‘Metamorphine’ (MM)

Morphine – Metamizole – Combination for use in pain therapy

New Structure – New Effects – New Potentials

Technology

In addition to more efficacious treatments, there is a need for drugs which are better-tolerated than opioid analgesics (less side effects, lower abuse potential). Admixtures of morphine and metamizole (trade name e.g. Novalgin) are used in Germany in PCA (patient controlled analgesia) pumps for analgesic cancer therapy. The combination of both drugs is part of the WHO analgesic scheme. However, the compatibility of morphine (an alkaloid; in solution as hydrochloride or sulphate) and metamizole (an acid; in solution as sodium salt) is problematic and the stability of the admixtures sets the limits for the durability of the therapy: In PCA bags the morphine content decreases over time below 80%, with >20% converted into a new chemical entity (NCE): the opioid »Metamorphine« (MM) with structure elements of morphine and metamizole. Since patients do not notice a loss of the analgetic potency or other side effects, it is likely that Metamorphine (i) has analgetic a/o spasmolytic potency, (ii) compared to morphine alone shows different effects on opioid receptors and (iii) is a stable molecule that (iv) combines effects of opioid and non-opioid analgesics.

Innovation/ Potentials

- MM could serve as a novel drug platform in the pain management field
- New, dual MoA likely: analgesic effect via both NMDA- and opioid-receptors and thus, analgesic potency in combination of peripher and central effects in one compound
- Stable in aqueous solutions - in contrast to mixtures
- Antispasmodic active component - due to metamizole fraction
- Less addictive potency
- Reduced (morphine) side effects (sedation, depression, obstipation)
- Qualitative optimization of opioid therapies - for different ratios between μ, κ- and δ-opioid receptors
- Strong competition, but if addressing “unmet needs” penetration potential of MM is rated to be reasonable high

Main Application

- Pain therapy: cancer, fibromyalgia and postoperative patients, dyspnoe (palliative care) and withdrawal symptoms …

Developmental Status

- Mass (LC-ESI-MS) and structure (13C- & 1H- NMR) determined
- Synthesis established (small-scale, non-GMP)
- First in vitro binding studies to morphine & NMDA receptors
- More detailed non-clinical study plans in place
- In man case series (phase IV) with PCA bags ongoing
- Subsequent study with synthesized MM planed

... to be sponsored …

Responsible Scientist

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- EP1989208, granted & validated in six major markets

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