



## MISTRAL Newsletter

April 2024

Dear MISTRAL colleagues,

Since our last newsletter, enrolment has moved forward significantly, thank you all for your hard work.

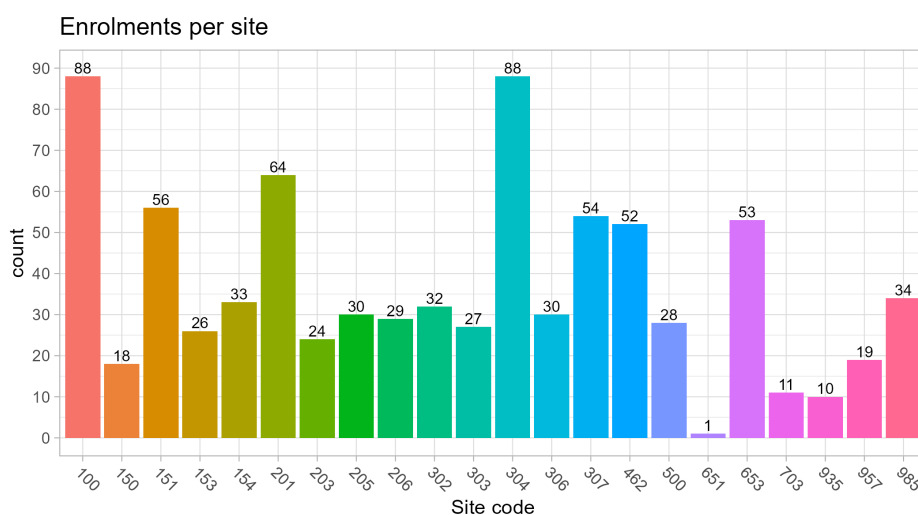
In this fourth MISTRAL study newsletter, we have gathered updates on the study, insights from the data collected so far, and some reminders to your sites. If you have any additional experiences or good ideas to share, feel free to contact us so we can share it with the other sites.

\MISTRAL team at CHIP

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### Site and enrolment status

There are now 22 sites open for enrolment in our MISTRAL work package. So far 813 participants have been enrolled and of these 295 were already part of EuroSIDA. In total, 68 participants have already returned to their clinic and completed their second visit.





## Cohort characteristics (as of 17.04.2024)

Similarly to our previous newsletter, the group still consists predominantly of white men who have sex with men (MSM). Their diet is mainly omnivorous, and the stool samples collected have mostly been of Type 4 of the Bristol Stool Chart.

We may not have yet reached full enrolment, but we can already see that we have a richly characterised cohort in relation to factors that may influence the microbiome and the risk of serious non-AIDS events. Preliminary assessments also highlight the need to treat these variables carefully given the observed correlations and small numbers of certain subgroups (e.g., women and non-white ethnicities).

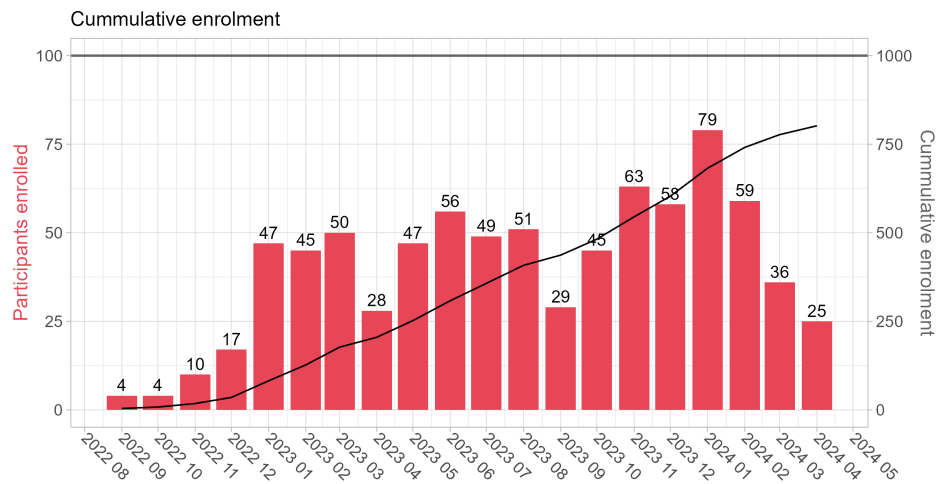
<b>Total participants, n (%)</b>	806 (100)
<b>EuroSIDA, n (%)</b>	290 (36)
<b>Age, median [min, max]</b>	59 [50, 86]
<b>Male, n (%)</b>	630 (78)
<b>Consented to genomics analysis, n (%)</b>	756 (94)
<b>Country of recruitment, n (%)</b>	
	Belgium 88 (11)
	Croatia 34 (4)
	Czechia 10 (1)
	Denmark 133 (17)
	Germany 231 (29)
	Israel 11 (1)
	Italy 52 (6)
	Luxembourg 28 (3)
	Poland 19 (2)
	Spain 54 (7)
	United Kingdom 146 (18)
<b>Ethnicity, n (%)*</b>	
	White 434 (84)
	Black 48 (9)
	Other 14 (3)
	Unknown 7 (1)
<b>Mode of HIV infection</b>	
	MSM 463 (57)
	Heterosexual contact 151 (19)
	Injecting drug user 20 (2)
	Sexual contact + injecting drug user 8 (1)
	Other 11 (1)
	Unknown 153 (19)
<b>Diet preference, n (%)</b>	
	Omnivore 709 (88)
	Pescetarian 24 (3)
	Vegetarian/vegan 21 (3)
	Unknown 52 (6)

\* Data only available for non-EuroSIDA patients

## Recruitment projections

Our original aim was to complete recruitment of 1,000 persons by December of last year to ensure adequate time for collection of follow-up samples for 1,000 participants within the EU reporting period. We have now decided to encourage you to continue enrolling new participants. We will let you know in due time when we plan to stop. However, we would like to reach our goal as soon as possible, so please continue enrolling! If there is anything we can do to help ease this process, please let us know.

