

Complex Trials, Simple Disclosures: Streamlined Transparency of Innovative Study Designs

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Agenda

1

- Introduction

Basket, Umbrella, & Platform Designs

2

- EU-CTIS

Multiple & Single Submissions

3

- clinicaltrials.gov

Multiple & Single Registrations
Results: Primary & Study Completion

4

- Conclusion

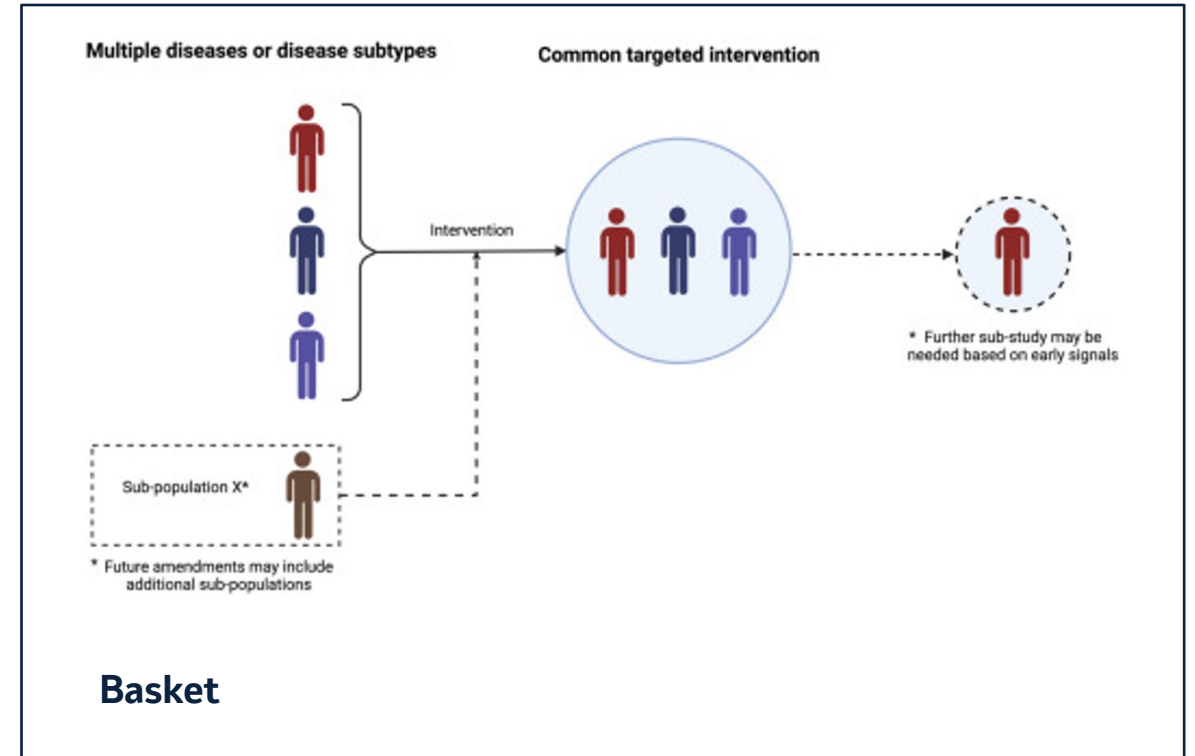
Key Takeaways

Note: This presentation is incomplete without accompanying verbal commentary. The views and opinions expressed are those of the individual presenter.

