A Randomized, Open-Label, Phase 3 Study of Cosibelimab (CK-301) in Combination with Platinum+Pemetrexed Chemotherapy in Subjects with First-Line Metastatic Non-squamous Non-Small Cell Lung Cancer

Protocol Number:	CK-301-301
EudraCT Number:	N/A
Trial Drug:	Cosibelimab (CK-301)
Sponsor:	Checkpoint Therapeutics, Inc. 2 Gansevoort Street, 9th floor New York, NY 10014, USA (212) 574-2830
Phase:	Phase 3
Version:	1.0
Date Final:	12 January 2021

CONFIDENTIAL

PROTOCOL SYNOPSIS

Title of Trial:	A Randomized, Open-Label, Phase 3 Study of Cosibelimab (CK-301) in Combination with Platinum+Pemetrexed Chemotherapy in Subjects with First-Line Metastatic Non-squamous Non-Small Cell Lung Cancer
Protocol Number:	CK-301-301
Sponsor:	Checkpoint Therapeutics, Inc.
Phase of Trial:	Phase 3
Introduction:	Cosibelimab (CK-301) is a fully human monoclonal antibody of IgG1 subtype that directly binds to Programmed Death-Ligand 1 (PD-L1) and blocks its interactions with the Programmed Death-1 (PD-1) and B7.1 receptors. Normally, PD-L1 binds to PD-1 or B7.1 to stop an immune response and prevent autoimmunity/promote self-tolerance. Cancer cells are able to express PD-L1 and can use this to evade the body's immune response. An anti-PD-L1 antibody, such as cosibelimab, could prevent PD-1/PD-L1 binding and reactivate the anti-tumor immune response. Clinical studies have shown that blockade of the PD-1/PD-L1 pathway by monoclonal antibodies can enhance the immune response and result in anti-tumor activity. PD-L1 is the primary PD-1 ligand that is up-regulated in solid tumors, where it can inhibit cytokine production and the cytolytic activity of PD-1+, tumor-infiltrating CD4+ and CD8+ T cells.[1,2,3] These properties make PD-L1 a target for cancer immunotherapy. In addition, by retaining a native Fc-region, cosibelimab may also be capable of mediating antibody-dependent cell-mediated cytotoxicity (ADCC) of tumor cells. In this trial, cosibelimab in combination with chemotherapy will be compared with chemotherapy alone in subjects with advanced or metastatic non-squamous, non-small cell lung cancer (NSCLC) who have not previously received systemic therapy. The primary objective of this trial is to evaluate the antitumor activity of cosibelimab in combination with chemotherapy compared with chemotherapy alone using Overall Survival (OS).
Trial Type:	Interventional.
Type of Control:	Active control, without placebo.
Trial Blinding:	Unblinded, open-label.
Treatment Groups:	There are 2 treatment arms: • Cosibelimab plus pemetrexed and carboplatin or cisplatin. • Pemetrexed and carboplatin or cisplatin.
# of Subjects:	Approximately 560 subjects are planned to be enrolled.
Randomization Ratio:	Randomized 2:1 to either receive cosibelimab combined with pemetrexed and platinum (investigator's choice of cisplatin or carboplatin), or pemetrexed and platinum (investigator's choice of cisplatin or carboplatin).
Estimated Duration of Trial:	The Sponsor estimates that the trial will require approximately 4 years from the time the first subject signs the informed consent until the last subject's last study-related phone call or visit.
Duration of Participation:	Subjects will participate in the trial from the time the subject signs the Informed Consent Form (ICF) through the final contact. After a screening phase of up to 28 days, eligible subjects will receive assigned treatment on Day 1 of each 3-week (Q3W) dosing cycle. Subjects randomized to the cosibelimab arm will continue treatment until the first occurrence of either: 1) confirmed and worsening radiographic progressive disease (PD),

