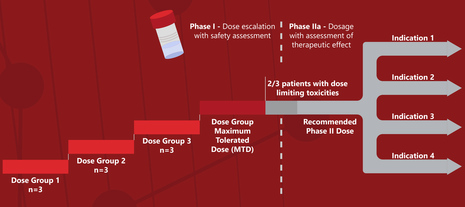
WHAT ONCOLOGY DRUG DEVELOPERS SHOULD EXPECT FROM THE FDA'S PROJECT OPTIMUS

Historically, the dosing strategy for oncology drugs has focused on the maximum tolerated dose.



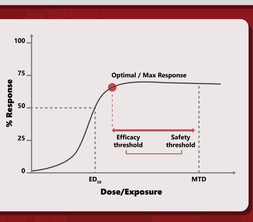
CHALLENGES OF THE MTD PARADIGM

This paradigm has resulted in drugs' pharmacokinetic (PK) profiles, pharmacokinetic/pharmacodynamic (PK/PD) relationships, and clinical target inhibition largely being ignored.

Thus, cancer patients often struggle to tolerate their medication doses long-term, requiring dose modifications including dose reductions and holidays. What's more, for many oncology drugs, their dosing or schedules have been modified to address safety or tolerability issues after regulatory approval.

WHAT'S THE IMPETUS FOR PROJECT OPTIMUS?

These challenges spurred the FDA's Oncology Center of Excellence to develop a new guidance called "Project Optimus" to address issues relating to dose optimization in clinical trials assessing the safety and efficacy of oncology drugs.



WHAT IS PROJECT OPTIMUS?

- Evaluation of additional dose levels for safety & efficacy/activity
- Dose & exposure response relationships
- Focus on dose intensity and adverse event time course
- Focus on toxicity past the dose limiting toxicity criteria
- Scrutiny of adverse events that effect patient quality of life
- Integrated data analyses

WHAT DO DRUG DEVELOPERS* THINK WILL BE THE MAJOR IMPACT OF PROJECT OPTIMUS ON ONCOLOGY DEVELOPMENT PROGRAMS?

INCREASED TIMELINE	38%
MORE STREAMLINED DEVELOPMENT	28%
INCREASED DEVELOPMENT COST	19%
APPROVAL DELAY	9%
HIGHER FAILURE RATE	6%

*Number of respondents = 576

WHAT STEPS SHOULD YOU TAKE TO BE PREPARED FOR PROJECT OPTIMUS?

Perform dose-finding studies in a pre-market setting

Focus on improving tolerability

Plan for interim analyses and allow for intra-patient dose escalation

Meet with the FDA as early as Pre-IND to discuss your dosing strategy

CERTARA CAN HELP YOU GET YOUR DOSE RIGHT THE FIRST TIME!

With deep experience in model-informed oncology drug development, dosing and regulatory strategy and submission, we've helped advance hundreds of oncology programs. Our proven, integrated approach using quantitative methods can help you to navigate this regulatory change.

Non-clinical Profiling	Predict Human Exposure	Predict Human Effect	Mitigate Risk
Toxicology & Toxicokinetics	Allometric Scaling	PK/PD	Risk Assessment
In Vitro Pharmacology	IVIVE	Systems Pharmacology	Safety Factor
In Vivo Pharmacology	PBPK		Monte Carlo Simulation

HUMAN STARTING DOSE

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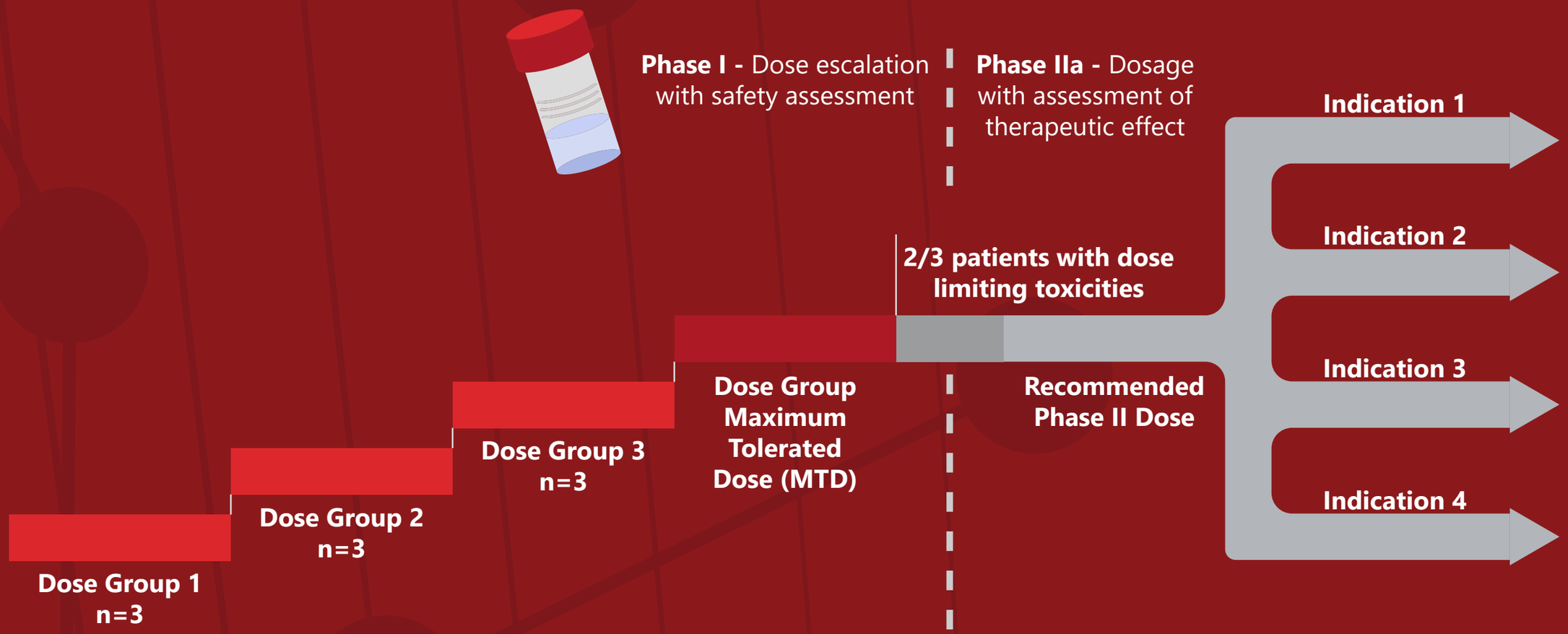

