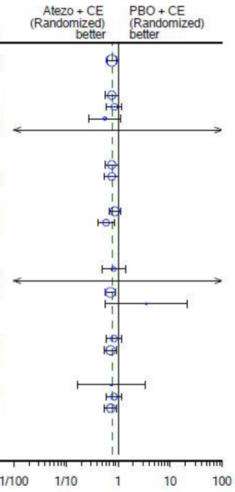
図 2.7.3.3.3.2-3　患者背景及びベースライン時の特性別の PFS の部分集団解析（GO30081試験）

Forest Plot - Subgroup Analysis of Progression Free Survival per RECIST v1.1 - Investigator, Intent-to-Treat Patients
Protocol: GO30081

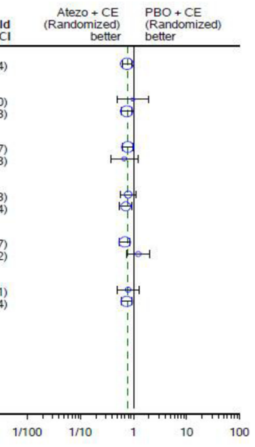
Baseline Risk Factors	Total n	PBO + CE (Randomized) (N=202) n	Events	Median (Months)	Atezo + CE (Randomized) (N=201) n	Events	Median (Months)	Hazard Ratio	95%Wald CI
All Patients	403	202	189	4.3	201	171	5.2	0.76	(0.61, 0.94)
Age Group 4 Categories (yr)									
<65	217	106	98	4.3	111	93	5.1	0.76	(0.57, 1.01)
65 - 74	145	74	69	5.3	71	64	5.3	0.85	(0.60, 1.20)
75 - 84	39	21	21	4.2	18	13	5.7	0.56	(0.28, 1.14)
>=85	2	1	1	0.5	1	1	4.2	<0.01	(0.00, NE)
Age Group 2 Categories (yr)									
< 65	217	106	98	4.3	111	93	5.1	0.76	(0.57, 1.01)
>= 65	186	96	91	4.6	90	78	5.3	0.76	(0.56, 1.03)
Sex (eCRF)									
Male	261	132	123	4.4	129	112	4.4	0.87	(0.67, 1.13)
Female	142	70	66	4.2	72	59	5.6	0.59	(0.41, 0.85)
Race									
American Indian or Alaska Native	1	1	1	5.6				NE	(NE , NE)
Asian	69	36	32	4.3	33	28	4.3	0.83	(0.49, 1.38)
Black or African American	3	2	2	4.2	1	1	8.3	<0.01	(0.00, NE)
White	322	159	150	4.3	163	139	5.4	0.72	(0.57, 0.91)
Unknown	8	4	4	6.5	4	3	4.2	3.49	(0.57, 21.55)
Baseline ECOG (eCRF)									
0	140	67	64	4.3	73	64	4.9	0.84	(0.59, 1.20)
1	263	135	125	4.3	128	107	5.4	0.72	(0.55, 0.94)
Tobacco Use									
Never	12	3	3	4.1	9	4	3.9	0.74	(0.16, 3.33)
Current	149	75	66	4.4	74	63	5.6	0.84	(0.59, 1.19)
Previous	242	124	120	4.2	118	104	5.2	0.73	(0.56, 0.95)



Medians were estimated from Kaplan-Meier method. NE = Not estimable.
Hazard ratios relative to PBO + CE and the associated confidence intervals were estimated using unstratified Cox regression.
The vertical dashed line indicates the hazard ratio for all patients.
The size of the symbol is proportional to the size of the population in the subgroup.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018
Program: /opt/BIOSTAT/prod/cdt30099/go30081/g_ef_tte_fp.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/g_ef_tte_fp_IT_pfsinv_p1_24APR2018_GO30081.pdf 06JUL2018 20:43

Forest Plot - Subgroup Analysis of Progression Free Survival per RECIST v1.1 - Investigator, Intent-to-Treat Patients
Protocol: GO30081

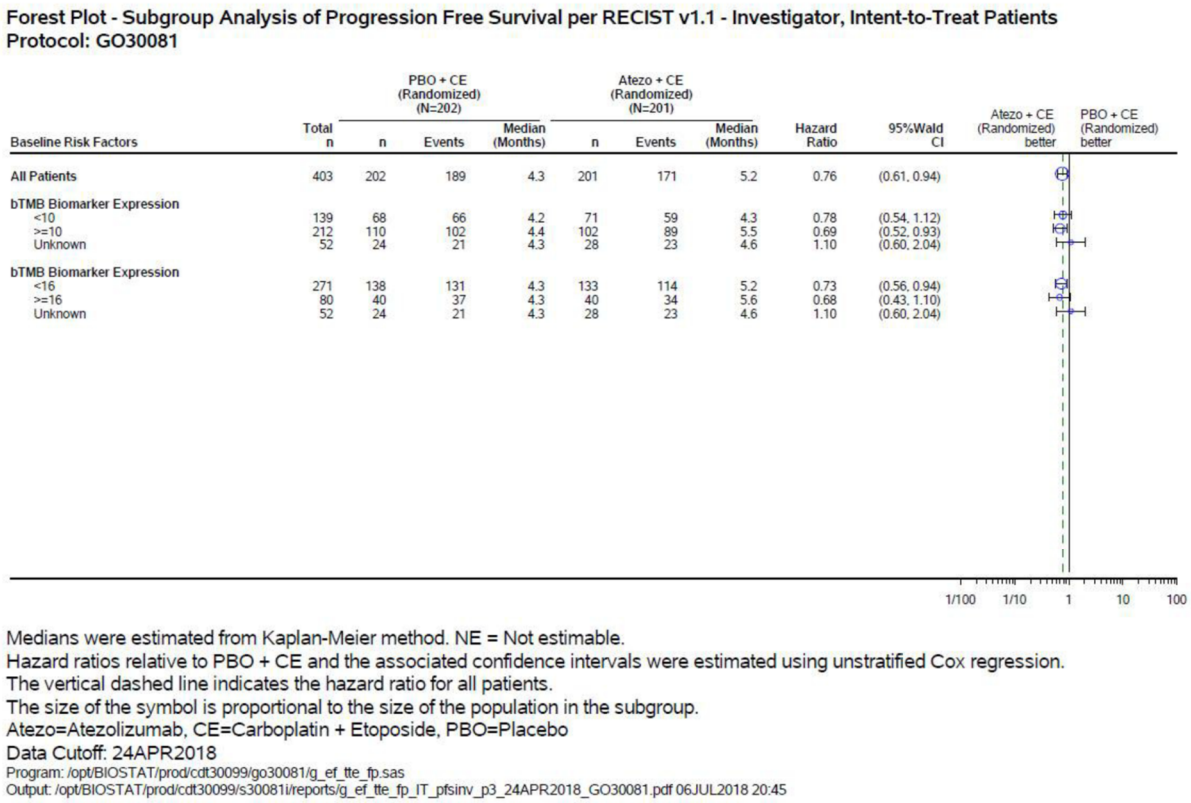
Baseline Risk Factors	Total n	PBO + CE (Randomized) (N=202) n	Events	Median (Months)	Atezo + CE (Randomized) (N=201) n	Events	Median (Months)	Hazard Ratio	95%Wald CI
All Patients	403	202	189	4.3	201	171	5.2	0.76	(0.61, 0.94)
Brain Metastases (eCRF)									
Yes	35	18	18	4.4	17	15	4.2	0.98	(0.49, 2.00)
No	368	184	171	4.3	184	156	5.3	0.75	(0.60, 0.93)
Lung Metastasis at Enrollment									
Yes	349	172	162	4.4	177	152	5.2	0.78	(0.62, 0.97)
No	54	30	27	4.1	24	19	5.4	0.67	(0.37, 1.23)
Liver Metastasis at Enrollment									
Yes	149	72	69	4.2	77	69	4.3	0.80	(0.57, 1.13)
No	254	130	120	4.4	124	102	5.6	0.72	(0.55, 0.94)
Lymph Node Metastasis at Enrollment									
Yes	328	168	158	4.2	160	137	5.4	0.69	(0.54, 0.87)
No	75	34	31	5.5	41	34	4.5	1.23	(0.75, 2.02)
Adrenal Gland Metastasis at Enrollment									
Yes	72	35	33	4.2	37	34	4.5	0.80	(0.49, 1.31)
No	331	167	156	4.3	164	137	5.3	0.75	(0.59, 0.94)



Medians were estimated from Kaplan-Meier method. NE = Not estimable.
Hazard ratios relative to PBO + CE and the associated confidence intervals were estimated using unstratified Cox regression.
The vertical dashed line indicates the hazard ratio for all patients.
The size of the symbol is proportional to the size of the population in the subgroup.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018
Program: /opt/BIOSTAT/prod/cdt30099/go30081/g_ef_tte_fp.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/g_ef_tte_fp_IT_pfsinv_p2_24APR2018_GO30081.pdf 06JUL2018 20:44

［5.3.5.1-1 Figure 10を再掲］

図 2.7.3.3.3.2-4　bTMB 別の PFS の部分集団解析（GO30081試験）



［5.3.5.1-1 Table 29を再掲］

2.7.3.4　推奨用法・用量に関する臨床情報の解析

本剤は，切除不能な進行・再発の非小細胞肺癌を効能・効果とし，1200 mg/body の3週間間隔点滴静注を用法・用量として承認されている。海外第 Ia 相臨床試験（PCD4989g 試験）の予備的な結果からは，被験者数が限られるものの，小細胞肺癌患者を対象とし本剤を単剤投与した場合，本剤の臨床活性が認められること及び安全性プロファイルが許容可能なものであることが確認された。海外第 Ib 相臨床試験（GP28328試験）の予備的な結果[2)]からは，本剤と白金製剤併用化学療法を併用した場合，有望な抗腫瘍活性が認められること及び安全性プロファイルが許容可能なものであることが示された。これらの知見を踏まえ，第 I/III 相臨床試験の GO30081試験では，本剤1200 mg/body を3週間間隔でカルボプラチン及びエトポシドと併用投与した。

GO30081試験では，主要評価項目の1つである OS がプラセボ併用群に対して本剤併用群で統計的有意かつ臨床的に意義のある延長を示し（層別 HR = 0.701，95%CI：0.541～0.909；層別 log-rank 検定：P = 0.0069），もう1つの主要評価項目である PFS でも統計的に有意な延長を示し（層別 HR = 0.772，95%CI：0.624～0.955；層別 log-rank 検定：P = 0.0170），本剤 + カルボプラチン + エトポシド併用療法の有効性が検証された。また，本剤をカルボプラチン及びエトポシドと併用することによる新たな安全性シグナルは認められず，本剤 + カルボプラチン + エトポシド併用療法は忍容であることが確認された。

GO30081試験の日本人部分集団の有効性及び安全性は，試験全体の結果と大きく異なるものではなく，上述の用法・用量での日本人の臨床的有用性が確認された。

以上から，小細胞肺癌患者に対し本剤の推奨用法・用量を「1200 mg/body を3週間間隔で点滴静脈内注射」とすることは妥当と考えた。

2.7.3.5 効果の持続，耐薬性

効果の持続及び耐薬性を検討する試験は実施していない。

GO30081試験の本剤併用群で，抗薬物抗体（ADA）の発現がみられた ADA 陽性集団と ADA の発現がみられなかった ADA 陰性集団の PFS 及び OS の要約を表 2.7.3.5-1に示す。

PFS の中央値及び無増悪生存割合（6カ月時点，12カ月時点）は，ADA 陽性集団と ADA 陰性集団で同程度であった。OS の中央値は，ADA 陰性集団より ADA 陽性集団で中央値が短い傾向がみられたが，95%CI は重なっていた。1年生存割合は ADA 陽性集団と ADA 陰性集団で同程度であり，いずれもプラセボ併用群より高かった。

表 2.7.3.5-1 ADA 陽性集団及び陰性集団の PFS 及び OS の要約（GO30081試験）

	PBO + CE (N＝202)	Atezo + CE (N＝188)	
	All patients	Atezo ADA-Negative	Atezo ADA-Positive
Progression Free Survival per Investigator			
N	n = 202	n = 153	n = 35
Patients with event (%)	189 (93.6%)	135 (88.2%)	30 (85.7%)
Median time to event (months) 95% CI	4.3 (4.2, 4.5)	5.1 (4.3, 5.6)	5.5 (5.2, 5.6)
6 Months			
Patients remaining at risk	44	49	9
Event Free Rate (%)	22.4	32.7	27.6
95% CI	(16.6, 28.2)	(25.2, 40.2)	(12.3, 42.9)
1 year			
Patients remaining at risk	9	18	3
Event Free Rate (%)	5.4	13.2	12.3
95% CI	(2.1, 8.6)	(7.7, 18.7)	(1.0, 23.5)
Overall Survival			
N	n = 202	n = 153	n = 35
Patients with event (%)	134 (66.3%)	82 (53.6%)	17 (48.6%)
Median time to event (months) 95% CI	10.3 (9.3, 11.3)	12.6 (11.1, 16.6)	10.9 (9.1, NE)
1 year			
Patients remaining at risk	59	63	11
Event Free Rate (%)	38.2	53.7	49.1
95% CI	(31.2, 45.3)	(45.5, 61.9)	(31.6, 66.7)
2 year			
Patients remaining at risk	NE	NE	NE
Event Free Rate (%)	NE	NE	NE
95% CI	NE	NE	NE

ADA＝anti-drug antibodies; Atezo + CE = atezolizumab in combination with carboplatin and etoposide; CI = confidence interval; NE = not estimable; OS = overall survival; PFS = progression-free survival; PBO + CE = placebo in combination with carboplatin and etoposide;

［5.3.5.1-1 Table 68を再掲］

2.7.3.6 参考文献

1) Ye Y, Li A, Liu L, Yao B. A group sequential Holm procedure with multiple primary endpoints. Stat Med. 2013; 32(7):1112-24.
2) Liu SV, Camidge DR, Gettinger SN, Giaccone G, Heist RS, Hodi FS, et al. Long-term survival follow-up of atezolizumab in combination with platinum-based doublet chemotherapy in patients with advanced non-small-cell lung cancer. Eur J Cancer. 2018; 101:114-22.

テセントリク点滴静注1200 mg
（アテゾリズマブ（遺伝子組換え））
［小細胞肺癌］

第2部　（モジュール2）：CTD の概要（サマリー）

2.7.4 臨床的安全性

中外製薬株式会社

略語一覧

略語	英名	和名
ADA	anti-drug antibody	抗薬物抗体
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human use	医薬品規制調和国際会議
MedDRA	Medical Dictionary for Regulatory Activities	ICH 国際医薬用語集
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events	National Cancer Institute 有害事象共通用語規準
PBRER	Periodic Benefit-Risk Evaluation Report	—
RECIST	Response Evaluation Criteria in Solid Tumors	固形癌の治療効果判定のための規準

目次

頁
2.7.4 臨床的安全性 5
2.7.4.1 医薬品への曝露 5
2.7.4.1.1 総括的安全性評価計画及び安全性試験の記述 5
2.7.4.1.1.1 安全性評価に用いた試験 5
2.7.4.1.1.2 安全性の評価方法 5
2.7.4.1.1.3 投与量変更（休薬又は減量）及び中止基準 6
2.7.4.1.2 全般的な曝露状況 8
2.7.4.1.3 治験対象集団の人口統計学的特性及びその他の特性 10
2.7.4.2 有害事象 10
2.7.4.2.1 有害事象の解析 10
2.7.4.2.1.1 比較的よくみられる有害事象 10
2.7.4.2.1.2 死亡 13
2.7.4.2.1.3 その他の重篤な有害事象 14
2.7.4.2.1.4 その他の重要な有害事象 17
2.7.4.2.1.4.1 治験薬の投与中止に至った有害事象 17
2.7.4.2.1.4.2 治験薬の投与量変更（休薬又は減量）に至った有害事象 18
2.7.4.2.1.5 器官別又は症候群別有害事象の解析 21
2.7.4.2.1.6 日本部分集団の結果 31
2.7.4.2.1.6.1 日本部分集団の安全性の結果 31
2.7.4.2.1.6.2 日本部分集団と外国部分集団との比較 42
2.7.4.2.2 個別有害事象の文章による説明 46
2.7.4.3 臨床検査値の評価 46
2.7.4.3.1 血液検査及び血液生化学検査 46
2.7.4.3.2 抗薬物抗体（ADA） 46
2.7.4.4 バイタルサイン，身体的所見及び安全性に関連する他の観察項目 47
2.7.4.4.1 心電図 47
2.7.4.4.2 バイタルサイン 47
2.7.4.5 特別な患者集団及び状況下における安全性 47
2.7.4.5.1 内因性要因 47
2.7.4.5.2 外因性要因 47
2.7.4.5.3 薬物相互作用 47
2.7.4.5.4 妊娠及び授乳時の使用 47
2.7.4.5.5 過量投与 47
2.7.4.5.6 薬物乱用 47
2.7.4.5.7 離脱症状及び反跳現象 47

2.7.4.5.8 自動車運転及び機械操作に対する影響又は精神機能の障害.....47
2.7.4.6 市販後データ.....48
2.7.4.6.1 海外における市販後の使用経験.....48
2.7.4.6.2 推定使用患者数.....48
2.7.4.6.3 有害事象.....48
2.7.4.6.4 市販後データの結論.....49
2.7.4.7 付録.....50
2.7.4.7.1 要約表.....50
2.7.4.7.2 一覧.....61

2.7.4 臨床的安全性

2.7.4.1 医薬品への曝露

2.7.4.1.1 総括的安全性評価計画及び安全性試験の記述

2.7.4.1.1.1 安全性評価に用いた試験

テセントリク点滴静注1200 mg（以下，本剤）は，アテゾリズマブ（遺伝子組換え）（以下，アテゾリズマブ）を有効成分として含有する点滴静脈内注射剤として開発されている。

本剤の安全性は，小細胞肺癌患者を対象とした日本を含む国際共同第 I/III 相臨床試験であるGO30081試験の結果に基づき評価した。

GO30081試験の本剤の用法・用量は，固定用量1200 mg を3週間に1回（1サイクル：21日）点滴静脈内投与であった。

本リーフでは主解析時（データカットオフ日：2018年4月24日）の結果を記載した。

2.7.4.1.1.2 安全性の評価方法

本リーフでは，被験者に投与された本剤/プラセボと，併用化学療法として投与されたカルボプラチン，エトポシドをまとめて，「治験薬」と表記する。

(1) 有害事象の定義

有害事象を，治験薬との因果関係を問わず，治験薬が投与された被験者に生じた，あらゆる好ましくない医療上の出来事と定義した。

下記のいずれかに該当するものは有害事象とした。

- 医薬品の使用と時間的に関連のある，あらゆる好ましくない，意図しない徴候（たとえば，臨床検査値の異常），症状又は疾病。当該医薬品との因果関係の有無は問わない。
- 新規疾患の発症，又は既存疾患の増悪（既知の状態の性質，頻度又は重症度の面からみた悪化）。ただし，原疾患の小細胞肺癌の病勢進行は除外した。
- ベースライン時にはみられなかった断続的な医学的状態（頭痛等）の再発。
- 臨床検査値やその他の検査（心電図，X 線等）における悪化で，症状を伴うもの，又は治験薬及び併用薬剤の変更や治験薬の投与中止に至ったもの
- 治験実施計画書に規定された処置に関連した有害事象。治験薬の割り付け前に発現したもの（たとえばスクリーニング時の生検などの侵襲的処置）も含む。

治験薬との因果関係は，「関連あり」，「関連なし」の2段階で判定し，「関連あり」と判定された有害事象を副作用（因果関係が否定できない有害事象）として取り扱った。

(2) 重篤な有害事象

有害事象の内，下記の事項のいずれか1つ以上に該当する事象を重篤な有害事象と定義した。

- 致死的なもの（実際に死因となる，又は死に至る有害事象）
- 生命を脅かすもの（治験責任（分担）医師の判断により，直ちに死亡する危険があると考えられる有害事象）
- 入院又は入院期間の延長を要するもの
- 永続的又は重大な障害・機能不全に至るもの（通常の生活機能を営む能力を著しく損なう有害事象）
- 治験薬に曝露された母親から生まれた新生児・乳児における先天異常・先天性欠損
- 治験責任（分担）医師により重要な医学的事象であると判断されるもの（例：被験者を危険

に曝す，又は上記のいずれかの転帰を防ぐために内科的又は外科的な処置を必要とする事象）

(3) 有害事象の評価基準

有害事象の重症度判定は National Cancer Institute 有害事象共通用語基準（NCI CTCAE）v4.0を，有害事象の読み替え用語集は ICH 国際医薬用語集（MedDRA）Version 21.0を用いた。

(4) 有害事象の収集

有害事象の収集範囲を表 2.7.4.1.1.2-1に示す。

表 2.7.4.1.1.2-1　有害事象の収集範囲（GO30081試験）

期間	対象
同意取得後，治験薬の投与開始前	治験実施計画書に規定された処置（例：生検などの侵襲的手法，治療の中止）に関連した重篤な有害事象
治験薬の投与開始後，治験薬最終投与日から90日間，又は別の全身抗癌療法開始のいずれかに該当するまで	すべての重篤な有害事象及び adverse event of special interest（治験薬との因果関係にかかわらない）
治験薬の投与開始後，治験薬最終投与日から30日間，又は別の全身抗癌療法開始のいずれかに該当するまで	その他のすべての有害事象（治験薬との因果関係にかかわらない）
以降	すべての死亡，治験薬に起因すると考えられる，重篤な有害事象及び adverse event of special interest

2.7.4.1.1.3　投与量変更（休薬又は減量）及び中止基準

(1) 投与量変更基準

1) 本剤/プラセボの休薬基準

被験者が休薬を要する有害事象を発現した場合，本剤/プラセボの投与を一時休薬することが可能であった。休薬期間が最終投与後105日を超えた場合には，本剤/プラセボの投与を中止した。例外的に対応する場合は，Medical Monitor の承認を必要とした。

有害事象の治療に用いたステロイド薬の漸減を必要とする被験者の場合，本剤/プラセボの休薬許容日数に関わらず，ステロイド薬による治療を終了又はプレドニゾン10 mg/日（又は相当量）以下となるまで本剤/プラセボの休薬が可能であった。許容される休薬期間の長さは治験責任（分担）医師と Medical Monitor の合意によって決められることとした。また，本剤/プラセボの減量は認めなかった。

2) カルボプラチン，エトポシドの投与量変更基準

カルボプラチン，エトポシドは，5.3.5.1-1 GO30081治験実施計画書5.1.7項に示した基準に従って投与量変更を行うこととした。

3) 治験薬全般に対する付記事項

重症度のグレードが異なる複数の毒性が同時に発現した場合は，最も高いグレードに従って用量変更を行うこととした。

毒性が単一の治験薬に起因すると治験責任（分担）医師が判定し，かつ治験実施計画書の規定に従って当該治験薬の投与延期又は用量変更を行った場合は，禁忌に該当しなければ他の治験薬を投与することを許容した。

本剤/プラセボ，カルボプラチン，エトポシドによる毒性のために投与を一時的に中止した場合は，本剤/プラセボの投与が化学療法のスケジュールと同調するように投与サイクルを再

開することとした。
毒性が単一の化学療法薬に起因すると治験責任（分担）医師が判定した場合は，他の化学療法薬の用量の変更は不要とした。

なお，治験責任（分担）医師は，被験者のコンプライアンス及び支持療法へのアクセスを最大限に高めることを目標として，毒性の重症度と被験者のリスク／ベネフィット評価に応じて，治験実施計画書に記載した用量変更ガイドラインを自身の裁量で変更することを許容した。

(2) 中止基準
以下の基準に該当する場合，治験薬の投与を中止することとした。

- 放射線画像データ，生検結果（入手可能な場合）及び臨床状態を総合的に評価した上で治験責任（分担）医師が判定した，病勢進行に起因した症状悪化
- 個々の被験者の治療に対する反応性と当該事象の重症度を考慮した上で治験責任（分担）医師が許容できないと判定した免疫を介した有害事象の発現など，本剤に関連した忍容できない毒性
- カルボプラチン又はエトポシドに関連した忍容できない毒性
- 忍容性に関する懸念から治験薬の1つを永久的に中止した場合は，治験責任（分担）医師と被験者が合意すれば，残りの治験薬を病勢進行まで継続可能とした。
- 投与を継続すれば被験者の安全を脅かす可能性がある医学的状態が発生した。
- 治験実施計画書外の別の抗癌療法を使用する。
- 妊娠
- 固形癌の治療効果判定のための規準（RECIST）v1.1に基づく病勢進行が認められた場合

ただし，標準的な臨床診療では，一次治療後に病勢進行が認められた進展型小細胞肺癌患者に対する治療選択肢は少なく，それらの選択肢も有効性が低く，毒性が高いことから，RECIST v1.1による画像所見上の病勢進行が認められた後も，以下の基準をすべて満たす場合に限り，被験者と適切な話し合いを行って同意を取得した上で，治験責任（分担）医師の裁量で被験者への投与継続を検討してもよいとした。

- 治験責任（分担）医師が判断した臨床的利益の証拠がある
- 病勢進行に起因すると考えられる Eastern Cooperative Oncology Group performance status の悪化がない
- 治験実施計画書で許容される医学的介入では管理不能な，重大な解剖学的部位における腫瘍の進行（例：軟膜・髄膜病変等）がない
- 最初に進行の所見を認めた時点で，他の治療選択肢を保留して治験薬の投与を継続することに同意する同意書を被験者から得ていなければならない

RECIST v1.1による画像所見上の病勢進行が認められた後も治験薬の投与を継続する場合は，被験者の臨床状態を慎重にモニタリングし，フォローアップ画像検査を6週間以内に，又は症状の悪化がみられた場合は直ちに実施することとした。病勢進行による臨床的悪化がみられた場合はいつでも，又はフォローアップ画像検査で腫瘍増殖の持続が確認された場合は，治験薬の投与を中止することとした。また，放射線画像データ及び臨床状態の総合的評価により，許容できない毒性又は病勢進行に起因する増悪の他の徴候・症状がみられると治験責任（分担）医師が判断した場合は，その被験者の治験参加を中止することとした。

2.7.4.1.2 全般的な曝露状況

(1) 安全性解析対象の被験者数

安全性解析対象の被験者数を表 2.7.4.1.2-1に示す。

少なくとも1回治験薬を投与された被験者を安全性解析対象集団とした。安全性解析対象は394例であった。

表 2.7.4.1.2-1 安全性解析対象の被験者数（GO30081試験）

レジメン	プラセボ + カルボプラチン + エトポシド	本剤 + カルボプラチン + エトポシド	合計
登録被験者数	202	201	403
安全性解析対象被験者数	196	198	394

［5.3.5.1-1 Table 14を改変］

(2) 曝露状況の要約

本剤/プラセボ，カルボプラチン及びエトポシドの曝露状況の要約を，それぞれ表 2.7.4.1.2-2及び表 2.7.4.1.2-3に示す。本剤/プラセボの投与期間の中央値は，プラセボ併用群が4.1カ月，本剤併用群が4.7カ月であり，本剤併用群でやや長かった。また，カルボプラチン及びエトポシドの投与期間，Dose Intensity 及び投与回数の中央値は，プラセボ併用群と本剤併用群で同程度であった。

表 2.7.4.1.2-2 本剤/プラセボの曝露状況の要約（GO30081試験）

Study Drug Exposure, Safety Evaluable Patients
Protocol: GO30081

Treatment: ATEZOLIZUMAB/PLACEBO

	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
Treatment duration (months)			
n	196	198	394
Mean (SD)	5.0 (3.5)	5.7 (4.4)	5.3 (3.9)
Median	4.1	4.7	4.2
Min - Max	0 - 21	0 - 21	0 - 21
Treatment duration			
n	196	198	394
0 to <= 3 months	41 (20.9%)	47 (23.7%)	88 (22.3%)
>3 months to <= 6 months	113 (57.7%)	87 (43.9%)	200 (50.8%)
>6 months to <= 12 months	30 (15.3%)	41 (20.7%)	71 (18.0%)
>12 months	12 (6.1%)	23 (11.6%)	35 (8.9%)
Dose Intensity (%)			
n	196	198	394
Mean (SD)	92.9 (7.2)	92.1 (9.3)	92.5 (8.4)
Median	94.7	94.9	94.7
Min - Max	60 - 102	16 - 100	16 - 102
Number of doses received			
n	196	198	394
Mean (SD)	7.7 (4.8)	8.5 (5.9)	8.1 (5.4)
Median	6.0	7.0	7.0
Min - Max	1 - 30	1 - 30	1 - 30
Total cumulative dose (mg)			
n	196	198	394
Mean (SD)	0.0 (0.0)	10193.0 (7166.6)	5122.4 (7196.2)
Median	0.0	8400.0	340.0
Min - Max	0 - 0	80 - 36000	0 - 36000

