Scaling clinical care for mpox. Using data to optimize standard of care. A basic approach to save lives?

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Objectives

To discuss:

1. Interplay between the virus, the host and the standard of care
2. What can we learn from other global threats (Ebola virus disease, EVD)
3. Where are we with mpox standard of care (SOC)

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Determinants of clinical outcomes in outbreaks

Virulence of pathogen and (interaction with host)

Fluctuating CFRs are commonly observed in outbreaks.

Therapeutics: antiviral, host-directed

Host factors (genetics, nutrition, immunity, age, chronic diseases, etc)

To understand risk factors, prognosis and the natural history it is essential to collect **standardized clinical data to** to inform clinical interventions and the design of intervention trials that may improve patient outcomes and save lives

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Learnings from other outbreaks: Ebola virus disease

During 2013-2016 West African EVD outbreak fluctuation in CFR observed

- **39.5% mean CFR** in the large majority of patients care for in West Africa
- **18.5% mean CFR** the few patients cared for in ICUs in US and Europe:

Suggesting that more aggressive supportive care interventions commonly used in high income countries (ICUs) may have reduced CFR.

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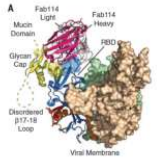
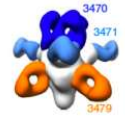
Learnings from other outbreaks: Ebola virus disease





In 2018-2019 EVD outbreak in DRC, the **hallmark PALM trial** evaluated two monoclonal antibodies, and one antiviral compared to Zmapp (control arm). WHO optimized supportive care served as standard of care (SOC).

Optimized Supportive Care for Ebola Virus Disease

CLINICAL MANAGEMENT STANDARD OPERATING PROCEDURES

oSOC included:
IV fluids, electrolyte replacement, treatment of co-infection, nutrient, etc. usually delivered in new treatment centre designed for easy access to patients to facilitate monitoring and interventions

28-day mortality

50% in Zmapp, 53% in remdesivir

34 % in **REG-EB3**, **35% MAb**114

10 % in R**EG-EB3 and MAb114 treated subgroup** with low viral load with either REG-EB3 or mab114

A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics | New England Journal of Medicine (nejm.org)

Fluctuating CFR in mpox…does it relate to SOC?

Quick look at literature…

- **1.4 % CFR** in adults and children in DRC 2007 to 2011 (prospective cohort)

https://doi.org/10.1371/journal.pntd.0010384

- **6% CFR** in cohort of adults and children during 2022-2023 outbreak in Nigeria (retrospective and prospective)

Clinical characteristics and predictors of human mpox outcome during the 2022 outbreak in Nigeria: a cohort study (thelancet.com)

- **0 % CFR** in children USA May – July 2022 (MMWR)

https://doi.org/10.15585/mmwr.mm7144a4

- **11 % CFR** paediatric and maternal mpox up to April 2023 (meta-analysis)

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(23)00607-1/fulltext

- **4.6% CFR pre-2022 outbreaks vs 0% CFR in 2022** multi-country outbreak (meta-analysis)

Clinical Features, Antiviral Treatment, and Patient Outcomes: A Systematic Review and Comparative Analysis of the Previous and the 2022 Mpox Outbreaks (eur.nl)

There remains variability in CFR.

Standardized clinical data collection and robust analysis needed to understand the CFR.

It is likely that improving the SOC can reduce CFR (and morbidity)

So, what is the current mpox standard of care?

Benefits:

- Released quickly
- Included both IPC and Clinical interventions
- Included home care and health facility-based care recommendations
- Addressed vulnerable populations (pregnant women, children, breastfeeding and immunocompromised patients)
- Included remarks on previously described complications: skin care, co-infections, eye care, nutrition, sepsis, hydration, etc.

