



Innovations for effective drug development

Promoting Effective Drug Development Programs: Opportunities and Priorities for FDA's Office of New Drugs

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November 7, 2019



Agenda

- Innovative approaches to accelerate development
- Design options for dose escalation
- Seamless Phase I/II design
- Considerations for more effective drug development

Survey demonstrates impact of innovations - low adoption rates and barriers

THE INNOVATION IMPERATIVE: THE FUTURE OF DRUG DEVELOPMENT

Innovation Type	Reduction In Enrollment Time	Likelihood of Launch	Adoption rate
Adaptive Trials	↓ 4.2 Months	13% ↑	0.6%
Precision Medicine Trials	↓ 5.2 Months (Oncology) ↓ 0.9 Months (Neurology) ↓ 10.6 Months (Rare Diseases)	10% ↑	5.2%
Patient Centricity	↓ 3 Months	19% ↑	13.7%
Real-World Data Trials	↓ 1 Month	21% ↑	0.3%

Enablers

Advanced Data Analytics

Workforce Readiness

Collaborative Partnerships

Early Regulator, Payer, & Patient Involvement

Barriers for Adoption



Vast, New and Fragmented Data



Small or Inadequate Workforce



Negative Perceptions of Pharma



Cultural Barriers

<https://druginnovation.eiu.com>
Commissioned by Parexel

Dose Escalation Designs used in Oncology

- **Rule based**

- Simple up and down, 3+3 type, **i3+3**, accelerated titration

- **Model Based**

- Continual Reassessment Method (CRM) and modifications
- Escalation with Overdose Control (EWOC)
- Bayesian Optimal INterval (BOIN) Design
- Modified toxicity probability interval design (mTPI , mTPI 2)
- Toxicity and efficacy probability interval (TEPI)

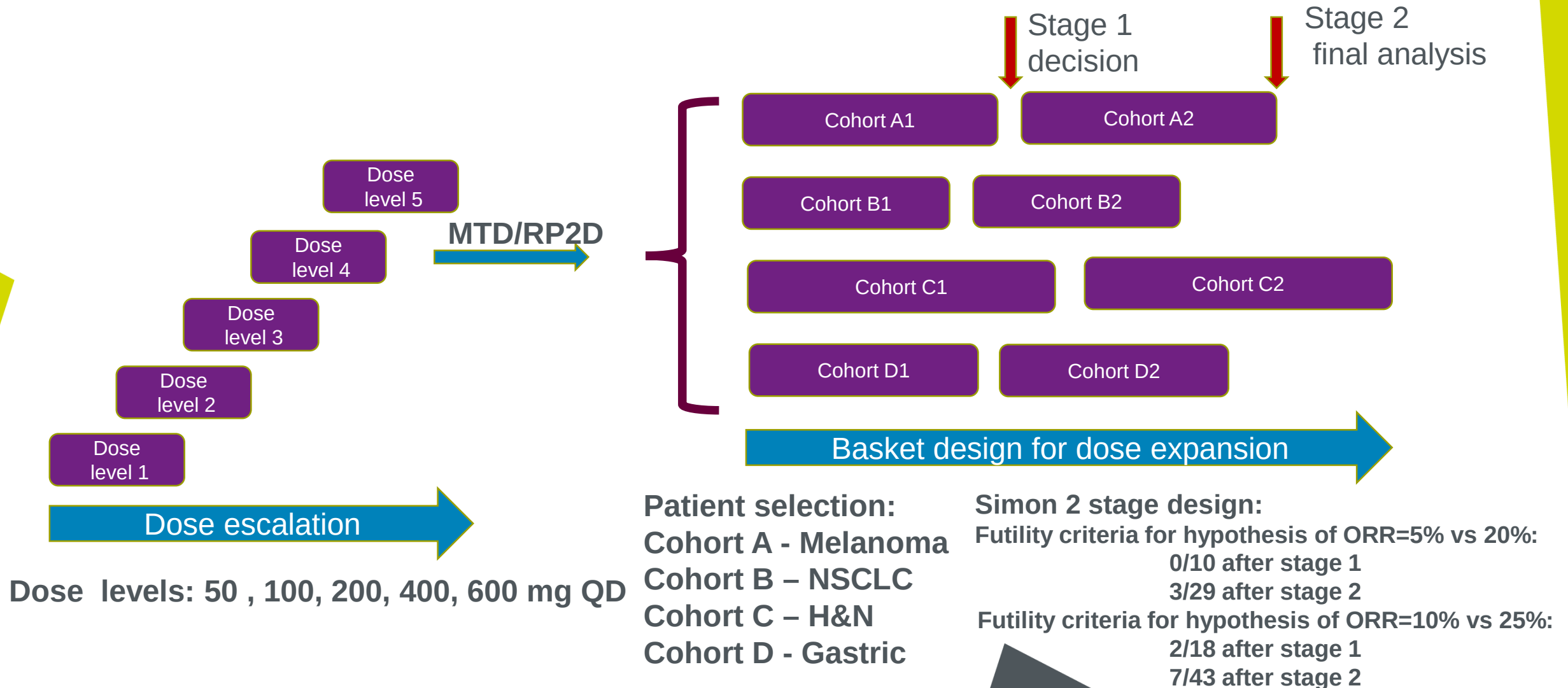
- **Comparison Rule/Model based Trials**

N=172 trials*	Rule-based	Model-based
Duration of trials	36 mo	26 mo
# Patients below RP2D	40	31
Safety: DLTs	14%	13%

*van Brummelen et al, The performance of model-based versus rule-based phase I clinical trials in oncology, June 2016

Seamless Phase I/II Study

Combining Dose Escalation and dose expansion



Synthetic Control Arm

Real World Evidence to Support Development of Drugs and Biologics

Single arm Clinical Study (CS)

RWD collection

- Patient-level data in similar patients

Matching algorithm applied to RWD

- Create a matching cohort to CS cohort

Comparative analysis CS vs RWD cohorts

- Demonstrate superiority of CS treatment vs RWD control cohort

<https://www.fda.gov/2018/08/update-fdas-historical-use-of-real-world-evidence/>

Considerations for more effective drug development

Use more efficient study designs in early development

- Apply innovations –Adaptive trial designs, Precision medicine, Patient centricity, RWD
- Apply model based dose escalation designs and expansion designs to oncology and non-oncology studies
- Consider RWD to support development through synthetic control arms
 - Agree on acceptable methodology



Thank you

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