	defined as an additional 10% or greater increase in tumor burden volume from time of initial radiographic disease progression (including all target lesions and new measurable lesions); 2) clinical deterioration suggesting that no further benefit from treatment is likely; 3) unacceptable adverse experiences; or 4) meets other criteria for discontinuation as outlined in Section 3.13 (Subject withdrawal/Discontinuation Criteria). Subjects with confirmed and worsening PD are permitted to continue cosibelimab treatment if there is clinical stability as assessed by the Investigator, as outlined in Section 3.13. Subjects randomized to the chemotherapy arm will continue treatment until the first occurrence of either: 1) confirmed radiographic PD; 2) clinical deterioration suggesting that no further benefit from treatment is likely; 3) unacceptable adverse experiences; or 4) meets other criteria for discontinuation as outlined in Section 3.13 (Subject withdrawal/Discontinuation Criteria). After the end of treatment, each subject will be followed for a minimum of 30 days for adverse event monitoring even if the subject started new anticancer treatment. Serious adverse events and immune-related adverse events (irAEs) will be collected for up to 90 days following cessation of cosibelimab treatment, or 30 days following cessation of treatment if the subject initiates new anticancer therapy, whichever is earlier. Subjects without radiographic progressive disease will have post-treatment follow-up visits for disease status, including radiographic imaging every 12 weeks, until initiating a non-study cancer treatment, experiencing disease progression, death, withdrawing consent, or becoming lost to follow-up. After documented disease progression each subject will be followed for OS until death or withdrawal of consent.
Study Objectives:	The primary study objective is to evaluate the antitumor activity of cosibelimab in combination with chemotherapy compared with chemotherapy alone using OS. The secondary study objectives include: • To evaluate the antitumor activity of cosibelimab in combination with chemotherapy compared with chemotherapy alone using investigator-assessed progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST 1.1). • To evaluate the antitumor activity of cosibelimab in combination with chemotherapy compared with chemotherapy alone using investigator-assessed objective response rate (ORR) per RECIST 1.1. • To evaluate the antitumor activity of cosibelimab in combination with chemotherapy compared with chemotherapy alone using investigator-assessed duration of response (DOR) per RECIST 1.1. • To evaluate the safety and tolerability profile of cosibelimab in combination with pemetrexed/platinum chemotherapy.
Subject Eligibility Criteria:	**<u>Inclusion Criteria:</u>** All subjects enrolling into the study must meet all of the following inclusion criteria: 1. Written consent on an IRB/IEC-approved Informed Consent Form (ICF) prior to any study-specific evaluation. 2. Age ≥ 18 years. 3. Life expectancy of at least 3 months. 4. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1. 5. Have a histologically-confirmed or cytologically-confirmed diagnosis of stage IV (M1a, M1b or M1c- AJCC 8th edition) non-squamous NSCLC. 6. Have confirmation that EGFR or ALK-directed therapy is not indicated (documentation of absence of tumor activating EGFR mutations AND absence of ALK gene rearrangements). 7. Measurable disease based on RECIST 1.1 as determined by the site. Target lesions situated in a previously irradiated area are considered measurable if progression has

