Imidazo[1,2-a]pyridines: Orally Active Positive Allosteric Modulators of the Metabotropic Glutamate 2 Receptor

Andrés A. Trabanco,^{a,*} Gary Tresadern,^b Gregor J. Macdonald,^c Juan Antonio Vega,^a Ana Isabel de Lucas,^a Encarnación Matesanz,^a Aránzazu García,^a María Lourdes Linares,^a Sergio A. Alonso de Diego, ^a José Manuel Alonso,^a Daniel Oehlrich, ^c Abdelah Ahnaou,^d Wilhelmus Drinkenburg,^d Claire Mackie,^e José Ignacio Andrés,^a Hilde Lavreysen,^d José María Cid^a

Supporting Information

Contents

- **Figure 5** Correlation between human and rat mGlu2 receptor GTPγS activity.
- **Table 5** Effects of oral administration of **27o** (10 mg/kg) or vehicle (20% CD + 2H2T) on duration of different sleep states during 20 h recording session.
- **Table 6** Effects of oral administration of **27o** (10 mg/kg) or vehicle (20% CD + 2H2T) on sleep parameters during 20 h recording session.
- **Table 7** Effects of oral administration of PAM **270** (10 mg/kg) or vehicle (20% CD + 2H2T) on states transitions during 20 h recording session.

^a Neuroscience Medicinal Chemistry, ^b Research Informatics and Integrative Genomics, Janssen Research & Development, Janssen-Cilag S.A., Jarama 75, 45007-Toledo, Spain. ^c Neuroscience Medicinal Chemistry, ^d Neuroscience Biology, ^e Discovery ADME/Tox, Janssen Research & Development, Turnhoutseweg 30, B-2340, Beerse, Belgium.

^{*} To whom correspondence should be addressed. Tel: +34 925245750, fax: +34 925 245771, e-mail: atrabanc@its.jnj.com.

Figure 5. Correlation between human and rat mGlu2 receptor GTPγS activity.

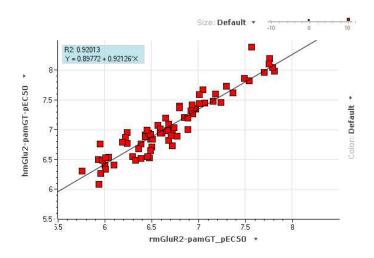


Table 5. Effects of oral administration of **27o** (10 mg/kg) or vehicle (20% CD + 2H2T) on duration of different sleep states during 20 h recording session.

	Duration (min)						
	AW	PW	IS	ISWS	dSWS	REM sleep	
Vehicle	588.81 ± 29.6	83.48 ± 12.5	11.23 ± 1.3	141.21 ± 24.5	284.91 ± 25.9	78.23 ± 4.1	
27o	576.13 ± 21.5	83.53 ± 7.1	9.31 ± 1.0	133.79 ± 13.0	313.56 ± 19.1	74.82 ± 5.8	

Mean values of 8 rats, expressed in min for the total duration of active wakefulness, passive wakefulness, light sleep, deep sleep and rapid eye movement sleep.

Table 6. Effects of oral administration of **27o** (10 mg/kg) or vehicle (20% CD + 2H2T) on sleep parameters during 20 h recording session.

	Total sleep time (min)						
	TST (min)	ISWS/TST (%)	dSWS/TST (%)	REM sleep/TST (%)	IS/TST (%)		
Vehicle	515.57 ± 39.0	26.59 ± 3.6	55.41 ± 3.1	15.73 ± 1.4	2.27 ± 0.3		
27 0	531.47 ± 21.3	25.09 ± 2.0	58.97 ± 2.6	14.17 ± 1.1	1.77 ± 0.2		

Mean values of 8 rats, expressed in min for the total duration of active wakefulness, passive wakefulness, light sleep, deep sleep and rapid eye movement sleep.

Table 7. Effects of oral administration of PAM **27o** (10 mg/kg) or vehicle (20% CD + 2H2T) on states transitions during 20 h recording session.

	State transition (number)						
	From ISWS to		From dSWS to		From REMS to		
	AW	PW	AW	PW	AW	PW	
Vehicle	219.38 ± 26.7	87.5 ± 8.4	48.00 ± 6.6	172.38 ± 34.0	66.63 ± 8.7	16.63 ± 2.9	
27 o	202.00 ± 18.8	118.13 ± 18.4	62.25 ± 12.4	199.50 ± 22.6	72.50 ± 12.8	20.25 ± 4.9	

Mean values of 8 rats, expressed in min for the total duration of active wakefulness, passive wakefulness, light sleep, deep sleep and rapid eye movement sleep.