Drugs in R&D

TITLE: EFFECT OF SEVERE RENAL IMPAIRMENT ON DORDAVIPRONE (ONC201) PHARMCOKINETICS

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Supplemental Information

Figure S1: Study Schema

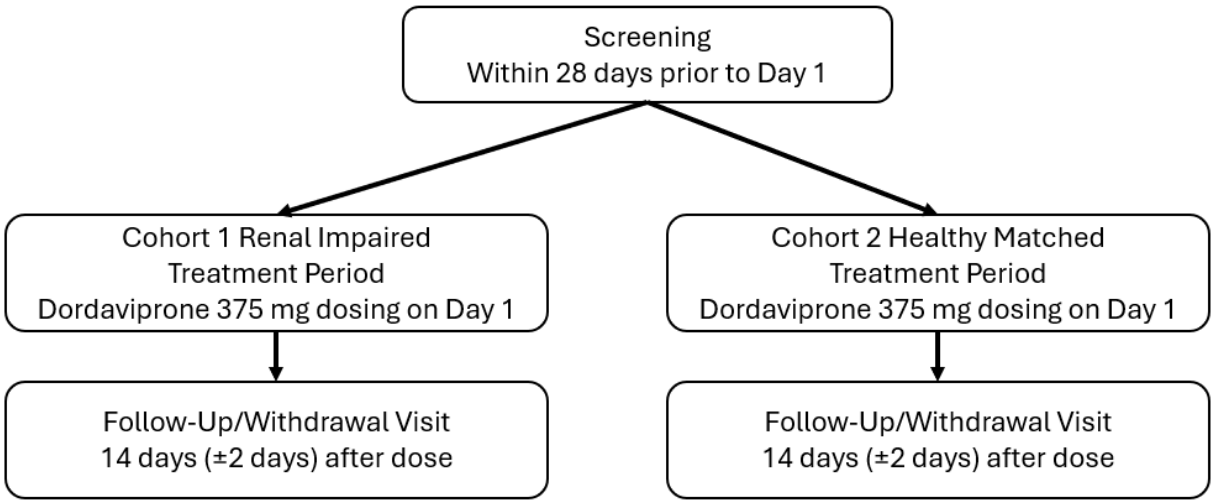
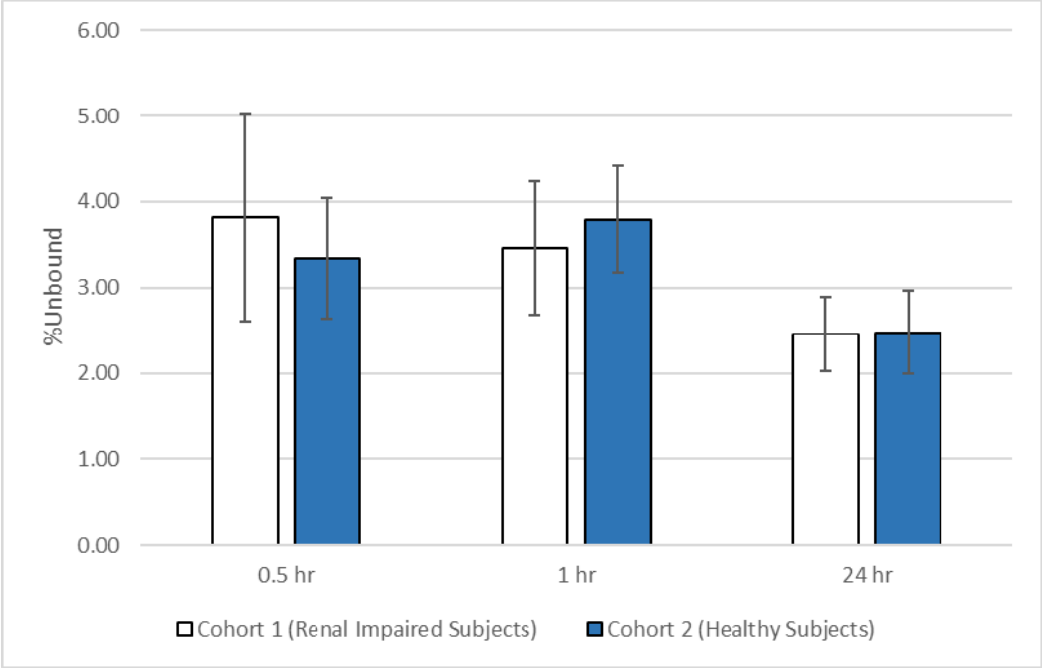
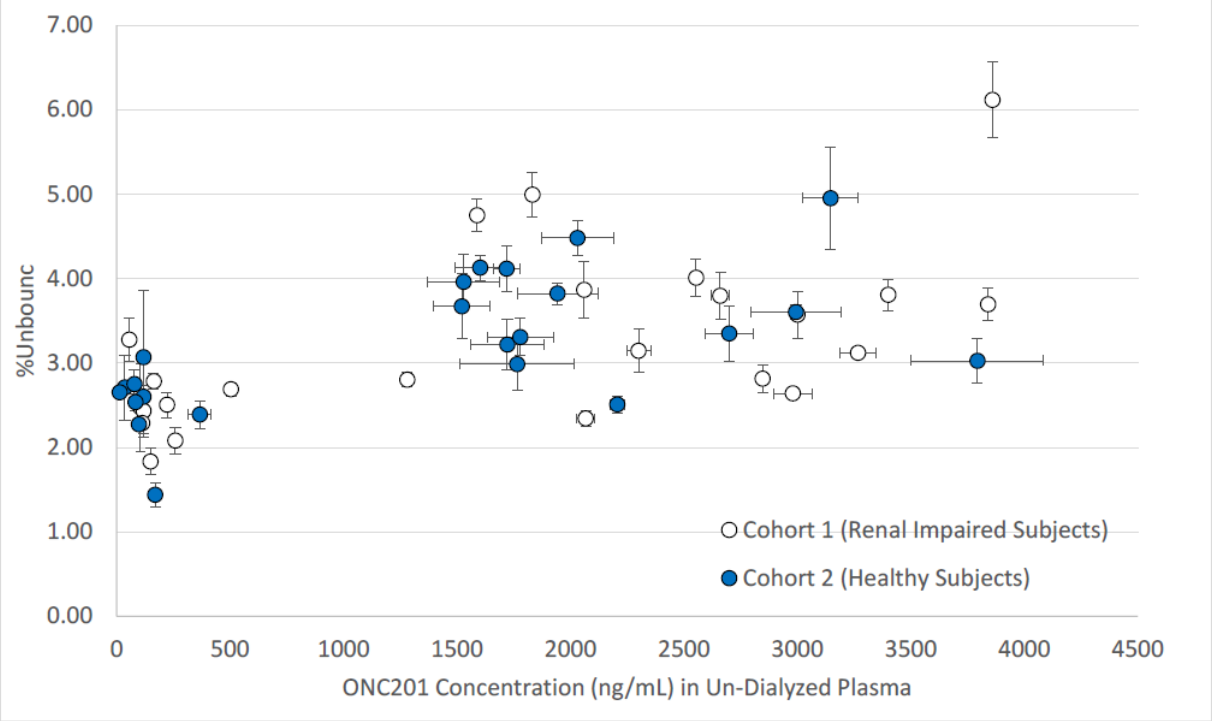


