

Acoziborole: Results of the safety study conducted in g-HAT seropositive non-parasitologically confirmed subjects

Acoziborole: Résultats de l'étude de sécurité menée chez des personnes séropositives à la THA due à Tb gambiense non confirmés par les tests parasitologiques.

37ème ISCRT

sept,16 2025

Guylain Mandula, on behalf of all the people who contributed to the OXA004 study

Guylain Mandula, au nom de toutes les personnes ayant contribué à l'étude OXA004

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Best Science for the Most Neglected

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STUDY RATIONAL & OBJECTIVES

RATIONNEL ET OBJECTIFS DE L'ETUDE

Background:

- **Acoziborole**: oral single dose treatment
- Study conducted from 2016 to 2020 in 208 g-HAT patients showed:
  - ✓ High efficacy (94.3%)
  - ✓ Very Good safety profile → benefit/risk ratio positive for patient indication

→ Acoziborole : a promising drug. Why not to envision as a treatment beyond the confirmed cases?

Contexte:

- **Acoziborole**: traitement oral à prise unique
- Une étude menée de 2016 à 2020 sur 208 patients atteints de la THA Tb gambiense a montré :
  - ✓ Une efficacité élevée (94,3%)
  - ✓ Un très bon profil de sécurité → rapport bénéfice/risque positif pour l'indication du patient

→ Acoziborole : un médicament prometteur. Pourquoi ne pas envisager son utilisation au-delà des cas confirmés ?

Primary study objective:

Assess the safety profile of acoziborole in serosuspects to g-HAT (i.e individuals seropositive to g-HAT but not diagnosed as patients by the parasitology assessment)

Objectif principal de l'étude:

Evaluer le profil de sécurité d'acoziborole chez les sero-suspects à la THA due à Tb gambiense (personnes seropositives à la THA mais non confirmés par les tests parasitologiques)

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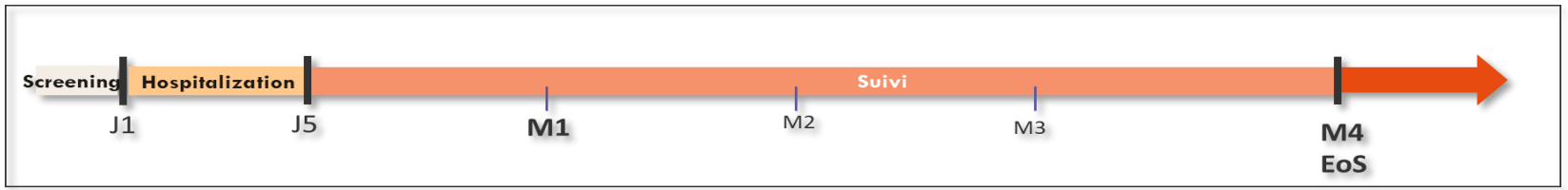
DNDI-OXA-04-HAT RESULTS

STUDY DESIGN

CONCEPTION DE L'ETUDE

- ✓ Study population: serosuspects to g-HAT (≥15 y.o)
- ✓ **Randomised, double-blinded and placebo controlled** (ratio 3:1 Acoziborole:placebo)
- ✓ One main **(safety)** + 1 exploratory sub-study conducted by Institut Pasteur (**TrypSkin**)
- ✓ Sample size: 1'200 participants
- ✓ 5 days of hospitalisation, on site follow-up visits at M1 and M4
- ✓ Lost to follow-up subjects had to be replaced

- ✓ Population de l'étude : adultes et adolescents (≥15 ans) sérosuspectes à la THA à Tb gambiense
- ✓ Etude **randomisée**, en **double aveugle** et contrôlée par placebo (ratio 3:1 Acoziborole:placebo)
- ✓ 1 étude principale **(safety)** + 1 sous-étude exploratoire (**TrypSkin**)
- ✓ Taille d'échantillon: 1'200 participants
- ✓ Période d'observation à l'hôpital de 5 jours of hospitalisation, 2 visites de suivi à M1 et M4
- ✓ Les sujets perdus de vue devaient être remplacés.



