The initial field testing of GS-441524 for FIP treatment involved subcutaneous injection. This route of administration was based on prior pharmacokinetic (PK) studies done on laboratory cats. Intravenous and subcutaneous routes of injection yielded similar high blood levels that were sustained at virus inhibitory concentrations for over 24 hours. Oral administration was also found to provide blood levels, but somewhat delayed and only at about 25% peak levels of subcutaneous and intravenous routes. Therefore, the subcutaneous route was chosen for field testing based on ease of administration and resulting blood levels.

Chinese suppliers of GS-441524 copied the diluent, drug concentration, subcutaneous route of administration that were used in the initial published field trial. The first company to offer GS-441524 on the unapproved market was Mutian. Mutian was also the first to research and offer an oral form of the drug. Mutian researchers found that effective blood levels of GS-441524 could be achieved by merely increasing the concentration of the drug in their oral preparations. Other companies (e.g., Aura, Lucky) subsequently offered their own versions of orally administered GS-441524. Currently, Mutian, Aura and Lucky brands are the most used oral forms of GS-441524 in the US.

Current brands of capsules/tablets are sold as supplements and their labels list several common innocuous chemical compounds and medicinal herbs and do not list GS-441524 as one of the ingredients. This is probably done to avoid scrutiny by customs. Regardless of the list of ingredients, the active component in all oral products is GS-441524. The exact concentration of GS-441524 in the various oral products is kept secret by the sellers, but it is obviously several times higher than would be needed if the drug were given by the subcutaneous route.

We were initially critical of the oral route for two reasons. First, oral forms were more wasteful of what was initially a rare and expensive resource. Second, published research on oral absorption of nucleosides (GS-441524 is a nucleoside) document a concentration limit or ceiling for oral absorption. This limitation would make it theoretically difficult to achieve the extremely high blood concentrations required to treat certain forms of FIP (e.g., neurological) and/or to overcome the problem of acquired drug resistance. Newer information obtained from field use of the oral forms of GS-441524 of Mutian and Aura brands, indicate that this problem may not be as serious as first believed as most forms of FIP respond equally well whether given pills or injections.

It appears that more and more owners and veterinarians are embracing oral GS-441524 for part or all the treatment. The cost of oral GS-441524 preparations has steadily declined over the last two years and quality increased. The problem of injection site reactions, coupled with more effective oral preparations of GS-441524, have encouraged the oral treatment. Steadily increasing numbers of cats are being treated with oral drug either for part or all of the treatment.
Formulation and Dosing

Suppliers of oral GS-441524 do not list the amount of active drug in their tablets or capsules. Instead, 1 tablet/capsule is usually recommended per kg body weight for wet/dry FIP and 2 pills per kg for ocular/neuro. This is comparable to dosage recommendations for the injectable form, i.e., wet and non-neurological/ocular forms of FIP require about one-half the dosage of the ocular and neurological forms. Some suppliers also provide pills with a higher concentration of GS-441524 for use in cats with ocular and neurological FIP in order to limit pills that must be given at one time. In addition, one supplier (Aura) has tablets labeled for administration every 12 hour (h) and yet another for every 24h. The 1 tablet/kg q12 h tablet contains one half as much GS-441524 as a 1 tablet/kg q24h tablet - the rationale being that the q12h dosing would prevent a fall-off in the blood concentration prior to 24h. This belief is inconsistent with the original pharmacokinetic data, which shows blood levels to be sustained at effective levels for at least 24h. Regardless, both the q12h and q24h Aura pills seem equally effective when given according to instructions, although most owners prefer dosing once a day.

All oral preparations, except for Mutian, are tablets. Tablets are all quite small, while the Mutian capsule is considerably larger. This makes the tablets easier to administer. Mutian capsules are also liquid rather than powder filled and if cats bite down on them the contents may be lost. Adverse reactions have been reported for cats who rupture the capsules.

Administration

All oral brands have similar instructions for administering capsules or tablets. Fasting for half an hour before and after giving the medication is generally recommended. A small amount of treat may encourage cats to take them, and many cats will consume them when put on a plate with a coating treat (e.g., Churu).

Cost

The price of oral GS has significantly decreased in the last year. Nevertheless, the relative cost of oral GS-441524 is 20-40% higher (depending on the supplier) than their injectable version. However, Mutian brands are exceptions, with the injectable form being as much as 4 times more expensive than the injectable forms of other brands. Interestingly, Mutian’s capsules contain less GS, dose for dose, than their injectable form.

