ペムブロリズマブ＋CDDP＋アリムタ療法(21日間/サイクル)　　肺癌

催吐リスク　High(apr)　　肺 PEM+アリムタ500＋

薬剤名	投与経路	投与量		希釈液			点滴時間（分）	投与日(day)
アプレピタント	内服	125	mg					1
			mg					
デキサメタゾン	注射	9.9	mg					1
グラニセトロン	注射	1	mg	生食	100	mL	30	1
キイトルーダ	200	mg/bo		生食	100	mL	30	1
アリムタ	500	mg/m2		生食	100	mL	10	1
シスプラチン	75	mg/m2		生食	500	mL	60	1
						mL		
						mL		

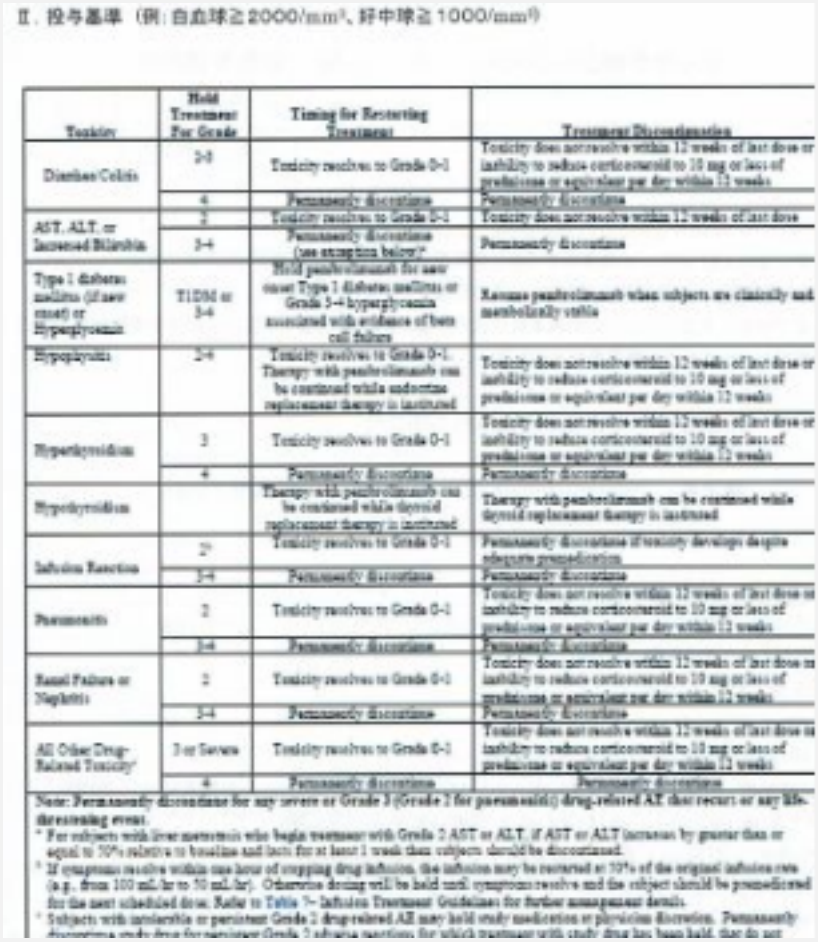
内服薬

アプレピタント 80mg 分1　朝食後　day2,3

デキサメタゾン 8mg 分2 朝昼食後　day2,3,4

オランザピン 5mg 分1　眠前　day1,2,3,4

投与基準等



II. 投与基準（例：白血球≧2000/mm³、好中球≧1000/mm³）

Toxicity	Hold Treatment For Grade	Timing for Restarting Treatment	Treatment Discontinuation
Diarrhea/Colitis	3-4	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
	4	Permanently discontinue	Permanently discontinue
AST, ALT, or Increased Bilirubin	3	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose
	3-4	Permanently discontinue (see exception below)[a]	Permanently discontinue
Type 1 diabetes mellitus (if new onset) or Hyperglycemia	T1DM or 3-4	Hold pembrolizumab for new onset Type 1 diabetes mellitus or Grade 3-4 hyperglycemia associated with evidence of beta cell failure	Resume pembrolizumab when subjects are clinically and metabolically stable
Hypophysitis	2-4	Toxicity resolves to Grade 0-1. Therapy with pembrolizumab can be continued while endocrine replacement therapy is instituted	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
Hyperthyroidism	3	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
	4	Permanently discontinue	Permanently discontinue
Hypothyroidism		Therapy with pembrolizumab can be continued while thyroid replacement therapy is instituted	Therapy with pembrolizumab can be continued while thyroid replacement therapy is instituted
Infusion Reaction	2	Toxicity resolves to Grade 0-1	Permanently discontinue if toxicity develops despite adequate premedication
	3-4	Permanently discontinue	Permanently discontinue
Pneumonitis	2	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
	3-4	Permanently discontinue	Permanently discontinue
Renal Failure or Nephritis	2	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
	3-4	Permanently discontinue	Permanently discontinue