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STUDY METHODOLOGY
METHODOLOGIE DE L'ETUDE

Collection of adverses events post drug administration (TEAE) and classification by:

- Severity (mild, moderate and severe)
- Seriousness (death, life threatening, requires hospitalization, results in persistent or significant disability, etc..)
- Relationship to the stud drug (related or not related)

Collection des événements indésirables (EI) post-administration du médicament et classification selon :

- Sévérité (légère, modérée et sévère)
- Gravité (décès, mettant la vie en danger, nécessite une hospitalisation, entraîne un handicap persistant ou significatif, etc.)
- Relation avec le traitement à l'étude (liée ou non liée)

STUDY RECRUITMENT/ RECRUTEMENT DE L'ETUDE

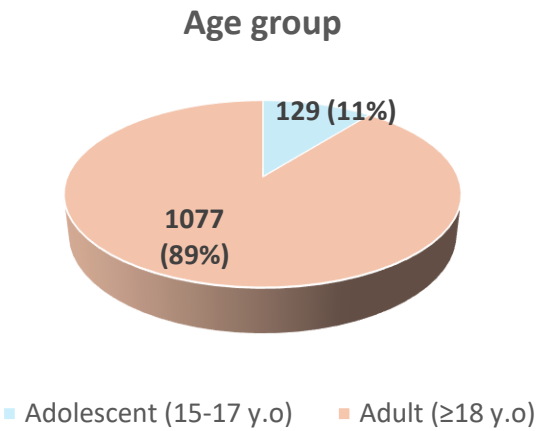
Site #	Site Name	Country	# ICF signed	# Screen failure	# Part. admin.	# Part. enrolled TrypSkin	M4 (EoS) completed	Comment
01	Bandundu	DRC	209	1	208	198	202 (97.1%)	5 lost to FU + 1 death (at D119)
03	Masi	DRC	256	8	248	202	248 (100%)	
04	Dipumba	DRC	222	30	192	NA	192 (100%)	
10	Bagata	DRC	165	5	160	160	160 (100%)	
12	Kwamouth	DRC	132	4	128	NA	127 (99.2%)	1 lost to FU
16	Idiofa	DRC	100	4	96	NA	94 (97.2%)	2 consent withdrawals at D4
20	Dubreka	Guinea	182	6	176	174	173 (98.3%)	2 lost to FU + 1 consent withdrawal (at D56)
TOTAL			**1266**	**58**	**1208**	**734**	**1196 (99.0%)**	

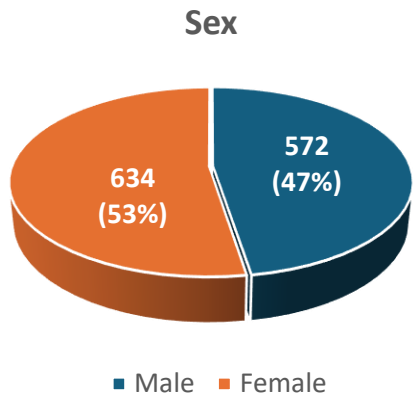
- 1208 participants administered with the study drug:
  - 907 with acoziborole
  - 301 with placebo
- Excellent completion rate

- 1208 participants ont reçu le traitement à l'étude:
  - 907 ont reçu l'acoziborole
  - 301 ont reçu le placebo
- Taux de complétude excellent

OXA004: A study with a high completion rate and baseline characteristics well balanced between groups

		Acoziborole	Placebo	Overall
Nb of participant screened		-	-	1266
Nb of participant administered (1)		907	301	1208
Nb of study completers (1)		898 (99.0%)	298 (99.0%)	1196 (99.0%)
Safety set (2)		**906**	**300**	**1206**
Sex	Male	430 (47.6%)	142 (47.3%)	572 (47.4%)
	Female	476 (52.5%)	158 (52.7%)	634 (52.6%)
Age (in year)	Mean (SD)	37.3 (17.35)	36.4 (16.38)	37.1 (17.11)
	[Min, Max]	[15, 90]	[15, 74]	[15, 90]
Age group	Adolescent (15-17 y.o)	101 (11.1%)	28 (9.3%)	129 (10.7%)
	Adult (≥18 y.o)	805 (88.9%)	272 (90.7%)	1077 (89.3%)
Compliance to treatement		906 (100%)	300 (100%)	1206 (100%)
Nb of part. with at least 1 medical history		367 (40.5%)	113 (37.7%)	480 (39.8%)





