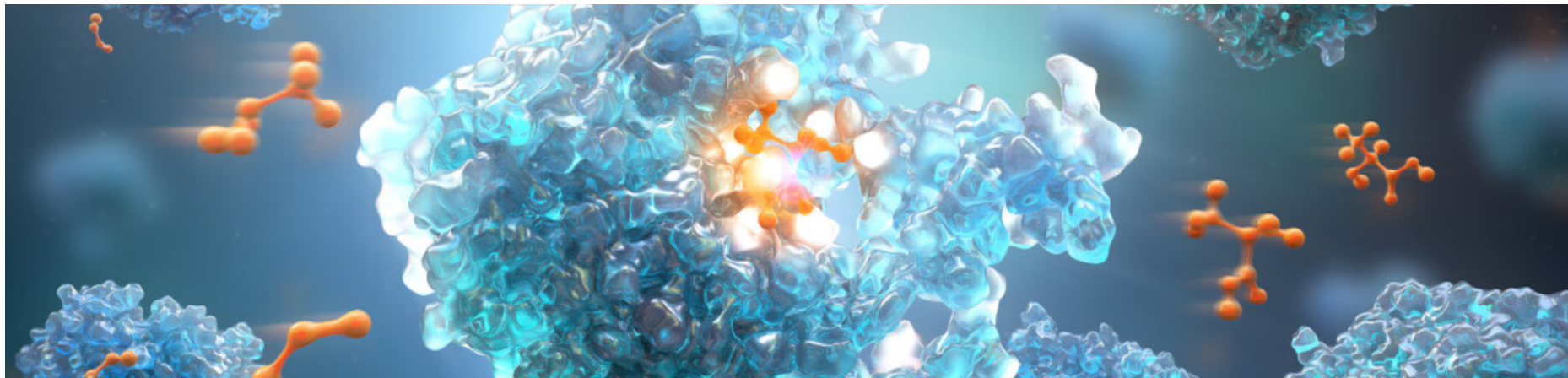


DH14: A Programmer's Journey Through an Early Oncology Adaptive Platform Trial

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PhUSE EU Connect 2020 - Liverpool

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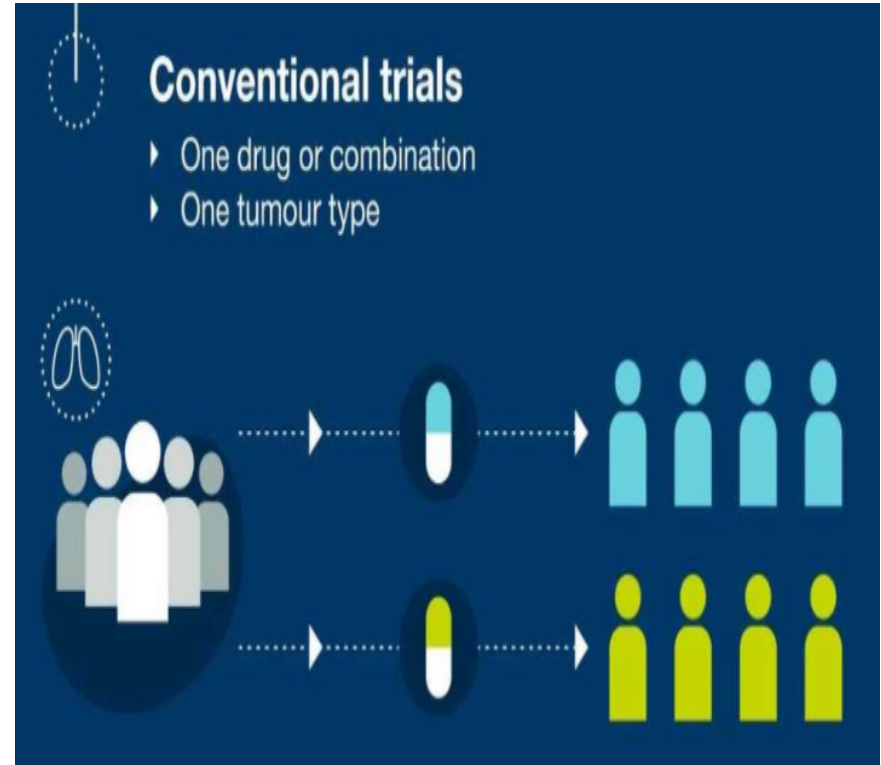


