BfArM
Bundesinstitut für Arzneimittel und Medizinprodukte

Alternative Monitoring Procedures in Investigator Initiated Trials (IITs) - International Workshop – Frankfurt, 03.04.2006

Implications for Monitoring of IITs – the German Experience of the Higher Federal Competent Authority (BfArM)

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Are there major differences between commercial and non-commercial clinical trials?

Statitistical evaluation of BfArM authorization requests in 2005

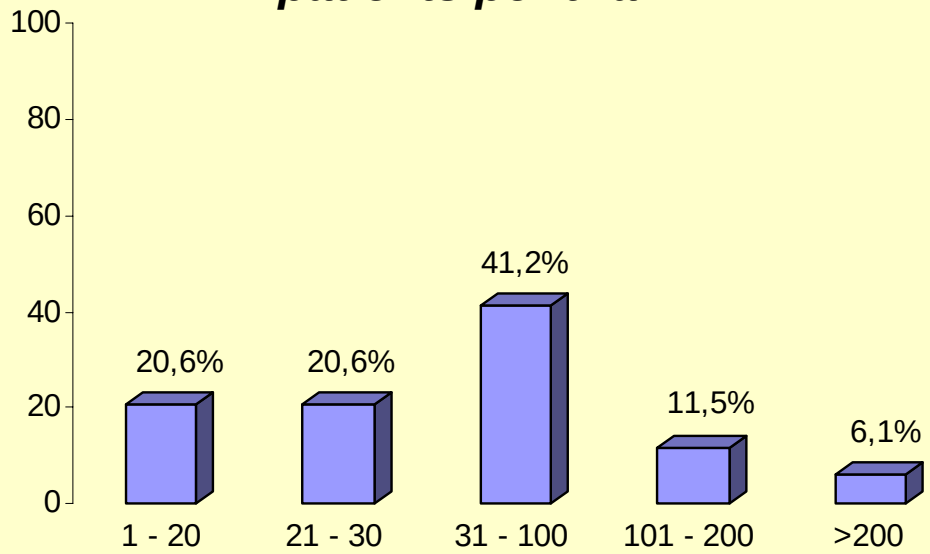
Evaluation period : ***01.01. – 31.12.2005***

- ***Number of authorization requests[1]:*** ***1099***
- ***Percentage of IITs:*** ***12%***

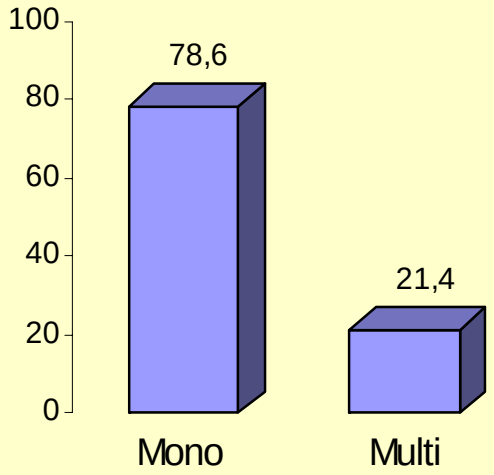
[1] ***Submissions according to the transitional provisions not included***

Statitistical evaluation of BfArM authorization requests in 2005

Number / percentage of patients per trial



Percentage of monocenter / multicenter trials



Only 5 % of the trials were multinational!

Statitistical evaluation of BfArM authorization requests in 2005

Trial objectives[1]

