Protocol Template- Radiotherapy Clinical Trials

The development of high-quality protocols allows the proper conduct of clinical trials.

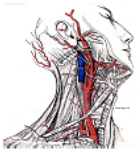
The intended purpose of the protocol template is to provide a guide to the minimum elements required for Phase II/III clinical trials involving radiotherapy with or with combination systemic therapy.

It provides an opportunity of promoting harmonization of protocols across the HNCIG membership, with the potential of facilitating inter-group collaboration and meta-analyses across clinical trials from different trial groups. It is not intended to replace Trial group-specific templates.

The template below is a draft version for further discussion and refinement and then modification by the Protocol & Endpoints Committee.

Sources/References

1. Templates from established clinical trials groups
2. SPIRIT 2013 explanation and elaboration; guidance for protocols of clinical trials. Chan AW et al. BMJ Research Methods and Reporting 2013.
3. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6 (R2). Version 4 (Nov 2016).



Head and Neck Cancer International Group (HNCIG)

HNCIG Protocol Number XX.XX

Lead Trial Group (Sponsor) – *insert name*
Collaborating Trial Groups – *insert name(s)*

Title – study design, population, intervention(s), trial acronym (if applicable)

Protocol Version – *insert number, insert date*

Trial Chairperson - *insert name & contact details*

Co-Chairperson - *insert name & contact details (where applicable)*

Trial Management Committee – *insert names, titles, role (eg statistician)*

Central Trial Centre/Organisation - *insert name and contact details*

Central Trial Coordinator - *insert name and contact details*

Abbreviations

Table of Contents

Trial Summary

- Disease type
- Study design (eg Phase III)
- Intervention (s)
- Key eligibility criteria (inclusion/exclusion)
- Target sample size
- Primary outcome(s)
- Key secondary outcomes
- Timing of registration
- Timing of consent
- Trial analyses timelines

Trial Schema

- diagram (preferably)

Introduction & Background

- Study disease
- Rationale
- Correlative/Exploratory studies background

Trial Objectives

- Hypothesis (es)
- Objectives
    - Primary
    - Secondary
    - Exploratory (if applicable)
- Endpoints
    - Primary
    - Secondary
    - Exploratory (if applicable)

Trial Design

- description of trial design eg randomized double blinded
- Intervention(s)
- Duration of therapy
- Duration of follow up

Participant selection and Eligibility

- Source of participants
- Accrual numbers & timelines
- Eligibility criteria
    - inclusion
    - exclusion

Registration and Randomisation

- insert registration and randomisation procedures
    - Site registration
    - Patient registration

Trial Participants assessment

- Pre-registration assessments (eg informed consent, eligibility)
- On-treatment assessments & timing (eg toxicity, disease status, bloods, imaging)
- Follow up assessments & timing (eg toxicity, disease status, bloods, imaging)

  (inserted timing as an appendix)

Screening

- rules about screening logs
- rules about informed consent
- rules about participation in other research/trials

Discontinuation/Withdrawal

- Protocol Treatment discontinuation rules (eg unacceptable toxicity)
- Withdrawal from trial (reasons and rules regarding collection of further data)

Endpoints Definitions/Measurement of Effect

- Local (complete/partial response/progression/recurrence)
- Regional (complete/partial response/progression/recurrence)
- Distant (complete/partial response/progression/recurrence)
- Other (eg biological markers)

  -description of management of progression/recurrence (if applicable)

  -will await Datecan project result for endpoint definition consensus

Radiotherapy Treatment Regimen

- Pre-trial treatment (eg patients require dental assessment)
- Treatment timelines (eg begin treatment within 6 weeks of surgery)
- Radiotherapy planning & delivery
    - Planning simulation/procedures
    - Target Volume definitions (GTV, CTV, PTV)
    - Organs at Risk Volumes
    - Techniques (eg IMRT)
- Dose prescription & constraints
- OAR dose constraints
- Dose reporting
- Treatment verification
- Treatment scheduling and management of gaps/delays

- Radiotherapy Quality Assurance

Systemic Therapy/Surgery (if applicable)

- **Chemotherapy/Systemic therapy**
    - Treatment schedule
    - Treatment regimens, dosing and administration
    - Known toxicities
    - Dose modifications & delays
    - Drug supply, storage, accountability and disposal

- **Surgery**
    - Surgery details
    - Treatment sequencing

Patient Reported Outcomes (where applicable)

- Instruments to be used
- Method of administration and scheduling
- Compliance recording
- Handling of missing data

Translation /Correlative Studies

- Rationale for studies
- Analysis(es) to be performed
- Sampling Collection
- Handling & Storage

Trial Administration & Quality Assurance

- Participating centres
- Investigator training
- Data acquisition (eg data collection with eCRF's)
- Definition of study end date
- Archiving rules
- Quality Assurance Reviews (what elements will be QA'd and when)

Adverse Event Reporting

- Definitions AE & SAE
- Definition of causality
- Reporting method
- Pregnancy

Statistical Considerations

- study design
- sample size/power calculations
- sequence generation
- endpoints definitions
- assessment of response
- statistical analysis plan for primary and secondary endpoints
- interim analyses and early termination criteria

- secondary analysis rules (where applicable)

Research Governance

- Sponsor & Funding
- Independent Data Safety Monitoring Committee

Patient protection & Ethical Considerations

- Ethical Principles and Regulatory Compliance
- Confidentiality
- Security and Back up handling of data
- Indemnity & insurance

Publication & Presentation Policy

References

Appendices