Limitations:

- Lack of evidence base, non -GRADED recommendations,
- High level remarks on how to treat complications were limited in detail.
- Needs to be updated
- Needs derivative operational guidance/tools to support implementation

PALM 007 preliminary results: may shed some light

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NEWS RELEASES

Thursday, August 15, 2024

The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo

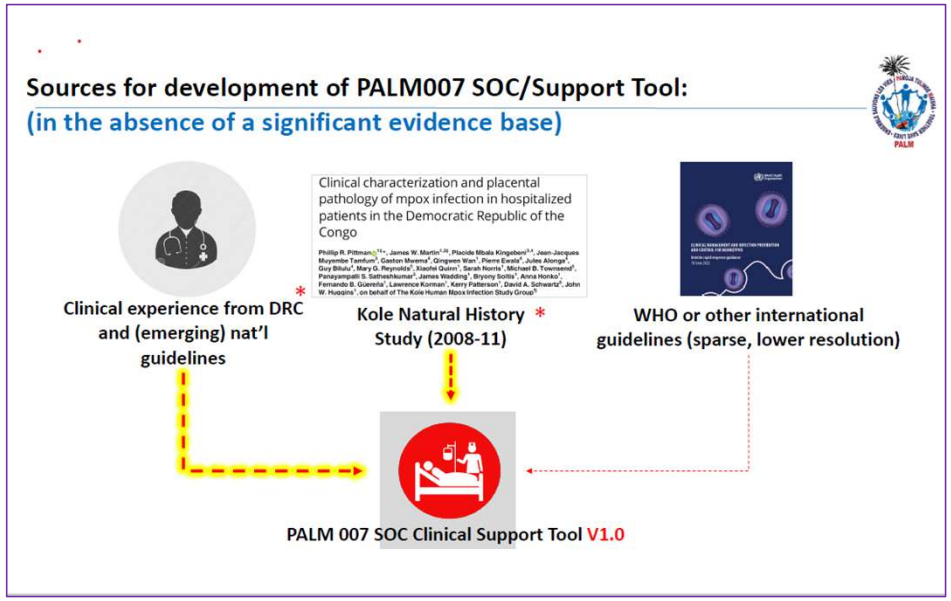
NIH-cosponsored study examined tecovirimat in mpox-endemic country.

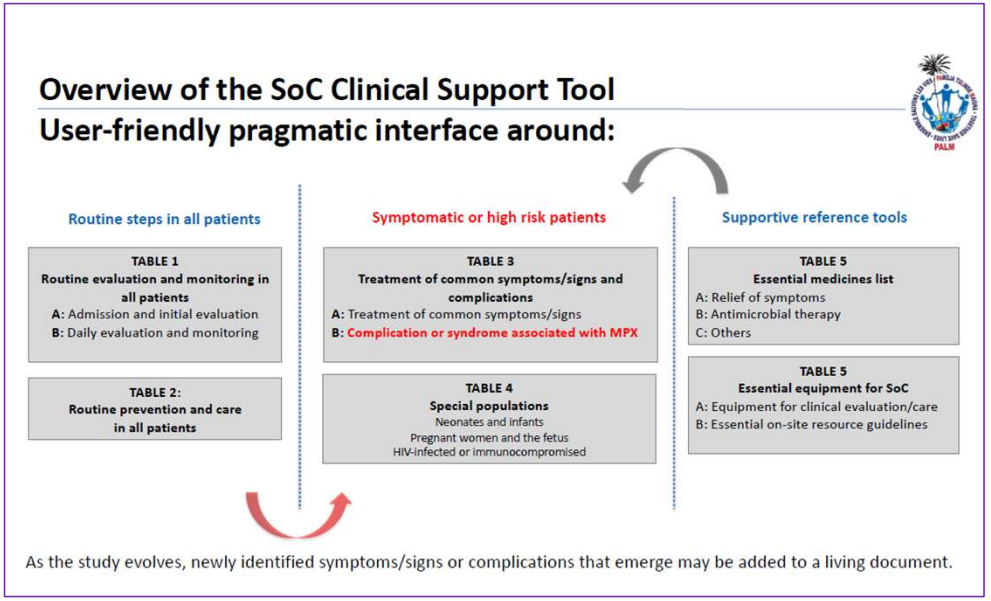
The antiviral drug tecovirimat did not reduce the duration of mpox lesions among children and adults with clade I mpox in the Democratic Republic of the Congo (DRC), based on an initial analysis of data from a randomized, placebo-controlled trial. However, the study's 1.7% overall mortality among enrollees, regardless of whether they received the drug or not, was much lower than the mpox mortality of 3.6% or higher reported among all cases in the DRC. This shows that better outcomes among people with mpox can be achieved when they are hospitalized and provided high-quality supportive care. The trial is sponsored by the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) and co-led through a government-to-government partnership with the DRC's Institut National de Recherche Biomédicale (INRB). Further analyses and detailed results will be released through scientific channels.

