Integrated Analysis Plan

Study Number:	MS200647-0054
Clinical Study Protocol Title:	An Open-label, Multicenter Follow-up Study to Collect Long-term Data on Participants from Multiple Bintrafusp alfa (M7824) Clinical Studies
Study Phase:	III
Merck Compound**:**	Bintrafusp alfa
Protocol Version:	30 November 2021/Version 2.0
Integrated Analysis Plan Author:	**Coordinating Author** PPD, EMD Serono — PPD **Function** — **Author(s) / Data Analyst(s)** PPD — PPD
Integrated Analysis Plan Date and Version:	13 November 2024 / Version 2.0
Integrated Analysis Plan Reviewers:	**Function** — **Name** PPD PPD, Merck Healthcare — PPD PPD Merck Healthcare — PPD PPD, Merck KGaA — PPD i PPD Merckgroup — PPD

Approval Page

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An Open-label, Multicenter Follow-up Study to Collect Long-term Data on Participants from Multiple Bintrafusp alfa (M7824) Clinical Studies

Approval of the IAP by all Merck Data Analysis Responsible must be documented within EDMS via eSignature. With the approval, the Merck responsible for each of the analysis also takes responsibility that all reviewers' comments are addressed adequately.

By using eSignature, the signature will appear at the end of the document.

1 Table of Contents

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2 List of Abbreviations and Definition of Terms

AE(s)	Adverse Event(s)
AESIs	Adverse Events of Special Interest
ATC	Anatomical Therapeutic Chemical
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CIPD	Clinically Important Protocol Deviation
COVID-19	Coronavirus Disease 2019
CR	Complete Response
CRF	Case report form
CSR	Clinical study report
CT	Computed tomography
DB	Database Lock
CCI	[redacted]
ECG	Electrocardiogram
EDMS	Electronic Document Management System
eCRF	Electronic case report form
EOT	End of Treatment
FAS	Full Analysis Set
GCP	Good Clinical Practice
IAP	Integrated Analysis Plan
ICH	International Council for Harmonisation
IPD	Important Protocol Deviation
irAEs	Immune-related adverse events
IRR	Infusion-related reactions
KM	Kaplan-Meier
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute-Common Terminology Criteria for Adverse Events
OS	Overall survival
OR	Objective Response
PD	Progressive disease

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PR	Partial response
PT	Preferred term
RECIST 1.1	Response Evaluation Criteria in Solid Tumors version 1.1
SAE(s)	Serious adverse event(s)
SAF	Safety Analysis Set
SD	Stable disease
SDTM	Study Data Tabulation Model
SOC	System Organ Class
SMQ	Standardized MedDRA Queries
TGFβ	Transforming growth factor β
TNM	Tumor, node and metastasis
TEAE(s)	Treatment-emergent adverse event(s)
TSH	Thyroid-Stimulating Hormone
WHO-DD	WHO Drug Dictionary

3 Modification History

Unique Identifier for Version	Date of IAP Version	Author	Changes from the Previous Version
1.0	08SEP2022	PPD	New document
2.0	13NOV2024		Section 5: Updated the table column “IAP section”
			CCI
			Section 10.1: Re-ordered the ineligible and eligible subjects in the disposition table to align with the TLFs.
			Section 10.2.1: Removed the summary presentation for PDs attributable to the COVID-19 pandemic.
			Section 11.1: Updated the age categories and split ethnicity in 2 separate lines.
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			Section 15.2.1: Added the additional analysis information for the presentation of TEAEs during the Rollover study.
			Section 15.2: Clarified the content of the overall summary of AEs table and tables of TEAEs by SOC and PT.
			Section 15.3.2: Added that SAEs will be presented for events that occurred during the on-treatment period as well as for events that occurred during the Rollover study to align with the new TLFs that were added.
			Section 15.3.3: Added details for the AESIs presentation
			Section 15.4: Added more details for the listings content
			Section 18.1: removed the details for the AESIs presentation, which were moved to Section 15.3.3.

4 Purpose of the Integrated Analysis Plan

The purpose of this IAP is to document technical and detailed specifications for the final analysis of data collected for Study MS200647-0054. Results of the analyses described in this IAP will be included in the CSR. Additionally, the planned analyses identified in this IAP may be included in regulatory submissions or future manuscripts. Any post-hoc, or unplanned analyses performed to provide results for inclusion in the CSR but not identified in this prospective IAP will be clearly identified in the CSR.

The IAP is based upon Section 9 (Statistical considerations) of the study protocol and protocol amendments and is prepared in compliance with ICH E9. It describes analyses planned in the protocol and protocol amendments.

The wording used in this IAP is chosen to best match the respective wording in the study protocol template, the Clinical Study Report (CSR) template, CDISC requirements and special requirements for table layouts. Therefore, the following approach is used:

Generally, the term 'participant' will be used instead of 'subject' or 'patient'. However, in tables and listings the term 'subject' will be used to match CDISC requirements, except for in-text tables where 'participant' will be used to match the CSR and protocol templates. Similarly, the term 'study intervention' will be used in this document instead of 'treatment' to match protocol and CSR templates, however, tables and listings will use 'treatment' for brevity reasons. Exceptions from this rule are commonly used terms like "on-treatment", "treatment-emergent", "treatment policy", "subject-years", "by-subject", or names of eCRF pages like "Treatment Termination" page.

5 Objectives and Endpoints

Objectives	Endpoints	IAP section
Primary		
To evaluate clinical safety of bintrafusp alfa in participants with solid tumors who continue treatment after completion of the primary/mainanalyses in parent bintrafusp alfa studies	Occurrence of AEs and treatment-related AEs, starting from baseline in parent study	15.1.1
Secondary		
To evaluate clinical efficacy of bintrafusp alfa based on OS	OS, starting from baseline in parent study	14.1.1
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6 Overview of Planned Analyses

A final analysis will be performed. This IAP covers the final analyses for efficacy and safety. Statistical analyses will be performed using cleaned Rollover eCRF data as well as data from the respective parent studies needed for the analysis but not collected in the Rollover eCRF.

6.1 Final Analysis

All final, planned analyses identified in the Clinical Study Protocol and in this IAP will be performed only after the last participant has completed the period of the study with all study data in-house, all data queries resolved, and the database locked.

