Clinical trials in paediatric haemato-oncology

different ways for HP to participate

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Conflict of interest

- Nothing to disclose

Entrance Questions

- Q1.When preparing the implementation of a clinical trial can all the information needed be found in the protocol, pharmacy manual and Investigator's brochure / Investigational medicinal product dossier ?

- Q2. If there is no information available regarding the potential carcinogenicity of a drug can you then regard it as non-carcinogenic ?

- Q3. A drug authorized for adults is now being tested in children. Can the preparation and volume of infusion be the same ?

Learning objectives

After this session one is able to:

- Describe the differences in preparation of clinical trial drugs for children
- Discuss problems of administration of clinical trial drugs in children

Contents

- Preparation phase
  - Information (not) available
- Obstacles
- Two case presentations
  - Intraveneous drug
  - Oral drug

Preparation phase

Available documents

- Protocol
- Pharmacy manual
- Investigational medicinal product dossier / Investigator's brochure

- Information from initiation visit
- Prior experience

Information available in documents (1)

1. Protocol

- Inclusion criteria: age group
- Specific (age-based) dosing recommendations
- Maximum dose

Information available in documents (2)

2. Pharmacy Manual

- IMP name: generic name; code name
- Risk classification: potentially carcinogenic drug
- Reconstitution volume & concentration
- Final concentration range
- Light-sensitive drug
- Stability, storage conditions, expiration
- Administration: rate (ml/hr), time, inline filter

Information available in documents (3)

3. Investigational Medicincal Product dossier / Investigator's Brochure

- Detailed information
- Risk classification: potentially carcinogenic drug

Information *not* always available (1)

1. Protocol

- Specific dosing recommendations
- Maximum dose
- Rounding off
- Administration issues
  - Nasal gastric tube
  - Masking (after)taste

Information *not* always available (2)

2. Pharmacy Manual

- Risk classification: potentially carcinogenic drug
- Appropriate iv container
- Small infusion volumes: dead volume
- Supplies: obligatory use ?
- Premedication
  - Administration times (iv bolus / short infusion)
  - Equivalent drug and dosage

Information *not* always available (3)

3. Investigational medicinal product dossier / Investigator's brochure

- Risk classification: potentially carcionogenic drug
  - Measures taken to minimize exposure
    - Nurses
    - Pharmacy technicians

Obstacles

- Getting the missing information
  - Who in lead ?
  - Who to contact ?
- Most pharma have little experience with pediatric oncology trials

10-year report to the European Commission (1)

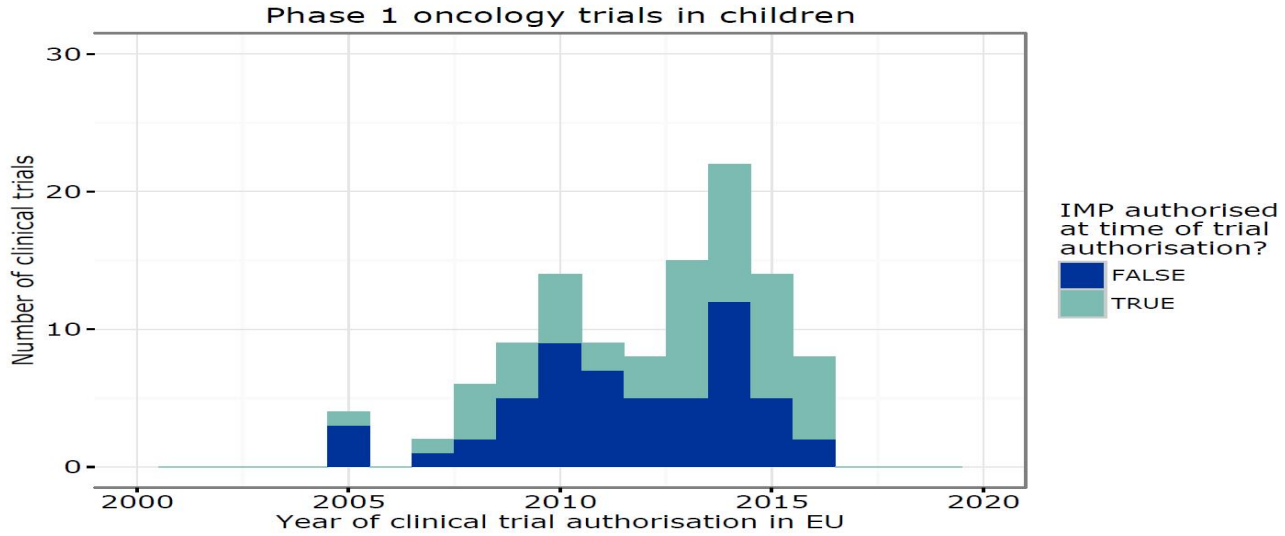
EMA/231225/2015

- 83 oncology PIPs for 68 anti-cancer medicines
- 10 developments completed
- 33 PIPs for age-appropriate formulations