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/t_ex_SE_24APR2018_GO30081.out
06JUL2018 20:12

［5.3.5.1-1 Table 35を再掲］

表 2.7.4.1.2-3 カルボプラチン及びエトポシドの曝露状況の要約（GO30081試験）

Study Drug Exposure, Safety Evaluable Patients
Protocol: GO30081

Treatment:	CARBOPLATIN		ETOPOSIDE	
	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Treatment duration (months)				
n	196	198	196	198
Mean (SD)	2.2 (0.6)	2.1 (0.7)	2.2 (0.6)	2.2 (0.7)
Median	2.2	2.3	2.2	2.3
Min - Max	0 - 4	0 - 4	0 - 4	0 - 4
Treatment duration				
n	196	198	196	198
0 to <= 3 months	191 (97.4%)	193 (97.5%)	191 (97.4%)	191 (96.5%)
>3 months to <= 6 months	5 (2.6%)	5 (2.5%)	5 (2.6%)	7 (3.5%)
Dose Intensity (%)				
n	196	198	196	198
Mean (SD)	92.0 (8.0)	91.0 (7.9)	89.6 (8.0)	88.1 (8.6)
Median	93.3	92.3	90.3	89.4
Min - Max	60 - 102	48 - 101	59 - 99	32 - 99
Number of doses received				
n	196	198	196	198
Mean (SD)	3.8 (0.6)	3.7 (0.8)	11.4 (2.0)	11.1 (2.5)
Median	4.0	4.0	12.0	12.0
Min - Max	1 - 5	1 - 6	2 - 15	1 - 18
Total cumulative dose (mg)				
n	196	198	196	198
Mean (SD)	2145.7 (645.0)	2019.2 (642.2)	2034.5 (477.2)	1965.8 (539.8)
Median	2175.0	2062.5	2131.7	2055.2
Min - Max	341 - 3691	380 - 3670	294 - 3240	8 - 3492

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/t_ex_SE_24APR2018_GO30081.out
06JUL2018 20:12

［5.3.5.1-1 Table 36を再掲］

2.7.4.1.3 治験対象集団の人口統計学的特性及びその他の特性

ITT 集団の人口統計学的特性及びその他の特性は2.7.3.3.1.2項に詳述した。

人口統計学的特性及びその他の特性に群間での大きな偏りは認められなかった。

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

2.7.4.2.1.1 比較的よくみられる有害事象

(1) 全 Grade の有害事象

いずれかの群で発現率が10%以上の有害事象の要約を表 2.7.4.2.1.1-1に示す。

有害事象の発現率は，プラセボ併用群96.4%（189/196例），本剤併用群100.0%（198/198例）であった。

プラセボ併用群で20%以上に認められた有害事象は，貧血35.2%，好中球減少症35.2%，脱毛症34.7%，悪心32.7%，便秘29.6%，疲労25.0%及び好中球数減少23.5%であった。本剤併用群で20%以上に認められた有害事象は，貧血43.4%，悪心37.9%，好中球減少症37.4%，脱毛症36.9%，疲労27.3%，食欲減退27.3%及び便秘25.8%であった。

両群で発現率に10%以上差が認められる有害事象はなかった。プラセボ併用群で本剤併用群より発現率が5%以上高かった有害事象は，低カリウム血症（プラセボ併用群9.2%，本剤併用群4.0%，以下同順）であり，本剤併用群でプラセボ併用群より発現率が5%以上高かった有害

事象は，差が大きい順に，甲状腺機能低下症（0.5%，10.1%），食欲減退（18.4%，27.3%），貧血（35.2%，43.4%），悪心（32.7%，37.9%）であった（5.3.5.1-1 Table 38）。

副作用の発現率は，プラセボ併用群92.3%（181/196例），本剤併用群94.9%（188/198例）であった。発現率が20%以上の副作用は，プラセボ併用群で好中球減少症34.7%，脱毛症33.7%，貧血33.2%，悪心30.1%及び好中球数減少23.0%，本剤併用群で貧血38.9%，好中球減少症36.4%，脱毛症34.8%，悪心31.8%，疲労21.2%及び食欲減退20.7%であった。

(2) Grade 3以上の有害事象

いずれかの群で発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.1-2に示す。Grade 3以上の有害事象の発現率は，プラセボ併用群69.4%（136/196例），本剤併用群69.2%（137/198例）であった。

いずれかの群で発現率が10%以上の有害事象の内，Grade 3以上の発現率が5%以上であった事象は，プラセボ併用群では，好中球減少症25.0%，好中球数減少16.8%，貧血13.3%及び血小板減少症8.7%であり，本剤併用群では好中球減少症23.2%，貧血15.7%，好中球数減少15.7%，血小板減少症10.1%及び白血球減少症5.1%であった。

表 2.7.4.2.1.1-1　いずれかの群で発現率が10%以上の有害事象の要約（GO30081試験）

Adverse Events with an Incidence Rate at Least 10% by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
Total number of patients with at least one adverse event	189 (96.4%)	181 (92.3%)	198 (100.0%)	188 (94.9%)
貧血	69 (35.2%)	65 (33.2%)	86 (43.4%)	77 (38.9%)
好中球減少症	69 (35.2%)	68 (34.7%)	74 (37.4%)	72 (36.4%)
脱毛症	68 (34.7%)	66 (33.7%)	73 (36.9%)	69 (34.8%)
悪心	64 (32.7%)	59 (30.1%)	75 (37.9%)	63 (31.8%)
便秘	58 (29.6%)	25 (12.8%)	51 (25.8%)	20 (10.1%)
疲労	49 (25.0%)	38 (19.4%)	54 (27.3%)	42 (21.2%)
好中球数減少	46 (23.5%)	45 (23.0%)	37 (18.7%)	35 (17.7%)
食欲減退	36 (18.4%)	26 (13.3%)	54 (27.3%)	41 (20.7%)
嘔吐	33 (16.8%)	22 (11.2%)	39 (19.7%)	27 (13.6%)
下痢	31 (15.8%)	19 (9.7%)	35 (17.7%)	19 (9.6%)
血小板減少症	31 (15.8%)	29 (14.8%)	33 (16.7%)	32 (16.2%)
血小板数減少	29 (14.8%)	28 (14.3%)	25 (12.6%)	24 (12.1%)
白血球数減少	25 (12.8%)	25 (12.8%)	18 (9.1%)	16 (8.1%)
咳嗽	25 (12.8%)	0	18 (9.1%)	0
頭痛	23 (11.7%)	4 (2.0%)	24 (12.1%)	4 (2.0%)
無力症	20 (10.2%)	14 (7.1%)	25 (12.6%)	17 (8.6%)
白血球減少症	19 (9.7%)	18 (9.2%)	25 (12.6%)	25 (12.6%)
呼吸困難	18 (9.2%)	0	20 (10.1%)	1 (0.5%)
発熱	16 (8.2%)	6 (3.1%)	20 (10.1%)	5 (2.5%)
体重減少	10 (5.1%)	4 (2.0%)	20 (10.1%)	8 (4.0%)
甲状腺機能低下症	1 (0.5%)	1 (0.5%)	20 (10.1%)	19 (9.6%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerelp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerelp10_SE_24APR2018_GO30081.out
13SEP2018 14:45　Page 1 of 1

［5.3.5.1-2 aerelp10_SE_24APR2018_GO30081を再掲］

表 2.7.4.2.1.1-2 いずれかの群で発現率が10%以上の有害事象の重症度別の要約（GO30081試験）

Adverse Events with an Incidence Rate at Least 10% by Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	PBO + CE (Actual) (N=196)		Atezo + CE (Actual) (N=198)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	189 (96.4%)	136 (69.4%)	198 (100.0%)	137 (69.2%)
血液およびリンパ系障害				
貧血	69 (35.2%)	26 (13.3%)	86 (43.4%)	31 (15.7%)
好中球減少症	69 (35.2%)	49 (25.0%)	74 (37.4%)	46 (23.2%)
血小板減少症	31 (15.8%)	17 (8.7%)	33 (16.7%)	20 (10.1%)
白血球減少症	19 (9.7%)	8 (4.1%)	25 (12.6%)	10 (5.1%)
胃腸障害				
悪心	64 (32.7%)	1 (0.5%)	75 (37.9%)	1 (0.5%)
便秘	58 (29.6%)	1 (0.5%)	51 (25.8%)	2 (1.0%)
嘔吐	33 (16.8%)	5 (2.6%)	39 (19.7%)	3 (1.5%)
下痢	31 (15.8%)	2 (1.0%)	35 (17.7%)	4 (2.0%)
一般・全身障害および投与部位の状態				
疲労	49 (25.0%)	1 (0.5%)	54 (27.3%)	5 (2.5%)
無力症	20 (10.2%)	4 (2.0%)	25 (12.6%)	5 (2.5%)
発熱	16 (8.2%)	0	20 (10.1%)	0
皮膚および皮下組織障害				
脱毛症	68 (34.7%)	0	73 (36.9%)	0
臨床検査				
好中球数減少	46 (23.5%)	33 (16.8%)	37 (18.7%)	31 (15.7%)
血小板数減少	29 (14.8%)	8 (4.1%)	25 (12.6%)	7 (3.5%)
白血球数減少	25 (12.8%)	9 (4.6%)	18 (9.1%)	7 (3.5%)
体重減少	10 (5.1%)	1 (0.5%)	20 (10.1%)	0
呼吸器、胸郭および縦隔障害				
咳嗽	25 (12.8%)	2 (1.0%)	18 (9.1%)	1 (0.5%)
呼吸困難	18 (9.2%)	2 (1.0%)	20 (10.1%)	3 (1.5%)
代謝および栄養障害				
食欲減退	36 (18.4%)	0	54 (27.3%)	2 (1.0%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_SE_24APR2018_GO30081.out
13SEP2018 14:48

Adverse Events with an Incidence Rate at Least 10% by Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	PBO + CE (Actual) (N=196) Any Grade No. (%)	PBO + CE (Actual) (N=196) >= Grade3 No. (%)	Atezo + CE (Actual) (N=198) Any Grade No. (%)	Atezo + CE (Actual) (N=198) >= Grade3 No. (%)
神経系障害				
頭痛	23 (11.7%)	0	24 (12.1%)	0
内分泌障害				
甲状腺機能低下症	1 (0.5%)	0	20 (10.1%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_SE_24APR2018_GO30081.out
13SEP2018 14:48　Page 2 of 2

［5.3.5.1-2 aegrdp10_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.2　死亡

治験期間中の死亡の要約を表 2.7.4.2.1.2-1に示す。また，すべての死亡例の一覧を5.3.5.1-1 l_dd_SE_24APR2018_GO30081に示した。死亡に至った有害事象の要約は表 2.7.4.2.1.2-2に，個別症例の詳細は5.3.5.1-1 NARRATIVES 1.1 NARRATIVES FOR PATIENTS WHO DIED DUE TO REASON OTHER THAN DISEASE PROGRESSION DURING THE STUDY に示した。

死亡した被験者数は，プラセボ併用群130/196例，本剤併用群103/198例であり，両群とも大部分が病勢進行による死亡であった。

表 2.7.4.2.1.2-1　死亡の要約（GO30081試験）

Death and Cause of Death, Safety Evaluable Patients
Protocol: GO30081

	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
All Deaths	130	103	233
Primary Cause of Death			
n	130	103	233
Adverse Event	11 (5.6%)	4 (2.0%)	15 (3.8%)
Progressive Disease	115 (58.7%)	90 (45.5%)	205 (52.0%)
Other	4 (2.0%)	9 (4.5%)	13 (3.3%)
n	4	9	13
Death Due to Cardiac Arrest	0	1 (0.5%)	1 (0.3%)
Death Due to Circulatory and Respiratory Failure	0	1 (0.5%)	1 (0.3%)
Death Due to Pneumonia	0	1 (0.5%)	1 (0.3%)
Death Due to Suicide	1 (0.5%)	1 (0.5%)	2 (0.5%)
Death Due to Unknown	1 (0.5%)	1 (0.5%)	2 (0.5%)
Post-study Reporting of Death	2 (1.0%)	4 (2.0%)	6 (1.5%)

Patient 10168 had grade 5 pneumonia which occurred after start of non-protocol second-line therapy, and Investigator considered unrelated to study drugs. This event is counted under Primary Cause of Death=Adverse Event.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_dd.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/t_dd_SE_24APR2018_GO30081.out
06JUL2018 20:19

［5.3.5.1-1 Table 41を再掲］

死亡に至った有害事象はプラセボ併用群で11例（5.6%），本剤併用群で4例（2.0%）に認められた。死亡に至った有害事象の内訳は，プラセボ併用群では肺炎が3例，心肺不全，敗血症性ショック，急性呼吸不全，心嚢液貯留，全身健康状態低下，敗血症，肺敗血症及び喀血が各1例であり，この内の肺炎1例，心肺不全及び敗血症性ショックは治験薬との因果関係が否定されなかった。本剤併用群では肺炎，好中球減少症，死亡及び呼吸不全が各1例であり，この内の肺炎，好中球減少症及び死亡は治験薬との因果関係が否定されなかった。

表 2.7.4.2.1.2-2　死亡に至った有害事象の要約（GO30081試験）

Adverse Events leading to Death by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
Total number of patients with at least one adverse event	11 (5.6%)	3 (1.5%)	4 (2.0%)	3 (1.5%)
肺炎	3 (1.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
心肺不全	1 (0.5%)	1 (0.5%)	0	0
敗血症性ショック	1 (0.5%)	1 (0.5%)	0	0
急性呼吸不全	1 (0.5%)	0	0	0
心嚢液貯留	1 (0.5%)	0	0	0
全身健康状態低下	1 (0.5%)	0	0	0
敗血症	1 (0.5%)	0	0	0
肺敗血症	1 (0.5%)	0	0	0
喀血	1 (0.5%)	0	0	0
好中球減少症	0	0	1 (0.5%)	1 (0.5%)
死亡	0	0	1 (0.5%)	1 (0.5%)
呼吸不全	0	0	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_dd.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_dd_SE_24APR2018_GO30081.out
14SEP2018 14:25　Page 1 of 1
［5.3.5.1-2 aerel_dd_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.3　その他の重篤な有害事象

重篤な有害事象の要約を表 2.7.4.2.1.3-1に示す。また，重篤な有害事象発現例の一覧を5.3.5.1-1 l_ae_ser_SE_24APR2018_GO30081に，治験薬との因果関係を否定できない重篤な有害事象を発現した個別症例の詳細は5.3.5.1-1 NARRATIVES 1.2 NARRATIVES FOR PATIENTS WHO EXPERIENCED SERIOUS ADVERSE EVENTS DURING THE STUDY に示した。

重篤な有害事象は，プラセボ併用群で34.7%（68/196例），本剤併用群で37.4%（74/198例）に認められ，重篤な副作用はプラセボ併用群で18.9%（37/196例），本剤併用群で22.7%（45/198例）に認められた。

発現率が3%以上の重篤な有害事象は，プラセボ併用群では発熱性好中球減少症4.6%（9/196例），好中球減少症4.1%（8/196例）及び肺炎3.6%（7/196例），本剤併用群では肺炎4.5%（9/198例）及び好中球減少症3.5%（7/198例）であった。

表 2.7.4.2.1.3-1 重篤な有害事象の要約（GO30081試験）

Serious Adverse Events by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
Total number of patients with at least one adverse event	68 (34.7%)	37 (18.9%)	74 (37.4%)	45 (22.7%)
発熱性好中球減少症	9 (4.6%)	9 (4.6%)	5 (2.5%)	4 (2.0%)
好中球減少症	8 (4.1%)	8 (4.1%)	7 (3.5%)	7 (3.5%)
肺炎	7 (3.6%)	1 (0.5%)	9 (4.5%)	4 (2.0%)
血小板減少症	4 (2.0%)	4 (2.0%)	5 (2.5%)	5 (2.5%)
低ナトリウム血症	4 (2.0%)	0	1 (0.5%)	0
汎血球減少症	4 (2.0%)	4 (2.0%)	0	0
嘔吐	3 (1.5%)	2 (1.0%)	3 (1.5%)	2 (1.0%)
肺感染	3 (1.5%)	2 (1.0%)	0	0
貧血	2 (1.0%)	2 (1.0%)	3 (1.5%)	3 (1.5%)
尿路感染	2 (1.0%)	1 (0.5%)	2 (1.0%)	0
慢性閉塞性肺疾患	2 (1.0%)	0	2 (1.0%)	0
注入に伴う反応	2 (1.0%)	2 (1.0%)	1 (0.5%)	1 (0.5%)
肺臓炎	2 (1.0%)	2 (1.0%)	1 (0.5%)	1 (0.5%)
呼吸困難	2 (1.0%)	0	1 (0.5%)	0
心房細動	2 (1.0%)	0	1 (0.5%)	0
血小板数減少	2 (1.0%)	2 (1.0%)	0	0
急性呼吸不全	2 (1.0%)	0	0	0
肺塞栓症	2 (1.0%)	0	0	0
下痢	1 (0.5%)	0	3 (1.5%)	3 (1.5%)
白血球減少症	1 (0.5%)	1 (0.5%)	2 (1.0%)	2 (1.0%)
無力症	1 (0.5%)	0	2 (1.0%)	2 (1.0%)
胸水	1 (0.5%)	0	2 (1.0%)	1 (0.5%)
喀血	1 (0.5%)	0	2 (1.0%)	1 (0.5%)
全身健康状態低下	1 (0.5%)	0	2 (1.0%)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5%)	0	1 (0.5%)	0
アラニンアミノトランスフェラーゼ増加	1 (0.5%)	0	1 (0.5%)	0
気道感染	1 (0.5%)	0	1 (0.5%)	0
心嚢液貯留	1 (0.5%)	0	1 (0.5%)	0
大腿骨骨折	1 (0.5%)	0	1 (0.5%)	0
好中球減少性敗血症	1 (0.5%)	1 (0.5%)	0	0
好中球数減少	1 (0.5%)	1 (0.5%)	0	0
心肺不全	1 (0.5%)	1 (0.5%)	0	0
低カリウム血症	1 (0.5%)	1 (0.5%)	0	0
低マグネシウム血症	1 (0.5%)	1 (0.5%)	0	0
敗血症性ショック	1 (0.5%)	1 (0.5%)	0	0
白血球数減少	1 (0.5%)	1 (0.5%)	0	0
膵炎	1 (0.5%)	1 (0.5%)	0	0
アルコール乱用	1 (0.5%)	0	0	0
クロストリジウム・ディフィシレ感染	1 (0.5%)	0	0	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_ser.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_ser_SE_24APR2018_GO30081.out
13SEP2018 14:52

Serious Adverse Events by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
胃腸出血	1 (0.5%)	0	0	0
気胸	1 (0.5%)	0	0	0
胸椎骨折	1 (0.5%)	0	0	0
胸痛	1 (0.5%)	0	0	0
抗利尿ホルモン不適合分泌	1 (0.5%)	0	0	0
高炭酸ガス血症	1 (0.5%)	0	0	0
腫瘍疼痛	1 (0.5%)	0	0	0
上気道感染	1 (0.5%)	0	0	0
上室性頻脈	1 (0.5%)	0	0	0
心不全	1 (0.5%)	0	0	0
脊髄浮腫	1 (0.5%)	0	0	0
穿孔性胃潰瘍	1 (0.5%)	0	0	0
全身性炎症反応症候群	1 (0.5%)	0	0	0
脳血管発作	1 (0.5%)	0	0	0
膿気胸	1 (0.5%)	0	0	0
播種性血管内凝固	1 (0.5%)	0	0	0
敗血症	1 (0.5%)	0	0	0
肺膿瘍	1 (0.5%)	0	0	0
肺敗血症	1 (0.5%)	0	0	0
白血球増加症	1 (0.5%)	0	0	0
発疹	1 (0.5%)	0	0	0
非心臓性胸痛	1 (0.5%)	0	0	0
変色便	1 (0.5%)	0	0	0
放射線性食道炎	1 (0.5%)	0	0	0
末梢動脈閉塞	1 (0.5%)	0	0	0
疲労	0	0	3 (1.5%)	1 (0.5%)
失神	0	0	3 (1.5%)	0
急性腎障害	0	0	2 (1.0%)	2 (1.0%)
自己免疫性甲状腺炎	0	0	2 (1.0%)	2 (1.0%)
下気道感染	0	0	2 (1.0%)	1 (0.5%)
気管支炎	0	0	2 (1.0%)	1 (0.5%)
大腸炎	0	0	2 (1.0%)	1 (0.5%)
高血糖	0	0	2 (1.0%)	0
発熱	0	0	2 (1.0%)	0
イレウス	0	0	1 (0.5%)	1 (0.5%)
ギラン・バレー症候群	0	0	1 (0.5%)	1 (0.5%)
サイトメガロウイルス感染	0	0	1 (0.5%)	1 (0.5%)
トランスアミナーゼ上昇	0	0	1 (0.5%)	1 (0.5%)
悪心	0	0	1 (0.5%)	1 (0.5%)
黄疸	0	0	1 (0.5%)	1 (0.5%)
完全房室ブロック	0	0	1 (0.5%)	1 (0.5%)
肝機能検査値上昇	0	0	1 (0.5%)	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_ser.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_ser_SE_24APR2018_GO30081.out
13SEP2018 14:52 Page 2 of 3

Serious Adverse Events by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
急性膵炎	0	0	1 (0.5%)	1 (0.5%)
憩室穿孔	0	0	1 (0.5%)	1 (0.5%)
血中クレアチニン増加	0	0	1 (0.5%)	1 (0.5%)
三叉神経痛	0	0	1 (0.5%)	1 (0.5%)
死亡	0	0	1 (0.5%)	1 (0.5%)
自己免疫性大腸炎	0	0	1 (0.5%)	1 (0.5%)
脱水	0	0	1 (0.5%)	1 (0.5%)
尿細管間質性腎炎	0	0	1 (0.5%)	1 (0.5%)
肺水腫	0	0	1 (0.5%)	1 (0.5%)
皮膚毒性	0	0	1 (0.5%)	1 (0.5%)
末梢性ニューロパチー	0	0	1 (0.5%)	1 (0.5%)
うつ病	0	0	1 (0.5%)	0
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.5%)	0
胃炎	0	0	1 (0.5%)	0
一過性脳虚血発作	0	0	1 (0.5%)	0
遠隔転移を伴う新生物	0	0	1 (0.5%)	0
関節痛	0	0	1 (0.5%)	0
気管支閉塞	0	0	1 (0.5%)	0
傾眠	0	0	1 (0.5%)	0
血栓性静脈炎	0	0	1 (0.5%)	0
血中アルカリホスファターゼ増加	0	0	1 (0.5%)	0
呼吸不全	0	0	1 (0.5%)	0
口唇浮腫	0	0	1 (0.5%)	0
四肢痛	0	0	1 (0.5%)	0
小腸閉塞	0	0	1 (0.5%)	0
上大静脈症候群	0	0	1 (0.5%)	0
心タンポナーデ	0	0	1 (0.5%)	0
胆管炎	0	0	1 (0.5%)	0
腸閉塞	0	0	1 (0.5%)	0
直腸炎	0	0	1 (0.5%)	0
頭部損傷	0	0	1 (0.5%)	0
腹痛	0	0	1 (0.5%)	0
腹部癒着	0	0	1 (0.5%)	0
末梢動脈閉塞性疾患	0	0	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_ser.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_ser_SE_24APR2018_GO30081.out
13SEP2018 14:52 Page 3 of 3

［5.3.5.1-2 aerel_ser_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.4 その他の重要な有害事象

2.7.4.2.1.4.1 治験薬の投与中止に至った有害事象

治験薬の投与中止に至った有害事象の要約を表 2.7.4.2.1.4.1-1に示す。

治験薬の投与中止に至った有害事象は，プラセボ併用群で3.1%（6/196例），本剤併用群で11.1%（22/198例）に認められた。

複数例に認められた治験薬の投与中止に至った有害事象は，プラセボ併用群では該当事象がなく，本剤併用群では注入に伴う反応が5例（2.5%）であった。

表 2.7.4.2.1.4.1-1 治験薬の投与中止に至った有害事象の要約（GO30081試験）

Adverse Events Leading to Discontinuation of Trial Treatment by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
Total number of patients with at least one adverse event	6 (3.1%)	3 (1.5%)	22 (11.1%)	18 (9.1%)
肺炎	1 (0.5%)	0	1 (0.5%)	1 (0.5%)
無力症	1 (0.5%)	0	1 (0.5%)	1 (0.5%)
悪心	1 (0.5%)	1 (0.5%)	0	0
下痢	1 (0.5%)	1 (0.5%)	0	0
肺臓炎	1 (0.5%)	1 (0.5%)	0	0
腹痛	1 (0.5%)	1 (0.5%)	0	0
膵炎	1 (0.5%)	1 (0.5%)	0	0
心嚢液貯留	1 (0.5%)	0	0	0
心房細動	1 (0.5%)	0	0	0
注入に伴う反応	0	0	5 (2.5%)	5 (2.5%)
アナフィラキシー反応	0	0	1 (0.5%)	1 (0.5%)
イレウス	0	0	1 (0.5%)	1 (0.5%)
トランスアミナーゼ上昇	0	0	1 (0.5%)	1 (0.5%)
黄疸	0	0	1 (0.5%)	1 (0.5%)
血小板減少症	0	0	1 (0.5%)	1 (0.5%)
好中球減少症	0	0	1 (0.5%)	1 (0.5%)
紅斑	0	0	1 (0.5%)	1 (0.5%)
三叉神経痛	0	0	1 (0.5%)	1 (0.5%)
低血圧	0	0	1 (0.5%)	1 (0.5%)
尿細管間質性腎炎	0	0	1 (0.5%)	1 (0.5%)
白血球減少症	0	0	1 (0.5%)	1 (0.5%)
腹部膨満	0	0	1 (0.5%)	1 (0.5%)
肛門出血	0	0	1 (0.5%)	1 (0.5%)
胃炎	0	0	1 (0.5%)	0
下気道感染	0	0	1 (0.5%)	0
上大静脈症候群	0	0	1 (0.5%)	0
全身健康状態低下	0	0	1 (0.5%)	0
尿路感染	0	0	1 (0.5%)	0
嘔吐	0	0	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_dis.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_dis_SE_24APR2018_GO30081.out
14SEP2018 14:32 Page 1 of 1

［5.3.5.1-2 aerel_dis_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.4.2 治験薬の投与量変更（休薬又は減量）に至った有害事象

治験薬の投与量変更に至った有害事象の要約を表 2.7.4.2.1.4.2-1に示す。

治験薬の投与量変更に至った有害事象は，プラセボ併用群で60.7%（119/196例），本剤併用群で69.7%（138/198例）に認められた。

発現率が5%以上の治験薬の投与量変更に至った有害事象は，プラセボ併用群では好中球減少症23.5%（46/196例），好中球数減少16.8%（33/196例），血小板減少症7.7%（15/196例），貧血6.1%（12/196例），血小板数減少及び白血球数減少が各5.1%（10/196例）であり，本剤併用群では好中球減少症26.8%（53/198例），好中球数減少12.6%（25/198例），貧血9.6%（19/198例），血小板減少症及び白血球減少症が各6.6%（13/198例），疲労5.1%（10/198例）であった。

