



Protocol No: SRF388-201

**A Randomized Phase 2 Trial of Atezolizumab and Bevacizumab in
Combination With CHS-388 (formerly known as SRF388) or Placebo in
Patients With Untreated Locally Advanced or Metastatic Hepatocellular
Carcinoma**

Statistical Analysis Plan

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SIGNATURE PAGE

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14-Aug-2025

Date

Coherus Oncology, Inc

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12-Aug-2025

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MODIFICATION HISTORY

DRAFT VERSION HISTORY			
Draft 0.1	19Nov2022	PPD	First Version based on Protocol Amendment 2.0 and 2.1 (Amendment 2.1 – South Korea)
Draft 0.2	03Feb2023		Update based on Surface's comments
Final 1.0	23Jun2023		Add KK in signature page
Draft 1.1	30Nov2023		Remove Randomization section due to early discontinuation and add Pharmacokinetics (PK) analysis
Draft 1.2	12Dec2023		Update PK section based on Coherus's comments, keep section 1~3 as they are for the consistency with the protocol. Add Section 4 for the deviation from the protocol
Draft 1.3	14Dec2023		Separate Response-Evaluable Analysis Set into two: RECIST and mRECIST on the version reviewed by Coherus
Draft 1.4	11Apr2024		Update Plasm to Serum for PK analysis Update treatment-boosted ADA definition Remove N (%) of patients without post-dose ADA positive
Final 2.0	15Feb 2025		Accept updates in version 1.4 Change drug name SRF388 to CHS-388
Draft 2.1	23May 2025		Add Disease control rate DCR2 and mDCR2 definition and summary. Add EBI3 Analysis Set and EBI3 related TFLs.
Final 3.0	04June 2025		Accept updates in version 2.1 and Coherus' edits
Final 4.0	11August 2025		Update TEAE definition to include SAE within 90 days after the last dose

ABBREVIATIONS

ADA	Antidrug antibody
AE	Adverse Event
AESI	Adverse Event of Special Interest
AFP	Alpha-fetoprotein
ALP	Alkaline phosphatase
ALT	Alanine transaminase
AST	Aspartate transaminase
ATC	Anatomical Therapeutic Chemical drug classification system
BCLC	Barcelona Clinic Liver Cancer
BOR	Best Overall Response
CI	Confidence Interval
CFB	Change From Baseline
CR	Complete Response
DCR	Disease control rate
DOR	Duration of Response
EBI3	Epstein-Barr Virus Induced Gene 3
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EoT	End of Treatment
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HR	Hazard Ratio
MedDRA	Medical Dictionary for Regulatory Activities
CTCAE	Common Terminology Criteria for Adverse events
NA	Not Available or Not Applicable
NE	Not Evaluable
ORR	Objective Response Rate
PFS	Progression Free Survival
PD	Progressive Disease
PK	Pharmacokinetics
PN	Preferred Name
PR	Partial Response
PT	Preferred Term
QTcF	QT Interval corrected with Fridericia's method
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Stable Disease
S.D.	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TTP	Time to Progression
TTR	Time to Response
ULN	Upper Limit of Normal Range

WHODrug	World Health Organization Drug Dictionary
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INTRODUCTION

The objective of this document is to detail the statistical methodology to be used in the summary and the final statistical analysis of clinical study protocol SRF388-201: “A Randomized Phase 2 Trial of Atezolizumab and Bevacizumab in Combination With SRF388 or Placebo in Patients With Untreated Locally Advanced or Metastatic Hepatocellular Carcinoma”. This study includes the Safety Lead-In, Lead-In Expansion, and Randomized Phase.

This SAP is based on Amendment 3 dated 19Sept2024, Amendment 3.1 – South Korea dated 19Sep2024, and CRFs version 11 dated on 18Dec2023.

Changes in Amendment 2.1 were made at the request of the South Korean Ministry of Food and Drug Safety and include two Exclusion Criteria and Protocol table 16. These changes have no impact on statistical analysis. In Amendment 3.0/3.1, SRF-388 was updated as CHS-388.

Pharmacodynamics analyses and reporting are not included in this analysis plan.

1.1 Primary analysis:

One primary analysis post DBL will be performed.

1.2 Changes to SAP

1.2.1 Changes to SAP Version 2.0 from Version 1.0

Surface (sponsor) terminated the study after 30 subjects received treatment in Safety Lead-In. Therefore, the analyses for Randomized Phase are removed from SAP. There is no Protocol Amendment for this change.

Update SRF388 to CHS-388.

1.2.2 Changes to SAP Version 3.0 from Version 2.0

Add Disease control rate DCR2 and mDCR2 definition and summary.

Add EBI3 Analysis Set and EBI3 related TFLs.

2 STUDY DESIGN

SRF388-201 is a Phase 2 trial composed of a Lead-In followed by a Randomized Phase designed to evaluate the efficacy and safety of CHS-388 in combination with atezolizumab plus bevacizumab (Arm A) compared to placebo in combination with atezolizumab plus bevacizumab (Arm B) in patients with first-line advanced or metastatic HCC.

After a Safety Lead-In of 6 patients who will receive open-label CHS-388 + atezolizumab + bevacizumab, approximately 24 additional patients will be enrolled in the Lead-In Expansion. The Randomized Phase follows the Lead-In Expansion and will randomize approximately 104 patients with a 1:1 allocation to Arm A or Arm B and stratified by geographic region (Asia excluding Japan vs. rest of world) and Barcelona Clinic Liver Cancer (BCLC) stage (B or C).

2.1 Study Objectives

All objectives are for both the Lead-In and Randomized Phase unless otherwise specified.

2.1.1 Primary Objectives

Lead-In:

- To evaluate the safety and tolerability of CHS-388 in combination with atezolizumab + bevacizumab

Randomized Phase:

- To evaluate the efficacy of CHS-388 in combination with atezolizumab + bevacizumab compared to placebo in combination with atezolizumab + bevacizumab as measured by PFS

2.1.2 Secondary Objectives

2.1.2.1 Efficacy Objectives

- To evaluate preliminary measures of efficacy of CHS-388 in combination with atezolizumab + bevacizumab in the Lead-In
- To evaluate additional measures of efficacy of CHS-388 in combination with atezolizumab + bevacizumab compared to placebo in combination with atezolizumab + bevacizumab in the Randomized Phase
- To evaluate the efficacy of CHS-388 in combination with atezolizumab + bevacizumab according to serum EBI3 levels in the Lead-In
- To evaluate the efficacy of CHS-388 in combination with atezolizumab + bevacizumab compared to placebo in combination with atezolizumab + bevacizumab according to serum EBI3 levels in the Randomized Phase

2.1.2.2 Safety Objective

- To evaluate the safety and tolerability of CHS-388 in combination with atezolizumab + bevacizumab compared to placebo in combination with atezolizumab + bevacizumab in the Randomized Phase

