催吐リスク　　乳ﾍﾟﾑﾌﾞﾛ200/d1+GEM1000+CBDCA2/d1,8/c21d

薬剤名	投与経路	投与量		希釈液			点滴時間（分）	投与日(day)
			mg					
			mg					
			mg					
			mg			mL		
キイトルーダ	200	mg/body		生食	100	mL	30	1
ゲムシタビン	1000	mg/m2		生食	100	mL	30	1,8
カルボプラチン	2	AUC		5%糖液	250	mL	60	1,8
						mL		
						mL		

内服薬

投与基準等

Ⅱ. 投与・休薬基準 （例：白血球≧2000/mm³、好中球≧1000/mm³）
好中球数 ≧1500/μL、血小板数 ≧10 万/μL、ヘモグロビン ≧9.0g/dL
クレアチニン <1.5×ULN または Ccr(GFR) ≧30mL/min クレアチニン＞1.5×ULN
総ビリルビン <1.5×ULN または 総ビリルビン>1.5×ULN で直接ビリルビン ≦ULN
アルブミン ≧3.0g/dL
INR または PT ≦1.5×ULN、aPTT ≦1.5×ULN

Ⅲ. 減量基準 （例：Grade3 以上の好中球減少時、次回より投与量を80%に減量）
ペムブロリズマブは減量なし

	Dose level 0	Dose level -1	Dose level -2	Dose level -3
ゲムシタビン	100mg/㎡	-20%	-20%	投与中止
カルボプラチン	AUC 2	AUC 1.5	AUC 1	投与中止

Ⅳ. 重大な副作用（例：好中球減少 Grade3 以上37．5%）

	Pembrolizumab–chemotherapy group (n=562)		Placebo–chemotherapy group (n=281)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any adverse event*	554 (99%)	438 (78%)	276 (98%)	207 (74%)
Treatment-related adverse event†				
Total	541 (96%)	383 (68%)	267 (95%)	188 (67%)
Anaemia	275 (49%)	92 (16%)	129 (46%)	41 (15%)
Neutropenia	231 (41%)	167 (30%)	107 (38%)	84 (30%)
Nausea	221 (39%)	9 (2%)	115 (41%)	4 (1%)
Alopecia	186 (33%)	5 (1%)	94 (33%)	3 (1%)
Fatigue	160 (28%)	16 (3%)	83 (30%)	7 (2%)
Neutrophil count decreased	125 (22%)	98 (17%)	74 (26%)	57 (20%)
Alanine aminotransferase increased	115 (20%)	33 (6%)	46 (16%)	13 (5%)
Immune-mediated adverse event‡				
Total	144 (26%)	29 (5%)	17 (6%)	0
Hypothyroidism	87 (15%)	2 (<1%)	9 (3%)	0
Hyperthyroidism	27 (5%)	1 (<1%)	3 (1%)	0
Pneumonitis	14 (2%)	6 (1%)	0	0
Colitis	10 (2%)	2 (<1%)	4 (1%)	0
Severe skin reactions	10 (2%)	10 (2%)	1 (<1%)	0

Data are n (%). *Listed are all adverse events that occurred during randomly allocated study treatment or within the 30 days thereafter (within 90 days for serious events). The as-treated population included all patients who underwent randomisation and received ≥1 dose of study treatment. Events are listed in descending order of frequency in the pembrolizumab–chemotherapy group. The severity of adverse events was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0. †Adverse events that were attributed to study treatment by the investigator. Treatment-related adverse events that occurred in at least 20% of patients are reported. Patients might have had more than one event. ‡Adverse events based on a list of terms specified by the sponsor and considered regardless of treatment attribution by the investigator that occurred in at least ten patients in the pembrolizumab–chemotherapy group are reported.

添付参考資料（文献・ガイドライン・治験計画書・研究計画書）

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