Electronic Supplementary Material

Phase I study of cabazitaxel plus cisplatin in patients with advanced solid tumors: study to evaluate the impact of cytochrome P450 3A inhibitors (aprepitant, ketoconazole) or inducers (rifampin) on the pharmacokinetics of cabazitaxel

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Keywords:

Cabazitaxel; aprepitant; ketoconazole; rifampin; cytochrome P450 3A; drug–drug interactions

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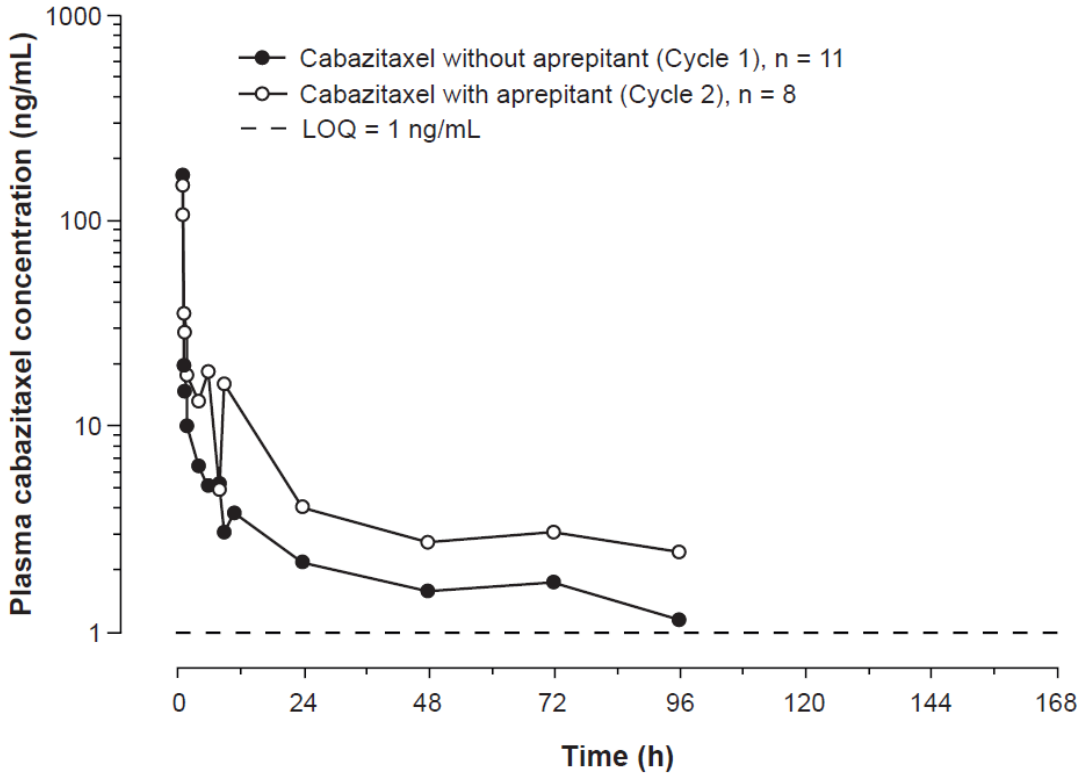
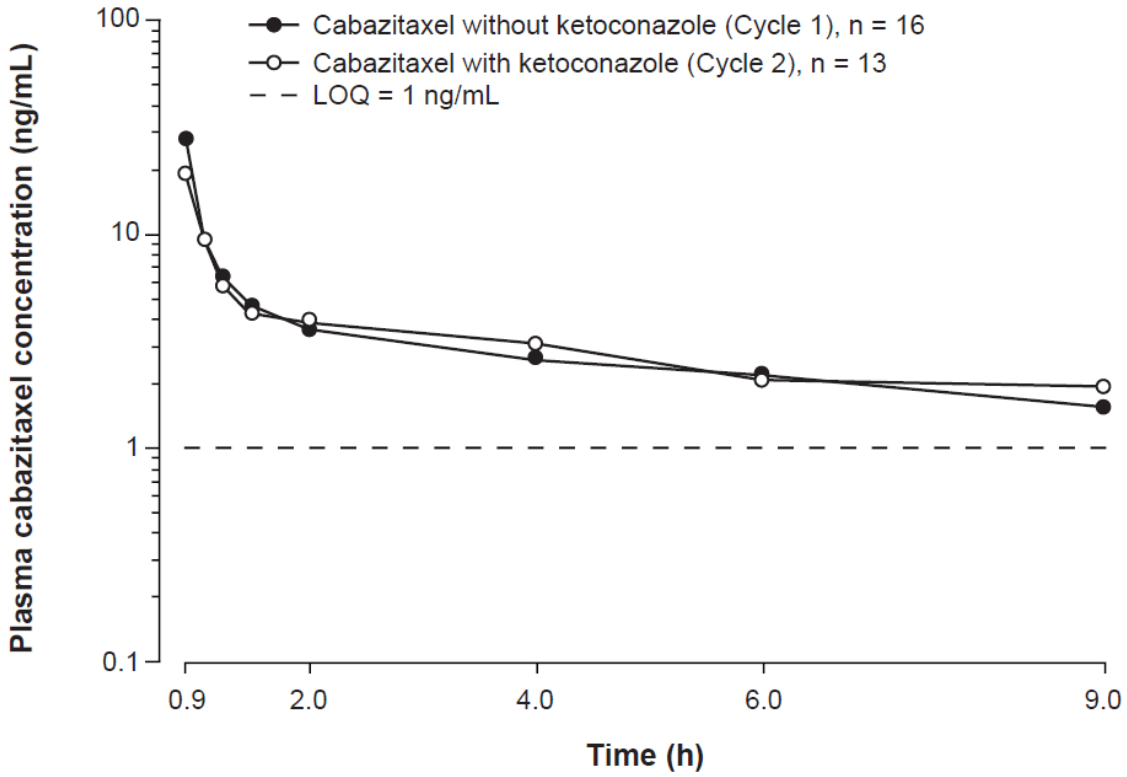
Online Resource 1: Mean plasma concentration–time profiles of cabazitaxel at Cycle 1 (without co-administered interacting drug) and Cycle 2 (with co-administered interacting drug) for a) aprepitant, b) ketoconazole and c) rifampin. LOQ = limit of quantification.