Subject survival follow-up will continue until up to a maximum of 5 years after the last participant receives the last dose of bintrafusp alfa. Therefore, the full database lock will take place either 5 years after the last subject receives the last dose of bintrafusp alfa or this duration may be shortened if the last patient was lost to follow-up or at the discretion of the Sponsor for any given indication. The Sponsor may terminate the study at any time once access to study intervention for participants still benefiting is provisioned via expanded access, marketed product, or another mechanism of access as appropriate.

A Data Review Meeting will be held prior to database lock. In addition, no database can be locked until this IAP has been approved.

7 Changes to the Planned Analyses in the Clinical Study Protocol

Subsections of COVID-19 impact on the study are added.

The final analysis will be performed after the last participant has completed the period of study, instead of 'the last participants is off treatment' as mentioned in the section 9.4.4 in the Clinical Study Protocol.

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8 Analysis Sets and Subgroups

8.1 Definition of Analysis Sets

Enrolled Analysis Set

All subjects consented for the Rollover study.

Full Analysis Set (FAS)

The FAS will be defined as in the protocol of the parent study and include all participants who receive at least one dose of study intervention in the Rollover study.

Safety Analysis Set (SAF)

The SAF will be defined as in the protocol of the parent study and include all participants who receive at least one dose of study intervention in the Rollover study.

The final decision to exclude participants from any analysis set will be made during the Data Review Meeting prior to database lock.

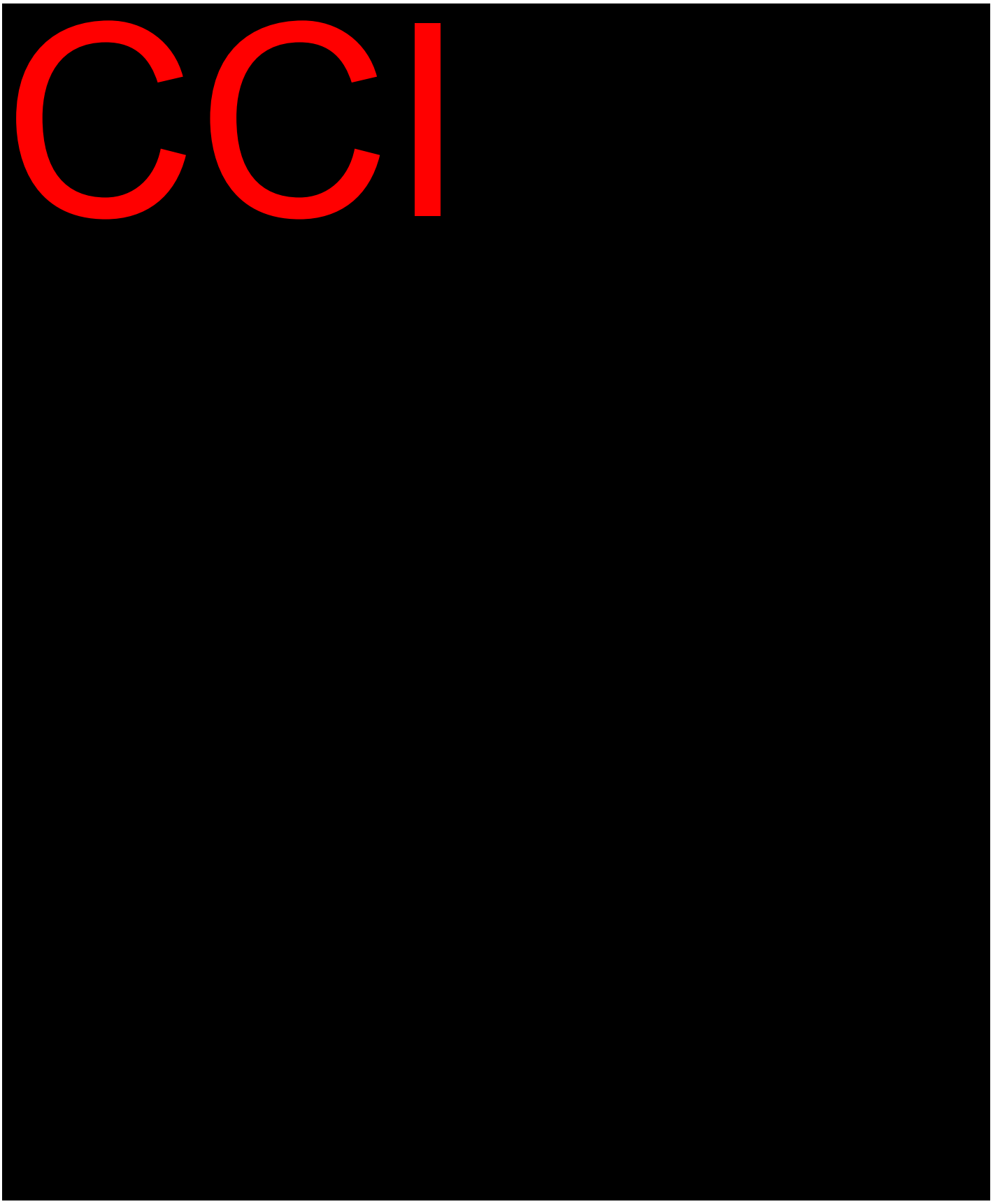
Analyses per Analysis Set

The following table summarizes the use of the analysis sets in the different analyses.