表 2.7.4.2.1.4.2-1 治験薬の投与量変更に至った有害事象の要約（GO30081試験）

Adverse Events Leading to Dose Modification or Interruption by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
Total number of patients with at least one adverse event	119 (60.7%)	108 (55.1%)	138 (69.7%)	123 (62.1%)
好中球減少症	46 (23.5%)	46 (23.5%)	53 (26.8%)	51 (25.8%)
好中球数減少	33 (16.8%)	33 (16.8%)	25 (12.6%)	23 (11.6%)
血小板減少症	15 (7.7%)	15 (7.7%)	13 (6.6%)	12 (6.1%)
貧血	12 (6.1%)	10 (5.1%)	19 (9.6%)	19 (9.6%)
血小板数減少	10 (5.1%)	10 (5.1%)	6 (3.0%)	6 (3.0%)
白血球数減少	10 (5.1%)	10 (5.1%)	4 (2.0%)	4 (2.0%)
注入に伴う反応	6 (3.1%)	6 (3.1%)	7 (3.5%)	6 (3.0%)
白血球減少症	5 (2.6%)	5 (2.6%)	13 (6.6%)	13 (6.6%)
発熱性好中球減少症	5 (2.6%)	5 (2.6%)	3 (1.5%)	2 (1.0%)
肺炎	4 (2.0%)	2 (1.0%)	4 (2.0%)	2 (1.0%)
上気道感染	3 (1.5%)	0	1 (0.5%)	0
嘔吐	2 (1.0%)	1 (0.5%)	3 (1.5%)	3 (1.5%)
低ナトリウム血症	2 (1.0%)	0	2 (1.0%)	1 (0.5%)
汎血球減少症	2 (1.0%)	2 (1.0%)	1 (0.5%)	1 (0.5%)
胸痛	2 (1.0%)	0	1 (0.5%)	0
無力症	2 (1.0%)	2 (1.0%)	0	0
Ｃ－反応性蛋白増加	2 (1.0%)	1 (0.5%)	0	0
気道感染	2 (1.0%)	1 (0.5%)	0	0
肺感染	2 (1.0%)	1 (0.5%)	0	0
インフルエンザ	2 (1.0%)	0	0	0
喀血	1 (0.5%)	0	2 (1.0%)	1 (0.5%)
下痢	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
甲状腺機能亢進症	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
肺臓炎	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
体重減少	1 (0.5%)	1 (0.5%)	1 (0.5%)	0
心房細動	1 (0.5%)	0	1 (0.5%)	1 (0.5%)
ヘモグロビン減少	1 (0.5%)	1 (0.5%)	0	0
過敏症	1 (0.5%)	1 (0.5%)	0	0
関節痛	1 (0.5%)	1 (0.5%)	0	0
帯状疱疹	1 (0.5%)	1 (0.5%)	0	0
脱毛症	1 (0.5%)	1 (0.5%)	0	0
注射部位漏出	1 (0.5%)	1 (0.5%)	0	0
副腎機能不全	1 (0.5%)	1 (0.5%)	0	0
扁桃の炎症	1 (0.5%)	1 (0.5%)	0	0
咳嗽	1 (0.5%)	0	0	0
気胸	1 (0.5%)	0	0	0
急性呼吸不全	1 (0.5%)	0	0	0
筋骨格痛	1 (0.5%)	0	0	0
憩室炎	1 (0.5%)	0	0	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_dosmod.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_dosmod_SE_24APR2018_GO30081.out
13SEP2018 14:55 Page 1 of 3

Adverse Events Leading to Dose Modification or Interruption by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
血管炎	1 (0.5%)	0	0	0
細菌感染	1 (0.5%)	0	0	0
心不全	1 (0.5%)	0	0	0
全身性炎症反応症候群	1 (0.5%)	0	0	0
足骨折	1 (0.5%)	0	0	0
多発ニューロパチー	1 (0.5%)	0	0	0
転倒	1 (0.5%)	0	0	0
尿路感染	1 (0.5%)	0	0	0
脳血管発作	1 (0.5%)	0	0	0
膿気胸	1 (0.5%)	0	0	0
白血球数増加	1 (0.5%)	0	0	0
白血球増加症	1 (0.5%)	0	0	0
不眠症	1 (0.5%)	0	0	0
浮腫	1 (0.5%)	0	0	0
末梢動脈閉塞	1 (0.5%)	0	0	0
膵炎	1 (0.5%)	0	0	0
疲労	0	0	10 (5.1%)	8 (4.0%)
アラニンアミノトランスフェラーゼ増加	0	0	4 (2.0%)	3 (1.5%)
発熱	0	0	4 (2.0%)	1 (0.5%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	3 (1.5%)	2 (1.0%)
悪心	0	0	3 (1.5%)	2 (1.0%)
γ－グルタミルトランスフェラーゼ増加	0	0	2 (1.0%)	2 (1.0%)
急性腎障害	0	0	2 (1.0%)	2 (1.0%)
甲状腺機能低下症	0	0	2 (1.0%)	2 (1.0%)
高血圧	0	0	2 (1.0%)	2 (1.0%)
末梢性ニューロパチー	0	0	2 (1.0%)	2 (1.0%)
胸水	0	0	2 (1.0%)	1 (0.5%)
血中アルカリホスファターゼ増加	0	0	2 (1.0%)	1 (0.5%)
血中クレアチニン増加	0	0	2 (1.0%)	1 (0.5%)
斑状丘疹状皮疹	0	0	2 (1.0%)	1 (0.5%)
トランスアミナーゼ上昇	0	0	1 (0.5%)	1 (0.5%)
横紋筋融解症	0	0	1 (0.5%)	1 (0.5%)
黄疸	0	0	1 (0.5%)	1 (0.5%)
下気道感染	0	0	1 (0.5%)	1 (0.5%)
乾癬	0	0	1 (0.5%)	1 (0.5%)
完全房室ブロック	0	0	1 (0.5%)	1 (0.5%)
肝機能検査値上昇	0	0	1 (0.5%)	1 (0.5%)
関節炎	0	0	1 (0.5%)	1 (0.5%)
気管支痙攣	0	0	1 (0.5%)	1 (0.5%)
急性膵炎	0	0	1 (0.5%)	1 (0.5%)
筋力低下	0	0	1 (0.5%)	1 (0.5%)
憩室穿孔	0	0	1 (0.5%)	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_dosmod.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_dosmod_SE_24APR2018_GO30081.out
13SEP2018 14:55

Adverse Events Leading to Dose Modification or Interruption by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=196) AE No. (%)	PBO + CE (Actual) (N=196) Related AE No. (%)	Atezo + CE (Actual) (N=198) AE No. (%)	Atezo + CE (Actual) (N=198) Related AE No. (%)
血液毒性	0	0	1 (0.5%)	1 (0.5%)
甲状腺炎	0	0	1 (0.5%)	1 (0.5%)
錯感覚	0	0	1 (0.5%)	1 (0.5%)
耳感染	0	0	1 (0.5%)	1 (0.5%)
自己免疫性大腸炎	0	0	1 (0.5%)	1 (0.5%)
失神	0	0	1 (0.5%)	1 (0.5%)
腎クレアチニン・クリアランス減少	0	0	1 (0.5%)	1 (0.5%)
体温上昇	0	0	1 (0.5%)	1 (0.5%)
大腸炎	0	0	1 (0.5%)	1 (0.5%)
糖尿病	0	0	1 (0.5%)	1 (0.5%)
粘液便	0	0	1 (0.5%)	1 (0.5%)
肺水腫	0	0	1 (0.5%)	1 (0.5%)
慢性腎臓病	0	0	1 (0.5%)	1 (0.5%)
薬物過敏症	0	0	1 (0.5%)	1 (0.5%)
膵酵素増加	0	0	1 (0.5%)	1 (0.5%)
アシドーシス	0	0	1 (0.5%)	0
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.5%)	0
外耳炎	0	0	1 (0.5%)	0
感染による慢性閉塞性気道疾患の増悪	0	0	1 (0.5%)	0
筋痙縮	0	0	1 (0.5%)	0
呼吸困難	0	0	1 (0.5%)	0
高血糖	0	0	1 (0.5%)	0
細菌性上気道感染	0	0	1 (0.5%)	0
歯感染	0	0	1 (0.5%)	0
歯痛	0	0	1 (0.5%)	0
小腸閉塞	0	0	1 (0.5%)	0
食欲減退	0	0	1 (0.5%)	0
大腿骨骨折	0	0	1 (0.5%)	0
低カルシウム血症	0	0	1 (0.5%)	0
低血圧	0	0	1 (0.5%)	0
皮膚乾燥	0	0	1 (0.5%)	0
末梢動脈閉塞性疾患	0	0	1 (0.5%)	0
冷感	0	0	1 (0.5%)	0
疼痛	0	0	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_dosmod.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_dosmod_SE_24APR2018_GO30081.out
13SEP2018 14:55 Page 3 of 3
［5.3.5.1-2 aerel_dosmod_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

本剤により過度の免疫反応に起因すると考えられる様々な事象が認められることから，本剤の注目すべき有害事象として，以後に記載した事象群を用いて評価した。

本剤の注目すべき有害事象の要約を表 2.7.4.7.1-1に，Grade 3以上の本剤の注目すべき有害事象の要約を表 2.7.4.7.1-2に，重篤な有害事象として報告された本剤の注目すべき有害事象の要約を表 2.7.4.7.1-3に，治験薬の投与中止に至った本剤の注目すべき有害事象の要約を表 2.7.4.7.1-4に，治験薬の投与量変更に至った本剤の注目すべき有害事象の要約を表 2.7.4.7.1-5に示した。なお，Grade 5の本剤の注目すべき有害事象は認められなかった（5.3.5.1-2 t_ae_si_SE_grade5_24APR2018_GO30081）。

(1) 間質性肺疾患

間質性肺疾患の要約を表 2.7.4.2.1.5-1に，重篤な有害事象として報告された間質性肺疾患の要約を表 2.7.4.2.1.5-2に示す。

間質性肺疾患の発現率は，プラセボ併用群2.6%（5/196例），本剤併用群2.0%（4/198例）であった。

重篤な有害事象として報告された間質性肺疾患はプラセボ併用群で2例（1.0%），本剤併用群で1例（0.5%）であった。治験薬の投与中止に至った間質性肺疾患はプラセボ併用群で1例（0.5%），本剤併用群で認められず，治験薬の投与量変更に至った間質性肺疾患はプラセボ併用群で1例（0.5%），本剤併用群で1例（0.5%）であった。

表 2.7.4.2.1.5-1 間質性肺疾患の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
間質性肺疾患		
Total number of patients with at least one adverse event	5 (2.6%)	4 (2.0%)
Total number of events	5	4
肺臓炎	4 (2.0%)	4 (2.0%)
放射線性肺臓炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-2 重篤な有害事象として報告された間質性肺疾患の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
間質性肺疾患		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	2	1
肺臓炎	2 (1.0%)	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(2) 肝機能障害

肝機能障害の要約を表 2.7.4.2.1.5-3に，重篤な有害事象として報告された肝機能障害の要約を表 2.7.4.2.1.5-4に示す。

肝機能障害の発現率は，プラセボ併用群4.6%（9/196例），本剤併用群7.1%（14/198例）であった。

重篤な有害事象として報告された肝機能障害は，プラセボ併用群で1例（0.5%），本剤併用群で3例（1.5%）であった。

治験薬の投与中止に至った肝機能障害は，プラセボ併用群で認められず，本剤併用群で1例（0.5%）であった。治験薬の投与量変更に至った肝機能障害は，プラセボ併用群で認められず，本剤併用群で5例（2.5%）であった。

表 2.7.4.2.1.5-3　肝機能障害の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
肝機能障害		
Total number of patients with at least one adverse event	9 (4.6%)	14 (7.1%)
Total number of events	16	29
アスパラギン酸アミノトランスフェラーゼ増加	6 (3.1%)	9 (4.5%)
アラニンアミノトランスフェラーゼ増加	7 (3.6%)	7 (3.5%)
γ－グルタミルトランスフェラーゼ増加	1 (0.5%)	2 (1.0%)
トランスアミナーゼ上昇	0	2 (1.0%)
肝機能検査値上昇	0	1 (0.5%)
肝酵素上昇	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-4　重篤な有害事象として報告された肝機能障害の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
肝機能障害		
Total number of patients with at least one adverse event	1 (0.5%)	3 (1.5%)
Total number of events	2	4
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5%)	1 (0.5%)
アラニンアミノトランスフェラーゼ増加	1 (0.5%)	1 (0.5%)
トランスアミナーゼ上昇	0	1 (0.5%)
肝機能検査値上昇	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(3)　大腸炎・下痢

大腸炎・下痢の要約を表 2.7.4.2.1.5-5に，重篤な有害事象として報告された大腸炎・下痢の要約を表 2.7.4.2.1.5-6に示す。

大腸炎の発現率は，プラセボ併用群0%（0/196例），本剤併用群1.5%（3/198例）であった。

本剤併用群で認められた事象の内，重篤な有害事象として報告された大腸炎は3例（1.5%）であり，治験薬の投与中止に至った大腸炎は認められなかった。治験薬の投与量変更に至った大腸炎は2例（1.0%）であった。

下痢の発現率は，プラセボ併用群15.8%（31/196例），本剤併用群17.7%（35/198例）であった。

重篤な有害事象として報告された下痢は，プラセボ併用群で1例（0.5%），本剤併用群で3例（1.5%）であった。

治験薬の投与中止に至った下痢は，プラセボ併用群で1例（0.5%）であり，本剤併用群では認められなかった。治験薬の投与量変更に至った下痢は，プラセボ併用群で1例（0.5%），本

剤併用群で1例（0.5%）であった。

表 2.7.4.2.1.5-5 大腸炎・下痢の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
大腸炎		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
大腸炎	0	2 (1.0%)
自己免疫性大腸炎	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	31 (15.8%)	35 (17.7%)
Total number of events	47	45
下痢	31 (15.8%)	35 (17.7%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-6 重篤な有害事象として報告された大腸炎・下痢の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
大腸炎		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
大腸炎	0	2 (1.0%)
自己免疫性大腸炎	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	1 (0.5%)	3 (1.5%)
Total number of events	1	3
下痢	1 (0.5%)	3 (1.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(4) 膵炎

膵炎の要約を表 2.7.4.2.1.5-7に，重篤な有害事象として報告された膵炎の要約を表 2.7.4.2.1.5-8に示す。

膵炎の発現率は，プラセボ併用群1.0%（2/196例），本剤併用群0.5%（1/198例）であった。

重篤な有害事象として報告された膵炎は，プラセボ併用群で1例（0.5%），本剤併用群で1例（0.5%）であった。

治験薬の投与中止に至った膵炎は，プラセボ併用群で1例（0.5%）であり，本剤併用群では認められなかった。治験薬の投与量変更に至った膵炎は，プラセボ併用群で1例（0.5%），本剤併用群で1例（0.5%）に認められた。

表 2.7.4.2.1.5-7　膵炎の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
膵炎		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	4	1
リパーゼ増加	1 (0.5%)	0
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-8　重篤な有害事象として報告された膵炎の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
膵炎		
Total number of patients with at least one adverse event	1 (0.5%)	1 (0.5%)
Total number of events	3	1
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(5)　1型糖尿病

1型糖尿病は認められなかった。

(6)　内分泌障害（甲状腺機能障害，副腎機能障害，下垂体機能障害）

内分泌障害の要約を表 2.7.4.2.1.5-9に，重篤な有害事象として報告された内分泌障害の要約を表 2.7.4.2.1.5-10に示す。

甲状腺機能障害の発現率は，プラセボ併用群3.1%（6/196例），本剤併用群15.2%（30/198例）であった。

重篤な有害事象として報告された甲状腺機能障害は，プラセボ併用群で認められず，本剤併用群で2例（1.0%）であった。

治験薬の投与中止に至った甲状腺機能障害は，両群とも認められなかった。治験薬の投与量変更に至った甲状腺機能障害は，プラセボ併用群で1例（0.5%），本剤併用群で4例（2.0%）に認められた。

副腎機能障害の発現率は，プラセボ併用群1.5%（3/196例），本剤併用群0%（0/198例）であった。

プラセボ併用群で認められた事象の内，重篤な有害事象として報告された副腎機能障害及び

治験薬の投与中止に至った副腎機能障害は認められず，治験薬の投与量変更に至った副腎機能障害は1例（0.5%）であった。

下垂体機能障害の発現率は，プラセボ併用群0%（0/196例），本剤併用群0.5%（1/198例）であった。

本剤併用群で認められた事象の内，重篤な有害事象として報告された下垂体機能障害，治験薬の投与中止に至った下垂体機能障害及び治験薬の投与量変更に至った下垂体機能障害はいずれも認められなかった。

表 2.7.4.2.1.5-9　内分泌障害の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
甲状腺機能障害		
Total number of patients with at least one adverse event	6 (3.1%)	30 (15.2%)
Total number of events	6	39
甲状腺機能低下症	1 (0.5%)	20 (10.1%)
甲状腺機能亢進症	5 (2.6%)	11 (5.6%)
自己免疫性甲状腺炎	0	3 (1.5%)
血中甲状腺刺激ホルモン減少	0	1 (0.5%)
血中甲状腺刺激ホルモン増加	0	1 (0.5%)
甲状腺炎	0	1 (0.5%)
遊離サイロキシン増加	0	1 (0.5%)
遊離トリヨードチロニン増加	0	1 (0.5%)
副腎機能障害		
Total number of patients with at least one adverse event	3 (1.5%)	0
Total number of events	3	0
副腎機能不全	2 (1.0%)	0
コルチゾール減少	1 (0.5%)	0
下垂体機能障害		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
体温調節障害	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-10　重篤な有害事象として報告された内分泌障害の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
甲状腺機能障害		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
自己免疫性甲状腺炎	0	2 (1.0%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(7) 脳炎・髄膜炎

脳炎・髄膜炎は認められなかった。

(8) 神経障害（ギラン・バレー症候群を含む）

神経障害の要約を表 2.7.4.2.1.5-11に，重篤な有害事象として報告された神経障害の要約を表2.7.4.2.1.5-12に示す。

神経障害の発現率は，プラセボ併用群4.6%（9/196例），本剤併用群9.1%（18/198例）であった。

重篤な有害事象として報告された神経障害は，プラセボ併用群で認められず，本剤併用群で2例（1.0%）であった。

治験薬の投与中止に至った神経障害は，両群とも認められなかった。治験薬の投与量変更に至った神経障害は，プラセボ併用群で1例（0.5%），本剤併用群で2例（1.0%）に認められた。

表 2.7.4.2.1.5-11　神経障害の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	9 (4.6%)	18 (9.1%)
Total number of events	10	18
末梢性ニューロパチー	5 (2.6%)	8 (4.0%)
末梢性感覚ニューロパチー	2 (1.0%)	8 (4.0%)
ギラン・バレー症候群	0	1 (0.5%)
多発ニューロパチー	1 (0.5%)	0
中毒性ニューロパチー	1 (0.5%)	0
末梢性運動ニューロパチー	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-12　重篤な有害事象として報告された神経障害の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
ギラン・バレー症候群	0	1 (0.5%)
末梢性ニューロパチー	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(9) 重症筋無力症

重症筋無力症は認められなかった。

(10) 皮膚障害

皮膚障害の要約を表 2.7.4.2.1.5-13に，重篤な有害事象として報告された皮膚障害の要約を表2.7.4.2.1.5-14に示す。

皮膚障害の発現率は，プラセボ併用群17.3%（34/196例），本剤併用群24.7%（49/198例）であった。

重篤な有害事象として報告された皮膚障害は，プラセボ併用群で1例（0.5%），本剤併用群で2例（1.0%）であった。

治験薬の投与中止に至った皮膚障害は，プラセボ併用群で認められず，本剤併用群で2例（1.0%）に認められた。治験薬の投与量変更に至った皮膚障害は，プラセボ併用群で認められず，本剤併用群で5例（2.5%）に認められた。

表 2.7.4.2.1.5-13　皮膚障害の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
重度の皮膚障害		
Total number of patients with at least one adverse event	34 (17.3%)	49 (24.7%)
Total number of events	45	80
発疹	12 (6.1%)	14 (7.1%)
そう痒症	9 (4.6%)	12 (6.1%)
斑状丘疹状皮疹	2 (1.0%)	10 (5.1%)
皮膚乾燥	5 (2.6%)	7 (3.5%)
紅斑	1 (0.5%)	5 (2.5%)
丘疹性皮疹	1 (0.5%)	2 (1.0%)
そう痒性皮疹	1 (0.5%)	1 (0.5%)
光線過敏性反応	0	2 (1.0%)
口角口唇炎	1 (0.5%)	1 (0.5%)
口唇炎	1 (0.5%)	1 (0.5%)
膿疱性皮疹	0	2 (1.0%)
皮膚病変	1 (0.5%)	1 (0.5%)
放射線皮膚損傷	1 (0.5%)	1 (0.5%)
ばら色粃糠疹	0	1 (0.5%)
アレルギー性そう痒症	0	1 (0.5%)
異汗性湿疹	1 (0.5%)	0
黄疸	0	1 (0.5%)
乾癬	0	1 (0.5%)
紅斑性皮疹	0	1 (0.5%)
挫傷	1 (0.5%)	0
水疱性皮膚炎	0	1 (0.5%)
全身性そう痒症	0	1 (0.5%)
全身性皮疹	1 (0.5%)	0
中毒性皮疹	0	1 (0.5%)
皮膚炎	0	1 (0.5%)
皮膚毒性	0	1 (0.5%)
皮膚反応	1 (0.5%)	0
皮膚疼痛	1 (0.5%)	0
毛孔性皮疹	1 (0.5%)	0
薬疹	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-14　重篤な有害事象として報告された皮膚障害の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
重度の皮膚障害		
Total number of patients with at least one adverse event	1 (0.5%)	2 (1.0%)
Total number of events	1	3
黄疸	0	1 (0.5%)
発疹	1 (0.5%)	0
皮膚毒性	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(11) 腎機能障害（尿細管間質性腎炎等）

腎機能障害の要約を表 2.7.4.2.1.5-15に，重篤な有害事象として報告された腎機能障害の要約を表 2.7.4.2.1.5-16に示す。

腎機能障害の発現率は，プラセボ併用群2.0%（4/196例），本剤併用群3.5%（7/198例）であった。

重篤な有害事象として報告された腎機能障害は，プラセボ併用群で認められず，本剤併用群で3例（1.5%）であった。

治験薬の投与中止に至った腎機能障害は，プラセボ併用群で認められず，本剤併用群で1例（0.5%）に認められた。治験薬の投与量変更に至った腎機能障害は，プラセボ併用群で認められず，本剤併用群で3例（1.5%）に認められた。

表 2.7.4.2.1.5-15　腎機能障害の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	4 (2.0%)	7 (3.5%)
Total number of events	4	11
急性腎障害	2 (1.0%)	5 (2.5%)
腎炎	1 (0.5%)	0
体液貯留	0	1 (0.5%)
尿細管間質性腎炎	0	1 (0.5%)
乏尿	1 (0.5%)	0
慢性腎臓病	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-16　重篤な有害事象として報告された腎機能障害の要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
急性腎障害	0	2 (1.0%)
尿細管間質性腎炎	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(12) 筋炎・横紋筋融解症

筋炎・横紋筋融解症の要約を表 2.7.4.2.1.5-17に示す。

筋炎は認められなかった。

横紋筋融解症の発現率は，プラセボ併用群0%（0/196例），本剤併用群0.5%（1/198例）であった。

本剤併用群で認められた事象の内，重篤な有害事象として報告された横紋筋融解症及び治験薬の投与中止に至った横紋筋融解症は認められず，治験薬の投与量変更に至った横紋筋融解症は1例（0.5%）に認められた。

表 2.7.4.2.1.5-17　筋炎・横紋筋融解症の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
横紋筋融解症		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
横紋筋融解症	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

(13) Infusion reaction

Infusion reaction の要約を表 2.7.4.2.1.5-18に，重篤な有害事象として報告された Infusion reaction の要約を表 2.7.4.2.1.5-19に示す。

Infusion reaction の発現率は，プラセボ併用群6.1%（12/196例），本剤併用群7.1%（14/198例）であった。

重篤な有害事象として報告された Infusion reaction は，プラセボ併用群で2例（1.0%），本剤併用群で1例（0.5%）であった。

治験薬の投与中止に至った Infusion reaction は，プラセボ併用群で認められず，本剤併用群で6例（3.0%）に認められた。治験薬の投与量変更に至った Infusion reaction は，プラセボ併用

群で7例（3.6%），本剤併用群で8例（4.0%）に認められた。

表 2.7.4.2.1.5-18 Infusion reactionの要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Infusion reaction		
Total number of patients with at least one adverse event	12 (6.1%)	14 (7.1%)
Total number of events	14	17
注入に伴う反応	10 (5.1%)	11 (5.6%)
過敏症	2 (1.0%)	0
薬物過敏症	0	2 (1.0%)
アナフィラキシー反応	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を改変］

表 2.7.4.2.1.5-19 重篤な有害事象として報告されたInfusion reactionの要約（GO30081試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Infusion reaction		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	2	1
注入に伴う反応	2 (1.0%)	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adaptation from output t_ae_si_SE_ser_24APR2018_GO30081
［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を改変］

(14) 心筋炎

心筋炎は認められなかった。

(15) 溶血性貧血

溶血性貧血は認められなかった。

(16) 免疫性血小板減少性紫斑病

免疫性血小板減少性紫斑病は認められなかった。

2.7.4.2.1.6 日本部分集団の結果

2.7.4.2.1.6.1 日本部分集団の安全性の結果

日本部分集団の曝露状況の要約を表 2.7.4.2.1.6.1-1に，いずれかの群で発現率が10%以上の有害事象の要約を表 2.7.4.2.1.6.1-2に，いずれかの群で発現率が10%以上の有害事象の重症度別の要約を表 2.7.4.2.1.6.1-3に，死亡に至った有害事象の要約を表 2.7.4.2.1.6.1-4に，重篤な有害事象の要約を表 2.7.4.2.1.6.1-5に示す。なお，日本部分集団で治験薬の投与中止に至った有害事象は認められなかった。

表 2.7.4.2.1.6.1-1　曝露状況の要約（GO30081試験, 日本部分集団）

Study Drug Exposure
Protocol: GO30081

Treatment: ATEZOLIZUMAB/PLACEBO

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Treatment duration (months)			
n	22	20	42
Mean (SD)	4.1 (3.3)	6.4 (4.1)	5.2 (3.8)
Median	3.3	4.7	3.7
Min - Max	0 - 15	2 - 17	0 - 17
Treatment duration			
n	22	20	42
0 to <= 3 months	10 (45.5%)	1 (5.0%)	11 (26.2%)
>3 months to <= 6 months	10 (45.5%)	12 (60.0%)	22 (52.4%)
>6 months to <= 12 months	1 (4.5%)	4 (20.0%)	5 (11.9%)
>12 months	1 (4.5%)	3 (15.0%)	4 (9.5%)
Dose Intensity (%)			
n	22	20	42
Mean (SD)	90.9 (8.1)	90.7 (6.0)	90.8 (7.1)
Median	93.9	92.9	93.4
Min - Max	72 - 100	77 - 99	72 - 100
Number of doses received			
n	22	20	42
Mean (SD)	6.3 (4.6)	9.4 (5.3)	7.8 (5.1)
Median	5.5	7.0	6.0
Min - Max	1 - 22	3 - 21	1 - 22

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

Study Drug Exposure
Protocol: GO30081

Treatment: ATEZOLIZUMAB/PLACEBO

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Total cumulative dose (mg)			
n	22	20	42
Mean (SD)	0.0 (0.0)	11280.0 (6366.5)	5371.4 (7162.0)
Median	0.0	8400.0	0.0
Min - Max	0 - 0	3600 - 25200	0 - 25200

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

Study Drug Exposure
Protocol: GO30081

Treatment: CARBOPLATIN

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Treatment duration (months)			
n	22	20	42
Mean (SD)	2.2 (0.8)	2.4 (0.3)	2.3 (0.6)
Median	2.3	2.3	2.3
Min - Max	0 - 4	2 - 3	0 - 4
Treatment duration			
n	22	20	42
0 to <= 3 months	21 (95.5%)	19 (95.0%)	40 (95.2%)
>3 months to <= 6 months	1 (4.5%)	1 (5.0%)	2 (4.8%)
Dose Intensity (%)			
n	22	20	42
Mean (SD)	89.2 (9.7)	86.8 (7.4)	88.1 (8.7)
Median	91.8	88.0	91.3
Min - Max	60 - 100	74 - 99	60 - 100
Number of doses received			
n	22	20	42
Mean (SD)	3.7 (0.8)	4.0 (0.2)	3.8 (0.6)
Median	4.0	4.0	4.0
Min - Max	1 - 4	3 - 4	1 - 4

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

Study Drug Exposure
Protocol: GO30081

Treatment: CARBOPLATIN

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Total cumulative dose (mg)			
n	22	20	42
Mean (SD)	1764.4 (606.8)	1877.0 (430.6)	1818.0 (527.0)
Median	1862.5	1771.1	1815.5
Min - Max	341 - 3000	1204 - 2800	341 - 3000