- 5 new anti-cancer medicines authorized since Pediatric Regulation

10-year report to the European Commission (2)

Figure 14. Number of phase 1 oncology trials newly started by year in the EU and US



Source: EudraCT database.

Case 1: intravenous drug A

Available information

- Cytotoxic drug
- Dose: 0.6 mg/m^2 (d1) – 0.4 mg/m^2 - (d8) – 0.4 mg/m^2 (d15)
- Concentration range after dilution: 0.025 - 0.1 mg/ml
- Infusion time: 1 hr – inline filter
- Patient range: 1-18 yr
- UV-light protection

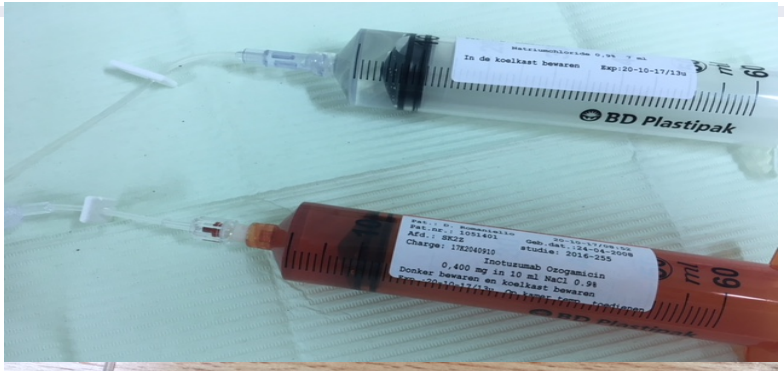
Case 1: intravenous drug A

Information not available:

- Specific guidance on administration in syringe given:
  - concentration range
  - doselevel
  - cytotoxic handling

- Correction for dead volume

Case 1: intravenous drug A



Case 1: intravenous drug A

Implementation

- Each doselevel: different infusion volume
- Intense collaboration with research nurses

Case 2: oral drug B

Available information

- Dose 1200 mg/m^2 b.i.d.
- ORA-Sweet® and powder (2 g & 7 g) → suspension 30 mg/ml
- Supplies for dispensing suspension

Case 2: oral drug B

Information not available

- Unsufficient formation for risk classification
  - request for additional information
  - on site risk classification → potentially carcinogenic

Open powder preparation with a potentially carcinogenic drug

Case 2: oral drug B

- Multicentre trial (EU and USA)

I would not say this preparation is to my satisfaction; We are running into the same issues, but just doing the best we can to not lose powder ***(Children's Health℠ Children's Medical Center Dallas)***

Two teleconferences with pharma: no changes

Case 2: oral drug B

- Open powder preparation: biohazard cabinet
- GMP: exposure ALARA principle

<u>Final procedures</u>

- P3 mask: extra precautions technician
- Stanley knife: open sealing of powder
- Graduated cylinders: measure ORA-Sweet®
- Funnel: transfer powder to (own)dispensing bottle
- Always last preparation of the day

Case 2: oral drug B

Conclusions & Take home messages

- Paediatric oncology trials are getting increasingly more complex yet pharma experience is (often) lacking behind
- HP with knowledge / experience in the following can make a difference:
  - Formulation / preparation issues
  - Paediatric iv administration
  - Drug dosing
  - Paediatric clinical trials
- Stay aware of your professional responsibilty

Answers

- Q1.When preparing the implementation of a clinical trial can all the information needed be found in protocol, pharmacy manual, IB / IMPD ?

  → *No*

- Q2. If there is no information available regarding the potential carcinogenicity of a drug can you then regard it as non-carcinogenic ?

  → *No*

- Q3. A drug authorized for adults is now being tested in children. Can the preparation and volume of infusion be the same ?

  → *No*

Questions…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photography