STATISTICAL ANALYSIS PLAN

Study Protocol Number:	BGB-A317-A1217-202
Study Protocol Title:	Phase 2 Study Investigating Efficacy and Safety of Anti-PD-1 Monoclonal Antibody Tislelizumab (BGB-A317) Combined With or Without Anti-TIGIT Monoclonal Antibody BGB-A1217 in Patients With Previously Treated Recurrent or Metastatic Cervical Cancer
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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Term
ADA	Antidrug antibody
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BOR	Best overall response
CBC	Complete blood count
CBR	Clinical benefit rate
CC	Cervical cancer
CI	Confidence interval
CL	Clearance
C_{max}	Maximum observed plasma concentration
C_{min}	Minimum observed plasma concentration
COVID-19	Coronavirus disease of 2019
CR	Complete response
CSR	Clinical Study Report
C_{trough}	Trough serum concentration
DCR	Disease control rate
dMMR	mismatch repair deficient
DOR	Duration of response
ECG	Electrocardiogram
ECOG PS	Eastern Cooperative Oncology Group Performance Status
eCRF	Electronic case report form

EDC	Electronic data capture
EORTC QLQ-C30	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30
EORTC QLQ-CX24	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cervical Cancer Module
EQ-5D-5L	European Quality of Life 5-Dimensions 5-Levels Health Questionnaire
GCP	Good Clinical Practice
HRQoL	Health-related quality of life
ICF	Informed consent form
ICH	International Conference on Harmonisation
imAE	Immune-mediated adverse event
IRC	Independent Review Committee
IV	Intravenous
LLN	Lower limit of normal
MedDRA	Medical Dictionary for Regulatory Activities
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NA	Not applicable
NE	Not evaluable
ORR	Objective response rate
OS	Overall survival
PD	Progressive disease
PD-1	Programmed cell death protein-1
PD-L1	Programmed death-ligand 1
PFS	Progression-free survival

PK	Pharmacokinetic(s)
PR	Partial response
RECIST	Response Evaluation Criteria in Solid Tumors
ROW	Rest of world
QoL	Quality of life
Q3W	Once every 3 weeks
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Stable disease
SOC	System Organ Class
$T_{1/2}$	Elimination half-life
T_{max}	Time to maximum plasma concentration
TA	Tumor assessment
TAP	Tumor area positive score
TE	Treatment-emergent
TEAE	Treatment-emergent adverse event
TIGIT	T-cell immunoreceptor with Ig and ITIM domains
TTR	Time to response
QTcF	Fridericia's correction formula
ULN	Upper limit of normal

1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the procedures and the statistical methods that will be used to analyze and report results for study BGB-A317-A1217-202 (AdvanTIG-202): Phase 2 Study Investigating Efficacy and Safety of Anti-PD-1 Monoclonal Antibody Tislelizumab (BGB-A317) Combined With or Without Anti-TIGIT Monoclonal Antibody Ociperlimab (BGB-A1217) in Patients With Previously Treated Recurrent or Metastatic Cervical Cancer. This SAP is based on BGB-A317-A1217-202 Original Protocol 0.0, dated on September 04, 2020. The focus of this SAP is for the planned analyses specified in the study protocol. The analysis details for Pharmacogenomics and Biomarker analyses are not described within this SAP. Separate analysis plans will be drafted if needed.

2. STUDY OVERVIEW

2.1. Study Design

This is an open-label, 2-cohort, multicenter, Phase 2 study to evaluate the efficacy and safety of tislelizumab combined with or without ociperlimab in patients with previously treated recurrent or metastatic cervical cancer. The study is composed of two stages:

- **Stage 1 (randomization)**: Approximately 80 patients whose tumor regardless of PD-L1 expression will be randomized at 1:1 ratio to receive either tislelizumab (200 mg intravenously [IV] once every 3 weeks [Q3W]) combined with ociperlimab (900 mg IV Q3W) or tislelizumab (200 mg IV Q3W) monotherapy.
- **Stage 2 (expansion)**: After the enrollment is completed in Stage 1, the sample size of the combination therapy cohort will continue to be expanded in Stage 2 with approximately 87 additional patients who will receive tislelizumab (200 mg IV Q3W) combined with ociperlimab (900 mg IV Q3W).

The total sample size of the combination therapy cohort (Cohort 1) will be approximately 127 patients. The total sample size of the tislelizumab monotherapy cohort (Cohort 2) will be approximately 40 patients.

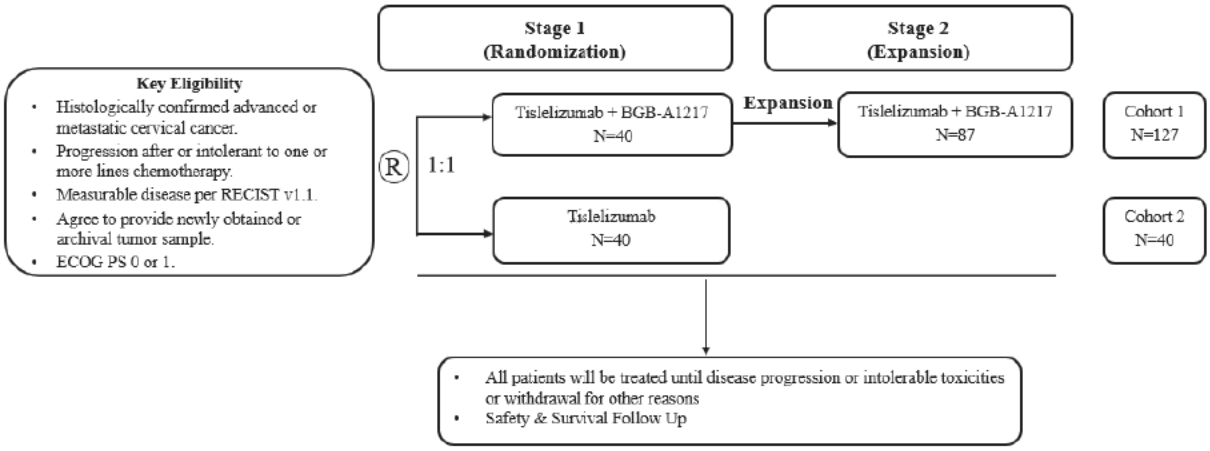
PD-L1 expression is determined by PD-L1 score assessed by tumor area positive score (TAP) (previously referred to visually-estimated Combined Positive (vCPS) Score in protocol), which is defined as the total percentage of the tumor area covered by tumor cells with any membrane staining above background and tumor-associated immune cells with any staining above background, using Ventana PD-L1 (SP263) assay.

