



Quality Imaging for Clinical Trials

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While the following is based on publicly available data, my work experience and feedback from colleagues in the industry, the opinions expressed are my own and not official company statements.

What do I think quality means for pharma?

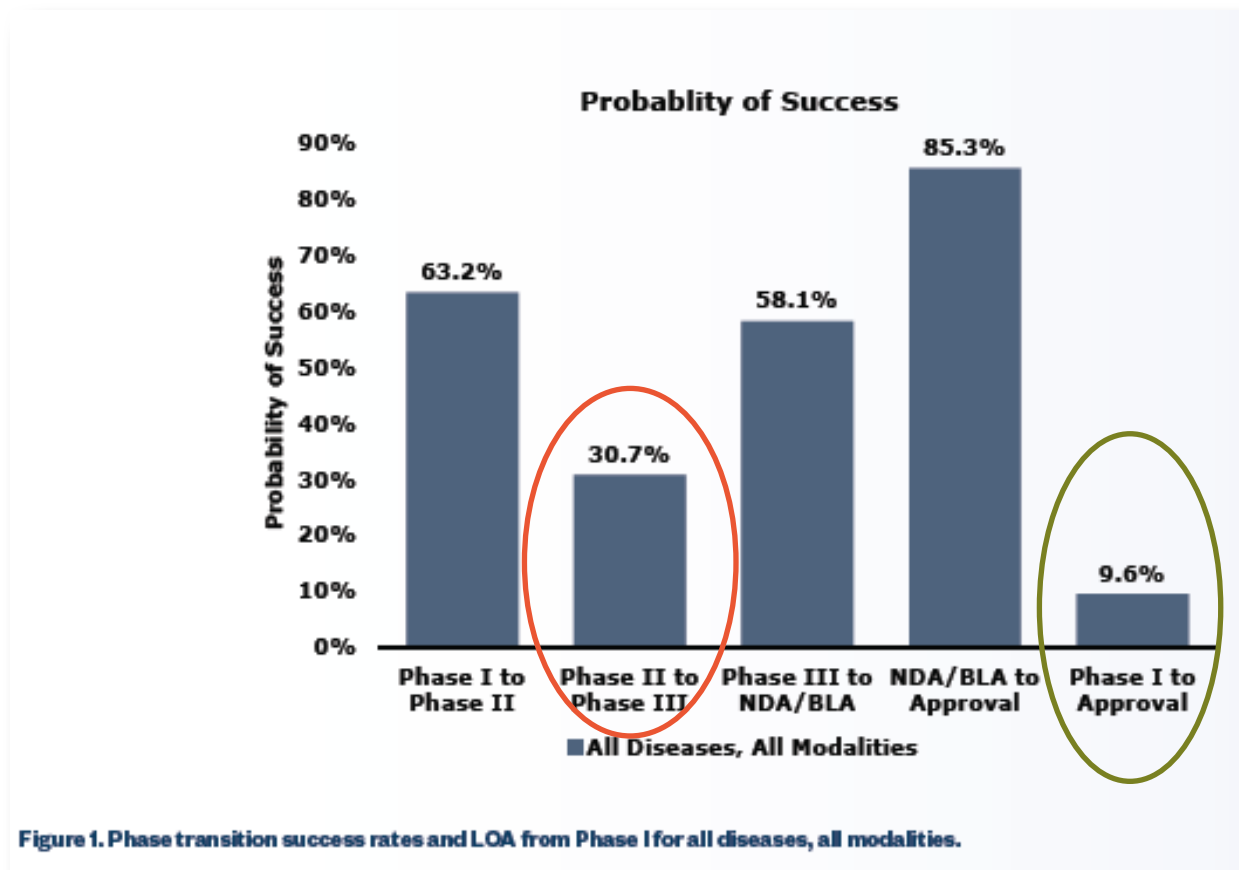


1. In clinical trials quality typically means Reproducibility and Standardization
 - Anecdotal evidence that push for quality works both ways from clinic to clinical trial and from clinical trial to clinic

2. In the translational and early space we are also looking for advancement
 - Are there alternative, better ways?
 - Can we demonstrate theoretical and clinical relevance ?
 - Is it feasible/ sufficiently practical?