Agenda

- Introduction
 - Why Adaptive Platform Trial
 - Adaptive platform trial
- Challenges and Solutions
 - Example study
 - Programming and data Handling challenges and solutions
- Conclusion

Introduction: Why Adaptive Platform Trial

- Traditional trials do not allow researchers to potentially adapt to the result during the study
- Studies can run for many years with inconclusive results because teams were less able to adapt to observed trends
- Potential for high costs, slow progress, and a lower success rate



Introduction: Typical success rate

Probability of Success² by Clinical Trial Phase and Therapeutic Area

	<i>P1 to P2</i>	<i>P2 to P3</i>	<i>P3 to Approval</i>	<i>Overall</i>
<i>Oncology</i>	57.6	32.7	35.5	3.4
<i>Metabolic/Endocrinology</i>	76.2	59.7	51.6	19.6
<i>Cardiovascular</i>	73.3	65.7	62.2	25.5
<i>Central Nervous System</i>	73.2	51.9	51.1	15.0
<i>Autoimmune/Inflammation</i>	69.8	45.7	63.7	15.1
<i>Genitourinary</i>	68.7	57.1	66.5	21.6
<i>Infectious Disease</i>	70.1	58.3	75.3	25.2
<i>Ophthalmology</i>	87.1	60.7	74.9	32.6
<i>Vaccines (Infectious Disease)</i>	76.8	58.2	85.4	33.4
<i>Overall</i>	66.4	48.6	59.0	13.8
<i>Overall (Excluding Oncology)</i>	73.0	55.7	63.6	20.9

Source: Chi Heem Wong, Kien Wei Siah, Andrew W Lo. "Estimation of clinical trial success rates and related parameters." *Biostatistics* 20(2): April 2019, Pages 273-286. Published online: 31 January 2018. DOI: 10.1093/biostatistics/kxx069

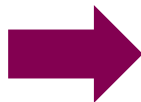
"Success" means that the drug or vaccine eventually received approval from a regulatory body like the FDA



Introduction: Change of focus in clinical trial

- Clinical trial design has evolved rapidly in the last decades
- The failure of promising agents in randomized studies has prompted reconsideration of the standard dose-finding paradigm in early phase studies
- The focus of oncology research has shifted

From
One tumour, one
population



To
Selecting treatment based on

- Genetic makeup of the tumour
- Patient's genotype
- Predicting individual outcomes

