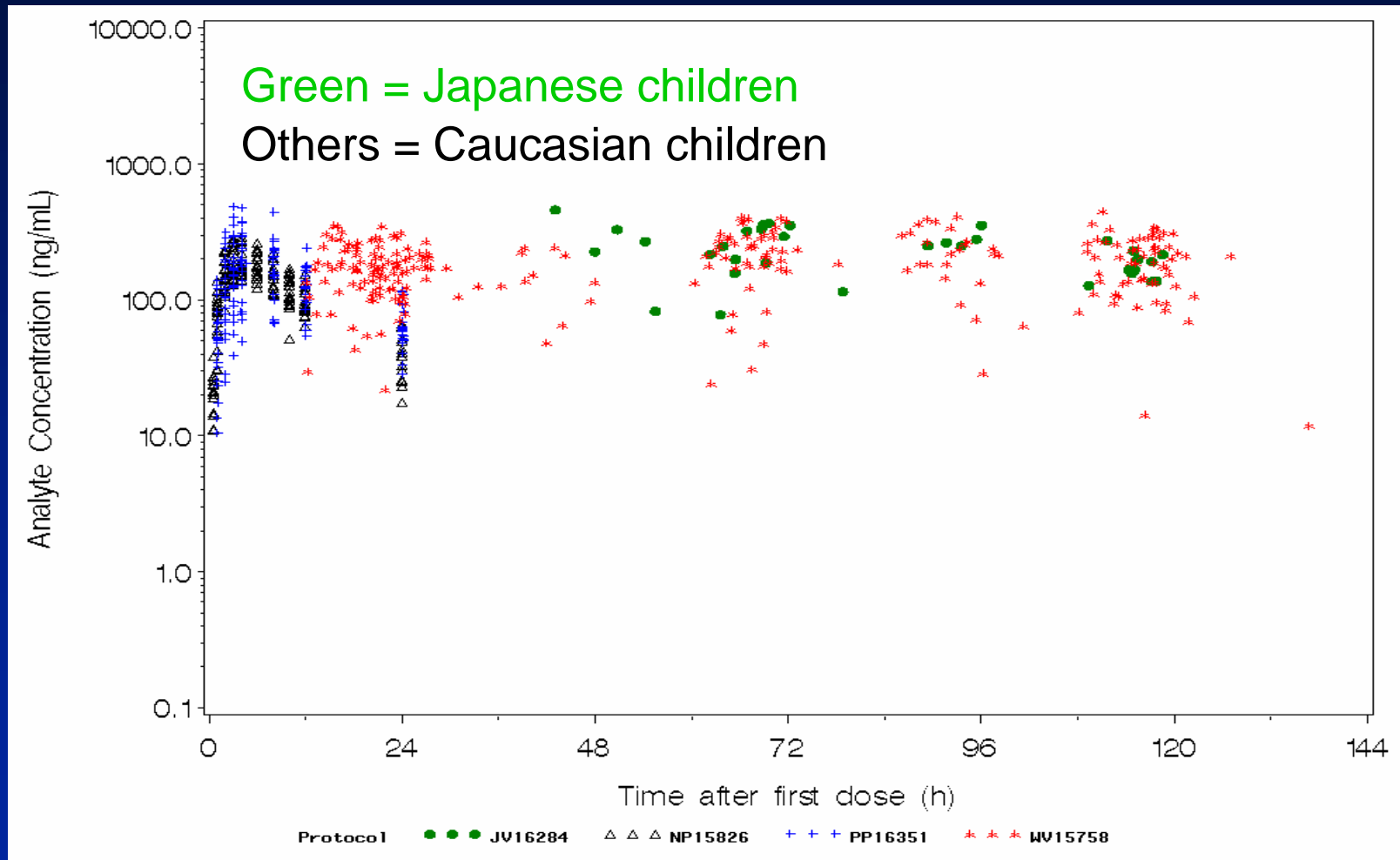


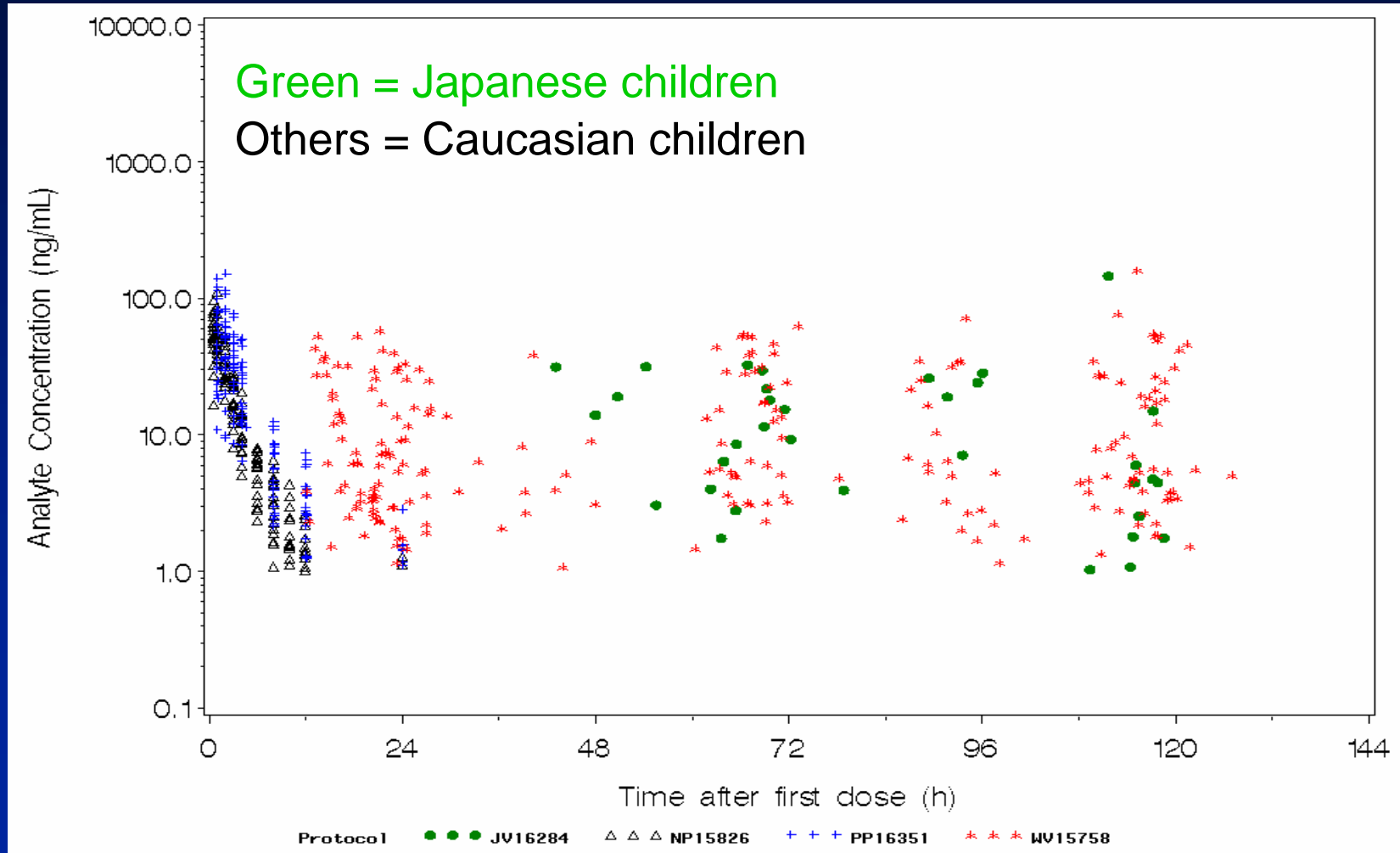
OP Concentrations Similar Between Japanese and Caucasian Children



