Statistical Analysis Report for Final Analysis of

A PHASE II SINGLE ARM TRIAL OF ELECTIVE VOLUME ADJUSTED DE-ESCALATION RADIOTHERAPY (EVADER) IN PATIENTS WITH LOW-RISK HPV-RELATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA

CCTG Protocol Number: **HN.10**

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1. Overview

This document is to describe the statistical analysis plan for HN.10 final analysis and serves as the guideline for the analyses generated for writing study report of this trial conducted by Canadian Cancer Trials Group (CCTG).

The data will be collected and cleaned by CCTG according to the data management plan for this study. Senior biostatistician in CCTG will perform all analyses and prepare a statistical analysis report.

1.1 Objective

To evaluate the efficacy of primary definitive radiotherapy (RT) or chemoradiotherapy (CRT) utilizing volume reduced elective nodal irradiation (ENI) as measured by 2-year event-free survival (EFS) in patients with low-risk HPV-related OPSCC.

Secondary objectives: To evaluate overall survival, local control, regional control, local-regional control, out-of-field regional control, distant metastasis free survival, early and late toxicities of treatment, subjective swallowing functions, quality of life (QOL), utilization of healthcare resources, work productivity, and prognostic biomarkers.

1.2 Sample size and power

The 2-year EFS was estimated to be 91% (Ha) for low-risk HPV-related OPSCC. Assuming that the experimental treatment will be considered as ineffective if the 2-year EFS is ≤ 85% (H0), with one-sided alpha of 0.1, a sample size of 100 patients will have 80% power to detect a 6% difference of 2-year EFS. With 3 years of accrual and 2 years of follow-up, the total duration of this study will be 5 years. A total of 304.7 person-years of follow-up is needed for the final analysis. The null hypothesis (H0) will be rejected when the observed survival rate is 88.85% or higher (i.e. if there are 18 or fewer EFS events observed).

1.3 Timeline

The analysis will include data accumulated until May 31, 2024 (estimated timing, specific timing decided until 304.7 person-years of follow-up are observed).

1.4 Data collection

Data are collected and entered by CCTG, Kingston, Ontario. Procedures for data collection, data editing and data transfer are described in the data management plan.

1.5 Interim analysis

A built-in interim futility analysis was conducted when 162.9 person-years of follow-up are observed. The alternative hypothesis (Ha) will be rejected at significant level 0.05 when 12 or more EFS events are observed. The DSMC reviewed the futility analysis at 2023 spring meeting and recommended the trial to continue.

1.6 Data set descriptions

A total of 103 patients were enrolled in HN.10. Out of 103, 99 are eligible; 4 patients are ineligible. Three type of analysis samples will be used:

Population	Definition	Sample size	Analysis
All patients	All patients who have been enrolled.	103	Baseline characteristics
Treated patients	All patients who have received any protocol treatment.	100	Protocol therapy exposure, off treatment, Safety analysis
Eligible patients	All patients who satisfy all eligible criteria.	99	Efficacy, quality of life analysis

2. RESULTS

2.1 Accrual

Number (%) of patients per study center (Table 1) (All patients).

2.2 Eligibility status

Number (%) of eligible and ineligible/ Inevaluable patients and reasons for ineligibility/inevaluability (Table 2).

2.3 Patient characteristics

Number (%) of patient characteristics at baseline (Table 3) (All patients):

- Age
- Sex
- ECOG performance status
- TNM Classification
  - T stage
  - N stage
- Smoking history
  - No smoking ever
  - Smoked ever
- Current smoking
  - Yes
  - No
  - Unknown
- Primary site
  - Base of tongue
  - Tonsil
  - Soft palate

2.4 Protocol therapy exposure

Dose intensity is summarized by actual cumulative dose for both radiotherapy and cisplatin in summary statistics. (Table 4)

The number and % of patients with at least one dose modification (interruption, dose adjustment, early discontinuation) will be summarized for both radiotherapy and cisplatin (Table 5).