3. Pragmatic approaches are great and may be cheaper and faster,
 - Yet, in an era of targeted therapies
 - Obligation to strive to better understand the effects of our treatments?
 - Aim for more scientific approaches to treatment decisions and drug development decisions?

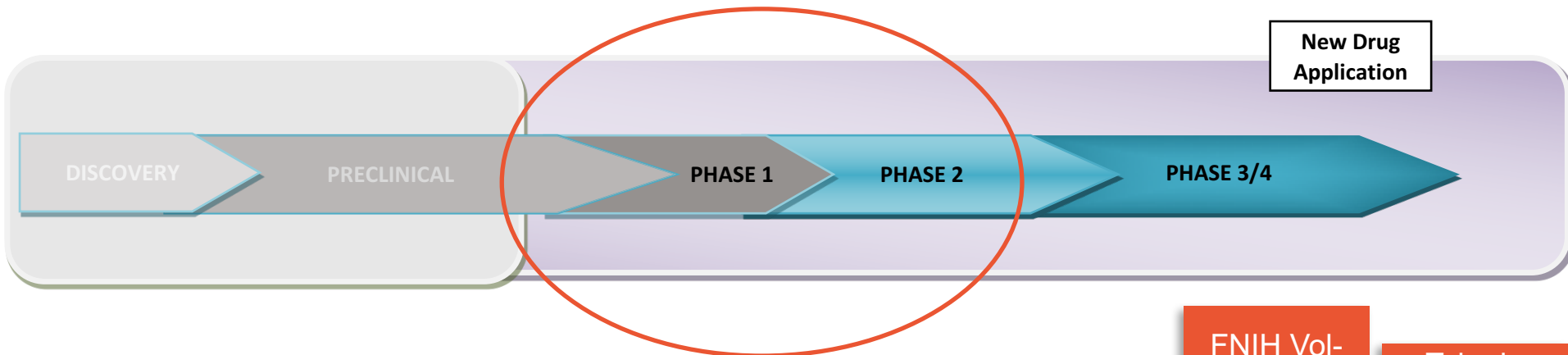
One of the drug development challenges



Bio June 2016 : " Clinical development success rates 2006-2015

<https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf>

(Semi) Quantitative Imaging Biomarker at Takeda



- Do we have the right efficacy biomarkers to predict efficacy?
- What are the critical parameter, can we standardize them?
- Do they need to be different in the targeted therapies?
- Can we identify more sensitive early predictors?
- Can we identify biomarkers that help us better understand the underlying biology?

FNIH Vol-PACT

Takeda internal efforts

QIBA

- “Standard” late phase solid tumor trial (CT/MRI arterial and portal venous phase contrast)
 - <10% of timepoints queried for slice thickness, anatomical coverage, patient positioning
 - <5% of timepoints queried for adequacy of timing and amount of contrast

Inconsistent Contrast Administration (e.g. mRECIST for HCC)



