# Statistical Analysis Plan Amendment 3

**Study ID:** 213410

**Official Title:** A Randomized, Open Label Phase 2/3 Study Comparing Cobolimab + Dostarlimab + Docetaxel To Dostarlimab + Docetaxel To Docetaxel Alone In Participants With Advanced Non-small Cell Lung Cancer Who Have Progressed On Prior Anti-PD-(L)1 Therapy And Chemotherapy (COSTAR Lung)

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# TITLE PAGE

**Protocol Title**: A Randomized, Open-Label Phase 2/3 Study Comparing Cobolimab + Dostarlimab + Docetaxel to Dostarlimab + Docetaxel to Docetaxel Alone in Participants with Advanced Non-small Cell Lung Cancer Who Have Progressed on Prior Anti-PD-(L)1 Therapy and Chemotherapy (COSTAR LUNG)

**Study Number:** 213410

**Compound Number:** GSK4069889A (Cobolimab)

GSK4057190A (Dostarlimab)

**Acronym:** COSTAR Lung

**Sponsor Name:** GSK Research & Development Limited

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# VERSION HISTORY

| SAP Version | Approval Date | Protocol Version (Date) on which SAP is Based | Change | Rationale |
|---|---|---|---|---|
| SAP | 23 September 2021 | Protocol Amendment 03 (22 December 2020) | Not Applicable | Original version |
| SAP Amendment 01 | 09 August 2024 | Protocol Amendment 06 (24 July 2024) | Old RAP template migrated to new SAP/OPS templates.<br><br>Updates to align with protocol amendments 4, 5 and 6<br><br>Interim Analysis 2 (IA-2) removed<br><br>Added early PK data access to designated representatives<br><br>Changes to statistical assumptions | New SAP template available in eTMF<br><br>Ensure all analyses aligned with most recent protocol(s)<br><br>Protocol amendment 05 removed IA-2<br><br>To support planned analyses<br><br>To reflect a change to the assumed true median OS for docetaxel from 9 to 11 months, and a change from Hochberg to Hierarchical |

| SAP Version | Approval Date | Protocol Version (Date) on which SAP is Based | Change | Rationale |
|---|---|---|---|---|
| | | | and testing procedure | Testing Procedure |
| | | | Update to spend a nominal level of alpha at IA-1 and adjust alpha at final analysis accordingly | To comply with recommendation by FDA |
| | | | Additions and clarifications required for analysis | To meet disclosure and reporting requirements. |
| | | | Added changes to protocol defined analyses | Clarifications |
| SAP Amendment 02 | 22 January 2025 | Protocol Amendment 07 (20 December 2024) | Updates to align with protocol amendment 7 | Ensure all analyses aligned with most recent protocol |
| | | | Changes to testing procedure | To revert to the original testing procedure to |

| SAP Version | Approval Date | Protocol Version (Date) on which SAP is Based | Change | Rationale |
|---|---|---|---|---|
| | | | CCI [redacted] | comply with FDA request<br><br>To meet reporting requirements<br><br>To meet reporting requirements |
| | | | Additions and clarifications required for analysis<br><br>Added changes to protocol defined analyses | To meet reporting requirements<br><br>Clarifications |
| SAP Amendment 03 | 25 Mar 2026 | Protocol Amendment 08 (04 September 2025) | CCI [redacted]<br><br>Added SOC to the non-serious treatment related TEAE table<br><br>Updated liver function test categories | To align with protocol amendment 8<br><br>To meet reporting requirements<br><br>To meet reporting requirements and be consistent with |

| SAP Version | Approval Date | Protocol Version (Date) on which SAP is Based | Change | Rationale |
|---|---|---|---|---|
| | | | Updated prior and concomitant medication definition along with imputation rules. | final analysis reporting.<br><br>To meet reporting requirements and be consistent with final analysis reporting. |

# 1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses to be included in the Clinical Study Report (CSR) for Study 213410. Details of the planned interim analysis, as well as the final analyses, are provided.

## 1.1. Objectives, Estimands and Endpoints

### 1.1.1. Objectives and Endpoints

| Objectives | Endpoints |
|---|---|
| Primary | |
| • To evaluate the efficacy of cobolimab + dostarlimab + docetaxel relative to docetaxel alone in participants with advanced NSCLC who have progressed on prior anti-PD-(L)1 therapy and chemotherapy | • OS defined as survival from the date of randomization to the date of death by any cause |
| • To evaluate the efficacy of dostarlimab + docetaxel relative to docetaxel alone in participants with advanced NSCLC who have progressed on prior anti-PD-(L)1 therapy and chemotherapy | • OS defined as survival from the date of randomization to the date of death by any cause |
| Secondary | |
| • To evaluate the efficacy of cobolimab + dostarlimab + docetaxel relative to dostarlimab + docetaxel | • OS defined as survival from the date of randomization to the date of death by any cause |
| • To evaluate additional measures of clinical benefit for cobolimab + dostarlimab + docetaxel relative to docetaxel alone | • Confirmed ORR defined as the proportion of participants who have achieved confirmed CR or confirmed PR, evaluated using RECIST v1.1 based on Investigator assessment<br>• PFS defined as the length of time until disease progression, from the time of randomization to the earliest date of assessment of disease progression based on RECIST v1.1 by Investigator assessment or death by any cause<br>• DOR defined as the time from first documented response (CR/PR) until the time of first documentation of disease progression based on RECIST v 1.1 by Investigator assessment or death, whichever occurs first<br>• TTD in lung cancer defined as time from randomization to meaningful deterioration on a composite endpoint of dyspnea, chest pain, and cough, from the EORTC-QLQ-LC13<br>• Change from baseline as assessed by the EORTC-QLQ-C30 and the EORTC-QLQ-LC13 domains |
| • To evaluate additional measures of clinical benefit for dostarlimab + docetaxel relative to docetaxel alone | • Confirmed ORR defined as the proportion of participants who have achieved confirmed CR or |

| Objectives | Endpoints |
|---|---|
| | confirmed PR, evaluated using RECIST v1.1 based on Investigator assessment<br>• PFS defined as the length of time until disease progression, from the time of randomization to the earliest date of assessment of disease progression based on RECIST v1.1 by Investigator assessment or death by any cause<br>• DOR defined as the time from first documented response (CR/PR) until the time of first documentation of disease progression based on RECIST v 1.1 by Investigator assessment or death, whichever occurs first<br>• TTD in lung cancer is defined as time from randomization to meaningful deterioration on a composite endpoint of dyspnea, chest pain, and cough, from the EORTC-QLQ-LC13<br>• Change from baseline as assessed by the EORTC-QLQ-C30 and the EORTC-QLQ-LC13 domains |
| • To evaluate additional measures of clinical benefit for cobolimab + dostarlimab + docetaxel relative to dostarlimab + docetaxel | • Confirmed ORR defined as the proportion of participants who have achieved confirmed CR or confirmed PR, evaluated using RECIST v1.1 based on Investigator assessment<br>• PFS defined as the length of time until disease progression, from the time of randomization to the earliest date of assessment of disease progression based on RECIST v1.1 by Investigator assessment or death by any cause.<br>• DOR defined as the time from first documented response (CR/PR) until the time of first documentation of disease progression based on RECIST v 1.1 by Investigator assessment or death, whichever occurs first<br>• TTD in lung cancer defined as time from randomization to meaningful deterioration on a composite endpoint of dyspnea, chest pain, and cough, from the EORTC-QLQ-LC13<br>• Change from baseline as assessed by the EORTC-QLQ-C30 and the EORTC-QLQ-LC13 domains |
| • To evaluate the safety and tolerability of cobolimab + dostarlimab + docetaxel and dostarlimab + docetaxel vs docetaxel alone | • The incidence of TEAEs, SAEs, imAEs, TEAEs leading to death, and AEs leading to discontinuation occurring while participants are on treatment or up to 90 days after the last dose of study treatment. Clinical laboratory parameters (hematology, chemistry, thyroid function, and urinalysis), vital signs, ECOG performance status, ECG parameters, physical examinations, and usage of concomitant medications will be collected. |

| Objectives | Endpoints |
|---|---|
| Exploratory | |
| CCI [redacted] | |

Abbreviations: ADA=anti-drug antibody; AE=adverse event; CD=cluster of differentiation; CD8 T=CD8+ cytotoxic T (cells); CR=complete response; ctDNA=circulating tumor DNA, DOR=duration of response; ECG=electrocardiogram; ECOG=Eastern Cooperative Oncology Group; EORTC-QLQ-C30=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core Module; EORTC-QLQ-LC13=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire 13-item Lung Cancer Module; CCI [redacted] CCI [redacted] CCI [redacted] iCPD=iRECIST-confirmed progressive disease; imAE=immune-mediated adverse event; iRECIST=modified Response Evaluation Criteria in Solid Tumors; NAb=neutralizing antibody; NSCLC=non-small cell lung cancer; NSCLC-SAQ=Non-small Cell Lung

Cancer-Symptom Assessment Questionnaire; ORR=objective response rate; OS=overall survival; PD-(L)1=programmed cell death protein 1/(programmed death-ligand 1); PFS=progression-free survival; CCI [redacted] PK=pharmacokinetics; PR=partial response; PRO=patient-reported outcome; PRO-CTCAE=Patient-reported Outcomes Version of the Common Term Criteria for Adverse Events; RECIST=Response Evaluation Criteria in Solid Tumors; SAE=serious adverse event; TEAE=treatment-emergent adverse events; TIM-3=T-cell immunoglobulin and mucin-domain containing-3; TTD=time to deterioration

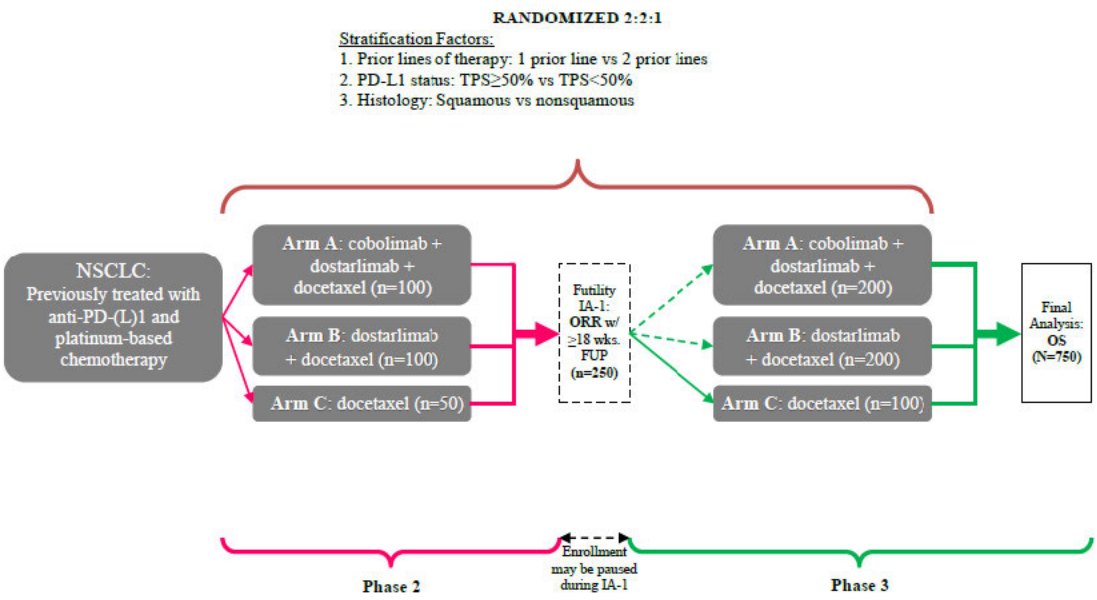
### 1.1.2. Estimands

| | | Estimand | | | |
|---|---|---|---|---|---|
| **Objective** | **Estimand Category** | **Variable/Endpoint** | **Population of interest** | **Intercurrent Event Strategy** | **Population Level Summary Measure** |
| Primary Objective 1: To evaluate the efficacy of cobolimab + dostarlimab + docetaxel relative to docetaxel alone in participants with advanced NSCLC who have progressed on prior anti-PD-(L)1 therapy and chemotherapy | Primary | OS | ITT | Follow up anti-cancer therapy: treatment policy Treatment discontinuation: treatment policy | Kaplan-Meier estimates and Hazard ratio for cobolimab + dostarlimab + docetaxel vs. docetaxel alone |
| | Supplementary 1 | | | Follow up anti-cancer therapy: hypothetical Treatment discontinuation: treatment policy | |
| Primary Objective 2: To evaluate the efficacy of dostarlimab + docetaxel relative to docetaxel alone in participants with advanced NSCLC who have progressed on prior anti-PD-(L)1 therapy and chemotherapy | Primary | OS | ITT | Follow up anti-cancer therapy: treatment policy Treatment discontinuation: treatment policy | Kaplan-Meier estimates and Hazard ratio for dostarlimab + docetaxel vs. docetaxel alone |
| | Supplementary 1 | | | Follow up anti-cancer therapy: hypothetical Treatment discontinuation: treatment policy | |

Abbreviations: NSCLC=non-small cell lung cancer; OS = overall survival; PD-(L)1 = programmed cell death protein 1/ (programmed death-ligand 1); ITT = Intent-to-treat

## 1.2. Study Design

**Overview of Study Design and Key Features**




Abbreviations: FUP=follow-up; IA=interim analysis; NSCLC=non-small cell lung cancer; ORR=objective response rate; OS=overall survival; PD(L)1=programmed cell death protein1/(programmed death-ligand 1); TPS=tumor proportion score. Note: Arm C represents current standard-of-care regimen and will continue through study completion regardless of IA-1 result. The 750 total participants include the 250 participants from the first futility analysis (IA-1).

| | |
|---|---|
| **Design Features** | • Design: multicenter, parallel-group treatment, Phase 2/3 open-label, 3-arm study comparing cobolimab + dostarlimab + docetaxel (Arm A) to dostarlimab + docetaxel (Arm B) to docetaxel alone (Arm C) for efficacy in male and female participants aged 18 years and older with advanced NSCLC who have progressed on prior anti-PD(L)1 therapy and chemotherapy.<br>• The study consists of a Screening Period (Day -28 to Day -1) for completion of all Screening assessments and subsequent randomization, a Treatment Period, an EOT Visit (within 7 days of the last dose/decision to discontinue treatment for any reason), a Safety Follow-up Visit 30 (±7) days and 90 (±7) days after the last dose of study treatment, and a Post-treatment Follow-up Period with assessments occurring every 90 (±14) days (from the 90 day Safety Follow Up Visit) and continuing until death, withdrawal of consent, loss to follow-up, or the end of study data collection. If the participant does not agree to continue in-person visits, a modified follow-up (telephone contact) must be arranged to ensure the collection of endpoints, safety information (adverse events-new or ongoing), new anti-cancer therapies, new medical conditions and vital status (see Protocol Section 7.1). |
| **Study intervention** | Cobolimab CCI and dostarlimab CCI each administered as a 30-minute intravenous (IV) infusion Q3W, docetaxel (75 mg/m²) administered as a 60-minute intravenous (IV) infusion Q3W for a minimum of 4 cycles.<br>CCI<br>CCI |
| **Study intervention Assignment** | Participants will be randomly assigned to receive the combination of cobolimab + dostarlimab + docetaxel, or the combination of dostarlimab + docetaxel, or docetaxel alone in a 2:2:1 ratio. Participants will be stratified according to 3 factors[1]:<br>• Prior lines of therapy: 1 prior line vs 2 prior lines<br>• Histology: Squamous vs nonsquamous |

| Overview of Study Design and Key Features | |
|---|---|
| | • PD-L1 status: TPS (Tumor Proportion Score) ≥ 50% vs TPS < 50%<br>Randomization will be completed in an unblinded manner. |
| CCI | [redacted] |
| **Final analysis** | The final analysis will be performed once the target number of OS events have been observed. If no combination arm is dropped after IA-1 futility analysis, the target number of OS events is 348 between each experimental arm and the control. If only one combination arm is left after IA-1 futility analysis, the target number of OS events is 348 between the remaining experimental arm and the control. |
| **End of main study analysis** | An end of main study analysis will be performed once the study is complete. |
| **Multiplicity adjustment** | The type I error is controlled at the one-sided 2.49% level for final analysis. The multiplicity strategy is described in Section 2.1. |

[1]Stratification factors changed in protocol amendment 3. Some participants have been randomized based on the factors defined in previous versions of the protocol, i.e., histology (squamous vs non-squamous) and prior lines of therapy (IO+chemotherapy vs IO followed by chemotherapy vs Chemotherapy followed by IO). These participants will be analyzed based on the protocol amendment 3 stratification factors.

# 2. STATISTICAL HYPOTHESES

The hypotheses tested are:

1. **Null**: There is no difference in overall survival (OS) between the cobolimab + dostarlimab + docetaxel (Arm A) combination treatment and the docetaxel (Arm C) treatment alone. **Alternative**: The cobolimab + dostarlimab + docetaxel (Arm A) combination treatment improves OS over the docetaxel (Arm C) treatment alone.
2. **Null**: There is no difference in OS between the dostarlimab + docetaxel (Arm B) combination treatment and the docetaxel (Arm C) treatment alone. **Alternative**: The dostarlimab + docetaxel (Arm B) combination treatment improves OS over the docetaxel (Arm C) treatment alone.

No formal hypothesis testing is conducted for ORR by BICR on which the interim futility assessment is based (IA-1). The comparison of cobolimab + dostarlimab + docetaxel (Arm A) to dostarlimab + docetaxel (Arm B) is descriptive.

## 2.1. Multiplicity Adjustment

If all 3 treatment arms are carried forward based on IA-1, then there will be 2 formal pairwise primary comparisons on OS: comparison between cobolimab + dostarlimab + docetaxel combination arm and docetaxel arm and comparison between dostarlimab + docetaxel combination arm and docetaxel arm. The Hochberg step-up procedure will be used for OS testing for the 2 comparisons at final analyses to preserve the overall type-1 error level at a 1-sided alpha of 0.0249. If both 1-sided p-values for the 2 combination arms vs the docetaxel arm comparison are less than the alpha boundary at the final analysis evaluated at a 1-sided alpha of 0.0249, then both combination arms are superior to docetaxel in OS; if the least significant (larger) p-value is greater than or equal to the alpha boundary at the final analysis, then the most significant (smaller) p-value needs to be compared with the alpha boundary at the final analysis evaluated at a 1-sided alpha of 0.01245. If only 1 of the 2 combination arms is carried forward based on the IA-1, then the p-value of the remaining combination arm will be compared to the alpha boundary at the final analysis evaluated at a 1-sided alpha of 0.01245.