	been demonstrated in such lesions. 8. Have not received prior systemic treatment for their advanced/metastatic NSCLC. Subjects who received adjuvant or neoadjuvant therapy are eligible if the adjuvant/neoadjuvant therapy was completed at least 6 months prior to the development of metastatic disease. 9. Adequate organ function, confirmed by the following laboratory values: a. Neutrophils (ANC) ≥ 1500/μL. b. Platelets ≥ 100,000/μL. c. Hemoglobin ≥ 9.0 g/dL or ≥ 5.6 mmol/L – without tranfusions within 4 weeks of first dose. d. Creatinine or CrCL* ≤ 1.5 X upper limit of normal (ULN) OR ≥ 50 mL/min for subjects with creatinine levels > 1.5 X ULN. e. AST and ALT ≤ 2.5 X ULN OR ≤ 5 X ULN for subjects with liver metastases. f. Total bilirubin ≤ 1.5 X ULN OR direct bilirubin ≤ ULN for subjects with total bilirubin levels > 1.5 X ULN. g. Alkaline Phosphate ≤ 2.5 X ULN OR ≤ 5 X ULN for subjects with liver or bone metastases. h. TSH Within normal limits. If TSH is not within normal limits at baseline, the subject may still be eligible if T3 and free T4 are within the normal limits. i. INR or PT ≤ 1.5 X ULN unless receiving anticoagulant therapy. j. aPTT≤ 1.5 X ULN unless receiving anticoagulant therapy. * Creatinine clearance (CrCl) should be calculated per institutional standard. If no local guideline is available, CrCL should be calculated using the Cockcroft-Gault Method): CrCl = ((140-age) x weight (kg) x (0.85 for females only)) / (72 x creatinine (mg/dL)). GFR can also be used in place of creatinine or CrCL. 10. Have provided tumor tissue from locations not radiated prior to biopsy; formalin-fixed specimens after the subject has been diagnosed with metastatic disease will be preferred for determination of PD-L1 status prior to randomization. Biopsies obtained prior to receipt of adjuvant/neoadjuvant chemotherapy will be permitted if recent biopsy is not feasible. 11. If female of childbearing potential (Section 3.10), have a negative urine or serum pregnancy test within 72 hours prior to receiving the first dose of study medication. 12. If female of childbearing potential (Section 3.10), be willing to use an adequate method of contraception as outlined in Section 3.10-Contraception, for the course of the study through 120 days after the last dose of study medication or through 180 days after last dose of chemotherapeutic agents as specified in the protocol. Note: Abstinence is acceptable if this is the established and preferred contraception for the subject. 13. If male subject with a female partner(s) of child-bearing potential, must agree to use an adequate method of contraception as outlined in Section 3.10-Contraception, starting with the first dose of study therapy through 180 days after the last dose of study therapy and chemotherapeutic agents as specified in the protocol. Males with pregnant partners must agree to use a condom; no additional method of contraception is required for the pregnant partner. Note: Abstinence is acceptable if this is the established and preferred contraception for the subject.

Exclusion Criteria:

Any of the following criteria will exclude subjects from study participation:

1. Has predominantly squamous cell histology NSCLC. Mixed tumors will be categorized by the predominant cell type; if small cell elements are present, the subject is ineligible.
2. Is currently participating and receiving study therapy or has participated in a study of an investigational agent and received study therapy or used an investigational device within 4 weeks prior to administration of cosibelimab.
3. Before the first dose of trial treatment:
   a. Has received prior systemic cytotoxic chemotherapy for metastatic disease
   b. Has received antineoplastic biological therapy (e.g., erlotinib, crizotinib, cetuximab) for metastatic disease
   c. Had major surgery (< 3 weeks prior to first dose)
4. Received radiation therapy to the lung that is > 30 Gy within 6 months of the first dose of trial treatment.
5. Completed palliative radiotherapy within 7 days of the first dose of trial treatment.
6. Is expected to require any other form of antineoplastic therapy while on study
7. Has received a live-virus vaccination within 30 days of planned treatment start. Seasonal flu vaccines that do not contain live virus are permitted.
8. Has clinically active diverticulitis, intra-abdominal abscess, GI obstruction, peritoneal carcinomatosis.
9. Has a known history of prior malignancy except if the subject has undergone potentially curative therapy with no evidence of that disease recurrence for 5 years since initiation of that therapy. Note: The time requirement for no evidence of disease for 5 years does not apply to the NSCLC tumor for which a subject is enrolled in the study. The time requirement also does not apply to subjects who underwent successful definitive resection of basal cell carcinoma of the skin, superficial bladder cancer, squamous cell carcinoma of the skin, in situ cervical cancer, or other in situ cancers.
10. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they are clinically stable for at least 2 weeks and, have no evidence of new or enlarging brain metastases and also are off steroids 3 days prior to dosing with study medication. Stable brain metastases by this definition should be established prior to the first dose of study medication. Subjects with known untreated, asymptomatic brain metastases (ie, no neurological symptoms, no requirements for corticosteroids, no or minimal surrounding edema, and no lesion > 1.5 cm) may participate but will require regular imaging of the brain as a site of disease.
11. Previously had a severe hypersensitivity reaction to treatment with another monoclonal antibody.
12. Has a known sensitivity to any component of cisplatin, carboplatin or pemetrexed.
13. Has active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
14. Immunosuppressive doses of systemic medications, such as steroids (doses > 10 mg/day prednisone or equivalent) must be discontinued at least 2 weeks before study drug administration.
15. Is on chronic systemic steroids. Subjects with asthma that require intermittent use of bronchodilators, inhaled steroids, or local steroid injections would not be excluded from