2.1.2.3 Immunogenicity Objectives

- To characterize the immunogenicity of CHS-388 and atezolizumab
- To explore potential correlations between immunogenicity and efficacy, safety, and PK outcomes

2.1.2.4 Pharmacokinetic Objectives

- To characterize the PK profile of CHS-388 when given in combination with atezolizumab + bevacizumab
- To explore the potential PK impact from drug interaction

2.1.2.5 Exploratory Biomarker Objectives

- To identify and evaluate potential blood or tissue biomarkers of response, resistance, and/or safety
- To evaluate the effects of CHS-388 in combination with atezolizumab + bevacizumab on peripheral blood immune cell subsets and circulating cytokines and chemokines

2.2 Sample Size Considerations

Trial SRF388-201 will enroll a total of approximately 134 patients; approximately 30 patients in the Lead-In followed by the Randomized Phase enrolling approximately 104 patients in a 1:1 randomization stratified by geographic location (Asia excluding Japan vs. rest of world) and BCLC stage (B or C) to assess a primary endpoint of PFS.

In the sample size calculation, the HR was calculated using the Weibull distribution with increasing hazard ($\kappa=1.92$), based on the shape of PFS curves in the literature. Of note, the exponential distribution is a special case of the Weibull distribution in that it has a constant hazard. Utilizing a larger alpha (1-sided alpha at 0.05, instead of a 1-sided alpha at 0.025) and appropriately modeling the HR based on the shape of the PFS curve for these patients, the protocol utilizes increased PFS as the primary endpoint. A clinically meaningful difference in median survival of 2.1 months (6.9 months vs 9 months) and the calculation of HR from a Weibull distribution of $[mPFS(\text{Control})/mPFS(\text{Experimental})]^{\kappa} = (6.9/9)^{1.92}$ result in the estimated HR of 0.6.

2.3 Study Endpoints and Evaluations

All endpoints are for both the Lead-In and Randomized Phase unless otherwise specified.

2.3.1 Primary Endpoints

Lead-In:

- Nature, frequency, and severity of AEs per National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0 or higher
- Timing of AEs

Randomized Phase:

- PFS, defined as time from randomization to occurrence of PD or death from any cause (whichever occurs first), as determined by Investigator review according to RECIST v1.1

2.3.2 Secondary Endpoints

2.3.2.1 Efficacy Endpoints

- PFS, defined as time from study drug initiation to occurrence of PD or death from any cause (whichever occurs first), as determined by Investigator review according to RECIST v1.1 (Lead-In only)
- PFS, defined as time from study drug initiation (Lead-In) or randomization to occurrence of PD or death from any cause (whichever occurs first), as determined by Investigator review according to HCC mRECIST
- ORR as determined by Investigator review according to:
 - RECIST v1.1
 - HCC mRECIST
- Duration of response (DoR), defined as time from initial documented objective response to PD or death from any cause (whichever occurs first), as determined by Investigator review according to:
 - RECIST v1.1
 - HCC mRECIST

- Disease control rate (DCR), defined as the proportion of patients who experience best overall response of complete response (CR), partial response (PR), or SD $\geq$ 12 weeks
- Time to progression (TTP), defined as time from study drug initiation (Lead-In) or randomization to occurrence of disease progression, as determined by Investigator review according to:
 - RECIST v1.1
 - HCC mRECIST
- OS, defined as time from study drug initiation (Lead-In) or randomization to death from any cause
- Time to response, defined as time from study drug initiation (Lead-In) or randomization to initial documented objective response, as determined by Investigator review according to:
 - RECIST v1.1
 - HCC mRECIST
- Time on therapy, defined as time from study drug initiation (Lead-In) or randomization to last treatment
- PFS, ORR, TTP, and OS by serum EBI3 concentrations

2.3.2.2 Safety Endpoints

Randomized Phase:

- Nature, frequency, and severity of AEs per National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) version 5.0 or higher
- Timing of AEs

2.3.2.3 Immunogenicity Endpoints

- Incidence of CHS-388 ADAs
- Incidence of atezolizumab ADAs
- Efficacy, safety, and PK endpoints by ADA status

2.3.2.4 Pharmacokinetic Endpoints

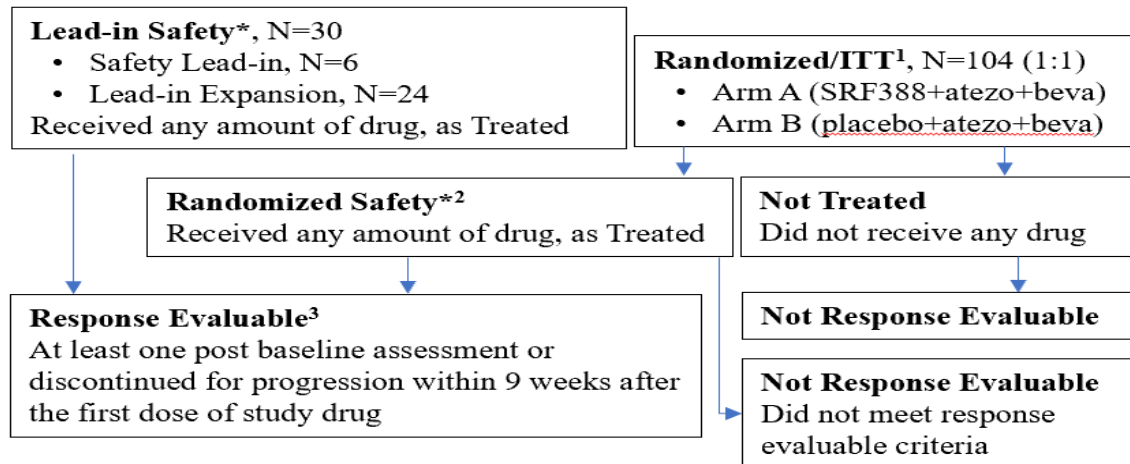
- Serum concentrations of CHS-388
- Serum concentrations of atezolizumab

2.3.2.5 Exploratory Biomarker Endpoints

- Assessment of selected blood-based and tumor tissue biomarkers, which may include cytokines, immune cell population subset enumeration and evaluation, PD-L1 expression, gene and protein expression levels, DNA mutation and copy number variations, and correlation of Baseline levels and changes in these markers with clinical outcomes (eg, PFS, ORR)
- Changes in peripheral blood immune cell populations by flow cytometry and gene expression

3 ANALYSIS SETS

The definitions of Safety Analysis Set, Intent-to-Treat Analysis Set, and Response Evaluable Analysis Set in lead-in phase and randomization phase are listed in the follow diagram:



*The following additional analysis sets should be in either Safety Lead-In or Randomized Safety and meet the condition(s) in each definition:

- PK Analysis Set: At least one measurable PK
- Immunogenicity Analysis Set: At least one measurable ADA
- Predictive Biomarker Analysis Set: At least one adequate baseline (C1D1 pre-dose or screening) biomarker result, and at least one RECIST response assessment. Note: This definition applies for each biomarker studied.
- PD Analysis Set: At least one baseline (C1D1 pre-dose or screening) biomarker result and one on therapy biomarker result. Note: This definition applies for each biomarker studied.
- EBI3 Analysis Set: At least 1 adequate baseline EBI3 assessment, including a Screening or C1D1 pre-dose assessment.

