Tipranavir (Aptivus)

Table of Contents

- Tipranavir Aptivus Editor's Summary
- Drug Summary
- Key Clinical Trials
- Adverse Effects
- Resistance
- Key Drug Interactions

Drug Summary

Tipranavir was developed as a protease inhibitor for salvage therapy for individuals who have developed resistance mutations to other protease inhibitors, but it also has been studied in initial therapy. Its use has been markedly limited by reports of adverse events, including fatal and nonfatal intracranial hemorrhage, as well as severe hepatotoxicity; the drug has a black box warning from the FDA for both of these potential toxicities. In addition, tipranavir requires twice-daily dosing with ritonavir boosting, and the required ritonavir dose is higher than with other protease inhibitors; the tipranavir plus ritonavir combination causes frequent gastrointestinal side effects and drug interactions.

Key Clinical Trials

In a randomized trial in treatment-naïve individuals, investigators compared twice-daily tipranavir plus ritonavir versus twice-daily lopinavir-ritonavir, each with tenofovir disoproxil fumarate (DF) and lamivudine, and showed similar rates of virologic suppression, but more discontinuations in the tipranavir arms due to adverse effects [BI-1182.33]. In two randomized, open-label trials of individuals with extensive treatment experience, ritonavir-boosted tipranavir was compared to investigator-chosen alternative boosted protease inhibitors, and the combined 48-week data demonstrated better treatment response with tipranavir (more individuals achieved and maintained virologic control and time to treatment failure was longer); however, gastrointestinal side effects, elevation of hepatic transaminases, and elevations of serum cholesterol and triglycerides were more frequent in the tipranavir arm [RESIST-1 and RESIST-2].

Adverse Effects

The tipranavir prescribing information includes FDA black box warnings for intracranial hemorrhage and hepatotoxicity. Tipranavir has been associated with fatal and nonfatal cases of intracranial hemorrhage, though an exact causal relationship has never been confirmed. Tipranavir has also
been associated with hepatotoxicity, which can be severe and occurs at a higher rate than with other protease inhibitors. Tipranavir may cause a number of other adverse effects, including rash, hyperglycemia, and elevation in serum lipid levels. Gastrointestinal side effects are common, perhaps caused by the required 200 mg twice-daily dosage of ritonavir. Tipranavir contains a sulfonamide moiety and thus should be used cautiously in individuals with a known sulfonamide allergy. Tipranavir is available in tablets and oral solution; the tipranavir oral solution contains vitamin E and patients taking the oral tipranavir solution should be counseled not to take supplemental vitamin E.

**Resistance**

For a listing of the most common clinically significant mutations associated with tipranavir (TPV) resistance, see the [PI Resistance Notes on the Stanford University HIV Drug Resistance Database](https://www.medicine.stanford.edu/content/pi-resistance).

**Key Drug Interactions**

For complete information on tipranavir-related drug interactions, see the [Drug Interactions section in the Tipranavir (Aptivus) Prescribing Information](https://www.medicine.stanford.edu/content/tpv-drug-interactions).

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