2.5 Efficacy

2.5.1 Event free survival (EFS)

Event free survival (EFS) is defined as the time from the date of registration to the date of first record of any of the following events:

- Progression. Investigator determined:
  - Local-regional progression or recurrence.
  - Distant metastasis.
- Surgery:
  - Surgery at any time for clinical or radiological (RECIST 1.1) disease persistence/progression/recurrence at the primary tumour site with tumour present/unknown on final pathology.
  - Neck dissection or surgery performed for clinical or radiological (RECIST 1.1) disease persistence/recurrence/progression within the target volumes > 20 weeks from the end of radiation therapy with tumour present/unknown on final pathology.
  - Neck dissection or surgery performed for clinical or radiological disease recurrence/progression outside the target volumes or without documentation of the site of failure at any time after registration with tumour present/unknown on final pathology.
- Non-protocol RT, chemotherapy, or biologic therapy (for the current cancer diagnosis) without documentation of the site of failure.
- Death due to any cause.

Kaplan Meier (KM) estimate of EFS will be reported in Figure 1.

Type of EFS event and reason of censoring will be list on Table 6. For simultaneous events, the following hierarchy will be used: Death due to any cause > progression (local-regional or distant metastasis) > surgery > non-protocol RT, chemotherapy, or biologic therapy.

Subgroup analysis for EFS based on baseline characteristics listed in Table 3 (plus chemotherapy or not(yes vs no)) will be reported in Table 11.

2.5.2 Overall survival (OS)

For patients who have died, overall survival is calculated in months from the day of registration to date of death. Otherwise, overall survival is censored at the last day the patient is known alive (LKA).

KM estimate of overall survival will be reported in Figure 2.

A frequency table for the number of patients who died, and cause of death will be listed in Table 7.

2.5.3 Local-regional control (LRC)

Local-regional control is defined as the time from the date of registration to the date of any of the following, whichever comes first:

- Surgery of primary tumour at any time performed for clinical or radiological (RECIST 1.1) disease persistence/progression/recurrence with tumour present/unknown on final pathology.
- Neck dissection > 20 weeks from the end of radiation therapy performed for clinical or radiological (RECIST 1.1) disease persistence/progression/recurrence within target volumes with tumour present/unknown on final pathology.
- Neck dissection at any time after registration performed for clinical or radiological (RECIST 1.1) disease recurrence/progression outside the target volumes or without documentation of the site of failure with tumour present/unknown on final pathology.
- the first record of appearance (radiological or clinical) of local or regional disease progression/recurrence.

KM estimate of time to LRC will be reported in Figure 3.

A frequency table for the number of patients with LRC events and type of LRC events in will be listed in Table 8.

2.5.4 Out-of-field regional control

Time to out-of-field regional failure is defined as the time from the date of registration to the date of the first record of appearance of regional progression/recurrence outside the treatment field, whichever comes first.

Local or distant recurrence/progression diagnosed before out-of-field regional failure and death in absence of out-of-field regional failure are not considered events of interest, but as competing risks events in the analysis of this endpoint. Subjects without any of the listed events (i.e. events of interest or competing risks events) are censored at the date of the most recent follow-up examination.

KM estimate of time to out-of-field regional control will be reported in Figure 4.

A frequency table for the number of patients with out-of-field regional control events and type of events in will be listed in Table 9.

2.5.5 Distant metastasis free survival (DMFS)

Distant metastasis free survival is defined as the time from the date of registration to the date of first record of appearance of distant metastasis or death for any cause. Local-regional failure or second cancers diagnosed before the distant metastases are not considered events of interest for this endpoint. Subjects alive and free of distant metastasis are censored at the date of the most recent follow-up examination.

KM estimate of time to DMFS will be reported in Figure 5.

A frequency table for the number of patients with DMFS events and type of events in will be listed in Table 10.

2.6 Safety

The safety analyses will be based on the treated population. Adverse events and laboratories are graded and categorized using the CTCAE v5.0 criteria except where CTCAE grades are not available.

The following variables are summarized.

- Adverse events: worst CTCAE grade per patient (Table 12)
- Serious adverse events: worst CTCAE grade per patient (Table 13)
- Drug related adverse events: worst CTCAE grade per patient (Table 14)
- Drug related serious adverse events: worse CTCAE grade per patient (Table 15)

2.7 Off treatment

- Number and (%) of patients and reasons off protocol treatment (Table 16).