¹Randomized/Intent-to-Treat Analysis Set

The Randomized/Intent-to-Treat Analysis Set is defined as all randomized patients in Randomization Phase. This analysis set will be the primary analysis set for the efficacy analyses for the Randomized Phase. Those without any post-treatment assessment are included and considered as non-responders in this analysis.

²Randomized Safety Analysis Set

The Randomized Safety Analysis Set is defined as all patients who received any amount of study drug (CHS-388/placebo, atezolizumab, or bevacizumab) in the Randomization Phase, with treatment group designated per actual study drug received. This analysis set will be the primary analysis set for all safety endpoints in the Randomization Phase.

³Response-Evaluable Analysis Set

The Lead-in and Randomization Response-Evaluable Analysis Set is defined as all patients with measurable disease at Baseline who received ≥ 1 dose of all assigned study drugs and had ≥ 1 post-Baseline response assessment or who discontinued the treatment phase due to radiographic or symptomatic disease progression (including death caused by disease progression) within 9 weeks after the first dose of study drug. Response-Evaluable Analysis Set for RECIST and mRECIST will be derived separately. This analysis set will be used as a sensitivity analysis for key efficacy endpoints in Randomization Phase and all efficacy endpoints in Lead-in Phase.

4 DEVIATION FROM PROTOCOL

On 5July3023, Surface announced that the Randomized Phase will not be started for this SRF388-201 study. All sites were notified on 12Jul2023. The patients who enrolled for Safety Lead-In treatment were permitted to continue the treatment per study protocol. Importantly, the early termination of SRF388-201 study was a business decision; there were no safety concerns. As of 12Jul2023, 30 subjects received treatment in Safety Lead-In.

There is no protocol amendment following this decision. Any descriptions/statements regarding the Randomized Phase of the study will be removed from this updated SAP.

5 GENERAL CONSIDERATIONS

5.1 Programming Environment

All analyses will be conducted using SAS[®] version 9.4 or later.

5.2 General Statistical Methods

The statistical analyses will be presented for the different analysis sets as defined in Section 3.

5.2.1 Analysis Groups

The summary will be presented as Lead-In.

5.2.2 Descriptive Summaries

In general, numerical variables will be summarized using descriptive statistics, displaying the number of patients in the respective analysis group, the number of patients with data, sample mean, sample standard deviation (calculated as the square root of an unbiased variance estimate), sample median, minimum (min) and maximum (max).

Categorical variables will be summarized by using frequency counts and percentages. In addition, the number of patients with missing values will be displayed. Unless otherwise specified, the denominators used for calculating sample proportions will be the number of patients for each level of the analysis group defined above in the specified statistical analysis set (or a subset of the statistical analysis set under use).

5.2.3 Presentation Conventions

Means and medians will be presented by 1 additional decimal place and standard deviation will be presented by 2 additional decimal places than the standard presentation level of the respective data. Minimum and maximum values will be presented using the same number of

decimal places as the original data. Confidence limits will be presented by 1 additional decimal place than corresponding point estimates.

If not otherwise stated, percentages will be presented to 1 decimal place. However, when the percentage (or estimated proportion) is 100% exactly, no decimal place will be shown, whereas a presented 100.0% implies that the percentage is in the half-open interval [99.95%, 100%). The number of decimal places may be adjusted, e.g., if the above default choices may lead to misinterpretation of the presented data.

In general, explicit rounding will only occur when presenting data but not when analyzing data. By default, presented data will be rounded to the nearest required presentation precision, with a “round half to even” tie-breaking rule according to IEEE 754-2019. However, when presenting confidence intervals, the lower limit will always be rounded down, and the upper limit will always be rounded up in order to preserve the claimed (exact or asymptotic) confidence level. When either limit is outside of the parameter space (e.g., below 0 or above 1 for proportions), the interval will be truncated at the boundary of the parameter space.

If the number of patients in a category is 0, then a percentage will not be displayed, and only a count of 0 will be shown. However, structural zeros (e.g., when the count is deemed to be 0 before obtaining actual data), missing data or inapplicable/unevaluable summaries will be presented as –, NA or NE.

In listings, data will be sorted by study part, arm, and patient. When appropriate by visit, scheduled timepoint or other identifiers for sequence or type of observation.

5.3 Covariates and Strata

Not applicable for Safety Lead-In.

5.4 Subgroups

No subgroup analysis for Safety Lead-In efficacy endpoints.

5.5 Multiple Comparison/Multiplicity

No multiple comparison will be performed.

6 DEFINITIONS & DATA HANDLING CONVENTIONS

6.1 Study Day, Duration, and Study Periods

6.1.1 Study Day

Day 1 will be the date corresponding to the first administration of CHS-388. Study Day = Assessment Date – Date of Day 1 + 1 for assessment dates on or after date of Day 1. Study Day = Assessment Date – Date of Day 1 for assessment prior to Day 1.

Unless otherwise specified, day is the primary time unit for derived time and durations. Derived time units include week=7 days, month=30.436875 days, and (Gregorian) year=365.2425 days=12 months. Thus, 1 month and 4 weeks are considered different.

6.1.2 Duration

Unless otherwise specified, duration of time is defined from the starting day through the ending day, inclusive of both boundary days.

6.1.3 Study Period

- Screening period: Beginning on the day of informed consent, or Study Day –30, whichever is latest, and ending on Study Day –1
- Treatment period: Beginning on Study Day 1 and ending on the last day of the end of treatment (EoT) visit. In case that the EoT visit is missed for any reason, the treatment period will end on the 21st day since the last dose of any study drug.
- Safety follow-up period: the Safety Follow-up visit should occur at 30 ($\pm$ 5) days after the last dose of any study drug (CHS-388, atezolizumab, or bevacizumab, whichever is later).
- Long-term follow-up period: The Long-term Follow-up Visit at 90 (+ 5) days after the last dose of study drug (CHS-388, atezolizumab, or bevacizumab, whichever is later). If possible, this visit should occur before the initiation of any subsequent anticancer therapy. Patients continuing to experience toxicity at this point following the discontinuation of treatment will continue to be followed at least monthly until resolution or determination in the clinical judgment of the Investigator that no further improvement is expected. A Safety Follow-up Visit is not required for patients who discontinue all study drugs due to a treatment interruption of CHS-388 and bevacizumab lasting > 42 days and atezolizumab lasting > 12 weeks. However, these patients must complete the Long-term Follow-up Visit and will be followed for survival.
- Survival follow-up period: All patients will be followed for survival every 6 months for 4 years from randomization. This assessment can be conducted by telephone interview or medical chart review. Information on initiation of other anticancer therapy, including start date, therapy type, and response on treatment, will be collected.

