developing and if so, how would this impact on future developments in the area of fusion inhibitors. But, on the other hand, non-participation in this trial may have rendered me more susceptible to opportunistic infections.

The trial also presented me with more practical issues — compliance, my mental ability to add this to the many pills that I already take and have to administer.

I finally decided to commence the trial, which was a real commitment to giving it a fair dinkum go.

The trial required extensive testing to establish [baseline](#) [5]1. Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. At this reference point, measurable values such as CD4 count are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values. data on issues such as heart, chest, eyes, cat scans, countless blood tests, bone density DEXA scans, etc.

The next step involved the [randomisation](#) [6]A method based on chance by which study participants are assigned to a treatment group. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant process. Two of every three trial participants are randomly selected to commence on T-20 injections plus their optimised background regimen of [antiviral](#) [7]A medication or substance which is active against one or more viruses. May include anti-HIV drugs, but these are more accurately termed antiretrovirals. drugs.

Those not selected for T-20 commenced treatment on their optimised regimen of antiviral drugs only. This was to determine whether any improvements were likely to be due to the change in medications or the introduction of T-20. I was pleased to hear that I had been randomised to commence T -20 injections.

The research staff at the Alfred Hospital in Melbourne were just great, and gave me all the time and training to make me feel as comfortable as possible with the concept of self-injecting. Each injection vial contains the T-20 in a semi-solid form. After allowing the vial to get to room temperature, you add water and wait for it to dissolve before actually injecting. This can take some fifteen to twenty minutes. It gets easier once you kind of establish a routine, however you need to schedule a minimum of half an hour per injection.

Over the first six weeks my viral load dropped from a high of 750,000 down to 622. Yes, you read correctly! Exciting stuff! In addition to this, a six-fold increase in T-cells really topped the already ecstatic results.

Injection sites continue to be a little tender to extremely sore at times, although they can be less painful if you can keep away from bony areas with little fat. I also try to rotate injection site areas as much as possible. Gentle rubbing of the area after injecting seems to reduce the discomfort.

Well on the way towards three years later, T-20 still forms an integral part of my HIV management. That in itself is a success story. All other drug treatments have all been terminated within a shorter period due to fatigue or toxicity. Generally speaking, my health remains good: I have not required any inpatient hospital treatment since commencing T-20. Previously, I was averaging some four too five hospitalisations per year!

Overall, while my level of fitness and energy has not improved all that much, my objective blood readings, (albeit not where I would like them to be) are much better and life continues merrily.

I have had to contend with many issues and challenges surrounding my decision to be part of the T-20 trial. There are privacy issues to consider when going out or sharing accommodation. Travelling continues to be a major issue as the amount of luggage you need to transport the drug is significant. In 2003 I managed a three-month visit to family and friends in Europe.

It was a daunting experience, when you consider that the medication requires refrigeration, the customs implications of unregistered trial drugs, boxes full of syringes and their security threats — not to mention the idea of baggage weight restrictions. Just physically carrying all your supplies can be overwhelming. This all has to be managed in addition to the other [antiretrovirals](#) [8]A medication or other substance which is active against retroviruses such as HIV., medicines and complementary health treatments.

The issue of adherence is one that has really been highlighted as a result of using T-20. Without wanting to carry on too much, we all know how important adherence is. Being the good lad that I am (ha ha!) I thought that since I was strictly complying with my tablets, another treatment would not be an issue. But it's been tempting to miss out just that once or twice! Just the thought of no injection!

So, my message is simple: if you cannot comply easily with a tablet regime, then think twice and very seriously before you take on T-20. It requires a hell of a lot more commitment.

## Tricks

I have learnt some tricks to make life a little easier with T-20: things like injecting the water into the vial and then attending to something else. Watching the T-20 slowly dissolve seems to take forever! You can dissolve an injection in advance, but there are practical issues associated with this such as use-by and temperature control.

This may sound repetitive, but a strict methodical rotation method for injection sites means overall less swelling, less hardness of skin and less scarring. Unless you have a lot of fat on your legs and arms, I suggest restricting injection sites to the stomach region. Give the buttocks a miss or you won't sit for the next two days!

I have tried many different 27 gauge syringes to inject and the 1 ml, 13 mm syringes have proven the best. I have found it best to keep away from longer needles as they penetrate the subcutaneous tissue too deeply, increasing the swelling and bruising. Also the larger volume needles (say 3 ml) tend to retain air bubbles more easily due to their increased width. Injecting air bubbles only increases swelling and bruising.

Another idea is to place the vial in a warm location when dissolving the powder. Ducted heater outlets or a ray of sunshine make all the difference to that stubborn dissolving process in cold weather. Better still, try a winter escape to warmer territories!

I have also found that the amount of bruising and swelling varies from injection to injection. After all the time I have been using, I have yet to find a reason for this — it's easier to just accept that it will sometimes be so. The worst-case scenarios seem to take up to 72 hours to resolve.

The NAPWA conference highlighted some concerns from other HIV positive people. There needs to be user support on an ongoing basis (such as a 'user hotline') to give advice, support and encouragement. This will need to be taken up with the drug's manufacturer, Roche.

Unexpectedly and somewhat surprisingly, a number of HIV-positive participants commented that having heard what was involved with injecting, they were now re-motivated to a strict adherence of their tablet regimen. It demonstrated that 'fear' tactics still have a role to play in HIV prevention and management.

However it needs to be reinforced that prospective T-20 users do not need to be scared of what lies ahead of them, but fully aware of what is involved and the commitment required.

## The future

The future holds the dream of a more user-friendly means of using fusion inhibitors, hopefully through reduced frequency of dosing, and eventually oral intake.

Ultimately, wouldn't it be magical if, for once, I did not need new drugs each time they became available for trial or special access. At this stage, I am happy with my decision to partake in the trial. It is now a matter of patience and continuing commitment in the hope that these achievements can be sustained without the complications of resistance and adverse side effects.

*This is an edited version of a presentation given at the 2003 NAPWA Conference.*

- [2003 Conference](#)
- [clinical trials](#)
- [enfuvirtide \(T-20\)](#)

## Links:

[1] <http://www.napwa.org.au/glossary/term/416>

[2] <http://www.napwa.org.au/glossary/term/125>

[3] <http://www.napwa.org.au/glossary/term/491>

[4] <http://www.napwa.org.au/glossary/term/109>

[5] <http://www.napwa.org.au/glossary/term/472>

[6] <http://www.napwa.org.au/glossary/term/513>

[7] <http://www.napwa.org.au/glossary/term/123>

[8] <http://www.napwa.org.au/glossary/term/122>