
PFS event
Treatment


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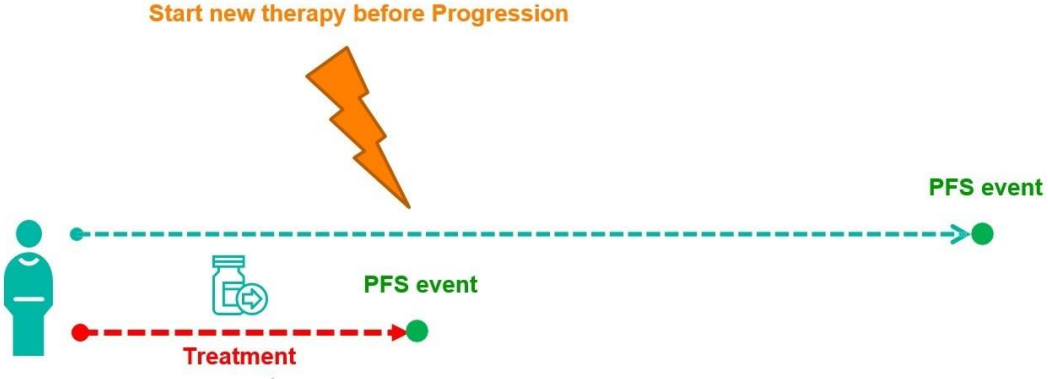
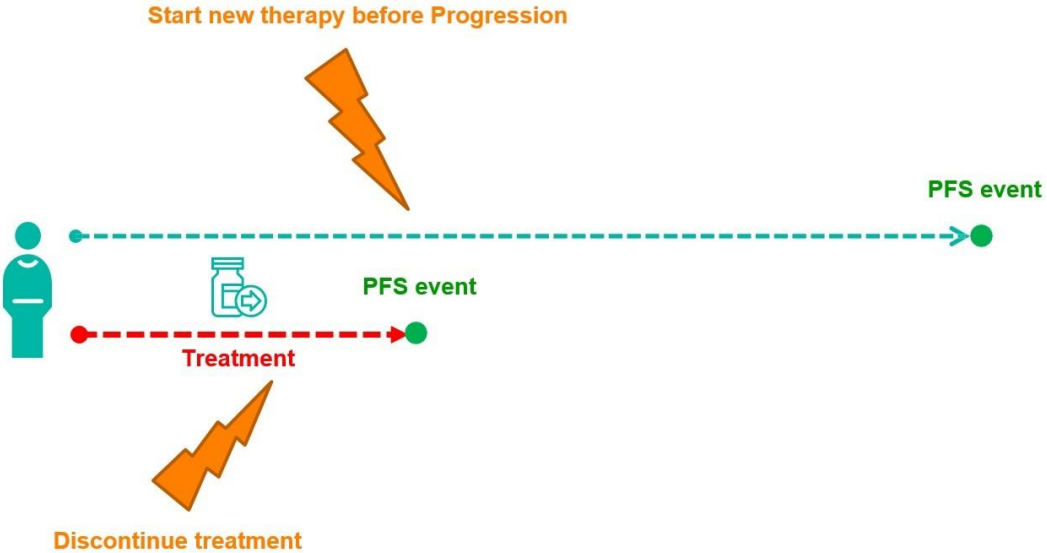

Start new therapy before Progression
PFS event
PFS event
Treatment


Start new therapy before Progression
PFS event
PFS event
Treatment
Discontinue treatment

Do these clinical events affect your interpretation of the treatment effect?

Is the treatment effect clearly defined?

What data would you collect?

If you do not know how to ask the right question, you discover nothing.

W.E. Deming, American Statistician

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3) **Data collection requirements unclear.**

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1) **Stakeholders not aligned.**

2) **Analysis method not aligned to scientific question.**

3) **Data collection requirements unclear.**

4) **Heterogeneity between trials.**

Present and future:

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ICH E9(R1) estimands addendum.

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Clear upfront definition of treatment effect of interest.

Have discussions upfront.

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Get clarity early on.

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Shorten filing timelines.

Polarix Oncologic Drugs Advisory Committee (ODAC).

