

HAT

In-hospital safety of NECT use
to treat 2nd stage *T.b. gambiense*
in African children, pregnant and breast-feeding women

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DNDi

Drugs for Neglected Diseases *initiative*

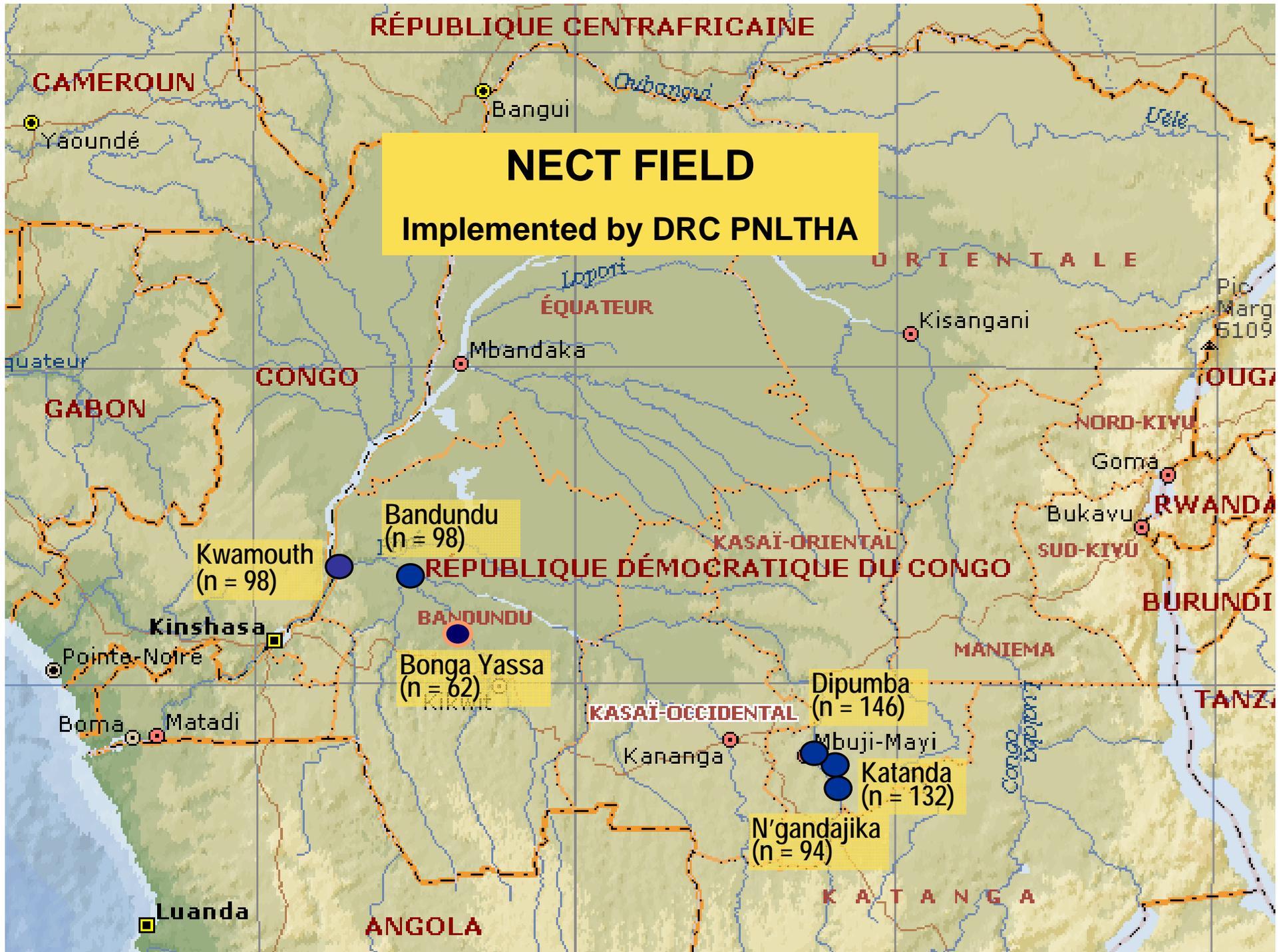
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Study objectives