	Analysis Set		
Analyses	**Enrolled Analysis Set**	**Full Analysis Set**	**Safety Analysis Set**
Disposition	✓		
Demographic and Baseline Assessments: Demographics, Medical History and Disease History		✓	
Previous and Concomitant Therapies		✓	
Compliance and Exposure			✓
Efficacy: Secondary Endpoint		✓	
Safety and Tolerability			✓

8.2 Subgroup Definition and Parameterization

No subgroup analyses will be performed in the study.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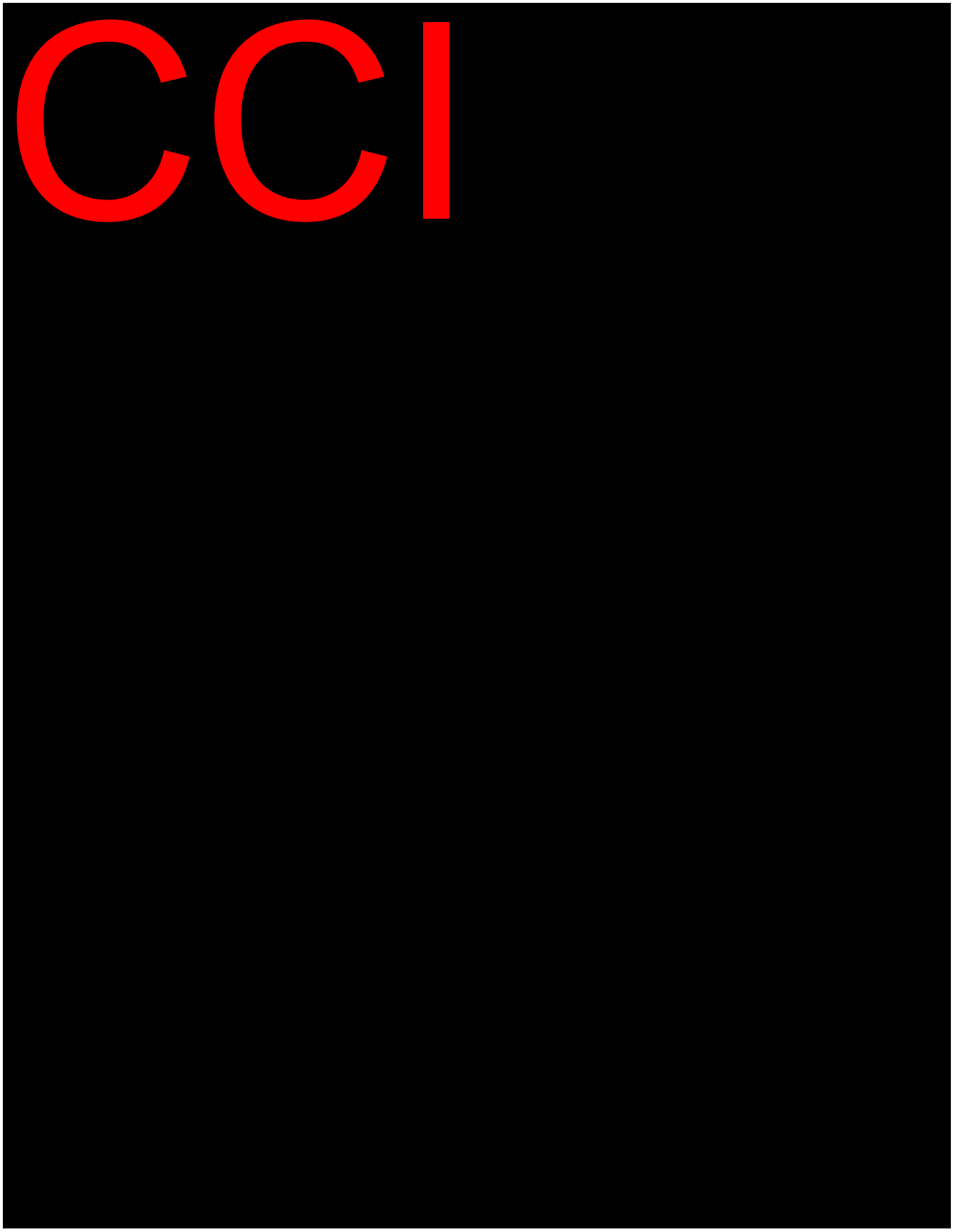
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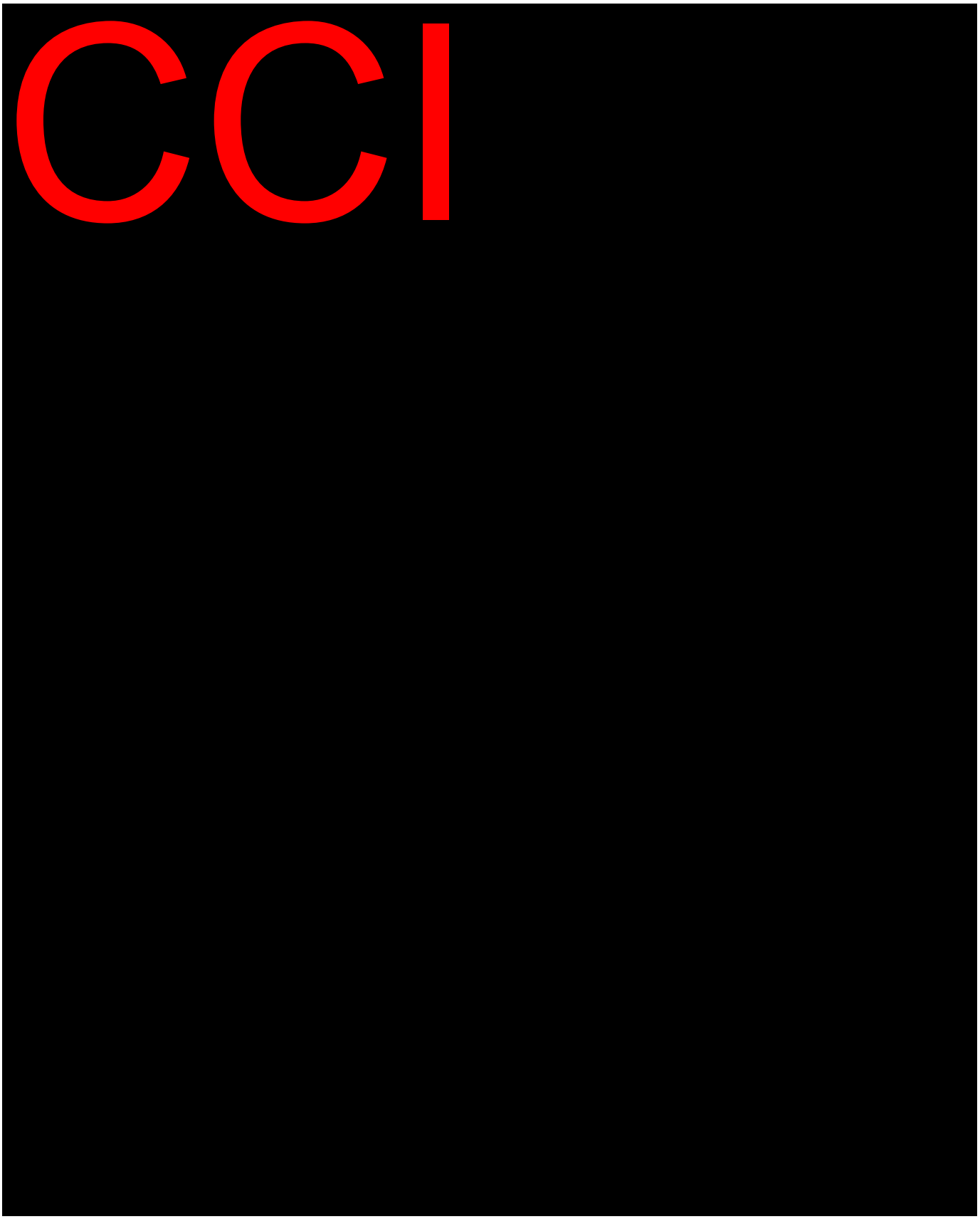
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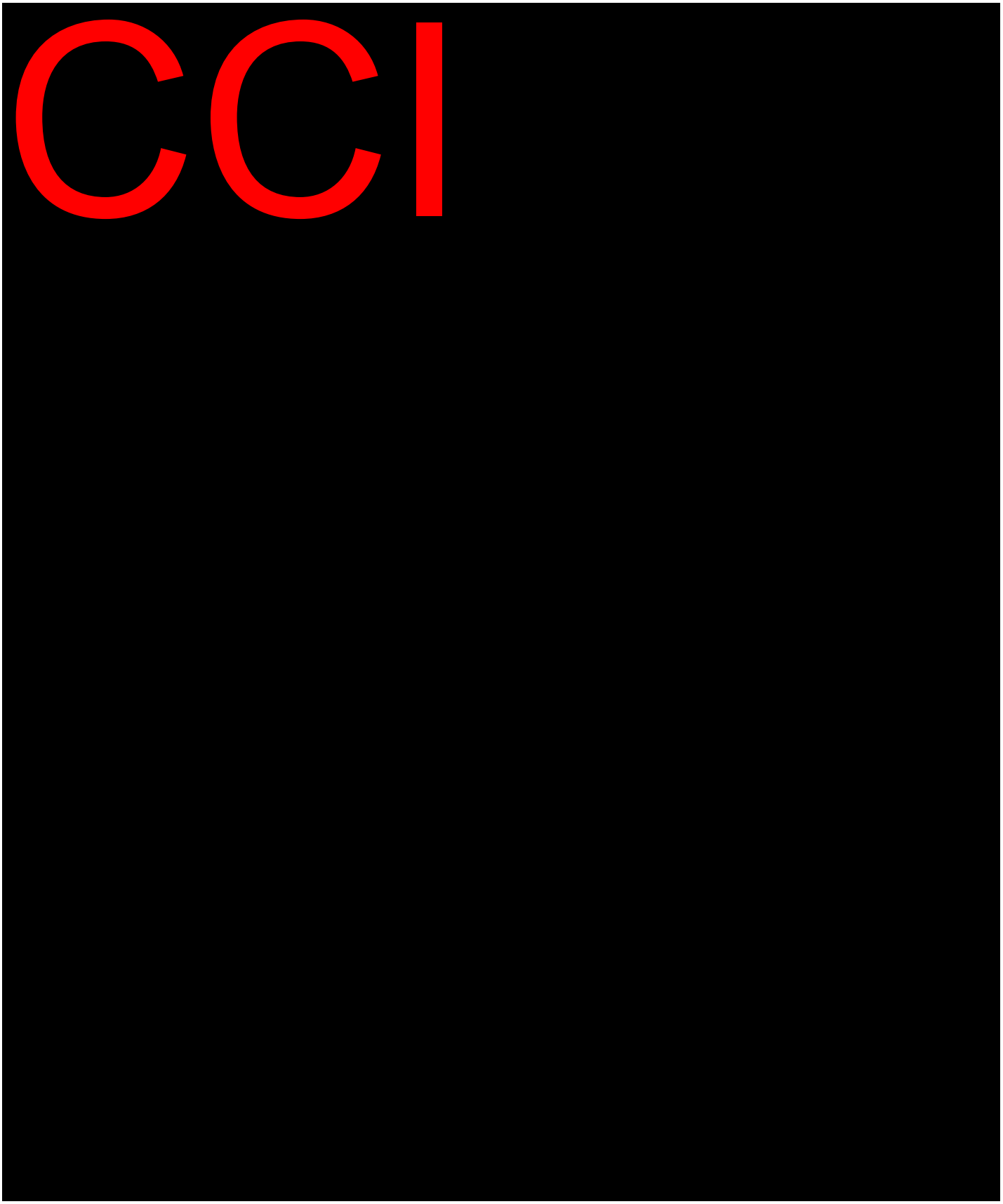
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10 Study Participants

