STATISTICAL ANALYSIS PLAN

A PHASE III STUDY OF PALLIATIVE RADIOTHERAPY FOR SYMPTOMATIC HEPATOCELLULAR CARCINOMA AND LIVER METASTASES

Protocol CCTG HE.1

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ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Serum Glutamic Oxaloacetic Transaminase
BPI	Brief Pain Inventory
BSC	Best Supportive Care
C. I.	Confidence Interval
CMH	Cochran-Mantel-Haenszel
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
CCTG	Canadian Cancer Trials Group
FACT-Hep	Functional Assessment of Cancer Therapy Hepatobiliary
FACT-G	FACT-General
EWB	Emotional Well-Being
FWB	Functional Well-Being
HBS	Hepatobiliary Subscale
HCC	Hepatocellular Carcinoma
ID	Patient Identification
IN	Inevaluable
INR	International Normalized Ratio
MPV	Major Protocol Violation
NA	Not Applicable
NC	Not Computed
NCI	National Cancer Institute
OME	Oral morphine equivalents
PWB	Physical Well-Being
QLQ	Quality of Life Questionnaire
QoL	Quality of Life
RT	Radiation Therapy
TOI	Trial Outcome Index
SAS	Statistical Analysis System
SFWB	Social and Family Well-Being
STD	Standard Deviation
UNL	Upper Normal Limit
WBC	White Blood Cells

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1. Background and Rationale

The purpose of this analysis plan is to describe the analysis performed by the Canadian Cancer Trials Group (CCTG) for the HE.1 trial. The data are collected and cleaned by CCTG. All analyses will be performed by a senior biostatistician in CCTG and a final statistical analysis report will be prepared.

2. Study Description

2.1 Background

Hepatocellular carcinoma (HCC) is a disease which is often diagnosed at an advanced stage with common symptoms of pain, anorexia and fatigue are common. The liver metastases are common for patients with a variety of gastrointestinal malignancies (e.g. colorectal and pancreatic cancer), as well as non-gastrointestinal malignancies, including, melanoma, breast and gynecological cancers. For HCC and liver metastases, majority of patients become refractory to all therapy for a period of time prior to death and a substantial proportion of these patients suffer from hepatic pain. Effective palliation of hepatic pain can be challenging for these patients and there is a need for improved palliative treatments.

A radiation therapy (RT) with the use of 8 Gy in one fraction to the whole (or near-whole) liver, with an anti-emetic to prevent nausea, was shown in a phase II clinical trial resulted in a clinically meaningful improvement in average index symptom intensity assessed using the BPI one month following RT with no differences between patients with HCC and liver metastases. This treatment was also shown well tolerated. This trial was designed to prospectively compare this radiotherapy with the best supportive care (BSC) in patients with HCC and liver metastases.

2.2 Research Hypothesis

The primary hypothesis in this study is that the radiotherapy combined with best supportive care (RT+BSC) will have a greater clinical improvement of an index symptom of pain or abdominal discomfort compared to best supportive care alone (BSC) in patients with symptomatic hepatocellular carcinoma (HCC) or liver metastases.

2.3 Study Design

CCTG HE.1 is a multi-center, open-label, randomized phase III trial which randomizes patients with end-stage, painful, symptomatic hepatocellular carcinoma (HCC) or liver metastases to receive RT+BSC or BSC after stratification by center and type of liver cancer (HCC vs. liver metastases).

This study was activated on July 23, 2015. The final analysis would be performed when 45 evaluable patients are available for analysis, which would be achieved after approximately 65 patients are randomized with an assumption of 25% drop out rate. The 66th patient was randomized on June 2, 2022, however, after a review, only 42 patients were evaluable from the 66 randomized patients. Because of the slow accrual, after consulting with the CCTG Data Safety Monitoring Committee (DSMC), the trial

committee decided to close the accrual on June 2, 2022, with the last expected date for the collection of trial data from all 66 randomized patients as September 8, 2022, which is therefore defined as the data cut-off date for final analysis. The final analysis will be performed after all data observed on or before this date are received and cleaned. This analysis plan describes the analyses performed for the final analysis.

The CCTG DSMC has been reviewing safety data every six months (usually at the time of the bi-annual CCTG Spring and Fall meetings) and as otherwise required. These analyses have been prepared by a CCTG/Queen's Senior Biostatistician.

3. Objectives

3.1 Primary

The primary objective of this study is to determine if patients with symptomatic liver tumours (either HCC or liver metastases) who undergo best supportive care (BSC) plus a single 8 Gy fraction of radiation therapy to the liver experience a significant improvement in symptoms (defined as a ≥ 2 point decrease in their pain 'intensity at worst' score on BPI) from baseline to 30 days as compared to patients receiving BSC alone.

3.2 Secondary

Secondary objectives are to compare the two treatment arms with respect to:

- Proportion of patients experiencing grade ≥ 2 adverse events at 30 days and 90 days.
- Proportion of patients alive at 90 days.
- Proportion of patients achieving improvement of liver cancer pain/discomfort by ≥ 2 points from baseline to day 30 and day 90 in all BPI pain scores.
- Proportion of patients reporting clinically significant improvement in QoL from baseline to day 30 and day 90 as defined by a ≥ 5 point change in the Functional Assessment of Cancer Therapy (FACT) Hepatobiliary Subscale (FACT-HBS) and Trial Outcome Index (FACT-TOI).
- Proportion of patients achieving a 25% reduction in opioid use at 30 days (employing daily morphine equivalence).

4. Endpoints

4.1 Primary Efficacy

The primary efficacy endpoint is proportion of patients achieving improvement of liver cancer/discomfort by ≥ 2 points in pain 'intensity at worst' on BPI from baseline to day 30.

4.2 Secondary Efficacy

The secondary efficacy endpoints are:

- Proportion of patients experiencing grade ≥ 2 adverse events at day 30 and day 90.
- Proportion of patients alive at day 90.

- Proportion of patients achieving improvement of liver cancer pain/discomfort by ≥ 2 points from baseline to day 30 and day 90 in all BPI pain scores.
- Proportion of patients reporting clinically significant improvement in QoL from baseline to day 30 and day 90 as defined by a ≥ 5 point change in the Functional Assessment of Cancer Therapy (FACT) Hepatobiliary Subscale (FACT-HBS) and Trial Outcome Index (FACT-TOI).
- Proportion of patients achieving a 25% reduction in opioid use at 30 days (employing daily morphine equivalence scale).
- Proportion of patients achieving improvement of liver cancer pain/discomfort by ≥ 2 points in pain 'intensity at worst' AND with no increase in opioid use (employing daily morphine equivalence sale) on BPI from baseline to 30 days.