	the study. 16. Is unable to interrupt aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs), other than an aspirin dose ≤ 1.3 g per day, for a 5-day period (8-day period for long-acting agents, such as piroxicam). 17. Is unable or unwilling to take folic acid or vitamin B_{12} supplementation. 18. Had prior treatment with any other anti-PD-1, or PD-L1 or PD-L2 agent or an antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways. 19. Has an active infection requiring therapy. 20. Has known history of Human Immunodeficiency Virus (HIV) (known HIV 1/2 antibodies positive). 21. Has known active Hepatitis B or C or tuberculosis. Active Hepatitis B is defined as a known positive HBsAg result. Active Hepatitis C is defined by a known positive Hep C Ab result and known quantitative HCV RNA results greater than the lower limits of detection of the assay. 22. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the subject's participation for the full duration of the study, or is not in the best interest of the subject to participate, in the opinion of the treating Investigator. 23. Has known psychiatric or substance abuse disorder that would interfere with cooperation with the requirements of the trial. 24. Is, at the time of signing informed consent, a known regular user of any illicit drugs or had a recent history (within the last year) of substance abuse (including alcohol). 25. Has symptomatic ascites or pleural effusion. A subject who is clinically stable following treatment for these conditions (including therapeutic thoraco- or paracentesis) is eligible. 26. Has active or history of interstitial lung disease or a history of (non-infectious) pneumonitis that required steroids or current pneumonitis. 27. Has had an allogeneic tissue/solid organ transplant. 28. Any known uncontrolled or significant cardiovascular disease including, but not limited to any of the following: a. Myocardial infarction within 6 months. b. Uncontrolled angina within 3 months. c. Congestive heart failure within 3 months. d. Left ventricular ejection fraction (LVEF) ≤ 50%. e. Any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or Torsades de Pointes). Controlled atrial fibrillation is not an exclusion criterion. 29. Is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study.
Study Efficacy Endpoints:	The primary efficacy endpoint is OS, defined as the time from randomization to death due to any cause. The secondary efficacy endpoints include: • PFS, defined as the time from randomization to the first documented disease progression per RECIST 1.1 based on investigator assessment or death due to any cause, whichever occurs first. • ORR, defined as the proportion of subjects who have complete response or partial response in accordance with RECIST 1.1 based on investigator assessment. • DOR, defined as the time from first documented evidence of complete response or partial response until disease progression or death.

Data Monitoring Committee:	To supplement the routine trial monitoring outlined in this protocol, an external Data Monitoring Committee (DMC) will monitor the interim safety data from this trial. The voting members of the committee are external to the Sponsor. The members of the DMC must not be involved with the trial in any other way (e.g., they cannot be trial investigators) and must have no competing interests that could affect their roles with respect to the trial.
Statistical Considerations:	Enrollment of 560 subjects is assumed to occur over 24 months at 2:1 ratio between the experimental and control groups. With 372 deaths at the Final Analysis (FA), the study has ~90% power for detecting a hazard ratio (HR) of 0.7 at a type I error rate of 0.025 (one-sided). The duration of OS in the control group is assumed to follow an exponential distribution with a median of 13 months based on historical data. The exponential dropout rate assumed for OS is 0.3% per month. The overall type I error rate for each efficacy endpoint included in the sequential tests is strictly controlled at 2.5% (one-sided). Between the endpoints, the type I error is controlled by the following gateway hypothesis testing procedure. First, the primary efficacy endpoint of OS is tested at the one-sided 0.025 level. If OS is found to be statistically significant, PFS will be tested using a one-sided 0.025 significance level. If PFS is found to be statistically significant, ORR will be tested at the one-sided 0.025 level. If OS or PFS are found to be not statistically significant in favor of cosibelimab combined with chemotherapy, the hypothesis testing procedure will stop and no further efficacy claims will be made. Full details of the statistical methodology for summary and analysis of data colleted in this study will be included in a separate Statistical Analysis Plan.

4. TRIAL FLOW CHART

4.1. Initial Treatment Phase

Details regarding the procedures listed in this table are outlined in Section 5.