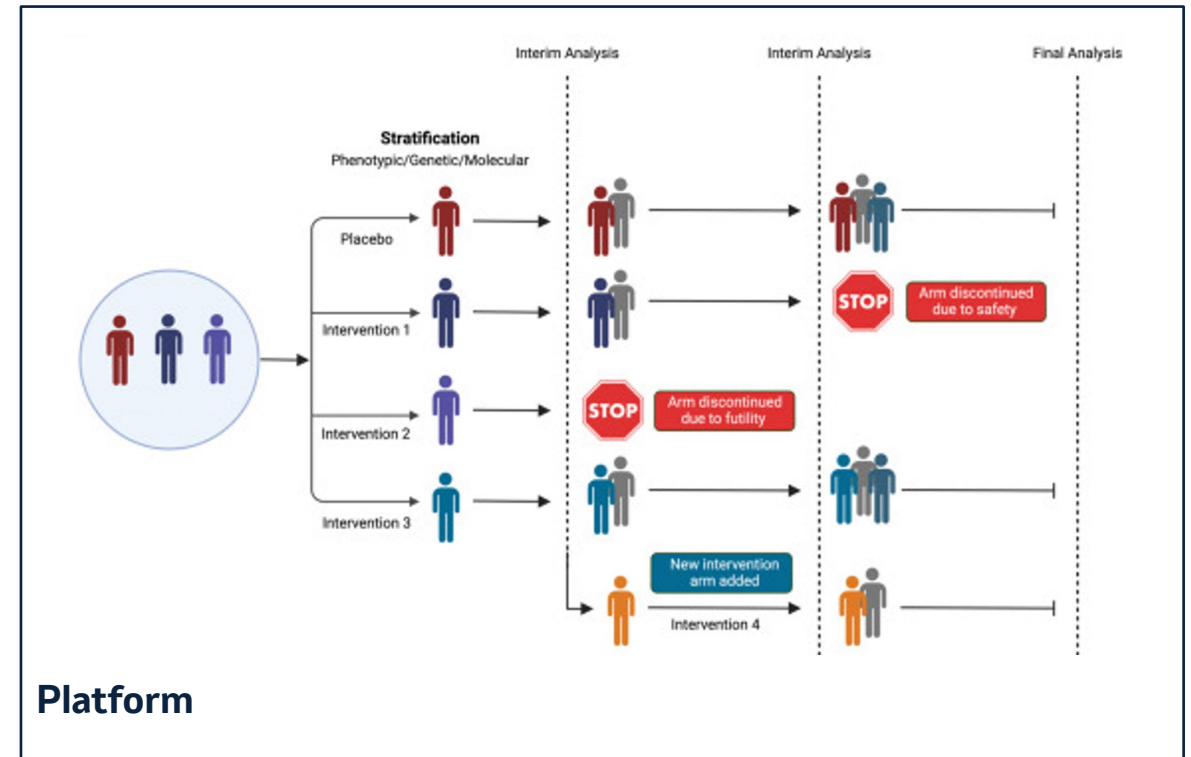
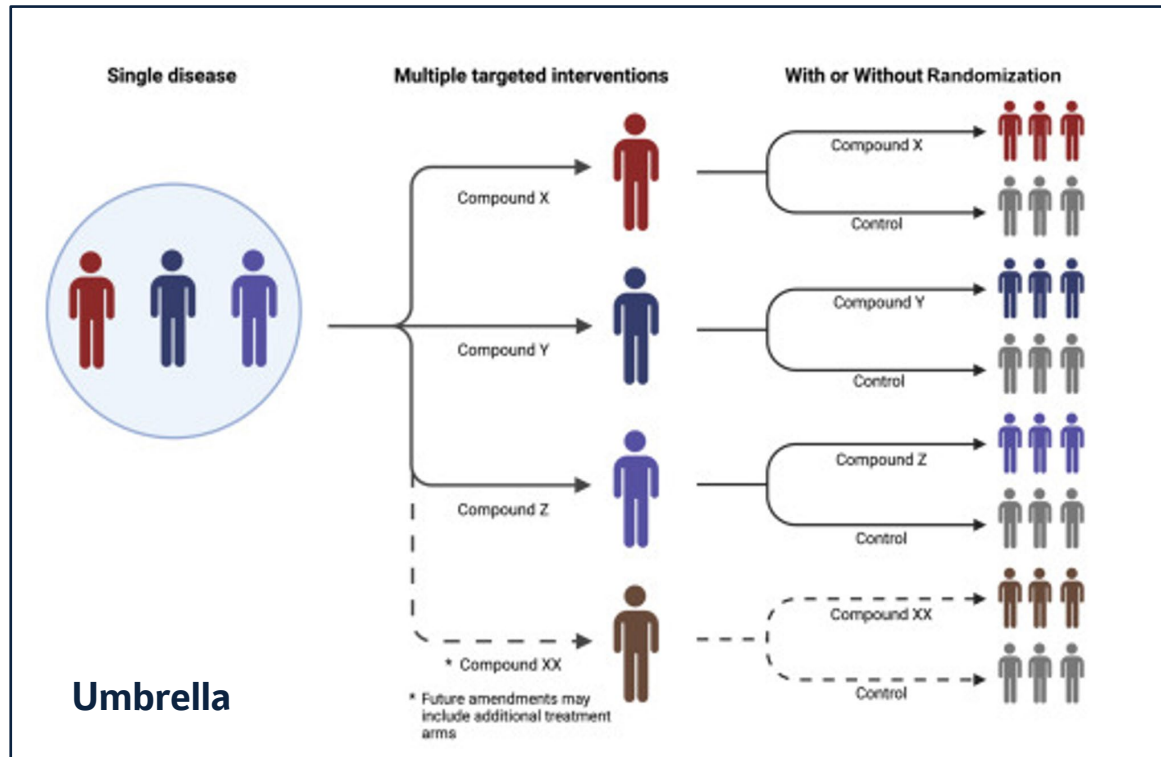
Introduction