The subsections in this section include specifications for reporting participant disposition and study intervention/study discontinuations. Additionally, procedures for reporting protocol deviations are provided.

10.1 Disposition of Participants and Discontinuations

The number and percentage of participants in each of the below disposition categories will be presented by total and per indication or per parent protocol of the corresponding parent study, where applicable. Percentages will be presented with respect to the number of consented participants in the Rollover study.

- Total number of participants consented (i.e. participants who gave informed consent)
- Number of ineligible subjects and reason for ineligibility (subject did not meet all eligibility criteria, withdrawal by-subject, PD, adverse event, lost to follow-up, death and other).
- Number of eligible subjects

  - Number of participants who enrolled before Start of COVID-19 pandemic.
  - Number of participants who enrolled after Start of COVID-19 pandemic.
- Number of participants who terminated the study treatment by main reason (adverse event, lost to follow-up, protocol non-compliance, death, PD, withdrawal by subjects and other).
- Number of participants who terminated the study treatment due to COVID-19.
- Number of participants who discontinued the study and primary reasons for study discontinuation (adverse event, lost to follow-up, protocol non-compliance, death, withdrawal by participants and other).
- Number of participants who discontinued the study due to COVID-19.
- Number and percentage of participants who re-initiated the bintrafusp alfa treatment.
  - Number and percentage of subjects who discontinued treatment after re-initiation.