(1) based on assigned treatment

(2) based on treatment received

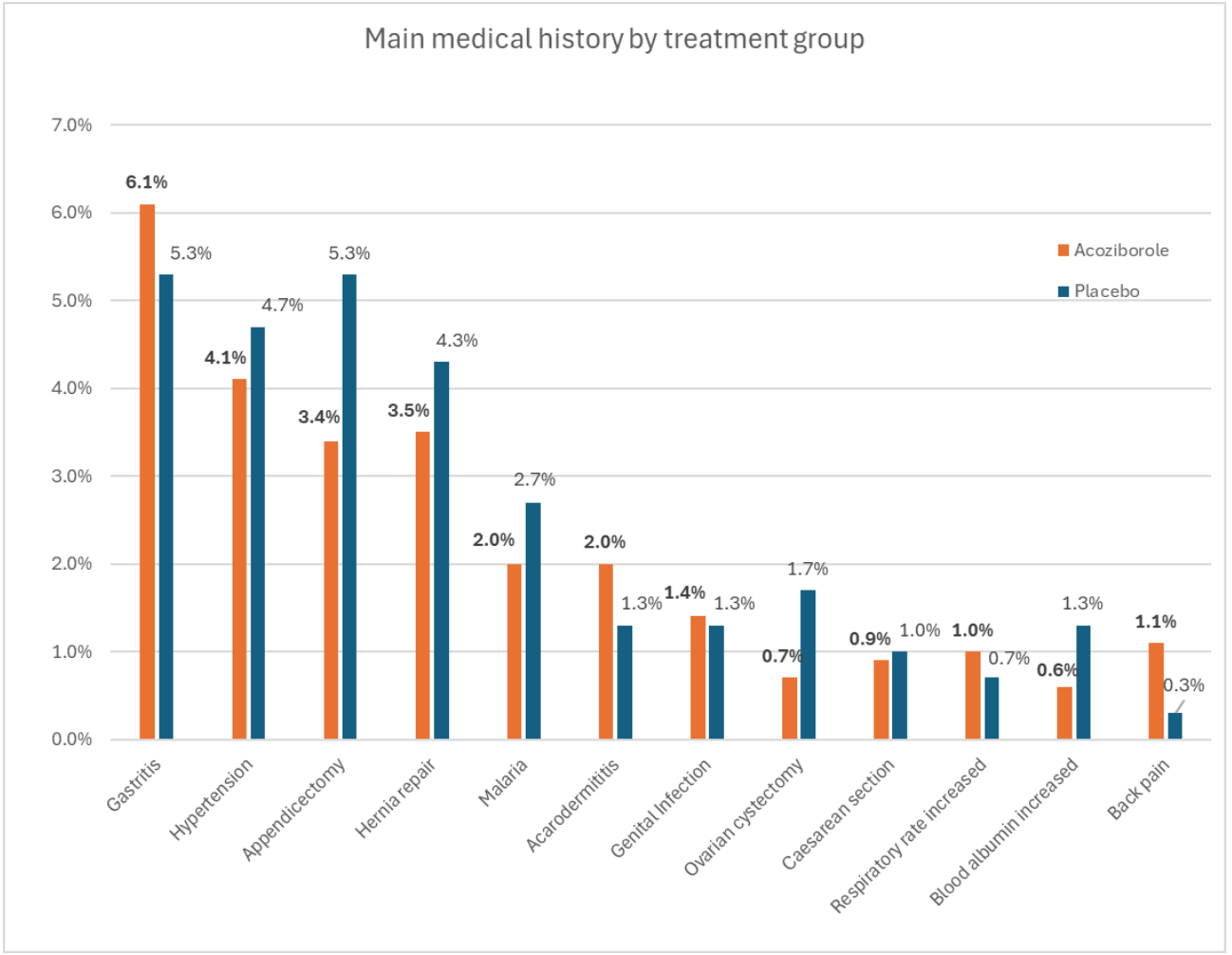
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Baseline characteristics – Medical History (safety set)

	Acoziborole (N=906)	Placebo (N=300)	Overall (N=1206)
Subject with at least one medical history	367 (**40.5%**)	113 (**37.7%**)	480 (**39.8%**)

- Medical history well balanced between both groups
- Main (≥1%) and relevant* medical history:
  1. Gastritis
  2. High blood pressure
  3. Surgical procedures (appendicectomy, hernia repair, overian ystectomy, caesarian section)
  4. Malaria
  5. Acarodermititis
  6. Genital infection

* Menopause (13.9% in Acoziborole and 11.7% in placebo) was recorded as medical history in the CRF but condition assessed as not relevant as baseline characterisitics



Source: Table 14.1.3.1

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STUDY RESULTS

RESULTATS DE L'ETUDE

- 21.9% of participants reported at least 1 TEAE (**21.5% in acoziborole** versus **23.0% in placebo,** Excess Rate: -1.5% 95% CI -7.2 : 3.7)
- Majority of TEAEs are mild or moderate
- No related severe and/or serious TEAE
- Overview of reported TEAEs :
  - **Common(1) TEAE with significant higher occurrence in Acoziborole:** Headaches (mild or moderate)
  - **Common (1) TEAE with no difference of occurrence between both groups**: malaria, scabies, abdominal pains, fatigue, enteritis and nausea
  - **Uncommon (2) TEAE observed in more than 2 participants in Acoziborole group:** Decreased appetite, dizziness, pyrexia, insomnia, hot flush, asthenia, diarrhoea, vomiting

(1) Common TEAE: TEAE occurring in more than or equal to 1% of participants
(2) Uncommon TEAE: TEAE occurring in less than 1% of participants