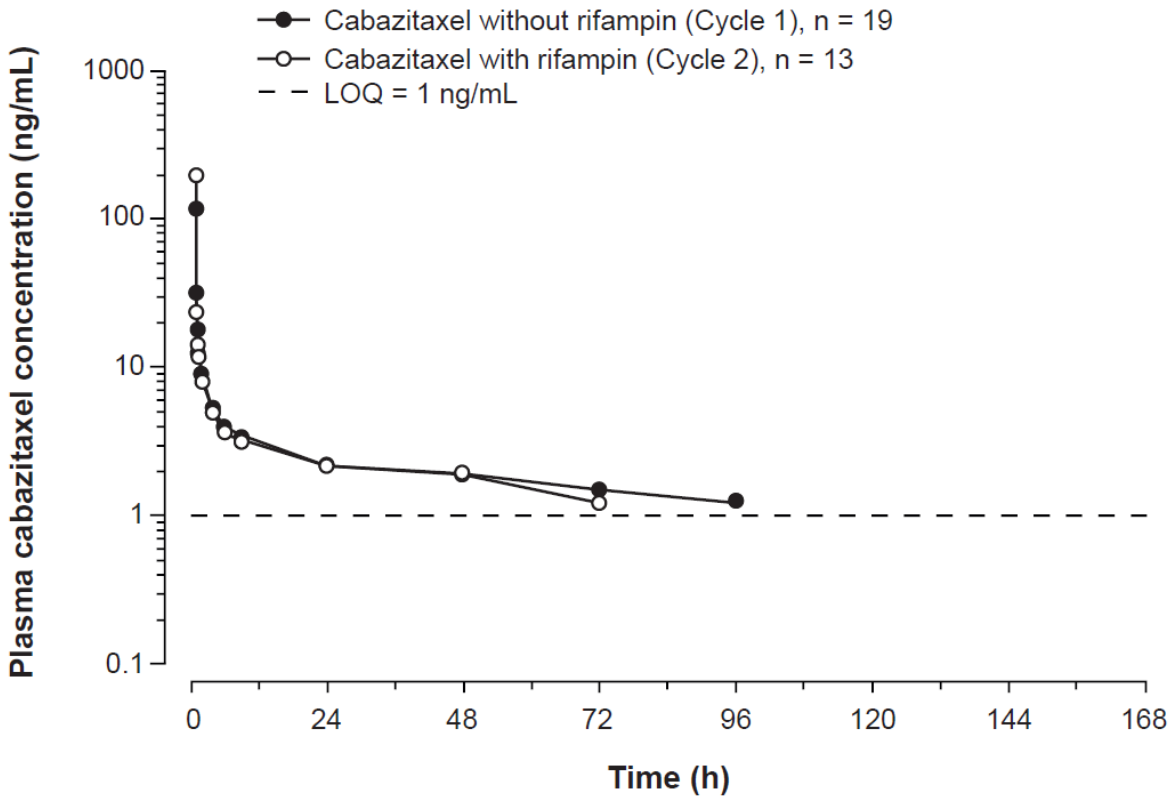
a)



b)


Cabazitaxel without ketoconazole (Cycle 1), n = 16
Cabazitaxel with ketoconazole (Cycle 2), n = 13
LOQ = 1 ng/mL
Plasma cabazitaxel concentration (ng/mL)
100
10
1
0.1
0.9
2.0
4.0
6.0
9.0
Time (h)

c)


Cabazitaxel without rifampin (Cycle 1), n = 19
Cabazitaxel with rifampin (Cycle 2), n = 13
LOQ = 1 ng/mL
Plasma cabazitaxel concentration (ng/mL)
1000
100
10
1
0.1
0
24
48
72
96
120
144
168
Time (h)

Online Resource 2: Hematologic abnormalities during on-treatment period in Parts 2, 3 and 4, presented as worst grade by patient (all-treated population)

Abnormality	Part 2, all-treated population (N = 15)		Part 3, all-treated population (N = 25)		Part 4, all-treated population (N = 23)	
	Grade ≥ 3, n (%)	All grades, n (%)	Grade ≥ 3, n (%)	All grades, n (%)	Grade ≥ 3, n (%)	All grades, n (%)
Anemia	5 (33.3)	12 (80.0)	6 (24.0)	25 (100)	3 (13.0)	23 (100)
Leukopenia	10 (66.7)	14 (93.3)	8 (32.0)	15 (60.0)	11 (47.8)	22 (95.7)
Lymphopenia	6 (40.0)	11 (73.3)	9 (36.0)	22 (88.0)	11 (47.8)	21 (91.3)
Neutropenia	11 (73.3)	13 (86.7)	7 (28.0)	10 (40.0)	14 (60.9)	19 (82.6)
Thrombocytopenia	2 (13.3)	13 (86.7)	2 (8.0)	16 (64.0)	3 (13.0)	16 (69.6)

Does not include toxicity Grade 0 or missing. Data are based on laboratory values, not AEs.