4.3 Safety

The safety endpoints are serious and non-serious adverse events (clinical and laboratory), laboratory parameters.

5. Sample Size and Power

The primary objective of this study was to determine a single 8 Gy dose of RT with best supportive care (BSC) would show an improvement of ≥ 2 pints in pain 'intensity at worst' on the Brief Pain Inventory (BPI) from baseline to day 30 relative to BSC alone in patients with painful liver tumours (either HCC or liver metastases). 45 evaluable patients with BPI at baseline and at day 30 were required to detect a change in proportion of patients with a significant improvement in BPI from 5% (no radiation) to 40% (with radiation therapy) with 80% power and two-sided 0.05 level. With 42 evaluable patients included in the final analysis, the study would have 77% power to detect the significant improvement in BPI from 5% (no radiation) to 40% (with radiation therapy) at two-sided 0.05 level or 80% power to detect the significant improvement in BPI from 5% (no radiation) to 42% (with radiation therapy) at two-sided 0.05 level.

6. Data Set Descriptions

Two types of analysis samples will be used:

All Randomized Patients:
All patients who have been randomized in the study with the treatment arm being as randomized.

All Treated Patients:
All patients who are randomized to RT+BSC arm and have received a single 8 Gy dose of RT and all patients who are randomized to BSC arm.

All Day 30 BPI Response Evaluable Patients:
All patients who have completed a baseline and 30 days follow-up BPI.

All Day 90 BPI Response Evaluable Patients:
All patients who have completed a baseline and a day 90 follow-up BPI.

All BPI Response from Day 30 to Day 90 Evaluable Patients:
All patients who have randomized to BSC arm and crossed over to RT+BSC arm after their day 30 assessment and also completed their day 30 and day 90 BPI.

All QoL (quality of life) Evaluable Patients:
All patients who have completed the quality of life questionnaire at baseline and on days 30 and 90.

All Change in Opioid Evaluable Patients:
All patients who have completed Pain/Discomfort and Medication Questionnaires at baseline and within 24 hours of the 30 day visit.

7. Statistical Analysis

7.1 General Methods

All comparisons between treatment arms will be carried out using a two-sided test at an alpha level of 5% unless otherwise specified.

When appropriate, discrete variables are summarized with the number and proportion of subjects falling into each category, and compared using Fisher's exact test. Continuous and ordinal categorical variables are summarized using the mean, median, standard error, minimum and maximum values and when appropriate, compared using the Wilcoxon test.

Percentages given in the summary tables will be rounded and may therefore not always add up to exactly 100%. Listings, tabulations, and statistical analyses will be carried out using the SAS (Statistical Analysis System, SAS Institute, North Carolina, USA) software.

Unless otherwise specified, date of randomization and stratification factors will be taken from the Centralized Randomization File.

Baseline evaluations will be those collected on CRF Eligibility Worksheet and Baseline Report and closest to, but no later than, the first day of study treatment for treated subjects and closest to, but no later than, the date of randomization, for subjects who were randomized but who never received treatment.

Laboratory results, adverse events, and other symptoms are coded and graded using the CTCAE Version 4.0 Criteria.

7.2 Study Conduct

All randomized patients are included in the analysis of study conduct. Information will be tabulated by randomized treatment (unless otherwise indicated) and pooled treatments.

7.2.1 Patient Disposition and Follow-up

- Number of patients randomized **(Table 1)**

- Number of patients on RT+BSC received and not received RT **(Table 1)**
- Reasons of patients on RT+BSC not received RT **(Table 1)**
- Number of patients on BSC received and not received RT after their day 30 assessment **(Table 1)**
- Reasons of patients on BSC not received RT after their day 30 assessment **(Table 1)**
- Number of alive patients **(Table 2)**
- Median (estimated by Kaplan-Meier method) and range (minimum and maximum) **(Table 2)** of the follow-up time (months) defined as time from the day of randomization (as recorded in centralized randomization file) to the last day the patient is known alive (LKA) as the last recorded date known alive or censored at the time of death and calculated as

  [(date of death or LKA − date of randomization) + 1)]/30.4375.

7.2.2 Accrual Patterns

- Number of patients accrued by center **(Table 3)**
- Number of patients by stratification factor (except center) at randomization **(Table 4)**
- Accrual of patients by calendar time **(Figure 1)**

7.2.3 Eligibility Violations/Protocol Deviations

Eligibility violations of inclusion or exclusion criteria are centrally reviewed by CCTG; a field (y/n) for eligibility status and reason for ineligibility is entered in the database. A major protocol violation (MPV) is defined as a deviation from the protocol, initiated by the center or the investigator, serious enough to mean that the patient's data contributes little, if any, information on the efficacy or toxicity of the regimen under study. MPVs are coded by CCTG based on its standard codes.

- Number of patients eligible, not eligible **(Table 5)**
- Reasons for ineligibility **(Table 5)**
- Major protocol violations: % for each type of violations **(Table 5)**

7.3 Study Population

All randomized patients are included in the study population analyses.

7.3.1 Patient Pretreatment Characteristics

- Gender: male, female **(Table 6)**
- Age: median, minimum, maximum values**;** number <65, ≥65 **(Table 6)**
- ECOG Performance Status: 0, 1, 2, 3, 4 **(Table 6)**
- BMI: median, minimum, maximum values **(Table 6)**

7.3.2 Patient Baseline Tumour Characteristics

- Months from initial diagnosis to randomization: median, minimum, maximum values **(Table 7)**
- Method of initial diagnosis **(Table 7)**
- Type of liver cancer **(Table 7)**

- Months from liver metastases diagnosis to randomization: median, minimum, maximum values **(Table 7)**
- Primary tumour type of liver metastases **(Table 7)**
- Presence of extrahepatic cancer **(Table 7)**
- Primary in place for extrahepatic cancer **(Table 7)**
- Sites of metastases **(Table 7)**
- Portal vein or other vascular invasion **(Table 7)**
- Type of other liver disease **(Table 7)**
- Extent of liver disease **(Table 7)**
- Child-Pugh class **(Table 7)**
- Child-Pugh score **(Table 7)**

7.3.3 Prior Cancer Therapy

- Number of patients with prior surgical/diagnostic procedures **(Table 8)**
- Procedure/site of prior surgery **(Table 8)**
- Number of patients with prior radiotherapy **(Table 9)**
- Prior radiotherapy by site with duration and total dose (cGy) **(Table 9)**
- Number of patients with prior systemic therapy **(Table 10)**
- Prior systemic therapy by drug or agent name **(Table 10)**
- Number of patients with regional therapy **(Table 11)**
- Prior regional therapy by therapy name **(Table 11)**