# 3. ANALYSIS SETS

| Analysis Set | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| Screened | All participants who signed the ICF. | Study Population |
| Enrolled | • All participants who entered the study.<br>• This includes participants identified to participate in the study on the Eligibility eCRF page or randomized into the trial.<br>• Note: screening failures (who never passed screening even if rescreened) and participants screened but never enrolled into the study (e.g., met eligibility but not needed) are excluded from the Enrolled Analysis set as they did not enter the study.<br>• Participants will be analyzed according to the randomized study treatment even if no study treatment was received. Non-randomized participants will be displayed as No Treatment. | Study Population |
| Safety (SAF) | • All participants who received at least one dose of study treatment.<br>• Data will be reported according to the actual study treatment they received. This will be different from the randomized treatment only if the incorrect treatment was received throughout the dosing period. | Safety |
| Intent-to-Treat (ITT) | • All participants who were randomized into the study.<br>• Participants will be analyzed according to the randomized study treatment even if no study treatment was received.<br>• Participants who were incorrectly stratified at randomization will be analyzed and presented according to the stratum assigned at randomization.<br>• Used for primary analysis of efficacy endpoints. | Study Population<br>Efficacy |
| Per-Protocol (PP) | • All participants randomized in the study who do not have protocol deviations that could significantly impact the interpretation of efficacy results.<br>• Participants who did not receive any dose of assigned treatment will be excluded. | Efficacy<br>The PP set will not be used for analyses if this analysis set |

| Analysis Set | Definition / Criteria | Analyses Evaluated |
|---|---|---|
| | • Protocol deviations that would exclude participants are the following critical eligibility criteria: Inclusion criteria 2, 3, and 5; Exclusion criteria 2, 3, and 4.<br>• Data will be reported according to the actual study treatment received.<br>• Used for supportive analysis of selected efficacy endpoints. | comprises more than 90% or less than 60% of the ITT analysis set. |

CCI

[redacted]

# 4. STATISTICAL ANALYSES

## 4.1. General Considerations

### 4.1.1. General Methodology

Data will be listed and summarized according to GSK reporting standards, where applicable.

Randomized participants who prematurely withdrew from study will not be replaced.

The ITT Analysis Set will be used for all efficacy analyses unless otherwise specified (e.g., screening status will be based on the Screened population, exposure will be based on the Safety population). The Safety Analysis Set will be used for all safety analyses unless otherwise specified.

In the case of wrong stratification assigned at the time of randomization, the analyses will be performed based on the assigned randomization and trial supply management (RTSM) strata levels at randomization.

Confidence intervals will use 95% confidence levels unless otherwise specified. For confidence intervals of KM estimates, a log-log transformation will be used.

Unless otherwise specified, continuous data will be summarized using descriptive statistics: n, mean, standard deviation (sd), median, minimum, maximum and first and third quartiles (Q1, Q3). Categorical data will be summarized as the number and percentage of participants in each category. Missing observations will be included in the denominator unless otherwise specified.

For by-visit outputs, the percentages will be based on the number of participants who are still in the study at that visit and have consented to it (some participants may opt out of safety follow-up visits but remain in the study for survival follow-up contact only).

For each statistical comparison between study treatments (e.g., OS for Arm A vs. Arm C, Arm B vs. Arm C), only data for these arms will be included in the corresponding model.

Further details including data display handling standards and handling conventions, reporting standards, rules for deriving data will be described in the OPS.

In this multicenter study, enrolment will be presented by country and site.

Data from all participating centers will be pooled and no controlling for center-effect will be considered in the statistical analyses. Participants are expected to be spread thinly across sites, so that summaries of data by center are not likely to be informative and will not be provided.

### 4.1.2. Stratified Analyses and Reporting of Stratification Factors

For all stratified analyses and reporting of stratification factors, the RTSM strata levels will be used unless other specified. Participants randomized effective protocol amendment 3 were randomized according to 3 stratification factors, prior lines of therapy (1 prior line vs 2 prior lines), PD-L1 status (TPS ≥50% vs TPS <50%), and histology (squamous vs nonsquamous).

For participants enrolled prior to protocol amendment 3, who were randomized according to 2 stratification factors, prior lines of therapy (IO followed by chemo vs chemo followed by IO vs chemo + IO) and histology (squamous vs non-squamous), the RTSM strata levels will be used for prior lines of therapy and histology, while PD-L1 status will be obtained from the eCRF, if available. For prior lines of therapy, IO followed by chemo and chemo followed by IO constitutes 2 lines of therapy and IO + chemo constitutes 1 line of therapy.

### 4.1.3. Baseline Definitions

For all endpoints unless otherwise specified, the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time (pre-dose/post-dose information) is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Unless otherwise stated, if baseline data is missing no imputation will be performed and baseline will be set to missing.

## 4.1.4. Examination of Covariates, Other Strata and Subgroups

### 4.1.4.1. Covariates and Other Strata

The list of covariates and other strata may be used in descriptive summaries and statistical analyses, some of which may also be used for subgroup analyses. Additional covariates and other strata of clinical interest may also be considered.

| Category | Details |
|---|---|
| Strata | • Prior lines of therapy: 1 line (Immuno-oncology therapy (IO) + chemotherapy) vs 2 lines (IO followed by chemotherapy or chemotherapy followed by IO)<br>• Histology: Squamous vs nonsquamous<br>• PD-L1 status: TPS (Tumor Proportion Score) ≥ 50% vs TPS < 50% |

### 4.1.4.2. Examination of Subgroups

The list of subgroups will be used to assess the consistency of the treatment effect on the primary endpoint (OS). See Section 4.2.3 for the analysis methodology. Additional subgroups of clinical interest may be considered.

- If the percentage of participants is small within a particular subgroup, then the subgroup categories may be refined prior to unblinding the trial.
- If the category cannot be refined further, then descriptive rather than statistical comparisons may be performed for the particular subgroup.
- If there are too few events (e.g. less than 20 events in a subgroup or there is no event in one treatment arm) available for a meaningful analysis of a particular subgroup, the subgroup will not be formally analyzed, and only descriptive summaries will be provided.

**Table 1 Table of subgroups**

| Subgroup | Categories |
|---|---|
| Age | ≤65 years vs > 65 years |
| Sex | female vs male |
| Race | Non-white vs white |
| ECOG status | 0 vs 1 |
| Geographic region of enrolling site[1] | North America vs East Asia vs Europe vs RoW |
| Smoking status | Never vs former vs current |
| Prior lines of therapy (according to the eCRF) | 1 line vs 2 lines |
| Histology (according to the eCRF) | Squamous vs non-squamous |
| PD-L1 status (according to the eCRF) | TPS ≥ 50% vs TPS < 50% |
| PD-L1 status (according to the eCRF) | TPS ≥ 1% vs TPS < 1% |
| Phase of Enrolment | Phase 2 (pre-IA-1) vs Phase 3 (post-IA-1) |
| Brain Metastases | Yes vs No |

| Subgroup | Categories |
|---|---|
| Liver Metastases | Yes vs No |

[1]See Section 6.3.3.1.

### 4.1.5. Other Considerations for Data Analysis and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

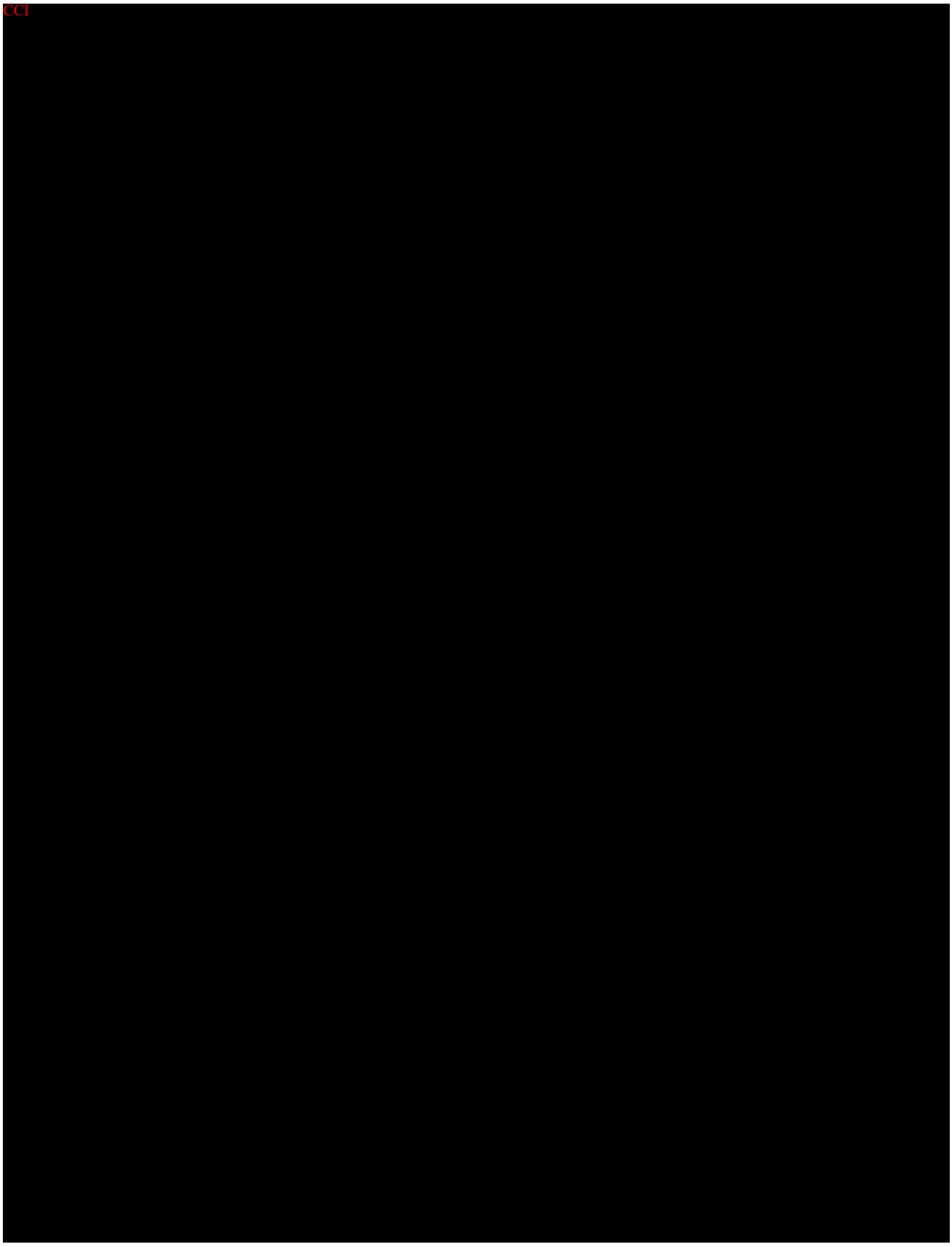
| Section | Component |
|---|---|
| 6.1 | Study Population Analyses |
| 6.2 | Electronic Clinical Outcome Assessment (eCOA) Compliance |
| 6.3 | Data Derivations Rule |

Note: participant-level data may be available interactively via RAPIDO Data Viewer at SAC.