6.2 Analysis Visit Windows

Subject visits will be presented according to the nominal visit as obtained upon the eCRF. All values will be included in the subject data listings.

6.3 Baseline and Change from Baseline

The baseline value is defined to be the last non-missing assessment prior to the first dose of CHS-388. For assessments performed at Day 1, if the time of the day is missing but scheduled timepoint is recorded as pre-dose, the assessment may be considered the baseline assessment for each of these respective study procedures. Unless otherwise specified, change from baseline (CFB) calculations for a treatment window assessment will be the applicable treatment window assessment minus the baseline assessment. If either the treatment window assessment value or the baseline value is/are missing, then CFB will be set to missing for descriptive analysis purposes, unless otherwise specified.

6.4 Missing Data

6.4.1 Partial or Missing Dates and Time

The incomplete dates (e.g., start and/or stop dates of AE, concomitant medication) will be assumed as the most conservative value possible. In general, unless the available parts of the partial date preclude an AE to be treatment-emergent, the AE will be considered treatment-emergent; similarly, unless the available parts of the partial date exclude a medication to be concomitant, the medication will be considered as a concomitant medication.

For example, if the start date has a missing day value, the first day of the month will be imputed for study day computations, etc. If a day is missing for an end date, the last day of the month will be imputed. If the start date has a missing month value, the first month of the year will be imputed for study day computations, etc. If month is missing for an end date, the last month of the year will be imputed. For determination of treatment-emergent status, the start date will be imputed as the date of the first dose of study drug, unless there is clear evidence (through comparison of partial dates/times) to suggest otherwise.

Date imputation will only be used for computational purposes such as treatment-emergent status, etc. Actual data values, as they appear in the original eCRFs, will be presented in the subject data listings. Non-monotone partial dates (e.g., day and month are non-missing, but year is missing) need to be queried and resolved before DBL.

6.4.2 Other Missing Values

Every effort will be made to obtain the required data at each scheduled evaluation from all patients who have been enrolled. In general, missing data will not be imputed and the data will be analyzed as they are recorded.

7 STUDY POPULATION AND DISPOSITION

7.1 Analysis Sets

The number and percentage of patients in each analysis set as defined in Section 3 will be summarized using Safety Analysis Set as described in Section 5.2.1.

Corresponding data listing will be provided using the Lead-in Safety Analysis Set.

7.2 Subject Disposition

The number and percentage of the following will be summarized using the Safety Analysis Set as described in Section 5.2.1, including:

- CHS-388 treatment ongoing
- CHS-388 treatment discontinuation
- Reason for CHS-388 treatment discontinuation
 - Adverse Event
 - Death
 - Progressive Disease – Radiographic
 - Progressive Disease – Clinical
 - Physician Decision
 - Withdrawal by Subject
 - <insert eCRF record>
 - Other
- Bevacizumab treatment ongoing
- Bevacizumab treatment discontinuation
- Reason for Bevacizumab treatment discontinuation
 - Adverse Event
 - Death
 - Progressive Disease – Radiographic
 - Progressive Disease – Clinical

- Physician Decision
- Withdrawal by Subject
- <insert eCRF record>
- Other
- Atezolizumab treatment ongoing
- Atezolizumab treatment discontinuation
- Reason for Atezolizumab treatment discontinuation
 - Adverse Event
 - Death
 - Progressive Disease – Radiographic
 - Progressive Disease – Clinical
 - Physician Decision
 - Withdrawal by Subject
 - <insert eCRF record>
 - Other
- Study ongoing
- Study discontinuation
- Reason for study discontinuation
 - Death
 - Adverse Event
 - Progressive Disease - Radiographic
 - Progressive Disease - Clinical
 - Physician Decision
 - Withdrawal by Subject
 - Study Terminated by Sponsor
 - <insert eCRF record>
 - Other

Time on therapy (weeks), defined as (the date of last treatment - the date of study drug initiation (Lead-In) + 21)/7, will be presented in swimmer plots. The visit response per RECIST 1.1 and the reason for CHS-388 treatment discontinuation will be labeled on the plots. Time on therapy will also be summarized using descriptive statistics.

Disposition of patients will be provided in a data listing using the using the Safety Analysis Set.

7.3 Protocol Deviations

Protocol Deviation Management Plan (PDMP) version: 1.0 dated 14Apr2022 defined the study specific procedures and responsibilities for managing Protocol Deviations. The document listed the definition of Bioclinica Deviation Description and Deviation Area, as well the Deviation Category (Important Protocol Deviation, Non-Important Protocol Deviation, GCP Compliance Issues). Subject level protocol deviations will be documented in the Clinical Trial Management System (CTMS). The Quarterly Protocol Deviation Review meeting will review protocol listing for quality control.

Major deviations from the clinical protocol may include, but are not limited to:

- ICF/Subject Information
- Ineligible Subject Enrolled
- IMP Dose Error

- IMP Other Error
- Prohibited Medication
- SAE or AESI Reporting Failure

All protocol deviations (both major and minor) will be provided in a data listing for all patients who signed the ICF. Protocol deviations due to COVID-19 will be provided in a separate listing.

8 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

8.1 Demographics

The following demographic characteristics will be summarized using the Safety Analysis Set as described in Section 5.2.1:

- Age at informed consent (years) (as reported in EDC)
- Sex (female [with childbearing potential, without childbearing potential], male, undifferentiated)
- Age ($\geq$ median, $<$ median)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, Other, Unknown/Not Reported)
- Ethnicity (Hispanic or Latino, not Hispanic or Latino, not reported, unknown)

Demographic characteristics will also be provided in a data listing using the Safety Analysis Set.

8.2 Primary Cancer History

The following primary hepatocellular carcinoma history characteristics will be summarized using the Safety Analysis Set as described in Section 5.2.1:

- Time since initial diagnosis (months), defined as time from the date of initial histopathological diagnosis to the date of first CHS-388 dose (lead-in phase) or date of randomization (randomization phase)
- Time since most recent disease progression (months), defined as time from date of most recent disease recurrence/progression to the date of first CHS-388 dose (lead-in phase) or date of randomization (randomization phase)
- Stage at initial diagnosis (0, I, II, III, IV)
- Current disease stage (III, IV)
- Characterization of disease at study entry
 - Locally advanced
 - Unresectable (Yes, No)
 - Metastatic
- Number of metastatic sites (0, 1, 2, 3, 4, 5, ≥ 6)
- Metastatic sites
 - Adrenal Gland
 - Bile duct
 - Bone
 - Brain
 - Breast

- Bronchus
- <insert eCRF record>
- Other

The primary cancer history will be listed using the Safety Analysis Set.