- 21,9% des participants ont signalé au moins 1 EI (**21,5% dans le group acoziborole** versus **23,0% dans le groupe placebo,** taux d'excès : -1.5% 95% CI -7.2 : 3.7)
- La majorité des EI sont légers ou modérés
- Aucun EI grave et/ou sévére relié au traitement
- Aperçu des EI signalés :
  - **EI courant (1) avec une survenue statistiquement plus élevée dans le groupe Acoziborole** : maux de tête (légers ou modérés)
  - **EI courant (1) avec une survenue similaire entre les deux groupes** : paludisme, gale, douleurs abdominales, fatigue, entérite et nausées
  - **EI rares (2) observés chez plus de 2 participants dans le groupe Acoziborole** : diminution de l'appétit, vertiges, pyrexie, insomnie, bouffées de chaleur, asthénie, diarrhée, vomissements

(1) EI courant: EI survenant chez plus de 1% des participants
(2) EI rare: EI survenant chez moins de 1% des participants

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Overview of Treatment Emergent Adverse Events (TEAE)

	Acoziborole* (N=906)	Placebo* (N=300)	Overall* (N=1206)	Excess rate xx% (95% CI)
Subject with at least 1 TEAE	195 (**21.5%**) [334]	69 (**23.0%**) [107]	264 (**21.9%**) 441	-1.5% (-7.2 : 3.7)
TEAE severity				
Mild/Moderate	183 (**20.2%**) [313]	65 (**21.75%**) [98]	248 (**20.6%**) [411]	-1.5% (-7.1 : 3.6)
Mild	115 (**12.7%**) [178]	42 (**14.0%**) [56]	157 (**13.0%**) [234]	NC
Moderate	92 (**10.2%**) [135]	32 (**10.7%**) [42]	124 (**10.3%**) [177]	NC
Severe	18 (**2.0%**) [21]	8 (**2.7%**) [8]	26 (**2.2%**) [29]	-0.7% (-3.3 : 1.1)
Related	-	-	-	NA
Not related	18 (2.0%) [21]	8 (2.7%) [8]	26 (2.2%) [29]	-0.7% (-3.3 : 1.1)
Life - threatening	-	-	-	NA
Death	-	1 (**0.3%**) [1]	1 (**0.1%**) [1]	NC
TEAE Drug relatedness				
Related	59 (**6.5%**) [82]	17 (**5.7%**) [22]	76 (**6.3%**) [104]	NC
Not related	159 (**17.5%**) [252]	58 (**19.3%**) [85]	217 (**18.0%**) [337]	NC
Serious TEAE				
Related	-	-	-	NA
Not related	3 (**0.3%**) [3]	4 (**1.3%**) [4]	7 (**0.6%**) [7]	-1.0% (-3.1 : 0.0)