- Primary objective
 - Assess the **clinical response** of NECT under field conditions (discharged alive from the hospital*)
- Secondary objectives:
 - Assess the incidence and type of **adverse events** (AE), and the capacity of the treatment centers to deal with these
 - Assess the **feasibility** of the implementation of NECT by the health center
 - Assess the **effectiveness** of NECT at 24 months after treatment

Study design

- Multicentre, open-labelled, non-controlled
 - All stage 2 HAT patients (diagnosed according local rules)
 - Pregnant/breastfeeding women, children
 - Other underlying disease, poor health, old age
 - At the decision of investigator or national rules
 - Target sample size: 620 patients
 - DSMB and stopping rule
 - Study duration 12 months (enrolment)
 - Follow up: for each patient 24 months (6, 12, 18, 24 months)



Results

Patient Characteristics	n	%
Patients treated	629	
Children 0 to 4 years	33	5
Children 5 to 11 years	64	11
Pregnant women	13	2
Breastfeeding women	34	5
Patients who previously had HAT	135	21
Sex ratio (male: female)		1.3
Age, mean (SD)	29,6	(16,2)

Primary efficacy

- Patients discharged alive: 98.4%
(Children 100%)
- Karnofski scale index improvement after treatment. (16% from 70 to 86)
- Reduced clinical signs and symptoms
 - Lymphadenopathy 54% to 22%
 - Neurological 89% to 37%
- Similar improvement among children, pregnant or breastfeeding women

Adverse Events

	NECT FIELD (in hospital safety) (N=629)	NECT (Priotto 2009) (N=143)	DFMO (N=143)
Average adverse events per patient	4	5	5
Patients having at least one Adverse event	578 (92%)	95%	96%
Severe Adverse Event (CTC grades 3-5)	77 (12%)	14%	29%
Serious Adverse Event (SAE)	32 (5.1%)	0.7%	4%
Fatalities	10 (1.6%)	0.6%	2.1%
Treatment cessations	5 (0.8%)	1.4%	8%

Mortality (in-hospital safety)

- SEX: 4 male and 6 female (1 pregnant).
- AGE: Average 42, range 18 to 77.
- DATE: Average after treatment start 12 days.
Range 2-23
 - 3 complex infections (2 respiratory; 1 septic shock)
 - 3 non specific diagnosis (1 sudden death)
 - 2 developed coma
 - 1 anaemia
 - 1 cardiogenic shock.

Confusing mortality analysis as symptoms were related with disease in a background of severely ill (at least 5 cases) and often malnourished patients.

Most Common Adverse Events %	All n=629	Children n=100	Pregnant n=14	Breast feeding n=33
Gastro-intestinal	61	43	93	64
Vomiting	43	31	79	58
Nausea	20	13	21	6
General disorders	46	57	86	61
Fever	30	44	29	42
Asthenia	18	13	57	27
Nervous system	34	21	57	24
Headache	14	8	36	12
Vertigo	10	0	14	6
Convulsions	9	10	0	9

Most Common Adverse Events %	All n=629	Children n=100	Pregnant n=14	Breast feeding n=33
Metabolic	26	22	29	12
Anorexia	25	21	29	9
Psychiatric	16	9	0	12
Agitation	6	5	0	12
Insomnia	6	3	0	0
Musculoskeletal (pain)	14	4	21	15
Respiratory	10	7	14	9
Skin disorders	9	9	7	6
Pruritus	7	6	7	6

Conclusions

- 629 patients, often in poor general health condition, treated with NECT
- In-hospital survival rate: data in field conditions (98.4%) similar to that observed in NECT clinical trial
- No new safety signal, especially in children
- Tolerability similar in children (less GI symptoms, more fever) and slightly lower in pregnant women (more headache, vomiting, asthenia, lumbar pain, no psychiatric symptoms)

**BTC CTB****Swiss TPH****epicentre**
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