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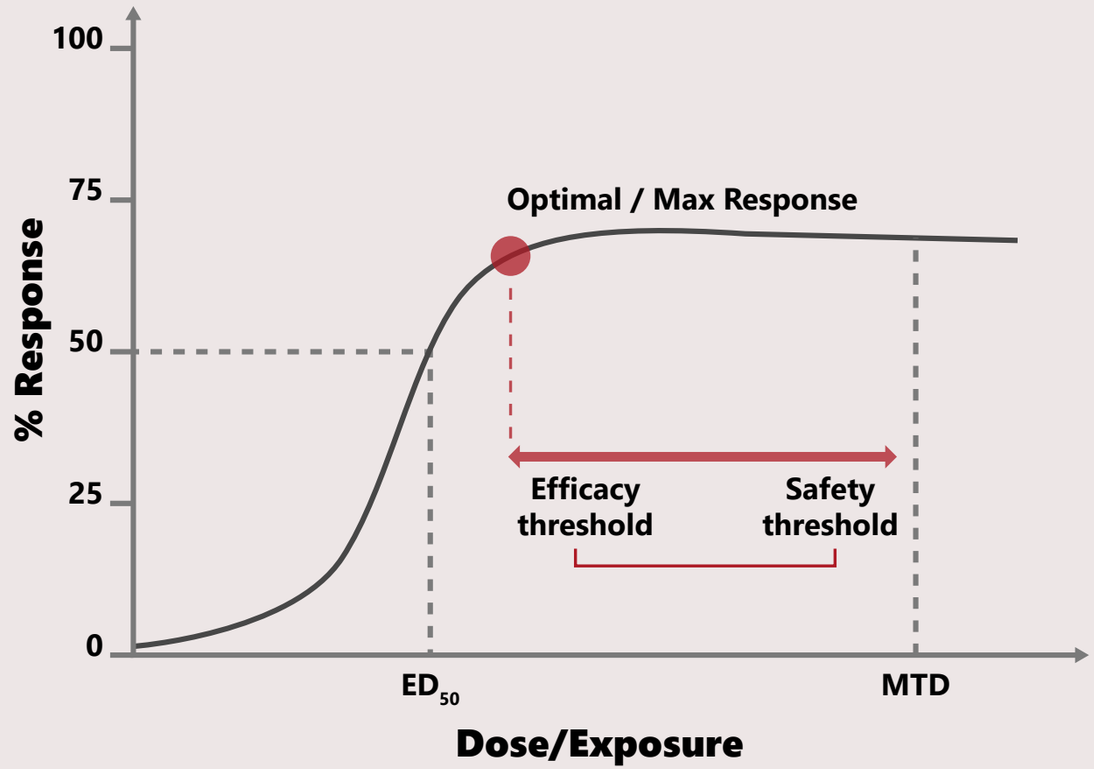

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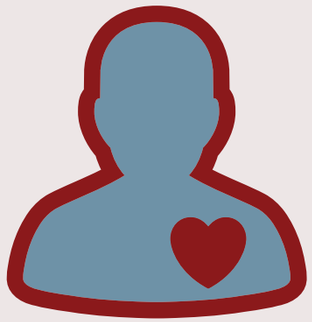

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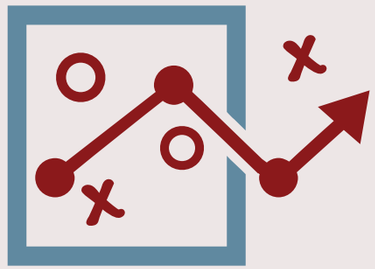

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