Basket, Umbrella, & Platform Designs

- Innovative trial designs have the potential to offer enhanced efficiency for precision medicine with increased utilization in drug development.
- These trials can allow investigators to examine multiple hypotheses through current sub-studies within the same overall trial structure, under one common protocol (called a “master protocol”).
- Interventional trials using a master protocol may assess several diseases or disease sub-types with a single treatment (basket trials), several therapies in one disease type (umbrella trials) or by sharing elements of these designs to allow continuous testing (platform trials).



Basket, Umbrella, & Platform Designs



- Multiple studies in Basket, Umbrella and Platform designs may be assigned individual sub-study protocols under the master protocol.
- Innovative study designs may also include multiple sub-studies in the same protocol, without a separate master protocol.

EU-CTIS

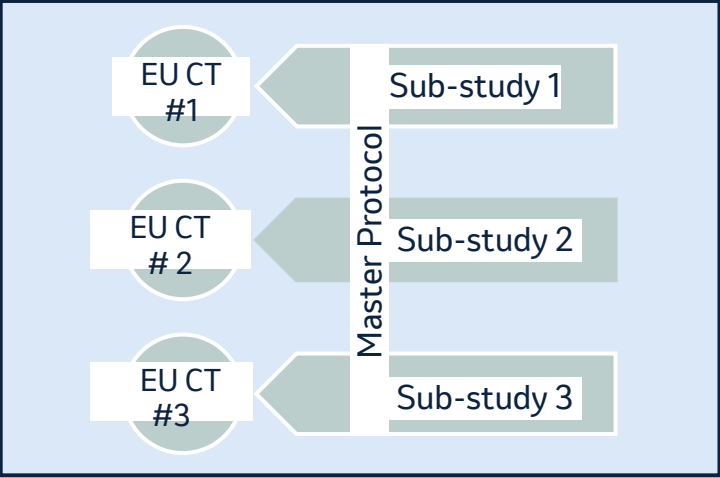
Multiple & Single Submissions

Multiple EU CT Numbers

Each sub-study protocol is treated as a standalone clinical trial

Independent authorization requested for each sub-protocol

Master protocol may not have a separate CTA, depending on study design

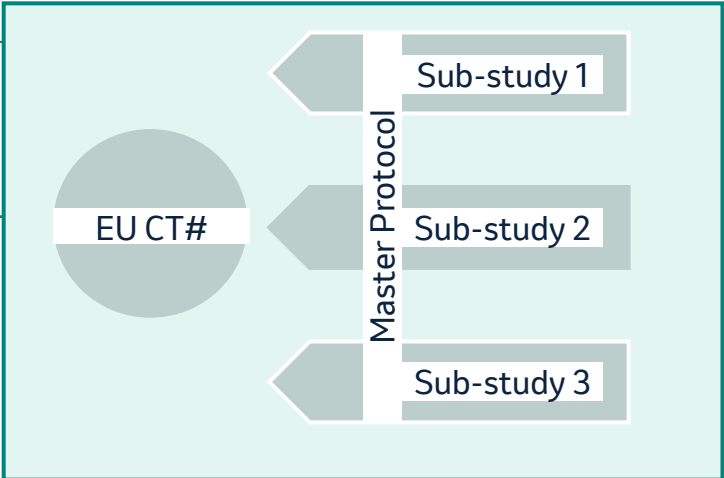


Single EU CT Numbers

Multiple sub-study protocols under a single CTA, centered around the common master protocol

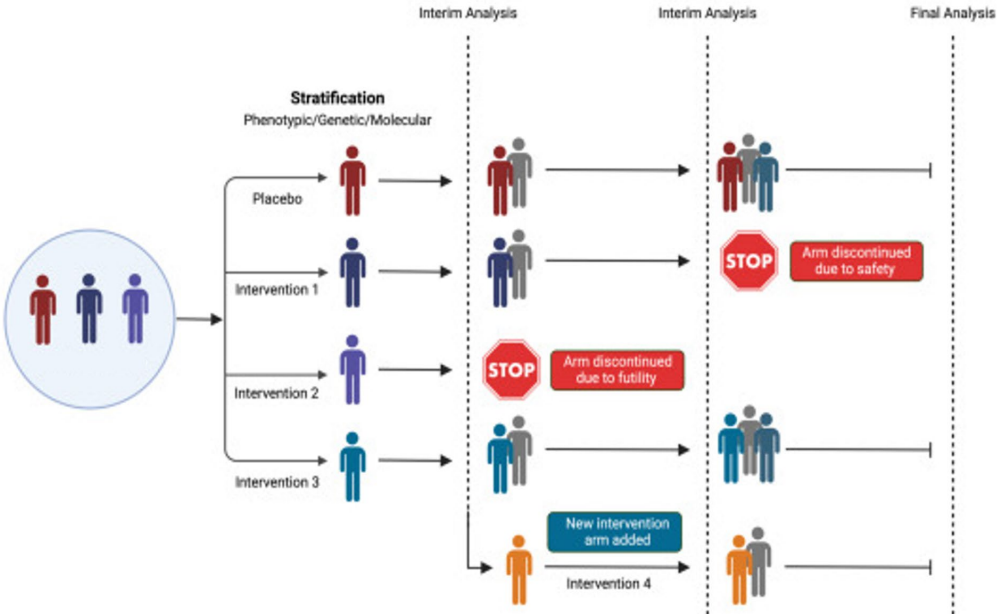
Clear scientific rationale to justify linking all sub-protocols under the same CTA

Justification for choice of control group is recommended, depending on study design



Multiple & Single Submissions

Multiple EU CT Numbers	Single EU CT Number
Substantial Modifications	
Changes substantial or otherwise may be segregated by the sub-protocol and applied to the relevant individual trial	Changes from multiple amendments (to different sub-protocols) may result in cumulative complex high-risk modifications to a single trial
Regulatory Compliance	
EoT defined by each individual sub-protocol	Interim reporting may be needed when different sub-protocols are at different stages of conduct and end of trial (EoT) is a ‘moving target’
Control Group	
In alignment with each sub-protocol, handled independently for each sub-study CTA.	Different investigational medicinal products (IMPs) evaluated over varying time periods across multiple sub-protocols require adequate justification to be maintained for choice of control group



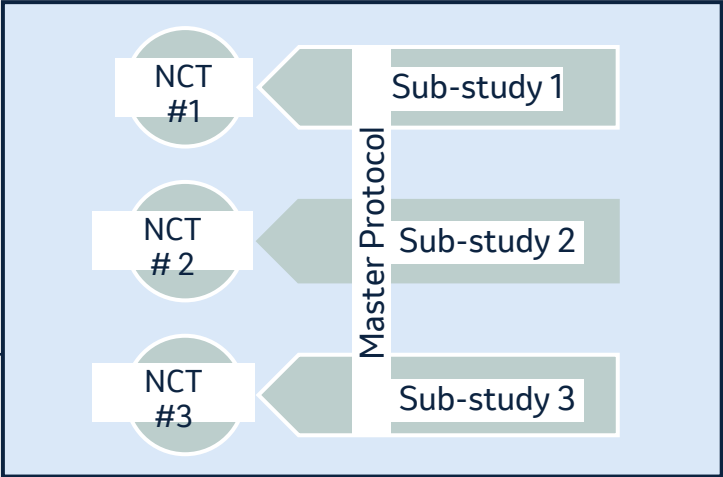
Source: Honap et al. Gastroenterology. 2024 Sep; 167 (4): 636-642.e2

clinicaltrials.gov

Multiple & Single Registrations

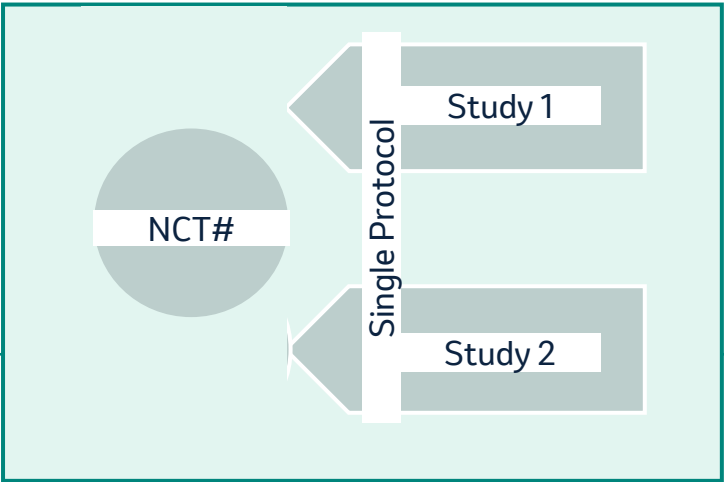
Multiple NCT Numbers

Each sub-study protocol is as a standalone registration; master protocol may not have a separate registration, depending on study design



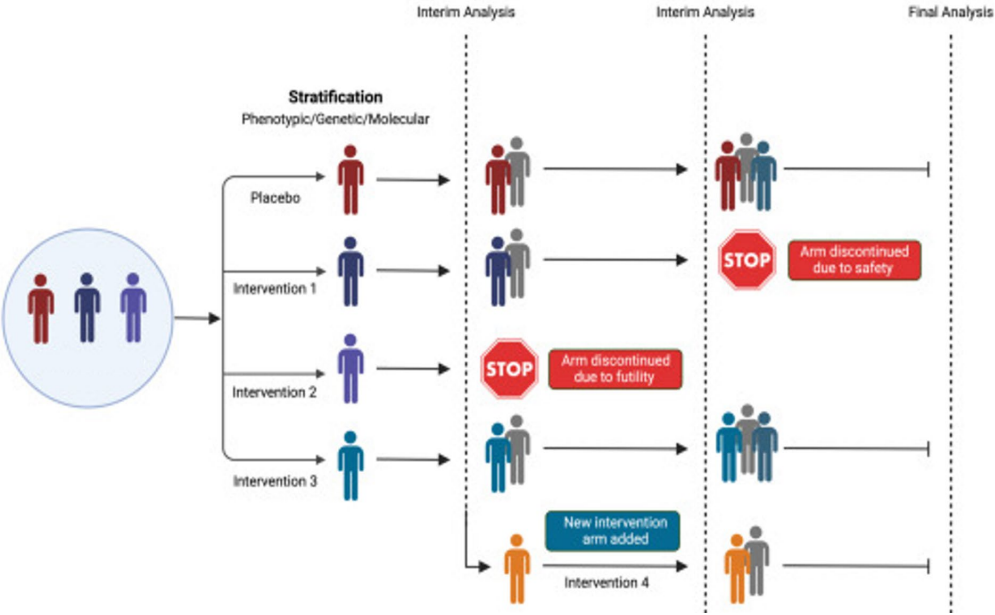
Single NCT Numbers

Multiple sub-studies in the same protocol included in a single registration



Multiple & Single Registrations

Multiple NCT Numbers	Single NCT Number
Detailed Description	
This field in each sub-study registration can be used to include information regarding the common unifying master protocol. Enrollment completion, arm discontinuation, new arm addition etc. or other features of rolling arm designs may also be clarified here, if needed.	If multiple studies/sub-studies are going to be included in the same registration, this field may be used to indicate distinguishing and unifying features of each study and any pre-specified rationale for inclusion in a single protocol, if needed.
Arms & Interventions; Outcome Measures	
In alignment with each sub-study protocol, handled independently for each sub-study registration.	Study arms and outcome measures are separated out for each study and contain identifiers for the relevant study. E.g., Study 1: Number of Participants with Adverse Event; Study 2: Number of Participants with Adverse Events



Source: Honap et al. Gastroenterology. 2024 Sep; 167 (4): 636-642.e2

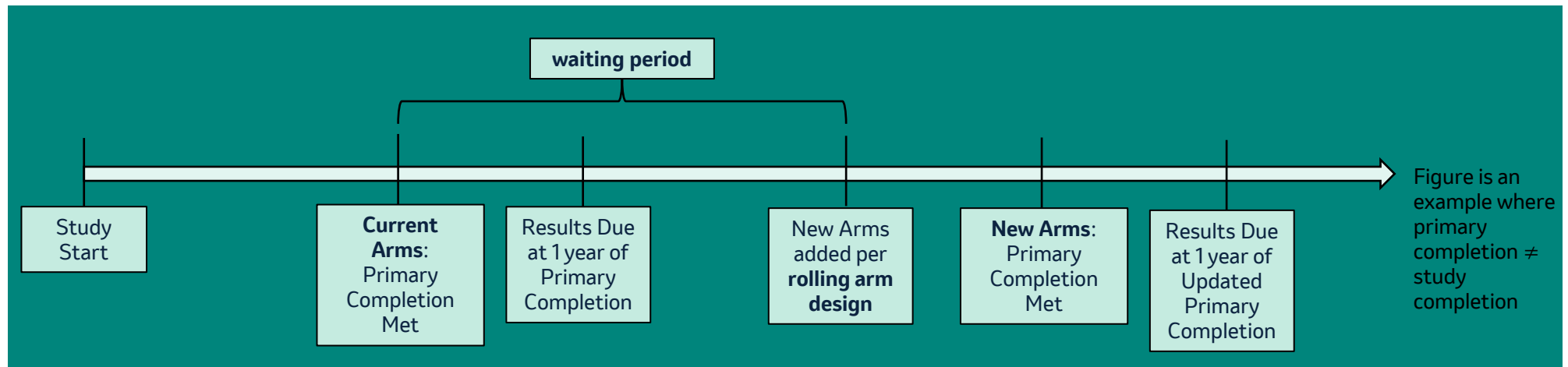
Results: Primary & Study Completion

Primary Completion Date: Final data collection for the **primary outcome measures** in the study



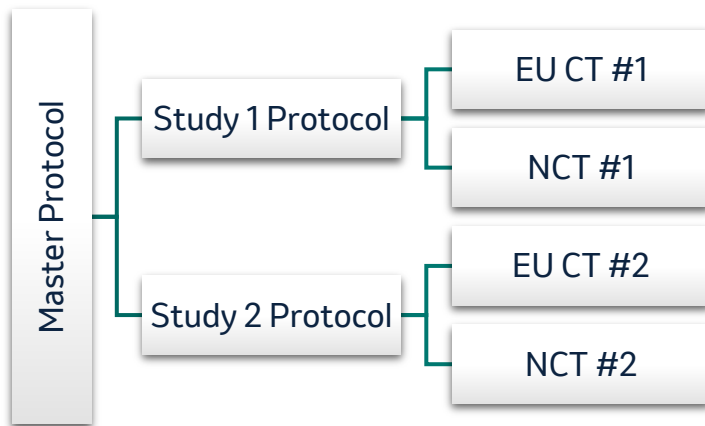
Study Completion Date: Final data collection in the study

- ❖ Protocol specified rolling arm designs allow the flexibility of adding new arms to an ongoing study; new arms may be added after the study has completed enrollment and/or data collection in existing arms
- ❖ A “waiting period” can ensue when the current arms in the study have completed follow-up and met primary completion, but new arms have not been added yet
 - ✓ Exploring the possibility of switching from an actualized primary completion to an estimated one, consistent with latest protocol amendment
 - ✓ Language in each sub-study protocol is key to defining and justifying Primary Completion and study completion



Conclusion

Key Takeaways



- Drug development is not necessarily “one size fits all”; innovative clinical trial designs can diversify development pipelines, enhance operational efficiency, and potentially expedite patient access to new treatments.
- Although parallel submissions for each individual study within a complex design may require additional upfront resources, this approach can be efficient over the long term. It facilitates clear understanding of key design features (e.g., control groups, rolling-arm enrollment), promotes consistency across trial registries, and supports both trial and data integrity.
- In certain circumstances, including some adaptive platform designs, a single consolidated submission may be appropriate and justified.
- Dynamic elements such as primary completion and overall study completion dates represent “moving targets” in complex designs and require tailored planning during protocol development, for disclosure and compliance.

Thank you