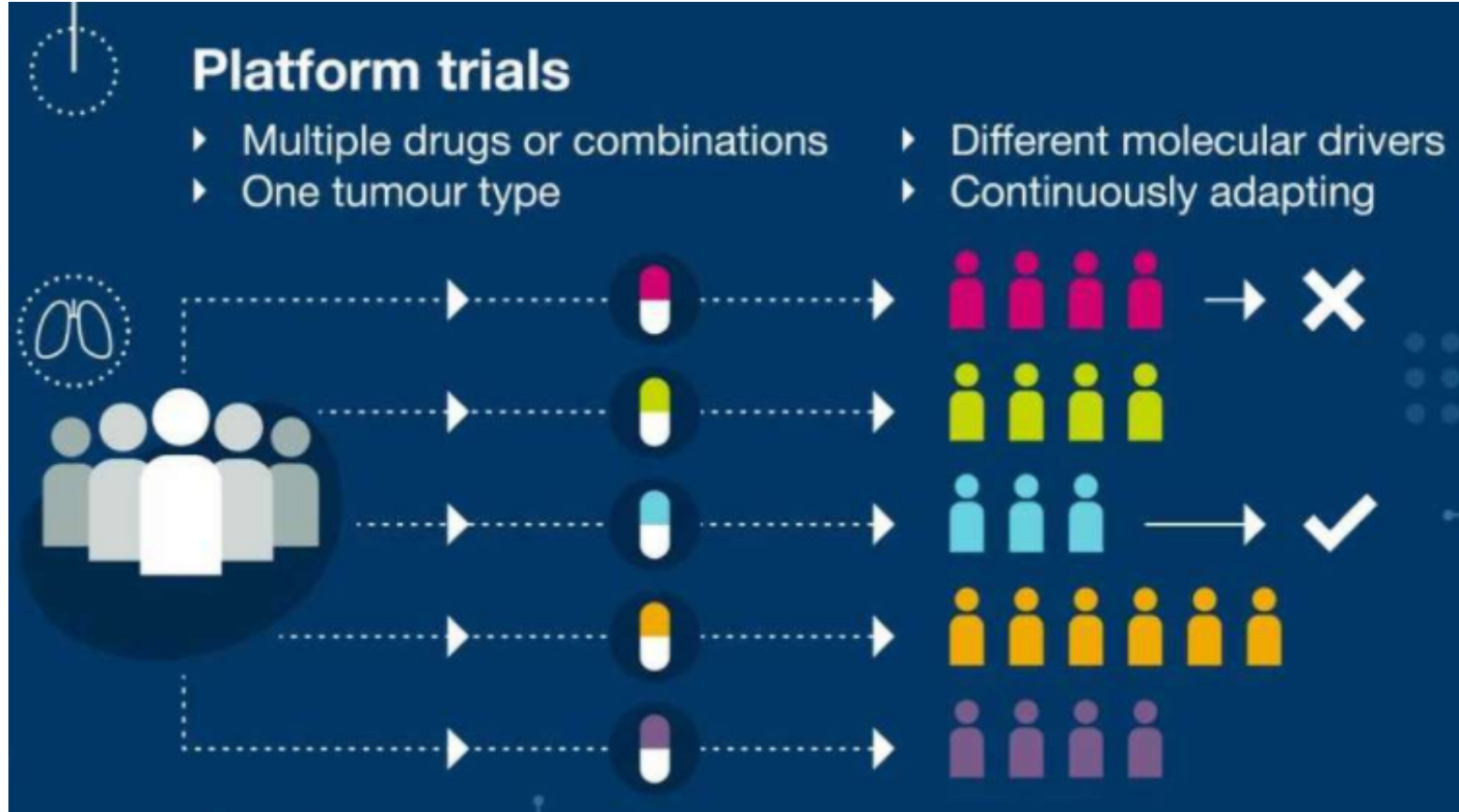


Introduction: Adaptive platform trial

- Adaptive platform trial evaluates multiple treatments simultaneously under one Master protocol
- Allows multiple treatments to enter or exit the trial over the course of the study based on a decision algorithm
- The aim is to answer more questions, more efficiently with less time
- Allows researchers the ability to adapt to results that are observed
- Allows modifications to key components of trial design while data are collected



Introduction: Adaptive platform trial



Introduction: Potential benefits of an adaptive platform trial to programming

- Dropping of inferior treatments or limit allocation of participants means a more lean delivery mechanism
- Multiple 'mini' studies within a master study protocol. Addition of new modules within one study protocol saves time and resources
- Combining resource into 'one' team across modules reduces time and potentially maximize efficiencies where repeating elements share commonalities
- Combined mini studies results in less redundancy within output generation

