Updating Dosage Optimization to Improve Tolerability for Patients with Cancer

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Disclaimer

- N/A

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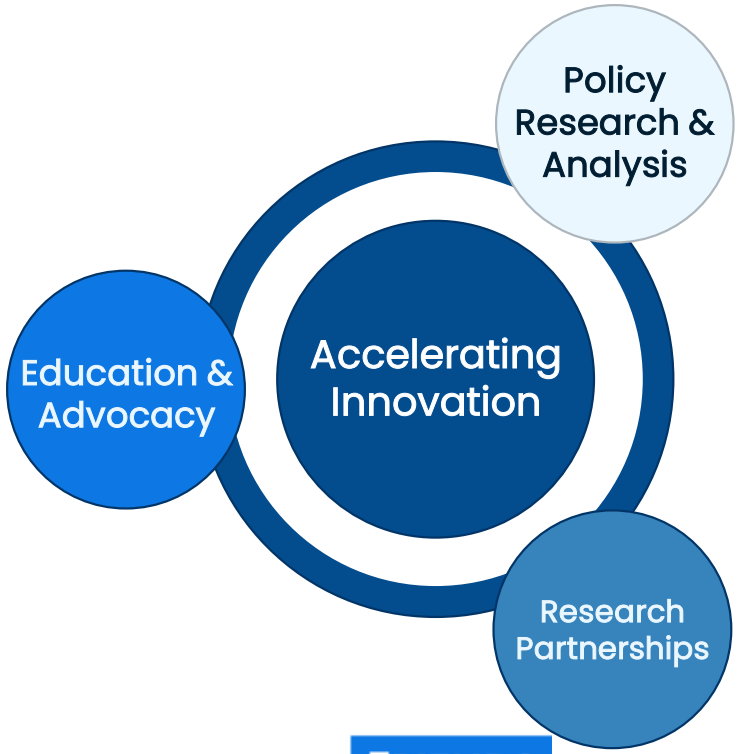
Friends of Cancer Research *(Friends)*

Friends works to accelerate policy change, support groundbreaking science, and deliver new therapies to patients quickly and safely.



Policy Research & Analysis

- Convene stakeholder meetings
- Assess drug development trends

Education & Advocacy

- Support advocates through education

Research Partnerships

- Work with stakeholders to generate novel data to support policy development

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The *Friends'* Collaborative Model

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Timeline of Friends' Dosing Projects

2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023

FDA Announces Project Optimus

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Expectations for Dosage Optimization Studies

Dosage Escalation Study	Dosage Expansion Study
• First in human trial • Test multiple doses in patients • Identifies a recommended dosage range to inform the Dosage Expansion Study	• Test at least two dosages in a randomized trial • Supports the selection of the dosage for registrational trial

Focus is not necessarily to identify the MTD, but to use a totality of evidence to select a dosage that is safe, effective, and tolerable

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Considerations for Dosage Optimization Strategies

PK and PD Metrics	Therapeutic Properties	Patient Populations
• Identify biomarkers that are well defined	• Differences like small molecule vs. antibody	• Heterogeneity in tumor type, stage, and comorbidities

Combination Products	Supplemental vs. Original Approval	Stakeholder Education
• Understand impacts of each agent in the combination	• Supplemental applications may require additional assessment	• Inform patients and providers about updates to the approach

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Defining Tolerability to Include the Patient Perspective

In 2018, *Friends* worked with stakeholders to define "tolerability"

Standard Assessment of Tolerability

Clinician Reported Outcomes

- Common Terminology Criteria for Adverse Events (CTCAE)

Case Report Data

- Dose modifications and discontinuations
- Dose interruptions
- Hospitalizations
- Death

Integration of Patient Experience

Patient-Reported Outcomes

- Patient-reported symptomatic adverse events
- Patient-reported overall burden of adverse events
- Patient-reported physical functioning
- Other types of functional assessments

A complete understanding of tolerability should include direct measurement from the patient on how they are feeling and functioning while on treatment.