10.2 Protocol Deviations / Exclusion from Analysis Sets

10.2.1 Important Protocol Deviations

Important protocol deviations (IPDs) are protocol deviations that might significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a participant's rights, safety, or well-being.

Important protocol deviations include:

- Participants enrolled and dosed on the study who did not satisfy enrolment criteria
- Participants that develop withdrawal criteria while on the study but are not withdrawn
- Participants that receive the wrong study intervention or an incorrect dose
- Participants that receive an excluded concomitant medication
- Failure to collect data necessary to interpret primary endpoints
- Failure to collect necessary key safety data
- Deviation from Good Clinical Practice (GCP)
- Any other protocol deviation that might significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a participant's rights, safety, or well-being.

Important protocol deviations will be identified for all participants by either site monitoring, medical review processes or programming and confirmed prior to or at the Data Review Meeting at the latest.

Any IPD is documented in SDTM datasets whether identified through site monitoring, medical review or programming. The management of protocol deviations is outside of this IAP document.

Clinically important protocol deviations (CIPDs) are a subset of IPDs that could impact the key objectives of the study and that would lead to the exclusion of a participant from an analysis set (see Section 8.1 Definition of Analysis Sets).

CIPDs may be identified during the course of the study but will not require amendments to this IAP.

A listing of IPDs will be provided based on the FAS.

Protocol deviations attributed to the impact of COVID-19 pandemic will be labeled accordingly. Both important and non-IPDs attributable to the COVID-19 pandemic will be included. A listing including protocol deviation impacted by COVID-19 will be provided.

10.2.2 Reasons Leading to the Exclusion from an Analysis Set

Not applicable.

11 Demographics and Other Baseline Characteristics

If not stated otherwise, the following analyses will be performed based on the FAS per indication or per parent protocol of the corresponding parent study.

11.1 Demographics

Demographic characteristics will be summarized descriptively using the following information from the parent study Baseline Visit eCRF pages.

The following demographic characteristics will be included:

- Sex: male, female,
- Race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, More than one race, Other, Not collected at this site
- Ethnicity: Hispanic or Latino/Not Hispanic or Latino
- Ethnicity: Japanese/Not Japanese
- Age (years) at parent study consent
- Age categories at parent study consent:

  < 65 years,

  ≥ 65 years

    65- < 75,

    75- < 85,

    ≥85 years

- Pooled Region (as applicable):
  - North America
  - Europe
  - Asia
  - Rest of the World
- Geographic Region:
  - North America
  - Latin America
  - Western Europe
  - Eastern Europe
  - Middle East
  - Australia
  - Asia

11.2 Medical History

The medical history will not be presented in table or listing, although the SDTM data is available.

11.3 Other Baseline Characteristics

Information on disease characteristics collected at parent study baseline will be summarized. Summary statistics will, if applicable, be presented for:

- Primary site of tumor,
- Time since initial disease diagnosis (in months) to parent study baseline,
- Tumor, Node and Metastasis (TNM) classification at initial diagnosis,
- TNM classification at parent study baseline,
- Histopathological classification (clear cell, sarcomatoid, other)

12 Concomitant Therapies/Procedures

The following analyses will be performed based on the Full Analysis Set per indication or per parent protocol of the corresponding parent study.

Concomitant medications are medications, other than study intervention, which are taken by participants any time during the on-treatment period, see Section 9.7.

Concomitant medication will be summarized by number and percentage of participants from the "Concomitant medications and/or Procedures" eCRF. Preferred term within ATC classification

code level 2 will be tabulated as given from the WHO-DD dictionary most current version at time of study database lock.

If concomitant medication is classified into multiple ATC classes, the medication will be summarized separately under each of these ATC classes.

The summary tables will be sorted by decreasing frequency of drug class and decreasing frequency of preferred term in each drug class. In case of equal frequency regarding ATC classification level 2 or preferred term, alphabetical order will be used.

In case any specific medication does not have an ATC classification level 2 coded term, it will be summarized under "Unavailable ATC classification" category. Each participant will only be counted once, even if he/she received the same medication at different times.

A listing of concomitant medications will be created with the relevant information collected on the "Concomitant Medications Details" eCRF page.

All **concomitant procedures**, which were undertaken during the on-treatment period will be summarized in a listing according to the information collected on the CRF page "Concurrent Procedures".

Subsequent anti-cancer therapy

Anti-cancer treatment after discontinuation will be provided in a listing with data retrieved from the "Anti-Cancer Treatment After Discontinuation Details", "Radiotherapy After Discontinuation Details", and "Surgery After Discontinuation Details" eCRF pages.

13 Study Intervention: Compliance and Exposure

The exposure duration (in weeks) of study intervention since first administration of study interventions in the parent study will be calculated based on the safety analysis set per indication or per parent protocol of the corresponding parent study. The detail on the calculation of exposure duration is described in Section 9.8.

14 Efficacy Analyses

The following analyses will be performed based on the FAS and presented as listings.

14.1 Secondary Endpoints

14.1.1 Secondary Objective: Analysis of the secondary endpoints

The below analysis will be performed per indication or parent protocol of the corresponding parent study cohort if there are at least 5 subjects enrolled per indication or parent protocol of the corresponding parent study cohort. Listings of the time-to-events will be presented.

Analysis (AnalysisSet)	Derivation	Statistical Analysis Methods
Secondary endpoint: OS, starting from baseline in parent study.		
Secondary (FAS)	OS time (in months) is defined as the date from baseline of parent study to the date of death due to any cause. For participants alive at the time of data analysis or who are lost to follow-up, the OS will be censored at the date of data cut-off or date of last contact defined in Section 9.5. OS (months) = (date of death/censoring – date of parent baseline + 1) / 30.4375	Date of death, with the reasons for censoring (alive, withdrawal of consent and lost to follow-up) will be presented in a participant listing. OS will be estimated by the KM method. Median time to event will be reported, along with 25th and 75th percentiles.

The tumor evaluation data will be listed.

