



What makes Oncology special?

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- Whether you are a SAS programmer in pharmaceutical industry, a bank or insurance company your job is to:
 - restructure data sets
 - program statistical analyses
 - create reports according to the provided requirements and specifications.
- With a few differences
- Even if still SAS is SAS and statistical reporting is still about tables, figures and listings.
- Wrong: Oncology is special!

Agenda



- Special Disease
- Special Data
- Special Analyses
- Special Reporting
- Conclusion



- Oncology is a very rapidly developing area in medicine, but also in science.
 - The investigation of molecular pathways and genetic mutations involved in tumour genesis is ongoing.

- Oncology will be the biggest therapeutic area in 20 years!

- A sense of Urgency
 - Many cancers develop very fast, and most clinical trials start as second line treatments of advanced carcinomas
 - Patients' median survival time as short as 6 months.
 - In Oncology clinical trials are either accelerated, priority or on fast track.



■ Trial design Ethics

- Placebo control arm or not
 - Settings: “prevention”, adjuvant, or early disease
 - Placebo-alone control usually not feasible in advanced cancer
 - Pot practical and ethical for cancer patient use a placebo-alone treatment arm
 - Placebo possible in combination therapy



- Special Schedule:
 - CRF organised in Cycle and not in Visit
- Tumor Assessment
- Concomitant medications:
 - Drug/drug interaction
- Additional data -> identify subpopulation for targeted therapies
 - Biomarkers
 - **Challenge for Programming:**
 - Always difficult to plan Programming for Biomarkers:
 - Late timelines
 - Standard Data structure is difficult -> often done in small local laboratories



■ CTCAE grades

- In Oncology, Laboratory grades are derived following the NCI-CTCAE definition:
 - The **NCI-CTCAE 4.2** (National Cancer Institute - Common Terminology Criteria for Adverse Events) provides definitions for AE terms and a grading (severity) scale for each AE. Eg below:

Investigations					
Adverse Event	Grade				
	1	2	3	4	5
Platelet count decreased	<LLN - 75,000/mm ³ ; <LLN - 75.0 x 10 ⁹ /L	<75,000 - 50,000/mm ³ ; <75.0 - 50.0 x 10 ⁹ /L	<50,000 - 25,000/mm ³ ; <50.0 - 25.0 x 10 ⁹ /L	<25,000/mm ³ ; <25.0 x 10 ⁹ /L	-
Definition: A finding based on laboratory test results that indicate a decrease in number of platelets in a blood specimen.					

- **Challenge for Programming:**
 - Use of local and/or Central lab
 - Conversion in standard Units
 - Missing units is also a problem when converting
 - Missing Lower/Upper Normal Ranges



■ Dosing information

- Compliance: **Relative Dose Intensity (RDI)**
 - RDI is a term that refers to the amount of a particular treatment given over a specific time in relation to what was ordered
- Dose reduction: A reduction is defined as a decrease in dose from the protocol planned dose or a decrease from the previous non-zero dose
- Dose interruption: An interruption is defined as a 0mg/0tablets dose given on one or more days.
- **Challenge for Programming:**
 - Dealing with dosing in relation to cycles
 - Definitions and derivations with different time schedule, unit...



■ Clinical Trial Endpoints

- Disease Free Survival (DFS) -> Recurrence, Death
- Progression Free Survival (PFS) -> Progression, Death
- Overall Survival (OS) -> Death
- Quality of Life (QoL) -> Side effect of the treatment, symptoms of the disease
 - EORTC QLQ-C30 (**E**uropean **O**rganization for **R**esearch and **T**reatment of **C**ancer **Q**uality of **L**ife **Q**uestionnaire-C30)
 - FACT – x (**F**unctional **A**ssessment of **C**hronic Illness **T**herapy)
 - ...



- Clinical Trial Endpoints (next)
 - Overall Response Rate -> sum of partial response (PR) plus complete response (CR)
 - For solid tumor the gold standard is provided by
 - RECIST (**R**esponse **E**valuation **C**riteria In **S**olid **T**umors) criteria published in 2000 by the European Organisation for Research and Treatment of Cancer (EORTC), NCI, and the National Cancer Institute of Canada Clinical Trials Group.
 - For Malignant Lymphoma
 - CHESON (Revised Response Criteria for Malignant Lymphoma)
 - ...
- Challenge for Programming:
 - RECIST is a complex algorithm with a lot of specifications to take into account...

Special Analyses



Table 1 – Time point response: patients with target (+/- non-target) disease.

Target lesions	Non-target lesions	New lesions	Overall response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-PD or not all evaluated	No	PR
SD	Non-PD or not all evaluated	No	SD
Not all evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, and NE = inevaluable.

- How to derive the Time point response?
 - Based on Tumor Assessment results
 - Target Lesions response
 - Non-Target Lesions response
 - Presence of New Lesions

- Ref: Eisenhauer EA, Therasse P, Bogaerts J. *et al.* **New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1).** *Eur J Cancer.* 2009;**45**:228-247

- **Challenge for programming:**
 - RECIST is simple. Using RECIST is not



■ Interim Analyses

- Analysis intended to assess treatment effect with respect to efficacy or safety at any time prior to completion of the clinical trial
- Ethical , Economic / Efficient, Scientific, Administrative

■ Independent Data Monitoring Committee (IDMC)

- Group of experts external to the study that reviews on regular basis accumulating data from an ongoing clinical trial
- An on-going review and evaluation of safety data and possibly efficacy data for one study or several studies within a development program.

■ Challenge for programming:

- Studies can be stopped prematurely
- Incomplete nature of the data and not fully cleaned
- Event driven analyses
 - Deliverables/timelines accelerated



- Planning of Programming Activities is challenging:
 - First need finalized Statistical Analysis Plan and Tables shells
 - Programmer must be flexible as:
 - Target is moving:
 - Data Base Lock depending on Last Patient Last Visit (LPLV)
 - Timelines and Resources estimation to be reviewed regularly
 - Importance of standard CRF, Data, output shells and programs to improve efficiency



- Pooled analyses for post-approval commitments
 - Oncologic Drugs Advisory Committee (ODAC) in USA
 - Yearly updates of the clinical study report until study end
-
- **Challenge for programming:**
 - To be ready on time even if the target is moving
 - To standardize programming



- Oncology is very challenging and very exciting for a Statistical Programmer:

ONCOLOGY IS SPECIAL

- To be one of the pioneers
- To deal with the moving timelines
- To understand and program algorithms such as the Lab Grading and RECIST
- To set-up the macros, programs and all dependencies to be ready for anything
- To unify derivations and naming conventions across studies for easier pooling
- To improve the lives of patients and caregivers



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