Norwegian Medical
Products Agency

HIV post-exposure prophylaxis (PEP)

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Disclaimer

- The views presented here are my personal views and do not represent the views of the European Medicines Agency or the Norwegian Medical Products Agency.

HIV PEP

- Established clinical practice reflected in HIV treatment guidelines
- Administration: as soon as possible, (4 - 72 hours)
- Duration: 28 days
- Objective is to prevent the establishment of HIV infection
- Determining the HIV status of the source of exposure requires consent
  - HIV status is unknown – PEP
  - HIV positive and viraemic – PEP (resistance profile to be taken into consideration)
  - HIV negative – PEP discontinued
  - HIV positive and well controlled – PEP discontinued
- PEP is considered highly effective if given promptly and there is complete adherence

HIV PEP

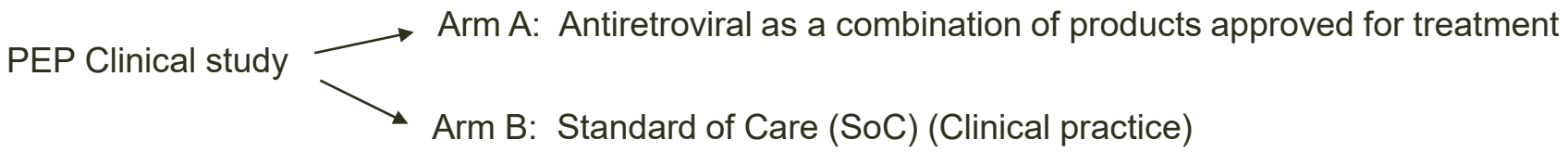
- PEP regimens used in clinical practice are approved for HIV treatment
- No antiretroviral therapy currently includes PEP as part of their indication
- PEP use in clinical practice is therefore ‘off-label’

- Adherence to PEP can vary* for different reasons including tolerability
- The development of longer-acting oral antiretrovirals may potentially improve adherence
- PEP candidates should attain pharmacological levels rapidly
- For longer-acting oral antiretrovirals (week/s), initiation with daily dosing may be required to assess adverse drug reactions

*https://pmc.ncbi.nlm.nih.gov/articles/PMC10836249/ Adherence, adverse drug reactions, and discontinuation associated with adverse drug reactions of HIV post-exposure prophylaxis: a meta-analysis based on cohort studies. Liu et al. 2023

Clinical trial considerations

- Antiretrovirals in development may seek a treatment indication first, followed by an extension of the indication to PEP if supported by appropriate data
- Clinical practice may be considered acceptable as a comparator in clinical trials for PEP candidates already approved for treatment



- Compliance is usually greater in clinical trials
- Feasibility
- Multiple trial centres

Clinical trials and clinical development

- Clinical trials have been carried out addressing occupational and non-occupational PEP including
  - Single arm trials – comparing to historical controls
  - Single arm trials - observational
  - Comparative studies to standard of care

- Product development towards a marketing authorisation may benefit from seeking scientific advice from regulators

- Marketing authorisation will be dependent on an assessment of quality, non-clinical and clinical development where the benefit/risk profile is positive

Interactions with regulators (EMA)

- No regulatory guidelines are currently available for the development of therapeutics for HIV PEP
- Regulatory guidelines can develop following dialogue between developers and regulators through the scientific advice procedure (EMA)
  - https://www.ema.europa.eu/en/human-regulatory-overview/research-development/scientific-advice-protocol-assistance
  - EMA then gives advice on the developer's proposals on how it plans to develop its medicine (Quality, Non-clinical, Clinical).
  - Scientific advice from EMA is not legally binding on EMA or on the medicine developer with regard to any future marketing authorisation applications for the medicine concerned.
  - Scientific advice is prospective in nature. EMA does not pre-evaluate the results of the studies and in no way concludes on whether the benefits of the medicine outweigh the risks.
- Procedure is 42 – 70 days

CTIS

- Clinical trials in Europe are approved centrally through the Clinical Trial Information System (CTIS)
  - https:www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system
- Any multinational clinical trial that plans to include clinical trial site(s) in Europe will need to submit an application through CTIS
- The dossier for the clinical trial application should also include any scientific advice that has been received

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