Safeguarding public health

MHRA

Cell-based products

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CAT-ESGCT WORKSHOP ATMPs: from regulation to reality

27th October 2011, Brighton, UK

DISCLAIMER

The views expressed are mine and not to be taken as representative of MHRA/EMA

General approach

- Clinical benefit is the ultimate aim, *but….*
  - The development path is not well established, therefore….
  - Preclinical aspects cannot be ignored
- A step-wise tailored approach needed
- Integrated plan advisable

Product features

- Scientific rationale
- Mode of action
  - Single or Multiple?
  - Predominant mechanism?
  - Evidence
  - Uncertainties
- How critical is the evidence on MoA?
- Absence does not automatically lead to refusal, but
- Useful to predict in-use behaviour

Dose and posology

- Dose finding studies
- Minimum effective dose
- Optimal dose – basis
- Maximal allowable (safe) dose
- No. of administrations and frequency
- Length of treatment
- Route of administration
- Associated procedures
- Use and role of any device

Pharmacokinetics

Standard PK parameters usually do not apply

- Viability
- Proliferation/differentiation
- Biodistribution
- Migration
- Functionality

Efficacy

- Target population
- Prospective vs retrospective
- Controlled vs uncontrolled
- Comparator
  - Placebo – methodologically clean but feasibility could be a problem
  - Standard of care
  - Active

Efficacy

- End-points
  - Clinical relevance
  - Consistency with therapeutic guidelines
- Results
  - Clinical meaningfulness
  - Statistical significance
- Is persistence of cells/tissue indicative of efficacy?
- Effect of concomitant therapy
- Contribution of the procedure
- Persistence of efficacy

Safety

- Size of the database
- Risk of the procedure
- Concomitant therapy
- Infections
- Immune response
- Tumourigenicity
- Long-term follow-up for safety/efficacy

Risk management plan

- Plan to gather post-marketing data
- Legal requirement
- Can include
  - Clinical trial
  - Registry
- Not a substitute for premature submission