- Deaths during protocol treatment or within 30 days of last protocol treatment: number of patients who died and cause of death from Date/Cause of Death Section of Death Report (Table 17)

2.8 Quality of life analysis

The quality of life of patients in this study is assessed at baseline, last week of RT, and 3, 6, 12, 24, 36 months post RT using FACT-G, FACT-H&N and MDADI.

2.8.1 Definitions and scoring

2.8.1.1 FACT-G

There are four functional domains from FACT-G questionnaires (see below for definitions). The scores are calculated by the corresponding formula below.

Physical well being: Questions: 1-7 (PWB)

Score=missing if number of above questions not answered is greater than 3; Otherwise,
Score = (4–(Total for the answered questions/Total questions answered))*7

Social/Family well being: Questions: 8-14 (SFWB)

Score=missing if number of above questions not answered is greater than 3; Otherwise,
Score = (Total for the answered questions/Total questions answered)*7

Emotional well being: Questions: 15-20 (EWB)

Score=missing if number of above questions not answered is greater than 2; Otherwise,
Score = (4 – (4 – score of GE2 + total of GE1, GE3-6) /Total questions answered)*6 if GE2 is not missing with other missing treated as with value of 0; or = (4 – (total score of GE1, GE3-6) /Total questions answered)*6 if GE2 is missing with other missing treated as with value of 0.

Functional well being: Questions: 21-27 (FWB)

Score=missing if number of above questions not answered is greater than 3; Otherwise,
Score = (Total for the answered questions/Total questions answered)*7.

The FACT-G Total score = (PWB+SFWB+EWB+FWB) when the overall item response rate is greater than 80% (e.g. at least 22 of 27 FACT-G) items complete, otherwise, FACT-G total score is considered to be missing.

2.8.1.2 FACT-HN

The FACT-H&N contains 12 items (hn1 to hn12, i.e. q28, to q39). The H&N subscale score is calculated by the corresponding formula below:

Item 2, 3, 6, 12 will be calculated in reverse scale:

hn2 = 4 – hn2
hn3 = 4 – hn3
hn6 = 4 – hn6
hn12 = 4 – hn6

Both hn8 (i.e. q35) and hn9 (i.e. q36) are not currently scored.

Score=missing if number of above questions not answered is greater than 5; Otherwise,
Score = (Total for the answered questions/Total questions answered)*10

The range of H&N scale score is 0 to 40. Trial Outcome index (TOI) for FACT-H&N is calculated by (PWB + FWB + H&N).

Overall FACT-H&N score is calculated by (FACT-G total + H&N).

2.8.1.3 MDADI

The MDADI consists of 20 items, one global item (scored individually) and 19 items organized into domains: emotional (6), physical (8) and functional (5). Each item is scored on a 1-5 scale (Two items have their scores reversed, E7 and F2; for all others, 5 points are given for "strongly disagree").

Global item: Question: 1

Score=missing if number of above question is not answered; Otherwise,
Score = (Score for question one - 1)*100/4

Emotional scale: Question: E1 to E6

Score=missing if number of above questions not answered is greater than 3; Otherwise,
Score = ((Total for the answered questions/Total questions answered)-1)*100/4

Physical scale: Question: P1 to P8

Score=missing if number of above questions not answered is greater than 4; Otherwise,
Score = ((Total for the answered questions/Total questions answered)-1)*100/4

Functional scale: Question: F1 to F5

Score=missing if number of above questions not answered is greater than 2; Otherwise,
Score = ((Total for the answered questions/Total questions answered)-1)*100/4

2.8.2 Analysis

All analyses on quality-of-life scores will include all eligible patients who have a measurement at baseline and at least one measurement after baseline.