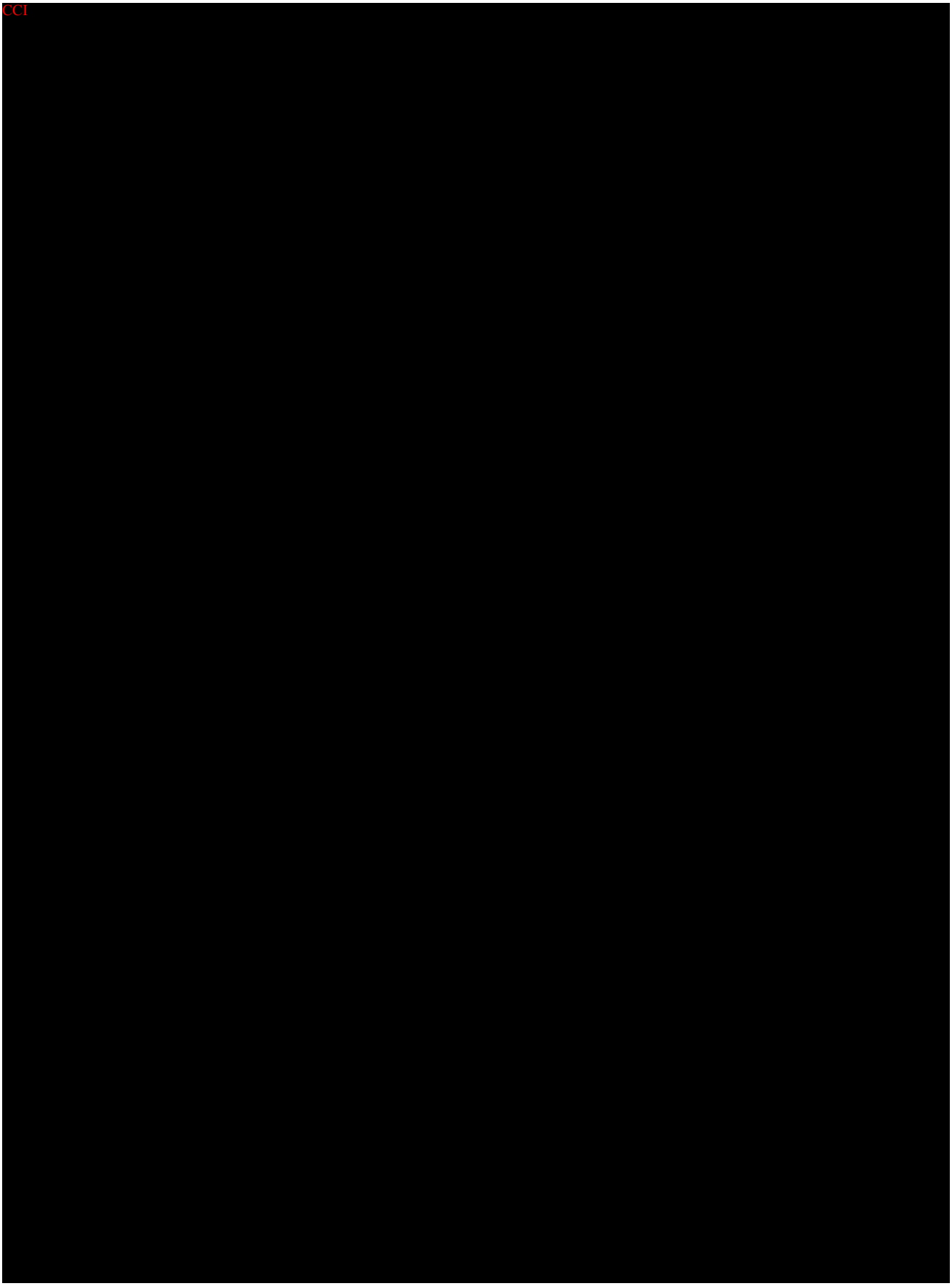
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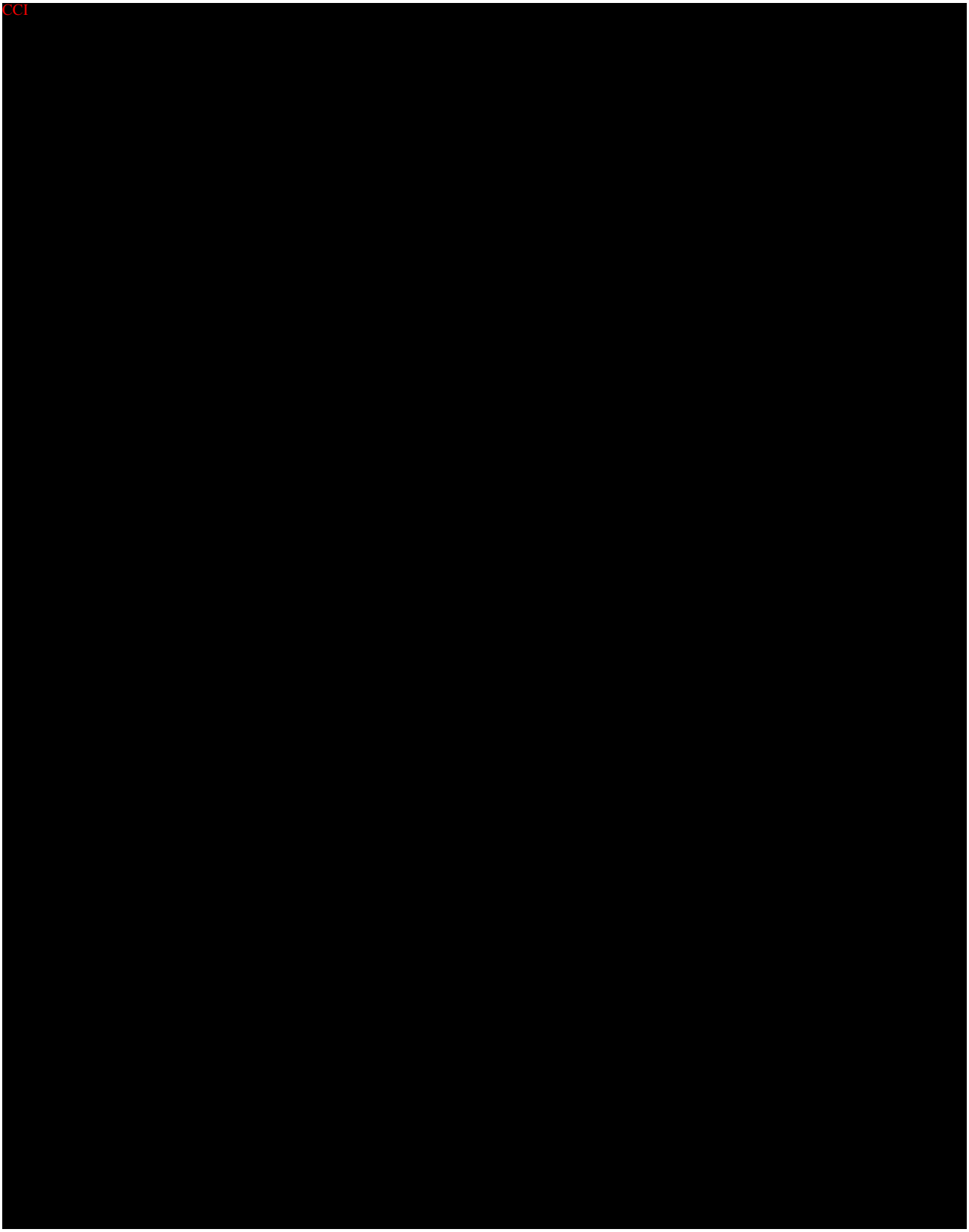
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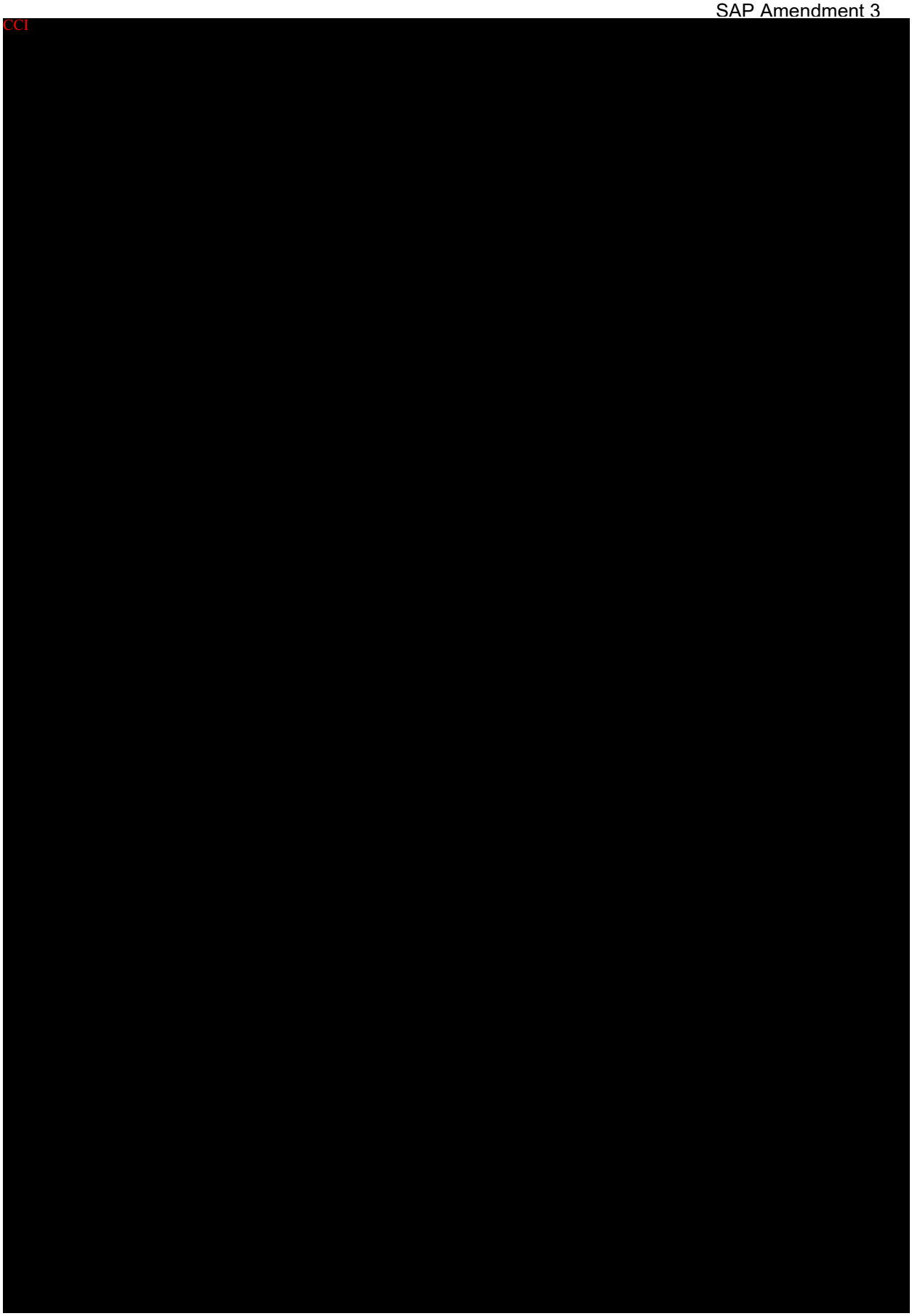
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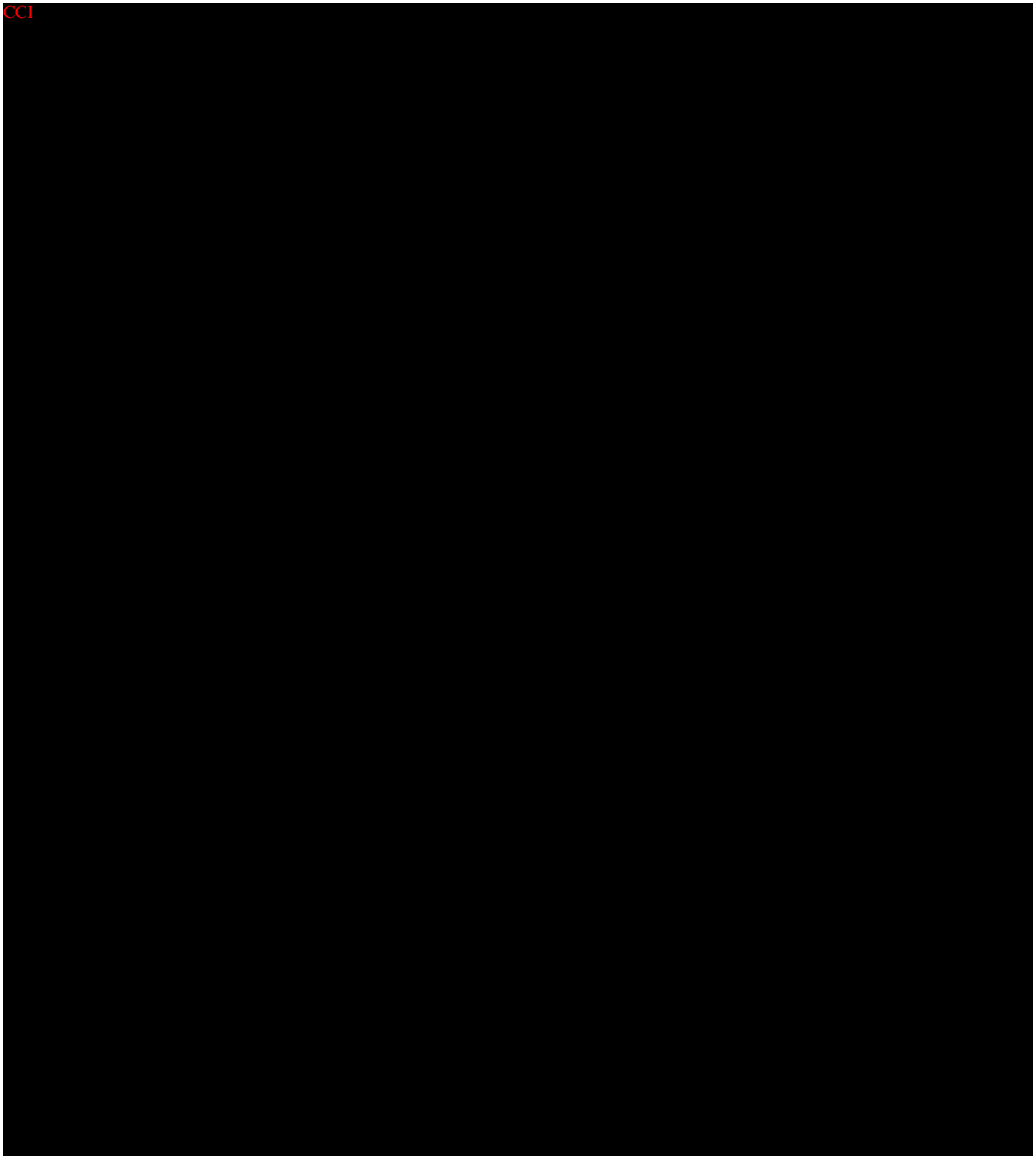
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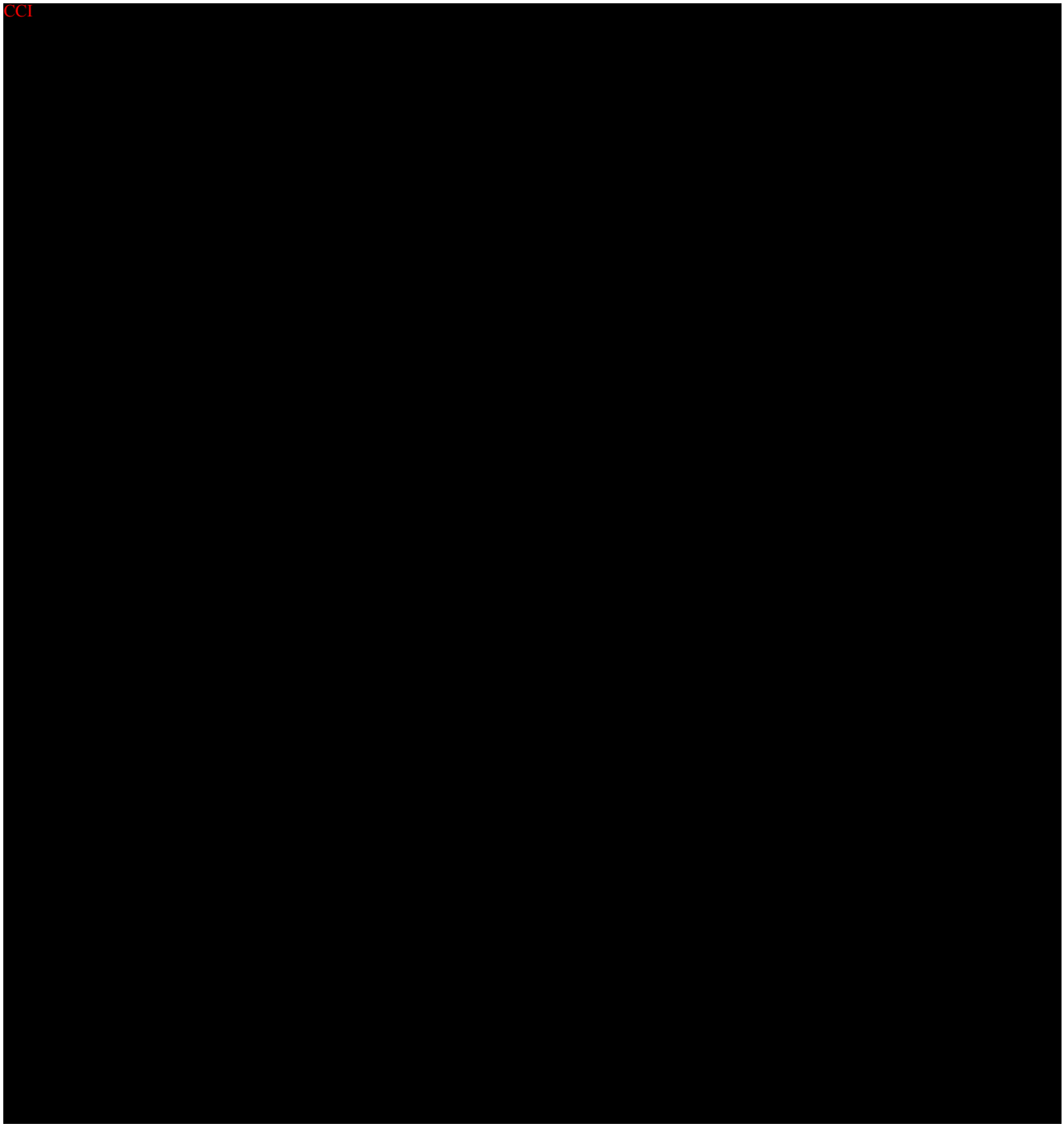
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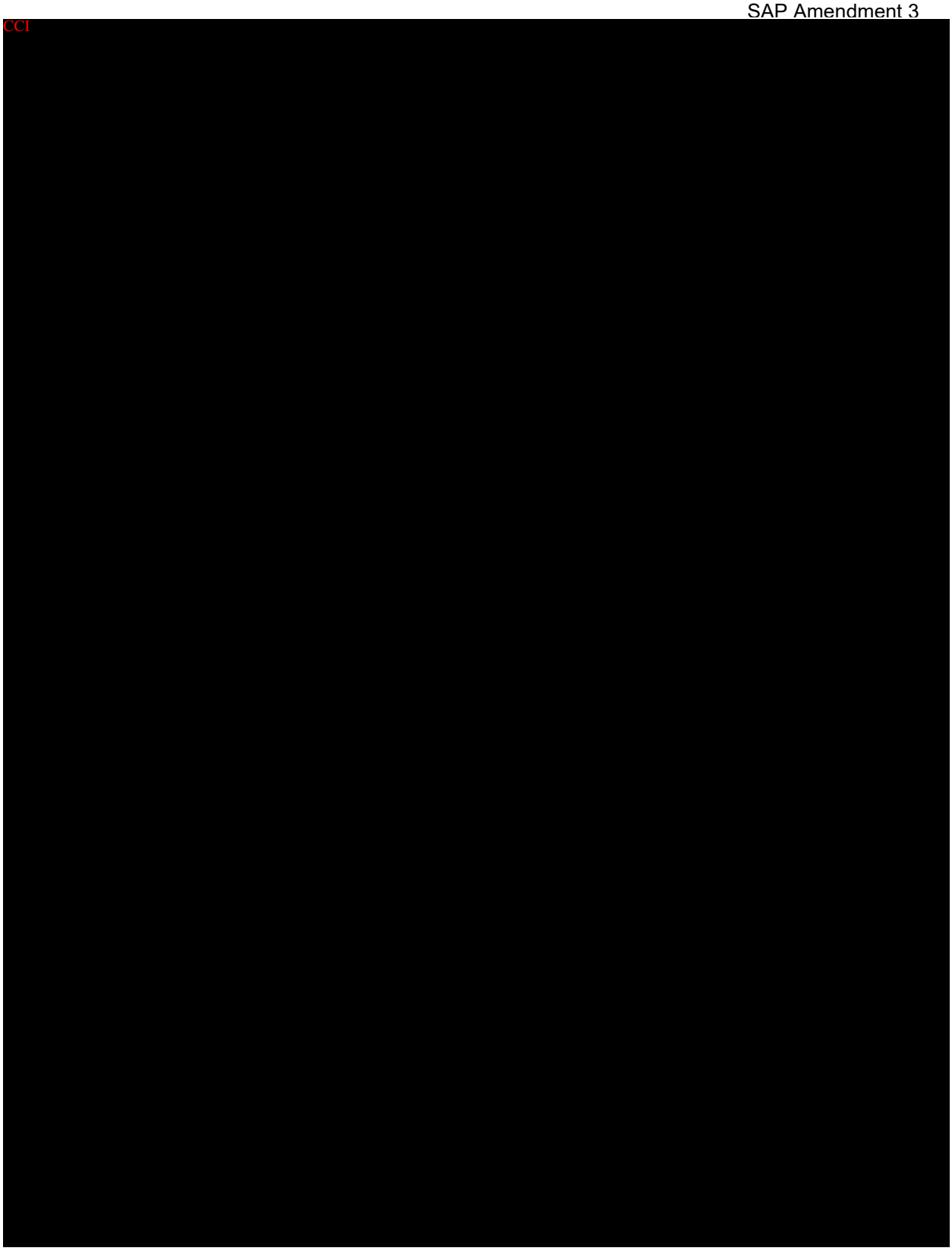
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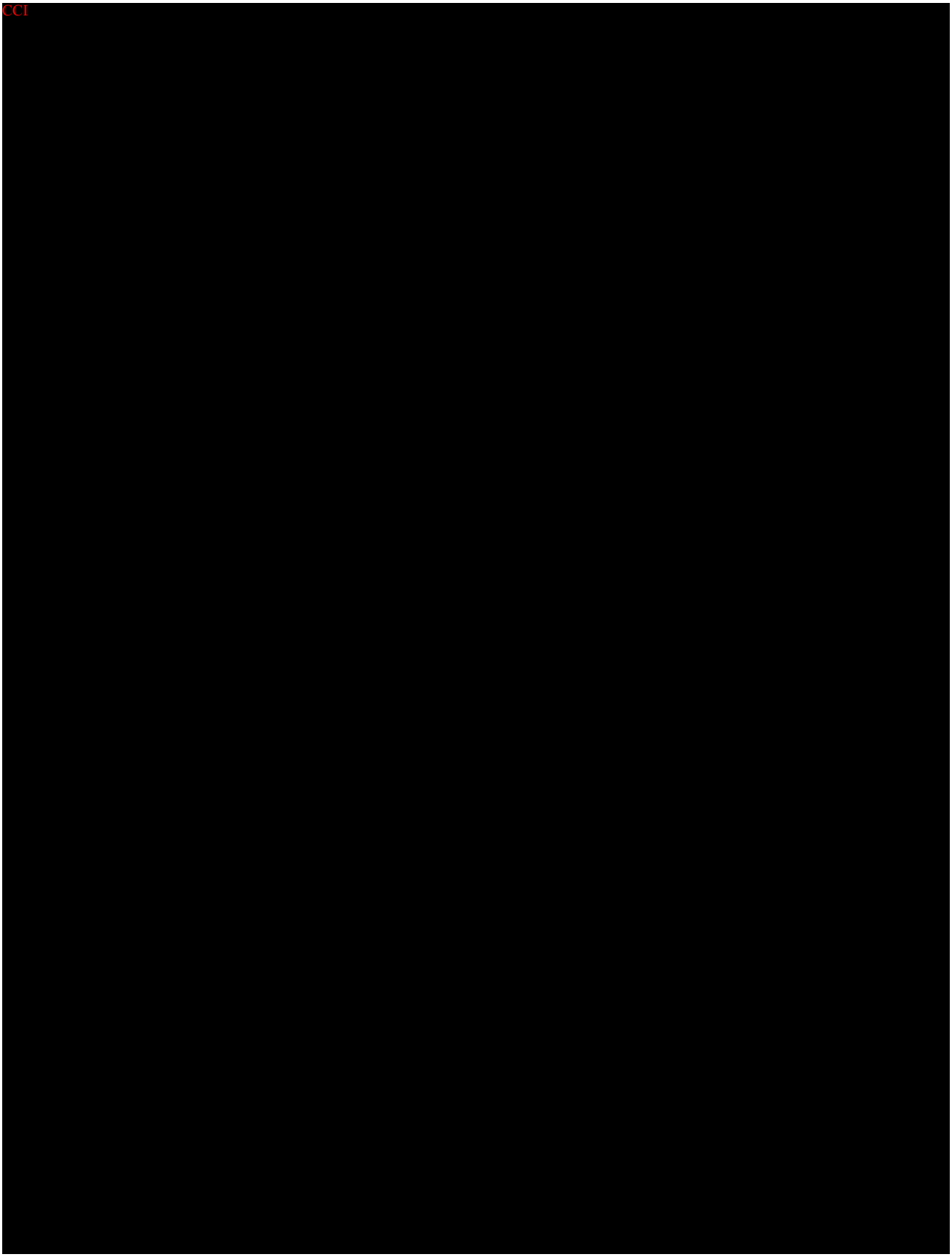