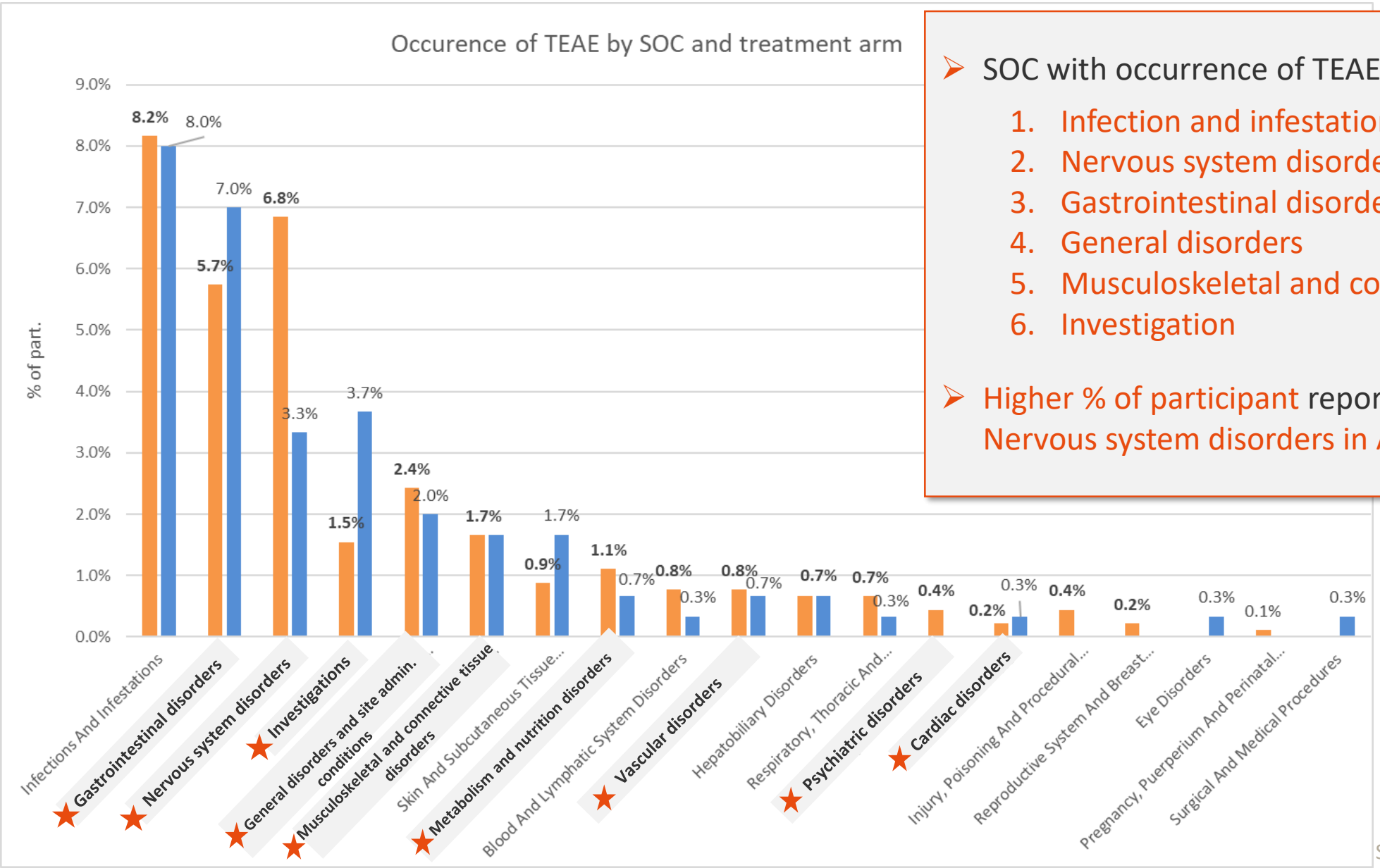
*Presentation of results: Nb of part. (% of part.) [Nb of TEAE]

- Occurrence of TEAE similar in both groups
- Majority of TEAE are mild or moderate
- No related severe and/or serious TEAE
- **6.5 %** of participants had at least 1 TEAE related to acoziborole (in OXA002: 13.9%)
- No death in acoziborole group

Source: Tables 14.3.1.1 & 14.3.1.14

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All TEAE reported by System Organ Class (SOC)



- SOC with occurrence of TEAE ≥1% in Acoziborole groups:
  1. Infection and infestations
  2. Nervous system disorders
  3. Gastrointestinal disorders
  4. General disorders
  5. Musculoskeletal and connective tissue disorders
  6. Investigation
- Higher % of participant reported TEAE related to Nervous system disorders in Acoziborole (vs placebo)