7.3.4 Baseline Exams

- Baseline grade 2 and higher adverse events (**Table 12)**
- Baseline hematology: hemoglobin, absolute neutrophil count, platelets **(Table 13)**
- Baseline biochemistry: total bilirubin, alkaline phosphatase, ALT, AST, albumin, serum creatinine, alpha-fetoprotein **(Table 14)**
- Baseline coagulation **(Table 15)**

7.3.5 Concomitant Medications at Baseline

- Number of patients with concomitant medication within 14 days prior to the date of randomization **(Table 16)**

7.4 Extent of Radiotherapy

Within 5 working days after randomization, the patients randomized to RT+BSC are planned to receive a single fraction of 8 Gy radiation therapy to the liver. The same radiation therapy may be given to the patients randomized to BSC who continue to be bothered by pain/discomfort following completion of the day 30 assessment. The following information will be summarized for patients who have received the radiotherapy:

- The number of fractions, plan dose, type of motion management, beam arrangement, planning, and position verification (**Table 17)**.
- Liver volumes, GTV, CTV, PTV **(Table 18)**
- Doses (**Table 19)**.

7.5 Efficacy

7.5.1 Patient-reported pain/discomfort symptoms

Patient-reported pain/discomfort symptoms in this study are assessed at baseline, and on days 30 and 90 from randomization by using BPI, which consists of 4 pain intensity and 7 pain interference 11- point Likert-scale questions (range 0-10). The following information on pain/discomfort assessment will be summarized:

- Number of patients who have completed the BPI pain/discomfort assessment at respectively baseline and days 30 and 90 (**Table 20)**.
- Reasons the assessments are not completed (**Table 20)**.
- Mean and standard deviation of BPI scores at baseline and days 30 and 90 (**Table 21**)

7.5.2 Proportion of patients who experience a significant improvement in symptoms

The primary endpoint of the study, the proportion of patients who experience significant improvement in symptoms from baseline to day 30, is estimated by the number of patients with ≥2 point reduction in 'worst' pain score on BPI from baseline to day 30 among all primary BPI response evaluable patients. A stratified Cochran-Mantel-Haenszel (CMH) test adjusting for the stratification factor (HCC versus liver metastases) will be used to compare this endpoint between two treatment arms **(Table 22).** A subgroup analysis will be performed based on the location of the metastases (HCC versus liver) **(Table 22).**

As a sensitivity analysis, this primary endpoint will also be estimated among all randomized patients by including those without assessment at day 30 after randomization in the 'no improvement' group **(Table 22)**.

The proportion of patients who experience significant improvement in symptoms from baseline to day 90, a secondary endpoint of the study, is estimated by the number of patients with a ≥2 point reduction in 'worst' pain score on BPI from baseline to day 90 among all secondary BPI response evaluable patients and analyzed similarly as the primary endpoint **(Table 22)**.

For patients who have randomized to BSC arm and crossed over to RT+BSC arm after their day 30 assessment, the proportion of patients who experience significant improvement in symptoms from day to day 90, another secondary endpoint of the study, is estimated by the number of patients with a ≥2 point reduction in 'worst' pain score on BPI from day 30 to day 90 among all BPI response from day 30 to day 90 evaluable patients **(Table 22)**.

7.5.3 Proportion of patients achieving improvement in other BPI pain scores

For all other BPI scores, the proportions of patients who had a ≥2 point reduction in from baseline to days 30 and 90 will be calculated among respectively all primary and secondary BPI response evaluable patients and analyzed similarly as the primary endpoint **(Table 23)**.

7.5.4 Opioid Intake

Number of patients using the opioid or non-opioid medications and the type and number of these medications as reported at baseline and 30 and 90 day follow-up visits are summarized in **Table 24.** Oral morphine equivalents (OME) calculated for all opioid medications are also summarized.

The proportion of patients who had achieved 25% reduction in opioid use at 30 days (employing daily morphine equivalence scale) will be compared between tow treatment arms using a stratified CMH test adjusting for the stratification factor (HCC versus liver metastases) **(Table 25**). In addition, the proportion of patients who improved liver cancer pain/discomfort by ≥ 2 points in pain 'intensity at worst' AND with no increase in opioid use (employing daily morphine equivalence scale) from baseline to 30 days will also be compared between two treatment arms using a stratified CMH test adjusting for the stratification factor (HCC versus liver metastases) **(Table 26)**.

7.5.5 Overall Survival

For all randomized patients, survival is calculated from the day of randomization (as recorded in CRF Eligibility Worksheet) to death (CRF Death Report). For alive patients, survival is censored at the last day the patient is known alive (LKA) as the last recorded date known alive (timing of the assessment at day 30 which is recorded in Section 1 of CRF Fellow-up Report 30 Day Visit, timing of the assessment at day 90 which is recorded in Section 1 of CRF Fellow-up Report 30 Day Visit**,** or the date of the radiotherapy delivered which is recorded in Section 1 of CRF: Radiotherapy Report). Survival time (in months) is defined as

$$[(\text{date of death or LKA} - \text{date of randomization}) + 1)]/30.4375.$$

The number of patients who died and the reason of death are presented in **Table 27**. The comparison of overall survival between the two treatment arms is the primary objective of this study. 90 days survival rates, based on Kaplan-Meier estimates, will be calculated by treatment arm and compared by the log-rank test **(Table 28)** stratified by the stratification factor (HCC versus liver metastases).

7.6 Safety

7.6.1 Adverse Events

Adverse events are assessed using the NCI Common Terminology Criteria for Adverse Events (CTCAE) v4.0 handbook and those with grade 2 or higher are recorded on the baseline report, 30 day follow-up report, and 90 day follow-up report. Events reported on 30 day follow-up report will be summarized respectively for patients who were randomized to RT+BSC arm and received radiotherapy and who were randomized to BSC. Events reported on 30 day follow-up report will be summarized by the following three groups: (1) patients who were randomized to RT+BSC arm and received radiotherapy; (2) patients who were randomized to BSC and crossed over to RT+BSC; (3) patients who were randomized to BSC but not crossed over to RT+BSC.

Radiotherapy related adverse events are those events with a relation to protocol therapy of 3=possible, 4=probable or 5=definite.

Severe adverse events are those events reported with a CTCAE Grade of 3 or higher.

- Grade 2 or higher adverse events at days 30 and days 90: CTCAE grade per patient **(Table 29)**
- Grade 2 or higher radiotherapy related adverse events at days 30 and days 90: CTCAE grade per patient **(Table 31)**
- Severe adverse events at days 30 and 90: CTCAE grade per patient **(Table 32)**

Proportions of patients experiencing any grade ≥ 2 adverse event at day 30 and day 90 will be compared between treatment arms is conducted by a stratified CMH test (**Table 30**).

