Additions and Corrections

2008, Volume 51

Ilse M. Zolle,* Michael L. Berger, Friedrich Hammerschmidt, Stefanie Hahner, Andreas Schirbel, and Biljana Peric-Simov: New Selective Inhibitors of Steroid 11β -Hydroxylation in the Adrenal Cortex. Synthesis and Structure—Activity Relationship of Potent Etomidate Analogues.

Pages 2244–2253. Recently, another manuscript presenting clinical data with the radiotracer ¹²³I-iodometomidate (¹²³I-IMTO) was published by Hahner et al. (Hahner, S.; Stuermer, A.; Kreissl, M.; Reiners, C.; Fassnacht, M.; Haenscheid, H.; Beuschlein, F.; Zink, M.; Lang, K.; Allolio, B.; Schirbel, A. ¹²³I-Iodometomidate for molecular imaging of adrenocortical CYP11B enzymes. J. Clin. Endocrinol. Metabol. 2008, 93, 2358-2365.). Two methods were presented for the evaluation of the inhibitory potency of ETO (1) derivatives based on direct measurements of cortisol secretion, produced either by human adrenocortical cancer cells (NCI-h295 cells), data shown in Table 6, or more specifically, by adrenocortical Y1 cells transfected with the human P-450c11 enzyme, using 11deoxycortisol as a substrate. The sensitivity of cortisol synthesis by these cells for inhibitors should therefore allow SAR studies of the human P-450c11 enzyme. The new IC₅₀ values for ETO $(1, 0.99 \pm 0.62 \text{ nM})$, MTO $(2, 4.60 \pm 2.39 \text{ nM})$, and FETO $(5, 4.60 \pm 2.39 \text{ nM})$ 2.94 ± 1.42 nM) are almost identical to the respective IC₅₀ values obtained by the displacement of ¹³¹I-IMTO from rat adrenal membranes: ETO (1, $1.08 \pm 0.42 \text{ nM}$), MTO (2, 3.69 \pm 1.92 nM), and FETO (5, 2.90 \pm 0.55 nM) (data from Table 6). Statistical analysis of differences support the following conclusions: Inhibition of high-affinity binding of ¹³¹I-IMTO on rat adrenal membranes and the inhibition of cortisol synthesis by the enzyme P-450c11 exhibit very similar SARs, most likely because the high-affinity binding site of ¹³¹I- IMTO on P-450c11 is located on, or very close to, the active site of the enzyme.

JM800920Y

10.1021/jm800920y Published on Web 11/06/2008