NECT: AN IMPROVED TREATMENT FOR STAGE 2 HAT. CLINICAL TRIAL RESULTS AND ONGOING RESEARCH

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AGENDA

I. Introduction
II. Objective of NECT
III. Nect design
IV. Implementation stages
V. Results
VI. Conclusion
VII. Perspectives

I. INTRODUCTION

Treatment of HAT in second stage

- **MELARSOPROL**: - high toxicity
  - treatment failure rates rising

- **EFLORNITHINE**: - less toxic
  - efficacious
  - resource intensive

- **NIFURTIMOX**: - cheap
  - easy to use
  - limited efficacy in monotherapy
  - not registered for HAT

Drug combinations can be avenues of improvement

II OBJECTIVE of NECT

- To compare

  eflornithine IV + nifurtimox *per os* to standard treatment with eflornithine IV regarding

  - efficacity
  - safety

+

VS

III. NECT DESIGN

- Randomized, controlled, open label, non-inferiority trial
- Enrollement criteria
  - **Confirmed case (parasites seen), Stage 2, >20 leukocytes/uL in CSF**
  - **Naive of second-stage treatment**
  - **≥15 yrs of age**
  - **Non-pregnant**
  - **Reasonable chances of follow-up**
- 286 patients included in two arms:
  - **E : Eflornithine 4X100mg/Kg/d X 14 d (iv infusion)**
  - **N+E: Nifurtimox 3X5mg/Kg/d X 10 d (per os)**
    Eflornithine 2X200mg/Kg/d X 7d (iv infusion)

IV IMPLEMENTATION STAGES

- 4 Sites in RoC and DRC 2003-2008 (Nkayi, Isangi, Dipumba, Katanda)

A) Site improvement
  - working conditions of the team
  - hospitalisation conditions of the patients

B) Equipment
  - Laboratory (improving diagnostic methods)
    - Reflotron, Centrifuge, Hemocue, Paracheck…
  - Nursery (physical examination and management of patients)
    - Aspirator, tensiometre, rechargeable solar lamps, cell phone…
  - Investigator
    - Motorcycle, fuel, air time

C) Training and capacity strengthening

V RESULT (safety)

Major AE	E (n=143)		N+E (n=143)	
	n	%	n	%
Seizures	6	4.2	6	4.2
Coma	3	2.1	1	0.7
Confusion	1	0.7	2	1.4
Hallucinations	1	0.7	1	0.7
Other neurological	2	1.4	3	2.1
Gastrointestinal	2	1.4	2	1.4
Fever	18	12.6	7	4.9
Infection	5	3.5	1	0.7
Hypertension	3	2.1	0	0.0
Headache	2	1.4	1	0.7
Acute Respiratory Distress	1	0.7	1	0.7
Other clinical AE	2	1.4	2	1.4
Anemia	1	0.7	2	1.4
Leucopenia	0	0.0	0	0.0
Neutropenia	10	7.2	2	1.4
Total	65		31	

RESULTS (efficacity)

- Excellent follow-up

	E (n=143)	N+E (n=143)
No follow-up	1 (0.7%)	2 (1.4%)
Partial follow-up	8 (5.6%)	9 (6.3%)
Complete follow-up until endpoint	133 (93.7%)	132 (92.3%)
Death due to AE	3 (2.1%)	1 (0.7%)
Relapsed	8 (5.6%)	2 (1.4%)
Cured	122 (91.7%)	129 (97.7%)

VII CONCLUSION

In the context of second-stage HAT, both treatments were well tolerated

Low fatality rate in both arms

Significant advantages of N+E:

- ➢Lower risk of major adverse events
- ➢Lower risk treatment interruptions
- ➢Lower risk of infections, diarrhea, fever peaks, neutropenia

VIII PERSPECTIVES

- EML WHO May/2009
- Publication LANCET June/2009
- NECT FIELD (to evaluate NECT in field setting)
  - Document safety, feasability and effectivity
  - Initiated 5 sites in DRC May 2009
  - 200 patients included so far
  - Objective: 620 patients to be enrolled in 12 months
- Agreement Ministry of Health DRC and CAR to use NECT (June 2009)

Progress made and Challenges ahead in Clinical Research and Development of New Treatments for Human African Trypanosomiasis

WHO and DNDi Symposium
ISCTRC Meeting, Kampala, Uganda
Tuesday, September 22, 2009
6 pm - 7:20 pm, in Victori Ballroom

World Health Organization

DNDi
Drugs for Neglected Diseases *initiative*

Thank you!

DNDi
Drugs for Neglected Diseases *initiative*

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