7.6.2 Laboratory Evaluations

Laboratory evaluations reported on the follow-up report 30 day visit and follow-up report 90 day will be classified according to the CTCAE if possible. Laboratory tests that are not covered by the CTCAE grading system will be summarized according to the following categories: normal and abnormal. Tabulations of laboratory adverse events will be presented by groups similarly as the adverse events.

7.6.2.1 Hematology

- Hemoglobin and platelets at days 30 and 90: CTCAE grade per patient **(Table 33)**

7.6.2.2 Serum Chemistry

- Total bilirubin, AST, ALT, albumin, serum creatinine, alpha-fetoprotein at days 30 and 90: CTCAE grade per patient **(Table 34)**

7.6.2.2 Coagulation

- INR at days 30 and 90: CTCAE grade per patient **(Table 35)**

7.7 Pre-medication, Concomitant Medications and Other Anti-Cancer Treatments

Patients who received RT may receive pre-medications before the RT. Treated patients may receive concomitant medications or other anti-cancer treatments during the whole study. Tabulations of pre-medications, concomitant medications and other anti-cancer treatments will be presented for both arms.

- Pre-medications for patients who received RT **(Table 36)**
- Concomitant medications for all randomized patients **(Table 36)**
- Anti-cancer treatments for patients before 30 days after randomization, by treatment group **(Table 37)**
- Anti-cancer treatments for all patients between 30 and 90 days after randomization, by treatment group **(Table 37)**

7.8 Quality of Life

Patient-reported QoL in this study is assessed at baseline and on days 30 and 90 from randomization by using Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) questionnaire. The following are the scoring algorithms for this instrument.

7.8.1 FACT-Hep

The FACT-Hep questionnaire is a 45-item instrument consisting of the 27-item cancer-specific QoL instrument FACT-G and a site-specific 18-item hepatobiliary subscale (HBS). The FACT-G consists of four subscales: (1) physical well-being (PWB); (2) social and family well-being (SFWB); (3) emotional well-being (EWB); and functional well-being (FWB). The FACT-Hep Trial Outcome Index (TOI) is the sum of the PWB, FWB, and HBS subscales. Individual scores for each subscale, FACT-G score, the trial outcome index (TOI), and the total FACT-HEP score will be scored according to FACT-Hep Scoring Guidelines as below with a subscale in which less than half of the items are completed treated as missing. The higher the score, the better the QoL.

- PWB subscale score = (28-GP1-GP2-CP3-GP4-GP5-GP6-GP7)* 7 / (number of items answered)
- SFWB subscale score = (GS1+GS2+CS3+GS4+GS5+GS6+GS7) * 7 / (number of items answered)
- EWB subscale score = (20-GE1+GE2 -GE3-GE4-GE5-GE6) * 6 / (number of items answered)
- FWB subscale score = (GF1+GF2+CF3+GF4+GF5+GF6+GF7) * 7 / (number of items answered)
- HBS subscale score = (56-C1-C2+C3+C4-C5+C6-Hep1-Cns7-Cx6-HI7+An7-Hep2-Hep3-Hep4-Hep5-Hep6-HN2-Hep8) * 18 / (number of items answered)
- FACT-G score = PWB score + SFWB score + EWB score + FWB score
- FACT-TOI = PWB subscale score + FWB subscale score + HBS subscale score
- FACT-HEP score = PWB score + SFWB score + EWB score + FWB score + HBS score

7.8.2 Data Sets

The analyses of quality of life data will be restricted to randomized patients who have completed the quality of life questionnaire at baseline and on days 30 or 90.

7.8.3 Compliance

Compliance will be described, for each time of evaluation, by the number and percentage of subjects who filled out a questionnaire in that time of evaluation. The denominator used in calculating the percentage for baseline will be all randomized subjects who are required to complete the assessment. The denominator used for days 30 and 90 assessments will be the number of subjects known to be alive at days 30 or 90 and who are required to complete the assessments **(Table 38).**

7.8.4 Baseline and Change Score Analysis

Descriptive statistics (mean and standard deviation) for FACT-Hep questionnaire scores at baseline will be presented for each subscale and total scores. The same statistics will be generated for change scores from baseline to day 30 and day 90. The comparability of mean baseline scores and change scores at day 30 and day 90 between treatment groups will be assessed using a Wilcoxon rank sum test (**Table 39 and Table 40**).

7.8.5 Proportion of Patients with Clinically Significant Improvement in QOL

A clinically significant improvement in QOL is defined by ≥ 5 points change in the Functional Assessment of Cancer Therapy (FACT) Hepatobiliary Subscale (FACT-HBS) and Trial Outcome Index (FACT-TOI) from baseline. Proportions of patients who had clinically significant improvement in QoL from baseline to day 30 and day 90 are summarized in **Table 41** and compared by a stratified CMH test adjusting for the stratification factor (HCC versus liver metastases) (**Table 41**).

8. Appendices

Appendix 1: Tables and Figure

Table 1: Patient Disposition

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC	BSC	Total
Randomized	N=**	N=**	N=**
Received RT	** (**)	NA[(1)]	NA[(1)]
Not received RT	** (**)	NA[(1)]	NA[(1)]
Reason for not received RT			
Progressive disease	** (**)	NA[(1)]	NA[(1)]
Intercurrent illness	** (**)	NA[(1)]	NA[(1)]
Patient refusal	** (**)	NA[(1)]	NA[(1)]
Adverse events	** (**)	NA[(1)]	NA[(1)]
Death	** (**)	NA[(1)]	NA[(1)]
Other	** (**)	NA[(1)]	NA[(1)]
Crossed over to RT	NA[(1)]	** (**)	NA[(1)]
Not crossed over to RT	NA[(1)]	** (**)	NA[(1)]
Reason for not crossed over to RT			
Progressive disease	NA[(1)]	** (**)	NA[(1)]
Intercurrent illness	NA[(1)]	** (**)	NA[(1)]
Patient refusal	NA[(1)]	** (**)	NA[(1)]
Adverse events	NA[(1)]	** (**)	NA[(1)]
Death	NA[(1)]	** (**)	NA[(1)]
Other	NA[(1)]	** (**)	NA[(1)]

[(1)] NA: Not Applicable

Table 2: Follow-up of patients

Data set: All Randomized Patients			
	Number of patients		
	RT+BSC N = **	BSC N = **	Total N = **
Number of patients alive	**	**	**
Follow-up (months)			
Median	**	**	**
Minimum-maximum	**-**	**-**	**-**

Table 3: Accrual by Center

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N = **	BSC N = **	Total N = **
Center #1	** (**)	** (**)	** (**)
Center #2	** (**)	** (**)	** (**)
Center #3	** (**)	** (**)	** (**)
...	** (**)	** (**)	** (**)