If we need to close for new enrolments prior to full enrolment, the power for associations with clinical events will be reduced. We would of course like to avoid doing this.



## Shipment and analysis of samples

### Shipment of samples

We recently shipped almost 8,000 samples from the first 500 enrolled participants to IrsiCaixa in Spain, who will be helping us with the analysis of the samples. Thank you so much for the effort you all put in sending your samples to us, we look forward to seeing some first results from the analyses!

### Analysis of samples

As part of our work package, we will be analysing the faecal, plasma and whole blood samples to use in various analyses. In the coming 12 months we will perform faecal shotgun metagenomic sequencing and faecal proteomics as plasma metabolomics, plasma lipidomics, and assessment of the inflammatory biomarkers IL-6, C-reactive protein (CRP) and D-dimer. Using bioinformatics and biostatistical methodologies, these data will be coupled with the clinical data collected through the REDCap questionnaires to elucidate the role of the microbiome in biomarkers of serious AIDS and non-AIDS events in people living with HIV. In the future, when we have sufficient power, we will also perform associations between these data and the clinical events themselves.

## Reminders and updates

### Plan for Visit 2

Please remember to plan the second study visit keeping in mind that the follow-up sample should be collected within 10-24 months after the first MISTRAL study visit.

### Reimbursement of REDCap forms

Forms that have a completed and locked status, i.e. enrolment forms (non-EuroSIDA participants only), questionnaire and samples (visit 1 and 2), event forms and CoDe forms, prior to **1 May 2024** will be reimbursed. Sites that also completed FU1 forms between October and December 2023 will also be reimbursed. Do not hesitate to ask if this raises any questions on your end.

### Finalising forms before April 2024

All REDCap enrolment forms with a completed and locked (validated) status prior to **1 May 2024** will be downloaded shortly after. In order to include enrolled participants for follow-up in Autumn 2024, you need to finalise their forms

before this deadline. Again, do not hesitate to contact us if this raises any questions on your end.

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## Frequently asked questions (FAQ)

**Q: Should the study staff or the patient complete the questionnaire?**

A: The questionnaire should be completed by the study staff.

**Q: A participant consents and takes the stool sample collection kit home with them, when do they have to return?**

A: The participant must return to the clinic with their stool sample within 48 hours of defecation. This should occur as early as possible to the consent, to ensure eligibility criteria are still met at the time of sample collection. However, we allow up to 3 months from date of consent for the participant to collect the stool and return the sample to the clinic.

**Q: Do the sample labels match, in any way, with the participants' PID numbers?**

A: No, you should use one set of labels per participant per visit in the order that you receive the samples. The labels will then be linked to the correct participant and visit when they are scanned into REDCap. You will also need to record which label IDs belong to which patient on the site List of Stored Samples. For more information see slides 43-48 in the [Training slides](#).

All frequently asked questions are gathered on our [website](#). If you have any questions not answered here, other solutions to the problems, or any general tips for participant recruitment/engagement, feel free to contact us at [mistral.rigshospitalet@regionh.dk](mailto:mistral.rigshospitalet@regionh.dk).

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## The MISTRAL consortium

MISTRAL is a large international consortium funded by EU. Research groups from all over Europe are engaged in the work, which has been split into several work packages each with their own aim.

The primary objective of the work led by CHIP is to strengthen and evaluate the understanding of the association between the gut microbiome composition and the risk of developing serious AIDS and non-AIDS events (SNAEs), including cardiovascular events.

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## Interesting research on the gut microbiome

**Heinken et al., “Genome-scale metabolic reconstruction of 7,302 human microorganisms for personalized medicine”, Nature Biotechnology (2023)**

AGORA2 predicts drug conversion/metabolism potential based on the gut microbiome. AGORA2 (assembly of gut organisms through reconstruction and analysis, version 2) accounts for 7,302 strains, includes strain-resolved drug degradation and biotransformation capabilities for 98 drugs. 10 of the 98 drugs they look at are lipid modifying (statins fx) which could be relevant for the MISTRAL cohort.

The full article is available here: <https://doi.org/10.1038/s41587-022-01628-0>.

## Learn more about MISTRAL

You can find all the study documents related to this MISTRAL project at <https://chip.dk/Research/Studies/MISTRAL/Study-documents>

General information about MISTRAL can be found on this website <https://chip.dk/Research/Studies/MISTRAL>

Information about all the work packages included in MISTRAL can be found at [www.mistral-hiv.eu](http://www.mistral-hiv.eu)

Finally, you can follow the MISTRAL consortium on Twitter <https://twitter.com/mistralhiv>

This was all we had for now. We look forward to sharing more updates with you in half a year. Wishing you all a lovely spring!

Sincerely,  
*The MISTRAL staff at CHIP*



Daniel D. Murray  
Scientific Lead



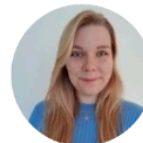
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