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# Tipranavir: A Ritonavir-Boosted Protease Inhibitor

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Mortality and morbidity related to HIV has decreased significantly with the introduction of protease inhibitors (PIs); however, over time this has lead to the emergence of HIV that is highly resistant to PIs. Hence, there is a great need for the development of new agents that are capable of suppressing viral replication in the presence of protease resistance.

Tipranavir is a novel non-peptidic PI that requires boosting with low-dose ritonavir and must be used in combination with other antiretroviral agents. The pivotal studies with this agent were done by comparing it to a boosted PI (CPI) that was selected based on the genotypic sensitivity of the HIV. In pooled data from RESIST-1 and RESIST-2 studies, tipranavir outperformed the comparator PI in all the primary and secondary analyses. Lopinavir accounted for up to 61% of the CPI.[1] However, in a secondary analysis there was no difference between lopinavir and tipranavir if patients were not receiving lopinavir at baseline or if the virus was sensitive to lopinavir at baseline.[2] The data also suggested that for both arms, the response to treatment improved progressively with the number of active agents available and the use of enfuvurtide. Based on these studies the US FDA's Antiviral Drugs Advisory Committee recommended the approval of tipranavir.

Unfortunately, the safety and tolerability of tipranavir was not as satisfactory as the efficacy. It was associated with significant gastrointestinal toxicity including nausea, vomiting and diarrhoea. Numerically more adverse events and discontinuations were seen among the patients on tipranavir, compared to the CPI arm. Grade 3 and 4 elevations of AST, ALT and lipids were also more common in the tipranavir arm.

The place of tipranavir in current HIV treatment strategy will be narrow. Based on the current studies, tipranavir may be used only in patients who have failed PIs. It has clearly demonstrated its superiority in salvage therapy; however, if HIV is sensitive to lopinavir there may be no great advantage. Tipranavir will be an excellent choice in combination with enfuvurtide for patients with limited universal PI mutations in whom treatment with lopinavir has failed. Finally, ritonavir-boosted tipranavir is also being evaluated for use in paediatric and treatment-naive patient populations in phase II and III studies that are currently underway. ▲

## References

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