Table 4: Accrual by Stratification Factor (except center) at Randomization

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N = **	BSC N=**	Total N = **
Type of Liver Cancer			
HCC	** (**)	** (**)	** (**)
Liver metastases	** (**)	** (**)	** (**)

Source: CRF Eligibility Worksheet

Figure 1: **Accrual by Calendar Time**

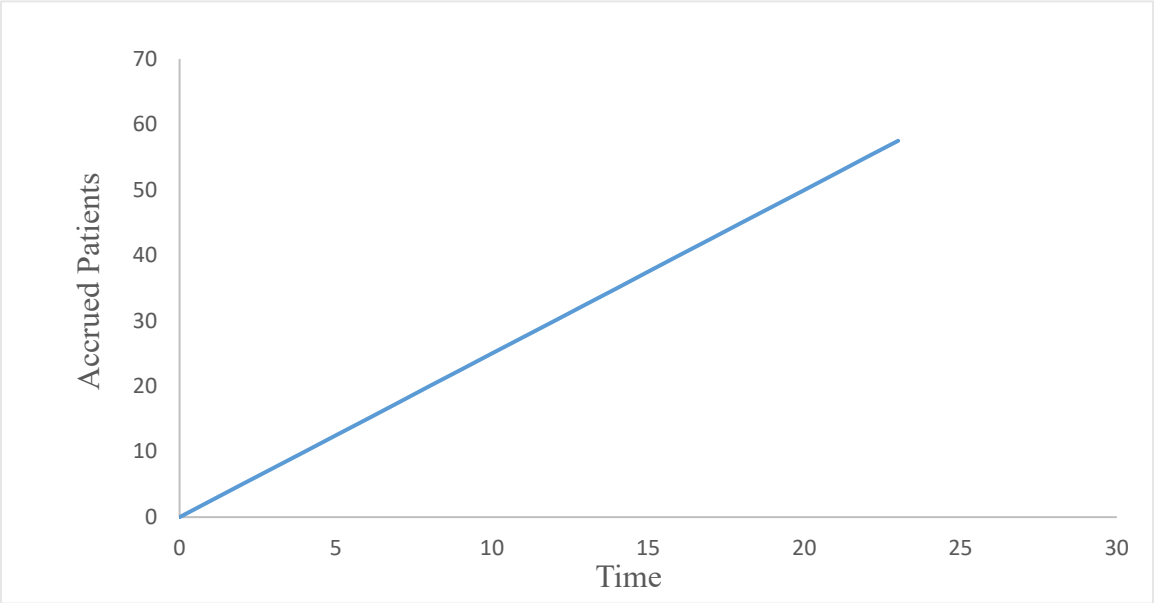

Table 5: Eligibility and Reasons for Ineligibility and Major Protocol Violations

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N = **	BSC N = **	Total N = **
Eligible	** (**)	** (**)	** (**)
Not Eligible	** (**)	** (**)	** (**)
Reason for ineligibility			
<Reason 1>	**	**	**
<Reason 2>	**	**	**
...	**	**	**
Major protocol violation			
<violation type 1>	**	**	**
<violation type 2>	**	**	**
...			

Table 6: Pre-treatment Characteristics at Baseline

Data set: All Randomized Patients

	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Gender			
Female	** (**)	** (**)	** (**)
Male	** (**)	** (**)	** (**)
Age (years)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
< 65	** (**)	** (**)	** (**)
≥ 65	** (**)	** (**)	** (**)
ECOG Performance Status			
0	** (**)	** (**)	** (**)
1	** (**)	** (**)	** (**)
2	** (**)	** (**)	** (**)
3	** (**)	** (**)	** (**)
4	** (**)	** (**)	** (**)
BMI (kg/m^2)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **

Table 7: Tumour Characteristics at Baseline

Data set: All Randomized Patients

	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Months from Initial Diagnosis to Randomization			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
Method of Initial Diagnosis			
Histology	** (**)	** (**)	** (**)
Cytology	** (**)	** (**)	** (**)
Standard Imaging Criteria	** (**)	** (**)	** (**)
Type of Liver Cancer			
HCC	** (**)	** (**)	** (**)
Liver Metastases	** (**)	** (**)	** (**)
Primary Tumour Type of Liver Metastases			
Type #1	** (**)	** (**)	** (**)
Type #2	** (**)	** (**)	** (**)
…	** (**)	** (**)	** (**)
Months From Liver Metastases Diagnosis to Randomization			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **
Presence of Extrahepatic Cancer			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Primary in Place for Extrahepatic Cancer			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Site of Metastases[(1)]			
Bone	** (**)	** (**)	** (**)
Abdominal (outside the liver)	** (**)	** (**)	** (**)
Lung	** (**)	** (**)	** (**)
Brain	** (**)	** (**)	** (**)
Other	** (**)	** (**)	** (**)
Portal Vein or Other Vascular Invasion			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Other Liver Disease			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Type of Other Liver Disease[(2)]			
Hepatitis B	** (**)	** (**)	** (**)
Hepatitis C	** (**)	** (**)	** (**)
Cirrhosis	** (**)	** (**)	** (**)
Other	** (**)	** (**)	** (**)

Extent of Liver Metastases			
Diffuse	** (**)	** (**)	** (**)
Multifocal	** (**)	** (**)	** (**)
Locally Advanced	** (**)	** (**)	** (**)
Child-Pugh Class			
A	** (**)	** (**)	** (**)
B	** (**)	** (**)	** (**)
C	** (**)	** (**)	** (**)
Child-Pugh Score			
5	** (**)	** (**)	** (**)
6	** (**)	** (**)	** (**)
7	** (**)	** (**)	** (**)
8	** (**)	** (**)	** (**)
9	** (**)	** (**)	** (**)
10	** (**)	** (**)	** (**)
11	** (**)	** (**)	** (**)
12	** (**)	** (**)	** (**)
13	** (**)	** (**)	** (**)
14	** (**)	** (**)	** (**)
15	** (**)	** (**)	** (**)

(1) Patient may have more than one site of metastases
(2) Patient may have more than one other liver disease

Table 8: Prior Surgery

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Prior surgical/diagnostic procedure			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Procedure / Site			
Procedure / Site 1	** (**)	** (**)	** (**)
Procedure / Site 2	** (**)	** (**)	** (**)
....	*** (**)	*** (**)	*** (**)