Factors affecting oral vs. injection

Cats currently experiencing vomiting/regurgitation and diarrhea are generally considered poor candidates for oral GS-441524. Therefore, cats with serious gastro-intestinal disease are often started on injections, at least until the problems are resolved. Most people, especially in the past, have started with injectable GS-441524. The injection form is cheaper, and the dosage is more accurately managed. Absorption of GS-441524 is also more reliable by the subcutaneous than oral route, which is often a critical factor in the initial treatment of cats that are severely ill and
unstable at the onset. Whether or not a cat continues injectable GS-441524 is often conditioned on the ability of the owner to do injections in the most effective manner, the willingness of the cat to adapt to the injection pain, and the occurrence of injection site sores. Oral medication is often a welcome respite for owner and feline patient in such situations.

**Comparison of treatment success between injectable and oral GS-441524**

Assuming that dosages are accurately calculated and dosing properly done, the success rate with oral GS-441524 currently mirrors that of injectable formulations. Nevertheless, differences in responses between oral and injectable GS-441524 have been reported. A small number of cats have not responded well to oral GS-441524 as initial treatment or have led to relapses when replacing injections. Alternatively, switching cats to oral GS-441524 at an equivalent dosage has resolved disease that was not responding well to injections. It is difficult to assign these dramatic differences in response to the drug form, as GS-441524 given by subcutaneous or oral routes ends up in the bloodstream and ultimately in the tissues. It is more likely that the brands of injectable or oral GS-441524 used prior to such switching were not good. Indeed, there have been many cases when switching to a different oral or injectable brand immediately improved the response.

It was assumed that only the injectable form of GS-441524 could achieve the extremely high blood and cerebrospinal fluid levels necessary to effectively treat neurological disease, especially in situations where the virus has evolved variable degrees of drug resistance. However, oral brands such as Aura/Lucky have been quite effective on cats with neurological FIP. This has also included some cats who were failing to respond to an extremely high dosage of injectable GS-441524. More and more cats with neurological FIP are being cured with entirely oral treatment. This is either due to more experience with oral treatment in difficult cases of FIP, or equally likely, to the increased quality of oral formulations.

**Summary of currently available brands of oral GS-441524**

*Mutian capsules* - This is the original and most well-known brand of oral GS-441524. It is currently sold in a liquid form within capsules in the US, but a newer tablet form has become available in other countries. The main complaint about Mutian capsules is the variability of therapeutic responses. Mutian capsules users also report more adverse side-effects than users of other oral brands. They can be more difficult to administer than tablet brands given their greater size. Mutian capsules are the most expensive oral option and are approximately double the cost (at equivalent dosage) of several of the other oral brands.

*Aural/Spark* – Aura tablets have been used in the US for nearly as long as Mutian and have been shown to be highly effective against all forms of FIP, including ocular and neurological FIP. They are marketed in q12h and q24h versions. The actual amount of GS-441524 in each tablet is not given, but it appears that the 1 tablet/kg q12 h tablet is equivalent to 2.5-3 mg of the injection form of GS-441524, 1 tablet/kg q24h is equivalent to 5-6 mg, the 1 tablet/3 kg q12h is equivalent to 7.5-9 mg, and the 1 tablet/2 kg q24h is equivalent to 10-12 mg.
**Lucky** - Lucky pills are sold as 1 tablet/kg q24h and are said to have an identical formulation to the comparable Aura tablet, although in a different shape. Lucky is one two brands that are currently the most affordable - the cost being only about 20% more than the lowest cost injectable. Early treatment results indicate that the performance of this this brand is equivalent to Aura.

**Brava/Rainman** - This brand is popular in China but rarely used in the US. It appears to have a solid reputation in countries where it is used.

**Capella** – Capella has only recently offered an oral version of GS-441524 and it has not been available long enough to rigorously evaluate results. (Several cats have used it but have not yet completed treatment.) However, as the brand’s injectable product has a solid reputation and the oral form is slightly less expensive than the Lucky brand, it is growing in popularity.

**Kitty Care** – This is another low-cost brand that now offers both injection and oral formulations of GS-441524. It has not been popular and there is little experience with it.