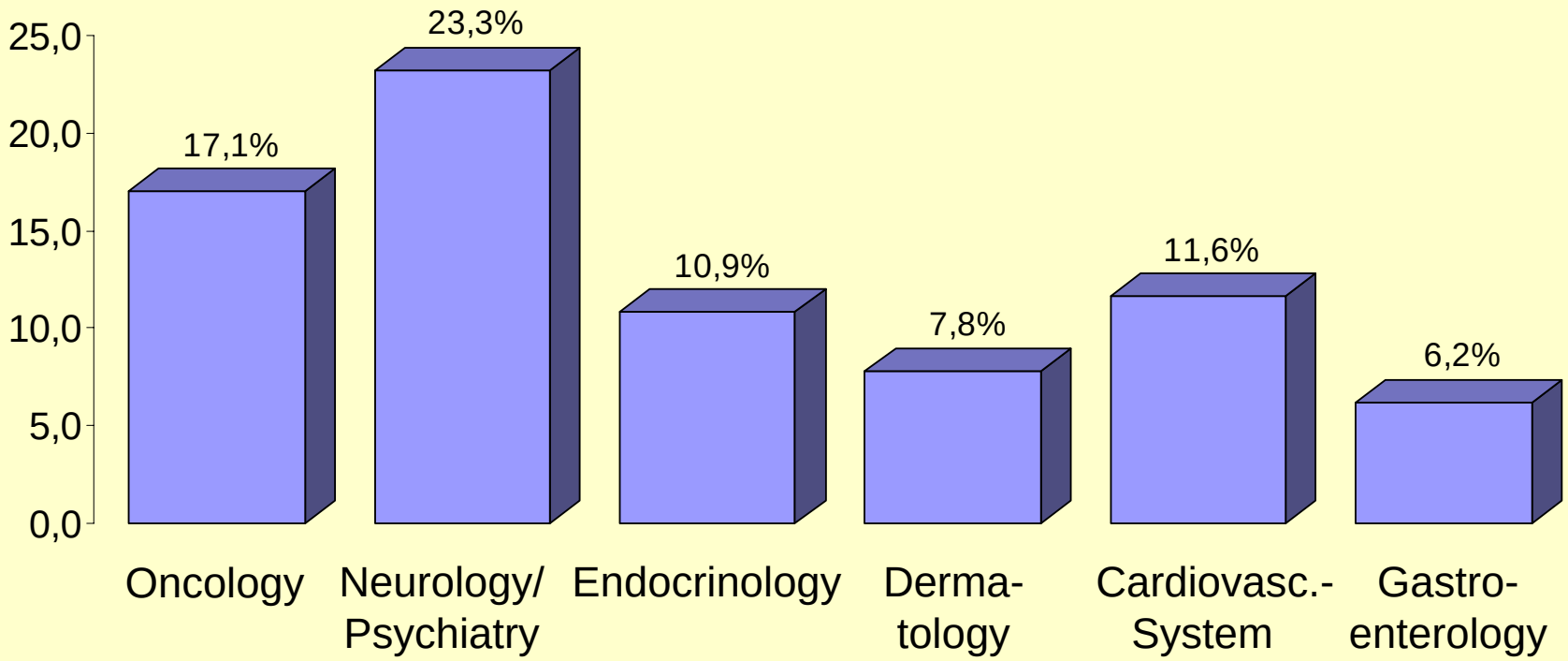
• ***Efficacy***	***54 %***
• ***Safety***	***45 %***
• ***Pharmacocinetic / -dynamic / -genetic***	***29 %***
• ***Others[2]***	***32 %***

[1] Multiple references possible

[2] e.g. research, pharmakoeconomics, diagnostic

Statitistical evaluation of BfArM authorization requests in 2005

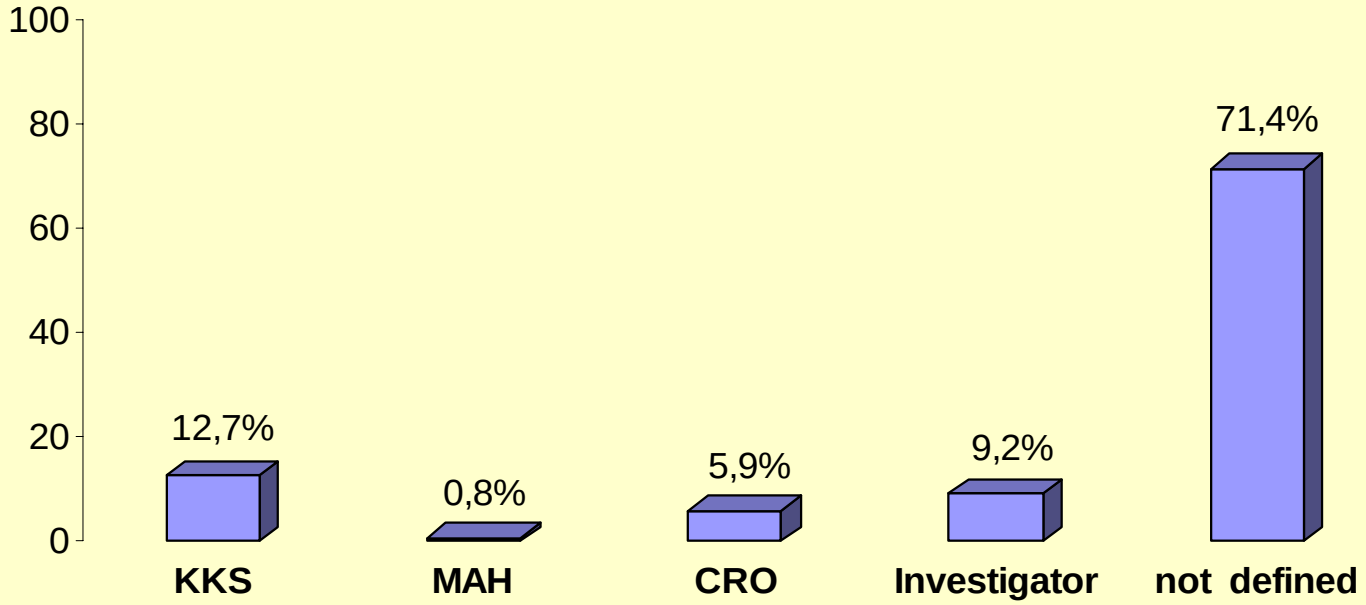
Indications[1]



