EBF Biomarker Focus Workshop
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Facilitate fast trial/project decisions and confirmation of context of use based on early PK and biomarker data

– The V I S T A Approach -

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Why? The starting point: Setting the scene

The Clinical Situation

Traditionally, clinical programs are driven by elaborate clinical efficacy endpoints

Today, Translational Medicine organizations suppor clinical programs in early phases with biomarker-based decision making

The Data Analysis

The conventional process to analyze clinical data is very formalistic, aiming for a static report

A holistic data analysis approach is desired allowing for an automated, interactive review of pharmacodynamics (PD), pharmacokinetics (PK), safety and covariates

The Biomarker dilemma

Exploratory biomarker data analysis is dominated by statistical hypothesis testing instead of biological insight generation

To define a CoU for exploratory biomarkers in the early clinical phase is difficult, but desirable

How can we streamline drug development, but maintain patient safety and efficacy?

How ? The Challenge: Create a change in mindset

Link lab sample analysis to clinical data evaluation

- BM based decision making is impacted by CoU and vice versa
- Connect the respective stakeholders (lab sample analyst & clinical data analyst)

Drive process automation from lab data to clinical decision making

- Too much hands-on in the process from lab bench to clinical decision
- Process from clinical protocol to clinical report takes too long

Enable customers to have a holistic view on all clinical data

- Look at all the data at once from different angles
- Do not perform isolated data analyses without context to other variables, such as PK, safety, covariates

Establish interactive and visual data analysis capabilities

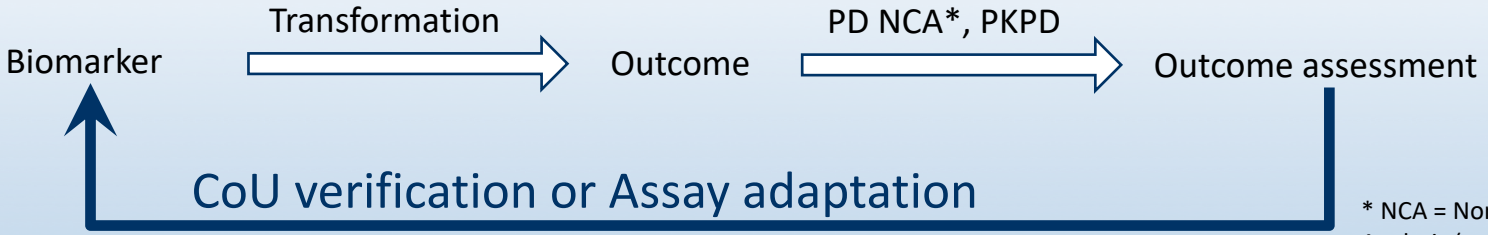
- Reduce complexity of data analysis by allowing interactive drill down
- „A picture is worth a thousand words“

What? Combine process and technology

VISTA – Visual & Integrated Support of Translational Analysis

- Provide **one** automated procedure to access, visualize & analyze clinical data…
  …interactively & flexible…for any open label trial…at any point in time
- Support trial teams with interactive trial analysis on PK, biomarkers & covariates
- Apply standard data structure shared with authorities
- Use powerful analysis technologies (Tibco Spotfire ®)