In Stage 1, the PD-L1 expression will be retrospectively tested centrally. In Stage 2, PD-L1 expression will be prospectively tested centrally, and only patients whose tumors are evaluable for PD-L1 expression will be enrolled. For Cohort 1 (including patients enrolled in Stage 1 and Stage 2), the percentage of patients whose tumors have PD-L1 score < 5% or whose tumors are not evaluable for PD-L1 expression would be capped to be no more than 40%, to reflect the natural distribution of PD-L1 expression in cervical cancer.

Study drugs will be administered until disease progression per RECIST v1.1 by IRC, unacceptable toxicity, or withdrawal for other reasons, whichever occurs first. End-of-Treatment (EOT), safety follow-up and survival follow-up visits will be conducted following study drug discontinuation.

The study design schema is shown in Figure 1.

Figure 1: Study Schema



Abbreviations: DCR, disease control rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HRQoL, Health-Related Quality of Life; INV, investigator; IRC, Independent Review Committee; ORR, overall response rate; OS, overall survival; PD-L1, programmed cell death protein-ligand 1; PFS, progression-free survival; QoL, Quality of Life; RECIST, Response Evaluation Criteria in Solid Tumors; vCPS, visually-estimated Combined Positive Score.

2.2. Study Assessments

Tumor imaging (computed tomography [CT] with or without contrast or magnetic resonance imaging [MRI]) must be performed within 28 days prior to first dose of study drug(s). On-study tumor assessments will occur every 6 weeks (±7 days) during the first 54 weeks and every 12 weeks (±7 days) thereafter based on RECIST v1.1. If a patient discontinues study treatment due to any reasons other than disease progression, tumor assessments will continue to be performed as scheduled until disease progression, loss to follow up, withdrawal of consent, death, or until the study terminates, whichever occurs first. If a tumor assessment is missed or conducted outside of the specified assessment window, all subsequent scans should be conducted according to the planned schedule.

After initiation of study drugs, all AEs and SAEs, regardless of relationship to study drugs, will be reported until either 30 days after last dose of study drugs, initiation of new anticancer therapy, death, withdrawal of consent, or loss to follow-up, whichever occurs first. Immune-mediated AEs (serious or nonserious) should be reported until 90 days after the last dose of study drugs (regardless of initiation of new anticancer therapy), death, withdrawal of consent, or loss to follow-up, whichever occurs first. All SAEs considered related to the study drug(s) that are brought to the attention of the investigator should be reported regardless of time since the last dose of treatment.

3. STUDY OBJECTIVES

3.1. Primary Objective

To evaluate the efficacy of ociperlimab combined with tislelizumab as measured by ORR according to RECIST v1.1, by Independent Review Committee (IRC) in patients who had previously treated recurrent or metastatic cervical cancer with PD-L1 Score ≥ 5% or regardless of PD-L1 expression

3.2. Secondary Objective

- To evaluate the efficacy of ociperlimab combined with tislelizumab as assessed by ORR by investigator review
- To evaluate the efficacy of tislelizumab monotherapy as assessed by ORR by both IRC and investigator review
- To evaluate the efficacy of ociperlimab combined with tislelizumab and tislelizumab monotherapy as measured by DOR, PFS, time to response (TTR), disease control rate (DCR), and clinical benefit rate (CBR) by both IRC and investigator review
- To evaluate the efficacy of ociperlimab combined with tislelizumab and tislelizumab monotherapy as measured by OS
- To evaluate Health Related Quality of Life (HRQoL) via cancer-specific patient-reported outcomes (PROs) in patients treated with ociperlimab combined with tislelizumab and tislelizumab monotherapy
- To evaluate the safety and tolerability of ociperlimab combined with tislelizumab and tislelizumab monotherapy
- To characterize the PK of ociperlimab and tislelizumab
- To assess host immunogenicity to ociperlimab and tislelizumab

3.3. Exploratory Objective

- To evaluate quality of life (QoL) via a generic PRO in patients treated with ociperlimab combined with tislelizumab and tislelizumab monotherapy
- To evaluate potential association of biomarkers with patient prognosis, response, or resistance of ociperlimab in combination with tislelizumab or tislelizumab alone

4. DEFINITION OF PRIMARY ESTIMAND

The primary clinical question of interest is: what is the efficacy of tislelizumab combined with ociperlimab as measured by the objective response rate (ORR) prior to disease progression in patients with previously treated recurrent or metastatic cervical cancer (R/M CC), before the patients start any new anticancer therapy prior to disease progression?

The primary estimand is described by the following attributes:

1) Treatment of interest:
   - The study treatment is tislelizumab 200mg IV Q3W combined with ociperlimab 900 mg IV Q3W.
2) Population:
   - All patients with R/M CC who had progression on or after one or more lines of chemotherapy and is not amenable to curative treatment (eg, systemic chemotherapy, surgery, or radiotherapy).
3) Variable:
   - The primary variable is a binary response variable of each patient, defined as whether or not the patient achieved objective response, including CR, or PR, as determined by independent review committee (IRC) per RECIST v1.1.
4) Handling of remaining intercurrent events:
   - New anticancer therapy started prior to disease progression or death: Patients starting any new anticancer therapy without achieving an objective response before will be considered as non-responders (composite strategy).
   - Discontinuation of treatment prior to disease progression or death: response assessment after discontinuation of treatment will be counted and used for analysis; however, if patients initiate new anticancer therapy prior to disease progression, the response assessment will not be counted or used for analysis (treatment policy strategy).
5) Population-level summary:
   - The ORR of the study treatment.

5. STUDY ENDPOINTS

5.1. Primary Endpoint(s)

- ORR, defined as the proportion of patients who had CR or PR assessed by IRC per RECIST v1.1 for Cohort 1

5.2. Secondary Endpoints

- ORR, defined as above assessed by investigator's review per RECIST v1.1 for Cohort 1
- ORR, defined as above assessed by both IRC and investigator's review per RECIST v1.1 for Cohort 2
- DOR, defined as the time from the first confirmed objective response until the first documentation of progression or death, whichever comes first, assessed by both IRC and investigator's review according to RECIST v1.1 for Cohorts 1 and 2
- Other efficacy endpoints (PFS, TTR, DCR, and CBR) that need tumor assessments by both IRC and investigator's review per RECIST v1.1 for Cohorts 1 and 2
  - PFS, defined as the time from the date of first dose of study drug to the date of first documentation of disease progression or death, whichever occurs first

  - TTR, defined as the time from the date of first dose of study drug to first documentation of response
  - DCR, defined as the proportion of patients who achieve CR, PR, or SD
  - CBR, defined as the proportion of patients who achieve CR, PR, or durable SD (SD ≥ 24 weeks)
- OS, defined as the time from the date of first dose of study drug until the date of death from any cause for Cohorts 1 and 2
- HRQoL questionnaires, assessment of the patient's overall health status using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Cervical Cancer Module (EORTC QLQ-CX24), for Cohorts 1 and 2
- AEs and SAEs as characterized by type, frequency, severity (as graded by National Cancer Institute-Common Terminology Criteria for Adverse Events version 5.0 [NCI-CTCAE v5.0]), timing, seriousness, and relationship to study drugs, physical examinations, electrocardiograms (ECGs), and laboratory assessments for Cohorts 1 and 2
- Serum ociperlimab and tislelizumab concentrations at specified timepoints
- Immunogenic responses to ociperlimab and tislelizumab, evaluated through the detection of ADAs

