**A flaw in a common treatment plan for Myeloma Bone Disease**

These comments are triggered by my unusually fast response to Zoledronic Acid and the treatment plan.

Apologies to grannies who already know how to suck eggs, but for completeness I must start with,,,

When a treatment is designed as a result of a clinical trial which indicated that some significant property was common to all participants there are two possibilities,

1. that property is also common to the population as a whole; and
2. a small minority of the population for whom that property does not hold has been missed.

*Only one of those possibilities can be true but there is absolutely no way of predicting which!* Therefore stating that one treatment fits all may well be true, but it cannot be regarded as an incontrovertible fact Regarding it as a fact is totally wrong. It can only be a working assumption.

As a working assumption it is therefore wrong to design a treatment plan which specifically prevents the discovery of such a small minority.

The normal treatment plan for the associated condition of Myeloma Bone Disease (MBD) presumes that all patients will have a slow response to Zoledronic Acid and hence is

1. A full body MRI scan is taken before treatment starts
2. Zoledronic Acid is given once every 4 weeks for 2 years, which is 26 doses
3. A further MRI scan is taken at the end of treatment

Now suppose that there really is a small minority who have a fast reaction. Using the normal treatment, how would anyone ever know? The total lack of any intermediate scan of any type means such people would be undetectable, hence the answer to “but we haven’t seen any fast reactions” is that yes you have but the standard procedure prevented you from recognising them.

Is that important?…..

Yes because

1. It was discovered by accident that my first treatment only needed 8 doses! Having had an unusually long first remission, an additional MRI scan was done at 10 years after treatment. *I was still free of MBD after 10 years*. My second treatment needed only 12 doses (we did 14 just to keep the consultant happy!). I cannot be the only fast reactor, therefore the previously unsuspected minority exists
2. Either of those numbers, 8 and 12 (14 if you insist) mean 26 doses would be a significant over use of the drug
3. The cause of the serious side effects of Osteonecrosis of the Jaw (ONJ) and Stress Fractures is the **over use** of the drug.

The failure of the above treatment plan to provide any intermediate scan means that it condemns patients with a fast reaction to the drug to a much increased risk of painful and expensive to fix those side effects The underlying problem is that we are all different and have different tolerance levels to medication and nobody knows the point at which individual patients become vulnerable because there is currently no way to find out. Is it unreasonable to suspect that a fast reaction to the beneficial effect of a drug may also indicate a fast reaching of the point of vulnerability to bad side effects?

To object to introducing intermediate scans on the basis of cost is false economy. Even though these side effects are not common, the cost of sorting out the consequences is vastly more than the cost of such scans, especially when you factor in all the costs starting from the initial ambulance all the way to after care.

But there is a cheap way of providing additional intermediate scans! Pick whatever scanning method you trust to show freedom from MBD, Identify an area of bone most affected by MBD and take just one small scan of that bone to see if that area appears to be clear of MBD. *One such scan per patient per treatment is therefore not a huge cost.*  I would suggest it be done after 8 doses as I was clear by then in my first remission period (but do it slightly later second and subsequent remission periods). The purpose of this scan is not to look for any other things, rather it is taken only to answer the one question “do we need to take a better look with a full body MRI scan” and that better look will only apply to a very small percentage of patients. For a few patients one might decide that a scan which indicates “almost clear” would indicate a second small scan should be taken later on.

I was discovered to be a fast reactor nearly 15 years ago. I naively assumed things would change. Out of curiosity I recently asked my consultant what had changed. The answer is nothing. In all that time nothing has been done, including the dissemination of the news of the existence of this minority group!

The above treatment plan is based upon (according to an Ask the Nurse reply from Myeloma UK)  *“... the available evidence and expert opinion, it is generally recommended that patients have bisphosphonate treatment for a minimum of two years after diagnosis.” T*he problem with that is that it becomes assumed that that should always be done, but as discussed above, that should not be the case for fast reactors. There needs to be a recommendation to include intermediate scans (as above) in order to detect the minority of patients who have a fast reaction and would therefore have a heightened risk of side effects..

That expert opinion was based on the assumption that all patients would have a slow reaction and hence being clear of MBD early it would only involve a few extra doses to complete the treatment which would enable more benefit from the drug’s other bone effects to happen. But, remember I had over 10 years of not needing those effects, and no one knows when vulnerability to side effects kicks in for any one individual. So, for slow reactors, the current scheme gambles some positive effects which the patient may not need against vulnerability to excruciating side effects which no one can tell when that vulnerability kicks in. Hence, those innocent looking few extra doses for slow reactors may be the very ones that cause vulnerability.

“But only a small number of patients get those side effects”. That is a bad argument because the number of people who become vulnerable may be very much higher than the number who go on to suffer those side effects for the simple reason that MM is still very much a killer disease so many may die before they get to undergo an event which would trigger a side effect. As we get better survival rates more people with that vulnerability will survive long enough to trigger side effects.

Another reason to adopt intermediate scans also comes from the limitation of statistics given above. Whilst no one has yet to be given the treatment for 2 years only to find that it hasn’t worked and was hence a waste of much money, the existence of such a seriously small minority for whom that is true can never be ruled out. Statistics says so!

Finally, can I note that expert opinion is only as valid as the data available. If that data is incomplete, as in this case, then if new data comes to light then that opinion becomes invalid until it is revised to reflect the new data which has become available.

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Myeloma patient with fast reactions to Zoledronic Acid.

I have instructed my consultant that my medical records be publicly available. My consultant is Dr. E. Renaudon-Smith at Frimley Park Hospital.