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

Study Drug Exposure
Protocol: GO30081

Treatment: ETOPOSIDE

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Treatment duration (months)			
n	22	20	42
Mean (SD)	2.2 (0.8)	2.5 (0.3)	2.4 (0.6)
Median	2.3	2.4	2.4
Min - Max	0 - 4	2 - 3	0 - 4
Treatment duration			
n	22	20	42
0 to <= 3 months	21 (95.5%)	19 (95.0%)	40 (95.2%)
>3 months to <= 6 months	1 (4.5%)	1 (5.0%)	2 (4.8%)
Dose Intensity (%)			
n	22	20	42
Mean (SD)	85.5 (11.1)	84.9 (7.0)	85.2 (9.3)
Median	89.4	86.2	88.9
Min - Max	59 - 98	72 - 97	59 - 98
Number of doses received			
n	22	20	42
Mean (SD)	11.0 (2.5)	11.9 (0.7)	11.4 (1.9)
Median	12.0	12.0	12.0
Min - Max	2 - 12	9 - 12	2 - 12

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

Study Drug Exposure
Protocol: GO30081

Treatment: ETOPOSIDE

	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)	All Patients (N=42)
Total cumulative dose (mg)			
n	22	20	42
Mean (SD)	1696.2 (493.0)	1786.2 (242.6)	1739.0 (392.2)
Median	1730.3	1800.0	1773.0
Min - Max	294 - 2328	1323 - 2220	294 - 2328

Dose intensity is the number of doses actually received divided by the expected number of doses.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ex.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ex_JPN_SE_24APR2018_GO30081.out
13SEP2018 15:42

［5.3.5.1-2 t_ex_JPN_SE_24APR2018_GO30081を再掲］

表 2.7.4.2.1.6.1-2　いずれかの群で発現率が10%以上の有害事象の要約（GO30081試験，日本部分集団）

Adverse Events with an Incidence Rate at Least 10% by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=22) AE No. (%)	PBO + CE (Actual) (N=22) Related AE No. (%)	Atezo + CE (Actual) (N=20) AE No. (%)	Atezo + CE (Actual) (N=20) Related AE No. (%)
Total number of patients with at least one adverse event	22 (100.0%)	22 (100.0%)	20 (100.0%)	20 (100.0%)
好中球数減少	15 (68.2%)	15 (68.2%)	15 (75.0%)	15 (75.0%)
便秘	15 (68.2%)	8 (36.4%)	13 (65.0%)	10 (50.0%)
血小板数減少	13 (59.1%)	13 (59.1%)	11 (55.0%)	11 (55.0%)
白血球数減少	13 (59.1%)	13 (59.1%)	8 (40.0%)	8 (40.0%)
貧血	12 (54.5%)	12 (54.5%)	10 (50.0%)	10 (50.0%)
脱毛症	11 (50.0%)	11 (50.0%)	14 (70.0%)	14 (70.0%)
好中球減少症	6 (27.3%)	6 (27.3%)	4 (20.0%)	4 (20.0%)
食欲減退	5 (22.7%)	5 (22.7%)	10 (50.0%)	10 (50.0%)
悪心	5 (22.7%)	4 (18.2%)	9 (45.0%)	9 (45.0%)
倦怠感	4 (18.2%)	3 (13.6%)	4 (20.0%)	4 (20.0%)
下痢	4 (18.2%)	2 (9.1%)	2 (10.0%)	0
発熱性好中球減少症	4 (18.2%)	4 (18.2%)	1 (5.0%)	1 (5.0%)
発熱	4 (18.2%)	2 (9.1%)	1 (5.0%)	0
白血球減少症	3 (13.6%)	3 (13.6%)	6 (30.0%)	6 (30.0%)
しゃっくり	3 (13.6%)	3 (13.6%)	2 (10.0%)	2 (10.0%)
肺感染	3 (13.6%)	2 (9.1%)	1 (5.0%)	1 (5.0%)
肺炎	3 (13.6%)	1 (4.5%)	1 (5.0%)	1 (5.0%)
口内炎	2 (9.1%)	2 (9.1%)	3 (15.0%)	3 (15.0%)
血小板減少症	2 (9.1%)	2 (9.1%)	2 (10.0%)	2 (10.0%)
嘔吐	2 (9.1%)	2 (9.1%)	2 (10.0%)	2 (10.0%)
味覚異常	1 (4.5%)	1 (4.5%)	3 (15.0%)	3 (15.0%)
咽頭炎	1 (4.5%)	0	2 (10.0%)	1 (5.0%)
血中クレアチニン増加	1 (4.5%)	0	2 (10.0%)	1 (5.0%)
高血糖	1 (4.5%)	0	2 (10.0%)	0
発疹	0	0	4 (20.0%)	4 (20.0%)
末梢性感覚ニューロパチー	0	0	3 (15.0%)	3 (15.0%)
皮膚乾燥	0	0	3 (15.0%)	2 (10.0%)
そう痒症	0	0	2 (10.0%)	2 (10.0%)
斑状丘疹状皮疹	0	0	2 (10.0%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerelp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerelp10_JPN_SE_24APR2018_GO30081.out
13SEP2018 14:47　Page 1 of 1

［5.3.5.1-2 aerelp10_JPN_SE_24APR2018_GO30081を再掲］

表 2.7.4.2.1.6.1-3 いずれかの群で発現率が10%以上の有害事象の重症度別の要約（GO30081試験，日本部分集団）

Adverse Events with an Incidence Rate at Least 10% by Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	PBO + CE (Actual) (N=22)		Atezo + CE (Actual) (N=20)	
	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	22 (100.0%)	21 (95.5%)	20 (100.0%)	19 (95.0%)
胃腸障害				
便秘	15 (68.2%)	0	13 (65.0%)	2 (10.0%)
悪心	5 (22.7%)	0	9 (45.0%)	0
下痢	4 (18.2%)	0	2 (10.0%)	0
口内炎	2 (9.1%)	0	3 (15.0%)	0
嘔吐	2 (9.1%)	0	2 (10.0%)	0
臨床検査				
好中球数減少	15 (68.2%)	15 (68.2%)	15 (75.0%)	14 (70.0%)
血小板数減少	13 (59.1%)	4 (18.2%)	11 (55.0%)	4 (20.0%)
白血球数減少	13 (59.1%)	7 (31.8%)	8 (40.0%)	3 (15.0%)
血中クレアチニン増加	1 (4.5%)	0	2 (10.0%)	0
血液およびリンパ系障害				
貧血	12 (54.5%)	2 (9.1%)	10 (50.0%)	3 (15.0%)
好中球減少症	6 (27.3%)	6 (27.3%)	4 (20.0%)	4 (20.0%)
発熱性好中球減少症	4 (18.2%)	4 (18.2%)	1 (5.0%)	1 (5.0%)
白血球減少症	3 (13.6%)	1 (4.5%)	6 (30.0%)	3 (15.0%)
血小板減少症	2 (9.1%)	0	2 (10.0%)	0
感染症および寄生虫症				
肺炎	3 (13.6%)	3 (13.6%)	1 (5.0%)	0
肺感染	3 (13.6%)	2 (9.1%)	1 (5.0%)	0
咽頭炎	1 (4.5%)	0	2 (10.0%)	0
皮膚および皮下組織障害				
脱毛症	11 (50.0%)	0	14 (70.0%)	0
発疹	0	0	4 (20.0%)	0
皮膚乾燥	0	0	3 (15.0%)	0
そう痒症	0	0	2 (10.0%)	0
斑状丘疹状皮疹	0	0	2 (10.0%)	0
代謝および栄養障害				
食欲減退	5 (22.7%)	0	10 (50.0%)	0
高血糖	1 (4.5%)	1 (4.5%)	2 (10.0%)	1 (5.0%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_JPN_SE_24APR2018_GO30081.out
13SEP2018 14:50

Adverse Events with an Incidence Rate at Least 10% by Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	PBO + CE (Actual) (N=22) Any Grade No. (%)	PBO + CE (Actual) (N=22) >= Grade3 No. (%)	Atezo + CE (Actual) (N=20) Any Grade No. (%)	Atezo + CE (Actual) (N=20) >= Grade3 No. (%)
一般・全身障害および投与部位の状態				
倦怠感	4 (18.2%)	0	4 (20.0%)	0
発熱	4 (18.2%)	0	1 (5.0%)	0
呼吸器、胸郭および縦隔障害				
しゃっくり	3 (13.6%)	0	2 (10.0%)	0
神経系障害				
味覚異常	1 (4.5%)	0	3 (15.0%)	0
末梢性感覚ニューロパチー	0	0	3 (15.0%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_JPN_SE_24APR2018_GO30081.out
13SEP2018 14:50 Page 2 of 2

［5.3.5.1-2 aegrdp10_JPN_SE_24APR2018_GO30081を再掲］

表 2.7.4.2.1.6.1-4　死亡に至った有害事象の要約（GO30081試験，日本部分集団）

Adverse Events leading to Death
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	PBO + CE (Actual) (N=22)
Total number of patients with at least one adverse event	2 (9.1%)
Overall total number of events	2
感染症および寄生虫症	
Total number of patients with at least one adverse event	2 (9.1%)
Total number of events	2
肺炎	2 (9.1%)

Percentages are based on N in the column headings.
Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aet02_dd.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aet02_dd_JPN_SE_24APR2018_GO30081.out
14SEP2018 14:11

［5.3.5.1-2 aet02_dd_JPN_SE_24APR2018_GO30081を再掲］

表 2.7.4.2.1.6.1-5　重篤な有害事象の要約（GO30081試験，日本部分集団）

Serious Adverse Events by Relation
Protocol: GO30081

MedDRA Preferred Term	PBO + CE (Actual) (N=22) AE No. (%)	PBO + CE (Actual) (N=22) Related AE No. (%)	Atezo + CE (Actual) (N=20) AE No. (%)	Atezo + CE (Actual) (N=20) Related AE No. (%)
Total number of patients with at least one adverse event	8 (36.4%)	6 (27.3%)	5 (25.0%)	4 (20.0%)
好中球減少症	2 (9.1%)	2 (9.1%)	1 (5.0%)	1 (5.0%)
肺感染	2 (9.1%)	2 (9.1%)	0	0
発熱性好中球減少症	2 (9.1%)	2 (9.1%)	0	0
肺炎	2 (9.1%)	0	0	0
好中球数減少	1 (4.5%)	1 (4.5%)	0	0
白血球数減少	1 (4.5%)	1 (4.5%)	0	0
胃腸出血	1 (4.5%)	0	0	0
心不全	1 (4.5%)	0	0	0
低ナトリウム血症	1 (4.5%)	0	0	0
播種性血管内凝固	1 (4.5%)	0	0	0
肺膿瘍	1 (4.5%)	0	0	0
末梢動脈閉塞	1 (4.5%)	0	0	0
サイトメガロウイルス感染	0	0	1 (5.0%)	1 (5.0%)
肝機能検査値上昇	0	0	1 (5.0%)	1 (5.0%)
急性膵炎	0	0	1 (5.0%)	1 (5.0%)
胸水	0	0	1 (5.0%)	1 (5.0%)
肺臓炎	0	0	1 (5.0%)	1 (5.0%)
高血糖	0	0	1 (5.0%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the closest relationship for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aerel_ser.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aerel_ser_JPN_SE_24APR2018_GO30081.out
13SEP2018 14:54　Page 1 of 1
［5.3.5.1-2 aerel_ser_JPN_SE_24APR2018_GO30081を再掲］

2.7.4.2.1.6.2　日本部分集団と外国部分集団との比較

日本部分集団と外国部分集団（日本部分集団を除いた被験者集団）のいずれかで，全 Grade の発現率が10%以上であった有害事象の要約を表 2.7.4.2.1.6.2-1に示す。

プラセボ併用群で外国部分集団と比較して日本部分集団で発現率が10%以上高かった有害事象は，便秘，好中球数減少，血小板数減少，白血球数減少，貧血，脱毛症，発熱，発熱性好中球減少症，倦怠感，しゃっくり，肺感染であった。これらの内，Grade 3以上の発現率も外国部分集団と比較して日本部分集団で10%以上高かった事象は，好中球数減少（日本部分集団68.2%，外国部分集団10.3%，以下同順），血小板数減少（18.2%，2.3%），白血球数減少（31.8%，1.1%）及び発熱性好中球減少症（18.2%，4.6%）であった。また，肺炎は全 Grade での発現率の差は10%以内であったが，Grade 3以上の発現率（13.6%，2.9%）は日本部分集団で10%以上高かった。

本剤併用群で外国部分集団と比較して日本部分集団で発現率が10%以上高かった有害事象は，便秘，好中球数減少，血小板数減少，白血球数減少，脱毛症，食欲減退，倦怠感，白血球減少症，口内炎，味覚異常，発疹，皮膚乾燥及び末梢性感覚ニューロパチーであった。これらの内，Grade 3以上の発現率も外国部分集団と比較して日本部分集団で10%以上高かった事象は，好中球数減少（日本部分集団70.0%，外国部分集団9.6%，以下同順），血小板数減少（20.0%，1.7%），白血球数減少（15.0%，2.2%），白血球減少症（15.0%，3.9%）及び便秘（10.0%，0%）であった。

表 2.7.4.2.1.6.2-1 日本部分集団と外国部分集団のいずれかで全 Grade の発現率が10%以上であった有害事象の要約（GO30081試験）

Adverse Events with an Incidence Rate at Least 10% by Intensity (Japanese vs. Non-Japanese)
Protocol: GO30081

	PBO + CE Japanese (N=22)		PBO + CE Non-Japanese (N=174)	
MedDRA Preferred Term	Any Grade No. (%)	>= Grade3 No. (%)	Any Grade No. (%)	>= Grade3 No. (%)
Total number of patients with at least one adverse event	22 (100.0%)	21 (95.5%)	167 (96.0%)	115 (66.1%)
便秘	15 (68.2%)	0	43 (24.7%)	1 (0.6%)
好中球数減少	15 (68.2%)	15 (68.2%)	31 (17.8%)	18 (10.3%)
血小板数減少	13 (59.1%)	4 (18.2%)	16 (9.2%)	4 (2.3%)
白血球数減少	13 (59.1%)	7 (31.8%)	12 (6.9%)	2 (1.1%)
貧血	12 (54.5%)	2 (9.1%)	57 (32.8%)	24 (13.8%)
脱毛症	11 (50.0%)	0	57 (32.8%)	0
好中球減少症	6 (27.3%)	6 (27.3%)	63 (36.2%)	43 (24.7%)
悪心	5 (22.7%)	0	59 (33.9%)	1 (0.6%)
食欲減退	5 (22.7%)	0	31 (17.8%)	0
下痢	4 (18.2%)	0	27 (15.5%)	2 (1.1%)
発熱	4 (18.2%)	0	12 (6.9%)	0
発熱性好中球減少症	4 (18.2%)	4 (18.2%)	8 (4.6%)	8 (4.6%)
倦怠感	4 (18.2%)	0	1 (0.6%)	0
白血球減少症	3 (13.6%)	1 (4.5%)	16 (9.2%)	7 (4.0%)
肺炎	3 (13.6%)	3 (13.6%)	9 (5.2%)	5 (2.9%)
しゃっくり	3 (13.6%)	0	2 (1.1%)	0
肺感染	3 (13.6%)	2 (9.1%)	1 (0.6%)	1 (0.6%)
嘔吐	2 (9.1%)	0	31 (17.8%)	5 (2.9%)
血小板減少症	2 (9.1%)	0	29 (16.7%)	17 (9.8%)
口内炎	2 (9.1%)	0	7 (4.0%)	0
頭痛	1 (4.5%)	0	22 (12.6%)	0
背部痛	1 (4.5%)	0	18 (10.3%)	1 (0.6%)
味覚異常	1 (4.5%)	0	8 (4.6%)	0
高血糖	1 (4.5%)	1 (4.5%)	3 (1.7%)	0
血中クレアチニン増加	1 (4.5%)	0	2 (1.1%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10_jnj.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_jnj_SE_24APR2018_GO30081.out
18SEP2018 18:55 Page 1 of 4

Adverse Events with an Incidence Rate at Least 10% by Intensity (Japanese vs. Non-Japanese)
Protocol: GO30081

MedDRA Preferred Term	PBO + CE Japanese (N=22) Any Grade No. (%)	PBO + CE Japanese (N=22) >= Grade3 No. (%)	PBO + CE Non-Japanese (N=174) Any Grade No. (%)	PBO + CE Non-Japanese (N=174) >= Grade3 No. (%)
咽頭炎	1 (4.5%)	0	0	0
疲労	0	0	49 (28.2%)	1 (0.6%)
咳嗽	0	0	25 (14.4%)	2 (1.1%)
無力症	0	0	20 (11.5%)	4 (2.3%)
呼吸困難	0	0	18 (10.3%)	2 (1.1%)
関節痛	0	0	13 (7.5%)	1 (0.6%)
発疹	0	0	12 (6.9%)	0
浮動性めまい	0	0	11 (6.3%)	0
体重減少	0	0	10 (5.7%)	1 (0.6%)
そう痒症	0	0	9 (5.2%)	0
皮膚乾燥	0	0	5 (2.9%)	0
末梢性感覚ニューロパチー	0	0	2 (1.1%)	0
斑状丘疹状皮疹	0	0	2 (1.1%)	0
甲状腺機能低下症	0	0	1 (0.6%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10_jnj.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_jnj_SE_24APR2018_GO30081.out
18SEP2018 18:55 Page 2 of 4

Adverse Events with an Incidence Rate at Least 10% by Intensity (Japanese vs. Non-Japanese)
Protocol: GO30081

MedDRA Preferred Term	Atezo + CE Japanese (N=20) Any Grade No. (%)	Atezo + CE Japanese (N=20) >= Grade3 No. (%)	Atezo + CE Non-Japanese (N=178) Any Grade No. (%)	Atezo + CE Non-Japanese (N=178) >= Grade3 No. (%)
Total number of patients with at least one adverse event	20 (100.0%)	19 (95.0%)	178 (100.0%)	118 (66.3%)
便秘	13 (65.0%)	2 (10.0%)	38 (21.3%)	0
好中球数減少	15 (75.0%)	14 (70.0%)	22 (12.4%)	17 (9.6%)
血小板数減少	11 (55.0%)	4 (20.0%)	14 (7.9%)	3 (1.7%)
白血球数減少	8 (40.0%)	3 (15.0%)	10 (5.6%)	4 (2.2%)
貧血	10 (50.0%)	3 (15.0%)	76 (42.7%)	28 (15.7%)
脱毛症	14 (70.0%)	0	59 (33.1%)	0
好中球減少症	4 (20.0%)	4 (20.0%)	70 (39.3%)	42 (23.6%)
悪心	9 (45.0%)	0	66 (37.1%)	1 (0.6%)
食欲減退	10 (50.0%)	0	44 (24.7%)	2 (1.1%)
下痢	2 (10.0%)	0	33 (18.5%)	4 (2.2%)
発熱	1 (5.0%)	0	19 (10.7%)	0
発熱性好中球減少症	1 (5.0%)	1 (5.0%)	6 (3.4%)	6 (3.4%)
倦怠感	4 (20.0%)	0	2 (1.1%)	0
白血球減少症	6 (30.0%)	3 (15.0%)	19 (10.7%)	7 (3.9%)
肺炎	1 (5.0%)	0	12 (6.7%)	7 (3.9%)
しゃっくり	2 (10.0%)	0	2 (1.1%)	0
肺感染	1 (5.0%)	0	2 (1.1%)	0
嘔吐	2 (10.0%)	0	37 (20.8%)	3 (1.7%)
血小板減少症	2 (10.0%)	0	31 (17.4%)	20 (11.2%)
口内炎	3 (15.0%)	0	8 (4.5%)	0
頭痛	0	0	24 (13.5%)	0
背部痛	1 (5.0%)	0	16 (9.0%)	0
味覚異常	3 (15.0%)	0	5 (2.8%)	0
高血糖	2 (10.0%)	1 (5.0%)	9 (5.1%)	3 (1.7%)
血中クレアチニン増加	2 (10.0%)	0	5 (2.8%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10_jnj.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_jnj_SE_24APR2018_GO30081.out
18SEP2018 18:55 Page 3 of 4

Adverse Events with an Incidence Rate at Least 10% by Intensity (Japanese vs. Non-Japanese)
Protocol: GO30081

MedDRA Preferred Term	Atezo + CE Japanese (N=20) Any Grade No. (%)	Atezo + CE Japanese (N=20) >= Grade3 No. (%)	Atezo + CE Non-Japanese (N=178) Any Grade No. (%)	Atezo + CE Non-Japanese (N=178) >= Grade3 No. (%)
咽頭炎	2 (10.0%)	0	1 (0.6%)	0
疲労	0	0	54 (30.3%)	5 (2.8%)
咳嗽	0	0	18 (10.1%)	1 (0.6%)
無力症	0	0	25 (14.0%)	5 (2.8%)
呼吸困難	0	0	20 (11.2%)	3 (1.7%)
関節痛	0	0	18 (10.1%)	0
発疹	4 (20.0%)	0	10 (5.6%)	0
浮動性めまい	0	0	19 (10.7%)	0
体重減少	1 (5.0%)	0	19 (10.7%)	0
そう痒症	2 (10.0%)	0	10 (5.6%)	0
皮膚乾燥	3 (15.0%)	0	4 (2.2%)	0
末梢性感覚ニューロパチー	3 (15.0%)	0	5 (2.8%)	0
斑状丘疹状皮疹	2 (10.0%)	0	8 (4.5%)	1 (0.6%)
甲状腺機能低下症	1 (5.0%)	0	19 (10.7%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the most severe grade for this preferred term.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/aegrdp10_jnj.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/aegrdp10_jnj_SE_24APR2018_GO30081.out
18SEP2018 18:55　Page 4 of 4
［5.3.5.1-2 aegrdp10_jnj_SE_24APR2018_GO30081を再掲］

2.7.4.2.2　個別有害事象の文章による説明

死亡例及び重篤な有害事象の叙述は2.7.6.2.2項に記載した。

2.7.4.3　臨床検査値の評価

2.7.4.3.1　血液検査及び血液生化学検査

ベースライン時に Grade 0，1又は2であり，治験薬投与後に Grade 3又は4となった臨床検査値の要約を5.3.5.1-1 Table 56に示す。

いずれの群でも，治験薬投与後に Grade 3又は Grade 4となった臨床検査値は稀であった。認められた変化の内大部分は散発的であり，発現率も各群で概ね同様であった。

2.7.4.3.2　抗薬物抗体（ADA）

(1) ADA の発現状況

治験薬投与後に ADA 評価対象となった被験者188例の内，ADA が陽性であった被験者は，35例（18.6%）であった（5.3.5.1-1 Table 66参照）。

(2) ADA の発現と安全性の関連

本剤併用群の ADA 陰性集団と ADA 陽性集団の有害事象の概要を5.3.5.1-1 Table 70に示す。ADA 陰性集団と ADA 陽性集団の有害事象の概要は概ね同様であった。Grade 3又は4の有害事象（ADA 陰性集団69.9%，ADA 陽性集団62.9%，以下同順），重篤な有害事象（35.3%，40.0%），本剤の投与量変更（休薬又は減量）に至った有害事象（58.8%，65.7%）の発現率は ADA 陰性集団と ADA 陽性集団でやや差が認められたが，発現した事象に特定の傾向は認められなかった。

本剤の投与中止に至った有害事象の発現率は，ADA 陽性集団（20.0%）で ADA 陰性集団（7.8%）より高かったが，複数例に認められた事象は注入に伴う反応（2例）のみであり，そ

の他の事象に特定の傾向は認められなかった（5.3.5.1-1 10.2.3項参照）。

2.7.4.4 バイタルサイン，身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1 心電図

スクリーニング時点で，プラセボ併用群の71例（36.6%），本剤併用群の74例（37.8%）に臨床的意義のない心電図の異常が認められ，プラセボ併用群の4例（2.1%），本剤併用群の1例（0.5%）に臨床的意義のある心電図異常が認められた。

治験薬投与開始後，プラセボ併用群の9例，本剤併用群の11例で心電図検査が実施された。この内，プラセボ併用群の3例（33.3%）で臨床的意義のある心電図異常が認められ，心臓に関連する有害事象が報告された。本剤併用群では臨床的意義のある心電図異常は認められなかった（5.3.5.1-1 8.13.1項参照）。

2.7.4.4.2 バイタルサイン

いずれの投与群でも治験薬の投与開始後にバイタルサインの大きな変動はみられなかった（5.3.5.1-1 8.13.2項参照）。

2.7.4.5 特別な患者集団及び状況下における安全性

2.7.4.5.1 内因性要因

日本部分集団の安全性の結果は，2.7.4.2.1.6.1項に示した。

その他の年齢，性別，人種等の内因性要因に関する部分集団解析は実施していない。

2.7.4.5.2 外因性要因

喫煙や飲酒等の外因性要因に関する部分集団解析は実施していない。

2.7.4.5.3 薬物相互作用

薬物間相互作用試験は実施していない。

2.7.4.5.4 妊娠及び授乳時の使用

これまでに，本剤について，妊婦及び授乳中の女性を対象にした臨床試験は実施していない。また，GO30081試験からも妊娠中，授乳中又は治験期間中に妊娠する予定のある女性を除外したため，新たな情報は得られていない。

2.7.4.5.5 過量投与

GO30081試験では，治験実施計画書で本剤の用量を固定用量の1200 mg と規定しており，過量投与に関する情報は得られなかった。

2.7.4.5.6 薬物乱用

これまでに実施された臨床試験で，本剤に対する依存性は報告されていない。

2.7.4.5.7 離脱症状及び反跳現象

これまでに実施された臨床試験で，本剤の離脱症状及び反跳現象は報告されていない。

2.7.4.5.8 自動車運転及び機械操作に対する影響又は精神機能の障害

これまでに実施された臨床試験で，自動車運転及び機械操作に影響すると考えられる有害事象に関し，対照群と比較して本剤群で明らかに発現率が高い事象は認められていない。

2.7.4.6 市販後データ

2.7.4.6.1 海外における市販後の使用経験

世界における本剤の市販後データを最新の Periodic Benefit-Risk Evaluation Report（PBRER）を元に記載した。

本剤は2016年5月18日に米国で最初に承認された。また，欧州連合においては2017年9月21日に承認された。2018年5月17日時点で，本剤は70の国で承認されていた。

2.7.4.6.2 推定使用患者数

推定使用患者数は国際誕生日から20[redacted]年[redacted]月末までの販売量（mg）に基づいて算出した。1患者あたりの平均投与量は用法・用量に基づき，3週間ごとに1200 mg を疾患進行まで継続したと仮定した。投与継続期間は各適応の臨床試験の結果より推定した。

以上の仮定に基づき，算出した結果，推定使用患者数は[redacted]人であった。内訳を表2.7.4.6.2-1に示す。

表 2.7.4.6.2-1 推定使用患者数

Indication	Gender		Age (years)			Dose and Formulation	Region			
	Male (%)	Female (%)	2 to ≤ 16	> 16 to ≤ 65	> 65	1200 mg Q3W, IV	Europe	U.S.	Japan	RoW
mUC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2L + NSCLC	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

mUC = metastatic urothelial carcinoma, NSCLC = non-small cell lung cancer, RoW = Rest of World, Q3W = Every three Weeks
Note: Rounding errors may be introduced during segment splits.

2.7.4.6.3 有害事象

海外における2016年5月18日から2018年5月17日までの市販後情報源からの累積の有害事象の入手状況を表 2.7.4.6.3-1に示す。報告件数の多かった器官別大分類別は，一般・全身障害および投与部位の状態，傷害、中毒および処置合併症，胃腸障害等であった。これらのデータから新たな安全性上の懸念は示唆されなかった。

表 2.7.4.6.3-1 市販後情報源からの累積有害事象報告

	Spontaneous, including health authority (worldwide) and literature			Non-interventional post-marketing study and reports from other solicited sources*
	serious	non-serious	Total	serious
SOC	cum.	cum.	cum.	cum.
Infections and infestations	64	21	85	156
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	30	10	40	50
Blood and lymphatic system disorders	28	16	44	38
Immune system disorders	3	5	8	5
Endocrine disorders	10	16	26	14
Metabolism and nutrition disorders	37	27	64	46
Psychiatric disorders	6	15	21	22
Nervous system disorders	38	46	84	34
Eye disorders	12	19	31	1
Ear and labyrinth disorders	2	1	3	4
Cardiac disorders	26	2	28	25
Vascular disorders	16	13	29	24
Respiratory, thoracic and mediastinal disorders	83	33	116	113
Gastrointestinal disorders	53	101	154	116
Hepatobiliary disorders	37	0	37	28
Skin and subcutaneous tissue disorders	14	111	125	12
Musculoskeletal and connective tissue disorders	16	55	71	36
Renal and urinary disorders	34	10	44	94
Pregnancy, puerperium and perinatal conditions	0	1	1	0
Reproductive system and breast disorders	0	3	3	4
General disorders and administration site conditions	157	442	599	371
Investigations	58	95	153	53
Injury, poisoning and procedural complications	25	433	458	34
Surgical and medical procedures	4	0	4	1
Social circumstances	1	0	1	1
Product issues	0	3	3	10
Total	754	1478	2232	1292

*This does not include interventional clinical trials.

