U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION & RESEARCH
OFFICE OF CLINICAL PHARMACOLOGY

Impossible Instructions—Food Intake and Concomitant Medications

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Optimizing Dosages for Oncology Drug Products
Session 3:
Understanding the Effects of Food and Drug-Drug Interactions on Dosage Optimization

Fundamental Questions About Dosing in Oncology

Does Food Impact the Drug?

- If so, do we give it fasted, or with food?
  - If yes, what kind of food?
  - What is the dosing interval?

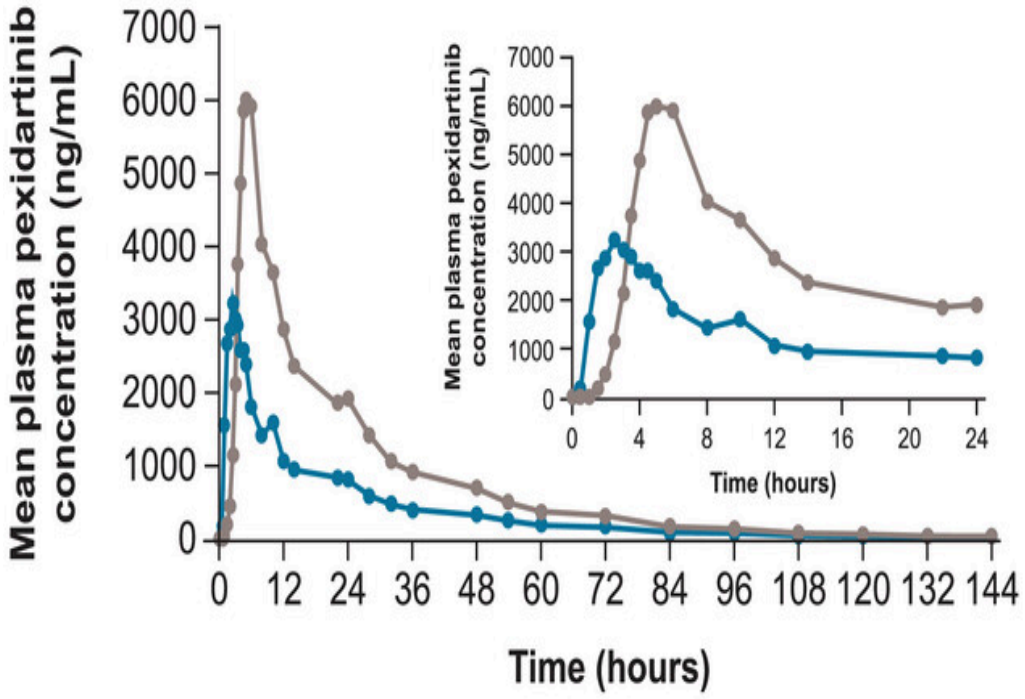
Is the Drug affected by other drugs?

- If yes, should we just avoid it?
- What if cannot be avoided?
- Anticonvulsants in GBM
- Antifungals in AML
- Commonly administered comedications

Fundamental Questions About Dosing in Oncology

Dose Impact Food Drug Exposure?

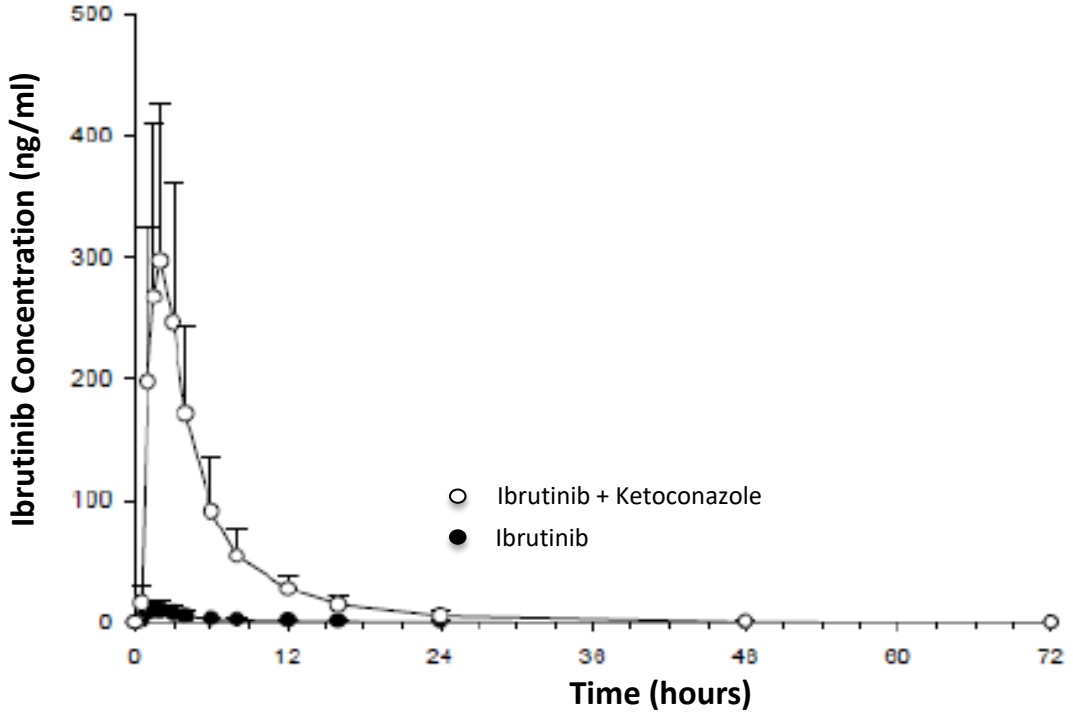
TURALIO (pexidartinib)



What about low fat meals?