5.3. Exploratory Endpoints

- Evaluate status of exploratory biomarkers including but not limited to expression of TIGIT, CD226, CD155, CD112 and PD-L1; gene expression profiling; tumor mutation burden; tumor infiltrating immune cells in archival and/or fresh tumor tissue and blood before study treatment, during study treatment, or at disease progression/reoccurrence; and the association between these biomarker and clinical efficacy, disease status, and resistance
- QoL is measured by assessment of the European Quality of Life 5-Dimensional - 5-Level Questionnaire (EQ-5D-5L)

6. SAMPLE SIZE CONSIDERATIONS

The sample size calculation of Cohort 1 was based on the power of the comparison between estimated ORR in the study and the historical rate in a sequential way with patients whose tumor with PD-L1 Score ≥ 5% followed by patients whose tumor regardless of PD-L1 expression. An assumed ORR of 30% in the patients whose tumor with PD-L1 Score ≥ 5% as compared to historical rate of 15%; an assumed ORR of 25% in the patients whose tumor regardless of PD-L1 expression as compared to historical rate of 15%.

- With 127 patients, the power is 0.807 to demonstrate that the ORR in the patient population whose tumor regardless of PD-L1 expression is statistically higher than the historical rate of 15% using a binomial exact test; the 95% CI of an observed 25% ORR is (17.9%, 33.7%).
- With 76 patients (60% whose tumor with PD-L1 Score ≥ 5%), the power is 0.860 to demonstrate that the ORR in patients whose tumor with PD-L1 Score ≥ 5% is statistically higher than the historical rate of 15% using a binomial exact test; the 95% CI of an observed 30% ORR is (20.2%, 41.9%).
- With 89 patients (70% whose tumor with PD-L1 Score ≥ 5%), the power is 0.927 to demonstrate that the ORR in patients whose tumor with PD-L1 Score ≥ 5% is statistically higher than the historical rate of 15% using a binomial exact test; the 95% CI of an observed 30% ORR is (21.0%, 40.0%).
- With 102 patients (80% whose tumor with PD-L1 Score ≥ 5%), the power is 0.940 to demonstrate that the ORR in patients whose tumor with PD-L1 Score ≥ 5% is statistically higher than the historical rate of 15% using a binomial exact test; the 95% CI of an observed 30% ORR is (21.7%, 40.3%).

The PD-L1 expression will be closely monitored for Cohort 1, and enrollment of patients whose tumors are PD-L1 Score < 5%/not evaluable will be stopped as necessary when reaching ~40%. This is to ensure that the percentage of patients whose tumor with PD-L1 Score ≥ 5% is no less than 60% of the Safety Analysis Set.

In addition, 40 patients will be enrolled in Cohort 2 to investigate the safety and efficacy of tislelizumab monotherapy in patients with previously treated recurrent or metastatic cervical cancer.

7. STATISTICAL METHODS

7.1. Analysis Sets

The Safety Analysis Set (SAS) includes all patients who received ≥ 1 dose of any study drug for each cohort. This will be the primary analysis set for efficacy analysis, and the analysis set for baseline characteristics and safety analysis.

The PD-L1 Score >= 5% Safety Analysis Set includes all treated patients (SAS) whose tumors have PD-L1 Score ≥ 5%. This will be one of the dual primary analysis sets for efficacy analyses.

The Efficacy Evaluable Analysis Set (EAS) includes all treated patients (SAS) who had measurable disease at baseline per RECIST v1.1 and who had ≥ 1 evaluable post-baseline tumor assessment by IRC unless discontinued due to clinical PD or death within 7 weeks after the first dose. It will be used for the sensitivity analysis of the primary efficacy endpoint ORR.

The PK Analysis Set includes all patients who received ≥ 1 dose of any component of study drug per the protocol, for whom any postdose PK data are available.

The Immunogenicity Analysis Set includes all patients who received at least 1 dose of any component of study drug for whom both baseline antidrug antibody result and at least 1 post-baseline antidrug antibody result are available.

7.2. Data Analysis General Considerations

7.2.1. Definitions and Computations

Study drugs include ociperlimab (BGB-A1217) and tislelizumab (BGB-A317).

Study day will be calculated in reference to the date of the first dose of study drug. For assessments conducted on or after the date of first dose of study drug, the study day will be calculated as assessment date – date of the first dose of study drug + 1). For assessments conducted before the date of first dose of study drug, study day is calculated as (assessment date – date of the first dose of study drug). There is no study day 0. In the situation where the event date is partial or missing, the date will appear partial or missing in the listings. Study day and any corresponding durations will be presented based on the imputations specified in Appendix 1.

Unless otherwise specified, a baseline value is defined as the last non-missing value collected before the first dose of study drug.

The following descriptive statistics will be used to summarize the trial data on the basis of their nature unless otherwise specified:

- Continuous variables: number of non-missing observations, mean, standard deviation, median, minimum, and maximum
- Categorical variables: frequencies and percentages
- Time-to-event variables: number of non-missing observations (N), median, minimum and maximum. Kaplan-Meier event rates may also be provided if applicable for specific time to event variables

All calculations and analyses will be conducted by the sponsor or designee after the data collection is completed and the database is locked and released, using SAS® Version 9.3 or higher (SAS Institute, Inc., Cary, North Carolina).

7.2.2. Conventions

The following conventions will be applied to all analyses:

- 1 year = 365.25 days. Number of years is calculated as (days/365.25) rounded up to 1 significant digit.
- 1 month = 30.4375 days. Number of months is calculated as (days/30.4375) rounded up to 1 significant digit.
- Age will be calculated as the integer part of (date of informed consent – date of birth + 1)/365.25 if not directly collected from eCRF.
- P-values will be rounded to 4 decimal places. P-values that round to 0.0000 will be presented as '< 0.0001' and p-values that round to 1.000 will be presented as '> 0.9999'.

- Duration of image-based event endpoints (such as PFS and DFS) will be based on the actual date the radiograph was obtained rather than the associated visit date.
- In the case results presented in numerical range, if lab results > (or >=) x then set as x; if < (or <=) x, then x/2).
- For by-visit observed data analyses, percentages will be calculated based on the number of patients with non-missing data as the denominator, unless otherwise specified.
- For continuous endpoints, summary statistics will include n, mean, standard deviation, median, Q1, Q3 and range (minimum and maximum).
- For discrete endpoints, summary statistics will include frequencies and percentages.