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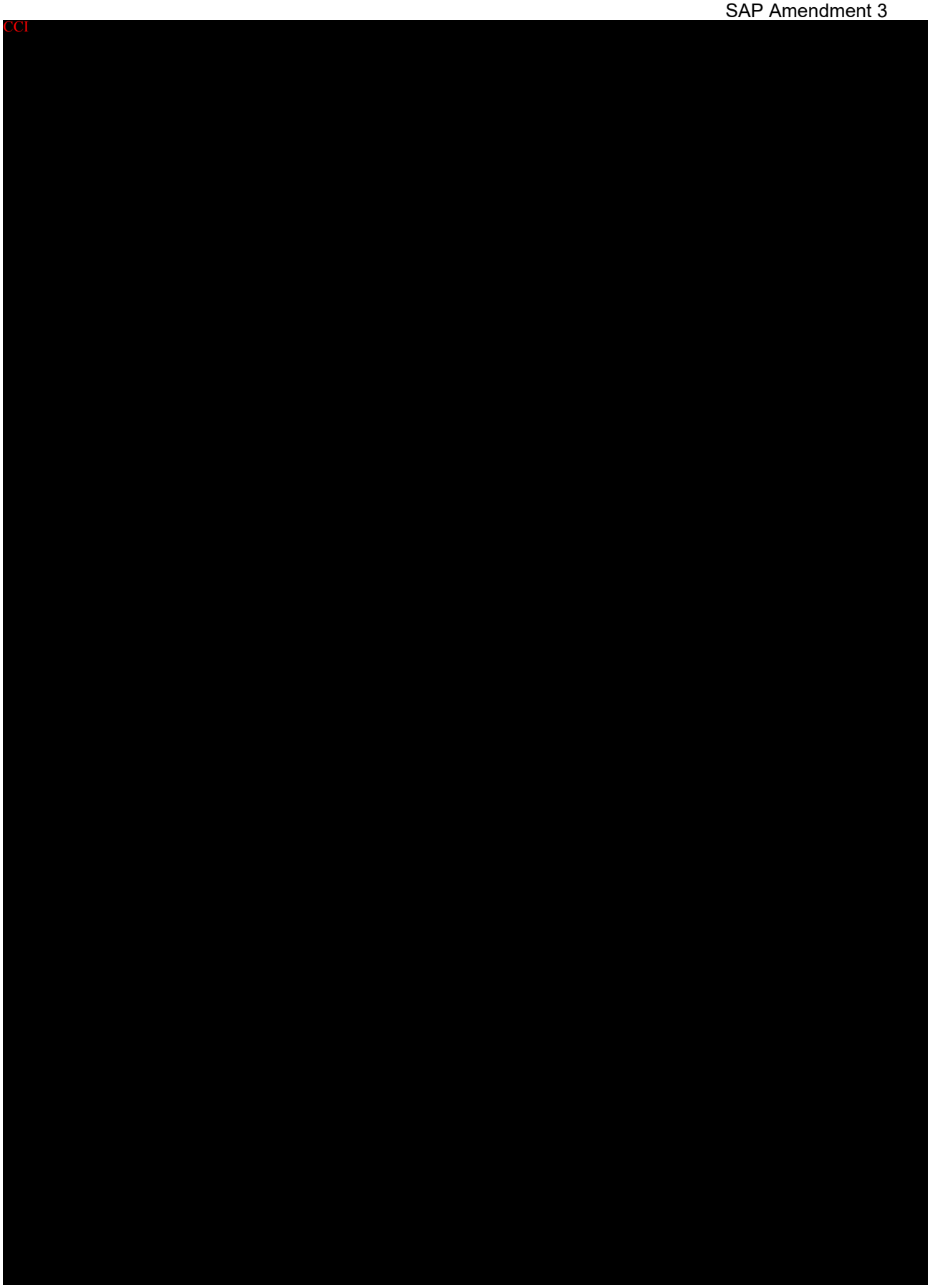
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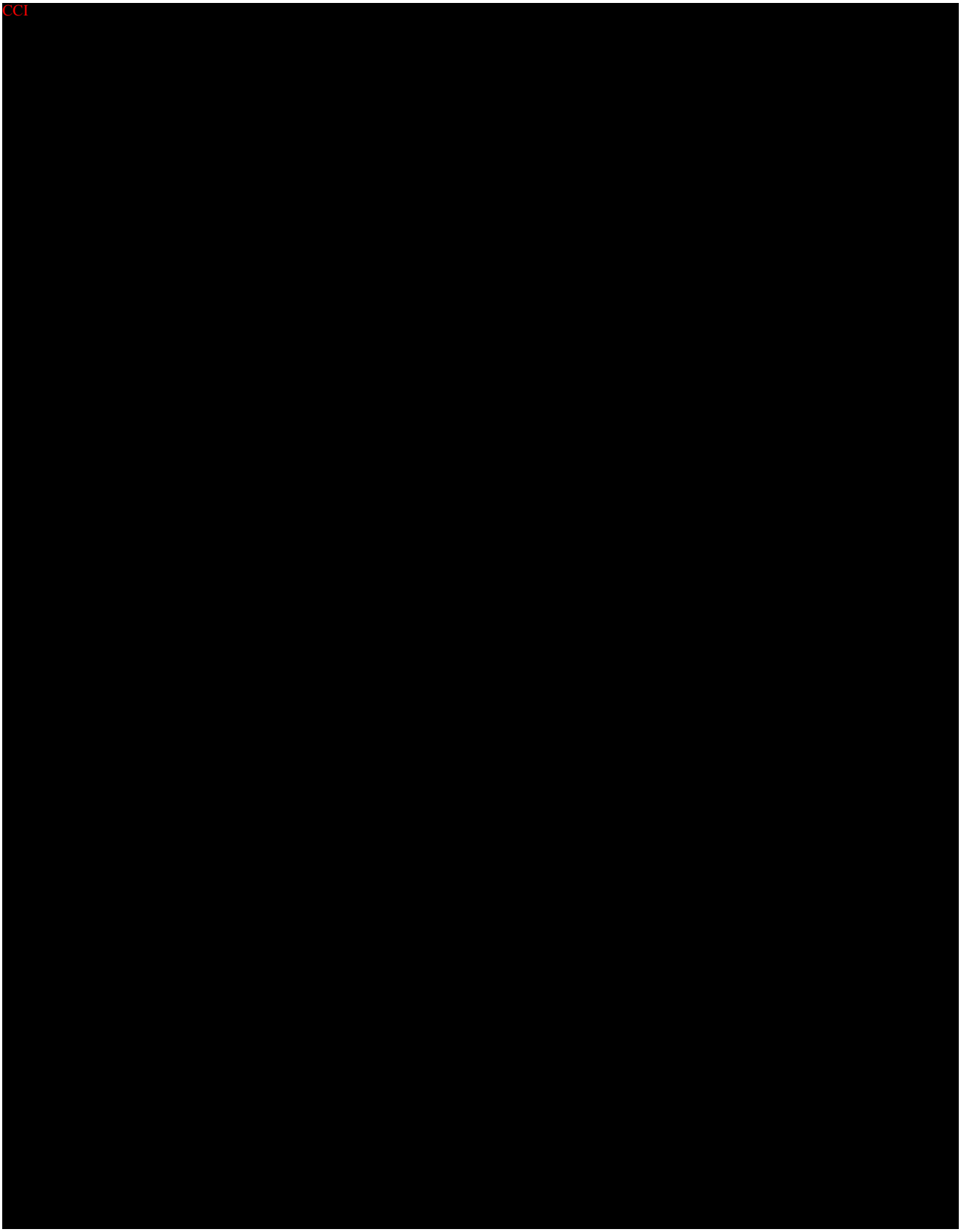
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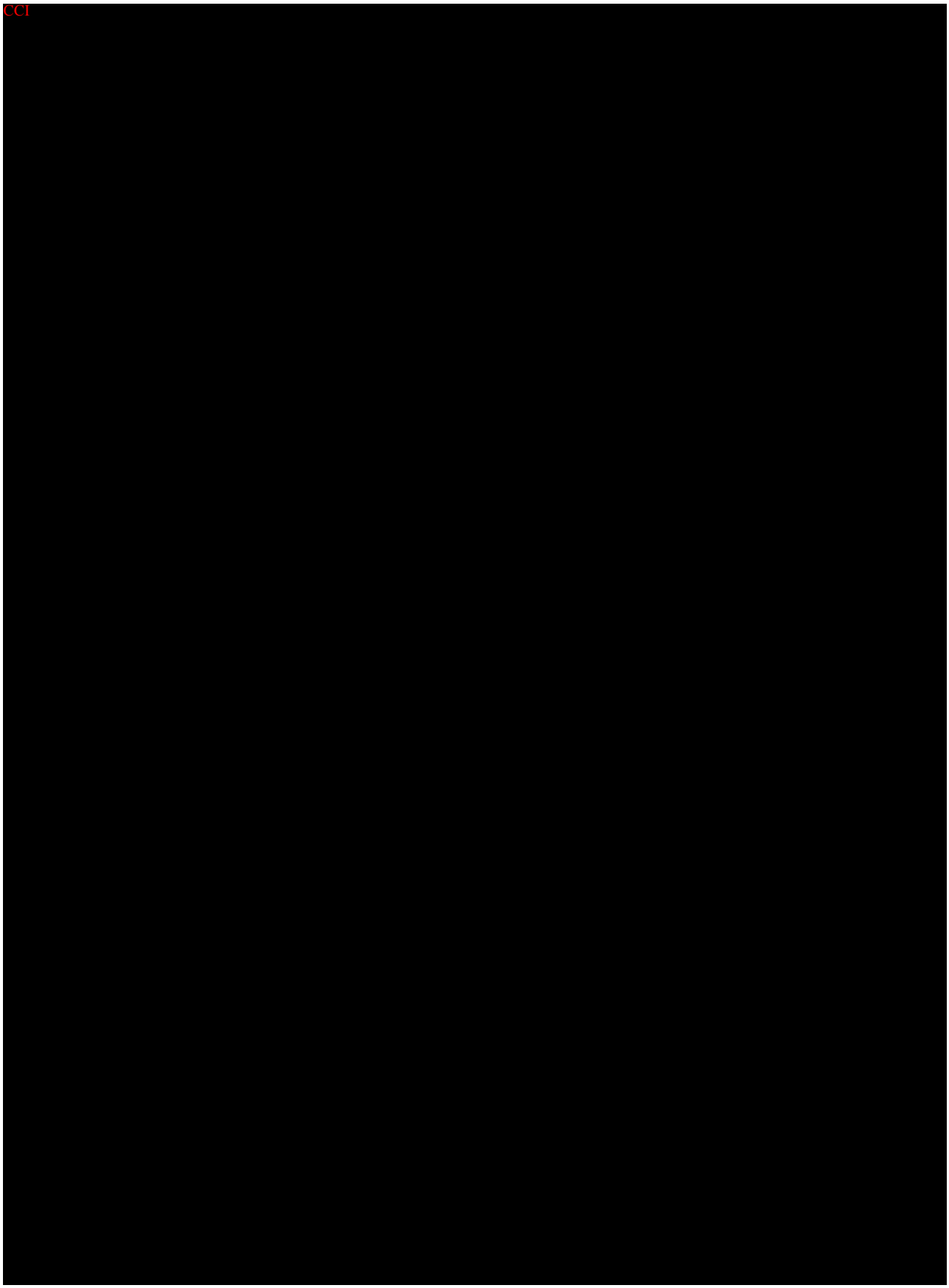
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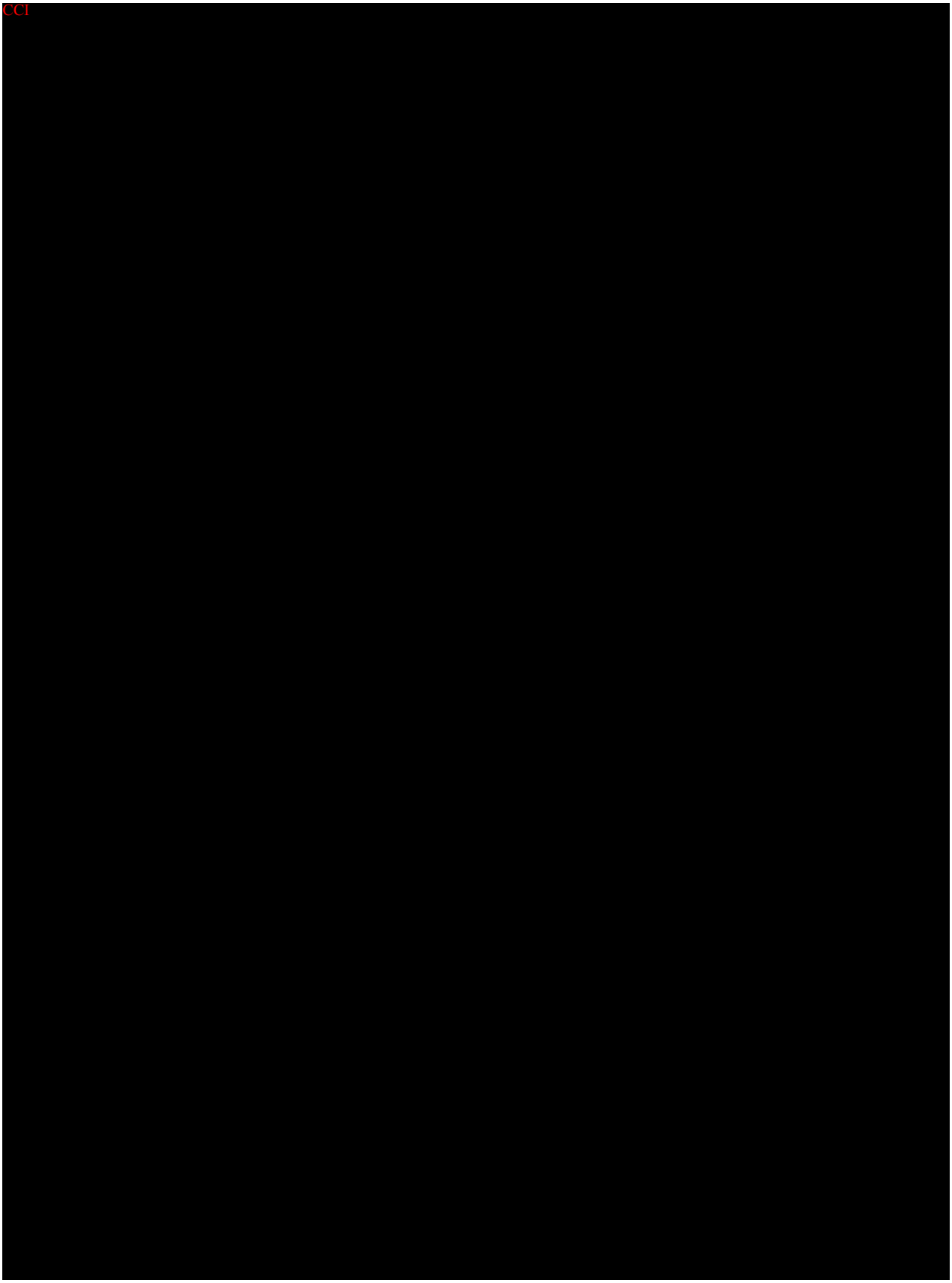
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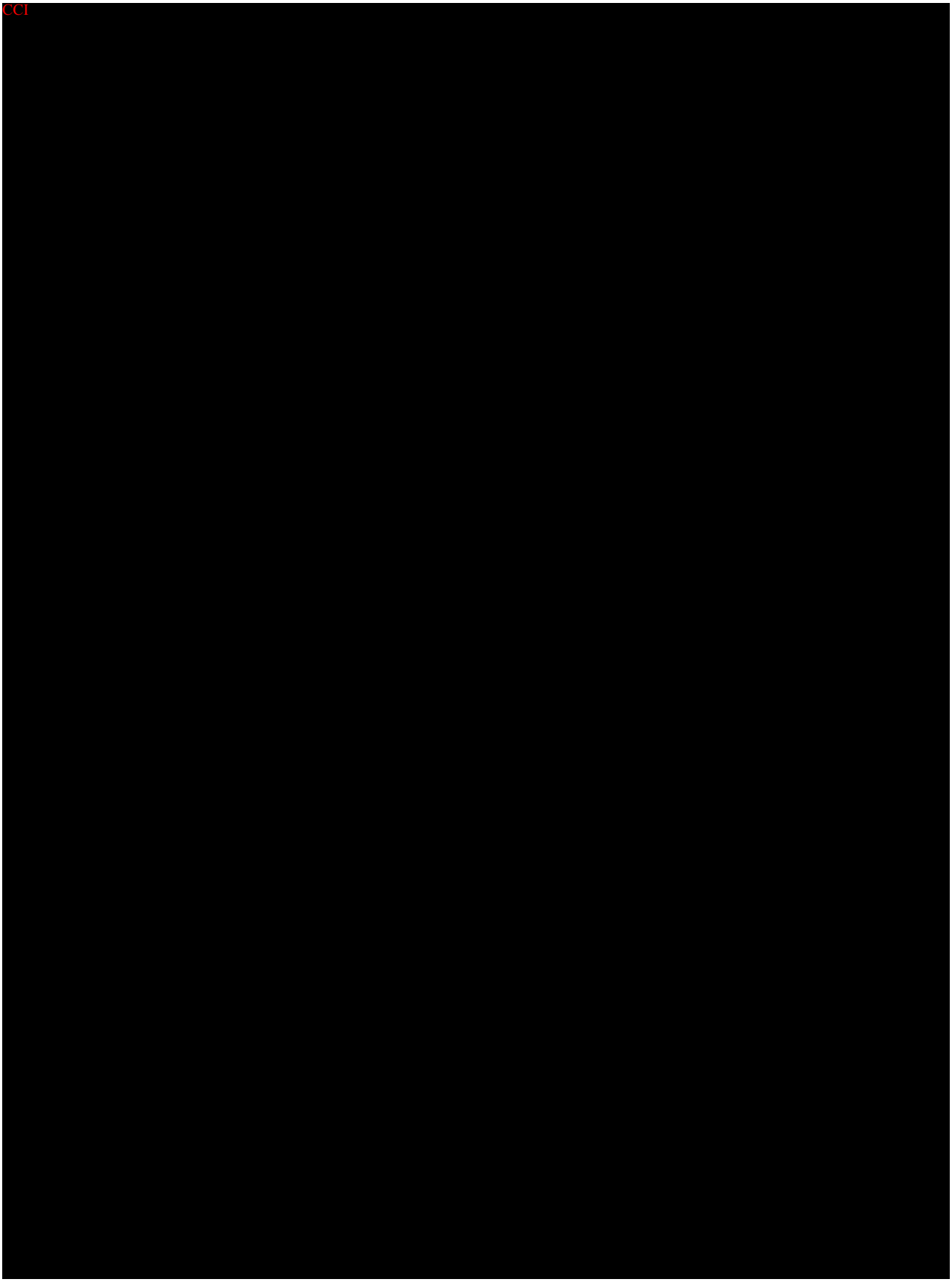
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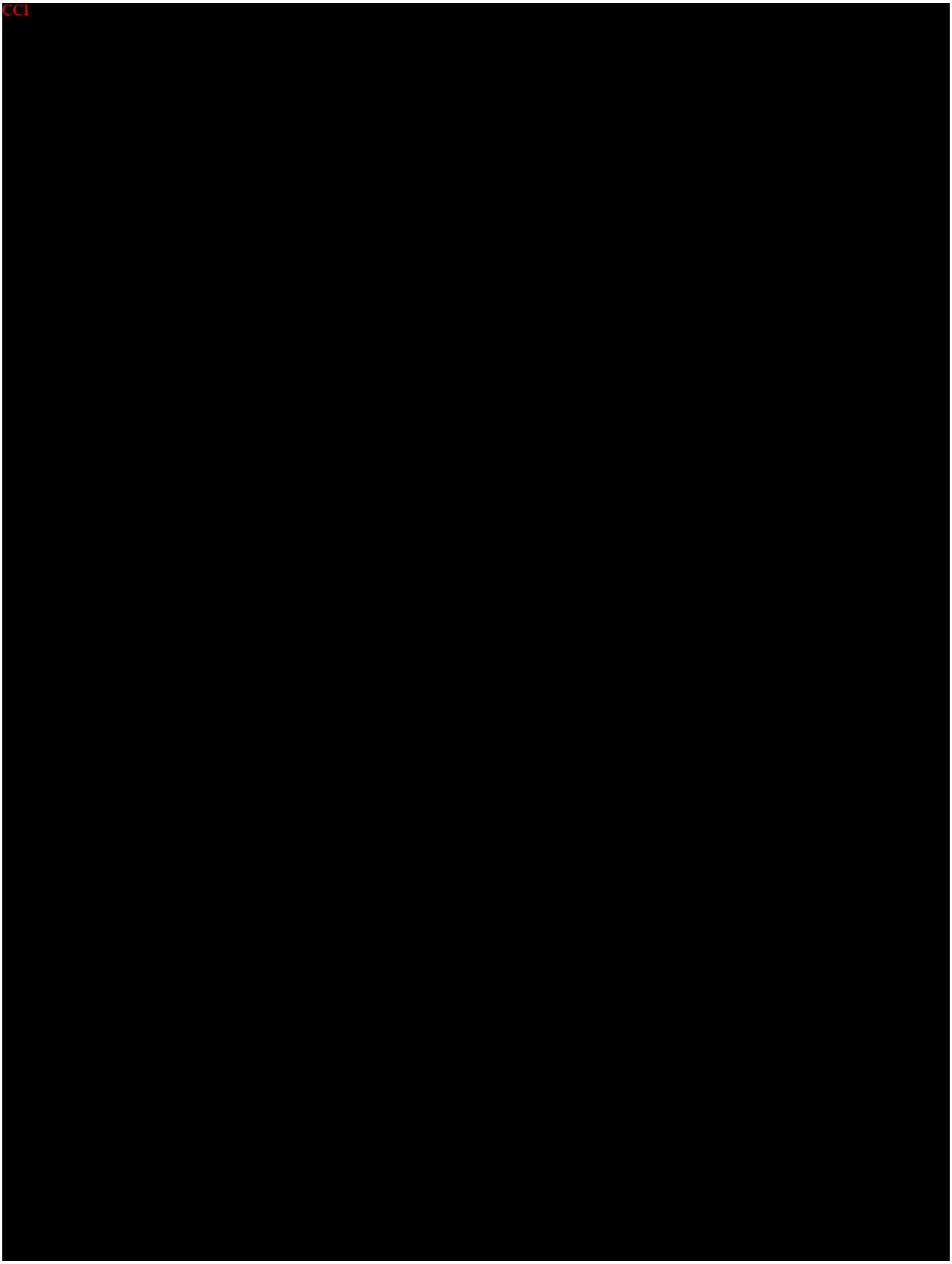