2.8.2.1 Determination of assessment times

The following will be the scheme to determining the time frame of all QOL assessments (FACT, MDADI):

1) Baseline: Baseline evaluation is the QOL questionnaire collected closest, but prior to, the date of treatment started (usually within 2 weeks);
2) Last week of radiotherapy: If the QOL is assessed two weeks before or after the last week of radiotherapy, this assessment is considered as last week of radiotherapy assessment;
3) 3 months off treatment: If 2 weeks < or = (QOL assessed date – off treatment date) < 4 .5 months, this assessment is considered as 3 months assessment;
4) 6 months off treatment: If 4.5 months < or = (QOL assessed date – off treatment date) < 9 months, this assessment is considered as 6 months assessment;
5) 12 months off treatment: If 9 months < or = (QOL assessed date – off treatment date) < 18 months, this assessment is considered as 12 months assessment;
6) 24 months off treatment: If 18 months < or = (QOL assessed date – off treatment date) < 30 months, this assessment is considered as 24 months assessment;
7) 36 months off treatment: 30 months < or = (QOL assessed date – off treatment date) < 42 months, this assessment is considered as 36 months assessment;

Note: when there was multiple recode for the same patient within a given interval, the one that is closest to the nominal time point should be used for analysis.

2.8.2.2 Calculation of Compliance Rates

The compliance rate is calculated as the number of forms received out of the number of forms expected at each assessment point defined based on the following principles:

1) At baseline: the number of forms expected is the total number of patients who are administrated to the study and required to fill out QOL questionnaires.
2) Last week of radiotherapy: the number expected at last week of radiotherapy is the total number of patients who completed the radiotherapy treatment. If radiotherapy terminated early, complete QOL on last day of radiotherapy treatment or as soon as possible after radiation;
3) After protocol treatment: the number expected is the total number of patients who were alive at the time of assessment and have not withdrawn (consent) from the trial.

Compliance for FACT-HN and MDADI will be summarized in Table 18.

2.8.2.3 Cross-sectional analysis

The mean and standard deviation of QOL scores at baseline and mean and standard deviation of QOL change scores from baseline at each assessment time will be calculated.

Summary statistics of baseline score for each domain in FACT-HN and MDADI will be summarized in Table 19. Mean QOL change score from baseline for each assessment time will be summarized in Table 20.

2.8.3 Analysis of FOIS and PSS-HN.

FOIS and PSS-HN are not a patient reported outcome however it is an important investigator-completed assessment of swallowing function and have been included in HN10. "Compliance" does not apply, and MID is not well defined for FOIS and PSS-HN. Thus, only the cross-sectional analysis specified in 2.8.2.3 will be conducted for both.

Cross-sectional analysis results related to FOIS and PSS-HN will be summarized in Table 21.

Figure 1. KM for EFS

Figure 2. KM for OS

Figure 3. KM for LRC

Figure 4. KM for out-of-field regional control

Figure 5. KM for DMFS

Figure 6. Boxplots for FACT domain score changes from baseline by assessment time

Figure 7. Boxplots for MDADI domain score changes from baseline by assessment time

Figure 8. Boxplots for FOIS domain score changes from baseline by assessment time

Figure 9. Boxplots for PSS-HN domain score changes from baseline by assessment time

Table 1. Accrual by center

Data set: All Patients

	Number of patients (%)
	Total N = ***
Canada	*** (**)
Center #1	*** (**)
Center #2	*** (**)
…	*** (**)
…	

Table 2. Eligibility and reasons for ineligibility

Data set: All Patients

	Number of patients (%)
	Total N = ***
Eligible/Evaluable	*** (**)
Not Eligible/Inevaluable	*** (**)
Major protocol violation	
<violation type 1>	**
<violation type 2>	**
...	

Table 3. Baseline patient characteristics

Data set: All Patients (N = 103)	
	Total N = 103
Age (years)	
N	
Median (Min-Max, Q1-Q3)	
Mean (SD)	
>/= 65	
<65	
Sex	
Female	
Male	
ECOG Performance Status	
0	
1	
T Stage	
T1	
T2	
T3	
T4[1]	
N Stage	
N0	
N1	
N2[2]	
Primary site	
Base of tongue	