15 Safety Analyses

This section includes specifications for summarizing safety endpoints that are common across clinical studies such as adverse events, laboratory tests and vital signs.

Safety analyses will be done on the safety analysis set.

15.1 Primary Endpoint

15.1.1 Primary Objective: Analysis of the Primary Endpoint

Analysis (Analysis Set)	Derivation	Statistical Analysis Methods	Missing Data Handling
Primary endpoint: Occurrence of TEAEs and treatment-related TEAEs.			
Primary (SAF)	**TEAEs** are those events with onset dates occurring during the on-treatment period for the first time, or if the worsening of an event is during the on-treatment period. **Treatment-related TEAEs** are the adverse events with relationship to study treatment (as recorded on the "Adverse Events Details" eCRF page, Relationship with bintrafusp alfa = Related) reported by the investigator and those of unknown relationship (i.e. no answer to the question "Relationship with bintrafusp alfa").	The following frequency table will be prepared by primary SOC and PT in alphabetical order of SOC for: • Any AE • Any related AE per indication or per parent protocol of the corresponding parent study. The listings of all AEs will also be provided with the relevant information with a flag for AEs with onset outside of the on-treatment period.	See Section 9.10

15.2 Adverse Events

Treatment-emergent adverse events (TEAE) are those events with onset or worsening (seriousness or severity) dates occurring within the on-treatment periods as defined in Section 9.7.

For immune-related AEs, an extended period of up to 90 days after last treatment is considered for analyses dedicated to irAEs. PTs belonging to irAEs will be considered as treatment-emergent up to 90 days for dedicated irAE analyses and up to 30 days for general AE analyses.

This includes also AEs ongoing at baseline, which first improve under study intervention and then worsen irrespective of baseline. Adverse events with changes in toxicity grade/severity, seriousness or outcome of AEs are recorded as separate entries in the eCRF with associated end and start dates. Records of the same AE will be considered as one event in the analysis. If the severity of the reported event worsens after start of treatment, the TEAE flag will be re-evaluated for the worse and the subsequent records as per the TEAE definition. If the worse record starts outside of the on-treatment period, it will not appear on the summaries/listings of TEAEs, unless otherwise specified. These events will be kept as separate records in the database in order to maintain the full detailed history of the events. The overall outcome of the adverse event is the

outcome of the last event in the sequence. When such AEs are listed, start, end date and outcome should be provided together with change date, toxicity grade/severity and seriousness per episode.

Adverse events related to study intervention are those events with relationship missing, unknown or yes.

Immune-Related Adverse Events (irAE) are identified according to the methodology outlined in Appendix 1 for a pre-specified search list of MedDRA PTs, documented in the Benefit Risk Strategy Document. Prior to DB lock these events are identified according to a pre-specified search list of MedDRA PTs, documented in a version-controlled repository maintained by the Sponsor and based on medical assessment prior to analysis of the current study. Details are included in Appendix 1.

Infusion-Related Reactions (IRR) are identified based on a list of MedDRA PTs. The detailed criteria of the timing relationship to infusions are specified in Table 1 of Appendix 1.

All analyses described in Section 15.2 will be based on TEAEs if not otherwise specified. The AE listings will include all AEs (whether treatment-emergent or not). AEs outside the on-treatment period will be flagged in the listings.

In addition, selected analyses will be repeated for the TEAEs that occurred during the Rollover study. TEAEs occurring during the Rollover study are defined as TEAEs with onset or worsening (seriousness or severity) date after the first dose of study intervention in the Rollover study.

Unless otherwise specified, TEAEs will be summarized by number and percentage of participants with the TEAE by primary SOC and PT in the category of interest in alphabetical order, per indication or per parent protocol of the parent study.

Each participant will be counted only once within each SOC or PT. If a participant experiences more than one AE within a SOC or PT for the same summary period, only the AE with the strongest relationship or the worst severity, as appropriate, will be included in the summaries of relationship and severity.

15.2.1 All Adverse Events

Adverse events will be summarized by worst severity (according to NCI-CTCAE version 5.0) per participant, using the latest version of MedDRA PT as event category and MedDRA primary SOC body term as Body System category.

In case a participant has events with missing and non-missing grades, the maximum of the non-missing grades will be displayed. No imputation of missing grades will be performed.

Incomplete AE-related dates will be handled as specified in Section 9.10.

The following tables will be created by group per indication/parent protocol:

- The overall summary of AEs table will include the frequency (number and percentage) of participants with each of the following:

- TEAEs
- TEAEs, Grade ≥ 3, Grade ≥ 4 [by severity]
- Related TEAEs
- Related TEAEs, Grade ≥ 3, Grade ≥ 4 [by severity]
- TEAEs leading to permanent discontinuation of study intervention
- Related TEAEs leading to permanent discontinuation of study intervention
- Serious TEAEs
- Non-Serious TEAEs
- Related Serious TEAEs
- TEAEs leading to death (AEs with Grade 5 or outcome "fatal" if Grade 5 not applicable)
- Related TEAEs leading to death
- Any AE of special interest:
  - IRRs
  - irAEs
  - TGFβ inhibition mediated skin reaction AEs
  - Anemia
- Any trial drug related AE of special interest:
  - Related IRRs
  - Related irAEs
  - Related TGFβ inhibition mediated skin reaction AEs
  - Related Anemia
- Any bleeding TEAE
- Any trial drug related bleeding AE

The overall summary of AEs table will be repeated for events that occurred or worsened (seriousness or severity) after the first dose of study intervention during the Rollover study.

In addition, the frequency of participants with TEAEs by SOC and PT will be produced for:

- TEAEs
  This table will be repeated for TEAEs that occurred or worsened (seriousness or severity) after the first dose of study intervention during the Rollover study.
- TEAEs by worst NCI-CTCAE grade (any grade, ≥3, ≥4 and 5)

- Related TEAEs
  This table will be repeated for TEAEs that occurred or worsened (seriousness or severity) after the first dose of study intervention during the Rollover study.
- TEAEs excluding SAEs, with frequency ≥ 5% in any group per indication/parent protocol by SOC and PT. "Number of subjects with at least one event" represents the number of participants with at least one AE among AEs which frequency is ≥ 5% in at least one study group per indication/parent protocol.