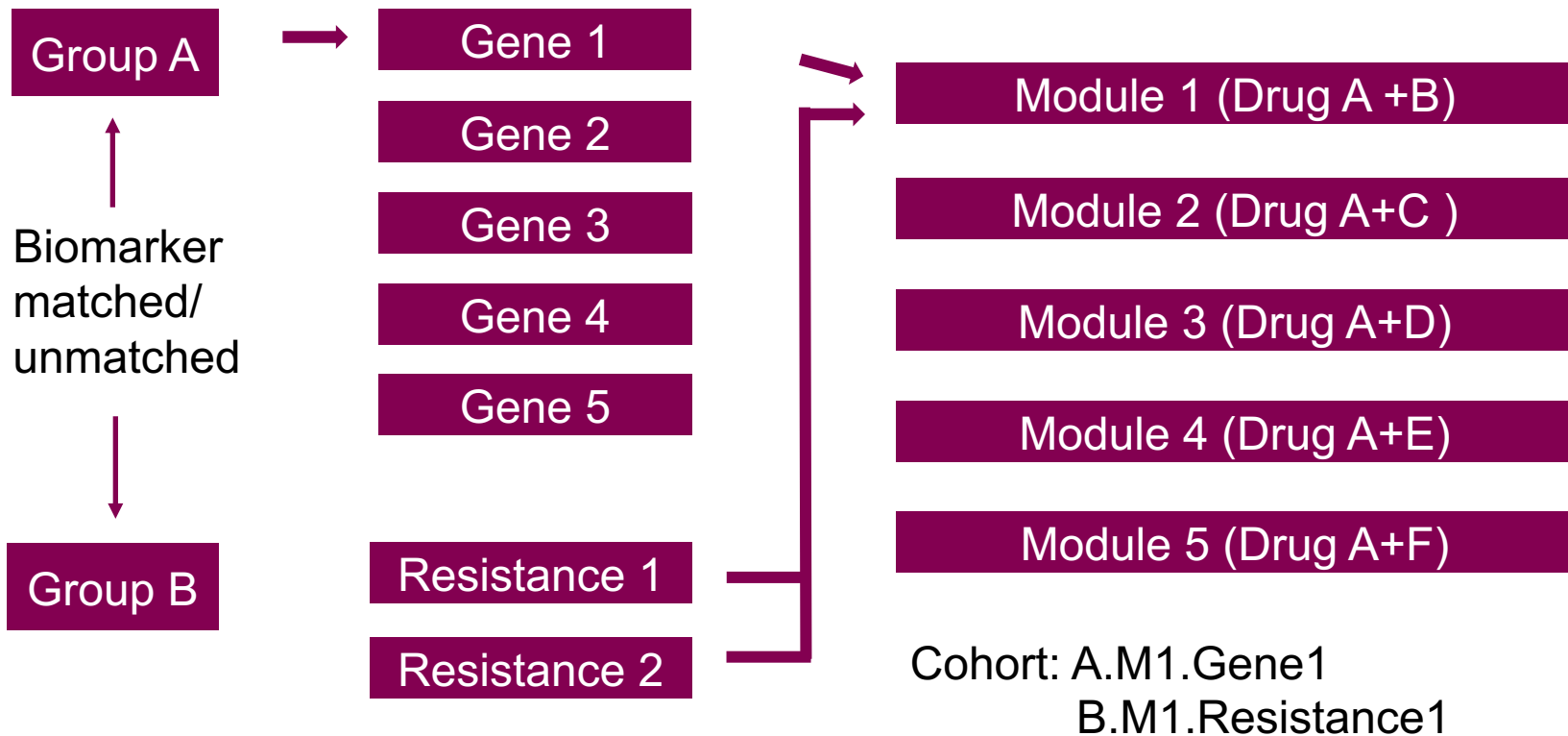


Challenges and Solutions: Example study

- An Open-Label, Multi-Drug, Biomarker-Directed Phase II Study in Patients with Non-Small Cell Lung Cancer
- Modular in design, consisting of a number of treatment cohorts, allowing evaluation of the efficacy, safety, and tolerability of multiple treatment arms
- Multiple interim analyses are planned to monitor the treatment outcomes
- Decision algorithm to include or exclude treatments are in place
- Multiple stakeholders



Challenges and Solutions: Example study



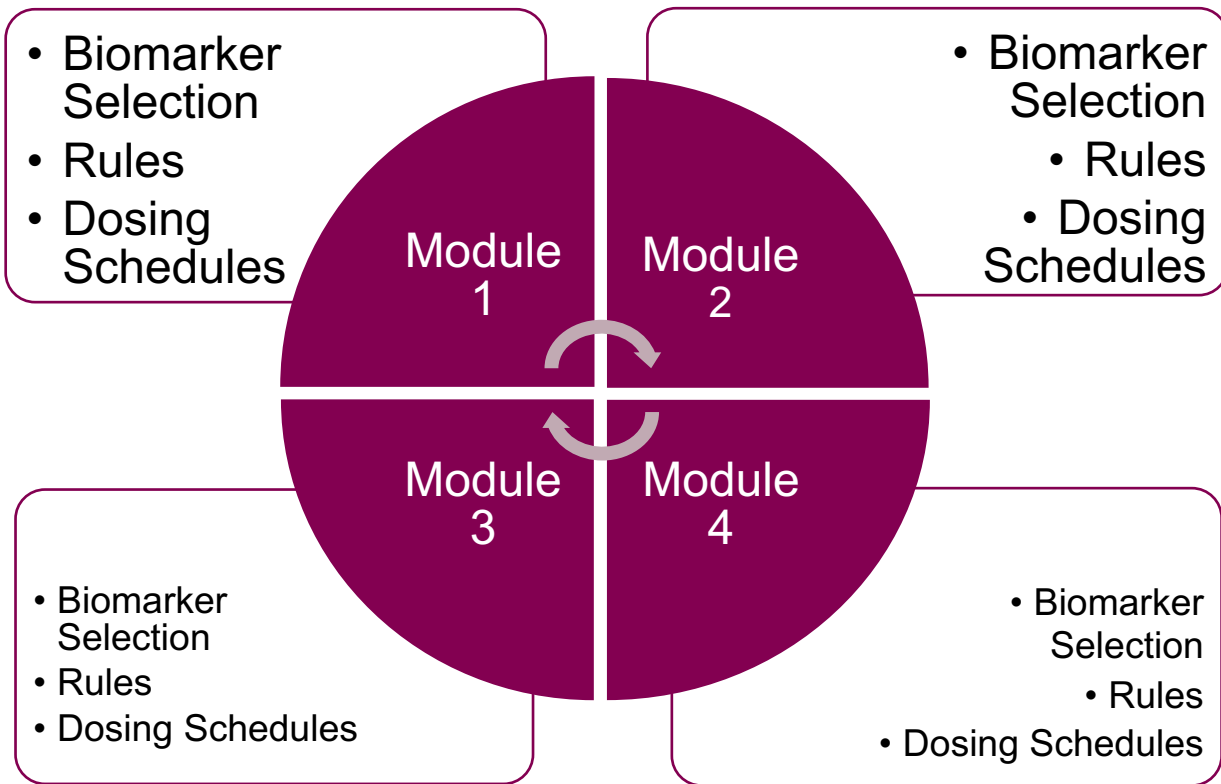
Challenges

- Programming and data handling

**CHALLENGE
ACCEPTED**



Multiple modules

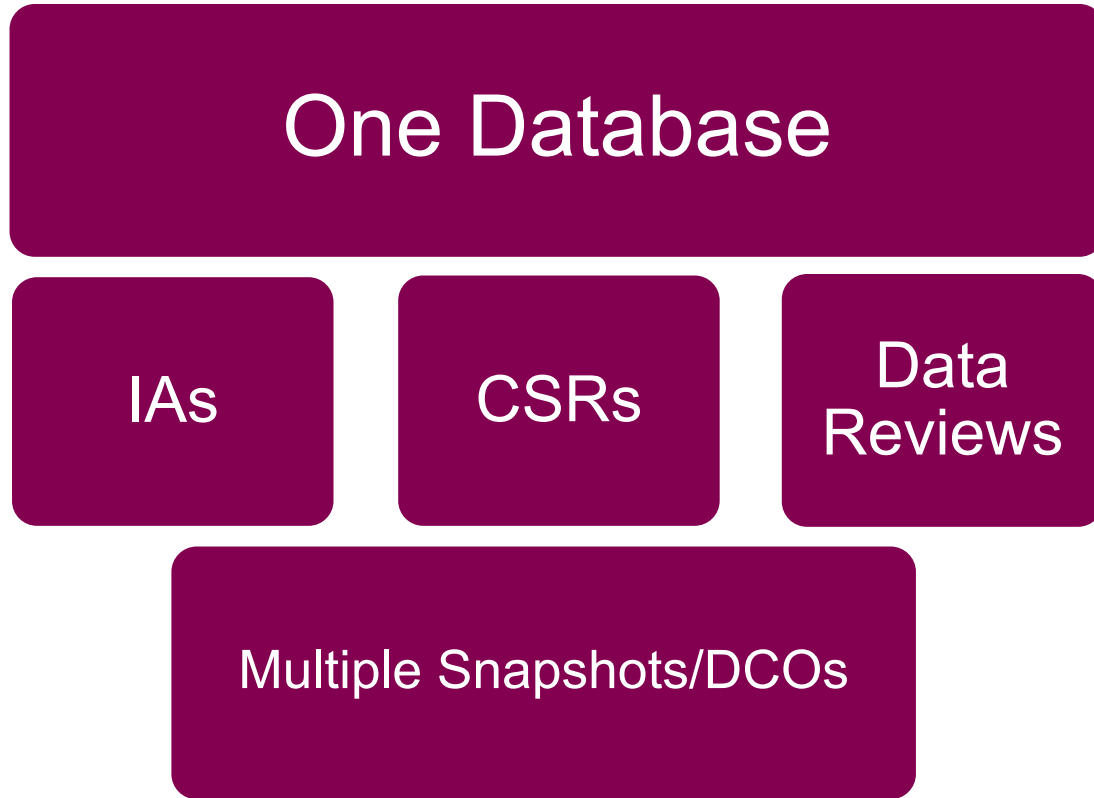


Solutions

- Appreciate commonalities and differences across modules in the protocol and SAP
- Master programs need to be designed for adaptability



Interim analyses/Multiple CSR

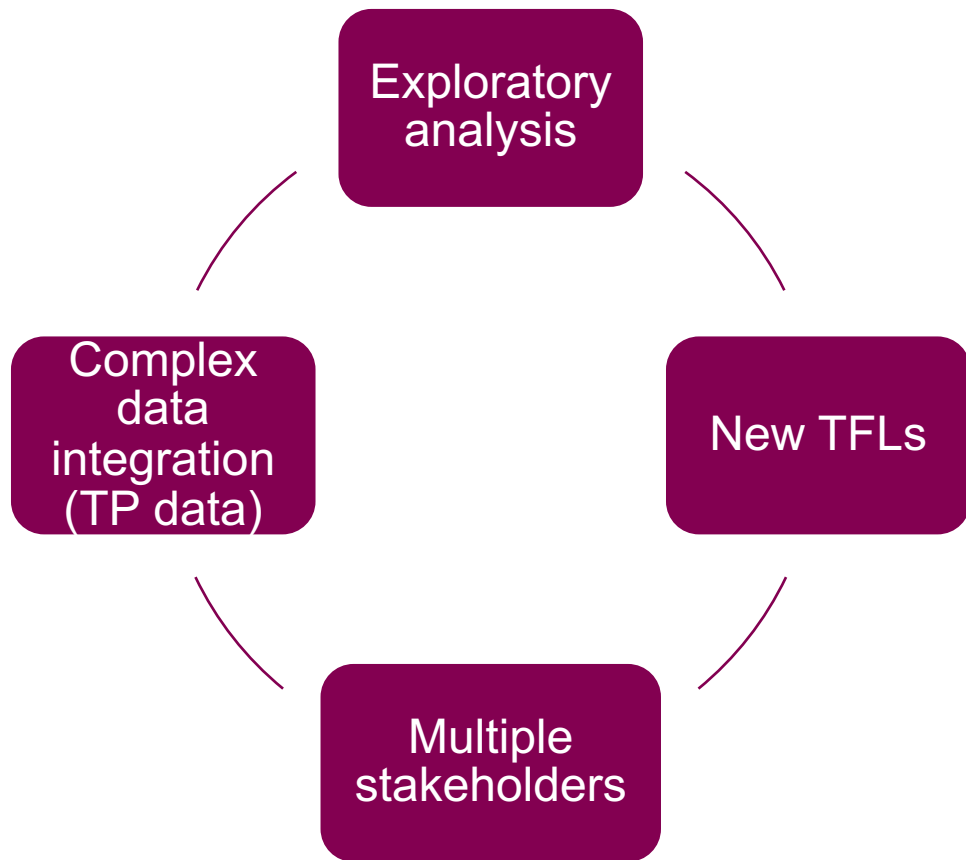


Solutions

- Master programs updated once for changes to all modules
- Adaptable macro based programs
- Clear DCO considerations for reporting events
- Validation Programs that focus on modules