	Screening Phase	**Treatment Cycles (3-Week Cycles)**							**End of Treatment**	**Post-Treatment**		
Treatment Cycle	**Screening**	**1**	**2**	**3**	**4**	**5**	**6 to 17**	**18+**	**Discon Visit**	**Safety Follow-Up Visit**	**Follow-Up Visits**	**Survival Follow-up[1]**
Scheduling Window (Days)[2]	-28 to -1	+ 3	+/- 3	+/- 3	+/- 3	+/- 3	+/- 3	+/- 3	At Time of Discon +/- 3 days	30 Days Post Discon +/- 3 days	Every 6 Weeks Post Safety Follow-up +/- 7 days	Every 12 Weeks +/- 14 days
Administrative Procedures												
Informed consent[14]	X											
Inclusion/exclusion	X											
Demographics/medical history	X											
Prior/concomitant medications	X	X	X	X	X	X	X	X	X	X	X[13]	X[13]
NSCLC disease details and prior treatment	X											
Obtain allocation number using IVRS/IWRS[11]		X										
Subsequent antineoplastic therapy status									X	X	X	X
Survival status[1]		Survival status at Sponsor's request										X
Clinical Procedures / Assessments												
Adverse events		X	X	X	X	X	X	X	X	X	X	
Full physical examination	X											
Directed physical examination		X	X	X	X	X	X	X	X	X		
Vital signs and weight	X[2]	X	X	X	X	X	X	X	X	X		
12-lead ECG	X[15]											
ECOG performance status	X[3]	X[12]	X	X	X	X	X	X	X	X	X	
Laboratory Procedures / Assessments: Local Laboratory[5]												
Pregnancy test – urine or serum β-HCG[4]	X											
PT/INR and aPTT/PTT[5]	X[3]											
CBC with differential[5]	X[3]		X	X	X	X	X	X	X	X		

	Screening Phase	Treatment Cycles (3-Week Cycles)							End of Treatment	Post-Treatment		
Treatment Cycle	**Screening**	**1**	**2**	**3**	**4**	**5**	**6 to 17**	**18+**	**Discon Visit**	**Safety Follow-Up Visit**	**Follow-Up Visits**	**Survival Follow-up[1]**
Scheduling Window (Days)[2]	-28 to -1	+ 3	+/- 3	+/- 3	+/- 3	+/- 3	+/- 3	+/- 3	At Time of Discon +/- 3 days	30 Days Post Discon +/- 3 days	Every 6 Weeks Post Safety Follow-up +/- 7 days	Every 12 Weeks +/- 14 days
Comprehensive chemistry panel[5]	X[3]		X	X	X	X	X	X	X	X		
Creatinine Clearance Calculation	X[3]		X	X	X	X	X	X	X	X		
Urinalysis[5]	X[3]						X[6]	X[6]	X	X		
TSH (with reflex to FT4, FT3)[5]	X[3]		X		X		X[7]	X[7]	X	X		
Laboratory Procedures / Assessments: Central Laboratory												
Cosibelimab pharmacokinetics		Serum collected according to schedule in Section 4.1.1										
Anti-cosibelimab antibodies		Serum collected according to schedule in Section 4.1.1										
Pharmacokinetics for pemetrexed, carboplatin and cisplatin (30 subjects per arm)		Serum collected according to schedule in Section 4.1.2										
Tumor Tissue Collection												
Tumor tissue collection for PD-L1 expression testing (ALK translocation and EGFR mutation testing, if unknown)	X											
Efficacy Measurements												
Tumor imaging	X			X[8]		X[8]	X[8]	X[9]	X[10]		X[10]	
Study Drug Administration												
Cisplatin or carboplatin		X	X	X	X							
Pemetrexed		X	X	X	X	X	X	X				
Cosibelimab		X	X	X	X	X	X	X				

1. After documented disease progression, or the start of new anti-cancer treatment; contacts are approximately every 12 weeks by telephone. Updated survival status may be requested by the Sponsor at any time during the course of the study. Upon Sponsor notification, all participants who do not/will not have a scheduled study visit or study contact during the Sponsor defined time period will be contacted for their survival status (excluding participants who have a death event previously recorded).
2. Height will be measured only at Screening.
3. ECOG and laboratory tests for screening are to be performed within 10 days prior to the first dose of trial treatment.

