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PROACTIVE COHORT MANAGEMENT
for Mastering Dose Escalation in Early-Phase Oncology Development

Goals in Dose Escalation Studies

- Escalate dose safely and efficiently to identify the optimal dose range
- Determine the Recommended Phase 2 Dose (RP2D)

Early Phase Oncology Trials & Proactive Cohort Management

- Early phase oncology trials are complex and fast-moving
- Delays between dose levels result in longer timelines and increased cost
- Proactive cohort management can keep studies on track and improve efficiency

Traditional Challenges	Proactive Cohort Management
Reactive decision-making	Planning ahead
Delayed data availability	Parallel workflows
Safety reviews scheduling	Proactive Project Management leadership
Patient readiness lag	Cross-functional team alignment

Success depends on early cross-functional alignment between Project Management, Medical and Clinical Pharmacology teams

Benefits of Proactive Cohort Management

- Keeps timelines on track and improves study efficiency
- Coordinates stakeholders: investigators, CRAs and sponsors
- Ensures real-time data capture, including dose-limiting toxicities and protocol deviations
- Anticipates risks and builds in contingencies before delays occur

Safety Review Committees (SRCs)

Their Role	Best Practices
Dose escalation decisions	Give SRCs flexibility to adjust dose or schedule without protocol amendments
RP2D or biologically effective dose (BED) determination	Allow for ad hoc SRC meetings if safety issues arise mid-cohort
Adjudication of unclear DLTs	

Committee Structures & Hybrid Models

Internal Committees
- PI, sponsor/CRO medical monitor, biostatistician
- Fast decision-making, familiar team
- May lack independence or external expertise

Hybrid Model
- Combines internal team with independent experts (open/closed sessions)
- Balanced expertise and flexibility
- Requires more planning and charter definition

External Committees
- Independent, non-PI medical experts
- Offers objectivity and fresh perspectives
- More complex to coordinate

Clinical Pharmacology's Expanding Role

With the new dosing paradigm, Clinical Pharmacology is more involved:

PK/PD analysis and interpretation

- NCA (Non-Compartmental Analysis): C_{max}/AUC
- Exposure-Response to support dose selection

Present Clinical Pharmacology Insights to Safety Review Committee

- Share PK/PD insights to inform SRC dose decisions

Enabling Smarter Decisions with Real-Time Data

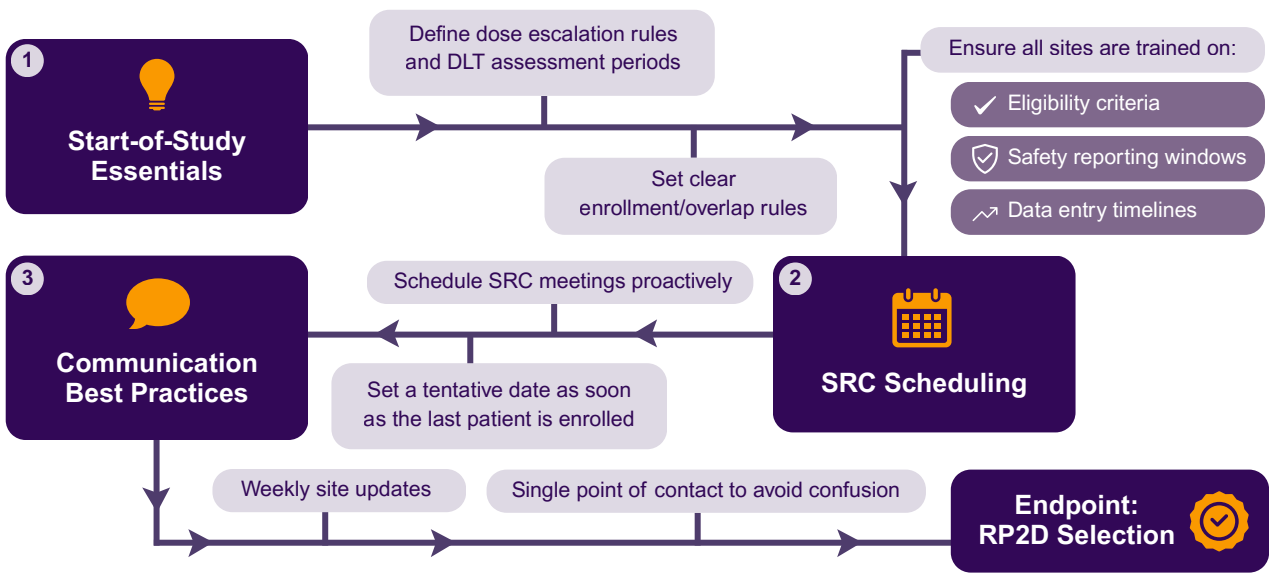
Electronic Data Capture (EDC) alerts provide instant notification of triggers of real-time data

- AE/AESI/ SAE
- DLT/ lab values
- Disease progression

EDC alerts are underutilized yet powerful

- Ensure relevant real-time safety data are transmitted promptly to the SRC
- Avoid having to wait for a scheduled committee meeting

Operational Tactics and Path for Success



Many of these processes run in parallel to expedite decisions

Successful dose escalation is about orchestration to reach RP2D efficiently and safely

Proactive cohort management can reduce delays and costs, and success comes from scenario planning and parallel workflows

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