Do Drug-Drug Interactions Impact Drug Exposure?

IBRUVICA (Ibrutinib)

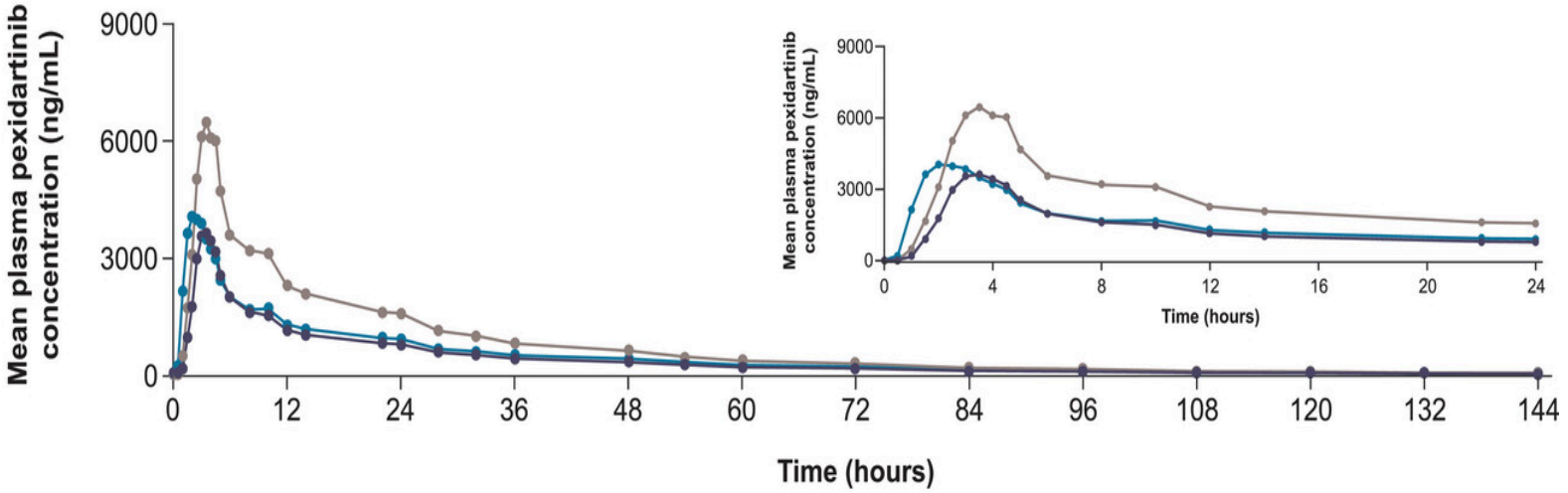


What about moderate inhibitors? Or weak inhibitors?

H. Zahir et al. 2023 Clinical Pharm Dug Develop 12(5): 475-483

http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/205552s007lbl.pdf

Food Drug Interaction: TURALIO



Food Drug Interaction: Low fat meal < High Fat

Fed drug administration more advantageous than fasted administration for long term treatment

Three years to complete PMR/label

H. Zahir et al. 2023 Clinical Pharm Dug Develop 12(5): 475-483

Food Effect and DDI Study Limitations

There are limits on conducting clinical studies

These studies do not answer all the questions about dosing

They are often conducted late in development ---often Post Marketing

Can MIDD Aid in Better Dose Selection for Food Drug Interactions?

Can we use MIDD early to assess different types of meals?

- Low fat?
- High fat?
- Other types of meals?

Can we use MIDD to better assess food/fasting dosing interval?

Can we use MIDD to assess differences in acute FE vs at steady state?

Can we use MIDD to assess patient risks under different fed conditions, and recommend better dosing strategies for testing?

Can MIDD Aid in Better Dose Selection for Drug-Drug Interactions?

Can we use MIDD to assess the doses needed in acute (short-term) DDI vs DDI effects at steady state?

Can we use MIDD to help design better dosing regimens for time-dependent inhibitors over the course of treatment?

Can we use MIDD to simulate/explore better dosing regimens when DDI cannot be avoided (or when we might want to leverage this phenomenon)?

Can we use MIDD to evaluate dosing in clinical scenario that are infeasible to conduct studies?

Can we use MIDD to assess patient risks under different fed conditions, and recommend better dosing strategies?

Can MIDD Aid in Better Dose Selection for Drug-Drug Interactions?

Can we use MIDD to assess patient risks under different fed conditions, and recommend better dosing strategies?

Can we use these MIDD tools in early in drug development to select better doses upfront?

Thank You

Stacy Shord
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