4. For women of reproductive potential, a urine pregnancy test should be performed within 72 hours prior to first dose of trial treatment. A serum test can be considered if urine is not appropriate. Monthly pregnancy testing should be conducted as per local regulations where applicable.
5. After Cycle 1, lab samples can be collected up to 3 days prior to Day 1 of subsequent cycles.
6. To be repeated every 6 cycles beginning with Cycle 6.
7. To be repeated every other Cycle beginning with Cycle 6.
8. Imaging performed at 6 weeks (+/- 7 days) and 12 weeks (+/- 7 days) and then every 9 weeks (63 days ± 7 days) for the first 48 weeks in the treatment period.
9. Imaging performed every 12 weeks (84 days +/- 7 days) subsequently.
10. If a previous scan was obtained within 4 weeks prior to the date of discontinuation, then a scan at treatment discontinuation is not mandatory. Follow up visit scans to be performed only for subjects that discontinued NOT for progressive disease, and using the same imaging schedule used while on treatment (that is, every 6 or 9 weeks in year 1 or 12 weeks after year 1).
11. Obtaining allocation number should be performed within 3 days prior to the first dose of trial treatment.
12. Does not have to be done if Screening ECOG was performed within 3 days prior to Cycle 1.
13. After the Safety Follow-up Visit, record all medications taken for SAEs and irAEs as defined in Section 6.
14. May be signed before Day -28. The screening period will then start with the first study-related assessment, excluding the tumor tissue collection and PD-L1/ALK/EGFR testing.
15. Following Screening, 12-lead ECG will be obtained when clinically indicated.

4.1.1. Pharmacokinetic and Anti-Cosibelimab Antibodies Collection Schedule for Cosibelimab

Study Day	Time (Relative to Dosing)	PK Blood Sample	Anti-cosibelimab Antibodies Blood Sample
Cycle 1 Day 1	0 (Predose)[a]	X	X
	EOI[b]	X	
	EOI + 60 min	X	
	EOI + 120 min	X	
	EOI + 240 min	X	
Cycle 2 Day 1	0 (Predose)[a]	X	X
	EOI[b]	X	
	EOI + 60 min	X	
Cycle 4 Day 1	0 (Predose)[a]	X	X
	EOI[b]	X	
	EOI + 60 min	X	
Cycle 8 Day 1 and every eight cycles Day 1 thereafter	0 (Predose)[a]	X	X
Safety Follow-up Visit[c]		X	X

EOI: End of Infusion.

a Predose samples will be drawn within 60 minutes before infusion. PK blood samples should be taken at the same time as blood collection for anti-cosibelimab antibodies.

b Should be drawn within 30 minutes after end of infusion.

c A single sample will be taken at the Safety Follow-up Visit.

Samples are to be drawn from a site other than the infusion site (i.e., contra lateral arm) on days of infusion. If drug was administered via a central venous catheter, sample collection for PK should be from a different site.

4.1.2. Pharmacokinetic Collection Schedule for Pemetrexed, Carboplatin and Cisplatin

At selected sites, a subset of 30 subjects in each arm will undergo the following additional pharmacokinetic assessments for pemetrexed, carboplatin and cisplatin.

Study Day	Time (Relative to Dosing)	Pemetrexed	Carboplatin	Cisplatin
Cycle 1 Day 1	0 (Predose)[a]	X	X	X
	EOI[b]	X	X	X
	EOI + 30 min	X		
	EOI + 60 min	X	X	X
	EOI + 120 min	X	X	X
	EOI + 240 min	X	X	X
Cycle 2 Day 1	0 (Predose)[a]	X	X	X
	EOI[b]	X	X	X
	EOI + 60 min	X	X	X
Cycle 4 Day 1	0 (Predose)[a]	X	X	X
	EOI[b]	X	X	X
	EOI + 60 min	X	X	X

EOI: End of Infusion.

a Predose samples will be drawn within 60 minutes before infusion.

b Should be drawn within 15 minutes after end of infusion. The infusion duration for pemetrexed is 10 minutes (0.17 hour), carboplatin is 15-60 minutes, and cisplatin is 30 minutes.

Samples are to be drawn from a site other than the infusion site (i.e., contra lateral arm) on days of infusion. If drug was administered via a central venous catheter, sample collection for PK should be from a different site.