FDA provides fastest drug approval

The US Food and Drug Administration (FDA) was faster than both the European Medicines Agency (EMA) and Health Canada in the review of applications for novel treatment agents approved between 2001 and 2010. A recent report compared the time taken for regulatory review of 510 drug applications approved by one or more agencies.

The FDA was quickest to complete the first review, needing a median time of 303 days (IQR 185–372) compared with 366 days (310–445) for the EMA and 352 days (255–420) for Health Canada ($p<0·001$ for the comparison between the three agencies). Similarly, the FDA was fastest to finish the total review, taking 44 days fewer than did the EMA and 71 fewer than did Health Canada.

Additionally, approval occurred first in the USA for most novel treatment agents approved by one or more regulators. Approval occurred earlier in the USA for 121 of 190 drugs approved both in the USA and in Europe, and for 132 of 154 new treatment agents approved both in the USA and in Canada. The FDA total review time was 90–100 days less than was that of the EMA and Health Canada for 72 drugs approved by all three regulators.

Author Nicholas Downing (School of Medicine, Yale University, CT, USA) told *The Lancet Oncology*: "There is a real interest in the length of time that the FDA takes for the review process. We believed that this benchmarking exercise—comparing regulators who face similar pressures—would be particularly helpful. And the FDA was 2–3 months faster on all the main metrics that we measured."

Ellen Sigal (Chair, Friends of Cancer Research, Washington, DC, USA) was an author on another study showing that during 2003–10, new oncology drugs approved by both the FDA and the EMA were available to patients sooner in the USA than in Europe. This finding was partly the result of more rapid drug reviews by the FDA than by the EMA. She stated that, "it is nice to see this follow-up study in the *New England Journal of Medicine* which confirms what we saw in the oncology field". However, she cautions, "this is not a race: this is not about lowering efficacy standards".

According to Jerry Avorn (Professor of Medicine, Harvard Medical School, MA, USA), "this paper is an important document that can put to rest any concerns about a supposed 'drug lag' between the USA and other countries".

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Mark Thomas/Science Photo Library

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For more on **time for review** see *N Engl J Med* 2012; published online May 16. DOI:10.1056/NEJMsa1200223

For more on **approval of oncology drugs** see *Health Aff* 2012. DOI:10.1377/hlthaff.2011.0231

New treatment option for untreated AML and MDS

Histone deacetylase inhibitors such as vorinostat are safe and efficacious in combination with standard first-line chemotherapy in acute myelogenous leukaemia (AML) or myelodysplastic syndrome (MDS) according to a new phase 2 study.

Guillermo Garcia-Manero and colleagues from MD Anderson Cancer Center, Houston, TX, USA, gave 75 patients with untreated AML or highest risk MDS standard induction treatment with idarubicin and cytarabine plus vorinostat. Patients in remission could be given five cycles of consolidation treatment and up to 12 months of maintenance treatment with vorinostat.

Addition of vorinostat yielded results that were more promising than are the expected outcomes for patients with AML treated with idarubicin and cytarabine. With a median follow-up of 82 weeks, median overall survival for the whole group was 82 weeks and event-free survival was 47 weeks. Similarly, the overall response rate was 85%, with 76% of patients achieving a complete response.

Some subgroups divided by genetic alterations had more favourable results with vorinostat than without this drug. For example, median overall survival and event-free survival were highest in patients with *FLT3* internal tandem duplication, although the difference between this group and unmutated patients was not significant ($p=0·067$).

The researchers investigated potential biomarkers and reported that upregulation of *NRF2* and *CYBB*—genes implicated in resistance to histone deacetylase inhibitors—were associated with improved survival. However, induction mortality and toxic effects were not significantly higher with addition of vorinostat than with idarubicin and cytarabine alone.

Suresh S Ramalingam (Winship Cancer Institute, Atlanta, GA, USA) notes that although the overall efficacy results are promising, the biomarker studies have provided some valuable clues. He adds, "follow-up studies should be adequately powered to verify the biomarker leads from the present study".

Garcia-Manero agrees that further studies are needed and says: "we will test this concept in a large phase 3 trial where vorinostat with idarubicin and cytarabine is going to be compared with standard AML therapy known as 7+3 or treatment without vorinostat". This study will investigate whether addition of vorinostat improves results of traditional treatment in patients with AML.

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For more on **the vorinostat study** see *J Clin Oncol* 2012; published online May 14. DOI:10.1200/JCO.2011.38.3265