8.3 Hepatocellular Carcinoma History at Baseline

The following cancer history characteristics will be summarized using the Safety Analysis Set:

- Child Pugh Total Points
- Child Pugh Score (Class A, Class B, Class C)
- Barcelona Clinic Liver Cancer Score (B, C)
- Subject have a history of varices
 - Yes
 - Present at screening
 - Not present at screening
 - No
 - Variceal banding in the last 6 months
 - Yes
 - No
 - Unknown
 - Unknown
- History of Cirrhosis
 - No
 - Yes
 - Unknown
- Etiology of HCC
 - HBV
 - HCV
 - Alcohol
 - NAFLD
 - Diabetes
 - Obesity
 - Other non-viral
 - Unknown
- Ascites history
 - Yes
 - Present at screening
 - Not present at screening
 - No
- Subject on diuretics for ascites (Yes, No)
- Paracentesis in the last 6 months (Yes, No, Unknown)
- Hepatic encephalopathy history
 - Yes
 - Present at screening
 - Not present at screening
 - No

- Unknown
- Medication for hepatic encephalopathy (Yes, No)
- Macrovascular hepatic vein invasion (Yes, No)
- Main portal vein invasion (Yes, No)
- Portal vein tumor thrombosis (Yes, No)
- Hepatic vein tumor thrombosis (Yes, No)
- IVC thrombosis (Yes, No)
- $\geq 50\%$ liver occupancy by HCC (Yes, No)
- Alcohol use
 - Current, Previous, Never, Unknown
 - Alcohol disorder or excessive use (Yes, No)
- History of HBV
 - Yes
 - Ongoing HBV infection
 - No ongoing HBV infection
 - No
- History of HCV
 - Yes
 - Treated with antiviral therapy
 - Not treated with antiviral therapy
 - Sustained virologic response (Yes, No)
 - No

The hepatocellular carcinoma history will be listed.

8.4 Tumor Genomic Alterations and Protein Expression

The following genomic alterations and protein expression will be summarized using the Safety Analysis Set:

- Mutation/Genetic Alteration Analysis Performed
 - Yes
 - No
- Specimen
 - Primary Liver Lesion
 - Metastatic Site
 - Serum/blood
- Organ Site
 - Adrenal Gland
 - Bile duct
 - Bone
 - Brain
 - Breast
 - <insert eCRF records>
 - Other
- MSI Status Known
 - No
 - Not Available
 - Yes

- MSI-H (microsatellite instability-high)
- MSI-L (microsatellite instability-low)
- MSS (microsatellite stable)
- dMMR (mismatch repair deficient)
 - No
 - Yes
 - Due to MLH1
 - Due to MSH2
 - Due to MSH6
 - Due to PMS2
- DNA Damage Repair (DDR) Alterations
 - ARID1A
 - ARID2
 - ATM
 - BARD1
 - BRCA1
 - BRCA2
 - <insert all that “Yes” is checked>
 - Other
- Tumor Mutation Burden (TMB) (≤ 10 , >10 , Unknown)
- PD-L1 Expression
 - Negative
 - Positive
 - $\leq 1\%$
 - $1\% - 5\%$
 - $5\% - 20\%$
 - $20\% - 50\%$
 - $\geq 50\%$
 - Unknown

The genomic alterations and protein expression will be listed.

8.5 Prior Systemic Anti-Cancer Therapies

The following prior systemic anti-cancer therapy characteristics will be summarized descriptively using the Safety Analysis Set as described in Section 5.2.1:

- Prior systemic anticancer therapies (Yes, No)
- Lines of prior systemic anticancer therapies (0, 1, 2, 3, 4,5, >5)
- Type of systemic therapy (Chemotherapy, Immunotherapy [aPD-1, aPD-L1, aCTLA4, Other], Hormonal, Targeted [VEGFR TKI, VEGF ab, VEGFR ab, Other], Other). A patient might be counted multiple time if the patient received multiple line of therapies with different type of therapy.
- Setting of therapy (Neoadjuvant, Adjuvant, Concurrent with liver directed therapy, Other). A patient might be counted multiple time if the patient received multiple line of therapies with different setting
- Best overall response (BOR) in all lines of prior systemic therapies (CR, PR, SD, PD, NE, Unknown). A patient might be counted multiple time if the patient received multiple line of therapies with different BOR
- BOR in the last line of prior systemic therapy (CR, PR, SD, PD, NE, Unknown)

- Reason for discontinuation in the last line of prior systemic therapy (Treatment completed, Progressive Disease, Toxicity, Adverse Event, Other)
- Primary reason for stopping treatment

Prior systemic cancer therapy information will also be provided in a data listing using the Safety Analysis Set.

8.6 Medical History

The medical history will be coded using MedDRA 24.1.

The number and percentage of patients with conditions coded to each system organ class (SOC) and preferred term (PT) will be summarized using the Safety Analysis Set as described in Section 5.2.1. If a patient has more than one medical condition within an SOC or PT, the patient will be counted only once for the respective SOC or PT.

Data listings of all medical history records will be provided using the Safety Analysis Set.

9 PROTOCOL-REQUIRED DRUG EXPOSURE AND COMPLIANCE

The dosing data for CHS-388, Atezolizumab, Bevacizumab be summarized descriptively using the Safety Analysis Set as described in Section 5.2.1.

The follow exposure parameters will be summarized will n. mean, standard deviation S.D.), median, min, max:

- **Number of cycles started** is defined as the maximum number of treatment cycles that a patient receives
- **Cumulative dose** (mg) is the sum of the actual dose administered that the patient receives across cycles as recorded in the eCRF
- **Total planned dose** (mg) is the sum of the planned total doses as recorded in the eCRF
- **Compliance** is $100 \times (\text{Cumulative dose} / \text{Total planned dose})$
- **Number of missing doses** (or called not administered in in the eCRF)
- **Number of interrupted** CCI

The number and percentage of patients with missing doses, interrupted CCI reasons for missing dose (COVID-19 Related, Other), reasons for interrupted CCI Reaction, Adverse Event other than CCI Reaction, Other) will be presented. All dosing data (including the above derived dosing parameters) will also be presented in a data listing using the Safety Analysis Set.

10 PRIOR AND CONCOMITANT THERAPIES

Safety Analysis Set will be used to summarize prior and concomitant therapies.

10.1 Prior and Concomitant Medications

Prior and concomitant medications will be coded according to the latest version of World Health Organization drug dictionary (WHO-Drug B3 Global version September 2021) with Anatomical Therapeutic Chemical Classification System (ATC) and preferred names (PN).

Prior medications include non-study drug medications that end before Day 1. Concomitant medications include non-study drug medications that are used on/after Day 1.

The number and percentage of patients with prior medication or concomitant medications will be summarized by ATC level 2 category and preferred name will be summarized using the Safety Analysis Set as described in Section 5.2.1. If a patient received more than 1 drug within an ATC2 or PN, the patient will be counted only once for this ATC2 and PN.