15.2.2 Adverse Events Leading to Discontinuation of Study Intervention

The data listing of all AEs will include the AEs leading to treatment discontinuation.

15.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

15.3.1 Deaths

All deaths, deaths within 30 days after last dose of study intervention, death within 60 days after first dose as well as reason for death, will be tabulated based on information from the "Report of Subject Death" and "Survival Follow-Up" CRFs pages, per indication or per parent protocol of the corresponding parent study.

- Number of Deaths
- Number of Deaths within 30 days after last dose of bintrafusp alfa
- Number of Deaths within 60 days after first dose of bintrafusp alfa
- Primary Reason of Death
  - Progression disease and/or disease related condition
  - Event unrelated to study treatment
  - Event related to study treatment
  - Unknown

In addition, date and cause of death will be provided in individual participant data listing together with selected dosing information (date of first / last administration, dose and number of infusions).

This listing will include:

- AEs with fatal outcome (list preferred terms of AEs with outcome=fatal)
- Flag for death within 30 days of last study intervention
- Flag for death within 60 days of first study intervention

15.3.2 Serious Adverse Events

The number of participants with SAEs will be described by SOC and PT and will be presented for events that occurred during the on-treatment period as well as for events that occurred during the Rollover study.

SAEs will be flagged in the TEAEs listing.

15.3.3 Other Significant Adverse Events

The frequency (number and percentage) of participants with each of the following adverse events of special interest (AESIs) will be presented per indication or per parent protocol of the corresponding parent study.

The following AESIs will be presented by worst grade (Any grade [including missing grade], Grade ≥ 3, Grade ≥ 4, Grade 5):

- irAEs.

  irAEs will be summarized in frequency tables presenting category, subcategory and sub-subcategory (if applicable) and PT sorted by alphabetical order.

- IRRs.

  IRR AEs will be summarized overall and by subcategories (Reactions / Signs and Symptoms) in a frequency table presenting SOC and PT sorted by alphabetical order.

- TGFβ inhibition mediated skin reactions.

  TGFβ inhibition mediated skin reactions will be summarized by PT categories (Narrow definition, Broad definition) and by PT sorted by alphabetical order.

- Anemia.

  Anemia TEAEs and related anemia TEAEs will be summarized in a frequency table presenting SOC and PT sorted by alphabetical order.

In addition, bleeding TEAEs will be presented by worst grade (Any grade [including missing grade], Grade 1, Grade 2, Grade 3, Grade 4, Grade 5):

- Bleeding TEAEs.

  Bleeding TEAEs and related bleeding TEAEs will be summarized in a frequency table presenting SOC and PT sorted by alphabetical order.

Details of AESIs are specified in Appendix 1.

AEs associated to COVID-19

A listing comprising all COVID-19 related AE terms will be presented. The relevant events will be identified based on the SMQ COVID-19 (narrow scope).

AEs associated to COVID-19 vaccines

The safety profile of the investigational treatment and vaccine may overlap. Investigators are asked to provide all AEs with potential COVID-19 vaccine related causality AEs as part of information on "Causality factors other than study treatment" and to enter "COVID19 vaccination" as free text on the AEDT eCRF page. Per this classification a focused analysis will be possible for potential vaccination associated AEs.

A listing comprising all COVID-19 vaccines related AE terms will be presented.

15.4 Clinical Laboratory Evaluation

All parameters collected on the eCRF will be listed in dedicated listings presenting all corresponding collected information on the eCRF based on SAF.

- Hematology
- Biochemistry.
- Free T4 and TSH

The listings of clinical laboratory evaluation will be provided for all laboratory parameters. The following information will be presented:

- Parameter (unit)
- Visit/Week
- Date of collection (Relative day)
- Value
- Lower Limit of Normal/Upper Limit of Normal
- Normal range indicator
- Worst On-treatment

The listings will be sorted by parameters and assessment dates or visits for each participant.

15.5 Vital Signs

The following vital signs will be collected:

- Body weight (kg/ lb),
- Diastolic blood pressure (mmHg),
- Systolic blood pressure (mmHg),
- Pulse (beats/min),
- Heart rate (beats/min),
- Temperature (Cº / Fº).

All significant vital signs abnormalities assessments will be listed.

15.6 Other Safety or Tolerability Evaluations

The following electrocardiogram (ECG) parameters will be collected:

- Heart rate (beats/min),
- PQ/PR duration (ms),
- RR duration (ms),
- QRS duration (ms),
- QT duration (ms),
- QTcB interval (Bazett's Correction Formula) (ms),
- Rhythm (sinus rhythm, atrial fibrillation and other).

