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Prophylaxis with lactoferrin and lactobacillusGG in Very Low Birth Weight (VLBW) neonates in Neonatal Intensive Care Unit (NICU): a double-blind, multicentre, placebo-controlled, randomised trial

Submission date 20/08/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/09/2007	**Overall study status** Completed	
Last Edited 15/02/2018	**Condition category** Neonatal Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Prophylaxis with lactoferrin and lactobacillusGG in Very Low Birth Weight (VLBW) neonates in Neonatal Intensive Care Unit (NICU): a double-blind, multicentre, placebo-controlled, randomised trial

Acronym
LF+LGG/PRETERMS

Study objectives
To evaluate the efficacy of lactoferrin (LF) (alone, or in combination with lactobacillusGG [LGG]) in prevention of bacterial and fungal colonization and infection, and Necrotising EnteroColitis (NEC), in preterm very low birth weight (i.e., <1500 g at birth) infants in NICUs.

Disease/condition/study domain:
1. Colonization by Candida species
2. Invasive infection by Candida species
3. Colonization by bacterial (Gram+ and Gram-) species
4. Invasive infection by bacterial (Gram+ and Gram-) species
5. NEC (surgical stages)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethical Committee of the Saint Anna Foundation (Fondazione Crescere Insieme al Santa Anna - ONLUS) on behalf of each participating institution, 18/06/2007

Study design
Multicentre prospective randomised double-blind placebo-controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Bacterial and fungal colonization and infection, and Necrotising EnteroColitis (NEC) in Very Low Birth Weight (VLBW) neonates

Interventions
The regimens in the two intervention groups will be:
Group A: LactobacillusGG, 6 x 109 Colony-Forming Units (CFU)/day (Dicoflor 60®, Dicofarm spa, Italy) plus Lactoferrin 100 mg (LF100®, Dicofarm spa, Italy), to be started within the first 36 h of life: single administration (added to prepared milk or to 1 ml of a 5% glucose solution), daily for 4 or 6 weeks.

Group B: Lactoferrin 100 mg (LF100®, Dicofarm spa, Italy), to be started within the first 36 h of life: single administration (added to prepared milk or to 1 ml of a 5% glucose solution), daily for 4 or 6 weeks.

The regimen in the placebo group will be:
Group C: Addition of 2 ml of 5% glucose solution to milk feeding, daily for 4 or 6 weeks.

Six weeks (in infants with birth weight less than 1000 g, i.e. Extremely Low Birth Weight [ELBW]) and four weeks (in the infants with birth weight 1001 g to 1500 g) are chosen as the duration of therapy on the basis of the currently published data, unless earlier discharge.

Neonates not feeding in the first 36 hours will receive the drug(s)/placebo by oral/naso-gastric tube and can be enrolled in the absence of gastric instability and/or repeated gastric residuals or vomit.

If they repeatedly display gastric instability, gastric residuals or vomit, they may be enrolled at any point during the first week of life, depending on the first "efficacious" feedings. The day of life on which they first received the drugs(s)/placebo will be recorded in the database, and their statistics will be limited to the days of administration exposure to intervention.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
LactobacillusGG , lactoferrin

Primary outcome(s)
Evaluation of the effectiveness of LF (alone, or in combination with the probiotic LGG) compared to placebo in the prevention of Bacterial and fungal colonization and infection, and of necrotizing enterocolitis (NEC), in the preterm very low birth weight neonates admitted to the participant NICUs. This will be based on the following outcome measures:

1. Assessment of the incidence of Gram-positive , Gram-negative and Candida sepsis prior to discharge
2. Mortality (overall, bacterial sepsis- and Candida-attributable) prior to discharge
3. Rate of progression from fungal colonization to fungal infection prior to discharge
4. Ligation of patent ductus arteriosus prior to discharge
5. Threshold retinopathy of prematurity requiring surgery at discharge
6. Severe (grade 3-4) intraventricular haemorrhage at discharge
7. Bronchopulmonary dysplasia at discharge
8. Incidence of organ locations (major complications) in infected patients prior to discharge
9. Absence of changes in the relative frequencies of the various Candida sub-species isolated at discharge

Key secondary outcome(s))
No secondary outcome measures

Completion date

31/07/2008

Eligibility

Key inclusion criteria
All neonates with birth weight <1500 g (i.e. VLBW) born within the study period, whether at one of the eighteen participating institutions or elsewhere, were eligible for the study.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Key exclusion criteria
1. Parental refusal
2. Admission after 12 hours of life
3. Death prior to 72 hours of life
4. Ongoing systemic antifungal management
5. Ongoing antifungal prophylaxis

Date of first enrolment
01/10/2007

Date of final enrolment
31/07/2008

Locations

Countries of recruitment
Italy

Study participating centre
Saint Anna Hospital
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Sponsor information

Organisation
Saint Anna Foundation (Fondazione Crescere Insieme al Santa Anna [ONLUS]) (Italy)

ROR
https://ror.org/00k065b17

Funder(s)

Funder type
Industry

Funder Name
Dicofarm S.p.A. will supply the LF, the LGG and placebo, and will provide financial support with a grant, but will not be involved in the concept, design, enrolment, data collection, analysis and interpretation of its results, and decision inherent the publication of the results.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	07/10/2009		Yes	No
Results article	results	01/01/2012		Yes	No
Results article	results	01/03/2014		Yes	No
Other publications	secondary analysis	01/02/2018		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes