1. Record Nr. UNINA9910959204203321

Titolo	Textbook of clinical trials in oncology : a statistical perspective / / edited by Susan Halabi, Stefan Michiels
Pubbl/distr/stampa	Boca Raton, Florida : , : CRC Press, , [2019]
ISBN	1-351-62097-5 1-351-62096-7 1-315-11208-6
Edizione	[1st ed.]
Descrizione fisica	1 online resource (645 pages)
Disciplina	616.99400727
Soggetti	Cancer - Research - Statistical methods Clinical trials - Statistical methods
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Note generali	"A Chapman & Hall Book"--Title page.
Nota di bibliografia	Includes bibliographical references and index.
Nota di contenuto	Cover -- Half Title -- Title Page -- Copyright Page -- Dedication -- Contents -- Acknowledgment -- Editors -- Contributors -- 1. Introduction to Clinical Trials -- 1.1 Scope and Motivation -- 1.2 Resources -- 1.3 Conclusion -- References -- Section I: Early to Middle Development -- 2. Selection of Endpoints -- 2.1 Introduction -- 2.2 Key Definitions and Endpoint Selection -- 2.3 Patient-Centered Endpoints -- 2.3.1 Overall Survival -- 2.3.2 Adverse Events and Toxicity -- 2.3.2.1 Dose-Limiting Toxicity -- 2.3.3 Health-Related Quality of Life -- 2.3.3.1 European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 30 Items -- 2.3.3.2 Functional Assessment of Cancer Therapy - General Version -- 2.3.3.3 Short-Form 36 Survey -- 2.4 Tumor-Centered Endpoints -- 2.4.1 Assessment of Response in Tumor-Centered Endpoints -- 2.4.2 Progression-Free Survival and Time to Progression -- 2.4.3 Disease-Free Survival -- 2.4.4 Time to Treatment Failure -- 2.4.5 Objective Response Rate and Duration of Response -- 2.5 Endpoints under Evaluation -- 2.5.1 Pathologic Complete Response (pCR) -- 2.5.2 Immune-Related Response Criteria (irRC) -- References -- 3. Innovative Phase I Trials -- 3.1 Early-Phase Designs for Cytotoxic Agents -- 3.1.1 Designs Based on Safety Endpoints -- 3.1.1.1 Rule-Based Algorithms: "A + B" Designs -- 3.1.1.2 Dose-Expansion Cohorts

(DECs) -- 3.1.1.3 Model-Based Designs -- 3.1.2 Designs Based on Safety and Efficacy Endpoints -- 3.2 Early-Phase Designs: Moving Beyond Cytotoxic Agents -- 3.2.1 The Bayesian Quasi-CRM for Continuous Toxicity Endpoints -- 3.2.1.1 Illustrative Example of Modeling Toxicity Scores: Quasi-CRM versus Conventional CRM -- 3.2.2 Novel Endpoints in Early-Phase Trials -- 3.2.2.1 Dose-Finding Designs Incorporating Pharmacokinetics (PK) Measures -- 3.2.2.2 Dose-Finding Designs for Immunotherapies.
3.3 Conclusion -- References -- 4. Current Issues in Phase II Cancer Clinical Trials -- 4.1 Introduction -- 4.2 Single-Arm Phase II Trials -- 4.2.1 Optimal Two-Stage Designs -- 4.2.2 Estimation of Response Rate -- 4.2.3 Confidence Interval -- 4.2.4 P-Value Calculation -- 4.3 Phase II Trials with Heterogeneous Patient Populations -- 4.3.1 Single-Stage Designs -- 4.3.2 Example 4.6 -- 4.3.3 Two-Stage Designs -- 4.3.4 Example 4.7 -- 4.3.5 Conditional P-Value -- 4.4 Randomized Phase II Trials -- 4.4.1 Single-Stage Design -- 4.4.2 Two-Stage Design -- 4.4.2.1 Choice of a1 and a2 -- 4.4.2.2 Choice of n1 and n2 -- 4.4.3 Numerical Studies -- 4.5 Conclusion -- References -- 5. Design and Analysis of Immunotherapy Clinical Trials -- 5.1 Introduction -- 5.2 Immune-Related Toxicity -- 5.3 Delayed Treatment Benefit -- 5.4 Marker Stratification -- 5.5 Treatment Benefit in a Subset of Patients -- 5.6 Conclusion -- Acknowledgment -- References -- 6. Adaptive Designs -- 6.1 Introduction -- 6.2 Adaptive Designs for Dose-Finding Studies -- 6.3 Population Finding -- 6.4 Response-Adaptive Randomization -- 6.5 Sample Size Re-Estimation -- 6.6 Adaptive Seamless Designs -- 6.7 Conclusion -- References -- Section II: Late Phase Clinical Trials -- 7. Sample Size Calculations for Phase III Trials in Oncology -- 7.1 Introduction -- 7.2 Basics of Sample Size Calculation in Phase III Oncology Trials -- 7.2.1 Required Parameters and Settings -- 7.2.2 Relationships among Survival Parameters -- 7.2.3 Basic Parameters: -- 7.2.4 Sample Size Calculations Using Additional Parameters -- 7.2.5 Sample Size Calculations Based on the Log-Rank Test -- 7.3 Software for Sample Size Calculations -- 7.4 Superiority Trials -- 7.4.1 Purpose of Superiority Trials -- 7.4.2 The Sample Size Calculation Methods Used in Various Software Programs -- 7.4.2.1 SAS Power Procedure: TWOSAMPLESURVIVAL Statement.
7.4.2.2 PASS: Log-Rank Tests and Tests for Two Survival Curves Using Cox's Proportional Hazards Model -- 7.4.2.3 SWOG Statistical Tool: Two-Arm Survival -- 7.4.3 Example of a Superiority Trial (the EAGLE Trial) -- 7.4.4 Comparison of the Sample Size Calculated with Each Software Program -- 7.4.4.1 SAS Power Procedure -- 7.4.4.2 PASS: Log-Rank Tests (Input Median Survival Times) -- 7.4.4.3 PASS: Tests for Two Survival Curves Using Cox's Proportional Hazards Model -- 7.4.4.4 SWOG Statistical Tool Website -- 7.4.4.5 Interpretation of the Results -- 7.5 Non-Inferiority Trials -- 7.5.1 Purpose of Non-Inferiority Trials and Formulas to Calculate the Sample Size -- 7.5.2 Specification of the Non-Inferiority Margin, -- 7.5.3 The Sample Size-Calculation Methods Used in Each Software Program -- 7.5.3.1 SAS -- 7.5.3.2 PASS: Non-Inferiority Log-Rank Tests and Tests for Two Survival Curves Using Cox's Proportional Hazards Model -- 7.5.3.3 SWOG Statistical Tool: Two-Arm Survival -- 7.5.4 Example Trial (JCOG0404 Trial) -- 7.5.5 Comparison of Sample Sizes Calculated with Each Software Program -- 7.5.5.1 SAS Power Procedure -- 7.5.5.2 PASS: Non-Inferiority Log-Rank Tests -- 7.5.5.3 PASS: Non-Inferiority Tests for Two Survival Curves Using Cox's Proportional Hazards Model -- 7.5.5.4 SWOG Statistical Tool Website -- 7.5.6 Interpretation of the Results -- 7.6 Other -- 7.6.1 Consideration for One-Sided or Two-Sided Tests -- 7.6.2 Violation of the Proportional-Hazards and