2.7.4.6.4 市販後データの結論

最新 PBRER に記載したデータを分析，検討した結果，安全性の懸念を示す知見は適切に医薬品リスク管理計画書に反映されており，医薬品リスク管理計画書に基づき実施される安全性監視計画及びリスク最小化計画により，本剤の市販後の安全性は確保されると考える。

2.7.4.7 付録

2.7.4.7.1 要約表

表 2.7.4.7.1-1 本剤の注目すべき有害事象の要約（GO30081試験）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Total number of patients with at least one adverse event	81 (41.3%)	122 (61.6%)
Overall total number of events	154	249
重度の皮膚障害		
Total number of patients with at least one adverse event	34 (17.3%)	49 (24.7%)
Total number of events	45	80
発疹	12 (6.1%)	14 (7.1%)
そう痒症	9 (4.6%)	12 (6.1%)
斑状丘疹状皮疹	2 (1.0%)	10 (5.1%)
皮膚乾燥	5 (2.6%)	7 (3.5%)
紅斑	1 (0.5%)	5 (2.5%)
丘疹性皮疹	1 (0.5%)	2 (1.0%)
そう痒性皮疹	1 (0.5%)	1 (0.5%)
光線過敏性反応	0	2 (1.0%)
口角口唇炎	1 (0.5%)	1 (0.5%)
口唇炎	1 (0.5%)	1 (0.5%)
膿疱性皮疹	0	2 (1.0%)
皮膚病変	1 (0.5%)	1 (0.5%)
放射線皮膚損傷	1 (0.5%)	1 (0.5%)
ばら色粃糠疹	0	1 (0.5%)
アレルギー性そう痒症	0	1 (0.5%)
異汗性湿疹	1 (0.5%)	0
黄疸	0	1 (0.5%)
乾癬	0	1 (0.5%)
紅斑性皮疹	0	1 (0.5%)
挫傷	1 (0.5%)	0
水疱性皮膚炎	0	1 (0.5%)
全身性そう痒症	0	1 (0.5%)
全身性皮疹	1 (0.5%)	0
中毒性皮疹	0	1 (0.5%)
皮膚炎	0	1 (0.5%)
皮膚毒性	0	1 (0.5%)
皮膚反応	1 (0.5%)	0
皮膚疼痛	1 (0.5%)	0
毛孔性皮疹	1 (0.5%)	0
薬疹	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	31 (15.8%)	35 (17.7%)
Total number of events	47	45
下痢	31 (15.8%)	35 (17.7%)
甲状腺機能障害		
Total number of patients with at least one adverse event	6 (3.1%)	30 (15.2%)
Total number of events	6	39
甲状腺機能低下症	1 (0.5%)	20 (10.1%)
甲状腺機能亢進症	5 (2.6%)	11 (5.6%)
自己免疫性甲状腺炎	0	3 (1.5%)
血中甲状腺刺激ホルモン減少	0	1 (0.5%)
血中甲状腺刺激ホルモン増加	0	1 (0.5%)
甲状腺炎	0	1 (0.5%)
遊離サイロキシン増加	0	1 (0.5%)
遊離トリヨードチロニン増加	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_24APR2018_GO30081.out
13SEP2018 16:34

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	9 (4.6%)	18 (9.1%)
Total number of events	10	18
末梢性ニューロパチー	5 (2.6%)	8 (4.0%)
末梢性感覚ニューロパチー	2 (1.0%)	8 (4.0%)
ギラン・バレー症候群	0	1 (0.5%)
多発ニューロパチー	1 (0.5%)	0
中毒性ニューロパチー	1 (0.5%)	0
末梢性運動ニューロパチー	0	1 (0.5%)
Infusion reaction		
Total number of patients with at least one adverse event	12 (6.1%)	14 (7.1%)
Total number of events	14	17
注入に伴う反応	10 (5.1%)	11 (5.6%)
過敏症	2 (1.0%)	0
薬物過敏症	0	2 (1.0%)
アナフィラキシー反応	0	1 (0.5%)
肝機能障害		
Total number of patients with at least one adverse event	9 (4.6%)	14 (7.1%)
Total number of events	16	29
アスパラギン酸アミノトランスフェラーゼ増加	6 (3.1%)	9 (4.5%)
アラニンアミノトランスフェラーゼ増加	7 (3.6%)	7 (3.5%)
γ－グルタミルトランスフェラーゼ増加	1 (0.5%)	2 (1.0%)
トランスアミナーゼ上昇	0	2 (1.0%)
肝機能検査値上昇	0	1 (0.5%)
肝酵素上昇	0	1 (0.5%)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	4 (2.0%)	7 (3.5%)
Total number of events	4	11
急性腎障害	2 (1.0%)	5 (2.5%)
腎炎	1 (0.5%)	0
体液貯留	0	1 (0.5%)
尿細管間質性腎炎	0	1 (0.5%)
乏尿	1 (0.5%)	0
慢性腎臓病	0	1 (0.5%)
間質性肺疾患		
Total number of patients with at least one adverse event	5 (2.6%)	4 (2.0%)
Total number of events	5	4
肺臓炎	4 (2.0%)	4 (2.0%)
放射線性肺臓炎	1 (0.5%)	0
大腸炎		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
大腸炎	0	2 (1.0%)
自己免疫性大腸炎	0	1 (0.5%)
副腎機能障害		
Total number of patients with at least one adverse event	3 (1.5%)	0
Total number of events	3	0
副腎機能不全	2 (1.0%)	0
コルチゾール減少	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_24APR2018_GO30081.out
13SEP2018 16:34

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
膵炎		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	4	1
リパーゼ増加	1 (0.5%)	0
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0
横紋筋融解症		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
横紋筋融解症	0	1 (0.5%)
下垂体機能障害		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
体温調節障害	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_24APR2018_GO30081.out
13SEP2018 16:34 Page 3 of 3

［5.3.5.1-2 t_ae_si_SE_24APR2018_GO30081を再掲］

表 2.7.4.7.1-2 Grade 3以上の本剤の注目すべき有害事象の要約（GO30081試験）

Grade3-5 Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Total number of patients with at least one adverse event	8 (4.1%)	28 (14.1%)
Overall total number of events	11	36
Infusion reaction		
Total number of patients with at least one adverse event	1 (0.5%)	5 (2.5%)
Total number of events	1	6
注入に伴う反応	1 (0.5%)	4 (2.0%)
アナフィラキシー反応	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	2 (1.0%)	4 (2.0%)
Total number of events	3	4
下痢	2 (1.0%)	4 (2.0%)
重度の皮膚障害		
Total number of patients with at least one adverse event	0	6 (3.0%)
Total number of events	0	7
黄疸	0	1 (0.5%)
乾癬	0	1 (0.5%)
紅斑	0	1 (0.5%)
膿疱性皮疹	0	1 (0.5%)
斑状丘疹状皮疹	0	1 (0.5%)
皮膚毒性	0	1 (0.5%)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	1 (0.5%)	4 (2.0%)
Total number of events	1	5
急性腎障害	0	3 (1.5%)
尿細管間質性腎炎	0	1 (0.5%)
乏尿	1 (0.5%)	0
慢性腎臓病	0	1 (0.5%)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	0	4 (2.0%)
Total number of events	0	4
末梢性ニューロパチー	0	3 (1.5%)
ギラン・バレー症候群	0	1 (0.5%)
肝機能障害		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	5
トランスアミナーゼ上昇	0	2 (1.0%)
アラニンアミノトランスフェラーゼ増加	0	1 (0.5%)
γ－グルタミルトランスフェラーゼ増加	0	1 (0.5%)
肝機能検査値上昇	0	1 (0.5%)
間質性肺疾患		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	2	1
肺臓炎	2 (1.0%)	1 (0.5%)
膵炎		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	4	1
リパーゼ増加	1 (0.5%)	0
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_g35_24APR2018_GO30081.out
13SEP2018 16:36

Grade3-5 Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
大腸炎		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
大腸炎	0	2 (1.0%)
横紋筋融解症		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
横紋筋融解症	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_g35_24APR2018_GO30081.out
13SEP2018 16:36 Page 2 of 2

［5.3.5.1-2 t_ae_si_SE_g35_24APR2018_GO30081を再掲］

表 2.7.4.7.1-3 重篤な有害事象として報告された本剤の注目すべき有害事象の要約（GO30081 試験）

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Total number of patients with at least one adverse event	8 (4.1%)	19 (9.6%)
Overall total number of events	11	23
下痢		
Total number of patients with at least one adverse event	1 (0.5%)	3 (1.5%)
Total number of events	1	3
下痢	1 (0.5%)	3 (1.5%)
肝機能障害		
Total number of patients with at least one adverse event	1 (0.5%)	3 (1.5%)
Total number of events	2	4
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5%)	1 (0.5%)
アラニンアミノトランスフェラーゼ増加	1 (0.5%)	1 (0.5%)
トランスアミナーゼ上昇	0	1 (0.5%)
肝機能検査値上昇	0	1 (0.5%)
Infusion reaction		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	2	1
注入に伴う反応	2 (1.0%)	1 (0.5%)
間質性肺疾患		
Total number of patients with at least one adverse event	2 (1.0%)	1 (0.5%)
Total number of events	2	1
肺臓炎	2 (1.0%)	1 (0.5%)
重度の皮膚障害		
Total number of patients with at least one adverse event	1 (0.5%)	2 (1.0%)
Total number of events	1	3
黄疸	0	1 (0.5%)
発疹	1 (0.5%)	0
皮膚毒性	0	1 (0.5%)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
急性腎障害	0	2 (1.0%)
尿細管間質性腎炎	0	1 (0.5%)
大腸炎		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
大腸炎	0	2 (1.0%)
自己免疫性大腸炎	0	1 (0.5%)
甲状腺機能障害		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
自己免疫性甲状腺炎	0	2 (1.0%)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
ギラン・バレー症候群	0	1 (0.5%)
末梢性ニューロパチー	0	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_ser_24APR2018_GO30081.out
13SEP2018 16:38

Serious Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
膵炎		
Total number of patients with at least one adverse event	1 (0.5%)	1 (0.5%)
Total number of events	3	1
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_ser_24APR2018_GO30081.out
13SEP2018 16:38 Page 2 of 2

［5.3.5.1-2 t_ae_si_SE_ser_24APR2018_GO30081を再掲］

表 2.7.4.7.1-4 治験薬の投与中止に至った本剤の注目すべき有害事象の要約（GO30081試験）

Targeted AE Leading to Study Treatment Withdrawal
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Total number of patients with at least one adverse event	3 (1.5%)	10 (5.1%)
Overall total number of events	3	11
Infusion reaction		
Total number of patients with at least one adverse event	0	6 (3.0%)
Total number of events	0	7
注入に伴う反応	0	5 (2.5%)
アナフィラキシー反応	0	1 (0.5%)
重度の皮膚障害		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
黄疸	0	1 (0.5%)
紅斑	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	1 (0.5%)	0
Total number of events	1	0
下痢	1 (0.5%)	0
肝機能障害		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
トランスアミナーゼ上昇	0	1 (0.5%)
間質性肺疾患		
Total number of patients with at least one adverse event	1 (0.5%)	0
Total number of events	1	0
肺臓炎	1 (0.5%)	0
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
尿細管間質性腎炎	0	1 (0.5%)
膵炎		
Total number of patients with at least one adverse event	1 (0.5%)	0
Total number of events	1	0
膵炎	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_aewithfl_24APR2018_GO30081.out
13SEP2018 16:39 Page 1 of 1

［5.3.5.1-2 t_ae_si_SE_aewithfl_24APR2018_GO30081を再掲］

表 2.7.4.7.1-5 治験薬の投与量変更に至った本剤の注目すべき有害事象の要約（GO30081試験）

Targeted AE Leading to Study Treatment Dose Modification/Interruption
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
Total number of patients with at least one adverse event	13 (6.6%)	30 (15.2%)
Overall total number of events	15	40
Infusion reaction		
Total number of patients with at least one adverse event	7 (3.6%)	8 (4.0%)
Total number of events	9	9
注入に伴う反応	6 (3.1%)	7 (3.5%)
過敏症	1 (0.5%)	0
薬物過敏症	0	1 (0.5%)
肝機能障害		
Total number of patients with at least one adverse event	0	5 (2.5%)
Total number of events	0	11
アラニンアミノトランスフェラーゼ増加	0	4 (2.0%)
アスパラギン酸アミノトランスフェラーゼ増加	0	3 (1.5%)
γ－グルタミルトランスフェラーゼ増加	0	2 (1.0%)
トランスアミナーゼ上昇	0	1 (0.5%)
肝機能検査値上昇	0	1 (0.5%)
甲状腺機能障害		
Total number of patients with at least one adverse event	1 (0.5%)	4 (2.0%)
Total number of events	1	4
甲状腺機能低下症	0	2 (1.0%)
甲状腺機能亢進症	1 (0.5%)	1 (0.5%)
甲状腺炎	0	1 (0.5%)
重度の皮膚障害		
Total number of patients with at least one adverse event	0	5 (2.5%)
Total number of events	0	5
斑状丘疹状皮疹	0	2 (1.0%)
黄疸	0	1 (0.5%)
乾癬	0	1 (0.5%)
皮膚乾燥	0	1 (0.5%)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	1 (0.5%)	2 (1.0%)
Total number of events	1	2
末梢性ニューロパチー	0	2 (1.0%)
多発ニューロパチー	1 (0.5%)	0
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	0	3 (1.5%)
Total number of events	0	3
急性腎障害	0	2 (1.0%)
慢性腎臓病	0	1 (0.5%)
下痢		
Total number of patients with at least one adverse event	1 (0.5%)	1 (0.5%)
Total number of events	1	1
下痢	1 (0.5%)	1 (0.5%)
間質性肺疾患		
Total number of patients with at least one adverse event	1 (0.5%)	1 (0.5%)
Total number of events	1	1
肺臓炎	1 (0.5%)	1 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_dsm_24APR2018_GO30081.out
13SEP2018 16:40

Targeted AE Leading to Study Treatment Dose Modification/Interruption
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)
大腸炎		
Total number of patients with at least one adverse event	0	2 (1.0%)
Total number of events	0	2
自己免疫性大腸炎	0	1 (0.5%)
大腸炎	0	1 (0.5%)
膵炎		
Total number of patients with at least one adverse event	1 (0.5%)	1 (0.5%)
Total number of events	1	1
急性膵炎	0	1 (0.5%)
膵炎	1 (0.5%)	0
横紋筋融解症		
Total number of patients with at least one adverse event	0	1 (0.5%)
Total number of events	0	1
横紋筋融解症	0	1 (0.5%)
副腎機能障害		
Total number of patients with at least one adverse event	1 (0.5%)	0
Total number of events	1	0
副腎機能不全	1 (0.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_SE_dsm_24APR2018_GO30081.out
13SEP2018 16:40 Page 2 of 2

［5.3.5.1-2 t_ae_si_SE_dsm_24APR2018_GO30081を再掲］

表 2.7.4.7.1-6　本剤の注目すべき有害事象の要約（GO30081試験，日本部分集団）

Targeted AE
Protocol: GO30081

AE of Special Interest Medical Concept MedDRA Preferred Term	PBO + CE (Actual) (N=22)	Atezo + CE (Actual) (N=20)
Total number of patients with at least one adverse event	9 (40.9%)	14 (70.0%)
Overall total number of events	11	33
重度の皮膚障害		
Total number of patients with at least one adverse event	1 (4.5%)	8 (40.0%)
Total number of events	1	15
発疹	0	4 (20.0%)
皮膚乾燥	0	3 (15.0%)
そう痒症	0	2 (10.0%)
口唇炎	1 (4.5%)	1 (5.0%)
斑状丘疹状皮疹	0	2 (10.0%)
口角口唇炎	0	1 (5.0%)
中毒性皮疹	0	1 (5.0%)
下痢		
Total number of patients with at least one adverse event	4 (18.2%)	2 (10.0%)
Total number of events	5	2
下痢	4 (18.2%)	2 (10.0%)
肝機能障害		
Total number of patients with at least one adverse event	2 (9.1%)	1 (5.0%)
Total number of events	3	9
アラニンアミノトランスフェラーゼ増加	2 (9.1%)	1 (5.0%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (4.5%)	1 (5.0%)
γ－グルタミルトランスフェラーゼ増加	0	1 (5.0%)
肝機能検査値上昇	0	1 (5.0%)
神経障害（ギラン・バレー症候群を含む）		
Total number of patients with at least one adverse event	0	3 (15.0%)
Total number of events	0	3
末梢性感覚ニューロパチー	0	3 (15.0%)
甲状腺機能障害		
Total number of patients with at least one adverse event	0	2 (10.0%)
Total number of events	0	2
甲状腺機能低下症	0	1 (5.0%)
甲状腺機能亢進症	0	1 (5.0%)
膵炎		
Total number of patients with at least one adverse event	1 (4.5%)	1 (5.0%)
Total number of events	1	1
リパーゼ増加	1 (4.5%)	0
急性膵炎	0	1 (5.0%)
間質性肺疾患		
Total number of patients with at least one adverse event	0	1 (5.0%)
Total number of events	0	1
肺臓炎	0	1 (5.0%)
腎機能障害(尿細管間質性腎炎等)		
Total number of patients with at least one adverse event	1 (4.5%)	0
Total number of events	1	0
乏尿	1 (4.5%)	0

Investigator text for AEs encoded using MedDRA version 21.0.
Multiple occurrences of the same AE in one individual are counted only once.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_si.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_si_JPN_SE_24APR2018_GO30081.out
13SEP2018 16:35　Page 1 of 1

［5.3.5.1-2 t_ae_si_JPN_SE_24APR2018_GO30081を再掲］

2.7.4.7.2 一覧

(1) 死亡した被験者の一覧（GO30081試験）
5.3.5.1-1 l_dd_SE_24APR2018_GO30081に示した。

(2) 重篤な有害事象を発現した被験者の一覧（GO30081試験）
5.3.5.1-1 l_ae_ser_SE_24APR2018_GO30081に示した。

テセントリク点滴静注1200 mg
（アテゾリズマブ（遺伝子組換え））
［小細胞肺癌］

第2部　（モジュール2）：CTD の概要（サマリー）

2.7.5 参考文献

中外製薬株式会社

目次

頁
2.7.5 参考文献 3

2.7.5 参考文献

(1) 2.7.1で引用した文献
該当なし

(2) 2.7.2で引用した文献
該当なし

(3) 2.7.3で引用した文献
2.7.3.6項に記載した。

(4) 2.7.4で引用した文献
該当なし

(5) 2.7.6で引用した文献
該当なし

テセントリク点滴静注1200 mg
（アテゾリズマブ（遺伝子組換え））
［小細胞肺癌］

第2部　（モジュール2）：CTD の概要（サマリー）

2.7.6 個々の試験のまとめ

中外製薬株式会社

目次

頁
2.7.6 個々の試験のまとめ 3
2.7.6.1 概要 3
2.7.6.1.1 GO30081 試験 3
2.7.6.2 付録 12
2.7.6.2.1 有害事象の集計表 12
2.7.6.2.1.1 GO30081 試験 12
2.7.6.2.2 個別症例の詳細 51

2.7.6　個々の試験のまとめ

表 2.7.6-1　臨床試験一覧表

地域	試験番号	相 (依頼者)	試験デザイン	対象	被験者数	用法・用量[a]	主要評価項目	CTD 番号 <資料区分>
国内及び海外	GO30081	I/III (Roche /Genentech 社)	ランダム化 二重盲検 2群	全身療法未治療の進展型小細胞肺癌患者	試験全体: 403 日本: 42	本剤併用群： 本剤 1200 mg/body カルボプラチン AUC 5 エトポシド 100 mg/m^2 プラセボ併用群： プラセボ カルボプラチン AUC 5 エトポシド 100 mg/m^2	PFS OS	5.3.5.1-1 <評価>

AUC =血中薬物濃度-時間曲線下面積；OS = 全生存期間；PFS = 無増悪生存期間
a: 21日を1サイクルとし，本剤，プラセボ及びカルボプラチンは各サイクルの Day 1に，エトポシドは各サイクルの Day 1,2,3に点滴静脈内投与した。

2.7.6.1　概要

2.7.6.1.1　GO30081試験

(1) 試験の標題

A Phase I/III, randomized, double-blind, placebo-controlled study of carboplatin plus etoposide with or without atezolizumab (anti-PD-L1 antibody) in patients with untreated extensive-stage small cell lung cancer

未治療の進展型小細胞肺癌患者を対象としたアテゾリズマブ（抗 PD-L1抗体）又はプラセボとカルボプラチン及びエトポシドの併用を検討する第 I/III 相二重盲検ランダム化試験

(2) 治験依頼者／実施地域

F. Hoffman-La Roche 社／21カ国，106施設（米国22施設，日本13施設，ポーランド6施設，ロシア6施設，スペイン6施設，イタリア6施設，ドイツ5施設，オーストリア4施設，ハンガリー4施設，韓国4施設，イギリス4施設，フランス4施設，チェコ共和国3施設，セルビア3施設，オーストラリア3施設，ギリシャ3施設，台湾3施設，ブラジル3施設，チリ2施設，メキシコ1施設，中国1施設）

(3) 治験実施期間

最初の被験者のランダム化実施日：2016年6月6日
最後の被験者のランダム化実施日：2017年5月31日
データカットオフ日：2018年4月24日

(4) フェーズ

第 I/III 相

(5) 目的

1) 有効性の目的

① 有効性主要目的

- Intent-to-treat（ITT）集団を対象として，主治医が「固形癌の治療効果判定のための新ガイドライン」（RECIST）v1.1に従って判定する無増悪生存期間（PFS）を指標としてアテゾリズマブ + カルボプラチン + エトポシド併用群（以下，本剤併用群）の有効性をプラセボ + カルボプラチン + エトポシド併用群（以下，プラセボ併用群）と比較する。

- ITT 集団を対象として，全生存期間（OS）を指標として本剤併用群の有効性をプラセボ併用群と比較する。

② 有効性副次的目的

ITT 集団を対象として，以下の指標を用いて本剤併用群の有効性をプラセボ併用群と比較する。

- 主治医が RECIST v1.1に従って判定する奏効率
- 主治医が RECIST v1.1に従って判定する奏効期間
- 各治療群の6カ月及び1年無増悪生存割合
- 各治療群の1年及び2年生存割合
- European Organisation for Research and Treatment of Cancer（EORTC）の QOL 質問票 Core 30（QLQ-C30）及び肺癌モジュール（QLQ-LC13）を用いた患者報告アウトカム（PRO）に基づく肺癌症状［咳嗽，呼吸困難（単項目及び複数項目の尺度評価），胸痛，腕／肩痛，疲労］の悪化までの期間（TTD）

2) 安全性の目的

- 本剤併用群の安全性及び忍容性を，プラセボ併用群と比較する。
- アテゾリズマブに対する抗薬物抗体（ADA）の発現率及び力価を評価する。また，免疫原性反応と薬物動態，安全性，有効性との関連性を探索する。

3) 薬物動態学的目的

化学療法歴のない進展型小細胞肺癌（SCLC）患者でのアテゾリズマブ，カルボプラチン及びエトポシドの薬物動態の特性を調べる。

(6) 治験デザイン

第 I/III 相多施設共同二重盲検ランダム化プラセボ対照試験

適格とされた被験者は，性別（男性 vs. 女性），Eastern Cooperative Oncology Group performance status（ECOG PS）（0 vs. 1），脳転移の有無（あり vs. なし）を割付因子として，以下の2つの投与群のいずれかに1 : 1でランダム割付けした。

- 本剤併用群：導入期間はアテゾリズマブ + カルボプラチン + エトポシド（21日を1サイクルとして4サイクル）。維持期間はアテゾリズマブ（21日を1サイクル）。
- プラセボ併用群：導入期間はプラセボ + カルボプラチン + エトポシド（21日を1サイクルとして4サイクル）。維持期間はプラセボ（21日を1サイクル）。

(7) 被験者数

予定登録被験者数：400例

登録被験者数：403例（本剤併用群：201例，プラセボ併用群：202例）

(8) 診断及び主な組入基準

- ECOG PS 0又は1
- 進展型 SCLC という診断が組織学的又は細胞学的に確認されていること［Veterans Administration Lung Study Group（VALG）staging system による］
- 進展型 SCLC に対する全身投与による治療歴がない。
- 限局型 SCLC に対する化学放射線療法の治療歴がある患者については，根治目的の治療を受けていなければならず，化学療法，放射線療法又は化学放射線療法の直近のサイクルから進展型 SCLC の診断までに6カ月以上の無治療期間がなければならない。

(9) 被験薬の投与量，投与方法

アテゾリズマブ及びプラセボ：臨床的利益が失われるまで，3週ごとに1200 mg を点滴静脈内投与。

(10) 併用薬の投与量，投与方法

カルボプラチン：導入期間（サイクル1～4）の各サイクルの Day 1に血中薬物濃度-時間曲線下面積（AUC）の目標値である5 mg/mL/min（Calvert 式）が得られるように点滴静脈内投与。

エトポシド：導入期間（サイクル1～4）の各サイクルの Day 1（カルボプラチン投与後），Day 2及び Day 3に100 mg/m^{2}を点滴静脈内投与。

(11) 評価項目

1) 有効性評価項目

① 有効性主要評価項目

主治医が RECIST v1.1に従って判定する PFS 及び OS

② 有効性副次的評価項目

主治医が判定する奏効率，奏効期間，無増悪生存割合，生存割合及び PRO（EORTC QLQ-C30及び QLQ-LC13）

2) PRO

投与群ごとの各評価時点の完遂率。各評価時点の EORTC QLQ-C30及び QLQ-LC13症状尺度のベースラインからの変化量。TTD。

3) 薬物動態に関する評価項目

アテゾリズマブの血清中濃度，カルボプラチン及びエトポシドの血漿中濃度。

4) 安全性評価項目

National Cancer Institute 有害事象共通用語基準（NCI CTCAE）v4.0に基づいて Grade 分類した有害事象，バイタルサイン，心電図，身体所見，臨床検査値，AE of special interest（AESI），全身性のステロイド投与を要した AESI，ステロイド以外の免疫抑制剤投与を要した有害事象。

5) 免疫原性

アテゾリズマブに対する ADA の発現率，ADA と薬物動態，安全性及び有効性の各種評価項目との関連性。

(12) 統計的手法

PFS 及び OS の解析は，ITT 集団を対象として実施した。

試験全体の第1種の過誤確率を両側5%以内に制御するため，group sequential Holm 法を適用し，主要解析としての PFS 及び OS の比較における両側有意水準はそれぞれ0.005及び0.045とした。

Kaplan-Meier 法を用いて，各治療群のイベント発生までの期間の中央値を推定した。Brookmeyer-Crowley 法を用いて，各治療群の PFS 中央値の95%信頼区間（CI）を算出した。

(13) 試験方法

同意取得後，適格とされた被験者は性別，ECOG PS，脳転移の有無によって層別し，本剤併用群及びプラセボ併用群のいずれかに1 : 1でランダム割付した。導入療法は21日を1サイクルとし，4サイクルとした。導入療法終了後は，3週ごとにアテゾリズマブ又はプラセボを投与する維持療法を継続した。両群とも，RECIST v1.1による病勢進行が認められた場合又は臨床的

利益が認められなくなった場合に治験薬の投与を中止した。

サイクル1の Day 1から48週間は6週（±7日）ごとに，48週目の腫瘍評価の完了以降は9週（±7日）ごとに腫瘍評価を実施した。腫瘍評価は，投与の遅れの有無にかかわらず，RECIST v1.1による画像所見上の病勢進行，同意の撤回，治験依頼者による治験終了，被験者の死亡のいずれかが起きるまで実施した。RECIST v1.1による画像所見上の病勢進行が認められた後も，治験薬投与により臨床的利益が得られている被験者は，主治医の裁量で治験薬の投与を継続することができることとした。

RECIST v1.1による画像所見上の病勢進行以外（毒性，臨床症状の悪化等）の理由で投与を中止した被験者でも，被験者が新しい抗癌療法を開始したか否かにかかわらず，RECIST v1.1による画像所見上の病勢進行，同意の撤回，治験依頼者による治験終了，被験者の死亡のいずれかが起きるまで，治験薬の投与を継続していた場合と同じ頻度で腫瘍評価を継続した。