Baseline



Week 6



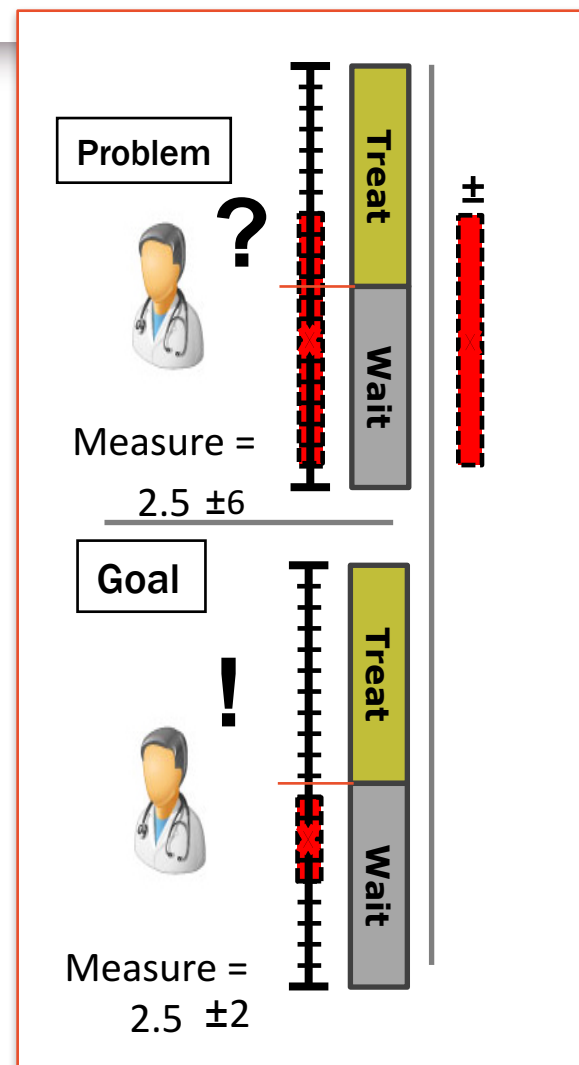
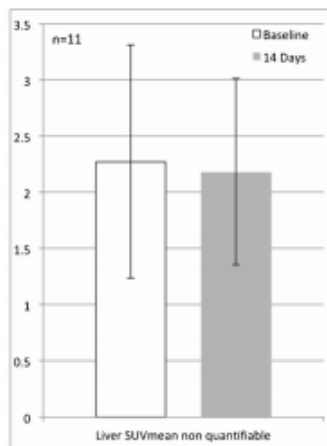
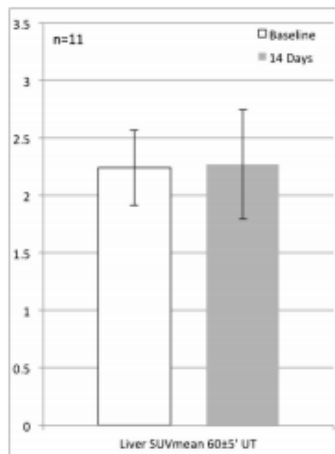
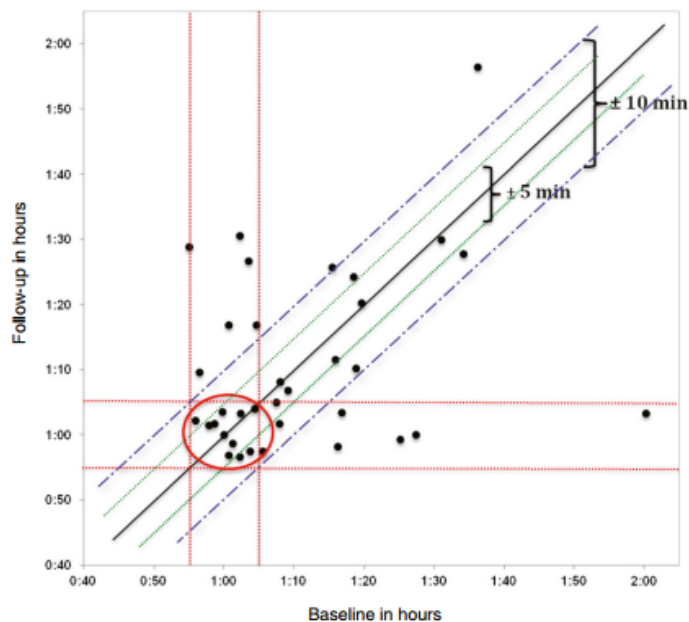
Week 23



PAREXEL Archives.

