# FW BM EBF 2020

In cyberspace, 16 September 2020

## Session 4
## Learnings and actions from the 2019 EBF FW

## Intro Round table & case studies

# **Learnings** and actions **from the 2019 EBF FW**

Biomarker assay validation = **F**it-**f**or-**P**urpose validation

- FFP assay validation means different criteria are required for each BM assay and even each particular use of the assay based on the specific CoU.
  No BM baskets are possible

  => remember the famous shoe slide from Lauren Stevenson

- „Fully validated assay“ does not mean PK criteria

PK is a specific purpose with specific validation criteria & pre-defined acceptance criteria

FFP validation does not mean less validation

BM assays are fully validated for their specific CoU!

# **Learnings** and actions **from the 2019 EBF FW**

Key challenge around the CoU = Communication

Same understanding of the specific CoU needed within BA and outside BA

- With the stakeholders
  - Identify and communicate with the relevant stakeholders
  - Understand what the data are used for & decisions based on these data
  - Communicate the limits of your assay
- With agencies
  - Regulatory expectations (FDA?)
  - No guidelines available => scientists feel uncomfortable and follow PK regulation

# **Learnings** and actions **from the 2019 EBF FW**

CoU statements need to be clearly defined and documented

Documented CoU statements in the bioanalytical report is important

- The CoU may change during drug development and the assay may no longer fit!
- For “known” biomarkers: available kit and/or published data may not be applicable for the CoU and may thus complicate discussion/agreement with stakeholders.

# **Learnings** and actions **from the 2019 EBF FW**

„Sense and nonsense of aligning CoU with development stage“

The development stage is important to know from a scientific point of view and for reporting, but

> CoU itself is independent of the development stage

“Exploratory” or “decision making”, “primary endpoint”… is not a CoU!

FFP not to be mixed with the scientific validation concept!

# Learnings and **actions from the 2019 EBF FW**


Interactive roundtable discussion on different CoU cases:

- Is the information sufficient to define the CoU? If not what info is missing and should be discussed with the stakeholder?
- What experiments need to be done during development, and then validation, to ensure that the assay is “fully validated”?

# Learnings and **actions from the 2019 EBF FW**


- Please stay on this zoom meeting, Magnus will divide all delegates in 8 teams now for roundtable discussion
- Every team discuss one BM assay request (4 CoU cases - 2 teams per case)

  1 Moderator per team:
  - Kyra
  - Michaela
  - Linda
  - Uli
  - Rob
  - Jo
  - Susanne
  - Lauren
- 1 Note taker per team => provide notes to your moderator or Michaela directly after the discussion. There will be an alarm message 2 min before a hard stop of the roundtables discussion.
- Summarised feedback on the discussions of all 4 cases at 18:30 (CET)

# Roundtable Case 1

A biomarker will be used to support dose escalation in a first in human study. The biomarker will decide the dose in a phase 1b PoC study. The biomarker is the drug target and is an intracellular protein expressed  in subpopulation of blood cells.  The clinical team has stipulated that when >95% target engagement has been achieved in all subjects at trough (in the multiple ascending dose), then the MAD study can stop.

The assay consists of 2 read outs (free and total) and the research team have provided a skeleton method that works in animal models.

- What info do you need to fully understand the CoU?
- What experiments need to be done during development, and then validation, to ensure that the assay is “fully validated” for that CoU?

# Roundtable Case 2

An explorative protein biomarker should be measured in plasma or serum in a phase IV placebo controlled double blind clinical study with hundreds of patients, pre- and several post-dose samples.

The biomarker should be tested whether it supports the hypothesis that it significantly changes during treatment as a disease modulating pharmacodynamic biomarker and as a possible further hint of drug efficacy (in addition to several other clinical endpoints).

Biomarker results will be evaluated as percent change from baseline.

The change during treatment is unknown, maybe quite low (< 20%) but expected to be significant when averaged over the whole population.

The study lasts for about three years with a one year treatment period per patient.

No interim evaluation of data is necessary.

Commercial immunoassay kits for the biomarker are available (RUO).

- What info do you need to fully understand the CoU?
- What experiments need to be done during development, and then validation, to ensure that the assay is “fully validated” for that CoU?

# Roundtable example 3

An exploratory, distal PD biomarker may be used for dose and dosing regimen decisions in the future, and could also potential serve to stratify untreated patients for pivotal studies.

The sponsor currently has a “validated” cynomolgus monkey assay, the data from which is being used for M&S efforts to support dose levels and dosing regimen for the SAD (healthy volunteers) and MAD studies (patients).

The program team is debating GO/NO GO criteria for the SAD study biomarker data, which is gating the MAD, based on published data to date by a competitor molecule, but in the meantime they expect to have a “fully validated” clinical assay before the start of the FIH study.

- What info do you need to fully understand the CoU?
- What experiments need to be done during development, and then validation, to ensure that the assay is “fully validated” for that CoU?

# Roundtable Case 4

BM data requested to support a PKPD trial in the development of a biosimilar.

The BM is well known  and accepted monitoring BM to establishing a drug's proof of concept in a patient population and is listed as primary endpoint in the clinical protocol of the trial.

Commercial immunoassay kits for the biomarker are available.

The project team request quantitative assessment using a validated assay to support a PKPD study and avoid the need of a phase III trial for submission.

- What info do you need to fully understand the CoU?
- What experiments need to be done during development, and then validation, to ensure that the assay is "fully validated" for that CoU?