すべての有害事象は，治験薬の最終投与日から30日間，若しくは治験薬の最終投与後に別の全身抗癌療法を開始するまでの，いずれか早い日まで報告することとした。この期間以降もすべての死亡は報告することとした。すべての重篤な有害事象及び AESI は，治験薬との因果関係にかかわらず，治験薬の最終投与後90日間，若しくは治験薬の最終投与後に別の全身抗癌療法を開始するまでの，いずれか早い日まで報告することとした。有害事象報告期間終了後は，主治医が重篤な有害事象又は AESI の発現を知り，治験薬投与との関連があると判断した場合に治験依頼者に報告することとした。

(14) 結果の要約

1) 人口統計学的特性及びベースライン時特性

ITT 集団の年齢中央値は64歳（範囲：26～90歳），男性は64.8%，白人は79.9%，アジア人は17.1%であった。大部分の被験者は喫煙経験があり（過去に喫煙歴あり：60.0%，現在喫煙者：37.0%），登録時に脳転移はなかった［脳転移なし：91.3%（eCRF データより）］。また，すべての被験者は治験実施計画書に従って，ベースライン時の全身状態が良好［ECOG PS 0：34.7%又は1：65.3%（eCRF データより）］であった。

2) 有効性の結果

本総括報告書では，PFS の主要解析，OS の治験実施計画書で事前に規定された中間解析，その他の副次的評価項目及び探索的評価項目の結果を示す。2018年4月24日のデータカットオフ時点で，238件の OS イベント及び360件の PFS イベントが認められた。有効性成績の概要を表 2.7.6.1.1-1に示した。主な結果を以下に示す。

主要評価項目である OS 及び主治医評価の PFS は治験実施計画書で事前に規定した基準を達成した。未治療の進展型小細胞肺癌患者を対象として，プラセボ併用群に対して本剤併用群で，統計学的に有意かつ臨床的に意義のある OS の延長及び統計学的に有意な主治医評価の PFS の延長が認められた。大部分の部分集団解析で，ITT 集団の結果と同様に，プラセボ併用群に対して本剤併用群で OS 及び PFS の延長が認められた。奏効率及び奏効期間は両群で同程度であった。データカットオフ時点で，プラセボ併用群と比較して本剤併用群で，より多くの被験者の奏効が継続していた。

表 2.7.6.1.1-1　有効性成績の概要（GO30081試験）

Parameter	PBO + CE	Atezo + CE
Co-Primary Efficacy Objectives		
Overall Survival		
ITT Population	N=202	N=201
Patients with event (%)	134 (66.3%)	104 (51.7%)
Median duration of survival (95% CI) (months)	10.3 (9.3, 11.3)	12.3 (10.8, 15.9)
Stratified Hazard Ratio (95% CI)	0.70 (0.54, 0.91)	
p-value (log-rank)	0.0069[a]	
1-year event-free rate (%)	38.2	51.7
(95% CI)	(31.2, 45.3)	(44.4, 59.0)
Progression-Free Survival		
ITT Population	N=202	N=201
Patients with event (%)	189 (93.6%)	171 (85.1%)
Median duration of PFS (95% CI) (months)	4.3 (4.2, 4.5)	5.2 (4.4, 5.6)
Stratified Hazard Ratio (95% CI)	0.77 (0.62, 0.96)	
p-value (log-rank)	0.0170[b]	
6-month event-free rate (%)	22.4	30.9
(95% CI)	(16.6, 28.2)	(24.3, 37.5)
1-year event-free rate (%)	5.4	12.6
(95% CI)	(2.1, 8.6)	(7.9, 17.4)
Other Key Efficacy Objectives		
Objective Response Rate		
ITT Population	N=202	N=201
Responders (%)	130 (64.4%)	121 (60.2%)
95% CI (Clopper-Pearson)	(57.3, 71.0)	(53.1, 67.0)

Parameter	PBO + CE	Atezo + CE
Other Key Efficacy Objectives		
Duration of Response		
ITT Population Responders	N = 130	N = 121
Patients with event, n (%)	123 (94.6%)	103 (85.1%)
Median DOR (months)	3.9	4.2
95% CI	(3.1, 4.2)	(4.1, 4.5)
Unstratified Hazard Ratio (95% CI)	0.69 (0.52, 0.90)	

Atezo = atezolizumab; CE=carboplatin + etoposide; CI=confidence interval; DOR = duration of response; ITT = intent-to-treat; OS = overall survival; PBO=placebo; PFS = progression-free survival.

[a] Interim Analysis OS was tested at two-sided α of 0.0193 (with 238 observed OS events at CCOD) to control the overall two-sided type I error for OS at 0.045 by Lan DeMets function approximating O'Brien-Fleming boundary.

[b] Since null hypothesis for OS was rejected at an overall two-sided significance level of 0.045, PFS was tested at two-sided type I error of 0.05.

［5.3.5.1-1 Synopsis Table 1を再掲］

3) PRO の結果

両群とも PRO データの入手率は，ベースライン時点で高く（85%～89%），その後も試験期間中はほとんどの時点で80%以上であった。

ベースラインからの変化量に関する解析から，プラセボ併用群の被験者と比較して，本剤併用群の被験者は肺癌症状（例えば，咳嗽，胸痛，呼吸困難，疲労）の臨床的に意義のある改善（すなわち，ベースラインから10ポイント以上の改善）が早くから認められ，全体的に長い期間，ベースラインを上回る改善が持続していた。プラセボ併用群と比較して，本剤併用群では呼吸困難が悪化するまでの期間が数値上長くなる傾向が認められた［層別ハザード比は0.63（95%CI：0.45～0.88）］。治療関連の症状（例えば，下痢，悪心，嘔吐，口内炎，末梢性ニューロパチー）の変化量は，導入期間及びその後54週目までほとんどの評価時点で，両群で同程度であった。両群とも治験薬投与開始後すぐに身体機能及び就労能力，余暇活動能力の改善が認められた。両群とも早期かつ顕著な健康関連 QOL の改善が認められた。臨床的に意義のある健康関連 QOL の改善（ベースラインから10ポイント以上の改善）は，プラセボ併用群の被験者では21週目以降次第に減少したのに対し，本剤併用群の被験者では54週目までほとんどの評価時点で継続していた。

4) 薬物動態の結果

アテゾリズマブの薬物動態は，カルボプラチン及びエトポシドとの併用時と単独投与時で同程度であった。カルボプラチン及びエトポシドの薬物動態は，プラセボ併用時とアテゾリズマブ併用時で同程度であった。アテゾリズマブ，カルボプラチン及びエトポシド併用時に薬物間相互作用は認められなかった。

5) 安全性の結果

安全性成績の概要は表 2.7.6.1.1-2に示した。主な結果を以下に示す。

- 本剤併用群の忍容性は良好であり，プラセボ併用群の安全性プロファイルと同様であった。
- 本剤併用群の安全性成績は，各薬剤でこれまでに認められている安全性プロファイルと概ね同様であり，併用投与による新たな安全性シグナルは認められなかった。
- 投与回数の中央値は，本剤併用群（アテゾリズマブ：7.0回，カルボプラチン：4.0回，エトポシド：12.0回）とプラセボ併用群（プラセボ：6.0回，カルボプラチン：4.0回，エトポシ

ド：12.0回）で同程度であった。併用化学療法の投与状況が両群とも同程度であったことから，アテゾリズマブ投与は化学療法投与に悪影響を与えないことが示された。

- Grade 3-4の有害事象の発現率は，両群で同程度（本剤併用群：67.2%，プラセボ併用群：63.8%）であり，発現した事象の種類や頻度にも特筆すべき違いは認められなかった。Grade 3-4の副作用の発現率も両群で同程度（本剤併用群：56.6%，プラセボ併用群：56.1%）であった。
- 重篤な有害事象の発現率は，両群で同程度（本剤併用群：37.4%，プラセボ併用群：34.7%）であり，発現した事象の種類や頻度にも特筆すべき違いは認められなかった。
- Grade 5の有害事象の発現率は，プラセボ併用群（5.6%）と比較して本剤併用群（2.0%）で低かった。
  - 本剤併用群では Grade 5の有害事象4例中3例は，主治医により治験薬との因果関係あり（1例はすべての治験薬と因果関係あり，2例はカルボプラチン及びエトポシドとの因果関係あり）と判断された。
  - プラセボ併用群では Grade 5の有害事象11例中3例は，主治医により治験薬との因果関係あり（1例はすべての治験薬と因果関係あり，1例はプラセボとの因果関係あり，1例はカルボプラチンとの因果関係あり）と判断された。
- いずれかの治験薬の投与中止に至った有害事象の発現率は，プラセボ併用群（3.1%）と比較して本剤併用群（11.1%）で高かった。両群で発現率に2%以上差があった事象は，注入に伴う反応（本剤併用群：2.5%，プラセボ併用群：0%）のみであった。
- 治験薬の投与量変更（休薬又は減量）に至った有害事象の発現率は，プラセボ併用群（60.7%）と比較して本剤併用群（69.7%）で高かった。
- AESI の発現率は，プラセボ併用群（24.5%）と比較して本剤併用群（39.9%）で高かったが，AESI の大部分は重症度が中等度又は軽度の事象であった。この発現率の違いは主に，本剤併用群で甲状腺機能低下症の発現例数が多いことによるものであった。

表 2.7.6.1.1-2　安全性成績の概要（GO30081試験）

Overall Summary of Adverse Events, Safety Evaluable Patients
Protocol: GO30081

	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
Total number of patients with at least one adverse event	189 (96.4%)	198 (100.0%)	387 (98.2%)
Total number of events	1861	2166	4027
Total number of patients with at least one			
Treatment-related AE	181 (92.3%)	188 (94.9%)	369 (93.7%)
Any Treatment	181 (92.3%)	188 (94.9%)	369 (93.7%)
Atezolizumab/Placebo	98 (50.0%)	128 (64.6%)	226 (57.4%)
Grade 3-4 AE	125 (63.8%)	133 (67.2%)	258 (65.5%)
Treatment-related Grade 3-4 AE	110 (56.1%)	112 (56.6%)	222 (56.3%)
Grade 5 AE	11 (5.6%)	4 (2.0%)	15 (3.8%)
Treatment-related Grade 5 AE	3 (1.5%)	3 (1.5%)	6 (1.5%)
Serious AE	68 (34.7%)	74 (37.4%)	142 (36.0%)
AE leading to withdrawal from treatment	6 (3.1%)	22 (11.1%)	28 (7.1%)
Any Treatment	6 (3.1%)	22 (11.1%)	28 (7.1%)
Atezolizumab/Placebo	5 (2.6%)	21 (10.6%)	26 (6.6%)
Carboplatin	1 (0.5%)	5 (2.5%)	6 (1.5%)
Etoposide	2 (1.0%)	8 (4.0%)	10 (2.5%)
AE leading to any dose modification/interruption	119 (60.7%)	138 (69.7%)	257 (65.2%)
Any Treatment	119 (60.7%)	138 (69.7%)	257 (65.2%)
Atezolizumab/Placebo	102 (52.0%)	117 (59.1%)	219 (55.6%)
Carboplatin	96 (49.0%)	111 (56.1%)	207 (52.5%)
Etoposide	95 (48.5%)	113 (57.1%)	208 (52.8%)

Investigator text for AEs encoded using MedDRA version 21.0.
Includes adverse events occurring on or after the start date of treatment.
Percentages are based on N in the column headings. Multiple occurrences of the same AE in an individual are counted only once. For frequency counts of "Total number of events" row, multiple occurrences of the same AE in an individual are counted separately. For "Grade 3-4 AE" and "Treatment-related Grade 3-4 AE", multiple occurrences of the same AE within Grade 3-4 is counted at the highest grade for an individual.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cdt30099/go30081/t_ae_summ.sas
Output: /opt/BIOSTAT/prod/cdt30099/s30081i/reports/t_ae_summ_SE_24APR2018_GO30081.out
06JUL2018 18:46

［5.3.5.1-1 Synopsis Table 2を再掲］

6)　免疫原性の結果

ベースライン後に ADA 陽性となった被験者は18.6%であり，これらの被験者はいずれもベースライン時は ADA 陰性であった。

ADA 陽性集団で曝露量がわずかに低くなる傾向が認められているが，ADA 陽性集団のいずれの被験者でもアテゾリズマブの最低血清中濃度（C_{min}）は標的血清中濃度（6 μg/mL）を超えており，臨床に関連するような薬物動態への影響はなかった。本剤併用群の ADA 陽性集団及び ADA 陰性集団はいずれもプラセボ併用群に対して臨床的有効性を示した。すべての有害事象及び AESI の発現率から，ADA 陽性集団と ADA 陰性集団のアテゾリズマブの安全性プロファイルは一致していた。

(15) 結論

- OS の中間解析において，主要評価項目である OS は治験実施計画書で事前に規定した基準を達成し，プラセボ併用群と比較して本剤併用群で，統計学的に有意かつ臨床的に意義のある OS の延長を示した。
- もう1つの主要評価項目である PFS も治験実施計画書で事前に規定した基準を達成し，プラセボ併用群と比較して本剤併用群で，統計学的に有意な延長を示した。
- 奏効率及び奏効期間は両群で同程度であった。データカットオフ時点で，プラセボ併用群と比較して本剤併用群で，より多くの被験者の奏効が継続していた。
- ランダム化から1年後の生存割合は，プラセボ併用群と比較して本剤併用群で13%高かった。データカットオフ時点で，2年生存割合は両群とも推定できなかった。
- 部分集団解析では，大部分の部分集団で本剤併用群の一貫した治療効果が示された。

- OS 及び PFS の延長効果は，血液検体中の腫瘍の遺伝子変異量（blood tumor mutation burden, bTMB）レベルにかかわらず認められた。
- 6カ月無増悪生存割合及び1年無増悪生存割合は，プラセボ併用群と比較して本剤併用群で数値上高かった。
- 患者報告によると，本剤併用群の肺癌症状及び身体機能に与える影響は全体的に顕著であり，良好であった。本剤併用群の被験者では，肺癌症状及び身体機能の早期かつ継続した改善が認められ，治療関連の症状による影響は最小限であった。更に，本剤併用群ではプラセボ併用群と比較してより明確で継続的な臨床的に意義のある健康関連 QOL の改善が認められた。
- アテゾリズマブをカルボプラチン及びエトポシドと併用投与することによる薬物間相互作用は認められなかった。
- ベースライン後に ADA 陽性となった被験者の割合は18.6%であった。ADA 発現は薬物動態及び安全性に臨床的に意義のある影響を与えなかった。本剤併用群の ADA 陽性集団及び ADA 陰性集団はいずれもプラセボ併用群に対して臨床的有効性を示した。
- 本剤併用群の忍容性は良好であった。本剤併用群とプラセボ併用群の安全性プロファイルは同様であり，各薬剤でこれまでに知られているリスクとも同様であった。アテゾリズマブと化学療法を併用することによる新たな又は予期せぬ安全性シグナルは認められなかった。