Simplify process from sample analysis to data evaluation including SOP landscape

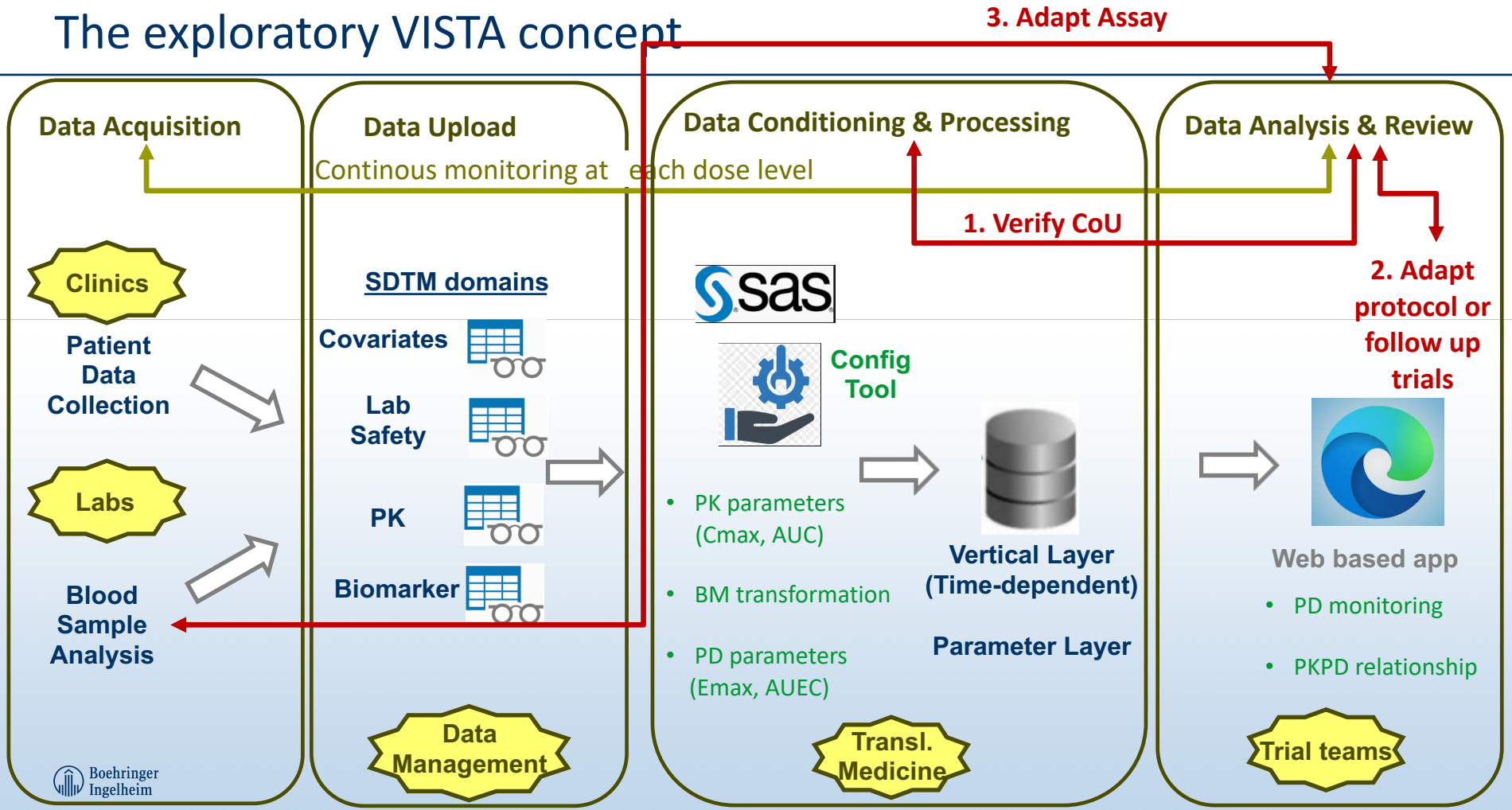


BMM SOP ** **DA SOP** **

* NCA = Noncompartmental Analysis (e.g. AUECs, Emax)

** BMM Biomarker Measurement
** DA Data Analysis

The exploratory VISTA concept



Conclusions

Reality check

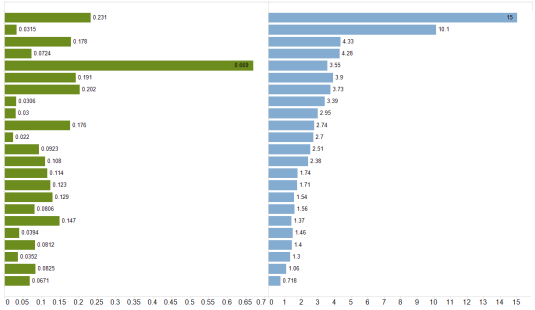
- **V I S T A Concept**: Go Live Q4/2018, mainly aiming for „online“ exploratory PK/PD data monitoring during trial conduct (but also safety)
- **Support Strategy**: TMCP support unit was built up with existing resources
- **Reality Check**: 74 trials requested support since rollout

Outlook

- Make better use of the VISTA approach for exploratory Biomarker data analysis
  - Eliminate sampling for non-responding biomarkers early
  - Verify context of use for biomarkers
  - Adapt biomarker assay setup to meet needs for clinical data analysis
  - Adapt trial protocols of follow up studies based on early data interpretation
  - Use Phase I studies for exploratory biomarker analysis instead of Phase 0, banked human samples or preclinical data

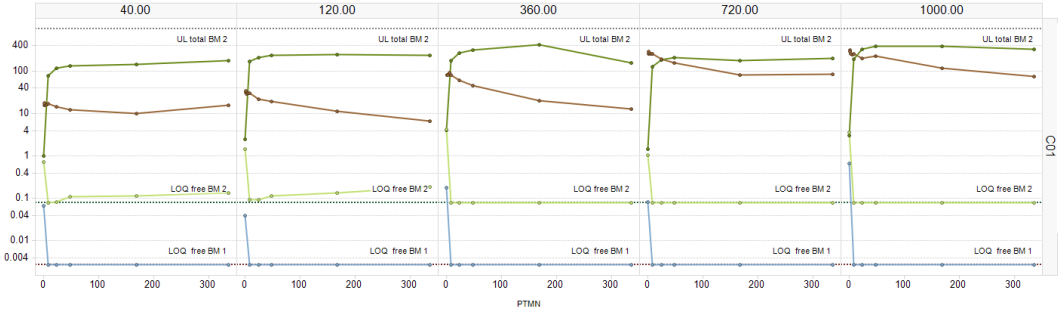
Use cases

Individual endogenous baseline levels of BM1 & BM2



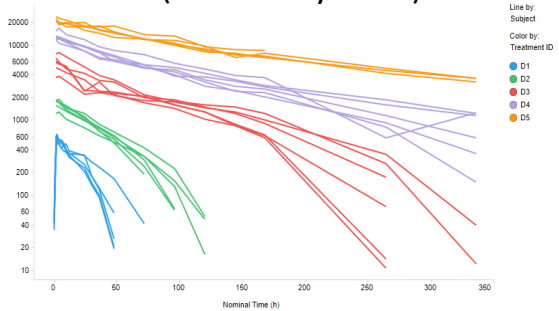
Concentration-time curves of Drug & Target per dose

Dose →

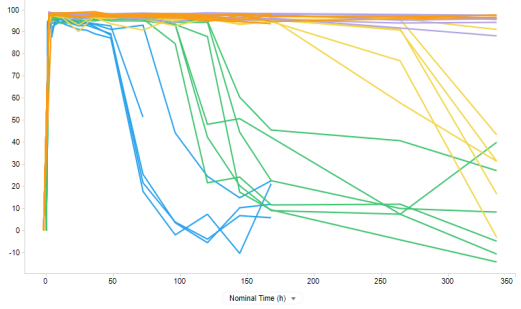


- Drug
- Free BM1
- Free BM2
- Total BM2

Pharmacokinetics of the Drug (colored by dose)



Pharmacodynamics of the Target (Receptor occupancy by the Drug)



PKPD relationship between Drug and Target