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2-arm RCT in DLBCL.
R-CHOP vs. R-CH-Polatuzumab-P.
Primary endpoint: ”PFS”.

Is it clear what "PFS" is?

Estimand attribute	Analysis 1 (pre-specified in SAP): PFS as per protocol	Analysis 2 (requested by FDA): PFS with censoring at NALT
Population	As per protocol	
Endpoint	PFS: time to PD or death	
Summary measure	Hazard ratio	
Treatment conditions	As per protocol	

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P-value	0.0177	0.0567
Implied scientific question	What is the time to PD / death irrespective of taking NALT?	What is the time to PD / death assuming NALT would not exist?

Do I need to care?

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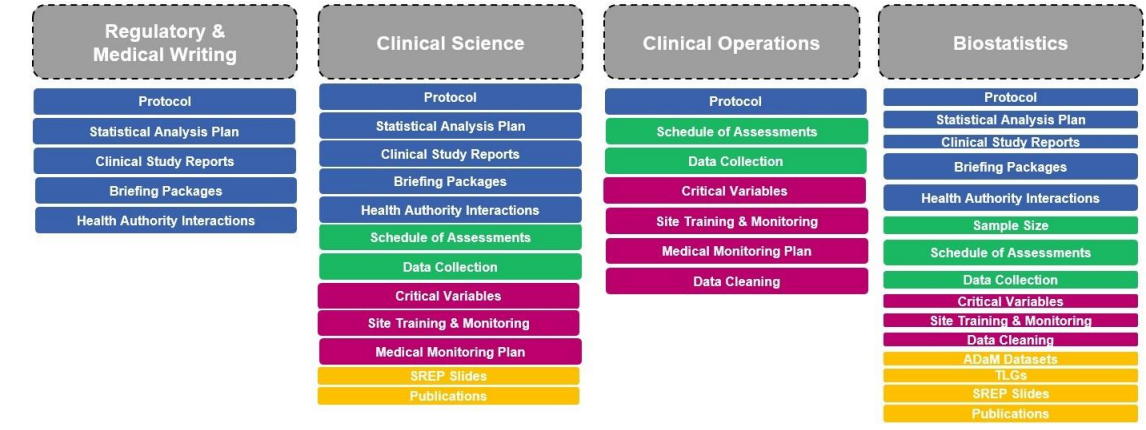
Yes!


Regulatory & Medical Writing
Protocol
Statistical Analysis Plan
Clinical Study Reports
Briefing Packages
Health Authority Interactions
Clinical Science
Protocol
Statistical Analysis Plan
Clinical Study Reports
Briefing Packages
Health Authority Interactions
Schedule of Assessments
Data Collection
Critical Variables
Site Training & Monitoring
Medical Monitoring Plan
SREP Slides
Publications
Clinical Operations
Protocol
Schedule of Assessments
Data Collection
Critical Variables
Site Training & Monitoring
Medical Monitoring Plan
Data Cleaning
Biostatistics
Protocol
Statistical Analysis Plan
Clinical Study Reports
Briefing Packages
Health Authority Interactions
Sample Size
Schedule of Assessments
Data Collection
Critical Variables
Site Training & Monitoring
Data Cleaning
ADaM Datasets
TLGs
SREP Slides
Publications
Regulatory Documentation
Trial Design
Study Conduct
Analysis & Reporting

Covid.

Covid.

Ukraine war.

Patients!

Patients!

Physicians. Investigators.

Patients!

Physicians. Investigators.

Trial developers.

Patients!

Physicians. Investigators.

Trial developers.

Regulators.

Patients!

Physicians. Investigators.

Trial developers.

Regulators.

HTA bodies.

It is not innovative if it does not work.

Mark Baillie, Statistician at Novartis in Basel

Thank you for your attention.

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Slides can be downloaded on
www.kasparrufibach.ch

Doing now what patients need next

R version and packages used to generate these slides:

R version: R version 4.2.3 (2023-03-15 ucrt)
Base packages: stats / graphics / grDevices / utils / datasets / methods / base
Other packages:

This document was generated on 2023-09-06 at 16:45:54.