

Study Title: The effect of a novel compound on disease progression in an acute MPTP induced Parkinson’s disease.

Study Objectives

The objective of this study was to assess the therapeutic potential of a novel compound to inhibit the onset and progression of cell loss and development of Parkinsonian pathology in an acute model of MPTP PD.

INTRODUCTION

Parkinson’s disease (PD) is a chronic, progressive, neurodegenerative disorder that affects approximately 1% of the population over 50 years of age and is the second most frequent degenerative disorder after Alzheimer’s disease. The motor deficits observed result from a loss of dopaminergic neurons in the substantia nigra pars compacta resulting in striatal dopamine deficiency. The MPTP animal models of PD are the most commonly used due to the similarity to humans in the brain pathology observed.

METHODS AND RECORDS

When the mice were at least 10 weeks of age and had achieved a body weight of at least 25 grams, the study began and mice underwent procedures as detailed below:

Five mice were used as naïve controls. All mice were grouped by mean body weight per cage.

The mice began treatment dosing on study day 1 and were dosed daily intraperitoneal (IP) for 19 days. On study day 8 the mice received daily subcutaneous injection (SC) of MPTP at 25 mg/kg for 5 days.

Cage side observations were made daily. Clinical observations were conducted twice weekly. Body weights were recorded daily as per dosing requirements.

Retro-orbital (RO) bleeds were performed post IP dosing of mice (at t=15min, t=1 hr. and t=4 hrs post last dose).

Mice were sacrificed 24 hours following the final dose. Blood was collected and processed to plasma and stored at -80°C. Brain was harvested and halved each half being snap frozen individually.

Blood Processing Details:

Blood Collected: Blood was processed for plasma by collection into an EDTA tube and spun for 12 minutes at 12,000 RPMs in a 4°C centrifuge, and then transferred to 0.5 mL microcentrifuge tubes for storage at -80°C until sent for analysis.

Treatment Protocol

Gp	n	Treatment	Dose (mg/kg/mouse)	Dose Route/Regimen
1A	5	Naïve	n/a	n/a
1B		Vehicle (10%DMSO in PBS)	33	IP, Daily for 19 days.

				On Day 8 they received Daily SQ injection of MPTP at 25 mg/kg for 5 days.
--	--	--	--	---

Procedural Timeline

	Receive mice		Body Weights																	Necroscopy							
Days	-6	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20		
Date	4/6	4/8	4/9	4/10	4/11	4/12	4/13	4/14	4/15	4/16	4/17	4/18	4/19	4/20	4/21	4/22	4/23	4/24	4/25	4/26	4/27	4/28	4/29	4/30	5/1		
			CO	CO	CO					CO	CO			CO			CO					CO			CO	Terminal Bleed	
																										Timed RO	Brain Harvest

Key:
 CO Clinical Observations
 IP Intraperitoneal
 RO Retro-orbital bleed
 SC Subcutaneous