Covid-19

HTAN Meeting, Oct 27th 2020
https://eunethta.eu/services/covid-19/

Claudia Wild, Director AIHTA, claudia.wild@aihta.at

In May 2020: RCR activities started

Rolling Collaborative Reviews (RCR) of therapies

1. **Rolling Review**:

- 1-15 therapies (HTW/ Wales, NIPN/ HU , KCE/ BE, AETSA&AEMPS/ SP, AIHTA/ AT, NIPH/ N, VVKT/ LT), https://eunethta.eu/rcr01-rcrxx/;
- 16+ pp

2. **Rapid Review**:

- **Remdesidir**: https://eunethta.eu/wp-content/uploads/2020/09/PTRCR15-Rapid-Collaborative-Review-Remdesivir-for-COVID-v1.0-1.pdf,
- **Dexamethasone** – ongoing (November)

Aim of EUnetHTA 'Rolling' Reviews'

- To **inform health policy** at the national, regional, and European levels at an early stage in the life-cycle of therapies, of which interventions are currently undergoing clinical trials.
- To **monitor permanently** – in the format of a living document – potential therapies against Covid-19.
- To **support** preparations for an evidence-based purchasing of regional/ national health politicians, if necessary.

The scope of the RCR is of a descriptive nature.

These **EUnetHTA Rolling Procedures are not meant to substitute a joint REA** adhering to the agreed procedures, aiming at critical appraisal of the clinical evidence submitted for approval.

Methodology

Three main sources of information:

- **Table 1** (Summary of findings/ SoF – efficacy and safety) is based on (peer reviewed) published RCTs: coop with DePlazio (NMA-PROPERO http://deplazio.net/farmacicovid/index.html for SoF (or https://covid-nma.com/. Sources: http://deplazio.net/farmacicovid/index.html for SoF (or https://covid-nma.com/)
- **Table 2** is based on published (peer reviewed) observational studies for safety results: Inclusion criteria: comparative or single-arm prospective studies and registries, > 50 patients, exclusion criteria: retrospective case series, case studies, sources: Living Map (NIPH/ N: https://www.fhi.no/en/qk/systematic-reviews-hta/map/
- **Table 3** is based on clinical trial registries: Inclusion criteria: RCTs or CTs only; ClinicalTrials.gov; EudraCT Register

Rolling collaborative reviews (= monitoring of therapies)(incl. combination therapies) – monthly updates

1.Convalescent plasma/ CPT (HTW/ Wales)

2.Lopinavir + Ritonavir (Kaletra®) (NIPN/ Hungary)

3.Tocilizumab (Roactemra®) (NIPN/ Hungary)

4.Camostat (Foipan®) (KCE/ Belgium)

5.Nafamostat (Futhan®) (KCE/ Belgium)

6.Solnatide (AIHTA/ Austria)

7.APN01 (rhACE2) (AEMPS&AETSA/ Spain)

Darunavir (Prezista®) (SNHTA/ Switzerland)

10. Favipiravir (Avigan®) (SNHTA/ Switzerland)

11. Sarilumab (Kevzara®) (NIPHNO/ Norway)

12. Interferon beta 1a (Novaferon, …) (NIPHNO/ Norway)

13. Gimsilumab (VVKT/ Lithuania)

14. Canakinumab (VVKT/ Lithuania)

15. Anakinra (Kineret®) (AIHTA/ Austria)

Rapid collaborative review (= assessing the evidence)

16. Remdesivir (INFARMED/ Portugal + NCPE/ Ireland)

17. Dexamethasone (AIHTA/ Austria + open)

Stopping and Starting Rules

Stopping rules

1. In EMA's marketing authorization process or positive marketing authorization decision
2. No clinical benefit: ≥ 2 RCTs with negative efficacy and/or safety results in the indication and population under review (phase III, of high or moderate quality/ high or moderate certainty of evidence, well powered)
3. MAH withdraws interest in compound (no interest in marketing authorization in COVID-19 indication)

Starting rules

1. Published results from ≥ 1 phase III RCT with positive efficacy and safety results in the indication and population under review (high or moderate quality, non peer-reviewed or peer-reviewed article)
2. Upcoming (promising) evidence of ≥ 2 phase III trials
3. Compound included as trial drug in a platform trial on COVID-19 treatments
4. Interest from ≥ 2 EUnetHTA Partners (via survey)
5. Interest from MAH to seek marketing approval
6. Interest from EC, HTA Network or EUnetHTA Stakeholder Groups

Incoming (in search for EUnetHTA authors)

Siltuximab (Sylvant®) - Phase 2, severe

Lenzilumab – Phase 3, severe

Mivrilimumab - cohort, severe

Leronlimab – Phase 2, mild/moderate/servere

Vazegepant – Phase 2, severe

AZD7442 – Phase 1- prevention / treatment

MK-4482 – Phase 2

Adalimumab (AVID-CC trial) - mild/moderate (ambulatory)

LY3009104/ Baricitinib (ACTT-2 trial) – Phase 3, moderate/severe

REGN-COV2 – Phase 2/3, mild/moderate (ambulatory)

LY-CoV555/LY3819253 **(ACTIV-3, ACTIV-2) – prevention**

European Trials + trial arms

Recovery: Dexamethasone, Azithromycin, Tocilizumab, CVP, REG-COV2

Solidarity (WHO): Remdesivir, Lopinavir/Ritonavir (stopped), Interferon beta-1a

Discovery: Remdesivir, Lopinavir/Ritonavir (stopped?), Interferon beta-1a

Coordination & Collaboration

Two main initiatives for coordination and collaboration:

Trial Coordination Board of EU Response:

- Input from/to Trial Coordinators of Recovery, Discovery, Solidarity, EU-Response, EMA

COVID-END: Coordination of international evidence resources