Table 9: Prior Radiotherapy

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Any Prior Radiotherapy			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Site of Prior Radiotherapy[(1)]			
Site #1	** (**)	** (**)	** (**)
Site #2	** (**)	** (**)	** (**)
Site #3	** (**)	** (**)	**(**)
...	** (**)	** (**)	** (**)
Total Dose of radiotherapy (cGy)			
N	**	**	**
Median	**	**	**
Min - Max	** - **	** - **	** - **

[(1)] Patient may have more than one site of radiotherapy

Table 10: Prior Systemic Therapy

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Any Prior Systemic Therapy			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Drug / Agent Name[1]			
Drug #1	** (**)	** (**)	** (**)
Drug #2	** (**)	** (**)	** (**)
Drug #3	** (**)	** (**)	**(**)
...	** (**)	** (**)	** (**)

[1] Patient may have more than one drug of prior systemic therapy

Table 11: Prior Regional Therapy

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N=**	BSC N=**	Total N=**
Any Prior Regional Therapy			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Therapy Name[1]			
TACE-DEB	** (**)	** (**)	** (**)
TACE-DEBIRI	** (**)	** (**)	** (**)
TAE-DEB	** (**)	** (**)	**(**)
TAE-DEBIRI	** (**)	** (**)	** (**)
Hepatic arterial chemotherapy	** (**)	** (**)	** (**)
Y90	** (**)	** (**)	** (**)
Other	** (**)	** (**)	** (**)

[1] Patient may have more than one therapy of prior regional therapy

Table 12: Baseline Grade 2 or Higher Adverse Events

Data set: All Randomized Patients									
	Number of patients (%)								
	RT+BSC N=**			BSC N=**			Total N=**		
	Grade			Grade			Grade		
	2	3	4	2	3	4	2	3	4
Patients with any AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE within category									
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...									
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...									

(1) Patients may have more than one event within a category.

Table 13: Baseline Hematology

Data set: All Randomized Patients			
	Number of Patients (%)		
	RT+BSC N = **	BSC N = **	Total N=**
Hemoglobin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)	** (**)
Platelet			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)	** (**)
Absolute Neutrophil Count			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)	** (**)

[(1)] Not done or outside the 14-day window prior to randomization

Table 14: Baseline Chemistry

Data set: All Randomized Patients			
	Number of Patients (%)		
	RT+BSC N = **	BSC N = **	Total N=**
Total bilirubin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Alkaline phosphatase			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
ALT			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
AST			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Albumin			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Serum Creatinine			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)
Alpha-Fetoprotein			
Normal	** (**)	** (**)	** (**)
High (2)	** (**)	** (**)	** (**)
Not reported (1)	** (**)	** (**)	** (**)

(1) Not done or outside the 14-day window prior to start of randomization
(2) High than upper lower limit

Table 15: Baseline Coagulation

Data set: All Randomized Patients			
	Number of Patients (%)		
	RT+BSC N = **	BSC N = **	Total N=**
INR			
Grade 0	** (**)	** (**)	** (**)
Grade 1	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)
Not reported [(1)]	** (**)	** (**)	** (**)

[(1)] Not done or outside the 14-day window prior to start of randomization

Table 16: Concomitant Medications at Baseline

Data set: All Randomized Patients			
	Number of patients (%)		
	RT+BSC N = **	BSC N = **	Total N=**
Any concomitant medication [(1)]			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)

[(1)]Any medication taken within 14 days prior to randomization.

Table 17: Summary of Radiotherapy

Data Set: All Radiotherapy Treated Patients		
	Within 30 days for patients on RT+BSC (%)	After 30 days for patients on BSC (%)
Number of Fractions		
N	**	**
Median	**	**
Min - Max	** - **	** - **
Maximum Planned Dose		
N	**	**
Median	**	**
Min - Max	** - **	** - **
Type of Motion Management		
None	** (**)	** (**)
ABC	** (**)	** (**)
4D CT	** (**)	** (**)
Other	** (**)	** (**)
Beam Arrangement		
APPA	** (**)	** (**)
Oblique POP	** (**)	** (**)
Other	** (**)	** (**)
Planning		
3D conformal	** (**)	** (**)
IMRT	** (**)	** (**)
VMAT	** (**)	** (**)
Other	** (**)	** (**)
Position Verification		
None	** (**)	** (**)
kV 2D	** (**)	** (**)
MV 2D	** (**)	** (**)
CBCT	** (**)	** (**)
Other	** (**)	** (**)

Table 18: Volumes of Radiotherapy

Data Set: All Radiotherapy Treated Patients		
	Within 30 days for patients on RT+BSC (%)	After 30 days for patients on BSC (%)
Liver Volume (cc)		
N	**	**
Median	**	**
Min - Max	** - **	** _ **
GTV Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
GTV Value (cc)		
N	**	**
Median	**	**
Min - Max	** - **	** _ **
CTV Value (cc)		
N	**	**
Median	**	**
Min - Max	** - **	** _ **
PTV Value (cc)		
N	**	**
Median	**	**
Min – Max	** - **	** - **

Table 19: Doses of Radiotherapy

Data Set: All Radiotherapy Treated Patients		
	Within 30 days for patients on RT+BSC N (%)	After 30 days for patients on BSC N (%)
Percent of ModPTV Encompassed by 8 Gy Prescribed Dose (%)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
ModPTV Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Maximum Dose to PTV (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Spinal Canal Maximum Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Liver Mean Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Right Kidney Mean Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Left Kidney Mean Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Bilateral Kidneys Mean Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Stomach Dose Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
Stomach Maximum Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Duodenum Dose Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
Duodenum Maximum Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **

Table 19 (Continued): Doses of Radiotherapy

Data Set: All Radiotherapy Treated Patients		
	Within 30 days for patients on RT+BSC N (%)	After 30 days for patients on BSC N (%)
Small Bowel Dose Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
Small Bowel Maximum Dose (Gy)		
N	**	**
Median	**	**
Min – Max	** _ **	** _ **
Large Bowel Dose Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
Large Bowel Maximum Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **
Peritoneal Dose Contoured		
Yes	** (**)	** (**)
No	** (**)	** (**)
Peritoneal Maximum Dose (Gy)		
N	**	**
Median	**	**
Min - Max	** _ **	** _ **

Table 20: Pain/Discomfort and Medication Assessment at Day 30 and Day 90

Data Set: All Randomized Patients		
	RT + BSC (%)	BSC (%)
Completion of Assessment at baseline		
Yes	** (**)	** (**)
No	** (**)	** (**)
Reason of Not Complete at baseline		
Patient too ill	** (**)	** (**)
Not documented / recalled	** (**)	** (**)
Patient confused	** (**)	** (**)
Patient refused for reason other than illness	** (**)	** (**)
Other	** (**)	** (**)
Completion of Assessment at Day 30		
Yes	** (**)	** (**)
No	** (**)	** (**)
Reason of Not Complete at Day 30		
Patient too ill	** (**)	** (**)
Not documented / recalled	** (**)	** (**)
Patient confused	** (**)	** (**)
Patient refused for reason other than illness	** (**)	** (**)
Other	** (**)	** (**)
Completion of Assessment at Day 90		
Yes	** (**)	** (**)
No	** (**)	** (**)
Reason of Not Complete at Day 90		
Patient too ill		
Not documented / recalled	** (**)	** (**)
Patient confused	** (**)	** (**)
Patient refused for reason other than illness	** (**)	** (**)
Other	** (**)	** (**)
	** (**)	** (**)

