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EMETIC CONCENTRATIONS IN PARAQUAT FORMULATIONS

Stuart,

To answer your question about the clinical data with the emetic ICI 63197 (PP796), I have studied all the evidence that exists at Pharmaceuticals including a summary report by Bayliss, PFC, PH20992B, 1973. As far as I am aware there is no further data with this compound in man.

The original human study for this Development compound was in 12 volunteers at Dundee in the early 1970s. This study identified nausea at doses of 0.5-8mg PP796 and vomiting in 2 out of the 12 volunteers. All trials subsequent to this were carried out using 2mg PP796 in a further total of 52 patients. The total incidence of vomiting was 7% of individuals receiving a 2mg dose (4/55). However, many of these patients received the compound three times a day for several weeks with no incidence of nausea or vomiting. Since no therapeutic effects were found in the specific disease areas targetted, together with the potential nausea/vomiting side effect, the compound was withdrawn from development. I have discussed this data together with the historical aspects of emetic in paraquat formulations with Lewis and he has agreed to arrange a meeting at Fernhurst to re-visit this issue.

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Clinical Trials with ICI 63197 (Bayliss 1973 PH 20992B)

All Trials used a dose of 2mg ICI 63197 (PP796).

Trialist	Centre	Disease	Nos Patients or Volunteers	Nos of Dosings to each person	Vomiting Incidences	
Crooks	Dundee	Normal Vol	3V	1	0/3	-
Davies	Manchester	Endocrinology	8V	1	1/8	at 45M
Davies	Manchester	Glucose Tol	2V	1	0/2	-
Kerr	Glasgow	Asthma	4P	1	1/4	no time quoted
Palmer	Aberdeen	Asthma	4P	1	1/4	no time quoted
Beumer	Utrecht	Emphysema	12P	1	0/12	-
Eccleston	Edinburgh	Depression	4P	63	0/252	21 day study TDS
Magnus	Birmingham	Schizophrenia	6P	21	0/126	7 day study TDS
Magnus	Birmingham	Anxiety	5P	21	1/105	Vomited once then settled 7 day study TDS
Zacharias	Bebington	Hypertension	3P	112	0/336	28 day study QDS
Davies	Manchester	Obesity	4P	126	0/504	6 week study TDS
		TOTALS	55			

% incidence by dosing
4/1356 or 0.3%

% incidence of individuals
4/55 or 7%
(but disease may predispose or exacerbate nausea/vomiting)