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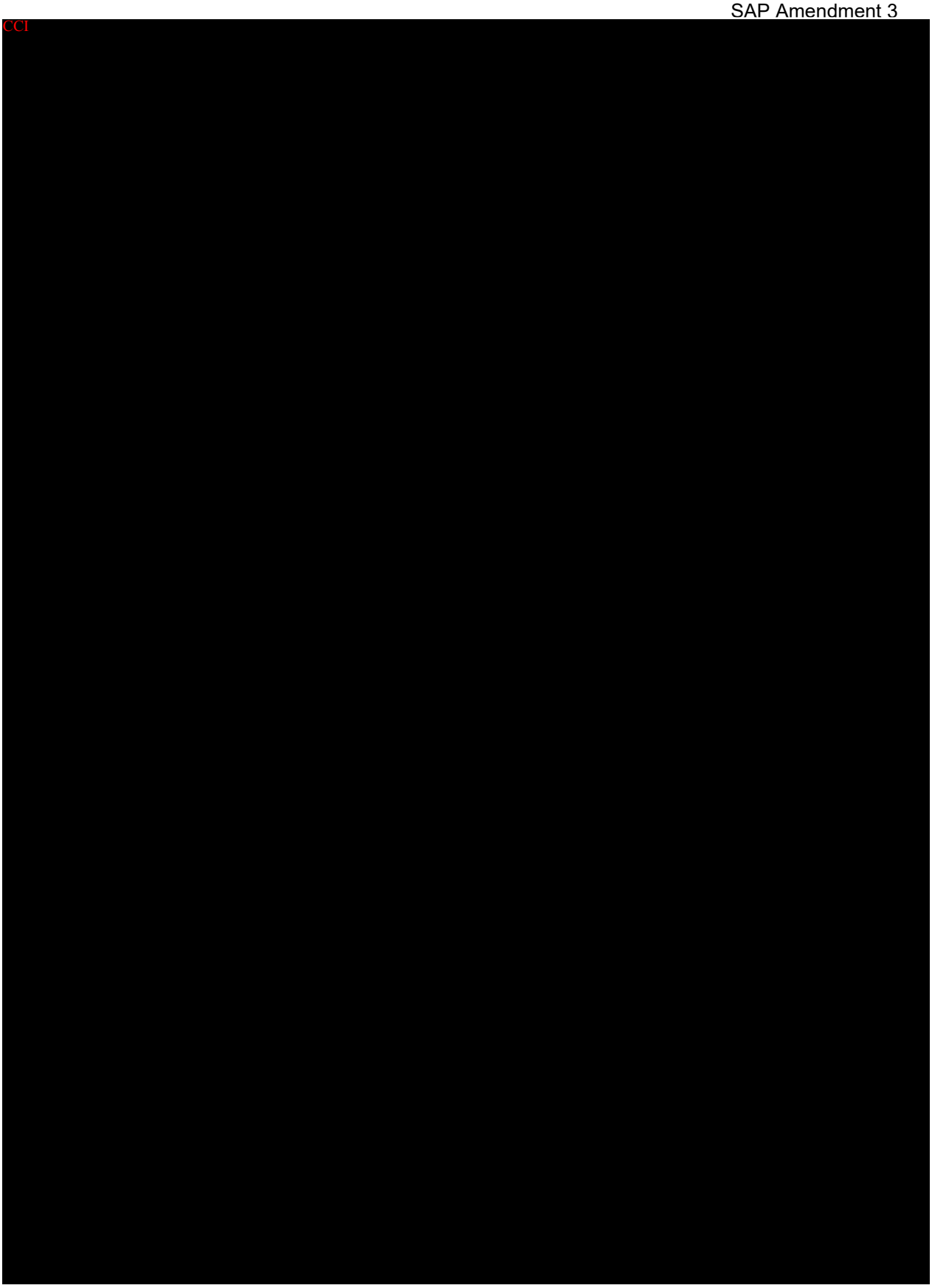
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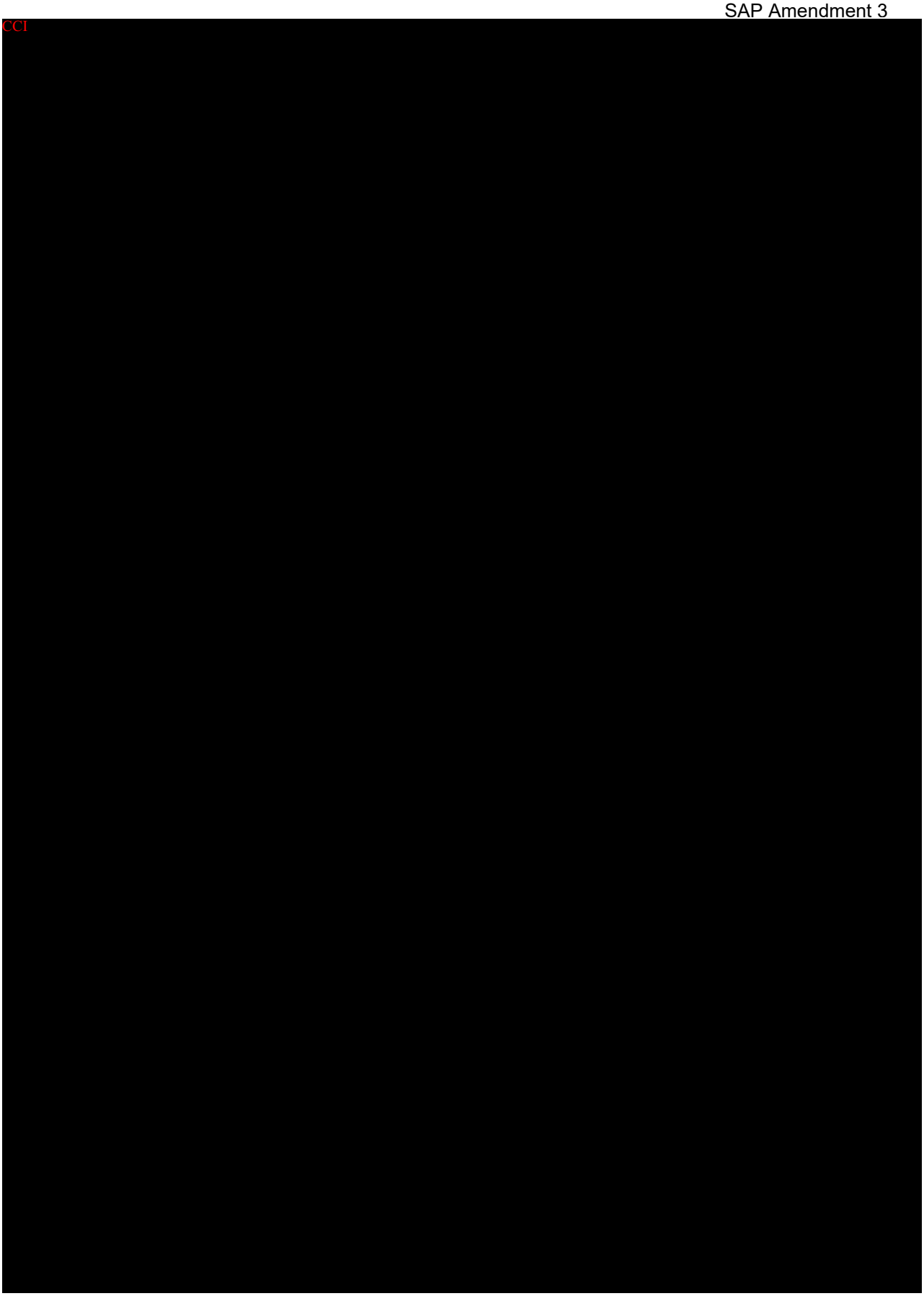
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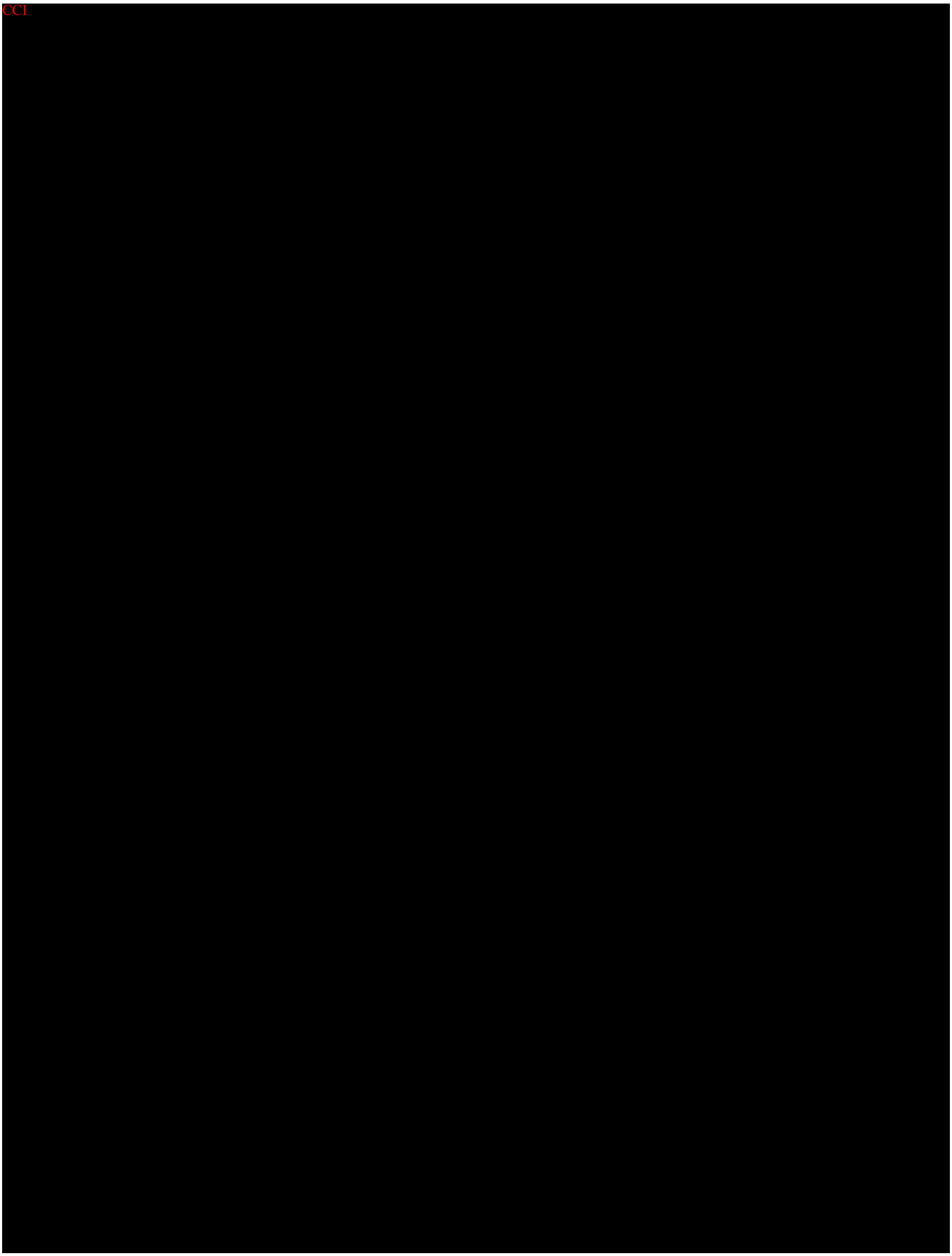
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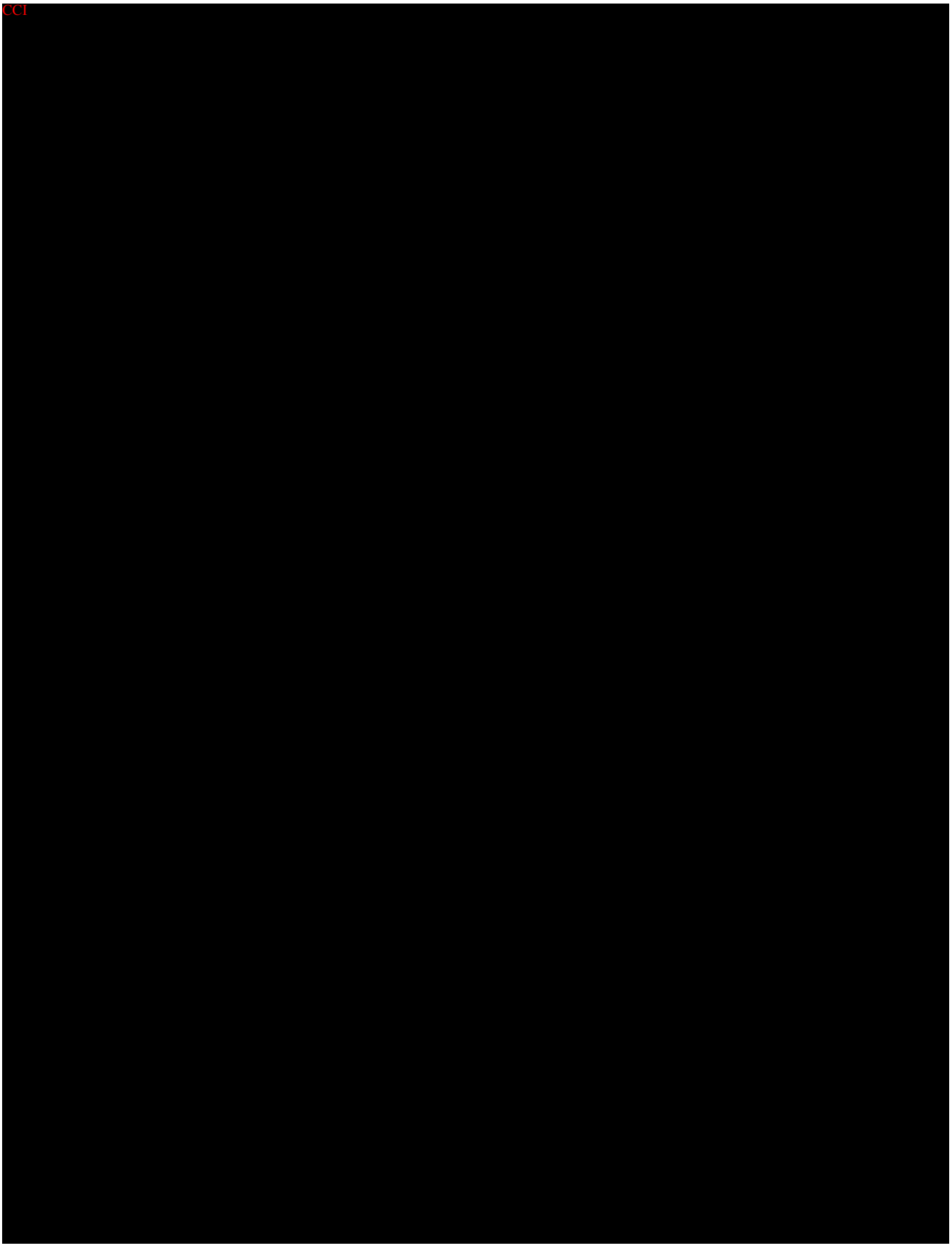
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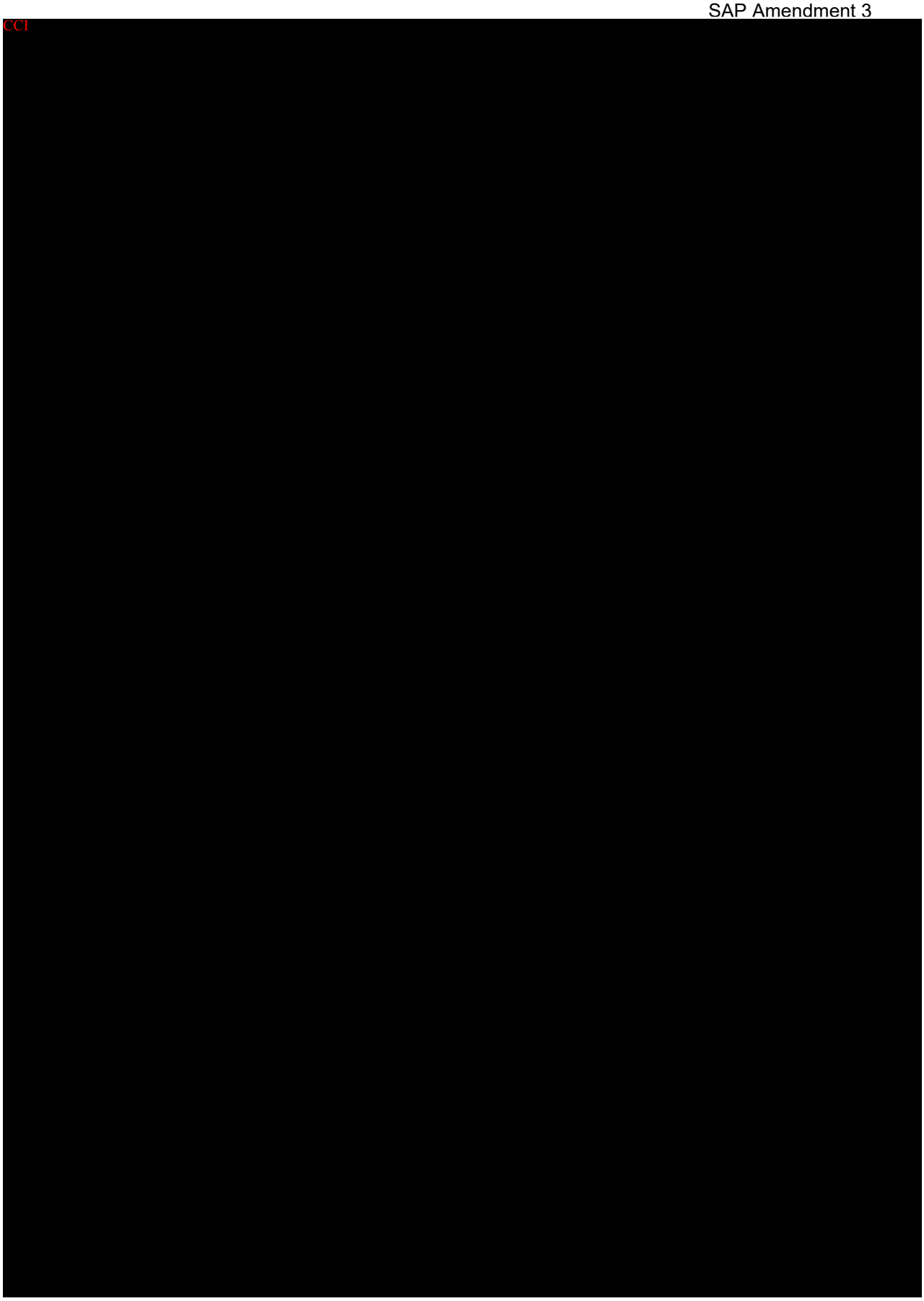
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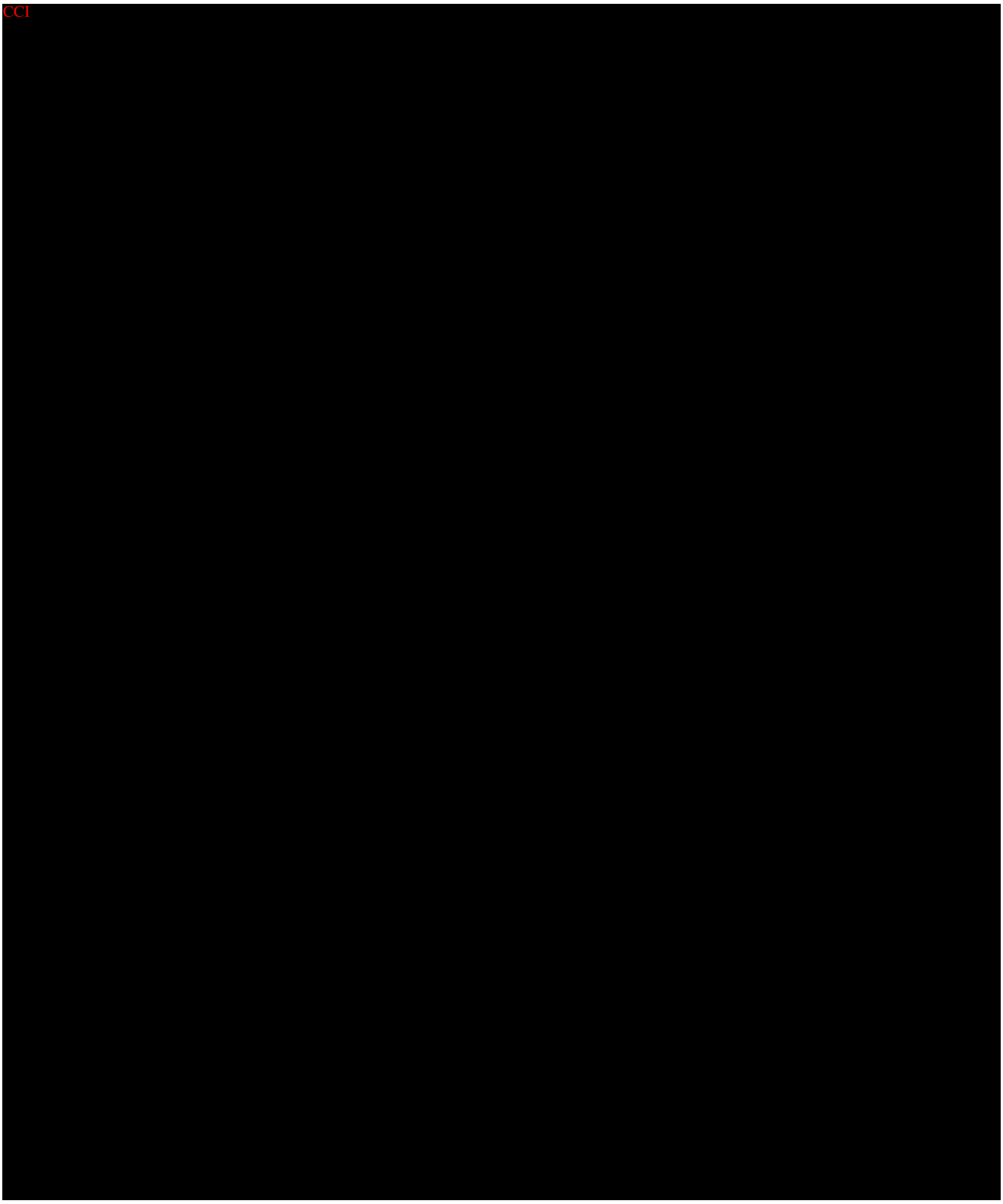


