EMA Scientific Advice on FIH studies

The new FIH EMA guideline: disruptive or Constructive?
EUFEMED 1st discussion forum

Presented by Stefano Ponzano on 19 September 2018
Clinical Pharmacology and Non-clinical Support Office
Methodology & Results

- Searched for the following key words in the EMA SA database: FIH, First-in-human, Phase 1, Phase I
- Time range: 2017-2018

Results:
Since 2017 16 EMA centralised SA have been requested with questions related to FIH studies

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
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<tbody>
<tr>
<td>ATMP</td>
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<tr>
<td>Biological</td>
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<td>Chemical</td>
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<td><strong>Grand Total</strong></td>
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Limited data to draw any conclusions on the impact of the revision of the FIH guideline

1 EMA Scientific Advice on FIH studies, 19 Sep 2018
Type of SA questions related to FIH studies

Design of FIH CT covers:
- Target population
- Choice of endpoints
- Dose selection
- Approach to determine the starting dose
- Safety monitoring
- Stopping criteria
- Safety measures
- Defined criteria to move from HV to patients under integrated protocol

Design of FIH CT

- Relevance of animal models
- Animal species selection
- Design of tox studies
- Adequacy of NC programme
- Design of FIH CT
CHMP Recommendations

• Further in vitro studies to better define:
  • Proof of concept
  • relevance of animal species before moving to in vivo

• Dose Selection for FIH CTs
  • Starting dose (level of uncertainty → NOAEL, MABEL and PAD)
  • Maximum dose beyond pharmacodynamic dose range (provide more justification → less aggressive dose escalation)
  • Transition from HV to patients under integrated protocol (different sensitivity of subjects should be considered for dose selection)
  • Justification for the use of a MTD
Harmonisation of FIH CTA- How can we support?

• EU Network training centre (NTC) **Assessors Training on Early Phase Clinical Trial applications** (March 2017)

• CTFG proposed training on **Clinical assessment training for NCA’s and ethics committees on FIH guideline** (2019)

• Implementation of the new **clinical trial portal and database** (access to clinical trial applications and authorisations within the EU)

• Close interaction **EMA-CTFG-NCAs** (detect/address issues, Q&A?)
• FIH Guideline

Thank you for your attention

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