7.2.3. Handling of Missing Data

Missing data will not be imputed unless otherwise specified elsewhere in this SAP. Missing dates or partially missing dates will be imputed conservatively for adverse events and prior/concomitant medications/procedures. Specific rules for the handling of missing or partially missing dates for adverse events and prior/concomitant medications/procedures are provided in Appendix 1.

By-visit endpoints will be analyzed using observed data unless otherwise specified. For observed data analyses, missing data will not be imputed, and only the observed records will be included.

7.2.4. Multiplicity Adjustment

The type I error will be strongly controlled at 0.025 (1-sided) in the primary analysis of ORR for Cohort 1 in PD-L1+ and safety analysis sets using sequential testing method. Hypothesis testing of ORR in safety analysis set will be performed only if the ORR in the PD-L1+ analysis set is statistically significant favoring tislelizumab + ociperlimab against historical control.

7.3. Patient Characteristics

7.3.1. Patient Disposition

The number (percentage) of patients treated, discontinued from the study/treatment, reasons for discontinued from the study/treatment, and the duration of study follow-up will be summarized in Safety Analysis Set. The primary reason for study drug and/or the study being discontinued will be summarized according to the categories from eCRF in Safety Analysis Set. The reasons for treatment/study discontinuation related to COVID-19 impact will also be summarized.

7.3.2. Protocol Deviations

Important protocol deviation criteria will be established, and patients with important protocol deviations will be identified and documented. Important protocol deviations will be summarized for all patients in the Safety Analysis Set and also listed by each category. Deviation categories are not mutually exclusive. Multiple deviations within the same category are counted once per patient.

Protocol deviations that are related to COVID-19 will be summarized. Patient data listing of COVID-19 related protocol deviation will be provided.

7.3.3. Demographic and Other Baseline Characteristics

Demographics and other baseline characteristics will be summarized using descriptive statistics in the Safety Analysis Set, including but not limited to the following variables:

- Age (continuously and by categories [≤65 or >65 years])
- Race
- Region/Country
- Weight
- BMI
- PD-L1 subgroup (PD-L1 Score < 5%, ≥5%, or NE)
- ECOG Performance Status

etc.

Continuous variables include age, weight, vital signs, etc. Categorical variables include ECOG Performance Status, region/country, race, PD-L1 subgroup, etc.

7.3.4. Disease History

The number (percentage) of patients reporting a history of disease and characteristics, as recorded on the eCRF, will be summarized in the Safety Analysis Set. Disease characteristics include histology, FIGO stage at initial diagnosis, time since initial cancer diagnosis to study entry, MSI or dMMR status, time since metastatic/recurrent disease diagnosis, etc. A listing of disease history will be provided.

7.3.5. Prior Anticancer Drug Therapies and Surgeries

Prior anti-cancer drug therapies, prior anti-cancer radiotherapy, and prior anti-cancer surgeries will be summarized in the Safety Analysis Set. The variables include number of patients with any prior anti-cancer therapy, number of prior regimens/lines, duration of last therapy, time from end of last disease progression to study entry, treatment setting, etc. for prior anti-cancer drug therapies. The therapies with the same sequence/regimen number are counted as one prior therapy.

7.3.6. Prior and Concomitant Medications

Prior medications are defined as medications that started and stopped before the first dose of study drug. Concomitant medications will be defined as medications that (1) started before the first dose of study drug and were continuing at the time of the first dose of study drug, or (2) started on or after the date of the first dose of study drug up to 30 days after the patient's last dose or the initiation of a new anti-cancer therapy (as of the on-site Safety Follow-up Visit).

Prior and concomitant medications will be coded using the latest version of World Health Organization Drug Dictionary (WHO DD) drug codes per BeiGene practice. They will be further classified to the appropriate Anatomical Therapeutic Chemical (ATC) code.

The number (percentage) of patients reporting prior and concomitant medications will be summarized by ATC medication class and WHO DD preferred name in the Safety Analysis Set. A listing of prior and concomitant medications will be provided.

7.3.7. Medical History

Medical History will be coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 24.0 or higher. The number (percentage) of patients reporting a history of any medical condition, as recorded on the CRF, will be summarized by system organ class and preferred term in the Safety Analysis Set. A listing of medical history will be provided.

7.3.8. Post Treatment Anti-cancer Therapy

Separate flags of start date of new anti-cancer therapy for efficacy and safety analyses are derived individually.

- As for efficacy analysis, start date of new anti-cancer therapy will be the earliest date of prohibited anti-cancer therapy taken during treatment, date of the post-treatment systemic anti-cancer therapy and date of other anti-cancer therapy such as post-treatment surgery and radiotherapy as deemed appropriate.
- The start date of new anti-cancer therapy in defining TEAE for safety is always the first date of new systemic anti-cancer therapy taken after the last study treatment.

Tumor response per RECIST or event driven endpoints have not been commonly used for the efficacy evaluation of traditional Chinese medicine (TCM). ORR, PFS or OS benefit of Chinese herbal medicines or Chinese patent medicines has not yet been established. Therefore, they will not be taken into account as new anti-cancer therapy in the efficacy and safety analyses.

Post treatment anti-cancer therapy is defined as the anti-cancer therapy started after the last dose date of study treatment. A summary of number and percentage of patients who received subsequent anti-cancer therapy in procedure or surgery/radiotherapy or systematic anti-cancer therapy/immunotherapy by cohort will be provided based on safety analysis set.

Time to first post-treatment systemic anti-cancer therapy will be summarized descriptively. Patient data listings of post-treatment systemic therapy will be provided.

7.4. Efficacy Analysis

ORR is the primary objective in the study. Response assessments will be determined by IRC and by investigator using RECIST v1.1.

Efficacy Analyses will be provided by subgroups as appropriate, such as PD-L1 subgroups, etc. Per-patient listings may be generated with limited patients for analysis.

7.4.1. Primary Efficacy Endpoints

Primary Analysis for Primary Estimand

The primary efficacy endpoint is confirmed ORR as determined by IRC using the RECIST v1.1 in Cohort 1.

ORR is defined as the proportion of patients achieving BOR of CR or PR. BOR is defined as the best response recorded from the first dose of study drug until data cut or the initiation of new anticancer treatment, whichever occurs earlier. Patients with no postbaseline response assessment (due to any reason) will be considered as non-responders for BOR. The proportion of patients in each response category will be presented.

The binomial exact test will be performed among the patients whose tumor with PD-L1 Score $\geq$ 5% and patients whose tumor regardless of PD-L1 expression in Safety Analysis Set in a sequential way.