Tonsil	
Soft palate	
Smoking history	
No smoking ever	
Smoked ever	
Greater than 100 cigarettes during lifetime	
100 or fewer cigarettes during lifetime	
Pipe or cigar smoker only	
Length of smoking in years	
N	
Median (Min-Max, Q1-Q3)	
Mean (SD)	
Current smoking	
Yes	
No	
Unknown or not answered	
Current average number of cigarettes smoked per day	
N	
Median (Min-Max, Q1-Q3)	
Mean (SD)	

1. Patient is ineligible since disease is T4.
2. Patient is ineligible since disease is N2.

Table 4. Actual dose intensity

Data set: All Treated Patients (n = 100)		
	Radiotherapy N = 100 (in Gy)	Cisplatin N = 50 (in mg)
Actual cumulative dose		
Median (Min-Max, Q1-Q3)		
Mean (SD)		
<200 mg	Not applicable	
>/= 200 mg	Not applicable	

Table 5. Number of patients with modifications of protocol therapy

Data set: All Treated Patients

	Number of patients (%)
	Radiotherapy N = ***
Patients with at least one cycle with (type of modification*) over all cycles	** (**)
Reason for (type of modification)	** (**)
Reason 1	** (**)
…	** (**)

Data set: All Treated Patients

	Number of patients (%)
	Chemotherapy N = ***
Patients with at least one cycle with (type of modification*) over all cycles	** (**)
Reason for (type of modification)	** (**)
Reason 1	** (**)
…	** (**)

Table 6. Type of event free survival (EFS) event and reason of censoring

Data set: All Eligible Patients

	Number of patients (%)
	Total N = ***
Patients who progressed	** (**)
Death due to any cause	** (**)
Progression (local-regional or distant metastasis)	** (**)
Surgery	** (**)
Non-protocol RT, chemo, or biologic therapy	** (**)
Patients who were censored	** (**)
Reason censored	

Lost to follow-up	** (**)
Withdraw of consent	** (**)
Not progressed	** (**)
…	

Table 7. All deaths

Data set: All Eligible Patients

	Number of patients (%)
	Total N = ***
Number of Patients who died	** (**)
Cause of death	
Reason 1	** (**)
Reason 2	** (**)
…	

Table 8. Type of Local-regional control (LRC) event and reason of censoring

Data set: All Eligible Patients

	Number of patients (%)
	Total N = ***
Patients who progressed	** (**)
Surgery of primary tumour	** (**)
Neck dissection within target volumes	** (**)
Neck dissection outside the target volumes	** (**)
Progression	** (**)
Patients who were censored	** (**)
Reason censored	
Lost to follow-up	** (**)
Withdraw of consent	** (**)
Not progressed	** (**)
…	

Table 9. Type of out-of-field regional control event and reason of censoring

Data set: All Eligible Patients

	Number of patients (%)
	Total N = ***
Patients who progressed	** (**)
Regional progression outside the treatment field	** (**)
Neck dissection within target volumes	** (**)
Patients who were censored	** (**)
Reason censored	
Lost to follow-up	** (**)
Withdraw of consent	** (**)
Not progressed	** (**)
…	

Table 10. Type of Distant metastasis free survival (DMFS) event and reason of censoring

Data set: All Eligible Patients

	Number of patients (%)
	Total N = ***
Patients who progressed	** (**)
Distant metastasis	** (**)
Death for any cause	** (**)
Patients who were censored	** (**)
Reason censored	
Lost to follow-up	** (**)
Withdraw of consent	** (**)
Not progressed	** (**)
…	

Table 11. Subgroup analysis for EFS

			Data set: All Eligible Patients (n = 99)		
Factor	Level	N	Number of events	2 year EFS rate (95% CI)	Hazard Ratio (95% CI)
Age	<= 65				
	>65				
Sex	Male				
	Female				
ECOG	1				
	0				
T stage	T1				
	T2				
	T3				
N stage	N0				
	N1				
Smoking history	No smoking ever				
	Ever smoked				
Chemotherapy	Yes				
	No				
Primary site	Base of tongue				
	Tonsil				
	Soft palate				

Table 12. Adverse Events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with AE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

Table 13. Serious adverse events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any SAE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with AE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

Table 14. Drug Related Adverse Events

Table 14.1. Radiotherapy Related Adverse Events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any drug-related AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with AE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

Table 14.2. Chemotherapy Related Adverse Events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any drug-related AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with AE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

Table 15. Drug Related Serious Adverse Events

Table 15.1. Radiotherapy Related Serious Adverse Events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any drug-related SAE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with SAE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

* Tables for cisplatin-related and radiotherapy-related SAE will also be presented.