Adhoc work

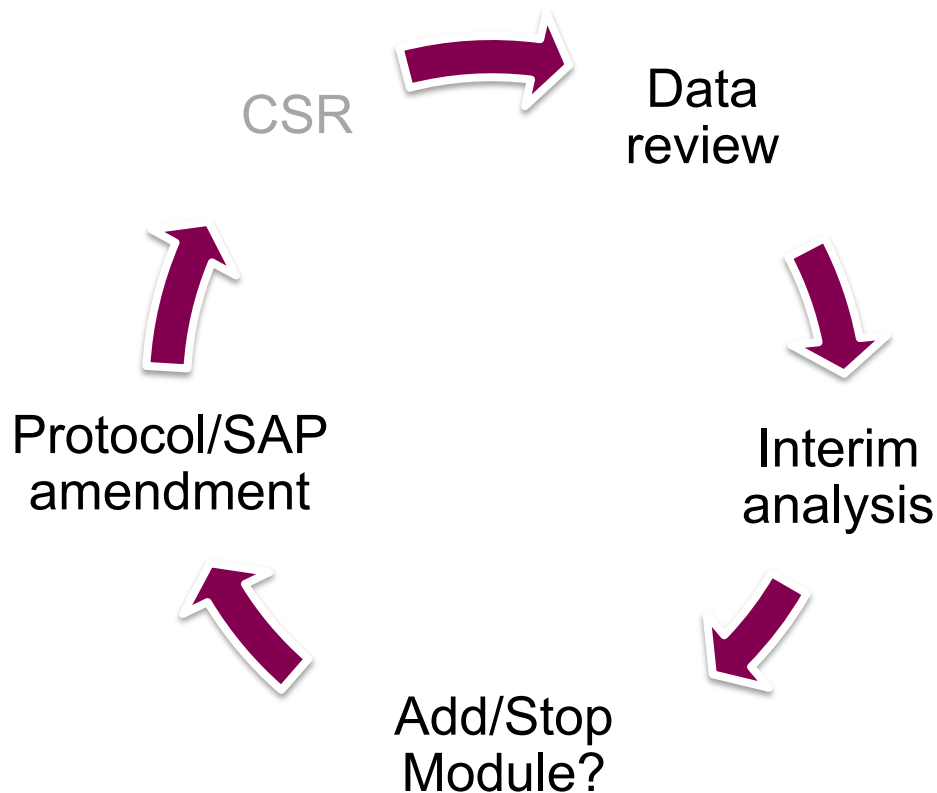


Solutions

- Efficient communication
- Documentation of requests
- Clarification of analysis
- Adhoc requests process
- Reusability of programs/macros
- Centralized documentation for all adhoc requests
- Data visualization tools



Volume of workload



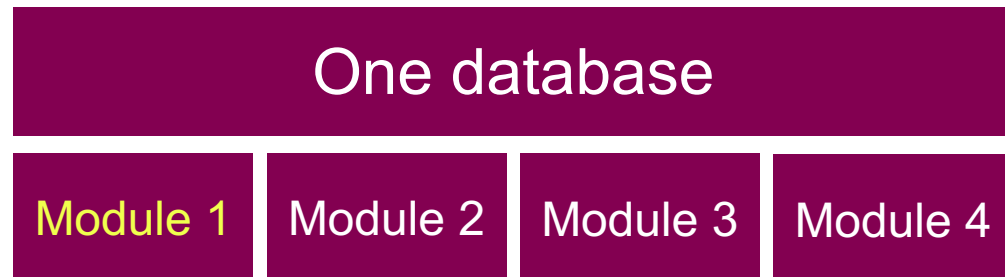
Solutions

- Managing peaks and troughs –reduced possibilities
- Planning ahead
- Use of spreadsheet



Database lock

Module CSR – Soft Lock



Final CSR – Hard Lock



Solutions

- Soft lock and hard lock
- Soft lock involves all the activities like hard lock
 - All data points cleaned and SDVed
 - PI signature applied
 - All TPV data/SAEs reconciled
 - Coding performed
 - Data points get frozen by site staff
- Maintain data integrity and time point comparison



Conclusion

- Adaptive platform trials offer an efficient model of running multiple modules trial under one Master protocol
- Multiple readout and reporting structure means adaptable and master level programs need to be developed and suitable for module changes
- Maximising resources in programming and understanding a more flat algorithm model is appropriate in comparison to a standard study due to continuous peaks
- An effective collaboration among different stakeholders is critical to make it successful when data sources vary
- Making sure data does not change between modules readout



Thank you very much for attending
and listening to this presentation!



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