The null and alternative hypotheses to be evaluated for ORR are:

$$H_0 : ORR \leq 15\%,$$

$$H_a : ORR > 15\%.$$

Binomial exact tests will be used to test the null hypothesis at the one-sided significance level of 0.025. If the null hypothesis is rejected, it will be concluded that the drug rules out a historical control of 15% ORR at the significance level, then it will be concluded that ociperlimab combined with tislelizumab statistically significantly increases ORR compared with the historical controls in the PD-L1 Score $\geq$ 5% or/and regard less of PD-L1 expression population.

The primary efficacy analysis will be conducted when ORR data is mature, which is 6 months (approximately 4 tumor assessments) after the last patient receives the first dose of study drug in Stage 2 and will be based on the Safety Analysis Set. Patients without postbaseline tumor assessment will be considered as non-responders. The number and proportion of patients who achieve the objective response will be summarized. Associated 2-sided 95% Clopper-Pearson confidence interval (CI) of ORR will be calculated to assess the precision of the rate estimate.

Approximately 4 months after the enrollment is completed in Stage 1, there will be a preliminary analysis of ORR and safety (using descriptive statistics) for the first 40 patients in Cohort 1 and all 40 patients in Cohort 2. Enrollment of Stage 2 will continue in parallel. At the time of preliminary analysis, if no more than 5 responders are observed in Cohort 1 SAS at Stage 1, which corresponds to a Bayesian predictive probability of success less than 0.1 with a non-informative prior, beta(1,1) (Chen et al 2019; Lee and Liu 2008), the study will be terminated.

7.4.2. Secondary Efficacy Endpoints

Objective Response Rate (ORR)

ORR as assessed by investigator's review will be summarized for secondary efficacy analysis in the Safety Analysis Set in Cohort 1, and ORR as assessed by both IRC and investigator will be summarized in Cohort 2. A 2-sided Clopper-Pearson 95% CI of ORR will be constructed to assess the precision of the point estimate of ORR.

Other efficacy endpoints with necessary tumor assessments, as well as OS, will be summarized for secondary efficacy analysis. The secondary efficacy analysis will be conducted by both IRC and investigator (if applicable) in Cohort 1 and Cohort 2.

Disease Control Rate (DCR)

DCR is defined as the proportion of patients who achieve CR, PR, or SD. DCR will be summarized similarly as ORR descriptively in the Safety Analysis Set and also in Efficacy Evaluable Analysis Set for sensitivity analysis.

Clinical Benefit Rate (CBR)

CBR is defined as the proportion of patients who achieve CR, PR, or durable SD (SD $\geq$ 24 weeks). CBR will be summarized similarly as ORR descriptively in the Safety Analysis Set and also in the Efficacy Evaluable Analysis Set for sensitivity analysis.

Progression Free Survival (PFS)

PFS is defined as the time from treatment initiation to disease progression or death due to any cause, whichever occurs first. PFS will be analyzed in the Safety Analysis Set.

Kaplan Meier methodology will be used to estimate median PFS, Q1 and Q3 of PFS, and the event-free rates. Ninety-five percent CIs for median and other quantiles of PFS will be estimated using the method of Brookmeyer and Crowley (Brookmeyer and Crowley, 1982). And 95% CIs for event-free rates will be estimated using Greenwood's formula (Greenwood, 1926). Kaplan Meier curves will be constructed to provide a visual description of the PFS change with time.

PFS will be censored at the last adequate tumor assessment if one of the following occurs: absence of event; the event occurred after a new anticancer therapy is given; the event occurred after missing two or more consecutive tumor assessments. The Table 1 shows the derivation rules for PFS in dealing with intercurrent events and missing value.

Table 1: Censoring Rules for Progression-free Survival Per RECIST Version 1.1

No.	Situation	Date of Progression or Censoring	Outcome
1	No baseline or any post-baseline tumor assessments and without death within 13 weeks from date of first dose of study drug(s)	Date of first dose of study drug(s)	Censored
2	Progression documented between scheduled visits	Date of first radiologic PD assessment	Event
3	No progression at the time of data cut-off or withdrawal from study	Date of last adequate radiologic assessment prior to or on date of data cut-off or withdrawal from study	Censored
4	New anticancer treatment started	Date of last adequate radiologic assessment prior to or on date of new anticancer treatment	Censored

5	Death before first PD assessment	Date of death	Event
6	Death between adequate assessment visits*	Date of death	Event
7	Death or progression after more than one missed visit**	Date of last adequate radiologic assessment before missed tumor assessments	Censored
8	No baseline or any post-baseline tumor assessments and died within 13 weeks from date of first dose of study drug(s)	Date of death	Event

*Adequate tumor assessment is a radiologic assessment of CR, PR, SD, non-CR/non-PD, or PD as determined by the BIRC.

** More than one missed visit is defined if the duration between the last tumor assessment and death or PD is longer than D2. The D2 is defined as two times protocol specified interval between tumor assessments (TAs) plus the protocol allowed window around the assessments. Since tumor assessment is scheduled as once every 6 weeks for first 54 weeks and once every 12 weeks afterwards with one-week window, D2 is 12 weeks + 1 week in the first 54 weeks and 24 weeks + 1 week afterwards.

Progression date for PFS event will be the earliest date of events defined in 2,5,6,8.

Duration of Response (DOR)

DOR is defined as the time from the first confirmed objective response to disease progression documented after treatment initiation or death, whichever occurs first.

DOR will be analyzed among the responders in the Safety Analysis Set. The censoring rule for DOR will follow the PFS censoring rule. Kaplan Meier methodology will be used to estimate the median duration, and the 95% confidence interval for the duration of response will be provided.

Time to Response (TTR)

TTR is defined as the time from treatment initiation to the first documented response.

TTR will be summarized for responders (who have achieved an objective response) only using sample statistics such as mean, median, and standard deviation.

Other analysis regarding tumor assessments

Waterfall plots will be provided for the maximum tumor shrinkage based on target lesion(s). The maximum tumor shrinkage based on target lesion(s) used in the plots will be listed. The post-baseline nadir will be summarized using descriptive statistics.

Overall Survival (OS)

OS is defined as the time from treatment initiation to death due to any cause.

OS will be analyzed in the Safety Analysis Set using similar methods to those described for PFS similarly, except for censoring rules. For patients who are alive by the clinical cutoff date, OS will be censored at the last known alive date (LKADT). The last known alive date will be defined as either the clinical data cutoff date for patients who are still on treatment, or last available date showing patients alive or cut-off date whichever comes first for other alive patients.

Note: Every effort should be made to ensure complete death dates. In the rare case, if day of death date is missing, death date is imputed as the max (last available date showing patients alive + 1, first day of year/month of death date). The patient with imputed death date will be considered as an event for OS analysis. Death with missing month and/or year will not be imputed for OS analysis.