WORST OVERALL GRADE 1 1 (1.0) (8.0)

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* Adverse events graded according to CTCAE V5.0

Table 15.2. Chemotherapy Related Serious Adverse Events

Data set: All treated patients							
	Number of patients (%) N=***						
	Worst grade					Any grade	
	1	2	3	4	5		
Patients with any drug-related SAE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	
Patients with SAE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)		**(**)
...							

* Tables for cisplatin-related and radiotherapy-related SAE will also be presented.

WORST OVERALL GRADE 1 1 (1.0) (8.0)

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* Adverse events graded according to CTCAE V5.0

Table 16. Number and (%) of patients off protocol treatment

Data set: All Treated Patients		
	Radiotherapy (%)	Cisplatin (%)
	Total N = ***	Total N = ***
Off Treatment	** (**)	** (**)
Reason off treatment		
Reason 1	** (**)	** (**)
Reason 2	** (**)	** (**)
…		

Table 17. Death on trial (on protocol treatment or within 30 days off treatment)

Data set: All Treated Patients

	Number of patients (%)
	Total N = ***
Number of Patients who died during or within 30 days of last protocol treatment	** (**)
Cause of death	
Reason 1	** (**)
Reason 2	** (**)
…	

Table 18. Compliance (Received/Expected) with QoL assessment.

Table 18.1 FACT

Data set: All Eligible Patients (n = 99)		
	Expected	Received (%)
Baseline		
Last week of Radiotherapy		
Follow up		
Month 3		
Month 6		
Month 12		
Month 24		
Month 36		

Table 18.2 MDADI

Data set: All Eligible Patients (n = 99)		
	Expected	Received (%)
Baseline		
Last week of Radiotherapy		
Follow up		
Month 3		

Month 6		
Month 12		
Month 24		
Month 36		

Table 18.3 FOIS

Data set: All Eligible Patients (n = 99)		
	Expected	Received (%)
Baseline		
Last week of Radiotherapy		
Follow up		
Month 3		
Month 6		
Month 12		
Month 24		
Month 36		

Table 18.2 PSS-HN

Data set: All Eligible Patients (n = 99)		
	Expected	Received (%)
Baseline		
Last week of Radiotherapy		
Follow up		
Month 3		
Month 6		
Month 12		
Month 24		
Month 36		

Table 19. Summary Baseline Scores.

	FACT-HN
Functional scales	
Physical	
N	***
Mean	***

STD	***
Social/Family	
N	***
Mean	***
STD	***
Emotional	
N	***
Mean	***
STD	***
Functional	
N	***
Mean	***
STD	***
FACT-G total	
N	***
Mean	***
STD	***
FACT-HN	
N	***
Mean	***
STD	***
FACT-HN total	
N	***
Mean	***
STD	***
…	…
	MDADI
Global	
N	***
Mean	***
STD	***
Emotional	
N	***
Mean	***
STD	***
Physical	
N	***
Mean	***
STD	***
Functional	
N	***
Mean	***

STD	***
MDADI total	
N	***
Mean	***
STD	***

Table 20. Change score from baseline for scale/domain/item at each time period.

	Scale/domain/item
Scale/Domain/Item	
Last week of RT	
N	***
Mean	***
STD	***
3 months post RT	
N	
Mean	***
STD	***
6 months post RT	
N	
Mean	***
STD	***
…	
N	
Mean	***
STD	***

* Table will be provided for each scale/domain/item.

Table 21. Change score from baseline for FOIS/PSS-HN at each time period.

	Scale/domain/item
Scale/Domain/Item	
Last week of RT	
N	***
Mean	***
STD	***
3 months post RT	
N	
Mean	***
STD	***

6 months post RT	
N	
Mean	***
STD	***
…	
N	
Mean	***
STD	***

* Table will be provided for each scale/domain/item.