Figure S2: Mean Percent Unbound of Dordaviprone in Plasma from Subjects at Each Time Point – Comparison of Cohort 1 and Cohort 2



Bar graph displays mean +/- SD

Figure S3: Percent Unbound of Dordaviprone A(ONC201) as a Function of Dordaviprone Concentration in un-Dialyzed Plasma Samples – Comparison of Cohort 1 and Cohort



The data are means of triplicate measurements with standard deviations as the error bars

Table S1: ONC207 Plasma Pharmacokinetic Parameters after a Single Oral Dose of 375 mg Dordaviprone to Severe Renal Impaired and Healthy Matched Participants

	Tmax (h)	Cmax (ng/mL)	AUClast (h.ng/mL)	AUCinf (h.ng/mL)	t½ (h)	M/P Ratio Cmax	M/P Ratio AUClast	M/P Ratio AUCinf
Severe Renal Impairment								
n	8	8	8	6	6	8	8	6
Mean (SD)	NC	518 (108)	34130 (7228)	39622 (8695)	59.7 (7.9)	0.208 (0.086)	2.56 (0.743)	3.26 (0.812)
CV%	NC	20.8	21.2	21.9	13.3	41.4	29	24.9
Geometric mean	NC	507	33461	38817	59.3	0.194	2.47	3.18
Geometric mean 95% CI	NC	(423, 608)	(27993, 39998)	(30711, 49064)	(51.7,67.9)	(0.138,0.272)	(1.95,3.13)	(2.48,4.08)
Geometric mean CV%	NC	21.9	21.6	22.6	13.1	42.5	28.9	24
Median	0.75	526	33971	38572	58.8	0.187	2.43	3.03
Range (min, max)	(0.50,24.02)	(356, 658)	(24171, 44653)	(28414, 49919)	(51.1,72.7)	(0.112,0.339)	(1.77,3.80)	(2.49,4.61)
Healthy								
n	8	8	8	8	8	8	8	8
Mean (SD)	NC	465 (140)	13196 (3423)	13895 (3657)	36.3 (6.8)	0.209 (0.094)	1.46 (0.461)	1.51 (0.485)
CV%	NC	30	25.9	26.3	18.6	44.9	31.5	32.2
Geometric mean	NC	447	12784	13458	35.7	0.193	1.4	1.44
Geometric mean 95% CI	NC	(349, 574)	(10157, 16090)	(10700, 16928)	(29.9,42.6)	(0.136,0.274)	(1.06,1.84)	(1.09,1.90)
Geometric mean CV%	NC	30.4	28	28	21.5	43.8	34	34.5
Median	0.75	432	13247	13754	37.6	0.181	1.4	1.45
Range (min, max)	(0.75,8.00)	(277, 677)	(7988, 18398)	(8752, 19642)	(22.5,42.8)	(0.114,0.376)	(0.805,2.12)	(0.831,2.27)

Abbreviations: AUCinf=area under the plasma concentration-time curve from time zero to infinity; AUClast=area under the plasma concentration-time curve from time zero to time of last measurable plasma concentration; CI=confidence interval; Cmax=maximum plasma concentration of the drug; CV%=percentage coefficient of variation; max=maximum; min=minimum; M/P=metabolite/parent (unadjusted for molecular weight differences); PK=pharmacokinetic; SD=standard deviation; t½=half-life associated with the terminal slope of the semi-logarithmic drug concentration-time curve; Tmax=time to maximum plasma concentration.

Table S2: ONC207 Urine Pharmacokinetic Parameters after a Single Oral Dose of 375 mg Dordaviprone to Severe Renal Impaired and Healthy Matched Participants

	Ae (mg)
Severe Renal Impairment	
n	8
Mean (SD)	11.3 (3.43)
CV%	30.3
Geometric mean	10.8
Geometric mean 95% CI	(8.07, 14.4)
Geometric mean CV%	35.6
Median	11.4
Range (min, max)	(5.80, 15.4)
Healthy Matched Participants	
n	8
Mean (SD)	37.6 (7.40)
CV%	19.7
Geometric mean	36.9
Geometric mean 95% CI	(31.1, 43.7)
Geometric mean CV%	20.5
Median	37.6
Range (min, max)	(26.6,47.4)

Abbreviations: Ae=cumulative amount of unchanged drug excreted into the urine; CI=confidence interval; CV%=percentage coefficient of variation; max=maximum; min=minimum; PK=pharmacokinetic; SD=standard deviation.