To be or not to be (Musings on IPF and Esbriet)

Updated: 25 March 2016

Another blog on my spouse having idiopathic pulmonary fibrosis (IPF) and its treatment with pirfenidone (Esbriet®). See *Further Reading* for additional resources.

The theme is how do patients with an incurable disease make decisions when the treatment has adverse side effects that make life miserable. Who helps them?

IPF - BACKGROUND

In brief, **idiopathic pulmonary fibrosis** (IPF) is an incurable,chronic progressive disease typically affecting people over 65, in which the lung's normal connective tissue is replaced by scar tissue. Scar tissue forms when the body has an injury anywhere, but in IPF, for unknown reasons, the scarring (fibrosis) does not stop as it normally does.

IPF's cause is unknown but the disease causes the lungs to become stiff and impairs their ability to function, i.e., move oxygen into the bloodstream and body tissues.

IPF has a median survival of 2-4 years from diagnosis. Most patients die within 3-5 years but some patients live much longer. See a simplified diagram of ways IPF typically progresses.

IPF - TREATMENT

Until pirfenidone (Esbriet®) no effective treatment existed for IPF. In clinical trials Esbriet® was shown to decrease scarring (fibrosis formation) and the incidence of death from all causes and from IPF alone. See below for more details.

Cost: Esbriet® was funded in the UK and elsewhere before in Canada but it now is, In Canada Esbriet® costs provincial governments ~$43,000 CDN per patient per year.

DILEMMA

Esbriet® gives IPF patients hope for a longer life but, to some, that comes at an incredible cost to quality of life due to side effects.

The good stuff

Although not a cure, Esbriet® offers the hope of maintaining lung function as measured by FVC (forced vital capacity - how much air a person can exhale during a forced breath). In IPF, FVC is a

key measure of disease progression. Esbriet® doesn't improve FCV but does slow its decline.

Esbriet® has also has been shown to offer patients better life expectancy. For example, after one year:

- 3.5% of patients on Esbriet® (n=22 of 278) died from all causes, versus 6.7% on placebo (n=42 of 277), areduction of ~48%.
- 1.1% (7 of 278) died from IPF related causes versus 3.5% (22 of 277), a reduction of ~68%.

Of course, given the type of IPF disease a patient has makes such statistics iffy at best. No one knows how an individual's IPF will progress.

The bad stuff

Unfortunately, Esbriet® has many side effects, also known as adverse events/reactions. It's important to recall that all drugs have side effects, ranging from harmless to severe reactions that require drug cessation.

Also, with any drug's side effects, an individual may experience none, some, or all. A given side effect may show up immediately or only after being on the drug for awhile. Plus some side effects occur more commonly, others are rare.

A complicating factor with side effects is that identifying them as directly related to the implicated drug can be difficult. The side effect may be due to drug interactions, a symptom of a co-existing disease, etc.

Identification is easier if a side effect is well documented as commonly occurring and stops when the drug is stopped, even temporarily. This applies to sun sensitivity and Esbriet® (see below).

Adverse events related to Esbriet® include:

- abdominal pain
- bloating
- gas
- nausea
- constipation
- diarrhea
- vomiting
- decreased appetite
- taste changes
- difficulty sleeping
- hot flushes
- itchy, dry, or red skin
- sun sensitivity (e.g., sunburn, skin rash, blistering or peeling skin)
- sweating
- tiredness
- weight loss
- muscle or joint aches or pains
- Cough or hoarseness
- sore throat
- sneezing

- headache
- indigestion, heartburn, or acid reflux
- ear congestion
- dizziness

From my spouse's experience:

- Suppose you cannot get proper sleep, night after night (insomnia), so you always wake up tired.
- Even when sleeping reasonably well, you're exhausted during the day.
- You have no appetite and what you eat tastes different (awful).
- You lose ~5 lbs every 10-14 days because you must force yourself to eat.
- After eating anything, you're always bloated, have a stomach pain, suffer indigestion, and feel nauseous, often gagging during meals.
- After eating (and taking Esbriet®), you feel dizzy for a short time.
- You alternate between diarrhea and constipation, the latter sometimes requiring extreme measures.
- Your throat is always sore and you think you're coming down with a cold but it doesn't happen.
- You spend 1 hour in the sun and develop a sunburn and measles-like rash on exposed skin which lasts for weeks and requires stopping Esbriet® for a month, then going back on in increasing doses until the optimum dosage is reached.
    - The rash also means in future wearing long sleeves and a wide-brimmed hat (even in summer with temperature 30^{o}C+) and lathering exposed skin with 50+ SPF lotion to walk outside and enjoy a sunny day.
- You regularly suffer severe headaches.

With these side effects eventually life becomes miserable. Do you

- Stay on Esbriet® because it extends your life?
- Stop taking Esbriet® and opt for a better of quality of life though it may be shorter than if on the drug?

DOCTOR INPUT

In general, respirologists/pulmonologists review lung function tests, and, if they see lab measures like FCV haven't decreased, assume you will stay on the drug because it's helping. Indeed, they want you to stay on the drug, because opting for life is paramount in their world.

Severe side effects seem to mean almost nil to physicians, presumably because they've never experienced such hell. Also, as physicians, naturally they want to believe they can do some good, even if a disease is devastating and incurable.

What doesn't happen is discussing the options and consequences (albeit uncertain), i.e., the reality of an incurable disease and what patients can expect, albeit based on population studies, which may or may nor apply to individual patients.

Often well meaning physicians assumes patients and their families want only hope and cannot deal with grim realities. Best to ignore them?

To be fair, I'm unsure what physicians could say, given the uncertainties. As well, they know that some patients may grab onto something they say and it could come back to bite them. And some doctors may not want to unduly influence patients one way or the other. Mind you, in other circumstances, I've found that's often not true. And so it goes....

But physician reluctance to discuss realities gives patients precious little upon which to base life and death decisions, even if definitive outcomes are unknown. Fortunately, I'm okay with reading the medical literature and research findings, but suspect many are not.

Perhaps that's how it must be. As in life, after all is said and done, individuals are responsible for their own choices. But it would be nice to make informed choices based on a physician's knowledge and experience of your circumstances combined with what population studies show.

BOTTOM LINE

How can patients with incurable diseases choose the best treatment option, even when one doesn't exist? In our case, my spouse went off Esbriet® for a month due to sun sensitivity adverse event (mandated by physician), then again later, due to other side effects that led to an unbearable quality of life. While off the drug, the symptoms lessened and many disappeared altogether.

He's back on Esbriet® now, opting for extending life and coping with drug's side effects. We'll see

how it goes. Sadly, we have no real support nor wise advice when making decisions. We could join a support group and may do that in time.

In closing, let me emphasize that there are far worse fates than developing IPF later in life. Overall, both I and my spouse feel pretty darn lucky, even with the latest side effects being a 'bummer', as we'd say in the 60s. Life is good, all things considered.

As always, comments are most welcome. Be aware that comments are moderated, but only to prevent spam.

FURTHER READING

Idiopathic pulmonary fibrosis: now a treatable disease and other highlights from the 2014 American Thoracic Society Annual Conference. CMAJ, May 27, 2014.

Brett Ley B, Harold R. Collard HR, and Talmadge E. King, Jr TE. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2011;183(4): 431-40.

King TE Jr, et al. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. N Engl J Med. 2014 May 29;370(22):2083-92. Epub 2014 May 18.

My earlier blogs on IPF

Labels: Alberta health, CADTH, Canadian Drug Expert Committee, Canadian Pulmonary Fibrosis Foundation,Esbriet, idiopathic pulmonary fibrosis, IPF, pirfenidone