(16) 報告書作成日

20[redacted]年[redacted]月[redacted]日

2.7.6.2 付録

2.7.6.2.1 有害事象の集計表

2.7.6.2.1.1 GO30081試験

表 2.7.6.2.1.1-1 有害事象の要約（GO30081試験）

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
- Any adverse events -	- Any Grade -	189 (96.4%)	198 (100.0%)	387 (98.2%)
	1	10 (5.1%)	9 (4.5%)	19 (4.8%)
	2	43 (21.9%)	52 (26.3%)	95 (24.1%)
	3	72 (36.7%)	81 (40.9%)	153 (38.8%)
	4	53 (27.0%)	52 (26.3%)	105 (26.6%)
	5	11 (5.6%)	4 (2.0%)	15 (3.8%)
血液およびリンパ系障害 - Overall -	- Any Grade -	120 (61.2%)	132 (66.7%)	252 (64.0%)
	1	8 (4.1%)	8 (4.0%)	16 (4.1%)
	2	32 (16.3%)	43 (21.7%)	75 (19.0%)
	3	46 (23.5%)	55 (27.8%)	101 (25.6%)
	4	34 (17.3%)	25 (12.6%)	59 (15.0%)
	5	0	1 (0.5%)	1 (0.3%)
貧血	- Any Grade -	69 (35.2%)	86 (43.4%)	155 (39.3%)
	1	10 (5.1%)	11 (5.6%)	21 (5.3%)
	2	33 (16.8%)	44 (22.2%)	77 (19.5%)
	3	23 (11.7%)	31 (15.7%)	54 (13.7%)
	4	3 (1.5%)	0	3 (0.8%)
好中球減少症	- Any Grade -	69 (35.2%)	74 (37.4%)	143 (36.3%)
	1	6 (3.1%)	1 (0.5%)	7 (1.8%)
	2	14 (7.1%)	27 (13.6%)	41 (10.4%)
	3	27 (13.8%)	26 (13.1%)	53 (13.5%)
	4	22 (11.2%)	19 (9.6%)	41 (10.4%)
	5	0	1 (0.5%)	1 (0.3%)
血小板減少症	- Any Grade -	31 (15.8%)	33 (16.7%)	64 (16.2%)
	1	5 (2.6%)	5 (2.5%)	10 (2.5%)
	2	9 (4.6%)	8 (4.0%)	17 (4.3%)
	3	11 (5.6%)	13 (6.6%)	24 (6.1%)
	4	6 (3.1%)	7 (3.5%)	13 (3.3%)
白血球減少症	- Any Grade -	19 (9.7%)	25 (12.6%)	44 (11.2%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	10 (5.1%)	13 (6.6%)	23 (5.8%)
	3	6 (3.1%)	4 (2.0%)	10 (2.5%)
	4	2 (1.0%)	6 (3.0%)	8 (2.0%)
発熱性好中球減少症	- Any Grade -	12 (6.1%)	7 (3.5%)	19 (4.8%)
	3	7 (3.6%)	5 (2.5%)	12 (3.0%)
	4	5 (2.6%)	2 (1.0%)	7 (1.8%)
汎血球減少症	- Any Grade -	4 (2.0%)	2 (1.0%)	6 (1.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
	4	2 (1.0%)	0	2 (0.5%)
白血球増加症	- Any Grade -	4 (2.0%)	1 (0.5%)	5 (1.3%)
	1	2 (1.0%)	0	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
	3	2 (1.0%)	0	2 (0.5%)
血小板増加症	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
リンパ球減少症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
巨赤芽球性貧血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
血液毒性	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
播種性血管内凝固	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
胃腸障害				
- Overall -	- Any Grade -	119 (60.7%)	127 (64.1%)	246 (62.4%)
	1	63 (32.1%)	53 (26.8%)	116 (29.4%)
	2	45 (23.0%)	56 (28.3%)	101 (25.6%)
	3	10 (5.1%)	18 (9.1%)	28 (7.1%)
	4	1 (0.5%)	0	1 (0.3%)
悪心	- Any Grade -	64 (32.7%)	75 (37.9%)	139 (35.3%)
	1	42 (21.4%)	44 (22.2%)	86 (21.8%)
	2	21 (10.7%)	30 (15.2%)	51 (12.9%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
便秘	- Any Grade -	58 (29.6%)	51 (25.8%)	109 (27.7%)
	1	44 (22.4%)	34 (17.2%)	78 (19.8%)
	2	13 (6.6%)	15 (7.6%)	28 (7.1%)
	3	1 (0.5%)	2 (1.0%)	3 (0.8%)
嘔吐	- Any Grade -	33 (16.8%)	39 (19.7%)	72 (18.3%)
	1	19 (9.7%)	26 (13.1%)	45 (11.4%)
	2	9 (4.6%)	10 (5.1%)	19 (4.8%)
	3	5 (2.6%)	3 (1.5%)	8 (2.0%)
下痢	- Any Grade -	31 (15.8%)	35 (17.7%)	66 (16.8%)
	1	22 (11.2%)	24 (12.1%)	46 (11.7%)
	2	7 (3.6%)	7 (3.5%)	14 (3.6%)
	3	2 (1.0%)	4 (2.0%)	6 (1.5%)
口内炎	- Any Grade -	9 (4.6%)	11 (5.6%)	20 (5.1%)
	1	5 (2.6%)	9 (4.5%)	14 (3.6%)
	2	4 (2.0%)	2 (1.0%)	6 (1.5%)
腹痛	- Any Grade -	9 (4.6%)	10 (5.1%)	19 (4.8%)
	1	6 (3.1%)	5 (2.5%)	11 (2.8%)
	2	3 (1.5%)	4 (2.0%)	7 (1.8%)
	3	0	1 (0.5%)	1 (0.3%)
上腹部痛	- Any Grade -	7 (3.6%)	4 (2.0%)	11 (2.8%)
	1	2 (1.0%)	4 (2.0%)	6 (1.5%)
	2	5 (2.6%)	0	5 (1.3%)
胃食道逆流性疾患	- Any Grade -	5 (2.6%)	4 (2.0%)	9 (2.3%)
	1	3 (1.5%)	0	3 (0.8%)
	2	2 (1.0%)	4 (2.0%)	6 (1.5%)
消化不良	- Any Grade -	3 (1.5%)	4 (2.0%)	7 (1.8%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
腹部膨満	- Any Grade -	2 (1.0%)	5 (2.5%)	7 (1.8%)
	1	1 (0.5%)	4 (2.0%)	5 (1.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
嚥下障害	- Any Grade -	3 (1.5%)	4 (2.0%)	7 (1.8%)
	1	3 (1.5%)	3 (1.5%)	6 (1.5%)
	2	0	1 (0.5%)	1 (0.3%)
胃炎	- Any Grade -	3 (1.5%)	3 (1.5%)	6 (1.5%)
	1	2 (1.0%)	0	2 (0.5%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
痔核	- Any Grade -	4 (2.0%)	2 (1.0%)	6 (1.5%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
鼓腸	- Any Grade -	2 (1.0%)	3 (1.5%)	5 (1.3%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
口内乾燥	- Any Grade -	3 (1.5%)	2 (1.0%)	5 (1.3%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	1 (0.5%)	0	1 (0.3%)
歯痛	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	0	1 (0.5%)	1 (0.3%)
食道炎	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	3 (1.5%)	3 (0.8%)
アフタ性潰瘍	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
口腔内痛	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
口唇炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
大腸炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	3	0	2 (1.0%)	2 (0.5%)
直腸炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	3	0	2 (1.0%)	2 (0.5%)
腹部不快感	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
嚥下痛	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
イレウス	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
レッチング	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
胃腸出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
胃排出不全	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
過敏性腸症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
急性膵炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
憩室穿孔	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血便排泄	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
呼気臭	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
口の感覚鈍麻	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
口腔障害	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
口腔内潰瘍形成	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
口唇腫脹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
口唇浮腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
歯肉出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
自己免疫性大腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
小腸閉塞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
舌痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
穿孔性胃潰瘍	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
大腸穿孔	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
腸閉塞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
直腸しぶり	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
直腸出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
吐血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
粘液便	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
腹部癒着	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
変色便	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
肛門失禁	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
肛門出血	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
肛門直腸不快感	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
膵炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
齲歯	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
一般・全身障害および投与部位の状態				
- Overall -	- Any Grade -	90 (45.9%)	114 (57.6%)	204 (51.8%)
	1	41 (20.9%)	51 (25.8%)	92 (23.4%)
	2	40 (20.4%)	50 (25.3%)	90 (22.8%)
	3	7 (3.6%)	12 (6.1%)	19 (4.8%)
	4	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	1 (0.5%)	2 (0.5%)
疲労	- Any Grade -	49 (25.0%)	54 (27.3%)	103 (26.1%)
	1	30 (15.3%)	19 (9.6%)	49 (12.4%)
	2	18 (9.2%)	30 (15.2%)	48 (12.2%)
	3	1 (0.5%)	5 (2.5%)	6 (1.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
無力症	- Any Grade -	20 (10.2%)	25 (12.6%)	45 (11.4%)
	1	8 (4.1%)	11 (5.6%)	19 (4.8%)
	2	8 (4.1%)	9 (4.5%)	17 (4.3%)
	3	4 (2.0%)	5 (2.5%)	9 (2.3%)
発熱	- Any Grade -	16 (8.2%)	20 (10.1%)	36 (9.1%)
	1	13 (6.6%)	16 (8.1%)	29 (7.4%)
	2	3 (1.5%)	4 (2.0%)	7 (1.8%)
胸痛	- Any Grade -	13 (6.6%)	16 (8.1%)	29 (7.4%)
	1	6 (3.1%)	9 (4.5%)	15 (3.8%)
	2	7 (3.6%)	6 (3.0%)	13 (3.3%)
	3	0	1 (0.5%)	1 (0.3%)
末梢性浮腫	- Any Grade -	7 (3.6%)	13 (6.6%)	20 (5.1%)
	1	2 (1.0%)	11 (5.6%)	13 (3.3%)
	2	5 (2.6%)	2 (1.0%)	7 (1.8%)
倦怠感	- Any Grade -	5 (2.6%)	6 (3.0%)	11 (2.8%)
	1	3 (1.5%)	5 (2.5%)	8 (2.0%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
粘膜の炎症	- Any Grade -	7 (3.6%)	4 (2.0%)	11 (2.8%)
	1	6 (3.1%)	2 (1.0%)	8 (2.0%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
非心臓性胸痛	- Any Grade -	4 (2.0%)	5 (2.5%)	9 (2.3%)
	1	3 (1.5%)	5 (2.5%)	8 (2.0%)
	3	1 (0.5%)	0	1 (0.3%)
疼痛	- Any Grade -	4 (2.0%)	5 (2.5%)	9 (2.3%)
	1	2 (1.0%)	3 (1.5%)	5 (1.3%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
胸部不快感	- Any Grade -	4 (2.0%)	2 (1.0%)	6 (1.5%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	3 (1.5%)	0	3 (0.8%)
インフルエンザ様疾患	- Any Grade -	3 (1.5%)	2 (1.0%)	5 (1.3%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	1 (0.5%)	0	1 (0.3%)
全身健康状態低下	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
	5	1 (0.5%)	0	1 (0.3%)
歩行障害	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	0	1 (0.5%)	1 (0.3%)
末梢腫脹	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	1 (0.5%)	0	1 (0.3%)
悪寒	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	3 (1.5%)	3 (0.8%)
溢出	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
顔面浮腫	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
注射部位疼痛	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
浮腫	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
炎症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
限局性浮腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
死亡	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	5	0	1 (0.5%)	1 (0.3%)
全身性炎症反応症候群	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
全身性浮腫	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
早期満腹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
体温調節障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
注射部位漏出	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
低体温	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
嚢胞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
冷感	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
皮膚および皮下組織障害				
- Overall -	- Any Grade -	89 (45.4%)	103 (52.0%)	192 (48.7%)
	1	49 (25.0%)	45 (22.7%)	94 (23.9%)
	2	40 (20.4%)	54 (27.3%)	94 (23.9%)
	3	0	4 (2.0%)	4 (1.0%)
脱毛症	- Any Grade -	68 (34.7%)	73 (36.9%)	141 (35.8%)
	1	32 (16.3%)	29 (14.6%)	61 (15.5%)
	2	36 (18.4%)	44 (22.2%)	80 (20.3%)
発疹	- Any Grade -	12 (6.1%)	14 (7.1%)	26 (6.6%)
	1	11 (5.6%)	13 (6.6%)	24 (6.1%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
そう痒症	- Any Grade -	9 (4.6%)	12 (6.1%)	21 (5.3%)
	1	7 (3.6%)	10 (5.1%)	17 (4.3%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
斑状丘疹状皮疹	- Any Grade -	2 (1.0%)	10 (5.1%)	12 (3.0%)
	1	0	5 (2.5%)	5 (1.3%)
	2	2 (1.0%)	4 (2.0%)	6 (1.5%)
	3	0	1 (0.5%)	1 (0.3%)
皮膚乾燥	- Any Grade -	5 (2.6%)	7 (3.5%)	12 (3.0%)
	1	5 (2.6%)	7 (3.5%)	12 (3.0%)
紅斑	- Any Grade -	1 (0.5%)	5 (2.5%)	6 (1.5%)
	1	1 (0.5%)	4 (2.0%)	5 (1.3%)
	3	0	1 (0.5%)	1 (0.3%)
顔面腫脹	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	3 (1.5%)	3 (0.8%)
丘疹性皮疹	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
多汗症	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
蕁麻疹	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
ざ瘡様皮膚炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
そう痒性皮疹	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
過角化	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
光線過敏性反応	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
皮膚潰瘍	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
皮膚病変	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
ばら色粃糠疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
アレルギー性そう痒症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
異汗性湿疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
乾癬	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
紅斑性皮疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
寝汗	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
尋常性白斑	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
水疱性皮膚炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
全身性そう痒症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
全身性皮疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
中毒性皮疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
皮膚炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
皮膚腫瘤	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
皮膚毒性	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
皮膚嚢腫	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
皮膚反応	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
皮膚疼痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
毛孔性皮疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
薬疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
臨床検査				
- Overall -	- Any Grade -	78 (39.8%)	87 (43.9%)	165 (41.9%)
	1	17 (8.7%)	25 (12.6%)	42 (10.7%)
	2	21 (10.7%)	24 (12.1%)	45 (11.4%)
	3	20 (10.2%)	18 (9.1%)	38 (9.6%)
	4	20 (10.2%)	20 (10.1%)	40 (10.2%)
好中球数減少	- Any Grade -	46 (23.5%)	37 (18.7%)	83 (21.1%)
	1	4 (2.0%)	2 (1.0%)	6 (1.5%)
	2	9 (4.6%)	4 (2.0%)	13 (3.3%)
	3	17 (8.7%)	12 (6.1%)	29 (7.4%)
	4	16 (8.2%)	19 (9.6%)	35 (8.9%)
血小板数減少	- Any Grade -	29 (14.8%)	25 (12.6%)	54 (13.7%)
	1	14 (7.1%)	11 (5.6%)	25 (6.3%)
	2	7 (3.6%)	7 (3.5%)	14 (3.6%)
	3	5 (2.6%)	5 (2.5%)	10 (2.5%)
	4	3 (1.5%)	2 (1.0%)	5 (1.3%)
白血球数減少	- Any Grade -	25 (12.8%)	18 (9.1%)	43 (10.9%)
	1	4 (2.0%)	3 (1.5%)	7 (1.8%)
	2	12 (6.1%)	8 (4.0%)	20 (5.1%)
	3	5 (2.6%)	6 (3.0%)	11 (2.8%)
	4	4 (2.0%)	1 (0.5%)	5 (1.3%)
体重減少	- Any Grade -	10 (5.1%)	20 (10.1%)	30 (7.6%)
	1	5 (2.6%)	8 (4.0%)	13 (3.3%)
	2	4 (2.0%)	12 (6.1%)	16 (4.1%)
	3	1 (0.5%)	0	1 (0.3%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	6 (3.1%)	9 (4.5%)	15 (3.8%)
	1	4 (2.0%)	5 (2.5%)	9 (2.3%)
	2	2 (1.0%)	4 (2.0%)	6 (1.5%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	7 (3.6%)	7 (3.5%)	14 (3.6%)
	1	6 (3.1%)	2 (1.0%)	8 (2.0%)
	2	1 (0.5%)	4 (2.0%)	5 (1.3%)
	3	0	1 (0.5%)	1 (0.3%)
血中アルカリホスファターゼ増加	- Any Grade -	3 (1.5%)	9 (4.5%)	12 (3.0%)
	1	2 (1.0%)	5 (2.5%)	7 (1.8%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	0	2 (1.0%)	2 (0.5%)
血中クレアチニン増加	- Any Grade -	3 (1.5%)	7 (3.5%)	10 (2.5%)
	1	3 (1.5%)	5 (2.5%)	8 (2.0%)
	2	0	2 (1.0%)	2 (0.5%)
体重増加	- Any Grade -	6 (3.1%)	3 (1.5%)	9 (2.3%)
	1	4 (2.0%)	2 (1.0%)	6 (1.5%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
ヘモグロビン減少	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
リンパ球数減少	- Any Grade -	0	4 (2.0%)	4 (1.0%)
	1	0	2 (1.0%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
血中マグネシウム減少	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	2 (1.0%)	0	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
Ｃ－反応性蛋白増加	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
トランスアミナーゼ上昇	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	3	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
腎クレアチニン・クリアランス減少	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	2	0	2 (1.0%)	2 (0.5%)
グリコヘモグロビン増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
コルチゾール減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
トレポネーマ検査陽性	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
ヘマトクリット減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
リパーゼ増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
肝機能検査値上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
肝酵素上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
血圧上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血小板数増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
血中カルシウム増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
血中クロール減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
血中甲状腺刺激ホルモン減少	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
血中甲状腺刺激ホルモン増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
血中乳酸脱水素酵素増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
血中尿素増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
赤血球数減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
体温上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
脳性ナトリウム利尿ペプチド前駆体Ｎ端フラグメント増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
白血球数増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
便潜血陽性	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 9 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
遊離サイロキシン増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
遊離トリヨードチロニン増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
膵酵素増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
代謝および栄養障害				
- Overall -	- Any Grade -	74 (37.8%)	82 (41.4%)	156 (39.6%)
	1	29 (14.8%)	35 (17.7%)	64 (16.2%)
	2	26 (13.3%)	29 (14.6%)	55 (14.0%)
	3	9 (4.6%)	11 (5.6%)	20 (5.1%)
	4	10 (5.1%)	7 (3.5%)	17 (4.3%)
食欲減退	- Any Grade -	36 (18.4%)	54 (27.3%)	90 (22.8%)
	1	23 (11.7%)	32 (16.2%)	55 (14.0%)
	2	13 (6.6%)	20 (10.1%)	33 (8.4%)
	3	0	2 (1.0%)	2 (0.5%)
低カリウム血症	- Any Grade -	18 (9.2%)	8 (4.0%)	26 (6.6%)
	1	11 (5.6%)	6 (3.0%)	17 (4.3%)
	2	4 (2.0%)	2 (1.0%)	6 (1.5%)
	3	2 (1.0%)	0	2 (0.5%)
	4	1 (0.5%)	0	1 (0.3%)
低ナトリウム血症	- Any Grade -	14 (7.1%)	11 (5.6%)	25 (6.3%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	6 (3.1%)	6 (3.0%)	12 (3.0%)
	4	7 (3.6%)	3 (1.5%)	10 (2.5%)
低マグネシウム血症	- Any Grade -	9 (4.6%)	12 (6.1%)	21 (5.3%)
	1	5 (2.6%)	11 (5.6%)	16 (4.1%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
	3	1 (0.5%)	0	1 (0.3%)
	4	2 (1.0%)	0	2 (0.5%)
脱水	- Any Grade -	9 (4.6%)	10 (5.1%)	19 (4.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	8 (4.1%)	8 (4.0%)	16 (4.1%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
高血糖	- Any Grade -	4 (2.0%)	11 (5.6%)	15 (3.8%)
	1	1 (0.5%)	5 (2.5%)	6 (1.5%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
	3	1 (0.5%)	2 (1.0%)	3 (0.8%)
	4	0	2 (1.0%)	2 (0.5%)
低カルシウム血症	- Any Grade -	5 (2.6%)	5 (2.5%)	10 (2.5%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
	3	2 (1.0%)	1 (0.5%)	3 (0.8%)
低アルブミン血症	- Any Grade -	2 (1.0%)	3 (1.5%)	5 (1.3%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	0	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
高コレステロール血症	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	2 (1.0%)	0	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
低リン酸血症	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
高ナトリウム血症	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
高尿酸血症	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
低クロール血症	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
低血糖	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
電解質失調	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
アシドーシス	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
ビタミンＢ１２欠乏	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
過小食	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
血液量増加症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
高トリグリセリド血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
高マグネシウム血症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
水分過負荷	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
多飲症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
体液貯留	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
糖尿病	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
呼吸器、胸郭および縦隔障害				
- Overall -	- Any Grade -	78 (39.8%)	77 (38.9%)	155 (39.3%)
	1	29 (14.8%)	37 (18.7%)	66 (16.8%)
	2	31 (15.8%)	27 (13.6%)	58 (14.7%)
	3	15 (7.7%)	12 (6.1%)	27 (6.9%)
	4	1 (0.5%)	0	1 (0.3%)
	5	2 (1.0%)	1 (0.5%)	3 (0.8%)
咳嗽	- Any Grade -	25 (12.8%)	18 (9.1%)	43 (10.9%)
	1	13 (6.6%)	10 (5.1%)	23 (5.8%)
	2	10 (5.1%)	7 (3.5%)	17 (4.3%)
	3	2 (1.0%)	1 (0.5%)	3 (0.8%)
呼吸困難	- Any Grade -	18 (9.2%)	20 (10.1%)	38 (9.6%)
	1	9 (4.6%)	9 (4.5%)	18 (4.6%)
	2	7 (3.6%)	8 (4.0%)	15 (3.8%)
	3	2 (1.0%)	3 (1.5%)	5 (1.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
喀血	- Any Grade -	11 (5.6%)	15 (7.6%)	26 (6.6%)
	1	9 (4.6%)	10 (5.1%)	19 (4.8%)
	2	1 (0.5%)	5 (2.5%)	6 (1.5%)
	5	1 (0.5%)	0	1 (0.3%)
湿性咳嗽	- Any Grade -	9 (4.6%)	10 (5.1%)	19 (4.8%)
	1	6 (3.1%)	8 (4.0%)	14 (3.6%)
	2	3 (1.5%)	2 (1.0%)	5 (1.3%)
口腔咽頭痛	- Any Grade -	5 (2.6%)	12 (6.1%)	17 (4.3%)
	1	4 (2.0%)	9 (4.5%)	13 (3.3%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
鼻出血	- Any Grade -	8 (4.1%)	3 (1.5%)	11 (2.8%)
	1	6 (3.1%)	3 (1.5%)	9 (2.3%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
慢性閉塞性肺疾患	- Any Grade -	5 (2.6%)	6 (3.0%)	11 (2.8%)
	2	2 (1.0%)	4 (2.0%)	6 (1.5%)
	3	3 (1.5%)	2 (1.0%)	5 (1.3%)
しゃっくり	- Any Grade -	5 (2.6%)	4 (2.0%)	9 (2.3%)
	1	3 (1.5%)	2 (1.0%)	5 (1.3%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
肺臓炎	- Any Grade -	4 (2.0%)	4 (2.0%)	8 (2.0%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
	3	2 (1.0%)	1 (0.5%)	3 (0.8%)
発声障害	- Any Grade -	3 (1.5%)	3 (1.5%)	6 (1.5%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
肺塞栓症	- Any Grade -	3 (1.5%)	2 (1.0%)	5 (1.3%)
	3	3 (1.5%)	2 (1.0%)	5 (1.3%)
アレルギー性鼻炎	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	0	1 (0.5%)	1 (0.3%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
胸水	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
低酸素症	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	0	1 (0.5%)	1 (0.3%)
喘鳴	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
労作性呼吸困難	- Any Grade -	3 (1.5%)	0	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	3	2 (1.0%)	0	2 (0.5%)
気胸	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
急性呼吸不全	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	4	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 12 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
呼吸不全	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	5	0	1 (0.5%)	1 (0.3%)
鼻閉	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
副鼻腔うっ血	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
副鼻腔痛	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
咽喉絞扼感	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
気管支閉塞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
気管支痙攣	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
起坐呼吸	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
胸膜痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
呼吸性アシドーシス	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
喉頭刺激感	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
喉頭痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
高炭酸ガス血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
上気道の炎症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
上気道咳症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
窒息	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
低換気	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
肺気腫	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
肺梗塞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
肺出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
肺水腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
鼻乾燥	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
鼻漏	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
頻呼吸	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
副鼻腔不快感	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 13 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
無気肺	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
扁桃の炎症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
感染症および寄生虫症				
- Overall -	- Any Grade -	72 (36.7%)	72 (36.4%)	144 (36.5%)
	1	17 (8.7%)	13 (6.6%)	30 (7.6%)
	2	35 (17.9%)	43 (21.7%)	78 (19.8%)
	3	13 (6.6%)	14 (7.1%)	27 (6.9%)
	4	1 (0.5%)	1 (0.5%)	2 (0.5%)
	5	6 (3.1%)	1 (0.5%)	7 (1.8%)
上気道感染	- Any Grade -	17 (8.7%)	14 (7.1%)	31 (7.9%)
	1	5 (2.6%)	6 (3.0%)	11 (2.8%)
	2	10 (5.1%)	7 (3.5%)	17 (4.3%)
	3	2 (1.0%)	1 (0.5%)	3 (0.8%)
肺炎	- Any Grade -	12 (6.1%)	13 (6.6%)	25 (6.3%)
	2	4 (2.0%)	6 (3.0%)	10 (2.5%)
	3	5 (2.6%)	5 (2.5%)	10 (2.5%)
	4	0	1 (0.5%)	1 (0.3%)
	5	3 (1.5%)	1 (0.5%)	4 (1.0%)
尿路感染	- Any Grade -	6 (3.1%)	13 (6.6%)	19 (4.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	4 (2.0%)	10 (5.1%)	14 (3.6%)
	3	2 (1.0%)	2 (1.0%)	4 (1.0%)
気管支炎	- Any Grade -	5 (2.6%)	9 (4.5%)	14 (3.6%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	4 (2.0%)	8 (4.0%)	12 (3.0%)
口腔カンジダ症	- Any Grade -	3 (1.5%)	6 (3.0%)	9 (2.3%)
	1	1 (0.5%)	5 (2.5%)	6 (1.5%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
気道感染	- Any Grade -	5 (2.6%)	2 (1.0%)	7 (1.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	4 (2.0%)	1 (0.5%)	5 (1.3%)
	3	0	1 (0.5%)	1 (0.3%)
肺感染	- Any Grade -	4 (2.0%)	3 (1.5%)	7 (1.8%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
	3	3 (1.5%)	0	3 (0.8%)
上咽頭炎	- Any Grade -	2 (1.0%)	4 (2.0%)	6 (1.5%)
	1	1 (0.5%)	4 (2.0%)	5 (1.3%)
	2	1 (0.5%)	0	1 (0.3%)
下気道感染	- Any Grade -	0	5 (2.5%)	5 (1.3%)
	2	0	3 (1.5%)	3 (0.8%)
	3	0	2 (1.0%)	2 (0.5%)
歯感染	- Any Grade -	2 (1.0%)	3 (1.5%)	5 (1.3%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
インフルエンザ	- Any Grade -	4 (2.0%)	0	4 (1.0%)
	1	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
咽頭炎	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 14 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
鼻炎	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
ウイルス性気道感染	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
医療機器関連感染	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
帯状疱疹	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
副鼻腔炎	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
ヘルペスウイルス感染	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
外耳炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
感染性嚢腫	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
結膜炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
口角口唇炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
口腔ヘルペス	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
耳感染	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	2	0	2 (1.0%)	2 (0.5%)
真菌感染	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
精巣上体炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
中耳炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
膿疱性皮疹	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
皮膚感染	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
毛包炎	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	2 (1.0%)	0	2 (0.5%)
膀胱炎	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
カンジダ感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
クロストリジウム・ディフィシレ感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
クロストリジウム・ディフィシレ大腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
コロナウイルス感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
サイトメガロウイルス感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
トリコモナス症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
胃腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
感染による慢性閉塞性気道疾患の増悪	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
気管気管支炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
憩室炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
限局性感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
口腔真菌感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
口唇感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
好中球減少性敗血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
細菌感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
細菌性上気道感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
四肢膿瘍	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
歯膿瘍	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
消化管感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
丹毒	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
単純ヘルペス	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
腸球菌性尿路感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
爪囲炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
膿気胸	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
敗血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
敗血症性ショック	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
肺膿瘍	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
肺敗血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
白癬感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
麦粒腫	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
皮下組織膿瘍	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
皮膚真菌感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
慢性副鼻腔炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
肛門カンジダ症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
膣感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
筋骨格系および結合組織障害				
- Overall -	- Any Grade -	63 (32.1%)	61 (30.8%)	124 (31.5%)
	1	31 (15.8%)	33 (16.7%)	64 (16.2%)
	2	28 (14.3%)	23 (11.6%)	51 (12.9%)
	3	4 (2.0%)	5 (2.5%)	9 (2.3%)
背部痛	- Any Grade -	19 (9.7%)	17 (8.6%)	36 (9.1%)
	1	11 (5.6%)	8 (4.0%)	19 (4.8%)
	2	7 (3.6%)	9 (4.5%)	16 (4.1%)
	3	1 (0.5%)	0	1 (0.3%)
関節痛	- Any Grade -	13 (6.6%)	18 (9.1%)	31 (7.9%)
	1	7 (3.6%)	13 (6.6%)	20 (5.1%)
	2	5 (2.6%)	5 (2.5%)	10 (2.5%)
	3	1 (0.5%)	0	1 (0.3%)
筋骨格痛	- Any Grade -	11 (5.6%)	12 (6.1%)	23 (5.8%)
	1	6 (3.1%)	7 (3.5%)	13 (3.3%)
	2	4 (2.0%)	5 (2.5%)	9 (2.3%)
	3	1 (0.5%)	0	1 (0.3%)
四肢痛	- Any Grade -	6 (3.1%)	13 (6.6%)	19 (4.8%)
	1	4 (2.0%)	7 (3.5%)	11 (2.8%)
	2	2 (1.0%)	5 (2.5%)	7 (1.8%)
	3	0	1 (0.5%)	1 (0.3%)
筋肉痛	- Any Grade -	8 (4.1%)	8 (4.0%)	16 (4.1%)
	1	5 (2.6%)	6 (3.0%)	11 (2.8%)
	2	3 (1.5%)	2 (1.0%)	5 (1.3%)
筋力低下	- Any Grade -	5 (2.6%)	7 (3.5%)	12 (3.0%)
	1	3 (1.5%)	3 (1.5%)	6 (1.5%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
	3	0	2 (1.0%)	2 (0.5%)
筋骨格系胸痛	- Any Grade -	4 (2.0%)	4 (2.0%)	8 (2.0%)
	1	2 (1.0%)	3 (1.5%)	5 (1.3%)
	2	2 (1.0%)	0	2 (0.5%)
	3	0	1 (0.5%)	1 (0.3%)
骨痛	- Any Grade -	6 (3.1%)	2 (1.0%)	8 (2.0%)
	1	0	1 (0.5%)	1 (0.3%)
	2	6 (3.1%)	1 (0.5%)	7 (1.8%)
頚部痛	- Any Grade -	5 (2.6%)	1 (0.5%)	6 (1.5%)
	1	4 (2.0%)	1 (0.5%)	5 (1.3%)
	2	1 (0.5%)	0	1 (0.3%)
筋痙縮	- Any Grade -	1 (0.5%)	4 (2.0%)	5 (1.3%)
	1	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 17 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
脊椎痛	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	1 (0.5%)	0	1 (0.3%)
関節炎	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
ミオパチー	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
横紋筋融解症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
顎痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
筋骨格硬直	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
筋骨格不快感	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
高クレアチン血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
側腹部痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
椎間板突出	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
病的骨折	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
変形性関節症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
肋軟骨炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
神経系障害				
- Overall -	- Any Grade -	50 (25.5%)	74 (37.4%)	124 (31.5%)
	1	33 (16.8%)	36 (18.2%)	69 (17.5%)
	2	15 (7.7%)	31 (15.7%)	46 (11.7%)
	3	2 (1.0%)	7 (3.5%)	9 (2.3%)
頭痛	- Any Grade -	23 (11.7%)	24 (12.1%)	47 (11.9%)
	1	16 (8.2%)	15 (7.6%)	31 (7.9%)
	2	7 (3.6%)	9 (4.5%)	16 (4.1%)
浮動性めまい	- Any Grade -	11 (5.6%)	19 (9.6%)	30 (7.6%)
	1	8 (4.1%)	15 (7.6%)	23 (5.8%)
	2	3 (1.5%)	4 (2.0%)	7 (1.8%)
味覚異常	- Any Grade -	9 (4.6%)	8 (4.0%)	17 (4.3%)
	1	8 (4.1%)	6 (3.0%)	14 (3.6%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
末梢性ニューロパチー	- Any Grade -	5 (2.6%)	8 (4.0%)	13 (3.3%)
	1	4 (2.0%)	3 (1.5%)	7 (1.8%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	0	3 (1.5%)	3 (0.8%)
末梢性感覚ニューロパチー	- Any Grade -	2 (1.0%)	8 (4.0%)	10 (2.5%)
	1	2 (1.0%)	7 (3.5%)	9 (2.3%)
	2	0	1 (0.5%)	1 (0.3%)
錯感覚	- Any Grade -	1 (0.5%)	7 (3.5%)	8 (2.0%)
	1	1 (0.5%)	4 (2.0%)	5 (1.3%)
	2	0	3 (1.5%)	3 (0.8%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 18 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
傾眠	- Any Grade -	1 (0.5%)	5 (2.5%)	6 (1.5%)
	1	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	0	2 (1.0%)	2 (0.5%)
失神	- Any Grade -	1 (0.5%)	5 (2.5%)	6 (1.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
	3	1 (0.5%)	2 (1.0%)	3 (0.8%)
記憶障害	- Any Grade -	1 (0.5%)	4 (2.0%)	5 (1.3%)
	1	1 (0.5%)	4 (2.0%)	5 (1.3%)
健忘	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
感覚鈍麻	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
嗜眠	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
構語障害	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
坐骨神経痛	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
失語症	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
失神寸前の状態	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
平衡障害	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
ギラン・バレー症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
ヘルペス後神経痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
悪性疾患に伴う多発ニューロパチー	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
異常感覚	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
一過性脳虚血発作	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
運動失調	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
下肢静止不能症候群	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
過眠症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
筋緊張低下	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
緊張性頭痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
三叉神経痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
手根管症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
振戦	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
声帯麻痺	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
脊髄浮腫	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
多発ニューロパチー	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
代謝性脳症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
中毒性ニューロパチー	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
脳血管発作	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
片頭痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
末梢性運動ニューロパチー	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
傷害、中毒および処置合併症				
- Overall -	- Any Grade -	24 (12.2%)	34 (17.2%)	58 (14.7%)
	1	8 (4.1%)	17 (8.6%)	25 (6.3%)
	2	12 (6.1%)	10 (5.1%)	22 (5.6%)
	3	3 (1.5%)	7 (3.5%)	10 (2.5%)
	4	1 (0.5%)	0	1 (0.3%)
注入に伴う反応	- Any Grade -	10 (5.1%)	11 (5.6%)	21 (5.3%)
	1	4 (2.0%)	1 (0.5%)	5 (1.3%)
	2	5 (2.6%)	6 (3.0%)	11 (2.8%)
	3	1 (0.5%)	4 (2.0%)	5 (1.3%)
転倒	- Any Grade -	4 (2.0%)	8 (4.0%)	12 (3.0%)
	1	2 (1.0%)	8 (4.0%)	10 (2.5%)
	2	2 (1.0%)	0	2 (0.5%)
熱傷	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
肋骨骨折	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
圧迫骨折	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
大腿骨骨折	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
頭部損傷	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
肉離れ	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
放射線皮膚損傷	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
気管出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
胸椎骨折	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 20 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
血管確保合併症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
股関節部骨折	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
腰椎骨折	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
骨折	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
鎖骨骨折	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
挫傷	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
処置による疼痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
脊椎圧迫骨折	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
切開部位痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
節足動物刺傷	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
足関節部骨折	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
足骨折	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
半月板損傷	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
皮下血腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
放射線関連痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
放射線心膜炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
放射線性食道炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
放射線性肺臓炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
放射線損傷	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血管障害				
- Overall -	- Any Grade -	21 (10.7%)	33 (16.7%)	54 (13.7%)
	1	7 (3.6%)	12 (6.1%)	19 (4.8%)
	2	10 (5.1%)	16 (8.1%)	26 (6.6%)
	3	4 (2.0%)	5 (2.5%)	9 (2.3%)
高血圧	- Any Grade -	6 (3.1%)	15 (7.6%)	21 (5.3%)
	1	0	5 (2.5%)	5 (1.3%)
	2	3 (1.5%)	7 (3.5%)	10 (2.5%)
	3	3 (1.5%)	3 (1.5%)	6 (1.5%)
低血圧	- Any Grade -	9 (4.6%)	8 (4.0%)	17 (4.3%)
	1	5 (2.6%)	3 (1.5%)	8 (2.0%)
	2	4 (2.0%)	5 (2.5%)	9 (2.3%)
上大静脈症候群	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
起立性低血圧	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血栓性静脈炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
深部静脈血栓症	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
静脈炎	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
ほてり	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
血管炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
上大静脈閉塞	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
静脈障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
大動脈瘤	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
潮紅	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
表在性血栓性静脈炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
末梢動脈閉塞	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
末梢動脈閉塞性疾患	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
精神障害				
- Overall -	- Any Grade -	24 (12.2%)	25 (12.6%)	49 (12.4%)
	1	13 (6.6%)	5 (2.5%)	18 (4.6%)
	2	10 (5.1%)	18 (9.1%)	28 (7.1%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
	4	0	1 (0.5%)	1 (0.3%)
不眠症	- Any Grade -	13 (6.6%)	15 (7.6%)	28 (7.1%)
	1	8 (4.1%)	5 (2.5%)	13 (3.3%)
	2	5 (2.6%)	10 (5.1%)	15 (3.8%)
不安	- Any Grade -	3 (1.5%)	6 (3.0%)	9 (2.3%)
	1	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	2 (1.0%)	3 (1.5%)	5 (1.3%)
うつ病	- Any Grade -	3 (1.5%)	5 (2.5%)	8 (2.0%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	2 (1.0%)	3 (1.5%)	5 (1.3%)
	4	0	1 (0.5%)	1 (0.3%)
錯乱状態	- Any Grade -	3 (1.5%)	3 (1.5%)	6 (1.5%)
	1	2 (1.0%)	0	2 (0.5%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 22 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
激越	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
抑うつ気分	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
譫妄	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	2	0	2 (1.0%)	2 (0.5%)
アルコール乱用	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
恐怖	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
幻覚	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
失見当識	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
人格変化	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
睡眠障害	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
閉所恐怖症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
落ち着きのなさ	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
内分泌障害				
- Overall -	- Any Grade -	9 (4.6%)	28 (14.1%)	37 (9.4%)
	1	6 (3.1%)	12 (6.1%)	18 (4.6%)
	2	2 (1.0%)	16 (8.1%)	18 (4.6%)
	4	1 (0.5%)	0	1 (0.3%)
甲状腺機能低下症	- Any Grade -	1 (0.5%)	20 (10.1%)	21 (5.3%)
	1	1 (0.5%)	8 (4.0%)	9 (2.3%)
	2	0	12 (6.1%)	12 (3.0%)
甲状腺機能亢進症	- Any Grade -	5 (2.6%)	11 (5.6%)	16 (4.1%)
	1	5 (2.6%)	8 (4.0%)	13 (3.3%)
	2	0	3 (1.5%)	3 (0.8%)
自己免疫性甲状腺炎	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
副腎機能不全	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
抗利尿ホルモン不適合分泌	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
甲状腺炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
腎および尿路障害				
- Overall -	- Any Grade -	16 (8.2%)	13 (6.6%)	29 (7.4%)
	1	10 (5.1%)	4 (2.0%)	14 (3.6%)
	2	5 (2.6%)	5 (2.5%)	10 (2.5%)
	3	1 (0.5%)	3 (1.5%)	4 (1.0%)
	4	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
急性腎障害	- Any Grade -	2 (1.0%)	5 (2.5%)	7 (1.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	0	3 (1.5%)	3 (0.8%)
頻尿	- Any Grade -	5 (2.6%)	1 (0.5%)	6 (1.5%)
	1	5 (2.6%)	0	5 (1.3%)
	2	0	1 (0.5%)	1 (0.3%)
排尿困難	- Any Grade -	3 (1.5%)	2 (1.0%)	5 (1.3%)
	1	3 (1.5%)	2 (1.0%)	5 (1.3%)
尿失禁	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	0	1 (0.3%)
尿閉	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	2 (1.0%)	0	2 (0.5%)
	2	0	2 (1.0%)	2 (0.5%)
血尿	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
尿流量減少	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	2 (1.0%)	0	2 (0.5%)
腎炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
切迫性尿失禁	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
蛋白尿	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
糖尿	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
尿細管間質性腎炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
排尿躊躇	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
乏尿	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
慢性腎臓病	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
夜間頻尿	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
心臓障害				
- Overall -	- Any Grade -	9 (4.6%)	14 (7.1%)	23 (5.8%)
	1	2 (1.0%)	6 (3.0%)	8 (2.0%)
	2	3 (1.5%)	5 (2.5%)	8 (2.0%)
	3	2 (1.0%)	2 (1.0%)	4 (1.0%)
	4	0	1 (0.5%)	1 (0.3%)
	5	2 (1.0%)	0	2 (0.5%)
心房細動	- Any Grade -	3 (1.5%)	5 (2.5%)	8 (2.0%)
	2	3 (1.5%)	4 (2.0%)	7 (1.8%)
	3	0	1 (0.5%)	1 (0.3%)
頻脈	- Any Grade -	0	5 (2.5%)	5 (1.3%)
	1	0	3 (1.5%)	3 (0.8%)
	2	0	2 (1.0%)	2 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 24 of 27