[1] *indications < 5 % not listed*

Statitistical evaluation of BfArM authorization requests in 2005

Details about monitoring



What is our experience of monitoring from GCP Inspections?

Experiences from GCP Inspections
Implications for Monitoring of IITs

- ***Monitoring is one of the elements with a major impact on the quality of clinical trial conduct***
- ***GCP inspections of non-commercial clinical trials without any monitoring or with poor monitoring revealed an unacceptable high number of critical GCP deviations***

Experiences from GCP Inspections
Implications for Monitoring of IITs

- ***Good monitoring has an educational impact by sharing good clinical practice techniques that have been successfully implemented at other institutions with the local staff***
- ***However even intense monitoring is not able to compensate lacking personnel resources of the local staff***

Experiences from GCP Inspections
Implications for Monitoring of IITs

- ***The qualification, training and experience of monitors itself is often not adequate. This refers to monitors of CROs as well as of commercial and non-commercial sponsors!***
- ***The consistency and quality in the conduct of on-site monitoring by adequate trial specific training (protocol, IB, procedures) of the monitors is often not ensured***

Experiences from GCP Inspections
Implications for Monitoring of IITs

- ***Trial specific monitoring strategies** taking into account the specifics of a clinical trial regarding IMP, study population, trial protocol, involved sites and trial organisation are often not developed*
- ***The sponsors´ follow-up to monitoring visits by taking appropriate corrective actions in a timely and effective manner is often lacking***

On-site versus central monitoring – options and limitations

On-site versus central monitoring
Implications for Monitoring of IITs

Some monitoring aspects might be covered by central monitoring e.g.

- ***site staff qualification***
- ***ensuring the supply with the current versions of trial protocol, IB, IC forms and any other written procedures or documents***
- ***verifying that the submitted CRFs are complete, plausible, timely, legible, dated and signed***

On-site versus central monitoring
Implications for Monitoring of IITs

However, central monitoring is limited

- ***to any data that are indeed submitted to the sponsor***
- ***by the time-point of submission***
- ***by the data entry to the database***
- ***by the sponsor´s software***

On-site versus central monitoring
Implications for Monitoring of IITs

Some other monitoring aspects need to be covered by on-site monitoring, e.g.

- ***verifying the site staff resources, adequacy of facilities and equipment***
- ***verifying different aspects of IMP handling***
- ***verifying compliance with the protocol and with the applicable regulatory requirements***

On-site versus central monitoring
Implications for Monitoring of IITs

- ***checking the accuracy and completeness of the CRFs entries against source documents and regarding e.g.***
- ***inclusion-, exclusion-, safety-, efficacy parameter***
- ***dosage regimen and dose***
- ***intercurrent illnesses and concomitant medications***
- ***(serious) adverse events/ reactions***

On-site versus central monitoring
Implications for Monitoring of IITs

- ***checking that the sponsor is aware of any complaints and any untoward occurrences or facts that might have an impact on the IMP manufacture or supply chain, subjects´ safety or the trial outcome***
- ***detecting patient/data generation or other fraudulent behaviour***

The challenge is to develop intelligent and efficient trial monitoring strategies!

Thank you
for your attention!

ANY QUESTIONS???