Legend

Acoziborole

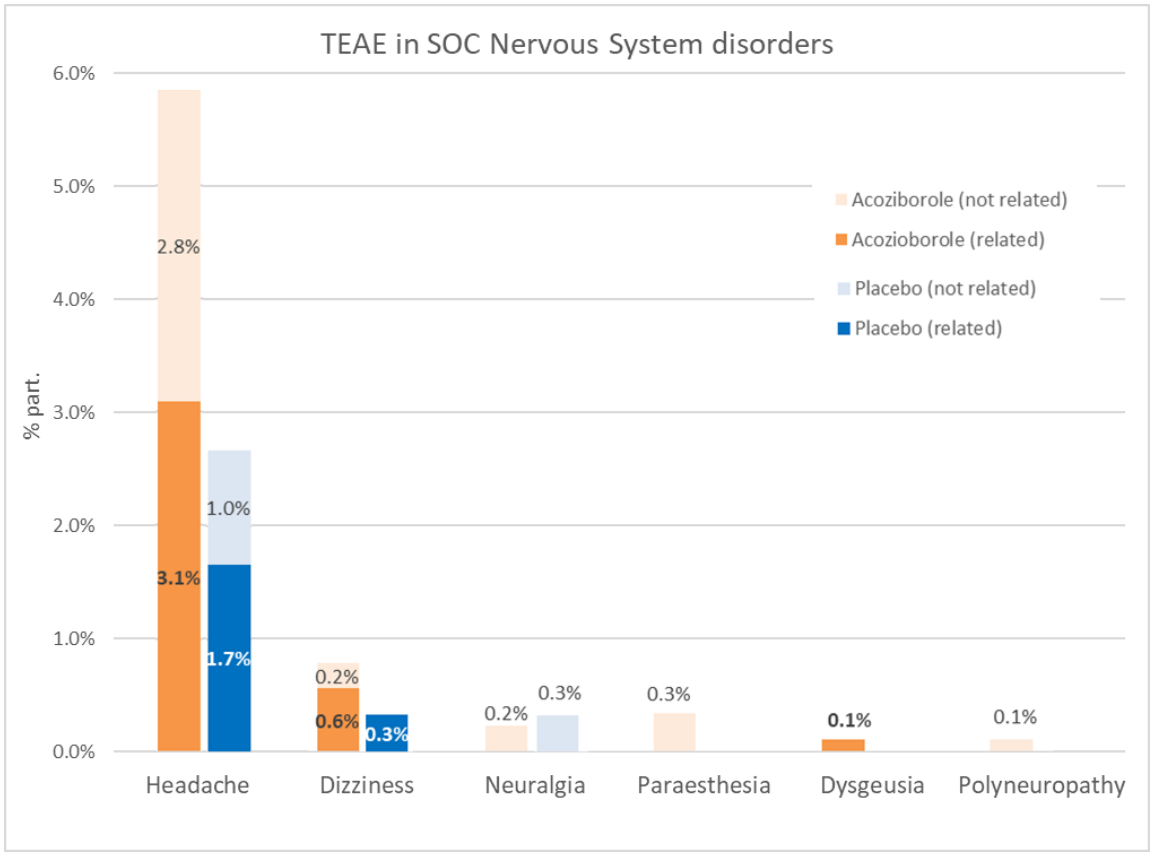
Placebo

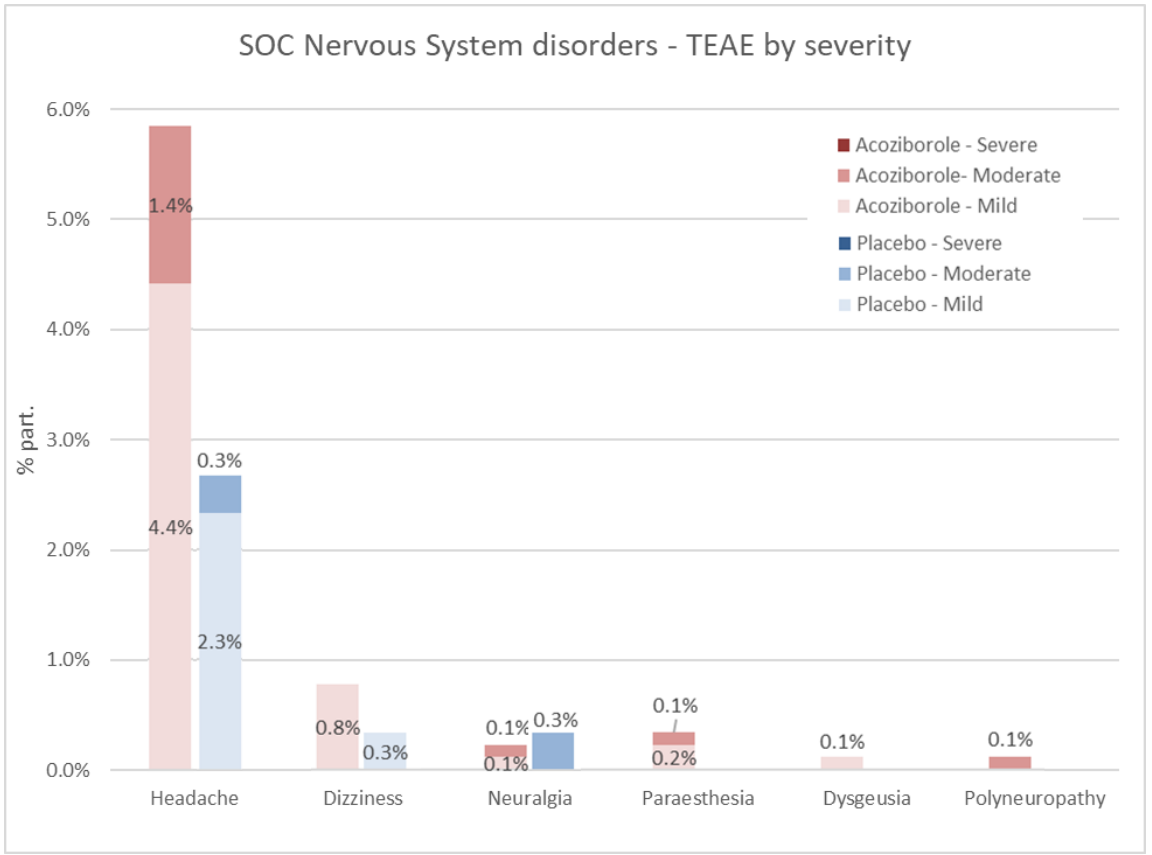
★ **SOC** where part. had at least 1 **TEAE related to the study drug**