## 4.6. Other Analyses

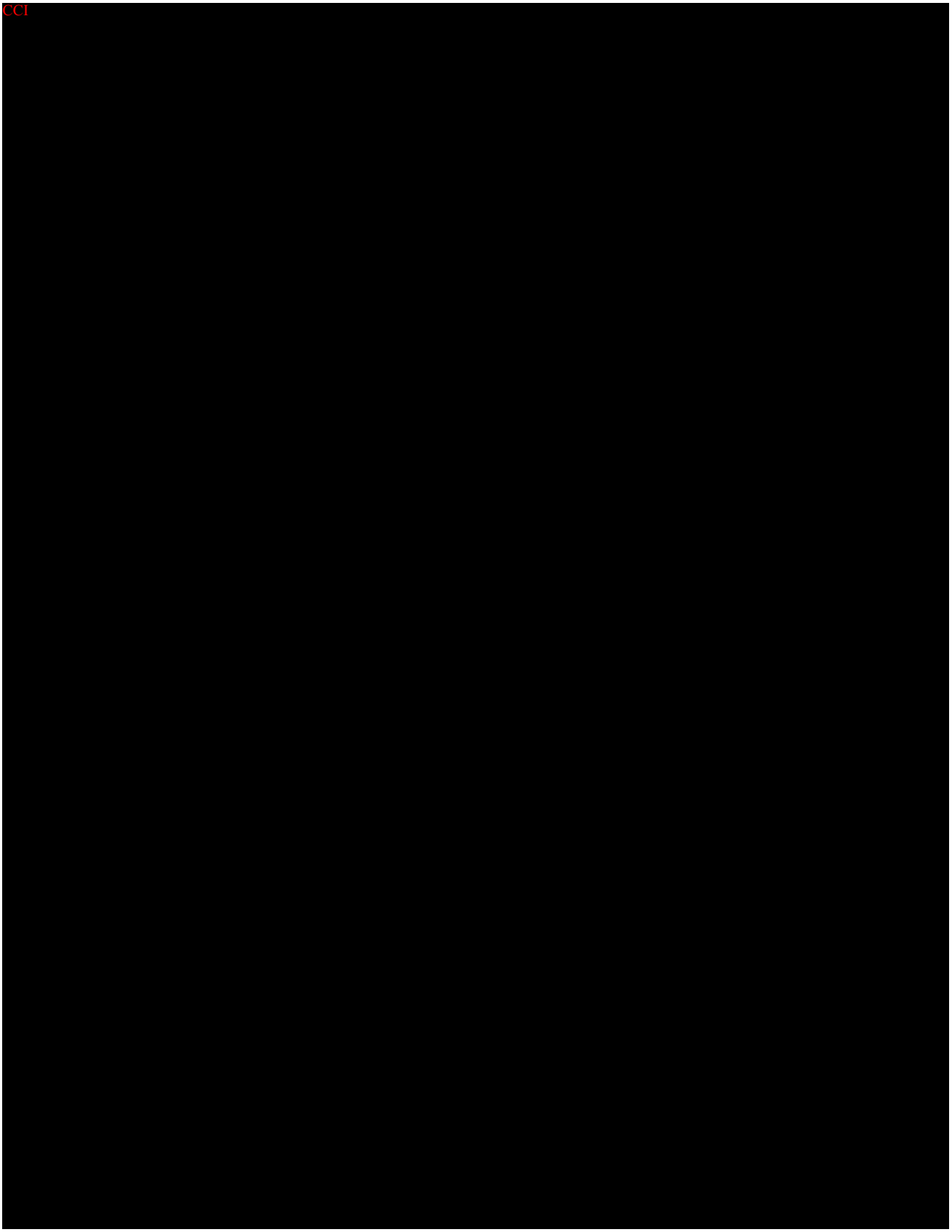
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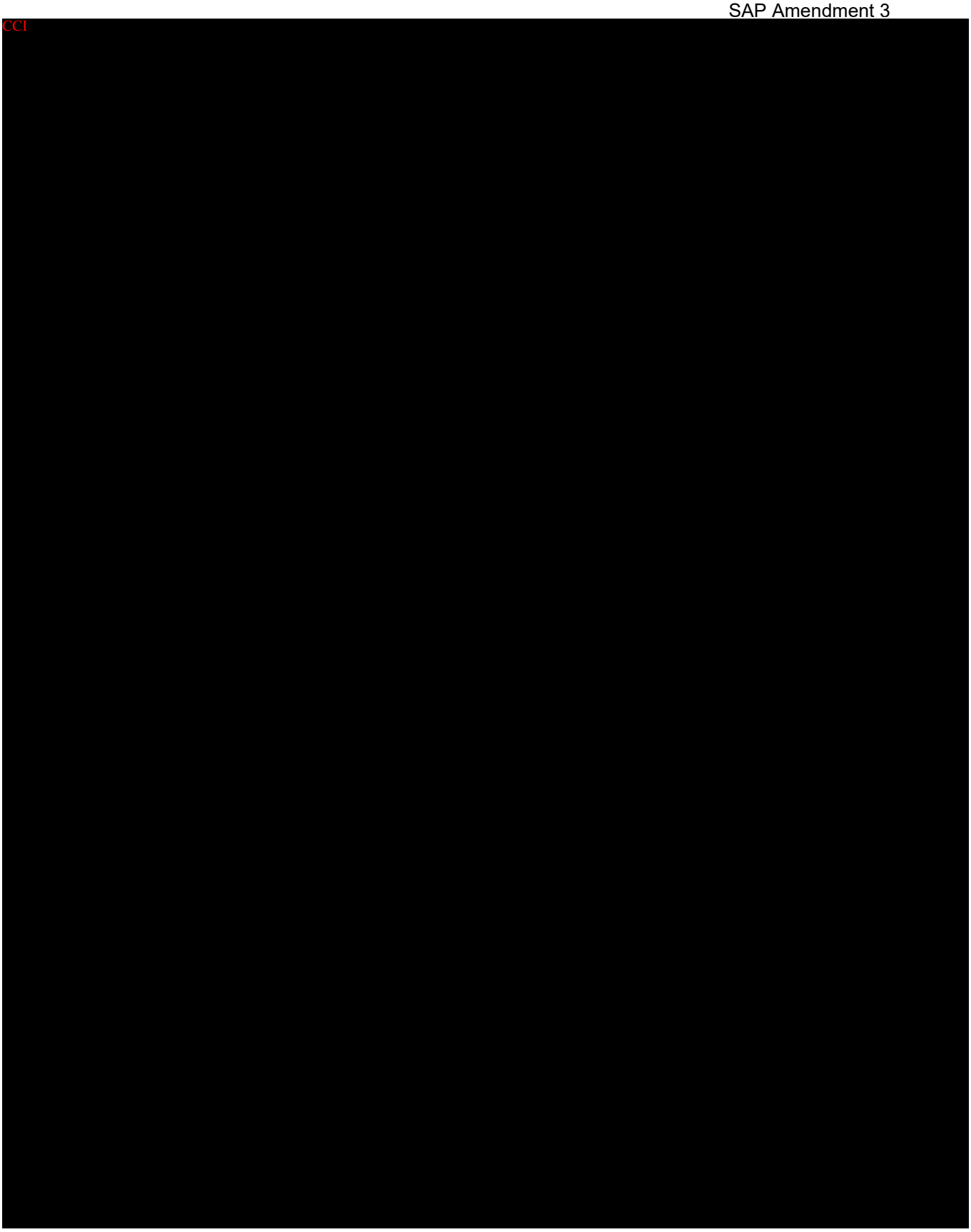
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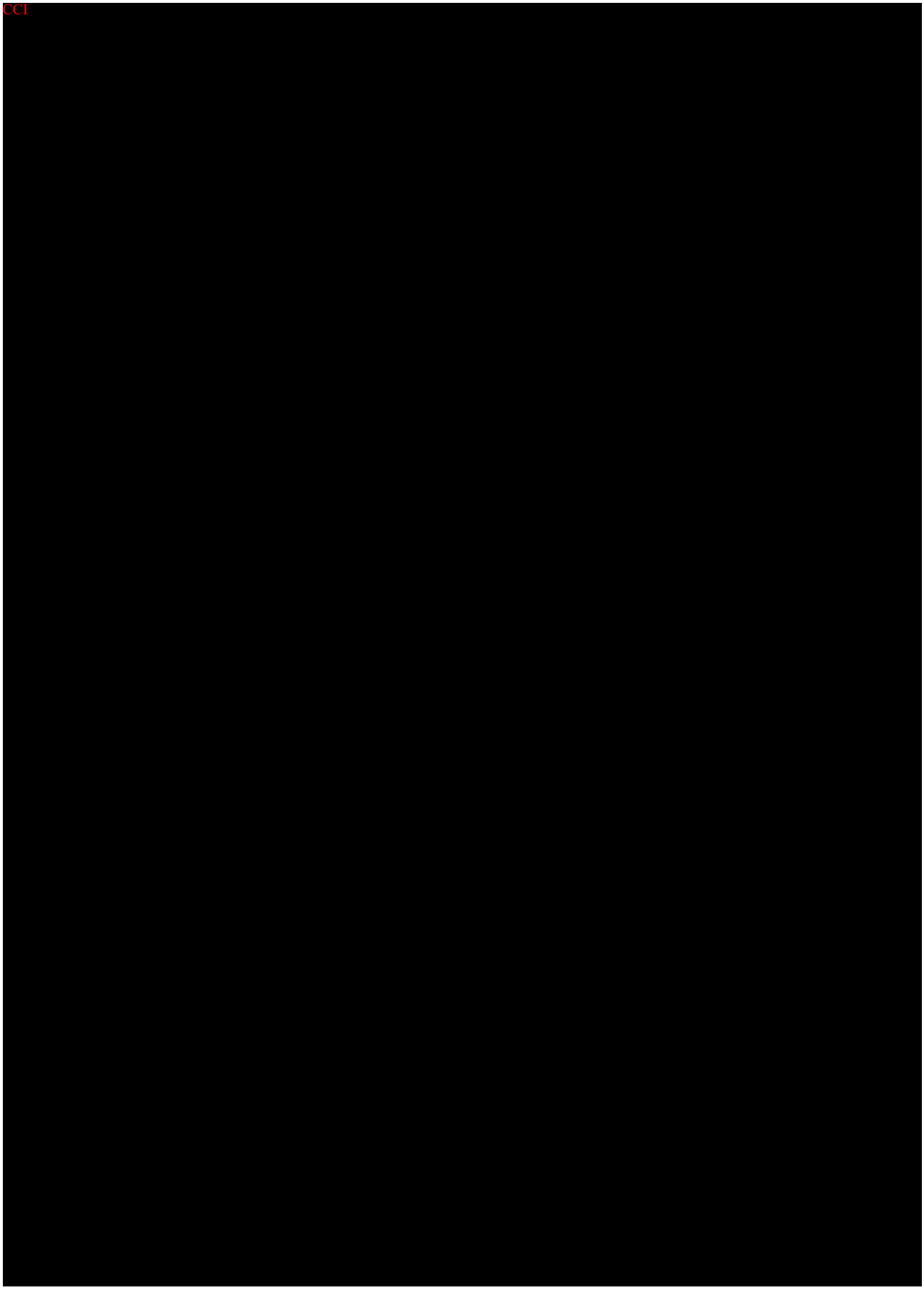
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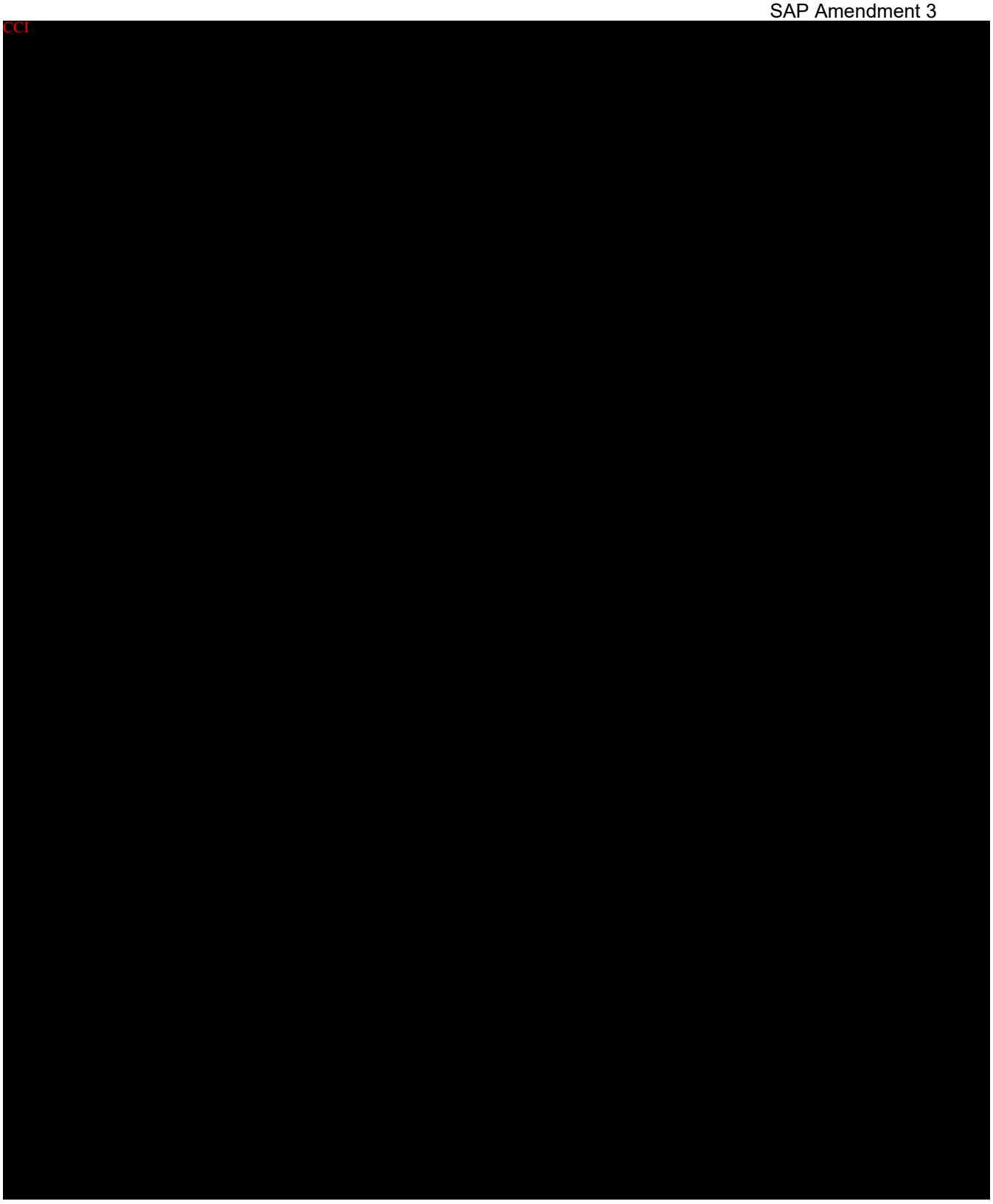
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## 4.8. Changes to Protocol Defined Analyses

Changes from the originally planned statistical analysis specified in the protocol are detailed in Table 9.