All Other Drug-Related Toxicity	3 or Severe	Toxicity resolves to Grade 0-1	Toxicity does not resolve within 12 weeks of last dose or inability to reduce corticosteroid to 10 mg or less of prednisone or equivalent per day within 12 weeks
	4	Permanently discontinue	Permanently discontinue

Note: Permanently discontinue for any severe or Grade 3 (Grade 2 for pneumonitis) drug-related AE that recurs or any life-threatening event.

[a] For subjects with liver metastasis who begin treatment with Grade 2 AST or ALT, if AST or ALT increases by greater than or equal to 50% relative to baseline and lasts for at least 1 week then subject should be discontinued.

[b] If symptoms resolve within one hour of stopping drug infusion, the infusion may be restarted at 50% of the original infusion rate (e.g., from 100 mL/hr to 50 mL/hr). Otherwise dosing will be held until symptoms resolve and the subject should be premedicated for the next scheduled dose. Refer to Table 7- Infusion Treatment Guidelines for further management details.

[c] Subjects with intolerable or persistent Grade 2 drug-related AE may hold study medication at physician discretion. Permanently discontinue study drug for persistent Grade 2 adverse reactions for which treatment with study drug has been held, that do not

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)

	Dose Level 0	Dose Level -1	Dose Level -2	Dose Level -3
Cisplatin	75 mg/m^2	56 mg/ m^2	38 mg/ m^2	Discontinue
Carboplatin	AUC 5 Maximum dose 750mg	AUC 3.75 Maximum dose 562.5mg	AUC 2.5 Maximum dose 375mg	Discontinue
Pemetrexed	500mg/m2	375 mg/m2	250 mg/m2	Discontinue
Pembrolizumab/placebo	200 mg fixed dose	Dose reductions are not permitted	Dose reductions are not permitted	Dose reductions are not permitted

Ⅳ. 重大な副作用 (例:好中球減少 Grade3 以上37. 5%)

<切除不能な進行・再発の非小細胞肺癌>

※ 併用投与時　国際共同第Ⅲ相試験(KEYNOTE-189試験)で、本剤200mgを3週間間隔で投された安全性解析対象例405例中372例(91.9%)(日本人4例中3例を含む)に副作用が認められた。主な副作用(20%以上)は、悪心187例(46.2%)、貧血154例(38.0%)、疲労134(33.1%)、好中球減少症101例(24.9%)及び食欲減退84例(20.7%)であった。
国際共同第Ⅲ相試験(KEYNOTE-407試験)で、本剤200mgを3週間間隔で投与された安全性析対象例278例中265例(95.3%)(日本人22例中22例を含む)に副作用が認められた。主な副用(20%以上)は、脱毛症126例(45.3%)、貧血123例(44.2%)、好中球減少症97例(34.9%悪心85例(30.6%)、血小板減少症81例(29.1%)及び下痢61例(21.9%)であった。(承認時)

添付参考資料(文献・ガイドライン・治験計画書・研究計画書)

N Engl J Med 2018, 378:2078-92