Reviewer's report

Title: Fatal case of sorafenib-associated hepatotoxicity in the adjuvant treatment of a patient with Renal Cell Carcinoma

Version: 2 Date: 23 July 2012

Reviewer: R E E Ferner

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The authors describe a patient who was treated with sorafenib and developed fatal liver failure. This is important if sorafenib is to be given for prophylaxis of recurrence of renal malignancies in patients who may not have such recurrences. Before it is accepted for publication, the authors should make good omissions in the chain of reasoning, and make the paper readable.

1. The reasons for concluding that sorafenib was the cause of the liver failure are not stated explicitly, and it is unclear which causality score was used, or why the score was '5b.'
2. The authors imply on page 6/16 that what they call 'idiosyncratic reactions' are not dose-dependent. Since delayed-type hypersensitivity reactions are demonstrably dose-dependent, and are assumed to lie behind adverse drug reactions of intermediate time-course, this is almost certainly wrong. [Drug Saf. 2005;28(10):851-70] What the authors almost certainly mean is that those with relevant HLA type are more susceptible.
3. The MHRA has a single fatal report of liver failure associated with sorafenib. Have the authors reported their own case? If not, what does the MHRA fatal case represent?
4. Page 2/16: The authors write: 'Here we report the case of a patient on the SORCE trial who died from liver failure associated with sorafenib treatment. Although this is an extremely uncommon occurrence, this case has important implications in the treatment of patients who are entirely asymptomatic and may indeed be free of cancer as well as alerting clinicians to this rare side effect.' This presupposes that the hepatic failure was drug-induced, and makes a statement about prevalence that cannot be based on a single case-report.
5. The report is badly written.

Matters of typography or style

Prefer 'adverse drug reaction' or 'adverse drug effect' to 'side effecte' throughout.
3/16: 'He was commenced on study medication' means 'He started taking...' or
'We gave him' [also 5/16]

3/16: 'he had symptom progression' means 'his symptoms had become worse.'

4/16: 'he had taken no other medications including over the counter analgesics, antibiotics or statins' means 'he had not take over-the-counter analgesics, antibiotics, statins, or any other medicine.'

4/16: 'Admission bloods revealed an acute hepatitis' means 'results of blood tests taken on admission showed acute hepatitis'

4/16: 'normal hepatic echogenicity texture' for 'normal hepatic echogenicity'

4/16: 'a septic source was not discerned' for 'we found [identified; discovered] no septic source'

5/16: Units for ammonia concentration not given, neither are reference ranges.

5/16: the reviewer gave up when confronted with 'Further radiology revealed mild peri-hepatic ascites only which was found to be transudative.'

If this is to be published, it should be translated into readable English.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

Only that I was a co-author of the cited reference - I guess that is why you chose me.