n=141 Caucasians, n= 18 Japanese children

Doses were 2mg/kg except PP16351 which was unit dosing

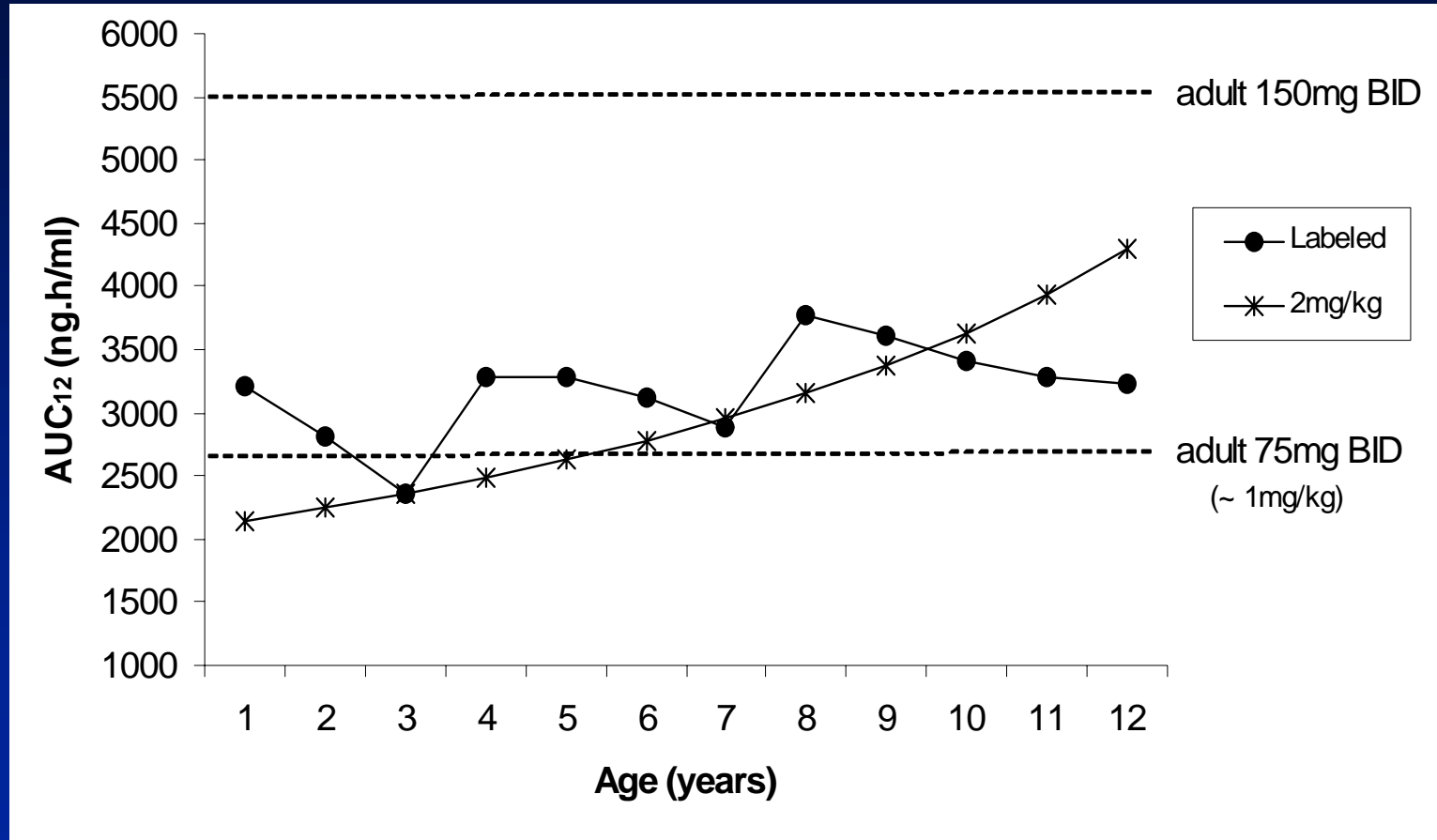
OC Concentrations Similar Between Japanese and Caucasian Children



n=141 Caucasians, n= 18 Japanese children

Doses were 2mg/kg except PP16351 which was unit dosing

Comparison of OC Exposures (AUC_{0-12}) based on 2mg/kg vs Unit dosing



Approved unit dosing Regimen: for children up to 15 kg: 30 mg BID, 16-23 kg: 45 mg BID; 24-40 kg: 60 mg BID; > 40 kg: 75 mg BID

Feasibility of Doing Pediatric Clinical Trial of Delirium-Like NPAEs

Background Rate of Delirium-Like NPAEs	Hypothesized Rate on Tamiflu	Excess Cases Seen per 10,000 Pts on Tamiflu	Patients per Treatment Arm
0.06%	0.18% (200% increase)	12	14,000
0.06%	0.12% (100% increase)	6	42,000
0.06%	0.09 (50% increase)	3	130,000

United HealthCare

Adjusted Exposure Odds Ratio

Oseltamivir vs. No Anti-viral

Age ≤ 17 Years

Outcome	Number of events (%)		Adjusted Exposure Odds Ratio	95% Confidence Interval	
	Oseltamivir	No Anti-viral		Lower	Upper
Any Neuropsych Events	251 (1.22)	1,032 (1.22)	0.96	0.83	1.12
Major Neuropsych Events	224 (1.09)	878 (1.03)	1.00	0.85	1.18
Specific to CNS Stimulation	157 (0.77)	605 (0.71)	1.03	0.85	1.25
296 Affective Psychoses	46 (0.22)	98 (0.12)	1.69	1.13	2.53
300 Neurotic Disorder	30 (0.15)	113 (0.13)	0.92	0.59	1.43
345 Epilepsy and Recurrent Seizures	7 (0.03)	31 (0.04)	1.05	0.43	2.61
346 Migraine	8 (0.04)	48 (0.06)	0.81	0.36	1.83
780 General Symptoms	28 (0.14)	127 (0.15)	0.97	0.62	1.53
784 Symptoms Involving Head & Neck	39 (0.19)	195 (0.23)	0.74	0.51	1.08

Propensity Score Matching

- In observational studies, characteristics of the treatment group and the untreated group are often significantly different
- Propensity score matching utilizes regression analysis to match patients of different groups based on a range of characteristics
 - e.g., Age, gender, region, presence of fever or pneumonia, and medical history
- After matching, the two study groups have similar distributions on these baseline characteristics
- Reduces selection bias and allows more accurate assessment of the impact of the treatment of interest