From TreatmentUpdate 160

Raltegravir—other issues

The data from clinical trials so far suggest that raltegravir has strong anti-HIV activity, even in treatment-experienced PHAs. Several additional points arising from the clinical trials are worth considering:

1. **A low genetic barrier**
   Although raltegravir has strong anti-HIV activity, it needs to be taken with an effective combination of drugs for a number of reasons. First, raltegravir has what researchers call a weak genetic barrier. This means that it takes only a few mutations for HIV to develop resistance to this drug. A similar situation exists with non-nukes—efavirenz and nevirapine. Therefore, care is required when selecting other drugs in a raltegravir-containing combination.

2. **Safety**
   Amazingly, raltegravir appears to have few obvious side effects. This may be due to the integrase enzyme being essential for HIV but not human cells. However, one laboratory-based study independent of Merck has found that very high concentrations of integrase inhibitors have the potential to weaken the immune system's capacity to make antibodies. But this only happened at concentrations 10 to 20 times above those that would normally be used in people. As long as raltegravir does not accumulate inside cells of the immune system at such high levels, such problems should not occur.

3. **Help from the immune system needed**
   In Benchmarks 1 and 2, there appeared to be a trend for raltegravir to be somewhat less effective in PHAs who had very low CD4+ counts (below 50 cells) or high viral loads (more than 100,000 copies). This is not surprising, as results from monkeys with an AIDS-causing virus suggest a similar effect. Overall, these findings highlight that a certain level of immunity is needed in order for raltegravir to be most useful.

4. **Access**
   Later this year, an expanded access program for treatment-experienced PHAs in Canada should become active. In the meantime, physicians with patients who urgently need this medication can contact Health Canada’s Special Access Program (SAP) to request the drug. For general information about the SAP, including contact information and how the program works, please see the following link: [http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/sapfs_pasfd_2002_e.html](http://www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/sapfs_pasfd_2002_e.html)

**REFERENCES:**


Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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