Source: Tables 14.3.1.15 & 14.3.1.20

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Preferred Terms in SOC Nervous system disorders



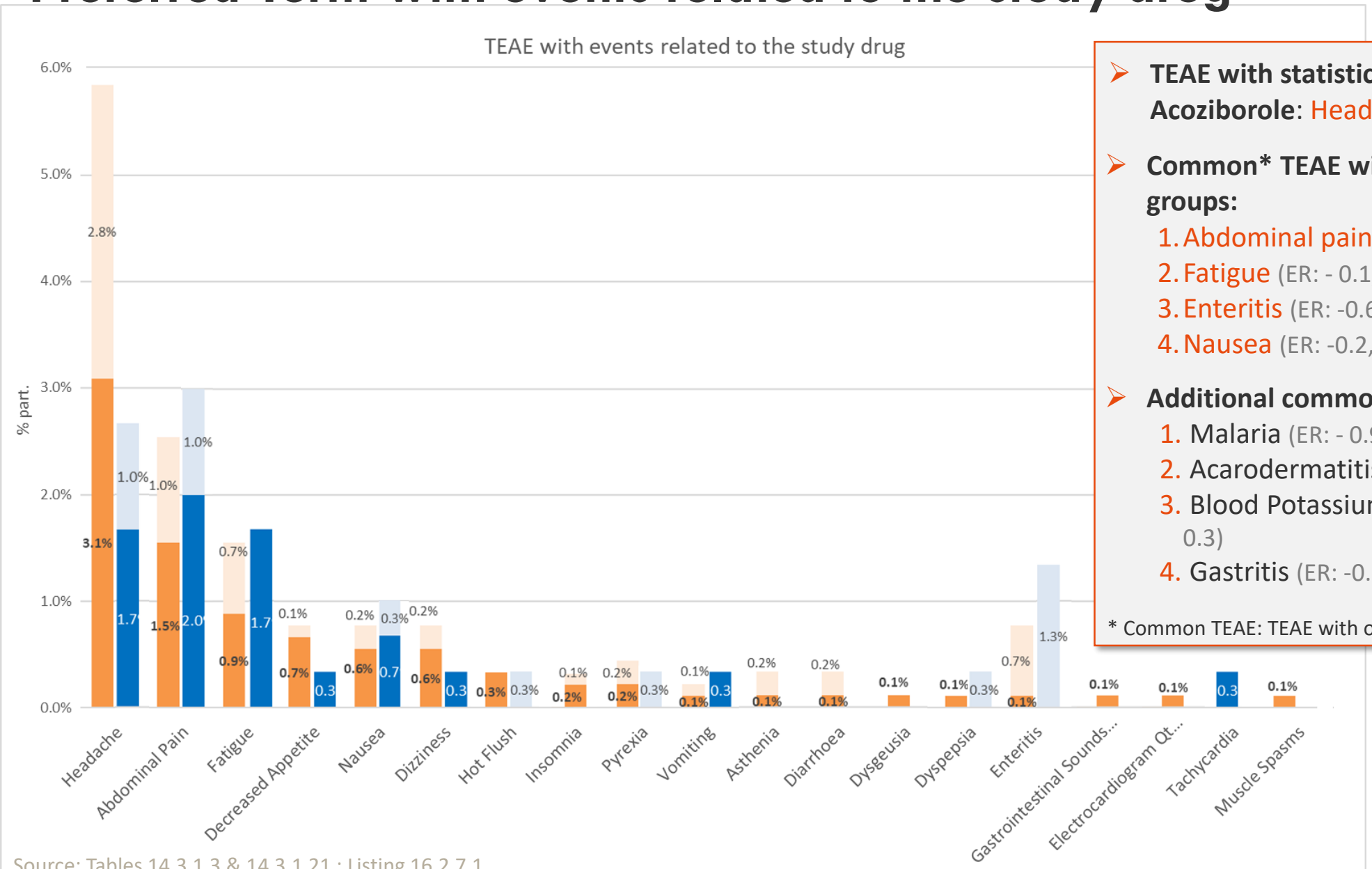


Source: Tables 14.3.1.15, 14.3.1.17a & 14.3.1.20

- Occurrence of headaches higher in acoziborole* group, all mild or moderate
- No severe TEAE
- 1 case of moderate polyneuropathy in Acoziborole group, not related (participant with drug and alcohol addictions)

* Excess rate: 3.2 (95% CI 0.3 : 5.3)