Exponential-Curve Assumptions -- 7.7 Conclusion -- References -- 8. Non-Inferiority Trial -- 8.1 Introduction -- 8.2 Assumptions for NI Trials -- 8.2.1 The Constancy of the Control Effect -- 8.2.2 Assay Sensitivity -- 8.3 Design -- 8.3.1 Selecting the Active Control -- 8.3.2 Determining the NI Margin -- 8.3.3 Statistical Algorithm for Assessing Non-Inferiority -- 8.3.3.1 The Fixed-Margin Approach.
8.3.3.2 Synthesis Approach -- 8.3.4 Sample Size -- 8.3.5 Other Design Alternatives and Issues -- 8.3.5.1 Three-Arm Studies -- 8.3.5.2 Switching between NI and Superiority -- 8.3.5.3 Interim Analyses -- 8.4 Trial Conduction -- 8.5 Analyses -- 8.5.1 Analysis Populations -- 8.5.2 Missing Data -- 8.5.3 NI and Superiority -- 8.6 Reporting -- 8.7 Examples -- References -- 9. Design of Multi-Arm, Multi-Stage Trials in Oncology -- 9.1 Introduction -- 9.2 Notation -- 9.2.1 Multi-Arm Trial -- 9.2.2 Multi-Arm, Multi-Stage -- 9.3 Determining Statistical Quantities for Multi-Arm Trials -- 9.3.1 Distribution of Test Statistics from a Multi-Arm Trial -- 9.3.1.1 Normal Outcomes -- 9.3.1.2 Binary Outcome -- 9.3.1.3 Time-to-Event Outcome -- 9.3.2 Evaluating the Operating Characteristics of a Multi-Arm Design -- 9.3.2.1 Type I Error Rate -- 9.3.3 Power -- 9.3.3.1 Conjunctive Power -- 9.3.3.2 Disjunctive Power -- 9.3.3.3 Least Favorable Configuration -- 9.3.3.4 Comparison of Power -- 9.3.4 Case Study -- 9.4 Designing Multi-Arm Multi-Stage Trials -- 9.4.1 Distribution of Test Statistics -- 9.4.2 Group-Sequential MAMS -- 9.4.2.1 Example -- 9.4.2.2 Extensions -- 9.4.3 Drop-the-Loser Multi-Arm Trials -- 9.4.3.1 Notation and Operating Characteristics -- 9.4.3.2 Extensions -- 9.4.4 Case Study -- 9.5 Conclusion -- References -- 10. Multiple Comparisons, Multiple Primary Endpoints and Subpopulation Analysis -- 10.1 Sources of Multiplicity in Oncology Trials -- 10.1.1 Introductory Example -- 10.2 Multiple Testing Procedures -- 10.2.1 Basic Concepts -- 10.2.1.1 Error Rate in Confirmatory Clinical Trials -- 10.2.1.2 Single-Step and Stepwise Procedures -- 10.2.1.3 Closed Testing Procedures -- 10.2.1.4 Adjusted Critical Values and Adjusted p-Values -- 10.2.1.5 Simultaneous Confidence Intervals -- 10.2.2 Common Multiple Testing Procedures -- 10.2.2.1 Bonferroni Test.
10.2.2.2 Holm Procedure -- 10.2.2.3 Hochberg Procedure -- 10.2.2.4 Numerical Illustration -- 10.2.3 Gatekeeping and Graphical Procedures Based on the CTP -- 10.2.3.1 Bonferroni-Based Graphical Procedures -- 10.2.3.2 Procedures Based on Asymptotic Normality -- 10.2.4 Multiplicity Adjustment for Other Types of Endpoints -- 10.3 Multiple Comparison Procedures in Oncology -- 10.3.1 The Scope of Multiplicity Adjustment -- 10.3.2 Multiple Endpoints Complications in Group Sequential Designs -- 10.3.3 Outlook on Future Developments -- 10.4 Conclusion -- References -- 11. Cluster Randomized Trials -- 11.1 Introduction -- 11.2 Randomization -- 11.2.1 Matching and Stratification -- 11.2.2 Constrained Randomization -- 11.2.3 Minimization -- 11.3 Analysis -- 11.3.1 Continuous Outcomes -- 11.3.1.1 Model -- 11.3.1.2 Estimation and Inference -- 11.3.1.3 Example -- 11.3.2 Dichotomous Outcomes -- 11.3.2.1 Cluster-Level Proportions Model -- 11.3.2.2 Cluster-Level Log-Odds Model -- 11.3.2.3 Estimation and Inference -- 11.3.2.4 Example -- 11.3.3 Other Analysis Methods -- 11.4 Sample Size and Power -- 11.4.1 Continuous Outcomes -- 11.4.1.1 Power -- 11.4.1.2 Sample Size: Number of Clusters -- 11.4.1.3 Sample Size per Cluster -- 11.4.1.4 Unequal ICCs in Treatment Arms -- 11.4.1.5 Unequal Allocation -- 11.4.1.6 Covariates -- 11.4.1.7 Varying Cluster Sizes -- 11.4.1.8 Matching and Stratification -- 11.4.2 Dichotomous Outcomes -- 11.4.2.1 Sample Size and Power -- 11.4.2.2 Sample Size per Cluster -- 11.4.2.3 Unequal ICCs in Treatment Arms -- 11.4.2.4 Unequal Allocation --

11.4.2.5 Covariates -- 11.4.2.6 Varying Cluster Sizes -- 11.5 Additional Resources -- 11.5.1 Resources for Other Designs -- 11.5.2 Resources for Power and Sample Size Calculation -- References -- 12. Statistical Monitoring of Safety and Efficacy -- 12.1 Introduction -- 12.2 Monitoring of Safety.
12.2.1 Introduction.

Sommario/riassunto

There is an increasing need for educational resources for statisticians and investigators. Reflecting this, the goal of this book is to provide readers with a sound foundation in the statistical design, conduct, and analysis of clinical trials. Furthermore, it is intended as a guide for statisticians and investigators with minimal clinical trial experience who are interested in pursuing a career in this area. The advancement in genetic and molecular technologies have revolutionized drug development. In recent years, clinical trials have become increasingly sophisticated as they incorporate genomic studies, and efficient designs (such as basket and umbrella trials) have permeated the field. This book offers the requisite background and expert guidance for the innovative statistical design and analysis of clinical trials in oncology. Key Features: Cutting-edge topics with appropriate technical background Built around case studies which give the work a "hands-on" approach Real examples of flaws in previously reported clinical trials and how to avoid them Access to statistical code on the book's website Chapters written by internationally recognized statisticians from academia and pharmaceutical companies Carefully edited to ensure consistency in style, level, and approach Topics covered include innovating phase I and II designs, trials in immune-oncology and rare diseases, among many others