Safeguarding public health

MHRA

Limbal Stem Cell Therapy

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EU Regulatory Workshop: regulatory view
28th October 2011, EMA, London

DISCLAIMER

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

Product features

- Mode of action
- Biopsy material
- Process of manufacturing
  - Starting materials
- Autologous vs allogeneic
- Release tests
- Transport/storage
- Scaffold/devices

Aim(s) of therapy?

- Symptomatic benefit
- Restoration of integrity
- Improvement in visual acuity

Early phase studies

- Biodistribution, migration, persistence
- Tolerability
- Proof-of-concept
- Dose-finding

Confirmatory studies

Dose and posology

- Number of cells
- Single and repeat treatment
- Immunosuppression (allogeneic)
- Surgical technique
- Training
- Restrictions on prescribing

Confirmatory studies

- Comparator

  Concurrent
  Vs
  Historical

  Placebo
  Vs
  Standard of care
  Vs
  Active comparator

Confirmatory studies

End-points

- Corneal integrity
  - Conjunctivalisation
    - Staining
    - Impression cytology – goblet cells
    - Con-focal microscopy
- Neovascularisation
  - Extent
  - Methodology – photos vs clinical

Confirmatory studies

End-points

- Visual acuity
  - Extent of improvement
  - Durability
  - Possible deterioration?
- Symptomatic improvement
  - Irritation, discomfort, pain
  - Watering
  - Cosmetic?

Confirmatory studies

Evaluation

- Investigator (unblinded)
- Independent committee (blinded)
- IC + investigator
- Management of bias

Confirmatory studies

Follow-up

- 12–24 months or until corneal graft
- Safety
  - Tumours
  - Infections
- Persistence of efficacy
- Success of future full-thickness graft