Health Related Quality of Life (HRQoL)

Details of the PROs scoring are specified according to the algorithm described in the EORTC QLQ-C30 scoring manual and EORTC QLQ-CX24 scoring manual (Fayers 2001). Summary of the scoring, scales and copy of the questionnaires are available in APPENDIX 2.

Compliance

Compliance for the EORTC QLQ-C30 and EORTC QLQ-CX24 modules, defined as the proportion of questionnaires actual received out of the expected number (i.e, number of patients on treatment), in the safety analysis set will be summarized for each assessment time point and cohort.

Descriptive Analysis

HRQoL is assessed using the EORTC QLQ-C30 and EORTC QLQ-CX24. The postbaseline scores of the scales and single items of the 2 questionnaires as well as the Index score of the QLQ-CX24 will be summarized for Cohorts 1 and 2, and the changes from the baseline scores will be summarized descriptively for both cohorts.

Key PRO Endpoints and key clinical cycles

The specific PRO end points in this trial are GHS, physical function and Pain of QLQ-C30 and index score as well as the scales of Symptom Experience, Lymphedema and Peripheral Neuropathy of QLQ-CX24, and the key clinical cycles postbaseline are Cycles 3 (Week 7) and 5 (Week 13).

More details about EORTC QLQ-C30 and EORTC QLQ-CX24 scorings could be found in Appendix 2.

7.4.3. Subgroup Analyses

Subgroup analysis on key efficacy endpoints (ORR, OS, etc.) will be conducted to explore the consistency of efficacy across a variety of subgroups, as appropriate. Subgroup variables may include but are not limited to age, gender, ECOG PS, FIGO stage at study entry, and PD-L1 expression.

7.4.4. Exploratory Efficacy Endpoints

EQ-5D-5L

QoL is measured by assessment of the European Quality of Life 5-Dimensional-5-Level Questionnaire (EQ-5D-5L). Details of scoring are specified according to the algorithm described in the EQ-5D-5L (https://euroqol.org/publications/user-guides/) (Appendix 2).

Five level response to EQ-5D-5L will be summarized as a categorical variable by tabulating frequency of each response category by visit. Scores of the visual analog scale (VAS) from baseline and post treatment will be summarized descriptively (n, mean, standard deviation, median, minimum, maximum).

7.5. Safety Analyses

All safety analyses will be performed by cohort based on the Safety Analysis Set. Safety and tolerability will be assessed, where applicable, by incidence, severity, and change from baseline values for relevant parameters including adverse events (AEs), laboratory values, vital signs, ECG findings, etc.

7.5.1. Extent of Exposure

The following measures of the extent of exposure will be summarized (One cycle is defined as 21 days of treatment):

- Duration of exposure (days): defined as the duration from the first dose date of study drug to the last dose date of the study drug. The duration of exposure will be calculated as (last date of exposure – date of first dose + 1).
  - If patients discontinued treatment (with non-missing EOT date), using min (CUOFFDT, death date, last dose date + 20) as the "last date of exposure" for tislelizumab and ociperlimab
  - otherwise if patient has treatment ongoing, using cutoff date as the "last date of exposure" to calculate duration of exposure
- Number of treatment cycles received: defined as the total number of treatment cycles in which at least one dose of the study drug is administered.
- Total dose received per patient (mg): defined as the cumulative dose of the study drug during the treatment period of the study. It will be calculated by summing all actual dosages per administration at all visits prior to the cutoff date.
- Actual dose intensity (mg/cycle): defined as the total dose received by a patient divided by the duration of exposure. Actual Dose Intensity (ADI) for tislelizumab (mg/cycle) = 21*total cumulative dose (mg) / (last dose date prior to cut off date+ 21 - first dose date).
- Relative dose intensity (%): defined as the ratio of the actual dose intensity and the planned dose intensity. Planned dose intensity is defined as the planned dose on study day 1 by a patient divided by the duration of exposure. Planned Dose Intensities for tislelizumab and ociperlimab (mg/cycle) are 200 mg/cycle and 900 mg/cycle, resp.

The number of patients with infusion rate decreased, dose delays and dose interruptions will be summarized by counts and percentages according to study drug. Number and percentage of patients with reason of dose modification in AE and COVID-19 will also be summarized.

Patient data listings will be provided for all dosing records, and for the above calculated summary statistics.

7.5.2. Adverse Events

AEs will be graded by the investigators using CTCAE version 5.0. The AE verbatim descriptions (investigator terms from the eCRF) will be classified into standardized medical terminology using MedDRA. Adverse events will be coded to the MedDRA Version 24.0 or higher lowest level term closest to the verbatim term, along with the linked MedDRA preferred term (PT) and primary system organ class (SOC).

7.5.2.1. Treatment-emergent Adverse Event

A treatment-emergent adverse event (TEAE) is defined as an AE that had onset or increase in severity level date on or after the date of the first dose of study drug(s) through 30 days after the last dose (permanent discontinuation of study drug) or the initiation of new anti-cancer therapy, whichever is earlier. Summary tables will generally focus on those AEs that were treatment-emergent (TE). All AEs, treatment-emergent or otherwise, will be presented in patient data listings. COVID-19 related adverse events will be summarized separately as appropriate.

An AE overview table, including the number and percentage of patients with TEAEs, treatment-emergent serious adverse events (SAEs), TEAEs with Grade 3 or above, TEAEs that led to death, TEAEs that led to treatment discontinuation, TEAEs that led to dose delay, TEAEs that led to infusion interruption/rate decrease, treatment-related TEAEs, infusion-related reactions will be provided. Treatment-related AEs include those events considered by the investigator to be related to study drug or with a missing assessment of the causal relationship.

The incidence of TEAEs will be reported as the number (percentage) of patients with TEAEs by SOC, PT and the worst grade. A patient will be counted only once by the highest severity grade within an SOC and PT, even if the patient experienced more than 1 TEAE within a specific SOC and PT. The number (percentage) of patients with treatment-emergent SAEs, treatment-related TEAEs, TEAEs with grade 3 or above, treatment-related SAEs, TEAEs that led to death, and TEAEs that led to treatment discontinuation, dose modification (dose delay, infusion interruption or infusion rate decrease), and infusion-related reactions will be summarized by SOC and PT. TEAEs with grade 3 or above will also be summarized by PT in descending order.

Patient data listings of all AEs, SAEs, AE related to COVID-19 will be provided.

7.5.2.2. Immune-mediated Adverse Events

Immune-mediated adverse events are of special interest and will be recorded until 90 days after discontinuation from tislelizumab, regardless of whether the patient starts a new anticancer therapy. Immune-mediated adverse events will be summarized by category within a pre-defined list. The identification of immune-mediated adverse events is described in immune-mediated adverse event charter.

