

UR-3216: A Manageable Oral GPIIb/IIIa Antagonist

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ABSTRACT

UR-3216, a prodrug, is a novel, selective, and orally active platelet surface glycoprotein (GPIIb/IIIa) receptor antagonist. The most important property of UR-3216 is the very tight binding of its active metabolite to platelets (K_i for resting platelets is <1 nM). UR-2992, the active form of UR-3216, binds to platelets for a long period of time, while the unbound drug is rapidly cleared. Therefore, after an initial loading dose of 0.1 mg/kg, only once daily repeated low maintenance doses of UR-3216 (<0.05 mg/kg p.o.) are required. This regimen maintains a high level of inhibition of platelet aggregation and, due to a small peak-to-trough ratio, severe bleeding is avoided. The therapy with UR-3216 is easy to manage, because it has low peak-to-trough ratio and high efficacy ($>80\%$ inhibition of platelet aggregation). In addition, UR-3216 does not produce excessive bleeding or thrombocytopenia and does not interact with abciximab. UR-3216 is excreted mostly in bile, so that it will not accumulate in patients with chronic renal dysfunction.

UR-2316 has the following abciximab-like features: (a) its half-lives for residence on platelets, inhibition of platelets aggregation and bleeding time prolongation are 60 to 80 h, 24, and 2 h, respectively; (b) its receptor binding occupancy is similar to that of abciximab (Mab1 is inhibited and Mab2 is unaltered). In conclusion, UR-3216 is a promising, orally active GPIIb/IIIa antagonist for the treatment of cardiovascular diseases.