Table 21: Summary of BPI Scores at Baseline, Day 30 and Day 90

	Data set: All Randomized Patients					
	Baseline		Day 30		Day 90	
	RT+BSC	BSC	RT+BSC	BSC	RT+BSC	BSC
Worst pain						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain at its least						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Average pain						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain Now						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Percentage relief in pain by treatment						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with general activity						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with mood						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with walking ability						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with normal work						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with relationship						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with sleep						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Pain interference with enjoyment of life						
N	**	**	**	**	**	**
Mean (standard deviation)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)

Table 22: Proportion of Patients Experiencing a Significant Improvement in Symptoms

	RT+BSC N (%)	BSC N (%)	P-value
All patients who had baseline and day 30 assessments			
Experiencing a Significant Improvement in Symptoms [2] at Day 30 from baseline	** (**.**)	** (**.**)	0.*** [1]
HCC patients who had baseline and day 30 assessments			
Experiencing a Significant Improvement in Symptoms [2] at Day 30 from baseline	** (**.**)	** (**.**)	0.***
Liver metastases patients who had baseline and day 30 assessments			
Experiencing a Significant Improvement in Symptoms [2] at Day 30 From baseline	** (**.**)	** (**.**)	0.***
All randomized patients [3]			
Experiencing a Significant Improvement in Symptoms [2] at Day 30 From baseline	** (**.**)	** (**.**)	0.*** [1]
All patients who had baseline and day 90 assessments			
Experiencing a Significant Improvement in Symptoms [2] at Day 90 From baseline	** (**.**)	** (**.**)	0.*** [1]
All patients on BSC who crossed over to receive RT after day 30 assessments			
Experiencing a Significant Improvement in Symptoms [2] at Day 90 from Day 30	NA[4]	** (**.**)	NA[4]

[1] Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)
[2] A Significant Improvement in Symptoms is defined as ≥ 2 points reduction in worst pain score on BPI.
[3] Those patients without assessment at day 30 are included in the "no improvement" group.
[4] Not applicable.

Table 23: Proportion of Patients Achieving Improvement (≥ 2 points reduction) in Other BPI Scores

	Baseline to Day 30 [1]			Baseline to Day 90 [2]			Days 30 to 90[3]
	RT+BSC N (%)	BSC N (%)	CMH P-value [4]	RT+BSC N (%)	BSC N (%)	CMH P-value [4]	BSC N (%)
Pain at its least	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Average pain	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain Now	** (**)	** (**)	0.***	** (**)	**(**)	0.***	**(**)
Percentage relief in pain by treatment	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with general activity	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with mood	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with walking ability	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with normal work	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with relationship	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with sleep	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)
Pain interference with enjoyment of life	** (**)	** (**)	0.***	** (**)	** (**)	0.***	** (**)

(1) For patients who had baseline and day 30 assessments;
(2) For patients who had baseline and day 90 assessments;
(3) For patients on BSC who crossed over to receive RT Arm after day 30 assessments
(4) Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)

Table 24: Opioid and Non-Opioid Intake

	Data set: All Randomized Patients					
	Baseline		Day 30		Day 90	
	RT+BSC	BSC	RT+BSC	BSC	RT+BSC	BSC
Any Opioid Medication Intake						
No	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Generic Opioid Name[1]						
Opioid #1	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Opioid #2	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Opioid #3	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
…	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Number of Opioid Taken[1]						
N	**	**	**	**	**	**
Median	**	**	**	**	**	**
Min - Max	** **	** **	** **	** **	** **	** **
Oral morphine equivalents						
N	**	**	**	**	**	**
Median	**	**	**	**	**	**
Min - Max	** **	** **	** **	** **	** **	** **
Any Non-Opioid Medication Intake						
No	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Generic Non-Opioid Name[1]						
Opioid #1	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Opioid #2	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Opioid #3	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
…	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Number of Non-Opioid Taken[1]						
N	**	**	**	**	**	**
Median	**	**	**	**	**	**
Min - Max	** **	** **	** **	** **	** **	** **

[1] Patient may have more than one opioid or non-opioid medications.

Table 25: Proportion of Patients with Reduction in Opioid Use at Day 30

Patients who have completed Pain/Discomfort and Medication Questionnaires at baseline and day 30	RT+BSC N (%)	BSC N (%)	CMH P-value [1]
Patients with 25% Reduction in Opioid Use[2]	** (**.**)	** (**.**)	0.***

[1] Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)
[2] 25% Reduction in opioid use from baseline to day 30 (employing daily morphine equivalence scale).

Table 26: Proportion of Patients with Improved BPI and no Increasing Opioid Use at Day 30

Patients who have completed Pain/Discomfort and Medication Questionnaires at baseline and day 30	RT+BSC N (%)	BSC N (%)	CMH P-value [*]
Patients with Improved BPI and no Increasing Opioid Use	** (**.**)	** (**.**)	0.***

* Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)

Table 27: All Deaths

Data set: All Randomized Patients		
	Number of Patients (%)	
	RT+BSC N=**	BSC N=**
Number of Patients who died	** (**)	** (**)
Cause of Death		
Cancer Only	**	**
Adverse Event Possibly/Probably/Definitely Related Protocol Treatment	**	**
Complication from a Non-protocol treatment for This Malignancy	**	**
Other Primary Malignancy	**	**
Other Condition or Circumstance	**	**

Table 28: Kaplan-Meier Estimate for Proportion of Patients Alive at Day 90

Data set: All Randomized Patients			
	N	Kaplan-Meier Estimate for Proportion of Patients Alive at Day 90 (95% CI)	Log Rank P-value[*]
Treatment Arm			0.***
RT+BSC	**	**.** (**.**, **.**)	
BSC	**	**.** (**.**, **.**)	

* Stratified Log Rank test adjusting for the stratification factor (HCC versus liver metastases)

Table 29: Grade 2 or Higher Adverse Events

	Number of patients (%)			
*Day 30 After Randomization for All Treated Patients on RT+BSC (N=**)*				
	Grade			
	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	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)
*Day 90 After Randomization for All Treated Patients on RT+BSC (N=**)*				
	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	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a category.