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
動悸	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	1 (0.5%)	0	1 (0.3%)
洞性頻脈	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
心嚢液貯留	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	4	0	1 (0.5%)	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
うっ血性心不全	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
完全房室ブロック	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
上室性期外収縮	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
上室性頻脈	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
心タンポナーデ	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
心肺不全	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
心不全	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
洞性徐脈	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
眼障害				
- Overall -	- Any Grade -	9 (4.6%)	9 (4.5%)	18 (4.6%)
	1	8 (4.1%)	4 (2.0%)	12 (3.0%)
	2	0	5 (2.5%)	5 (1.3%)
	3	1 (0.5%)	0	1 (0.3%)
霧視	- Any Grade -	3 (1.5%)	2 (1.0%)	5 (1.3%)
	1	3 (1.5%)	1 (0.5%)	4 (1.0%)
	2	0	1 (0.5%)	1 (0.3%)
硝子体浮遊物	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
眼窩周囲浮腫	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
白内障	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
遠視	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
眼そう痒症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
眼乾燥	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
眼球浮腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
眼刺激	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
眼痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
近視	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
結膜出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
視力障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
複視	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
流涙増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
耳および迷路障害				
- Overall -	- Any Grade -	8 (4.1%)	8 (4.0%)	16 (4.1%)
	1	6 (3.1%)	5 (2.5%)	11 (2.8%)
	2	2 (1.0%)	3 (1.5%)	5 (1.3%)
回転性めまい	- Any Grade -	6 (3.1%)	3 (1.5%)	9 (2.3%)
	1	4 (2.0%)	3 (1.5%)	7 (1.8%)
	2	2 (1.0%)	0	2 (0.5%)
耳痛	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
耳鳴	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
耳そう痒症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
耳閉	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
聴覚障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
片耳難聴	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
生殖系および乳房障害				
- Overall -	- Any Grade -	5 (2.6%)	4 (2.0%)	9 (2.3%)
	1	3 (1.5%)	2 (1.0%)	5 (1.3%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	1 (0.5%)	0	1 (0.3%)
良性前立腺肥大症	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
乳房痛	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
月経過多	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
乳房腫脹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
勃起不全	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
腟出血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
腟分泌物	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）				
- Overall -	- Any Grade -	5 (2.6%)	2 (1.0%)	7 (1.8%)
	1	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
腫瘍疼痛	- Any Grade -	4 (2.0%)	0	4 (1.0%)
	1	2 (1.0%)	0	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
遠隔転移を伴う新生物	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
癌疼痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
浸潤性乳管癌	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
免疫系障害				
- Overall -	- Any Grade -	2 (1.0%)	4 (2.0%)	6 (1.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
	3	0	1 (0.5%)	1 (0.3%)
過敏症	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
薬物過敏症	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
アナフィラキシー反応	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
造影剤反応	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
肝胆道系障害				
- Overall -	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	3	0	2 (1.0%)	2 (0.5%)
黄疸	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
胆管炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_24APR2018_GO30081.out
13SEP2018 18:43 Page 27 of 27

［5.3.5.1-2 t_ae_ctc_SE_24APR2018_GO30081を再掲］

表 2.7.6.2.1.1-2 因果関係が否定できない有害事象の要約（GO30081試験）

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
- Any adverse events -	- Any Grade -	181 (92.3%)	188 (94.9%)	369 (93.7%)
	1	29 (14.8%)	12 (6.1%)	41 (10.4%)
	2	39 (19.9%)	61 (30.8%)	100 (25.4%)
	3	60 (30.6%)	67 (33.8%)	127 (32.2%)
	4	50 (25.5%)	45 (22.7%)	95 (24.1%)
	5	3 (1.5%)	3 (1.5%)	6 (1.5%)
血液およびリンパ系障害				
- Overall -	- Any Grade -	115 (58.7%)	122 (61.6%)	237 (60.2%)
	1	8 (4.1%)	7 (3.5%)	15 (3.8%)
	2	32 (16.3%)	38 (19.2%)	70 (17.8%)
	3	42 (21.4%)	51 (25.8%)	93 (23.6%)
	4	33 (16.8%)	25 (12.6%)	58 (14.7%)
	5	0	1 (0.5%)	1 (0.3%)
貧血	- Any Grade -	65 (33.2%)	77 (38.9%)	142 (36.0%)
	1	9 (4.6%)	10 (5.1%)	19 (4.8%)
	2	32 (16.3%)	39 (19.7%)	71 (18.0%)
	3	21 (10.7%)	28 (14.1%)	49 (12.4%)
	4	3 (1.5%)	0	3 (0.8%)
好中球減少症	- Any Grade -	68 (34.7%)	72 (36.4%)	140 (35.5%)
	1	6 (3.1%)	1 (0.5%)	7 (1.8%)
	2	14 (7.1%)	25 (12.6%)	39 (9.9%)
	3	26 (13.3%)	26 (13.1%)	52 (13.2%)
	4	22 (11.2%)	19 (9.6%)	41 (10.4%)
	5	0	1 (0.5%)	1 (0.3%)
血小板減少症	- Any Grade -	29 (14.8%)	32 (16.2%)	61 (15.5%)
	1	5 (2.6%)	5 (2.5%)	10 (2.5%)
	2	9 (4.6%)	7 (3.5%)	16 (4.1%)
	3	9 (4.6%)	13 (6.6%)	22 (5.6%)
	4	6 (3.1%)	7 (3.5%)	13 (3.3%)
白血球減少症	- Any Grade -	18 (9.2%)	25 (12.6%)	43 (10.9%)
	1	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	9 (4.6%)	12 (6.1%)	21 (5.3%)
	3	6 (3.1%)	4 (2.0%)	10 (2.5%)
	4	2 (1.0%)	6 (3.0%)	8 (2.0%)
発熱性好中球減少症	- Any Grade -	12 (6.1%)	6 (3.0%)	18 (4.6%)
	3	7 (3.6%)	4 (2.0%)	11 (2.8%)
	4	5 (2.6%)	2 (1.0%)	7 (1.8%)
汎血球減少症	- Any Grade -	4 (2.0%)	2 (1.0%)	6 (1.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
	4	2 (1.0%)	0	2 (0.5%)
巨赤芽球性貧血	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
血液毒性	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血小板増加症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
白血球増加症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 1 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
胃腸障害				
- Overall -	- Any Grade -	84 (42.9%)	96 (48.5%)	180 (45.7%)
	1	52 (26.5%)	51 (25.8%)	103 (26.1%)
	2	27 (13.8%)	33 (16.7%)	60 (15.2%)
	3	5 (2.6%)	12 (6.1%)	17 (4.3%)
悪心	- Any Grade -	59 (30.1%)	63 (31.8%)	122 (31.0%)
	1	37 (18.9%)	37 (18.7%)	74 (18.8%)
	2	21 (10.7%)	25 (12.6%)	46 (11.7%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
嘔吐	- Any Grade -	22 (11.2%)	27 (13.6%)	49 (12.4%)
	1	11 (5.6%)	16 (8.1%)	27 (6.9%)
	2	8 (4.1%)	9 (4.5%)	17 (4.3%)
	3	3 (1.5%)	2 (1.0%)	5 (1.3%)
便秘	- Any Grade -	25 (12.8%)	20 (10.1%)	45 (11.4%)
	1	21 (10.7%)	15 (7.6%)	36 (9.1%)
	2	4 (2.0%)	4 (2.0%)	8 (2.0%)
	3	0	1 (0.5%)	1 (0.3%)
下痢	- Any Grade -	19 (9.7%)	19 (9.6%)	38 (9.6%)
	1	14 (7.1%)	12 (6.1%)	26 (6.6%)
	2	4 (2.0%)	3 (1.5%)	7 (1.8%)
	3	1 (0.5%)	4 (2.0%)	5 (1.3%)
口内炎	- Any Grade -	6 (3.1%)	8 (4.0%)	14 (3.6%)
	1	3 (1.5%)	7 (3.5%)	10 (2.5%)
	2	3 (1.5%)	1 (0.5%)	4 (1.0%)
上腹部痛	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
口唇炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
口内乾燥	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	2 (1.0%)	0	2 (0.5%)
腹部膨満	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
アフタ性潰瘍	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
イレウス	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
レッチング	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
急性膵炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
憩室穿孔	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
口腔障害	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
口腔内潰瘍形成	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
自己免疫性大腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
消化不良	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 2 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
大腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
直腸炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
粘液便	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
腹痛	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
腹部不快感	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
肛門失禁	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
肛門出血	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
膵炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
皮膚および皮下組織障害				
- Overall -	- Any Grade -	78 (39.8%)	90 (45.5%)	168 (42.6%)
	1	39 (19.9%)	44 (22.2%)	83 (21.1%)
	2	39 (19.9%)	42 (21.2%)	81 (20.6%)
	3	0	4 (2.0%)	4 (1.0%)
脱毛症	- Any Grade -	66 (33.7%)	69 (34.8%)	135 (34.3%)
	1	30 (15.3%)	30 (15.2%)	60 (15.2%)
	2	36 (18.4%)	39 (19.7%)	75 (19.0%)
発疹	- Any Grade -	9 (4.6%)	12 (6.1%)	21 (5.3%)
	1	8 (4.1%)	11 (5.6%)	19 (4.8%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
そう痒症	- Any Grade -	5 (2.6%)	9 (4.5%)	14 (3.6%)
	1	4 (2.0%)	7 (3.5%)	11 (2.8%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
斑状丘疹状皮疹	- Any Grade -	2 (1.0%)	6 (3.0%)	8 (2.0%)
	1	0	3 (1.5%)	3 (0.8%)
	2	2 (1.0%)	2 (1.0%)	4 (1.0%)
	3	0	1 (0.5%)	1 (0.3%)
皮膚乾燥	- Any Grade -	4 (2.0%)	3 (1.5%)	7 (1.8%)
	1	4 (2.0%)	3 (1.5%)	7 (1.8%)
紅斑	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	3	0	1 (0.5%)	1 (0.3%)
ざ瘡様皮膚炎	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
そう痒性皮疹	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
丘疹性皮疹	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
蕁麻疹	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
過角化	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
乾癬	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
顔面腫脹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
光線過敏性反応	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
紅斑性皮疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
尋常性白斑	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
全身性そう痒症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
全身性皮疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
中毒性皮疹	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
皮膚炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
皮膚毒性	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
皮膚病変	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
毛孔性皮疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
一般・全身障害および投与部位の状態				
- Overall -	- Any Grade -	60 (30.6%)	70 (35.4%)	130 (33.0%)
	1	32 (16.3%)	26 (13.1%)	58 (14.7%)
	2	24 (12.2%)	37 (18.7%)	61 (15.5%)
	3	4 (2.0%)	6 (3.0%)	10 (2.5%)
	5	0	1 (0.5%)	1 (0.3%)
疲労	- Any Grade -	38 (19.4%)	42 (21.2%)	80 (20.3%)
	1	23 (11.7%)	13 (6.6%)	36 (9.1%)
	2	14 (7.1%)	26 (13.1%)	40 (10.2%)
	3	1 (0.5%)	3 (1.5%)	4 (1.0%)
無力症	- Any Grade -	14 (7.1%)	17 (8.6%)	31 (7.9%)
	1	5 (2.6%)	7 (3.5%)	12 (3.0%)
	2	7 (3.6%)	7 (3.5%)	14 (3.6%)
	3	2 (1.0%)	3 (1.5%)	5 (1.3%)
発熱	- Any Grade -	6 (3.1%)	5 (2.5%)	11 (2.8%)
	1	6 (3.1%)	3 (1.5%)	9 (2.3%)
	2	0	2 (1.0%)	2 (0.5%)
粘膜の炎症	- Any Grade -	7 (3.6%)	3 (1.5%)	10 (2.5%)
	1	6 (3.1%)	2 (1.0%)	8 (2.0%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
倦怠感	- Any Grade -	3 (1.5%)	4 (2.0%)	7 (1.8%)
	1	2 (1.0%)	3 (1.5%)	5 (1.3%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
末梢性浮腫	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
溢出	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
疼痛	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
悪寒	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
インフルエンザ様疾患	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
顔面浮腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
死亡	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	5	0	1 (0.5%)	1 (0.3%)
全身健康状態低下	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
注射部位漏出	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
臨床検査				
- Overall -	- Any Grade -	65 (33.2%)	60 (30.3%)	125 (31.7%)
	1	11 (5.6%)	13 (6.6%)	24 (6.1%)
	2	16 (8.2%)	15 (7.6%)	31 (7.9%)
	3	18 (9.2%)	13 (6.6%)	31 (7.9%)
	4	20 (10.2%)	19 (9.6%)	39 (9.9%)
好中球数減少	- Any Grade -	45 (23.0%)	35 (17.7%)	80 (20.3%)
	1	4 (2.0%)	2 (1.0%)	6 (1.5%)
	2	8 (4.1%)	5 (2.5%)	13 (3.3%)
	3	17 (8.7%)	10 (5.1%)	27 (6.9%)
	4	16 (8.2%)	18 (9.1%)	34 (8.6%)
血小板数減少	- Any Grade -	28 (14.3%)	24 (12.1%)	52 (13.2%)
	1	14 (7.1%)	10 (5.1%)	24 (6.1%)
	2	7 (3.6%)	7 (3.5%)	14 (3.6%)
	3	4 (2.0%)	5 (2.5%)	9 (2.3%)
	4	3 (1.5%)	2 (1.0%)	5 (1.3%)
白血球数減少	- Any Grade -	25 (12.8%)	16 (8.1%)	41 (10.4%)
	1	4 (2.0%)	2 (1.0%)	6 (1.5%)
	2	12 (6.1%)	8 (4.0%)	20 (5.1%)
	3	5 (2.6%)	5 (2.5%)	10 (2.5%)
	4	4 (2.0%)	1 (0.5%)	5 (1.3%)
体重減少	- Any Grade -	4 (2.0%)	8 (4.0%)	12 (3.0%)
	1	2 (1.0%)	4 (2.0%)	6 (1.5%)
	2	1 (0.5%)	4 (2.0%)	5 (1.3%)
	3	1 (0.5%)	0	1 (0.3%)
アラニンアミノトランスフェラーゼ増加	- Any Grade -	3 (1.5%)	5 (2.5%)	8 (2.0%)
	1	3 (1.5%)	1 (0.5%)	4 (1.0%)
	2	0	3 (1.5%)	3 (0.8%)
	3	0	1 (0.5%)	1 (0.3%)
アスパラギン酸アミノトランスフェラーゼ増加	- Any Grade -	2 (1.0%)	3 (1.5%)	5 (1.3%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	0	2 (1.0%)	2 (0.5%)
血中アルカリホスファターゼ増加	- Any Grade -	1 (0.5%)	4 (2.0%)	5 (1.3%)
	1	1 (0.5%)	3 (1.5%)	4 (1.0%)
	3	0	1 (0.5%)	1 (0.3%)
ヘモグロビン減少	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 5 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
γ－グルタミルトランスフェラーゼ増加	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
血中クレアチニン増加	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
リンパ球数減少	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
血中マグネシウム減少	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	1	2 (1.0%)	0	2 (0.5%)
Ｃ－反応性蛋白増加	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
コルチゾール減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
トランスアミナーゼ上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
ヘマトクリット減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
肝機能検査値上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
腎クレアチニン・クリアランス減少	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
赤血球数減少	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
体温上昇	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
脳性ナトリウム利尿ペプチド前駆体Ｎ端フラグメント増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
遊離サイロキシン増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
遊離トリヨードチロニン増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
膵酵素増加	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
代謝および栄養障害				
- Overall -	- Any Grade -	41 (20.9%)	48 (24.2%)	89 (22.6%)
	1	24 (12.2%)	28 (14.1%)	52 (13.2%)
	2	13 (6.6%)	17 (8.6%)	30 (7.6%)
	3	2 (1.0%)	3 (1.5%)	5 (1.3%)
	4	2 (1.0%)	0	2 (0.5%)
食欲減退	- Any Grade -	26 (13.3%)	41 (20.7%)	67 (17.0%)
	1	18 (9.2%)	26 (13.1%)	44 (11.2%)
	2	8 (4.1%)	13 (6.6%)	21 (5.3%)
	3	0	2 (1.0%)	2 (0.5%)
低マグネシウム血症	- Any Grade -	7 (3.6%)	7 (3.5%)	14 (3.6%)
	1	4 (2.0%)	6 (3.0%)	10 (2.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
	3	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 6 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
脱水	- Any Grade -	6 (3.1%)	4 (2.0%)	10 (2.5%)
	2	5 (2.6%)	3 (1.5%)	8 (2.0%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
低カリウム血症	- Any Grade -	6 (3.1%)	2 (1.0%)	8 (2.0%)
	1	4 (2.0%)	1 (0.5%)	5 (1.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
低カルシウム血症	- Any Grade -	3 (1.5%)	0	3 (0.8%)
	1	2 (1.0%)	0	2 (0.5%)
	3	1 (0.5%)	0	1 (0.3%)
低アルブミン血症	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
過小食	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
血液量増加症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
高コレステロール血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
低ナトリウム血症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
低リン酸血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
糖尿病	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
神経系障害				
- Overall -	- Any Grade -	22 (11.2%)	29 (14.6%)	51 (12.9%)
	1	18 (9.2%)	17 (8.6%)	35 (8.9%)
	2	4 (2.0%)	9 (4.5%)	13 (3.3%)
	3	0	3 (1.5%)	3 (0.8%)
味覚異常	- Any Grade -	8 (4.1%)	5 (2.5%)	13 (3.3%)
	1	7 (3.6%)	5 (2.5%)	12 (3.0%)
	2	1 (0.5%)	0	1 (0.3%)
末梢性ニューロパチー	- Any Grade -	4 (2.0%)	6 (3.0%)	10 (2.5%)
	1	4 (2.0%)	3 (1.5%)	7 (1.8%)
	2	0	1 (0.5%)	1 (0.3%)
	3	0	2 (1.0%)	2 (0.5%)
頭痛	- Any Grade -	4 (2.0%)	4 (2.0%)	8 (2.0%)
	1	3 (1.5%)	2 (1.0%)	5 (1.3%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
末梢性感覚ニューロパチー	- Any Grade -	1 (0.5%)	7 (3.5%)	8 (2.0%)
	1	1 (0.5%)	6 (3.0%)	7 (1.8%)
	2	0	1 (0.5%)	1 (0.3%)
浮動性めまい	- Any Grade -	1 (0.5%)	4 (2.0%)	5 (1.3%)
	1	1 (0.5%)	2 (1.0%)	3 (0.8%)
	2	0	2 (1.0%)	2 (0.5%)
錯感覚	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
傾眠	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 7 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
ギラン・バレー症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
感覚鈍麻	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
記憶障害	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
三叉神経痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
失語症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
失神	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
失神寸前の状態	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
振戦	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
多発ニューロパチー	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
中毒性ニューロパチー	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
嗜眠	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
感染症および寄生虫症				
- Overall -	- Any Grade -	17 (8.7%)	19 (9.6%)	36 (9.1%)
	1	3 (1.5%)	3 (1.5%)	6 (1.5%)
	2	8 (4.1%)	10 (5.1%)	18 (4.6%)
	3	3 (1.5%)	4 (2.0%)	7 (1.8%)
	4	1 (0.5%)	1 (0.5%)	2 (0.5%)
	5	2 (1.0%)	1 (0.5%)	3 (0.8%)
肺炎	- Any Grade -	3 (1.5%)	5 (2.5%)	8 (2.0%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	0	2 (1.0%)	2 (0.5%)
	4	0	1 (0.5%)	1 (0.3%)
	5	1 (0.5%)	1 (0.5%)	2 (0.5%)
気管支炎	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	1 (0.5%)	0	1 (0.3%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
上気道感染	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
肺感染	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	2	0	1 (0.5%)	1 (0.3%)
	3	2 (1.0%)	0	2 (0.5%)
口腔カンジダ症	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
尿路感染	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	0	1 (0.5%)	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
膿疱性皮疹	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
サイトメガロウイルス感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 8 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
医療機器関連感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
咽頭炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
下気道感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
外耳炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
気道感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
結膜炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
口角口唇炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
口唇感染	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
好中球減少性敗血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	4	1 (0.5%)	0	1 (0.3%)
耳感染	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
上咽頭炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
帯状疱疹	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
中耳炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
敗血症性ショック	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
毛包炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
内分泌障害				
- Overall -	- Any Grade -	6 (3.1%)	26 (13.1%)	32 (8.1%)
	1	4 (2.0%)	11 (5.6%)	15 (3.8%)
	2	2 (1.0%)	15 (7.6%)	17 (4.3%)
甲状腺機能低下症	- Any Grade -	1 (0.5%)	19 (9.6%)	20 (5.1%)
	1	1 (0.5%)	7 (3.5%)	8 (2.0%)
	2	0	12 (6.1%)	12 (3.0%)
甲状腺機能亢進症	- Any Grade -	3 (1.5%)	10 (5.1%)	13 (3.3%)
	1	3 (1.5%)	8 (4.0%)	11 (2.8%)
	2	0	2 (1.0%)	2 (0.5%)
自己免疫性甲状腺炎	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
副腎機能不全	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
甲状腺炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
呼吸器、胸郭および縦隔障害				
- Overall -	- Any Grade -	11 (5.6%)	14 (7.1%)	25 (6.3%)
	1	5 (2.6%)	7 (3.5%)	12 (3.0%)
	2	3 (1.5%)	5 (2.5%)	8 (2.0%)
	3	3 (1.5%)	2 (1.0%)	5 (1.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
しゃっくり	- Any Grade -	3 (1.5%)	4 (2.0%)	7 (1.8%)
	1	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
肺臓炎	- Any Grade -	4 (2.0%)	3 (1.5%)	7 (1.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
	3	2 (1.0%)	1 (0.5%)	3 (0.8%)
鼻出血	- Any Grade -	3 (1.5%)	1 (0.5%)	4 (1.0%)
	1	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	1 (0.5%)	0	1 (0.3%)
口腔咽頭痛	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	2 (1.0%)	2 (0.5%)
喀血	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
気管支痙攣	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
胸水	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
呼吸困難	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
肺水腫	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
発声障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
扁桃の炎症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
筋骨格系および結合組織障害				
- Overall -	- Any Grade -	8 (4.1%)	16 (8.1%)	24 (6.1%)
	1	5 (2.6%)	7 (3.5%)	12 (3.0%)
	2	2 (1.0%)	7 (3.5%)	9 (2.3%)
	3	1 (0.5%)	2 (1.0%)	3 (0.8%)
関節痛	- Any Grade -	5 (2.6%)	3 (1.5%)	8 (2.0%)
	1	2 (1.0%)	3 (1.5%)	5 (1.3%)
	2	2 (1.0%)	0	2 (0.5%)
	3	1 (0.5%)	0	1 (0.3%)
筋肉痛	- Any Grade -	1 (0.5%)	6 (3.0%)	7 (1.8%)
	1	0	4 (2.0%)	4 (1.0%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
筋力低下	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
	3	0	1 (0.5%)	1 (0.3%)
筋骨格痛	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
関節炎	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	1 (0.5%)	2 (0.5%)
四肢痛	- Any Grade -	1 (0.5%)	1 (0.5%)	2 (0.5%)
	1	1 (0.5%)	0	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
横紋筋融解症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
筋痙縮	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
高クレアチン血症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)
背部痛	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
変形性関節症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
傷害、中毒および処置合併症				
- Overall -	- Any Grade -	10 (5.1%)	10 (5.1%)	20 (5.1%)
	1	4 (2.0%)	1 (0.5%)	5 (1.3%)
	2	5 (2.6%)	5 (2.5%)	10 (2.5%)
	3	1 (0.5%)	4 (2.0%)	5 (1.3%)
注入に伴う反応	- Any Grade -	10 (5.1%)	10 (5.1%)	20 (5.1%)
	1	4 (2.0%)	1 (0.5%)	5 (1.3%)
	2	5 (2.6%)	5 (2.5%)	10 (2.5%)
	3	1 (0.5%)	4 (2.0%)	5 (1.3%)
血管障害				
- Overall -	- Any Grade -	2 (1.0%)	8 (4.0%)	10 (2.5%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	5 (2.5%)	6 (1.5%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
高血圧	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	2	0	2 (1.0%)	2 (0.5%)
	3	1 (0.5%)	1 (0.5%)	2 (0.5%)
低血圧	- Any Grade -	0	3 (1.5%)	3 (0.8%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	2 (1.0%)	2 (0.5%)
上大静脈症候群	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
静脈炎	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
静脈障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
腎および尿路障害				
- Overall -	- Any Grade -	2 (1.0%)	8 (4.0%)	10 (2.5%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	3 (1.5%)	4 (1.0%)
	3	1 (0.5%)	2 (1.0%)	3 (0.8%)
	4	0	1 (0.5%)	1 (0.3%)
急性腎障害	- Any Grade -	1 (0.5%)	4 (2.0%)	5 (1.3%)
	2	1 (0.5%)	2 (1.0%)	3 (0.8%)
	3	0	2 (1.0%)	2 (0.5%)
糖尿	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
尿細管間質性腎炎	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
尿閉	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
排尿困難	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 11 of 13

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
乏尿	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	3	1 (0.5%)	0	1 (0.3%)
慢性腎臓病	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	4	0	1 (0.5%)	1 (0.3%)
耳および迷路障害				
- Overall -	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	0	3 (1.5%)	3 (0.8%)
	2	1 (0.5%)	0	1 (0.3%)
回転性めまい	- Any Grade -	1 (0.5%)	2 (1.0%)	3 (0.8%)
	1	0	2 (1.0%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
耳鳴	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
聴覚障害	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
心臓障害				
- Overall -	- Any Grade -	1 (0.5%)	3 (1.5%)	4 (1.0%)
	1	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
完全房室ブロック	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
心肺不全	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	5	1 (0.5%)	0	1 (0.3%)
心房細動	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
動悸	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
免疫系障害				
- Overall -	- Any Grade -	2 (1.0%)	2 (1.0%)	4 (1.0%)
	2	2 (1.0%)	1 (0.5%)	3 (0.8%)
	3	0	1 (0.5%)	1 (0.3%)
過敏症	- Any Grade -	2 (1.0%)	0	2 (0.5%)
	2	2 (1.0%)	0	2 (0.5%)
アナフィラキシー反応	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
薬物過敏症	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
精神障害				
- Overall -	- Any Grade -	2 (1.0%)	1 (0.5%)	3 (0.8%)
	1	1 (0.5%)	1 (0.5%)	2 (0.5%)
	2	1 (0.5%)	0	1 (0.3%)
うつ病	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
不眠症	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	2	1 (0.5%)	0	1 (0.3%)
抑うつ気分	- Any Grade -	1 (0.5%)	0	1 (0.3%)
	1	1 (0.5%)	0	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Related Adverse Events by Highest NCI CTCAE Grade
Protocol: GO30081

MedDRA System Organ Class MedDRA Preferred Term	Grade	PBO + CE (Actual) (N=196)	Atezo + CE (Actual) (N=198)	All Patients (N=394)
眼障害				
- Overall -	- Any Grade -	0	2 (1.0%)	2 (0.5%)
	2	0	2 (1.0%)	2 (0.5%)
眼刺激	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
硝子体浮遊物	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	1	0	1 (0.5%)	1 (0.3%)
霧視	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	2	0	1 (0.5%)	1 (0.3%)
肝胆道系障害				
- Overall -	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)
黄疸	- Any Grade -	0	1 (0.5%)	1 (0.3%)
	3	0	1 (0.5%)	1 (0.3%)

Investigator text for AEs encoded using MedDRA version 21.0.
All counts represent patients. Multiple occurrences of the same AE in one individual are counted once at the highest grade for this patient.
To the SOC Overall row counts, a patient contributes only with the AE occurring with the highest grade within the SOC.
Percentages are based on N in the column headings.
Atezo=Atezolizumab, CE=Carboplatin + Etoposide, PBO=Placebo
Data Cutoff: 24APR2018

Program: /opt/BIOSTAT/prod/cd30099a/j30081a/t_ae_ctc.sas
Output: /opt/BIOSTAT/prod/cd30099a/j30081a/reports/t_ae_ctc_SE_rel_24APR2018_GO30081.out
13SEP2018 18:46 Page 13 of 13

［5.3.5.1-2 t_ae_ctc_SE_rel_24APR2018_GO30081を再掲］

2.7.6.2.2 個別症例の詳細

5.3.5.1-1 1.NARRATIVES page 200に記載した。