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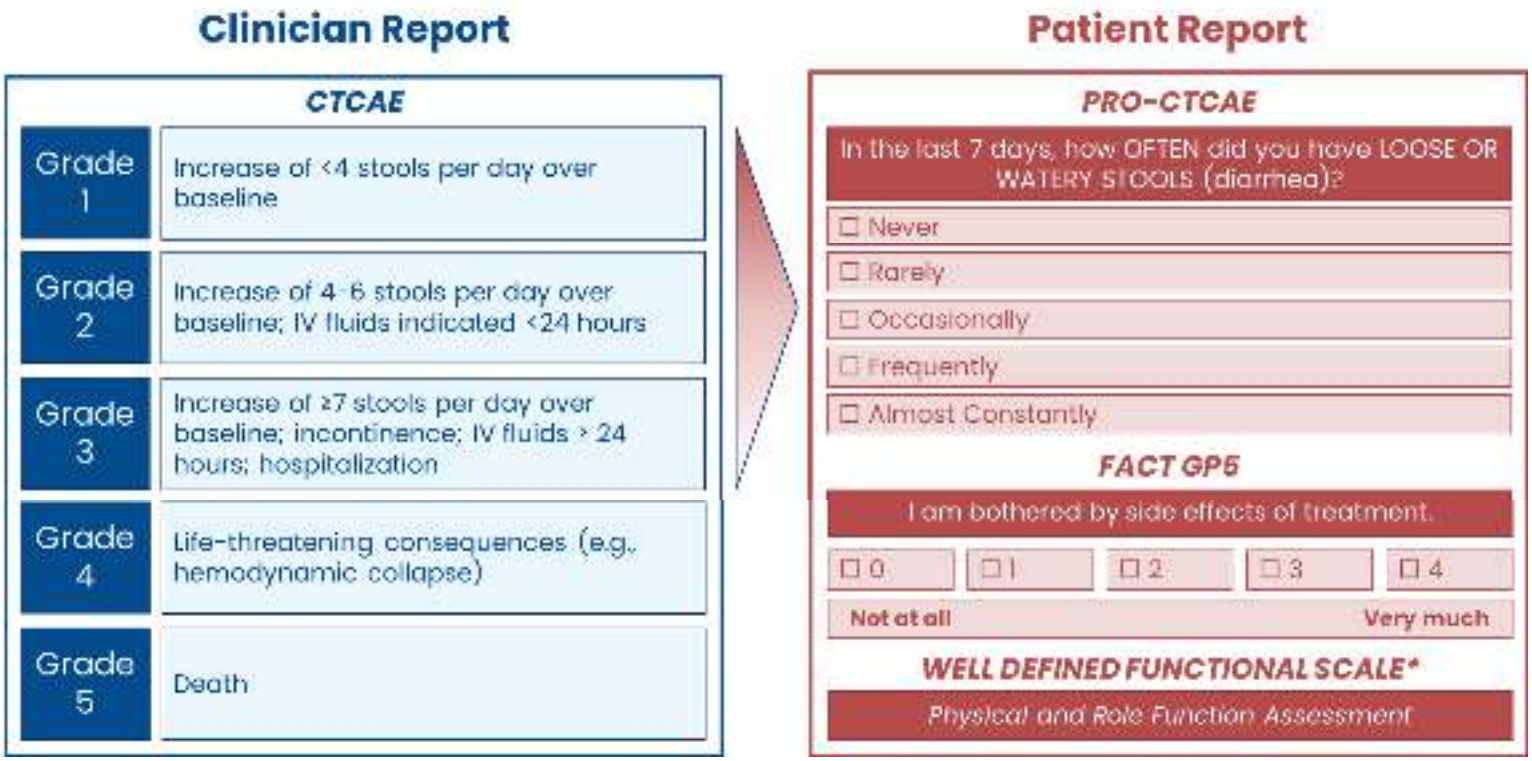
How PROs Enhance an Understanding of Tolerability



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Incorporating PROs into Dosing Studies

Dosage Escalation Study	Dosage Expansion Study
• Performing high frequency systematic assessment can add power to pharmacokinetic exposure-response analyses • Collecting a breadth of PROs for a smaller proportion of patients can inform targeted PROs for later phases • A free text PRO item can help identify unknown AEs	• PRO data including descriptive trends in severity and duration should be evaluated • Consider PRO questions that are relevant and minimize duplication • Perform assessments more frequently in the first few treatment cycles

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Conclusion and Next Steps

- Sponsors should perform robust dosage escalation and dosage expansion studies during early phases of clinical trials to define the optimal dose
- Incorporating PROs can provide a better understanding of the tolerability and inform dosage selection
- Understanding implementation and interpretation of early phase clinical trials and how they inform dose selection will be critical

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