Prior and concomitant medications information will also be provided in a data listing using the Safety Analysis Set.

10.2 Prior and Concomitant Procedures

Prior and concomitant procedures will also be provided in a data listing using the Safety Analysis Set.

11 EFFICACY ANALYSES

Imaging will be performed every 9 weeks (ie, beginning C4D1 [$\pm$ 7 days] followed by C7D1, C10D1, C13D1, etc.) and should include imaging consistent with anatomic areas and modality used at Screening. Tumor responses are assessed based on RECIST (v1.1) criteria and mRECIST criteria by Investigator. The overall tumor response per visit includes Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Not Evaluable (NE) per RECIST 1.1 and mRECIST criteria by Investigator.

The efficacy endpoints will be presented using Response-Evaluable Analysis Set For efficacy endpoints derived from progression and/or response status, disease assessments after the start of new anticancer therapy will be excluded from consideration.

11.1 Definitions of Efficacy Variables

11.1.1 Progression-free Survival

The progression-free survival (month) is calculated from the date of first CHS-388 dose to the date of disease progression using RECIST 1.1 (PFS)/mRECIST (mPFS) criteria or death, whichever occurs first. The patients without disease progression or death will be censored on the date of last disease assessment. Disease assessments after the start of new anticancer therapy will be excluded from the derivation. PFS and mPFS will be derived separately. See below for event/censor rules.

Situation	Date of Event or Censoring	Event or Censoring
No post baseline disease assessment	Date of first CHS-388 dose/ randomization	Censored
Progression after one or none missing assessment	Date of progression	Event
Death after one or none missing assessment	Date of death	Event
No progression (or death)	Date of last assessment	Censored
Progression or death after two or more missing assessment	Date of last assessment prior to missed assessments	Censored

11.1.2 Best Overall Response

The best overall response of RECIST 1.1 (BOR) and mRECIST (mBOR) will be derived from the overall responses of all visits per patients, excluding the visit (s) after the date of subsequent anti-cancer therapy and/or the date of first documented PD. BOR and mBOR include CR, PR, SD, PD, NE. CR or PR needs to be confirmed by a second scan performed at least 4 weeks later. Unconfirmed CR or PR will be categorized as SD. The patients in response-evaluable analysis set without any visit overall response will be categorized as NE.

11.1.3 Objective Response Rate

Objective response rate is the proportion of patients that achieve the best overall response of PR/CR per RECIST 1.1 (ORR) and mRECIST (mORR). As defined in BOR, PR/CR needs to be confirmed by a second scan performed at least 4 weeks later.

11.1.4 Disease Control Rate

Disease control rate is the proportion of patients that achieve BOR of confirmed CR, confirmed PR, or SD lasting a minimum of 12 weeks per RECIST 1.1 (DCR1) and mRECIST (mDCR1) or the proportion of patients that achieve BOR of confirmed CR, confirmed PR, or SD per RECIST 1.1 (DCR2) and mRECIST (mDCR2).

11.1.5 Duration of Response

Duration of response (month), reported in patients achieving a confirmed CR or confirmed PR, is calculated from the date of first observation of CR or PR to the date of disease progression using RECIST 1.1 (DOR)/mRECIST (mDOR) or death, whichever occurs first. The patients without disease progression or death will be censored on the date of last disease assessment. Disease assessments after the start of new anticancer therapy will be excluded from the derivation. See below for event/censor rules.

Situation	Date of Event or Censoring	Event or Censoring
Progression after one or none missing assessment	Date of progression	Event
Death after one or none missing assessment	Date of death	Event
No progression (or death)	Date of last assessment	Censored
Progression or death after two or more missing assessment	Date of last assessment prior to missed assessments	Censored

11.1.6 Time to Response

Time to response (month), reported in patients achieving a confirmed CR or confirmed PR, is defined as time from the date of first CHS-388 dose to the date of first documented CR or PR as determined by Investigator review according to RECIST v1.1 (TTR) and mRECIST (mTTR).

11.1.7 Time to Progression

Time to progression (month), is defined as time from the date of first CHS-388 dose to the date if first documented disease progression as determined by Investigator review according to RECIST v1.1 (TTP) and mRECIST (mTTP). The patients without disease progression will be censored on the date of last disease assessment. Disease assessments after the start of new anticancer therapy will be excluded from the derivation. See below for event/censor rules.

Situation	Date of Event or Censoring	Event or Censoring
No post baseline disease assessment	Date of first CHS-388 dose/ randomization	Censored
Progression after one or none missing assessment	Date of progression	Event
No progression	Date of last assessment	Censored
Progression after two or more missing assessment	Date of last assessment prior to missed assessments	Censored

11.1.8 Overall Survival

Overall Survival (OS, month) is defined as time from the date of first CHS-388 dose to the date of death for any reason. The patients who alive at the end of study or date of data cut will be censored on the date of last known alive.

11.2 Analysis of Efficacy Variables

11.2.1 Time to Response

Time to Response (TTR and mTTR) will be summarized using descriptive statistics (n, mean, S.D., median, minimum, and maximum).

11.2.2 Other Time to Events

Time to event analyses include DOR, mDOR, TTP, mTTP, mPFS, PFS and OS. The number and percentage of patients with events or censored, the time when 25%, median, 75% of the events occurring, 95% confidence interval of the selected times will be estimated with the Kaplan-Meier methods. Event-free rate at 6 months, 12 months, 18 months, 24 months, and their 95% CIs will be calculated with the Kaplan-Meier methods as well.

11.2.3 Best Overall Response and Objective Response Rate

The number and percentage of patients with each BOR and mBOR will be summarized, respectively. SD will be further presented as <12 weeks or ≥12 weeks. ORR and ORRm along with the 2-sided 80%, 90% and 95% exact confidence intervals will be estimated using Clopper–Pearson method.

The best percentage change of target lesion change from baseline (maximum decrease or minimum increase if no decrease) per RECIST 1.1 and mRECIST will be presented with water fall plots.

11.2.4 Disease Control Rate

DCR1, mDCR1, DCR2, mDCR2 and their 2-sided 80%, 90% and 95% exact confidence intervals will be estimated using Clopper–Pearson method.

11.2.5 Sensitivity Analyses of BOR, ORR and DCR

The sensitivity analyses of BOR, mBOR, ORR, mORR, DCR and mDCR will be performed with unconfirmed RECIST 1.1 and mRECIST response. BOR/mBOR will be selected from all visit responses per patients, excluding the visit (s) after the date of subsequent anti-cancer therapy and/or the date of first documented PD, based on the following hierarchy: CR, PR, SD, PD, NE per each response criteria. The patients in response-evaluable analysis set without any visit overall response will be categorized as NE. The definitions and derivations of ORR and DCR are same as the descriptions in the sections 10.1.2, 10.1.3 and 10.1.4, except for the confirmation of BOR.

