PhUSE Single Day Event – Frankfurt 06MAY2014

Lead Statistical Programmer interacting and meeting face-to-face with the FDA * – experiences from an oncology filing and recommendations

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* “Tornados, Nervousness, Sweating, Suit, Correct Behaviour, …Meeting with the FDA…”

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Agenda

- Background of the FDA meeting (BLA)
  - Application Meeting
  - Technical Walkthrough Meeting
- Preparations for the FDA meeting
- Regulatory Gateway System
- Stat. Prog. experiences from questions received from the FDA and other health authorities
- Stat. Prog. attendance at the early/mid/late cycle FDA BLA review meetings
- Recommendations / Conclusions

Background of the FDA meeting (BLA)

- Phase III Oncology Filing Activities
  - → Approval occurred on 01NOV2013 (**GAZYVA**)
  - → "GAZYVA, in combination with Chlorambucil, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)"
- Breakthrough Designation / Accelerated Review Timelines
- http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm341027.htm
- Washington DC, FDA Headquarters, June 2013
- Orientation Meeting with the FDA to discuss the BLA submitted in Spring 2013
  - → NEW meeting, no fixed list of people who should attend
  - → Stat. Prog. recommended / needed due to technical part
- Actual Orientation Meeting with the FDA consisted of two parts:
  - Application Meeting (large audience)
    - → General Presentation 1.5 h (Study & Results) (→ next slides)
  - Technical Walkthrough Meeting (small audience with the actual BLA reviewers)
    - → Technical Presentation 0.5 -1 h (Regulatory Gateway System) (→ next slides)

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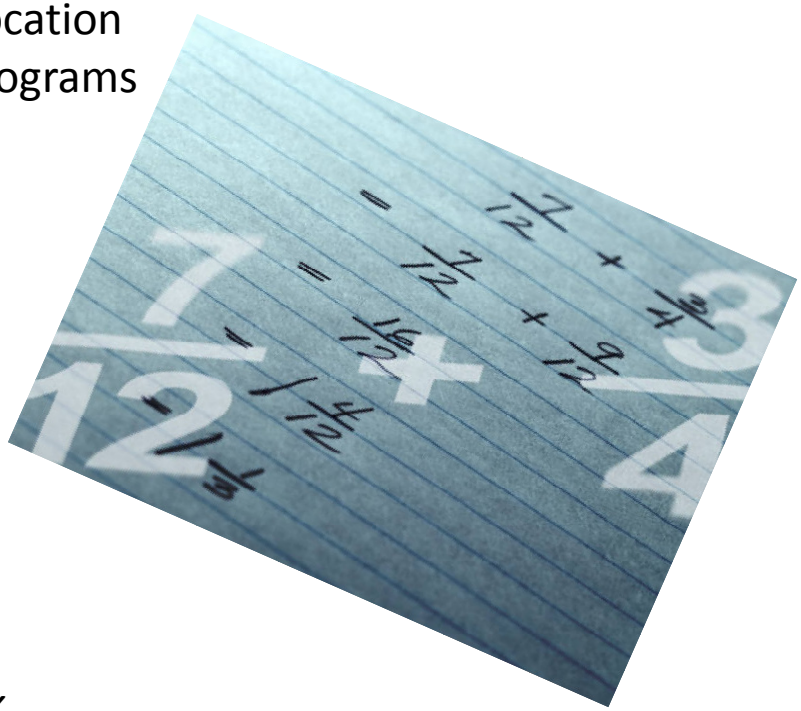
Application Meeting

- Content:
  - Around 80 slides (incl. back-up-slides)
  - Regulatory Overview
  - Participants
  - Proposed Indication and Dosing
  - FDA Key Interactions (BLA)
  - Mechanism of Action (Drug)
  - Studies included in BLA
  - Rationale for Study
  - Proposed Indication and Dosing
  - Study Design /Statistical Design
  - Safety & Efficacy Results
  - Baseline Characteristics
  - Pharmacology
  - ……..
  - Q & A

→ Presentation given by Science

Technical Walkthrough

- Content:
  - Overall organization of the BLA
  - Datasets and Supporting Documents & Location
  - Format of the ISS and ISE Datasets and programs
  - Navigation of BLA and CRFs
  - Efficacy and Safety Data
  - PK Data
  - Review Guides (Content)
  - Define-files
  - Raw Data & Derived Data
  - …….
  - **Q & A**



→ Presentation given by Stat. Prog/STATS/PK

Preparations for the FDA Meeting I

- Regular Filing Team Meeting TCs starting weeks before
- Slides review sessions
- Experiences from other project teams (previously asked questions)
- Possible questions that might be asked by the FDA
- Rehearsing the presentations
- 1-day F2F Washington Hotel meeting on the Sunday before with all team members
- Understand the overall proceedings – what do we have to expect?

  → yes, we WERE nervous!
- Get used to Regulatory Gateway system (→ next slides)
- Get familiar with the overall CSR Content

Preparations for the FDA Meeting II

- Buy a suit and dress up!

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Preparations for the FDA Meeting III

- Drive there!

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Preparations for the FDA Meeting IV

- Survive Tornados in Washington!

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Preparations for the FDA Meeting V

- First wait !

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Preparations for the FDA Meeting VI

- Learn how to behave when being there!

→ Regulatory Policies:

“Interactions with Regulatory Authorities”

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Regulatory Gateway System

- The Gateway
- Pre-defined folder structure
- All deliverables go in there
- Structured in modules
- Large folder trees
- Everyone needs to be aware where deliverables are

Stat. Prog. experiences from questions

- Fast turnaround timelines → accelerated review
- Due to positive results not many questions
- Most were clarifications of the data in the reports or label
- Additional datasets and outputs to be submitted

→ working closely with esub team

- Stat. Prog. part of BLA response team
- Explanations needed to be written
- Discussion on submitted data and analyses performed by the agency
- Availability needs to be ensured
- Time-difference
- Tight timelines
- Inspection dataset
- Label discussions

SPA attendance at the early/mid/late cycle FDA BLA review meetings

- Stat. Prog. needs to be ready for any possible questions
- Might be F2F or TC
- Agenda-driven Stat. Prog. attendance
- Short turn-around timelines

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Recommendations / Conclusions

- BLA reviewers from the Agency in attendance included Clinical, Safety, PK, Nonclinical ….. reviewers
- The Application meeting was well attended
- Who is going next……?
- Especially when Stat. Prog. = “Biometrics Submission Team Lead”

  → Stat. Prog. should attend the meeting
- Lead Stat. attends the meeting as a subject matter expert on statistics and other content
- Presence of the lead Stat. Prog. is required for various technical and content questions (outputs, analysis datasets, raw datasets, derivations, overall structure of the BLA, etc) that might arise during the meeting
- Although there is no fixed list of people given who should attend the FDA BLA Orientation Meeting

  → highly recommended that lead Stat. Prog. of the respective project is attending this meeting together with lead statistician

  → make the team ready to confidently answer a broad spectrum of possible questions
- It is therefore important that Stat. Prog. has a fixed role within the filing team

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