7.5.2.3. Infusion-related Reactions

The PT list of infusion-related reactions (IRRs) included fever/pyrexia, chills/rigor, nausea, pruritus, angioedema, hypotension, headache, bronchospasm, urticaria, rash, vomiting, myalgia, dizziness, hypertension, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, IRR, and transfusion reaction. The following process was used for the final determination of IRRs:

a. The investigator/site must have checked the IRR box on the AE pages in the CRF.

b. The event term must have matched (or been equivalent) to the IRR terms listed above (such as fever or chills), with the exception of events that happened concurrently with one of the terms on this list (such as fever + back pain + chest pain – all would be included).

c. Only events that started on the day of an infusion or the day after an infusion were included.

For IRRs, a summary of incidence by SOC, PT and maximum severity will be provided, sorted by descending order of incidence within each SOC and PT based on Cohort 1.

7.5.2.4. Deaths

All deaths and causes of death will be summarized by treatment group, including those occurred during the study treatment period and those reported during the survival follow-up period after treatment completion/discontinuation.

7.5.3. Laboratory Values

Laboratory safety tests will be evaluated for the laboratory parameters and serum chemistry and hematology parameters are described in Table 2.

Descriptive statistics (n, mean, standard deviation, median, minimum, maximum for continuous variables; n [%] for categorical variables) for laboratory parameters will be summarized as appropriate. Abnormal laboratory values will be flagged and identified as those outside (above or below) the normal range. Reference (normal) ranges for laboratory parameters will be included in the CSR for this protocol.

Laboratory parameters that are graded in NCI CTCAE Version 5.0 will be summarized by shifts from baseline CTCAE grades to maximum post-baseline grades. In the summary of laboratory parameters by CTCAE grade, parameters with CTCAE grading in both high and low directions will be summarized separately.

Hy's Law for liver injury will also be summarized.

Box-whisker plots will be generated for parameters of interest.

Patient data listings will be provided as appropriate.

Table 2: Serum Chemistry and Hematology Laboratory Tests

Serum Chemistry	Hematology
Alkaline phosphatase	Hemoglobin
Alanine aminotransferase	Hematocrit
Aspartate aminotransferase	Platelet counts

Serum Chemistry	Hematology
Albumin	White blood cell count
Total bilirubin	Red blood cell count
Direct bilirubin	Neutrophil (Absolute)
Blood Urea Nitrogen	Lymphocyte (Absolute)
Chloride	Monocyte (Absolute)
Creatinine	Basophil (Absolute)
Calcium	Eosinophil (Absolute)
Phosphate	
Glucose	
Lactate dehydrogenase	
Total Protein	
Potassium	
Sodium	
Urea	

7.5.4. Vital Signs

Patient data listing of vital signs will be provided.

7.5.5. Electrocardiograms (ECG)

The number and percentage of patients satisfying the following QTcF conditions at any time post-baseline will be summarized:

- > 450, > 480, or > 500 msec
- > 30, or > 60 msec increase from baseline

7.5.6. Eastern Cooperative Oncology Group (ECOG) Performance Status

A shift table from baseline to worst post-baseline in ECOG performance status will be summarized by cohort.

7.6. Pharmacokinetic Analyses

The following analysis plan provides the framework for the summarization of the PK data from study AdvanTIG-202. The objective is to summarize available ociperlimab and tislelizumab PK concentrations following an IV administration. PK parameters will not be characterized as only sparse samples were collected.

Any additional PK analyses, including population PK analyses and exposure-response analyses (efficacy or safety endpoints), may be conducted as appropriate and the results of such analyses may be reported separately from the CSR.

7.6.1. Reporting of Pharmacokinetic Concentrations for Descriptive Statistics

The ociperlimab and tislelizumab serum concentration data will be listed and tabulated by visit/cycle at which these concentrations are collected per the study design. Descriptive statistics in tables will include means, medians, ranges, standard deviations, coefficient of variation (CV%), geometric mean and geometric CV%, as appropriate.

8. IMMUNOGENICITY ANALYSES

The scope of anti-drug antibodies (ADA) calculations used for characterizing clinical immunogenicity depend on the incidence and kinetics of detected ADA. Therefore, not all parameters described below may be derived.

The immunogenicity results will be summarized using descriptive statistics by the number and percentage of subjects who develop detectable ADAs per the study design. The effect of immunogenicity on PK, efficacy, and safety may be evaluated if data allows, and reported separately from the CSR. The incidence of positive and neutralizing ADAs (as applicable) will be reported for ADA-evaluable subjects according to the following definitions:

ADA attributes:

- **Treatment boosted ADA** is defined as ADA positive at baseline that was boosted to a 4-fold or higher-level following drug administration.
- **Treatment-induced ADA** is defined as ADA negative at baseline and ADA positive post-baseline.
- **Transient ADA response** is defined as Treatment-emergent ADA detected only at 1 time point during treatment or follow-up, excluding last time point; or detected at 2 or more time points during treatment or follow-up, where the first and last positive samples are separated by less than 16 weeks and the last time point is negative.
- **Persistent ADA response** is defined as Treatment-induced ADA detected at 2 or more time points during treatment or follow-up, where the first and last ADA positive samples are separated by 16 weeks or longer; or detected only in the last time point or at a time point less than 16 weeks before a negative last sample.
- **Neutralizing ADA** is defined as ADA that inhibits or reduces the pharmacological activity.

ADA response endpoints:

- **ADA incidence** is defined as sum of treatment-induced and treatment-boosted ADA-positive patients as a proportion of the ADA evaluable population.
- **ADA prevalence** is defined as proportion of all patients that are ADA positive, including pre-existing ADA, at any time point.

9. CHANGES IN THE PLANNED ANALYSIS

As in protocol, "The Efficacy Evaluable Analysis Set (EAS) includes all treated patients (SAS) without critical protocol deviation of each cohort who had measurable disease at baseline per

RECIST v1.1 by IRC and who had ≥ 1 evaluable post-baseline tumor assessment unless discontinued due to clinical PD or death within 7 weeks after the first dose." For courtesy of estimand framework for this SAP, patients with critical protocol deviations will also be included in EAS.

All imAEs that are recorded up to 90 days after the last dose of the study drugs, regardless of whether the patient starts a subsequent anticancer therapy, would be counted as TEAE in protocol. While in this SAP, imAEs and TEAEs were analyzed separately to look into the safety profile in more details.

10. REFERENCES

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APPENDIX 1. IMPUTATION OF MISSING OR PARTIALLY MISSING DATES

Detailed imputation rule are documented in project level programming specs.

APPENDIX 2. HRQOL SCORING, SCALES AND QUESTIONNAIRES

EORTC-QLQ-C30, QLQ-CX24

EORTC QLQ-C30: measures HRQoL of general cancer and includes two items that measure Global health status and quality of life (GHS). The instrument is also consisted of 5 functional scales and 9 single-item symptoms. . GHS includes 2 items, and the functional scales include Physical (5 items), Role (2 items), Emotional (4 items), Cognitive (2 items) and Social (2 items) functioning. Symptom scales include Fatigue (3 items), Nausea and vomitting (2 items), Pain (2 items), and single-items include Dyspnoea, Insomnia, Appetite loss, Constipation, Diarrhoea and Financial Difficulties. Higher scores in GHS and functional scales indicate better HRQoL, and lower scores in symptom scales and items better HRQoL.