BOR, mBOR, ORR, mORR, DCR and mDCR will be presented in separate tables using the methods being described in section 10.2.3 and 10.2.4.

12 SAFETY ANALYSES

The Safety Analysis Set as defined in section 3 will be used to evaluate the safety and adverse event endpoints.

12.1 Adverse Events

Adverse events (AE) will be coded using MedDRA 26.1 and graded according to the NCI-CTCAE version 5.0.

Summaries of AEs will be based on treatment-emergent AEs (TEAEs). A TEAE is an AE that emerges or worsens in the period from the first dose of any study drug (including Placebo) to 30 days after the last dose of any study drug for AEs or 90 days after the last dose of any study drug for SAEs. TEAE summaries will be presented by System Organ Class (SOC) and Preferred Term (PT). Although AEs may be reported more than once for a PT or SOC in a patient, each patient will only be counted once per SOC and PT.

If CTCAE toxicity grade is missing, the event will be graded as severe (Grade 3) for analysis. The TEAE will be categorized as 'related' to study drug if the relationship of 'Possible', 'Probable', 'Definite' is selected. If the relationship to study drug is missing, the TEAE will be conservatively assessed as related.

An overview of Treatment Emergent Adverse Events (TEAEs), including number and percent of patients who had any TEAE, TEAE related to study drug, serious TEAEs, serious TEAEs related to study drug, TEAE leading to treatment withdrawn, TEAEs leading to treatment interrupted, TEAEs leading to CHS-388 dose reduced, adverse events of special interest (AESIs), TEAEs $\geq$ grade 3 in severity, TEAE being considered as CCI reaction, TEAE leading to death will be presented.

Number and percentages of patients with TEAEs will be presented by SOC and PT in the following summaries:

- TEAEs
- TEAEs related to CHS-388 only
- TEAEs related to Bevacizumab only
- TEAEs related to Atezolizumab only
- TEAEs related to any study drug
- TEAEs with grade 3 or higher
- TEAEs with grade 3 or higher related to CHS-388 only
- TEAEs with grade 3 or higher related to Bevacizumab only
- TEAEs with grade 3 or higher related to Atezolizumab only
- TEAEs with grade 3 or higher related to any study drug
- Serious TEAEs
- Serious TEAEs related to CHS-388 only
- Serious TEAEs related to Bevacizumab only
- Serious TEAEs related to Atezolizumab only
- Serious TEAEs related to any study drug
- TEAEs leading to CHS-388 withdrawn only

- TEAEs leading to Bevacizumab withdrawn only
- TEAEs leading to Atezolizumab withdrawn only
- TEAEs leading to any study drug withdrawn
- TEAEs leading to CHS-388 interrupted only
- TEAEs leading to Bevacizumab interrupted only
- TEAEs leading to Atezolizumab interrupted only
- TEAEs leading to study drug interrupted
- TEAEs leading to CHS-388 dose reduced
- TEAE leading to CCI reaction
- TEAEs of special interest
- TEAEs leading to death

Number and percentages of patients with TEAEs will be presented by PT in the following summaries:

- TEAEs
- TEAEs related to CHS-388 only
- TEAEs related to Bevacizumab only
- TEAEs related to Atezolizumab only
- TEAEs related to any study drug
- Serious TEAEs
- Serious TEAEs related to CHS-388 only
- Serious TEAEs related to Bevacizumab only
- Serious TEAEs related to Atezolizumab only
- Serious TEAEs related to any study drug

Number and percentages of patients with TEAEs will be presented by SOC, PT and maximum CTCAE grade in the following summaries:

- TEAEs
- TEAEs related to CHS-388 only
- TEAEs related to any study drug
- Serious TEAEs
- Serious TEAEs related to CHS-388 only
- Serious TEAEs related to any study drug

Subject listings will be provided for patients with all AEs, serious AEs, special interest TEAEs, CCI reactions, TEAE leading to withdrawal of any study drug, TEAEs leading to treatment interrupted, TEAEs leading to CHS-388 dose reduced, and TEAEs leading to death.

12.2 Deaths

Death information will be provided in a listing.

12.3 Pregnancies

Pregnancy test information will be provided in a data listing.

12.4 Vital Signs

Vital signs and body measurements (including weight, temperature, systolic and diastolic blood pressure, heart rate, and respiratory rate) and change from baseline (CFB) values will be summarized descriptively over time as described in Section 4.2.

The number and percentage of patients with the following notably abnormal vital signs and body measurements will be presented by visit:

- Clinically notable elevated values:
 - Systolic BP: ≥ 180 mmHg and an increase ≥ 20 mmHg from baseline
 - Diastolic BP: ≥ 105 mmHg and an increase ≥ 15 mmHg from baseline
 - Weight: Increase of $\geq 10\%$ from baseline
 - Heart rate: ≥ 120 bpm with an increase of ≥ 15 bpm from baseline
 - Temperature: $> 38^{\circ}$ C
- Clinically notable below normal values:
 - Systolic BP: ≤ 90 mmHg and a decrease ≥ 20 mmHg from baseline
 - Diastolic BP: ≤ 50 mmHg and a decrease ≥ 15 mmHg from baseline
 - Weight: decrease of $\geq 10\%$ from baseline
 - Heart rate: ≤ 50 bpm and a decrease ≥ 15 bpm from baseline
 - Temperature: $< 35^{\circ}$ C

Vital signs information will also be provided in a data listing.

12.5 Clinical Laboratory

For lab values in the form of $< x$, $\leq x$, below lower quantification limit, etc., the value will be imputed as $x/2$ or half of the lower quantification limit for the purpose of numerical descriptive summary. For lab values in the form of $> x$, $\geq x$, above upper quantification limit, etc., the value will be imputed as x or upper quantification limit for the purpose of numerical descriptive summary. When such imputation occurs, footnotes will be presented to clarify the imputation rule. The original lab values will be presented in data listings.

12.5.1 Hematology, Coagulation, Clinical Chemistry, Fasting Lipid Panel, AFP

The Laboratory test value, change from baseline, and percentage change from baseline for continuous parameters over hematology tests, chemistry tests, coagulation tests, fasting lipid panel, and AFP will be summarized using descriptive statistics (n, mean, S.D., median, minimum, maximum) by visit.

Shift of hematology tests, coagulation tests, and chemistry tests from baseline CTCAE grade to the worst postbaseline CTCAE grade will be presented. If a parameter includes both hypo- and hyper- CTCAE grade derivation, hypo- and hyper- will be tabulated separately. If the baseline is not CTCAE gradable (e.g., AST increase), the baseline measurement will be categorized as low/normal/high according to reference ranges.

An extremely high level of AFP in blood (greater than 400 ng/mL) could be a sign of liver tumors. The shift of AFP categories (< 400 ng/mL vs ≥ 400 ng/mL) from baseline to highest postbaseline will be prepared.