**Table 9 Changes to Protocol Defined Analysis Plan**

| Protocol Defined Analysis | SAP Defined Analysis | Rationale for Changes |
|---|---|---|
| • Physical examination data are listed as an endpoint under the safety and tolerability secondary objective. | • No planned analysis will be generated. | • Physical examination data were not collected in the eCRF and captured in the clinical database |
| • In Protocol Appendix 1, BOR is defined as "best response recorded from the start of the treatment until disease progression/recurrence". | • The BOR definition uses randomization instead of the start of treatment. | • Clarification for a randomized trial. |
| • To be assigned a status of SD, follow-up disease assessment must have met the SD criteria at least once after randomization at a minimum interval of 84 (±14) days. | • To be assigned a status of SD, follow-up disease assessment must have met the SD criteria at least once after randomization at a minimum interval of 42 (±7) days. | • Align with internal guidance. |
| • The exploratory efficacy endpoints of ORR and PFS by iRECIST based on Investigator assessment will be analyzed in the same manner as for the secondary efficacy endpoints of ORR and PFS by RECIST v1.1 based on Investigator assessment. | • ORR and PFS by iRECIST will not be analyzed. | • In an FDA pooled analysis [Mulkey, 2020], the authors conclude "the magnitudes of treatment effects on ORR and PFS, as well as associations of PFS with OS, as calculated by iRECIST or RECIST V1.1 appeared similar". |

# 5. SAMPLE SIZE DETERMINATION

A total of 750 participants will be randomized using a 2:2:1 allocation ratio (cobolimab + dostarlimab + docetaxel:dostarlimab + docetaxel:docetaxel, i.e., Arm A:Arm B:Arm C). The sample size is driven by the primary efficacy analysis comparing the OS distributions of each of the combination arms vs the docetaxel arm. Based on several studies in the literature, including CANOPY-2 [Paz-Ares, 2024], CONTACT-01 [Neal, 2024], LEAP-008 [Leighl, 2023], the median OS for docetaxel is expected to be approximately 11 months. Assuming the true HR of 0.691 (ie, 11 months vs 15.9 months)

for each combination arm vs docetaxel comparison, a total of approximately 348 OS events between 1 combination arm and the docetaxel arm will provide at least 90% power to detect a statistically significant treatment benefit at an overall 1-sided, 0.0249 significance level adjusted for multiple comparisons using the Hochberg procedure (at the final analysis) as described in Section 2.1. Assuming a 77% OS event maturity rate, 750 patients (300:300:150 in Arm A:Arm B:Arm C) will need to be randomized.

The final analysis will be performed when a total of approximately 348 OS events are reached for each combination arm and the docetaxel arm.

An external unblinded statistician will monitor the number of events to determine the timing of the final analysis.

The sample size calculations were performed using Cytel East 6.4.

# 6. SUPPORTING DOCUMENTATION

## 6.1. Appendix 1 Study Population Analyses

### 6.1.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the Intent-to-Treat population, unless otherwise specified (i.e., screening status will be based on the screened population, exposure will be based on the safety population).

Demographic and baseline characteristics summaries will be presented overall and by phase of enrolment (Phase 2 vs Phase 3).

Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure will be based on GSK Core Data Standards. Details of the planned displays are presented in the OPS.

### 6.1.2. Participant Disposition

The following participant disposition summaries will be summarized by treatment arm and overall:

- Screening status (participants screened, participants entered the study, screen failures and reasons for failure, based on the Screened population)
- Participant status (ongoing on-study treatment, ongoing in follow-up, completed the study [died, study is closed/terminated], withdrawn from study and reason for study withdrawal)
- Treatment status (ongoing, discontinued and reason for discontinuation overall and for each drug)

- Number and percentage of screened participants belonging to each analysis population (e.g., ITT, safety, per-protocol etc.) displayed by randomized treatment. The number of participants randomized but not treated (i.e., who are part of the ITT set but not part of the safety set) can be derived from that summary. Non randomized participants are displayed in a no treatment column.
- Participant status (randomized, completed, withdrawn, ongoing) presented overall and by phase of enrolment (Phase 2 vs Phase 3).
- Participants in the enrolled population will be summarized by country and site ID.
- Summary of randomization strata by RTSM and eCRF as well as a comparison between sources. See Section 4.1.2 for further details on the strata reporting.

Study withdrawal, treatment discontinuation, inclusion/exclusion criteria deviations, exclusions from study populations and reasons for screening failures will be listed.

### 6.1.3. Protocol Deviations

Protocol deviations will be tracked by the study team throughout the conduct of the study.

- Data will be reviewed prior to freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis populations are captured and categorized on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarized by treatment arm and overall and listed.

### 6.1.4. Demographic and Baseline Characteristics

#### 6.1.4.1. Demographic characteristics and Smoking Status

Demographic characteristics and smoking status are collected in the *Demographics* eCRF page. ECOG performance status at Screening is collected in the *ECOG Performance Status* page. Height and weight are captured on the *Vital Signs Screening* page. Body surface area (BSA) will be derived based on height and weight at screening using the Mosteller formula (see Section 6.3.2).

Demographic characteristics and smoking status will be summarized by treatment arm and overall and include the following categories:

- Sex: Male, Female
- Age (years): summary statistics
- Age Group (years): < 18, 18-64, 65-75, ≥75

- Ethnicity: Hispanic or Latino, not Hispanic or Latino, not reported, unknown
- Race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Mixed Race, not reported, unknown.
- Race Detail: American Indian or Alaska Native, Asian – Central/South Asian heritage, Asian – East Asian heritage, Asian – Japanese heritage, Asian – South East Asian heritage, Black or African American, Native Hawaiian or other Pacific Islander, White – Arabic/North African heritage, White – White/Caucasian/European heritage, mixed Asian race, mixed White race, multiple, not reported, unknown
- Smoking Status: never, current, former
- Height (cm): summary statistics
- Weight (kg): summary statistics
- BMI ($kg/m^2$): summary statistics (=weight (kg) / [height (m)]$^2$)
- BSA ($m^2$): summary statistics
- ECOG performance status at Screening: 0, 1

If the summary of demographics meets the criteria for de-identification, as described in the relevant procedural document, a de-identified version should be produced.

Age ranges (Adult [18-64 years], >=65-84 years, >=85 years) will also be displayed by the enrolled population. Demography characteristics will also be listed.

#### 6.1.4.2. Disease Characteristics

Disease characteristics are collected in the *Advanced/Metastatic NSCLC History* eCRF page. PD-L1 status is collected in the *PD-L1* eCRF page. Histology and PD-L1 TPS are also captured in the RTSM system.

Disease characteristics will be summarized by treatment arm and overall and include the following categories:

- Primary tumor type: Adenocarcinoma, Squamous cell carcinoma, Large cell carcinoma
- Time from initial diagnosis to randomization (days): summary statistics
- Time from diagnosis of advanced/metastatic disease to randomization (days): summary statistics
- Histology (eCRF): Squamous, Nonsquamous
- Histology (RTSM): Squamous, Nonsquamous
- PD-L1 TPS: ≥50%, < 50% - per RTSM for participants after protocol amendment 3, per eCRF for participants prior to protocol amendment 3
- PD-L1 Status (according to the eCRF): TPS ≥50%, TPS < 50%
- PD-L1 Status (according to the eCRF): TPS ≥1%, TPS <1%

- Stage at initial diagnosis: as captured in eCRF advanced/metastatic NSCLC history page
- Stage at Screening: as captured in eCRF advanced/metastatic NSCLC history page
- Metastatic disease site and number of metastatic sites: as captured in eCRF advanced/metastatic NSCLC history page. Where pre-specified sites are similar, these will be grouped and only counted once in the number of metastatic sites.

### 6.1.5. Medical Conditions

Medical conditions at screening are collected in the *Medical History* eCRF page. A summary of the number and percentage of subjects who report medical conditions at screening will be displayed by classification (system organ class), treatment arm and overall.

### 6.1.6. Prior Anti-Cancer Therapy for Advanced/Metastatic Lung Cancer

Prior anti-cancer therapy is collected in the *Prior Anti-Cancer Therapy for Lung Cancer*, *Prior Surgery for Primary Lung Cancer* and *Prior Radiotherapy* eCRF pages. The number of prior lines of therapy (1 prior line vs 2 prior lines) is also captured in the RTSM system.

Prior anti-cancer therapy for lung cancer in the advanced/metastatic setting will be summarized by treatment arm and overall and will include the following categories:

- Number of participants with at least one prior anti-cancer drug therapy for lung cancer (eCRF data) by number of prior lines (0-5). Additional rows for >0 and >2 lines of therapy will be included. Two lines of therapy will be categorized into the order and combination of IO [anti-PD-(L)1)] and platinum chemotherapy received.
- Number of participants with at least one prior anti-cancer drug therapy for lung cancer in the advanced/metastatic setting (RTSM data):
  - 1 prior line of therapy – IO + chemo
  - 2 prior lines of therapy – IO followed by chemo, chemo followed by IO
- Time from end of last anticancer therapy to randomization (days): summary statistics
- Number of participants with any prior anti-cancer therapy for lung cancer by type of therapy category

The number of participants with prior surgery and the number of participants with prior radiotherapy for participants with at least one therapy in the advanced/metastatic setting will also be included.

The best response to the most recent prior anti-cancer drug therapy in the advanced/metastatic setting will also be summarized.

### 6.1.7. Prior and Concomitant Medications

Prior and concomitant medications are collected in the *Prior and Concomitant Medication/Therapy* eCRF page.

Prior and concomitant medications will be coded using the current version of the World Health Organization (WHO) Drug dictionary (latest version available at time of reporting). **Concomitant medications** are medications, other than study treatment, that started on or after the first dose of study treatment and prior to the end of the on-treatment period (defined in Section 6.3.6). **Prior medications** are medications, other than study treatment, that started and stopped prior to the first dose of study treatment. **Prior and Concomitant medications** are medications, other than study treatment, that started prior to the first dose of study treatment and stopped on or after the first dose of study treatment.

Prior and concomitant medications will be summarized by treatment arm and overall with separate displays for prior, concomitant and prior and concomitant medications. The summary will be presented by Anatomical Therapeutic Chemical (ATC) Class (the lowest level of ATC term available from WHO Drug Dictionary) and ingredient. Participants with more than 1 medication in a given ATC and ingredient category will only be counted once in that category.

Prior and concomitant medications will be listed with whether the medication is prior and ongoing included.

### 6.1.8. Follow Up Anti-Cancer Therapy

Follow up anti-cancer therapy is collected in the *Follow Up Anti-Cancer Therapy* eCRF page.

The number and percentage of participants initiating follow up anti-cancer therapy will be summarized by treatment arm and overall. The summary will include the type of anti-cancer therapy as collected in the eCRF and the time from study treatment discontinuation to start of anti-cancer therapy. To derive the time to subsequent anti-cancer therapy, any partial dates will be imputed using the rules outlined in Section 6.3.7.3.

### 6.1.9. Additional Analyses Due to the COVID-19 Pandemic

To address the impact of the COVID-19 pandemic on trial results, the following outputs will be generated:

- Summary of COVID-19 assessments for participants with suspected, probable or confirmed COVID-19 case diagnosis.
- Summary of exposure adjusted incidence rates of TEAEs, any treatment-emergent SAEs and Any Grade ≥ 3 TEAEs over time
- Summary of exposure adjusted incidence rates of common (>= 5%) TEAEs

For the exposure adjusted incidence rate displays, event rates are reported by calendar time, in pre-defined time blocks that are defined in Table 10.

Pandemic measures began in different countries at different times. A dataset containing the date when pandemic measures began, as determined by the GSK country Issue Management Teams (IMT), will be used to determine the start date of pandemic measures within each country. A copy of this dataset will be taken at the time of database lock (DBL). The alert levels are escalated and de-escalated over time and the scale used for the recording of alerts is standardized: green (low impact), yellow (low to moderate impact), orange (moderate to high impact), red (high impact), and black (high impact with severe disruption). Date of when pandemic measures began was defined based on the IMT alert levels and used in analyses.

Adverse events will be summarized according to whether the onset date was before, during or after the start of the COVID-19 pandemic measures.

The initial start date is being defined as when the COVID-19 IMT alerts for each country were all initially activated with an alert level of Yellow or above. The end date is defined as when the alert level was de-escalated to green for each country. Where an end date is not provided for a country, the date when the WHO emergency committee de-escalated COVID-19 worldwide will be used. On 5 May 2023, the Director-General accepted the recommendation by the WHO Emergency Committee on COVID-19 that the disease no longer fits the definition of a public health emergency of international concern [World Health Organization, 2024].

**Table 10 Definition of when COVID-19 Pandemic Measures Began**

| Pandemic Measures Phase | Definition |
|---|---|
| Pre | AE onset date < pandemic measures start date |
| During | Pandemic measures start date ≤ AE onset date < pandemic measures end date |
| Post | AE onset date ≥ pandemic measures end date |

Exposure adjusted incidence rate (rate/100 PY) = (number of participants with occurrence of a specific treatment-emergent adverse event /total exposure duration in years across all participants at risk at the start of the given time interval)*100. Exposure duration is defined as:

- (date of last dose of any study treatment component[1] – date of first dose of study treatment[2] + 1)/365.25 for participants who DO NOT experience the event
- (start date of TEAE – date of first dose of study treatment[2] + 1)/365.25 for participants that DO experience the event

[1] or end date of time block, whichever occurs sooner.

[2] or start date of time block, whichever occurs later.

For recurring common TEAEs events, the first occurrence of an event (by MedDRA preferred term) will be reported, with the appropriate corresponding exposure years.

## 6.2. Appendix 2 Electronic Clinical Outcome Assessment (eCOA) Compliance

Summary measures of the overall participant compliance rate, and the participant compliance rate over time for each PRO instrument will be derived, respectively. These will be based upon the following definitions:

- Expected questionnaire: a questionnaire that is expected to be completed at a scheduled assessment time e.g. a questionnaire from a participant who is still under PRO follow-up at the specified assessment time.
- Evaluable questionnaire: a questionnaire with a completion date and at least one subscale that is non-missing.

Overall participant compliance rate for each PRO endpoint is defined for each randomized treatment group as: Total number of participants with an evaluable baseline and at least one evaluable follow-up questionnaire, divided by the total number of participants expected to have completed at least a baseline questionnaire multiplied by 100. The target compliance for each instrument is 80%.

Participant compliance over time is calculated separately for each scheduled assessment (including baseline) as the number of participants providing an evaluable assessment at that assessment divided by the number of participants expected to have provided an assessment.

Overall study-level compliance rate across the PRO instruments will also be summarized by treatment arm and overall.

## 6.3. Appendix 3 Data Derivations Rule

Additional data derivation rules may be described in the OPS if applicable.

### 6.3.1. General

| **Multiple Measurements at One Analysis Time Point** |
|---|
| • Mean of the measurements may be calculated and used in any derivation of summary statistics but if listed, all data will be presented.<br>• Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables. |
| **Study/Treatment Day** |
| Study Day (Efficacy/Non-safety Parameters)<br>• Calculated as the number of days from Randomization Date:<br>o Ref Date = Missing → Study Day = Missing<br>o Ref Date < Randomization Date → Study Day = Ref Date – Randomization Date<br>o Ref Data ≥ Randomization Date → Study Day = Ref Date – (Randomization Date) + 1<br>Treatment Day (Safety Parameters)<br>• Calculated as the number of days from First Dose Date:<br>o Ref Date = Missing → Study Day = Missing |

| |
|---|
| ○ Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date<br>○ Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1 |
| **Change from Baseline** |
| • Change from Baseline = Post-Baseline Visit Value – Baseline<br>• % Change from Baseline= 100 x (Post-Baseline Visit Value – Baseline) / Baseline<br>• Maximum Increase/Decrease from Baseline = maximum (Increase/Decrease from Baseline)<br>• If either the Baseline or Post-Baseline Visit Value is missing, Change from Baseline and % Change from Baseline is set to missing |
| **Time Unit Conversion Factors** |
| • Weeks = Number of Days/7<br>• Months = Number of Days/30.4375<br>• Years = Number of Days/365.25 |
| **Duration** |
| Durations (e.g., the duration of an adverse event, duration of exposure, etc.) are calculated as:<br>Stop Date – Start Date + 1<br>The time since an event (e.g., time since initial diagnosis) is calculated as:<br>• Ref Date = Missing → Time since an event = Missing<br>• Ref Date < Event Date → Time since an event = Ref Date – Event Date<br>• Ref Data ≥ Event Date → Time since an event = Ref Date – (Event Date) + 1 |

### 6.3.2. Study Population

| |
|---|
| **Age** |
| • Analysis age will be calculated from birth date to date of randomization.<br>• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows:<br>○ Missing day and month will be imputed to "30th June"<br>• Birth date will be presented in listings as "YYYY". |
| **BSA** |
| • BSA ($m^2$) will be derived using the Mosteller formula, where H = height (cm) and W = weight (kg)<br>$$\sqrt{\frac{HxW}{3600}}$$<br>• For exposure, this will use the most recent height and weight measurement prior to dose. For demographics, this will use height and weight at screening. |

### 6.3.3. Efficacy

#### 6.3.3.1. Geographic Region of Enrolling Sites

The geographic region of enrolling sites will be categorized into the following categories:

- North America: Canada, Mexico, United States
- East Asia: Japan, Republic of Korea, Taiwan
- Europe: Belgium, Finland, France, Germany, Greece, Italy, Netherlands, Poland, Romania, Russia Federation, Spain, Sweden, United Kingdom
- RoW: Argentina, Australia, Brazil, Thailand, Turkey

#### 6.3.3.2. Derived Date of Last Contact

For participants not known to have died, the date of last contact will be derived using the maximum complete collection/assessment date from among these selected data domains within the clinical database:

- Disposition dates, excluding date of study discontinuation for reasons of lost-to follow-up and death
- Participant assessment dates (blood sampling [laboratory, PK, biomarker], vital signs, ECGs, tumor assessment, etc.)
- Start and end dates of healthcare encounters
- Start and end date of AEs
- Start and end date of study treatment
- Start and end date of concomitant medications/procedures
- Start and end date of follow up anti-cancer therapies administered after study treatment discontinuation
- Last date of contact recorded on the survival follow-up for current participant status
- Date last known alive on the *Participant Survival Status - Post Study Withdrawal* eCRF page for participants that discontinued study for reasons other than death.

#### 6.3.3.3. Extended Time Without Adequate Assessment for PFS/iPFS Endpoints

CCI [redacted]
CCI [redacted]
CCI [redacted] If death or PD follow 2 missed consecutive visits, then PFS is censored at the time of the last adequate tumor assessment (LATA). If death follows 2 missed consecutive visits, then iPFS is censored at the time of LATA.

The definition of 2 missed consecutive visits varies according to the scan schedule and is defined by matching the LATA prior to an event (PD/death) to a scheduled visit using the midpoint in Table 11 LATA before the midpoint is assigned to the scheduled visit prior to it. LATA after the midpoint is assigned to the scheduled visit after it.

**Table 11 Mapping of Tumor Assessment to Scheduled Visit**

| Assessment Schedule | Scheduled visit – 1 week (7 days) | Scheduled visit (weeks from randomization) | Scheduled visit + 1 week (7 days) | Midpoint (floor for non-integers) |
|---|---|---|---|---|
| Q6W | 5 | 6 | 7 | 9 |
| | 11 | 12 | 13 | 15 |
| | 17 | 18 | 19 | 22 |
| Q9W | 26 | 27 | 28 | 31 |
| | 35 | 36 | 37 | 40 |
| | 44 | 45 | 46 | 49 |
| | 53 | 54 | 55 | 60 |
| Q12W | 65 | 66 | 67 | 72 |
| | 77 | 78 | 79 | 84 |
| | 89 | 90 | 91 | 96 |
| | 101 | 102 | 103 | 108 |

Any event occurring after LATA + T2, is considered to have occurred after 2 consecutive missed assessments, where T2 is defined as follows:

- If LATA prior to event is within 9 weeks, T2 = 42*2 + 7*2 = 98 days
- If LATA prior to event is after 9 weeks but within 15 weeks, T2 = 42+63+7*2 = 119 days
- If LATA prior to event is after 15 weeks but within 40 weeks, T2 = 63*2+7*2 = 140 days
- If LATA prior to event is after 40 weeks but within 49 weeks, T2 = 63+84+7*2 = 161 days
- If LATA prior to event is after 49 weeks, T2 = 84*2 + 7*2 = 182 days

#### 6.3.3.4. Extended Time Without Adequate Assessment for PRO Endpoints

EORTC-QLQ-LC13 and EORTC-QLQ-C30 are collected on C1D1, every 3 weeks until C6, every 9 weeks until C18, and every 12 weeks thereafter. For participants who discontinue treatment, assessments are collected at the EOT visit, at the 30 (±7)-day Safety Follow-Up Visit and 90 (±14) days after the last dose. For participants who agree to modified follow up, the last assessments will be collected at the EOT Visit.