- For FDG-PET study (aiming to determine SUVs)
 - Compliance may be as low as 30% of imaging timepoints
 - Uptake time/ Wait time
 - Blood Glucose levels

Lack of quality hurts clinical patient management



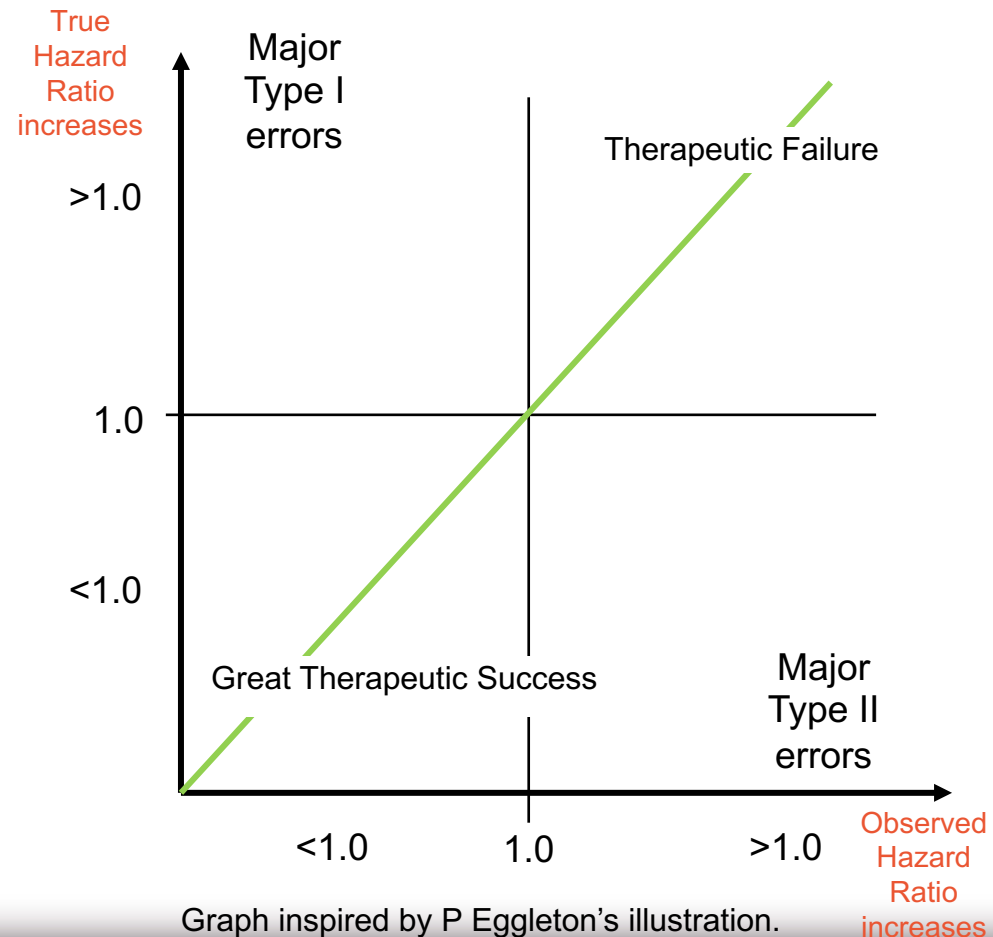
Hristova et al., Eur J Nucl Med Mol Imaging (2015) 42:848–857.

Illustration courtesy of K. O'Donnell

Lack of quality hurts clinical patient management AND drug development



1. For successful drug development (including or especially in targeted therapies) need to understand the biology
2. Low reproducibility of imaging biomarker reduces the clinical value
3. Low reproducibility of imaging biomarker reduces the clinical trial value and drug development value
 - Greater challenge to achieve significant differences
 - Need for larger trials
 - Greater challenge to formulate future strategy



Thank you



Takeda Pharmaceutical Company Limited