Preferred Term with events related to the study drug



- **TEAE with statistically higher occurrence in Acoziborole**: Headaches (ER: +3.2, 95% CI 0.3 : 5.3)
- **Common* TEAE with similar occurrence in both groups:**
  1. Abdominal pains (ER: - 0.5, 95% CI -3.2 : 1.4)
  2. Fatigue (ER: - 0.1, 95% CI -3.4 : 1.3)
  3. Enteritis (ER: -0.6, 95% CI -3.4 : 1.3)
  4. Nausea (ER: -0.2, 95% CI -2.2 : 0.8)
- **Additional common* TEAE, not related** :
  1. Malaria (ER: - 0.9, 95% CI -4.1 : 1.4)
  2. Acarodermatitis (ER: +0.4, 95% CI -1.6: 1.6)
  3. Blood Potassium Increase (ER: -1.1, 95% CI -3.5 : 0.3)
  4. Gastritis (ER: -0.3, 95% CI -2.3:0.7)

* Common TEAE: TEAE with occurrence ≥1%

Source: Tables 14.3.1.3 & 14.3.1.21 ; Listing 16.2.7.1

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Reporting of Serious Adverse Events (SAE)

Déclaration des évènements Indésirables graves

In ACOZIBOROLE group:

- 8 SAEs in 7 participants (0.8% of participants), not related:
  - **3 SAEs within reporting period**: Uterine prolapse, vaginal haemorrhage and abortion (probably induced)
  - **5 additional SAEs (onset> 9 months)**, **linked to outcome of pregnancy** : Vaginal bleeding, Umbilical cord prolapse, Fetopelvic disproportion, Premature rupture of membranes, Fetal distress
- All recovered, 1 delivery with fetal death

In PLACEBO group:

- 5 SAEs in 5 participants (1.7% of participants), not related
  - **4 SAEs within reporting period**: acute appendicitis, infected wound, complicated malaria and elective abortion
  - **1 additional SAE (onset> 5 months)**, **linked to outcome of pregnancy** : spontaneous abortion
- 1 fatal outcome (complicated malaria)

Dans le groupe ACOZIBOROLE:

- **8 EIG** chez 7 participants (0.8% of participants), non relié au traitement:
  - **3 EIGs survenus avant M4**: prolapse utérin, hémorragie vaginale et avortement (probablement provoqué)
  - **5 EIGs supplémentaire (apparition > 9 mois), liés à l'issue de grossesses non prévues**
- Tous les participants se sont rétablis

Dans le groupe PLACEBO:

- **5 EIG** chez 5 participants (1,7% des participants), non relié au traitement:
  - **4 EIG survenus avant M4** : appendicite aiguë, plaie infectée, paludisme compliqué et avortement provoqué
  - **1 EIG supplémentaire** (apparition > 5 mois), lié à l'issue d'une grossesse non prévue
- 4 participants se sont rétablis
- 1 participant est décédé suite à un paludisme compliqué

Reporting of exposures during incidental pregnancies
Déclaration des expositions pendant des grossesses non prévues

In ACOZIBOROLE group: 8 grossesses

- **6 infants born healthy and developing normally** (3 normal deliveries and 3 deliveries by C-section)
- 1 fetal death (due to umbilical cord prolapse)
- 1 abortion (probably induced)

In PLACEBO group: 3 grossesses

- **1 infant born healthy and developing normally**
- 1 elective abortion
- 1 spontaneous abortion

Dans le groupe ACOZIBOROLE: 8 grossesses

- **6 nourrissons nés en bonne santé et se développant normalement** (3 accouchements normaux et 3 accouchements par césarienne)
- 1 décès fœtal (dû à un prolapsus du cordon ombilical)
- 1 avortement (probablement provoqué)

Dans le groupe PLACEBO: 3 grossesses

- **1 nourrisson né en bonne santé et se développant normalement**
- 1 avortement provoqué
- 1 avortement spontané

DNDI-OXA04-HAT RESULTS

CONCLUSION

- **Excellent safety profile of acoziborole in g-HAT seropositive subjects**
  - 78.9% of participants administered with acoziborole did not report any TEAEs
  - The majority of TEAE were of mild or moderate intensity
  - No serious nor severe related TEAEs
  - Only the occurrence of headaches has been identified as a potential risk with acoziborole

- **Very supportive data for a future extended use of acoziborole**

- **Profil de sécurité de l'acoziborole chez les participants séropositifs à la THA due à Tb gambiense excellent**
  - 78.9% des participants ayant reçus acoziborole n'ont rapporté aucun EI
  - La majorité des EI étaient d'intensité légère ou modérée
  - Pas d'EI severe ou grave relié à la prise d'acoziborole
  - Seuls la survenue des maux de têtes est un risque identifié comme potentiel avec la prise d'acoziborole

- **Les données sont très encourageantes pour une extension future de l'utilisation de l'acoziborole.**

Thank You
Merci

AKSANTI SANA,
Matondo mingi

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