QLQ-CX24: is the cervical cancer module of the QLQ-C30. CX24 is comprised of 3 symptom scales and 6 single symptom items. The scales include: Symptom Experience (11 items), Body Image (3 items) and Sexual/vaginal Functioning (4 items); and single symptom items include Lymphedema, Peripheral Neuropathy, Menopausal Symptoms, Sexual Worry, Sexual Activity and Sexual Enjoyment. Lower scores indicate better HRQoL.

Scoring

The principle for scoring applies to all scales/scores: Raw scores are calculated as the average of the items that contribute to the scale.

Missing Items

If at least half of the items for a scale are answered, then all the completed items are used to calculate the score. Otherwise, the scale score is set to missing.

A linear transformation to standardize the raw scores is utilized, so that the scores are ranged from 0 to 100. Increases in scores for functional domains (e.g., physical, role, social, emotional, etc.) are improvements while increases in scores for symptoms (e.g., fatigue, vomiting and nausea, diarrhea, pain, etc.) are deteriorations.

Derived Scale

The derived scales are obtained from the raw scores as defined in the EORTC manual. The derived scales have a more intuitive interpretation: larger function scale or global health status / QoL are improvements while larger symptom scales (e.g., pain, nausea, etc.) are deteriorations.

Technical Summary

In practical terms, if items $I_1, I_2, \ldots I_n$ are included in a scale, the procedure is as follows:

Raw score
Calculate the raw score
$RawScore = RS = (I_1 + I_2 + \ldots + I_n)/n$

Linear transformation
Apply the linear transformation to 0-100 to obtain the score S,

Functional scales: $S = \left\{1 - \frac{(RS-1)}{range}\right\} \times 100$

Symptom scales / items: $S = \{(RS-1)/range\} \times 100$

Global health status / QoL: $S = \{(RS-1)/range\} \times 100$

Range is the difference between the maximum possible value of *RS* and the minimum possible value. The QLQ-C30 has been designed so that all items in any scale take the same range of values. Therefore, the range of *RS* equals the range of the item values. Most items are scored 1 to 4, giving *range* = 3. The exceptions are the items contributing to the global health status / QoL, which are 7-point questions with *range* = 6, and the initial yes/no items on the earlier versions of the QLQ-C30 which have *range* = 1.

*Index Score for QLQ-CX24 = average score:

[∑(domain scores + single item scores)]÷number of available domains and single items

Scales

EORTC QLQ-C30

	Number of items	Item range	Item Numbers
Global health status/ QoL	2	6	29,30
Functional Scales			
• Physical functioning	5	3	1, 2, 3, 4, 5
• Role functioning	2	3	6, 7
• Emotional functioning	4	3	21, 22, 23, 24
• Cognitive functioning	2	3	20, 25
• Social functioning	2	3	26, 27
Symptom Scales/ items			

	Number of items	Item range	Item Numbers
• Fatigue	3	3	10, 12, 18
• Nausea and vomiting	2	3	14, 15
• Pain	2	3	9, 19
• Dyspnoea	1	3	8
• Insomnia	1	3	11
• Appetite loss	1	3	13
• Constipation	1	3	16
• Diarrhoea	1	3	17
• Financial Difficulties	1	3	28

QLQ-CX24

	Number of items	Item range	Item Numbers
Symptom Scales			
• Symptom experience	11	4	31, 32, 33, 34, 35, 36, 37, 39, 41, 42, 43
• Body image	3	4	45, 46, 47
• Sexual/Vaginal functioning	4	4	50, 51, 52, 53
• Lymphoedema	1	4	38
• Peripheral neuropathy	1	4	40
• Menopausal symptoms	1	4	44
• Sexual worry	1	4	48
• Sexual activity	1	4	49
• Sexual enjoyment	1	4	54

ENGLISH

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: _____
Your birthdate (Day, Month, Year): _____
Today's date (Day, Month, Year): 31 _____

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

ENGLISH

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

ENGLISH

EORTC QLQ – CX24

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems, please answer by circling the number that best applies to you.

During the past week:		Not at all	A little	Quite a bit	Very much
31.	Have you had cramps in your abdomen?	1	2	3	4
32.	Have you had difficulty in controlling your bowels?	1	2	3	4
33.	Have you had blood in your stools (motions)?	1	2	3	4
34.	Did you pass water/urine frequently?	1	2	3	4
35.	Have you had pain or a burning feeling when passing water/urinating?	1	2	3	4
36.	Have you had leaking of urine?	1	2	3	4
37.	Have you had difficulty emptying your bladder?	1	2	3	4
38.	Have you had swelling in one or both legs?	1	2	3	4
39.	Have you had pain in your lower back?	1	2	3	4
40.	Have you had tingling or numbness in your hands or feet?	1	2	3	4
41.	Have you had irritation or soreness in your vagina or vulva?	1	2	3	4
42.	Have you had discharge from your vagina?	1	2	3	4
43.	Have you had abnormal bleeding from your vagina?	1	2	3	4
44.	Have you had hot flushes and/or sweats?	1	2	3	4
45.	Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
46.	Have you felt less feminine as a result of your disease or treatment?	1	2	3	4
47.	Have you felt dissatisfied with your body?	1	2	3	4

Please go on to the next page

ENGLISH

During the past 4 weeks:	Not at all	A little	Quite a bit	Very much
48. Have you worried that sex would be painful?	1	2	3	4
49. Have you been sexually active?	1	2	3	4

Answer these questions only if you have been sexually active during the past 4 weeks:	Not at all	A little	Quite a bit	Very much
50. Has your vagina felt dry during sexual activity?	1	2	3	4
51. Has your vagina felt short?	1	2	3	4
52. Has your vagina felt tight?	1	2	3	4
53. Have you had pain during sexual intercourse or other sexual activity?	1	2	3	4
54. Was sexual activity enjoyable for you?	1	2	3	4

EQ-5D-5L

EQ5D-5L measures general HRQoL consists for 5 scales (descriptive dimension) and a Visual Analogue Scale (VAS). The descriptive Dimensions scale includes Mobility, Self-Care, Usual Aactivities, Pain/Discomfort and Anxiety/Depression. Within the 5 Dimensions, level 1 "indicates no problem" and level 5 "indicates unable to/extreme problems". The self-rated health state scale, Visual Analog Scale (VAS), is scaled 0 to 100, with 0=worse health and 100=best health you can imagine.

Health Questionnaire

English version for the UK

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

2

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