"This shows that better outcomes among people with mpox can be achieved when they are hospitalized and provided high quality supportive care"

So, what may become the mpox standard of care?

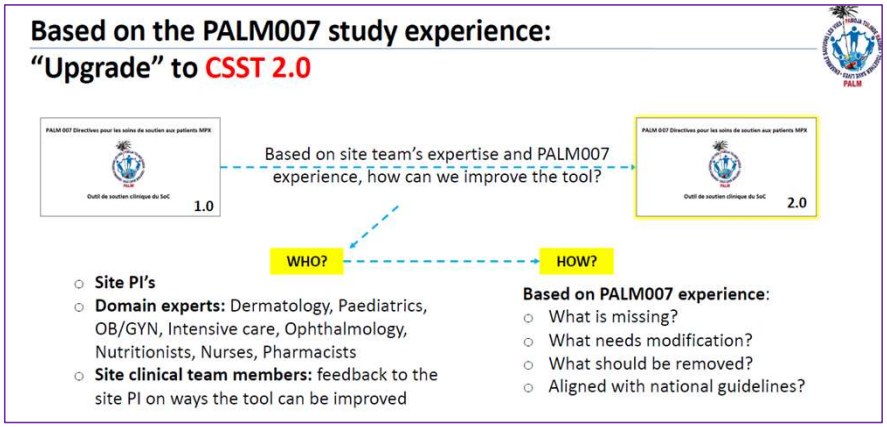
Development of the PALM007 Clinical SOC Support Tool





Slide courtesy of PALM 007 Clinical Management Team (Leads: Jean-Luc Biampata, Placide Mbala, Ian Crozier)

Next steps for a Global optimized SOC….



WHO in collaboration with INRB and NIH, to bring this **PALM 007 SOC clinical tool v2.0** to international experts at a Global meeting to validate this tool and create a WHO optimized supportive care for mpox guidance and tools. Coming soon…

What can member states do now?

Establish standardized clinical data collection in mpox patients to understand the disease, complications, outcomes and prognosis.

- can be done using already in place EMR, where in place.

WHO platform supports MS, facilities and partners with eCRF, analytics, dashboard and contribute to regional and global analysis (global good).

This serves as **initial step** to build clinical research capacity…**data registries, observational studies** and **clinical trials.**

Standard clinical data collection should be part of **implementing standard of care protocols** in all settings caring for mpox patients.

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Conclusions

1. The **standard of care matters** and **improves patient outcomes.** As we wait for effective therapeutics it is essential to do the basics well.

2. **Clinical trials are necessary** to evaluate efficacy on interventions such as therapeutics. Efforts to improve SOC during trials can have meaningful impact on health systems over time.

3. WHO will use the PALM 007 trial SOC protocol and trial results to inform the its development of **Global oSOC for mpox** in near future.

4. WHO **appreciates** the **investigators**, enrolled **patients** and their **families** for participating in trials to advance knowledge and science for global good.

Thank you!