Note: The same type of table will be made for BSC arm and at day 90 only for patients on BSC who crossed over to RT after day 30 assessment.

Table 30: Proportion of Patients with Grade ≥ 2 Adverse Event at Day 30 and Day 90

All Treated Patients			
	RT+BSC	BSC	CMH P-value [(*)]
Any Grade ≥ 2 Adverse Event at Day 30	** (**.**)	** (**.**)	0.***
Any Grade ≥ 2 Adverse Event at Day 90	** (**.**)	** (**.**)	0.***

* Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)

Table 31: Grade 2 or Higher Radiotherapy Related Adverse Events

	Number of patients (%)				
*Day 30 After Randomization for All Treated Patients on RT+BSC (N=**)*					
	Grade				Any ≥2 grade
	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	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)
*Day 90 After Randomization for All Treated Patients on RT+BSC (N=**)*					
	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	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)
*Day 90 After Randomization for patients on BSC who crossed over to RT after day 30 assessment (N=**)*					
	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	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a category.

Table 32: Severe Adverse Events: Any and Severe

	Number of patients (%)			
*Day 30 After Randomization for All Treated Patients on RT+BSC (N=**)*				
	Grade			Any ≥ 3 grade
	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	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)
*Day 90 After Randomization for All Treated Patients on RT+BSC (N=**)*				
	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	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a category.

Note: The same type of table will be made for BSC arm and at day 90 only for patients on BSC who crossed over to RT after day 30 assessment.

Table 33: Hematology During Follow-up

	Day 30 for all treated patients		Day 90 for all treated patients		Day 90 for all BSC patients crossed over to RT
	RT+BSC N = **	BSC N = **	RT+BSC N = **	BSC N = **	BSC N = **
Platelets					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)
Hemoglobin					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)

Table 34: Serum Chemistry During Follow-up

	Day 30 for all treated patients		Day 90 for all treated patients		Day 90 for all BSC patients crossed over to RT
	RT+BSC N = **	BSC N = **	RT+BSC N = **	BSC N = **	BSC N = **
Total bilirubin					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)
Albumin					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)
ALT					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)
AST					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)
Alpha-Fetoprotein					
Normal	** (**)	** (**)	** (**)	** (**)	** (**)
High[(1)]	** (**)	** (**)	** (**)	** (**)	** (**)
Serum Creatinine					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)

(1) High than upper lower limit

Table 35: Coagulation Test During Follow-up

	Day 30 for all treated patients		Day 90 for all treated patients		Day 90 for all BSC patients crossed over to RT
	RT+BSC N = **	BSC N = **	RT+BSC N = **	BSC N = **	BSC N = **
INR					
Grade 1	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 2	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 3	** (**)	** (**)	** (**)	** (**)	** (**)
Grade 4	** (**)	** (**)	** (**)	** (**)	** (**)

Table 36: Pre-medication and Concomitant Medication

Data set: All Treated Patients		
	Number of patients (%)	
	RT+BSC	BSC
Any pre-medication before radiotherapy[1]		
No	** (**)	** (**)
Yes	** (**)	** (**)
Any concomitant medication[2]		
No	** (**)	** (**)
Yes	** (**)	** (**)

[1] Within 30 days from randomization for patients on RT+BSC and after 30 days for patients on BSC crossed over to RT.
[2] Patients may have received more than one concomitant medication.

Table 37: Anti-Cancer Treatment

Data set: All Randomized Patients		
	Number of patients (%)	
	RT+BSC N=**	BSC N =**
Any anti-cancer treatment before 30 days after randomization	** (**)	** (**)
Systemic therapy [1]	** (**)	** (**)
Drug 1 …	** (**)	** (**)
Radiotherapy [1]	** (**)	** (**)
Site 1 …	** (**)	** (**)
Surgery [1]	** (**)	** (**)
Procedure 1 …	** (**)	** (**)
Other [1]	** (**)	** (**)
Therapy 1 …	** (**)	** (**)
Any anti-cancer treatment between 30 and 90 days after randomization	** (**)	** (**)
Systemic therapy [1]	** (**)	** (**)
Drug 1 …	** (**)	** (**)
Radiotherapy [1]	** (**)	** (**)
Site 1 …	** (**)	** (**)
Surgery [1]	** (**)	** (**)
Procedure 1 …	** (**)	** (**)
Other [1]	** (**)	** (**)
Therapy 1 …	** (**)	** (**)

[1] Patients could have more than one type of anti-cancer treatment.

Table 38: Compliance Rate with QoL Assessment by Treatment Arm

	RT+BSC		BSC	
	N[(1)]	Received (%)	N[(1)]	Received (%)
Baseline	**	** (**)	**	** (**)
Day 30	**	** (**)	**	** (**)
Day 90	**	** (**)	**	** (**)

[(1)] The denominator used in calculating the percentage for baseline will be all randomized subjects. The denominator used for all other time points will be the number of alive subjects required to complete the specific follow-up assessment.

Table 39: Summary of Baseline QoL Scores

	RT+BSC	BSC	P value*
Subscale Scores			
PWB			0.***
N	**	**	
Mean	**	**	
STD	**	**	
...	...	...	
FACT-G			0.***
N	**	**	
Mean	**	**	
STD	**	**	
The total FACT-Hep			0.***
N	**	***	
Mean	**	***	
STD	**	***	
FACT-TOI			0.***
N	**	**	
Mean	**	**	
STD	**	**	

* Wilcoxon rank sum test

Table 40: Summary of QOL Change Scores from Baseline at Each Time Period

	RT+BSC	BSC	P Value**
Subscale Scores*			
At Day 30			.**
N	**	**	
Mean	**	**	
STD	**	**	
At Day 90			.**
N			
Mean	**	**	
STD	**	**	

* Table will be provided for each subscale scores.
** Wilcoxon rank sum test

Table 41: Proportion of Patients with Clinically Significant Improvement in QoL

	RT+BSC N (%)	BSC N (%)	CMH P-value (*)
Patients with QoL at baseline and day 30	**	**	**
With Clinically significant improvement (**) in QoL	** (**.**)	** (**.**)	0.***
≥5 point change in FACT-HBS	** (**.**)	** (**.**)	0.***
≥5 point change in FACT-TOI	** (**.**)	** (**.**)	0.***
Patients with QoL at baseline and day 90	**	**	
With Clinically significant improvement (**) in QoL	** (**.**)	** (**.**)	0.***
≥5 point change in FACT-HBS	** (**.**)	** (**.**)	0.***
≥5 point change in FACT-TOI	** (**.**)	** (**.**)	0.***

* Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)
** ≥5 point change in both FACT-HBS and FACT-TOI