Additionally, the liver function tests (AST, ALT, ALP, and Total Bilirubin (TBL)) will be summarized in the following categories:

- Aspartate Aminotransferase (AST)

- 3 to < 5 x ULN
- 5 to < 10 x ULN
- 10 to < 20 x ULN
- ≥ 20 x ULN
- Alanine Aminotransferase (ALT)
 - 3 to < 5 x ULN
 - 5 to < 10 x ULN
 - 10 to < 20 x ULN
 - ≥ 20 x ULN
- AST or ALT
 - 3 to < 5 x ULN
 - 5 to < 10 x ULN
 - 10 to < 20 x ULN
 - ≥ 20 x ULN
- Total Bilirubin (TBL)
 - 1.5 x ULN to < 2 x ULN
 - ≥ 2 x ULN
- Alkaline Phosphatase (ALP)
 - < 2 x ULN
- (AST or ALT) and TBL
 - AST or ALT ≥ 3 x ULN and TBL ≥ 1.5 x ULN
 - AST or ALT ≥ 3 x ULN and TBL ≥ 2 x ULN
- (AST or ALT) and ALP and TBL
 - AST or ALT ≥ 3 x ULN and ALP < 2 x ULN and TBL ≥ 2 x ULN

Laboratory hematology, chemistry, coagulation, fasting lipid panel, Thyroid Function Testing, and AFP will be provided in data listings by patient.

12.5.2 Urinalysis and Urine Protein

Data listings of all urinalysis tests and 24 Hr. Urine Protein will be provided.

12.5.3 Virology

HIV tests, hepatitis (HBV surface antigen (HBsAG), anti-HCV antibody, HCV RNA, HBV DNA Viral Count, and HCV RNA Viral Load) will be listed.

12.6 ECG

QTcF Interval (msec) will be collected. QTcF Interval value, change from baseline, and percentage change from baseline at each visit/timepoint will be summarized using descriptive statistics (n, mean, S.D., median, minimum, and maximum)

The number and percentage of patients in the following QTcF category will also be summarized:

- QTcF at Baseline
 - QTcF >450 msec
 - QTcF >480 msec
 - QTcF >500 msec
- QTcF Highest Post-Baseline
 - QTcF >450 msec

- QTcF >480 msec
- QTcF >500 msec
- QTcF Highest Change from Baseline
 - >30 msec
 - >60 msec

All ECG data (scheduled or unscheduled) will be displayed in a data listing.

12.7 Eastern Cooperative Oncology Group (ECOG) Performance Status

Shift of ECOG at each visit from baseline will be summarized, All ECOG performance status will be provided in a data listing using Safety Analysis Set.

13 OTHER ANALYSES

13.1 Pharmacokinetics

The schedules of the blood sample collections for CHS-388 and Atezolizumab PK analysis are listed below:

Cycle	Day	Scheduled time point	CHS-388 PK sample ^a	Atezolizumab PK sample
1	1	Immediately CC1 (+ 30 min)	X	X
2 and 3	1	CC1	X	X
4	1	CC1	X	X
5 and beyond	1	Immediately CC1 (+ 30 min)	X	X ^c
EoT	--	--	X	X

Abbreviations: EoT = End of Treatment; PK = pharmacokinetics.

^a An additional blood sample for CHS-388 PK should be drawn at the time of any unusual safety event (ie, an AE different in type and severity from that which is expected in the setting of CHS-388, atezolizumab, or bevacizumab use).

^b **CC1** is defined as prior to **CC1** of all study drugs.

^c After Cycle 4, atezolizumab PK samples should only be collected on Day 1 of Cycle 8, Cycle 12, and Cycle 16, as well as EoT.

Serum concentrations will be summarized at each nominal timepoint using descriptive statistics (n, mean, standard deviation, coefficient of variation, median, minimum, maximum, and geometric mean) for CHS-388 and Atezolizumab separately.

Individual serum concentration will be plotted for CHS-388 and Atezolizumab on a linear scale against actual sampling time points relative to the first dosing time. Mean ($\pm$ S.D.) concentration troughs will be plotted on a linear scale against nominal time points for CHS-388 and Atezolizumab separately, when available. LLOQ (Lower Limit of Quantification) of CHS-388 or Atezolizumab will be plotted as a reference line.

For the individual concentration calculation of study treatment, the following rules will be applied:

- If one or more values below the limit of quantification (BLQ) occur before the first measurable concentration, they will be assigned a value of zero.
- If BLQ values occur between measurable concentrations in a profile, the BLQ should be omitted (set to missing).

- If BLQ values occur after the last measurable concentration in a profile, the BLQ should be omitted (set to missing).

For the concentration summary and mean concentration plot preparation of study treatment, the following rules will be applied:

- Mean concentration at any individual time point will only be calculated if at least half of the patients have valid values (i.e. quantifiable and not missing) at this time point for study treatment.
- In cases where a mean value is not calculated due to the above criterion not being met, the value will be set to missing.
- BLQ values will be set to zero.

Individual plasma concentrations will also be listed for the PK analysis set.

13.2 Pharmacodynamics

The pharmacodynamics analysis will be described in a separate plan.

13.3 Immunogenicity

Anti-drug antibody (ADA) data of CHS-388 will be provided in a listing using Immunogenicity Analysis Set. ADA will be summarized in tabular by the following categories:

- N (%) of patients with ADA positive at baseline (i.e. ADA detectable in the Cycle 1 Day 1 pre-dose sample)
- N (%) of patients with ADA negative at baseline (i.e. ADA detectable in the Cycle 1 Day 1 pre-dose sample)
- N (%) of patients with post-dose ADA positive (i.e. ADA detectable in any pre-dose sample from Cycle 2 on)
- N (%) of patients with treatment-emergent ADA, defined as those patients with a negative ADA result at baseline and one or more post-treatment (Cycle 2 on) ADA-positive samples. Patients with treatment-boosted ADA, defined as patients with a positive baseline ADA result who had one or more post-treatment (Cycle 2 on) ADA result with the titer increased at least 4-fold.

13.4 Biomarkers

13.4.1 EBI3

Serum EBI3 test value, change from baseline, and percentage change from baseline will be descriptively summarized by visit. Baseline serum EBI3 value will be summarized by BOR (RECIST1.1) status. The Kaplan-Meier method plots and summaries will be generated for PFS, TTP and OS by Baseline Serum EBI3 Status: $\leq$ Median Baseline EBI3 vs. $>$ Median Baseline EBI3. Scatter plot for correlation between BOR(RECIST1.1) status vs. baseline serum EBI3 for individual patients will be prepared. EBI3 Analysis Set will be used for these analyses. Serum EBI3 will be listed.

13.4.2 Other Biomarkers

PMBC immunophenotyping data, pharmacogenomics, and tumor biopsies may be further analyzed according to a separate analysis plan.

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