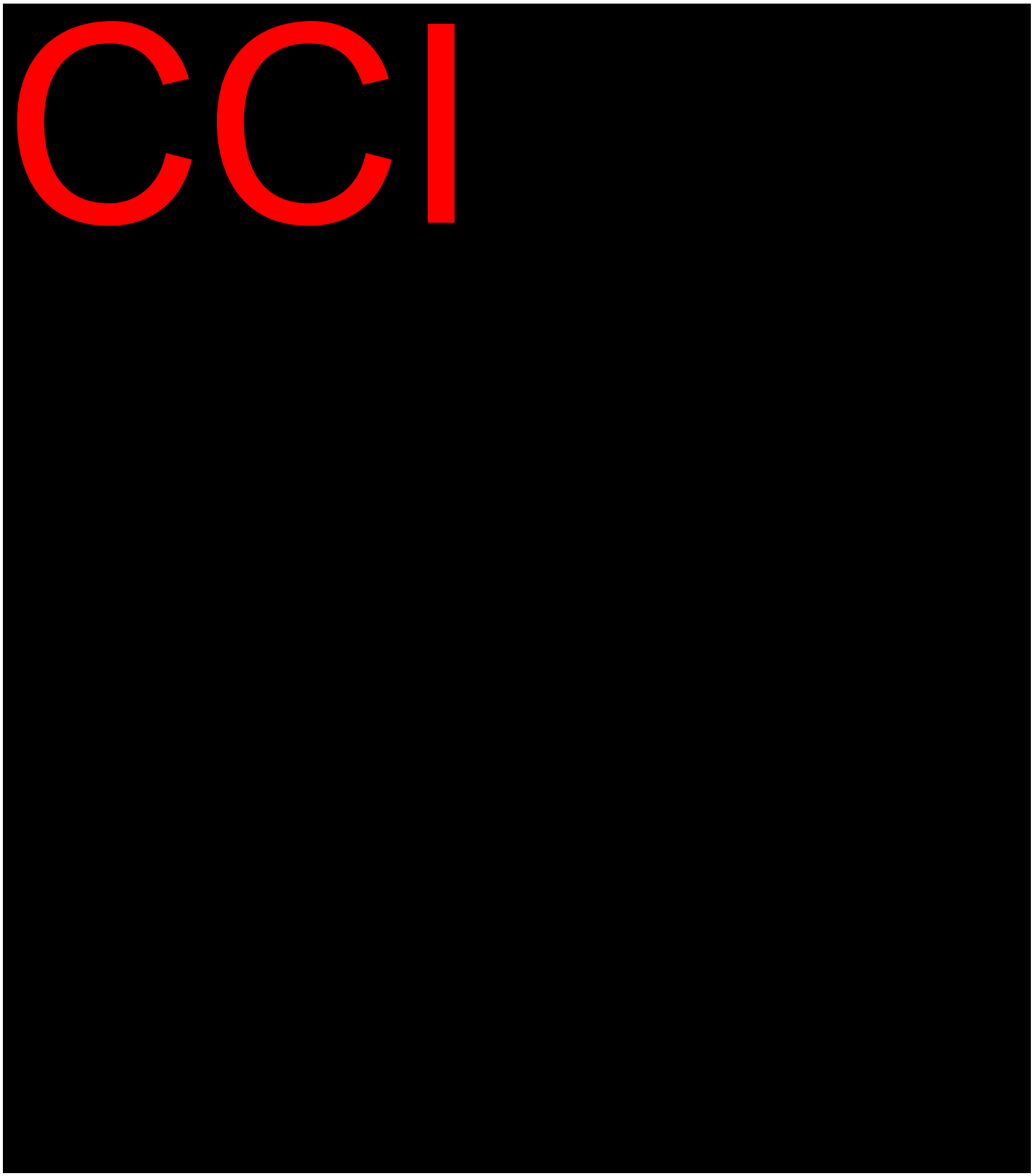
All ECG significant abnormal assessments will be listed.

16 Analyses of Other Endpoints

Not applicable.

17 References

No references.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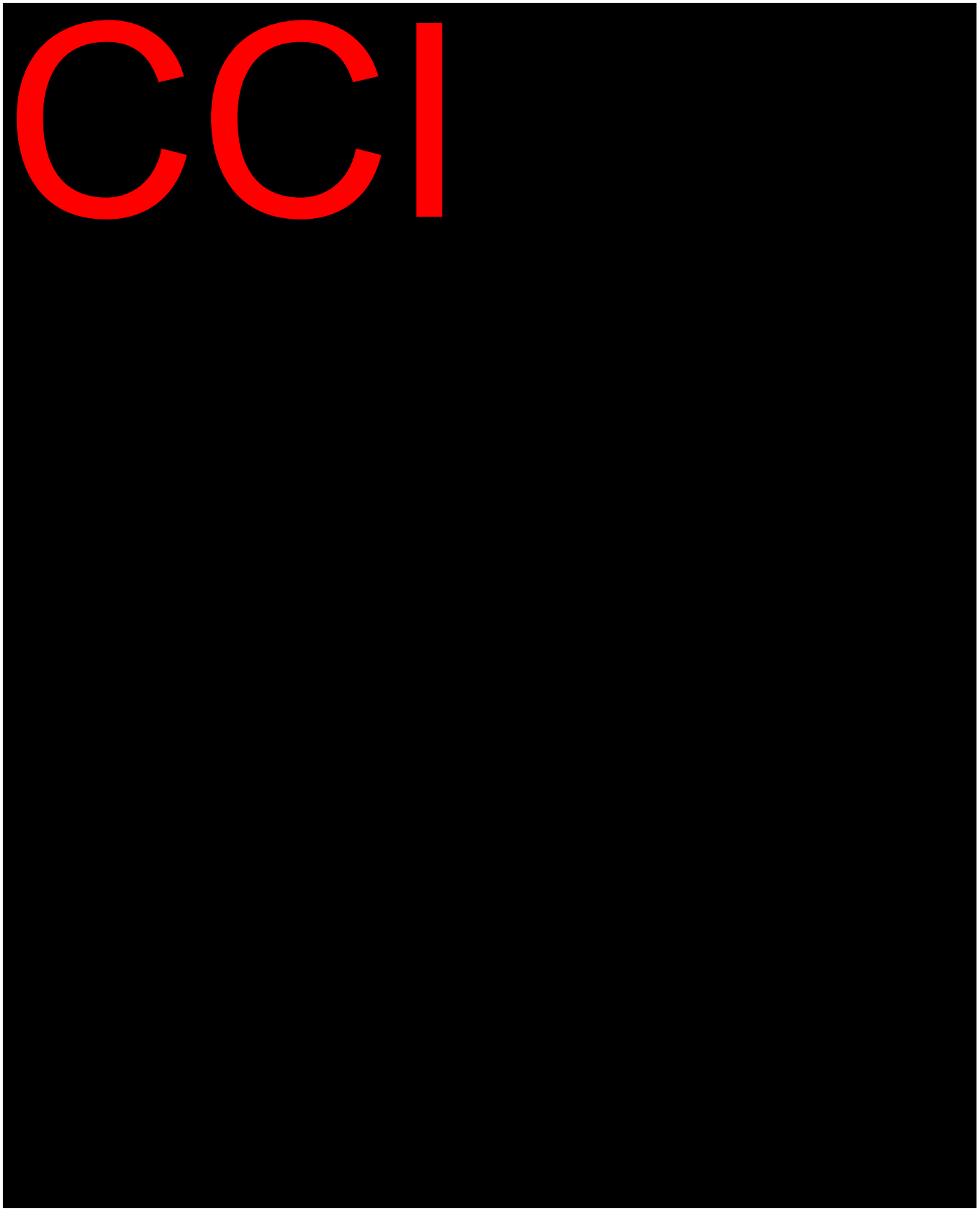
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