If deterioration follows 2 missed consecutive visits, then TTD is censored at the time of the last PRO assessment. The definition of 2 missed consecutive visits varies according to the PRO schedule and is defined by matching the last PRO assessment prior to an event (deterioration), similar to the methodology for PFS described above.

Any event occurring after last PRO assessment + T2, is considered to have occurred after 2 consecutive missed assessments, where T2 is defined as follows:

- If last PRO assessment prior to event is within 12 weeks, T2 = 2*21 + 2*3 = 48 days
- If last PRO assessment prior to event is after 12 weeks but within 15 weeks, T2 = 21 + 63 + 2*3 = 90 days
- If last PRO assessment prior to event is after 15 weeks but within 42 weeks, T2 = 2*63 + 2*3 = 132 days
- If last PRO assessment prior to event is after 42 weeks but within 51 weeks, T2 = 63 + 84 + 2*3 = 153 days
- If last PRO assessment prior to event is after 51 weeks but before EOT, T2 = 2*84 + 2*3 = 174 days
- If last PRO assessment prior to event is less than 12 weeks before EOT, T2 = 84 + 3 + 30 + 7 = 124 days
- If last PRO assessment prior to event is EOT, T2 = 90 + 14 = 104 days

## 6.3.4. Safety

### 6.3.4.1. Immune-mediated Adverse Events

Below is a list of imAE categories that will be used to identify immune-mediated adverse events.

Programmatically defined, imAEs are identified as any IO treatment related ≥Grade 2 AEs based on a pre-specified search list of preferred terms (PTs) using the most recent MedDRA version, finalized for analysis of the current study data prior to database lock. imAEs will be identified using the following GSK Terms of Interest (TOI):

| imAE_Category | TOI Code | TOI category name |
|---|---|---|
| Immune-mediated Pulmonary | 322669 | Dostarlimab Immune-mediated Pulmonary |
| Immune-mediated Gastrointestinal | 322661 | Dostarlimab Immune-mediated Gastrointestinal |
| Immune-mediated hepatic | 322663 | Dostarlimab Immune-mediated hepatic |
| Immune-mediated endocrinopathies | 322660 | Dostarlimab Immune-mediated endocrinopathies |
| Immune-mediated renal | 322670 | Dostarlimab Immune-mediated renal |
| Immune-mediated skin adverse reactions | 322671 | Dostarlimab Immune-mediated skin adverse reactions |
| Immune-mediated pancreatitis | 322668 | Dostarlimab Immune-mediated pancreatitis |
| Immune-mediated hematologic | 322662 | Dostarlimab Immune-mediated hematologic |
| Immune-mediated musculoskeletal | 322664 | Dostarlimab Immune-mediated musculoskeletal |
| Immune-mediated nervous system | 322665 | Dostarlimab Immune-mediated nervous system |

| imAE_Category | TOI Code | TOI category name |
|---|---|---|
| Immune-mediated Ocular | 322666 | Dostarlimab Immune-mediated Ocular |
| Immune-mediated cardiovascular | 322659 | Dostarlimab Immune-mediated cardiovascular |
| Hypersensitivity | 322658 | Dostarlimab Hypersensitivity |
| Immune-mediated Others | 322667 | Dostarlimab Immune-mediated Others |

### 6.3.4.2. Laboratory Values

**Laboratory Values**

- If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.
  - Example 1: 2 Significant Digits = '< x ' becomes x – 0.01
  - Example 2: 1 Significant Digit = '> x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x – 1

### 6.3.4.3. ECG

**ECG**

If QTcF is not available in the eCRF, it will be calculated based on the following formula: $QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$

- Where the calculated values have decimal places, values will be rounded down to the nearest integer for grading. For example, 480.9 would be considered as Grade 1.

### 6.3.4.4. Treatment-emergent Flag for Adverse Events

| Flag | Definition |
|---|---|
| Treatment Emergent | For AEs:<br>• If AE onset date is on or after treatment start date & on or before treatment stop date (plus 30 days or up to initiation of follow up anti-cancer therapy, whichever comes first).<br>  ○ Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date [+ 30 days or up to initiation of follow up anti-cancer therapy, whichever comes first].<br>• If AE onset date is before treatment start date and worsens in either intensity or frequency following exposure to study treatment.<br>  ○ Study Treatment Start Date ≤ AE Worsening Date ≤ Study Treatment Stop Date [+ 30 days or up to initiation of follow up anti-cancer therapy, whichever comes first].<br>For SAEs:<br>• If AE onset date is on or after treatment start date & on or before treatment stop date (plus 90 days follow-up or up to initiation of follow up anti-cancer therapy, whichever comes first).<br>  ○ Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date [+ 90 days or up to initiation of follow up anti-cancer therapy, whichever comes first].<br>• If AE onset date is before treatment start date and worsens in either intensity or frequency following exposure to study treatment.<br>• Study Treatment Start Date ≤ AE Worsening Date ≤ Study Treatment Stop Date [+ 90 days or up to initiation of follow up anti-cancer therapy, whichever comes first]. |

**NOTES:**

- If AE onset date is missing, then the AE will be considered to be On-Treatment.
- If the study treatment stop date is missing, then the AE will be considered to be On-Treatment.
- Time of study treatment dosing and start/stop time of AEs should be considered, if collected.

### 6.3.5. Criteria for Potential Clinical Importance

#### 6.3.5.1. Laboratory Values

Not applicable. Reference ranges for all laboratory parameters will be supplied by each local laboratory. See Clinical Laboratory analysis section (Section 4.5.3.1) for grading.

#### 6.3.5.2. ECG

PCI is defined as QTc >450 or QTc increase of >30 msec. See ECG analysis section (Section 4.5.3.3) for grading.

#### 6.3.5.3. Vital Signs

See Vital Signs analysis section (Section 4.5.3.2) for grading of systolic and diastolic pressure. The clinical concern ranges for the other parameters are shown below.

| Vital Sign Parameter (Absolute) | Units | Clinical Concern Range | |
|---|---|---|---|
| | | Lower | Upper |
| Weight | kg | <90% of baseline weight | ≥110% of baseline weight |
| Heart Rate | bpm | <60 | >100 |
| Temperature | C | ≤35 | ≥38 |
| Oxygen Saturation | % | <95% | NA |
| Respiratory Rate | bpm | <10 | >20 |

Bpm = beats per minute for heart rate and breaths per minute for respiratory rate;

### 6.3.6. Study Phases

| Study Phase | Definition |
|---|---|
| On-Treatment | Study Treatment Start Date ≤ Date ≤ Study Treatment Stop Date [+ 30 days] or Date of Initiation of Follow Up Anti-Cancer Therapy, whichever comes first. |

#### 6.3.6.1. Study Phases for Concomitant Medication

| Study Phase | Definition |
|---|---|
| Prior | Start Date and Stop Date < Study Treatment Start Date or Study Treatment Start Date is missing |
| Concomitant | Study Treatment Start Date ≤ Start Date and Start Date is within the on-treatment period (see Section 6.3.6). |
| Prior and Concomitant | Start Date < Study Treatment Start date and Stop Date ≥ Study Treatment Start Date. |

**NOTES:**

- Please refer to Section 6.3.7.3: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

## 6.3.7. Reporting Standards for Missing Data

### 6.3.7.1. Premature Withdrawals

| Element | Reporting Detail |
|---|---|
| General | • Withdrawn participants were not replaced in the study.<br>• All available data from participants who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. |

### 6.3.7.2. Handling of Missing Data

| Element | Reporting Detail |
|---|---|
| General | Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument:<br>• These data will be indicated by the use of a "blank" in participant listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table.<br>• Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.<br>• Missing baseline data will not be imputed and baseline will be set to missing. |
| Outliers | • Any participants excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report. |
| Overall Response Rate | • Participants with unknown/not evaluable or missing best overall response will be assumed to be non-responders and will be included in the denominator for percentage calculation |

### 6.3.7.3. Handling of Missing Data and Partial Dates

| Element | Reporting Detail | | |
|---|---|---|---|
| General | • Partial dates will be displayed as captured in participant listing displays.<br>• Where necessary, display macros may impute dates as temporary variables for sorting data in listings only. In addition, partial dates may be imputed for 'slotting' data to study phases or for specific analysis purposes as outlined below.<br>• In general, imputed partial dates will not be used to derive study day, time to onset or duration (e.g., time to onset or duration of adverse events), or elapsed time variables (e.g., time since diagnosis). In case the imputed dates are used in any analysis other than sorting or slotting data, a footnote will be added to the display to clarify the use of imputed dates. In addition, imputed dates are not used for deriving the last contact date in overall survival analysis dataset. | | |
| Adverse Events | • The eCRF does not allow entry of partial dates.<br>• Completely missing end dates will not be imputed.<br>• A missing start date will be imputed as the study treatment start date. If the resulting onset date is after a reported end date, the start date will be set equal to the end date. | | |
| Prior/Concomitant Medications | • Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: | | |
| | | Missing start day | • If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = 1st of month.<br>• Else if study treatment start date is not missing:<br>o If month and year of start date = month and year of study treatment start date then<br>▪ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 1st of month.<br>▪ Else set start date = study treatment start date. |

<table>
<tr><th>Element</th><th>Reporting Detail</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td>• Else set start date = 1st of month.</td></tr>
<tr><td>Missing start day and month</td><td>• If study treatment start date is missing (i.e. participant did not start study treatment), then set start date = January 1.<br>• Else if study treatment start date is not missing:<br>o If year of start date = year of study treatment start date then<br>▪ If stop date contains a full date or stop date is partial and there's clear evidence that it is earlier than study treatment start date then set start date = January 1.<br>▪ Else set start date = study treatment start date.<br>• Else set start date = January 1.</td></tr>
<tr><td>Missing end day</td><td>A"28/29/30/3" will be used for the day (dependent on the month and year) or date of death, whichever is earlier.</td></tr>
<tr><td>Missing end day and month</td><td>A"3" will be used for the day and 'Dec' will be used for the month or date of death, whichever is earlier.</td></tr>
<tr><td>Completely missing start/end date</td><td>No imputation<br>If both start and end dates are missing: categorized as prior and concomitant.<br>If start date is missing but end date is available: If end date < first dose date, then categorized as prior. If end date >= treatment start date then categorized as prior and concomitant.<br>If end date is missing but start date is available: If start date >= treatment start date, then categorized as concomitant. If start date < treatment start date, then categorized as prior and concomitant.</td></tr>
</table>
• The recorded partial date will be displayed in listings.
</td></tr>
<tr><td>Disease Characteristics (Initial diagnosis date, Date of diagnosis of advanced/metastatic disease)</td><td>
<table>
<tr><td>Missing start day</td><td>Set date to 1st of month</td></tr>
<tr><td>Missing start day and month</td><td>Set date to January 1.</td></tr>
<tr><td>Completely missing date</td><td>No imputation</td></tr>
</table>
</td></tr>
<tr><td>Prior Anticancer Therapy End Date</td><td>• If the end day is missing, the day will be imputed to the last day of the month.<br>• If both the end day and month are missing, the day and month will be assumed as last day of the year i.e. December 31.<br>• If the imputed end date is after the randomization date, use the randomization date as the imputed end date.</td></tr>
<tr><td>Follow Up Therapy</td><td>• Start dates for follow-up therapy will be temporarily imputed in order to define event and censoring rules, such as for progression-free survival, response rate, or duration of response (i.e. start date for new anti-cancer therapy). Dates will only be imputed when month and year are available, but the day is missing. The following rules will be used to impute the date:<br>• No imputation for completely missing start dates<br>• No imputation for missing start day and month<br>• For missing start day:<br>o If partial start date falls in the same month as the last dose of study treatment, then assign to earlier of (date of last dose of study treatment+1, last day of month).<br>o If partial start date falls in the same month as the participant's last assessment and the participant's last assessment is progressive disease (PD), then assign to earlier of (date of PD+1, last day of month).<br>o If both rules above apply, then assign to latest of the 2 dates</td></tr>
</table>

| Element | Reporting Detail |
|---|---|
| | ○ Otherwise, impute missing day to the first of the month. |
| Exposure Date (Last Dose of Treatment) | • The eCRF does not allow entry of partial infusion dates.<br>• Completely missing exposure dates will not be imputed. |
| Death | • If only 'day' is missing, then impute day with first day of the month<br>• If 'day' and 'month' are missing, and 'year' is not missing and the same as the year of last contact date, then impute as date of last contact + 1 day<br>• If 'day' and 'month' are missing, and 'year' is not missing and greater than the year of last contact date, then impute as 1st January of that year.<br>• If the imputed death date is less than last contact date, then set to last contact date + 1. |

## 6.4. Appendix 4 Abbreviations

| Abbreviation | Description |
|---|---|
| AAC | All Analysis Complete |
| ADA | Anti-Drug Antibody |
| ADaM | Analysis Data Model |
| AE | Adverse Event |
| AESI | Adverse Event of Special Interest |
| ALP | Alkaline Phosphate |
| ALT | Alanine Aminotransferase |
| AST | Aspartate Aminotransferase |
| ATC | Anatomical Therapeutic Chemical |
| BICR | Blinded Independent Central Review |
| BMI | Body-Mass Index |
| BOR | Best Overall Response per RECIST v1.1 |
| BPM | Beats Per Minute |
| BSA | Body Surface Area |
| CD8 T | CD8+ cytotoxic T (cells) |
| CDISC | Clinical Data Interchange Standards Consortium |

| Abbreviation | Description |
|---|---|
| CI | Confidence Interval |
| COVID-19 | Coronavirus Disease 2019 |
| CPMS | Clinical Pharmacology Modelling & Simulation |
| CR | Complete Response |
| CSR | Clinical Study Report |
| CxDx | Cycle X Day X |
| DBF | Database Freeze |
| DBL | Database lock |
| DBL | Database Lock |
| DBP | Diastolic Blood Pressure |
| DCO | Data cut-off |
| DOR | Duration Of Response |
| DP | Decimal Places |
| ECG | Electrocardiogram |
| eCOA | Electronic Clinical Outcome Assessment |
| ECOG | Eastern Cooperative Oncology Group |
| eCRF | Electronic Case Record Form |
| eDISH | evaluation of Drug-Induced Serious Hepatotoxicity |
| CCI [redacted] | |
| EOT | End-of-Treatment |
| EQ-5D-3L | European Quality of Life 5 Dimensions 3 Level Scale |

| Abbreviation | Description |
|---|---|
| FA | Final Analysis |
| FACT-GP | Functional Assessment of Cancer Therapy-General Population |
| FACT-GP5 | Functional Assessment of Cancer Therapy-General Population 5-category Response Scale |
| FDAAA | Food and Drug Administration Clinical Results Disclosure Requirements |
| GGT | Gamma glutamyl transferase |
| HR | Hazard Ratio |
| IA | Interim Analysis |
| iBOR | Best Overall Response per iRECIST |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| iCPD | iRECIST-confirmed progressive disease |
| iCR | iRECIST-complete response |
| CCI | [redacted] |
| IDSL | Integrated Data Standards Library (GSK Standards Library) |
| imAE | Immune-mediated Adverse Event |
| IMT | Issue Management Teams |
| imTEAEs | Immune-mediated Treatment-emergent Adverse Event |
| IND | Investigational New Drug |
| IO | Immuno-Oncology |
| iORR | Objective Response Rate per iRECIST |
| iPFS | Progression Free Survival per iRECIST |
| iPR | iRECIST-partial response |

| Abbreviation | Description |
|---|---|
| IQR | Interquartile Range |
| iRECIST | modified Response Evaluation Criteria in Solid Tumors |
| IRR | Infusion-Related Reaction |
| iSD | iRECIST-stable disease |
| ITT | Intent-To-Treat |
| iUPD | iRECIST-confirmed progressive disease |
| IV | Intravenous |
| KM | Kaplan-Meier |
| LATA | Last Adequate Tumor Assessment |
| LLN | Lower Limit of Normal |
| MedDRA | Medical Dictionary for Regulatory Activities |
| NA | Not Applicable |
| NAb | Neutralizing Antibody |
| NCI-CTCAE | National Cancer Institute-Common Terminology Criteria for Adverse Events |
| ND | Not Done |
| NE | Non-Evaluable |
| NQ | Non-quantifiable |
| NSCLC | Non-small Cell Lung Cancer |
| NSCLC-SAQ | Non-Small Cell Lung Cancer-Symptom Assessment Questionnaire |
| OPS | Output and Programming Specifications |
| ORR | Objective Response Rate per RECIST v1.1 |
| OS | Overall Survival |

| Abbreviation | Description |
|---|---|
| PCI | Potential Clinical Importance |
| PD | Progressive Disease |
| PD-1 | programmed cell death protein 1 |
| PD-L1 | programmed death-ligand 1 |
| PDMP | Protocol Deviation Management Plan |
| PFS | Progression Free Survival per RECIST v1.1 |
| CCI | [redacted] |
| PK | Pharmacokinetic |
| PopPK | Population PK |
| PP | Per Protocol |
| PR | Partial Response |
| PRO | Patient-reported Outcome |
| PRO-CTCAE | Patient-reported Outcomes Version of the Common Term Criteria for Adverse Events |
| PT | Preferred Term |
| PY | Person-Years |
| QoL | Quality of Life |
| QTc | Corrected QT Interval |
| QTcF | Frederica's QT Interval Corrected for Heart Rate |
| QxW | Every x Weeks |
| RAP | Reporting & Analysis Plan |
| RECIST | Response Evaluation Criteria in Solid Tumors |
| RMST | Restricted Mean Survival Time |

| Abbreviation | Description |
|---|---|
| RoW | Rest of World |
| RS | Raw Score |
| RTSM | Randomization and Trial Supply Management |
| SAC | Statistical Analysis Complete |
| SAE | Serious Adverse Event |
| SAF | Safety Population |
| SBP | Systolic Blood Pressure |
| sd | Standard Deviation |
| SD | Stable Disease |
| SDTM | Study Data Tabulation Model |
| SOC | System Organ Class |
| SOP | Standard Operation Procedure |
| TEAE | Treatment-Emergent Adverse Event |
| TFL | Tables, Figures & Listings |
| TIM-3 | T-cell immunoglobulin and mucin-domain containing-3 |
| TMF | Trial Master File |
| TOI | Terms of Interest |
| TPS | Tumor Proportion Score |
| TTD | Time to Deterioration |
| TTE | Time to Event |
| TTR | Time to response |
| ULN | Upper Limit of Normal |
| VAS | Visual Analogue Scale |

| Abbreviation | Description |
|---|---|
| WHO | World Health Organisation |

## 6.5. Appendix 5 Trademarks

| Trademarks of the GlaxoSmithKline Group of Companies | | Trademarks not owned by the GlaxoSmithKline Group of Companies |
|---|---|---|
| NA | | MedDRA |
| NA | | PRO-CTCAE |
| NA | | SAS |

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