FACULTY OF PHARMACEUTICAL SCIENCES

LABORATORY OF PHARMACEUTICAL TECHNOLOGY

GHENT UNIVERSITY

SAFETY AND ACCEPTABILITY OF PLACEBO PELLETS CO-ADMINISTERED WITH A SWALLOWING GEL IN HEALTHY ADULT VOLUNTEERS

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1. Introduction

- **Pellets**
  - Personalized dosing
  - Age-appropriate formulation
  - Less risk of dose dumping of sustained release formulation
- **Patients with swallowing difficulties**
  - Difficulties in swallowing oral solid dosage forms e.g. tablets and capsules
  - Reduced therapy adherence
  - Increased risk of aspiration pneumonia
  - Unauthorized modification of dosage form
- **Need for patient-centric development of suitable oral solid dosage form**
  - Co-administration of high drug-loaded pellets with a commercially available swallowing gel

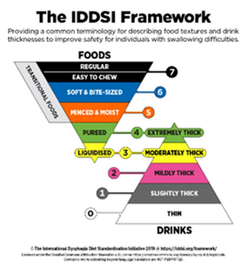
2. Objective

Investigate the **safety** and **acceptability** of **oral administration** of **placebo pellets** in combination with commercially available CE-marked **swallowing gels** in **healthy adult volunteers**

3. Materials & Methods

Materials

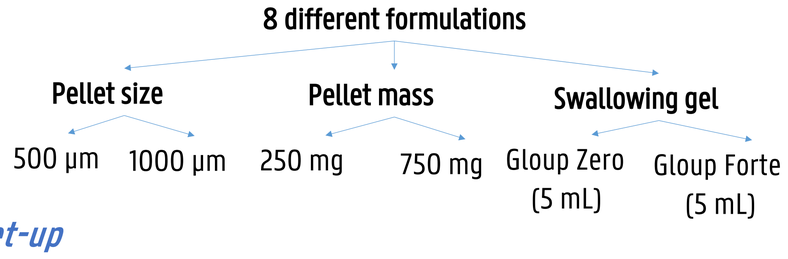
Placebo microcrystalline cellulose pellets	Cellets 500 Cellets 1000	500-710 µm 1000-1400 µm
Swallowing gels (class I medical device, CE-marked)	Gloup Zero (GZ) Gloup Forte (GF)	IDDSI level 3 IDDSI level 4



Methods

Trial design

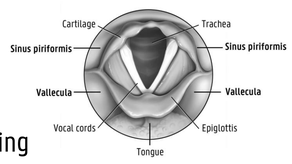
- **2x2x2 factorial randomized balanced incomplete block design**



Trial set-up

- Inclusion criteria:
  - > 18 years old and < 65 years old
  - No swallowing problems (EAT-10 score < 3)
- Participant-reported swallowability (VAS)
- Investigator-reported swallowability (PAS and YPRSRS)
  - Anatomical regions monitored for residual pellets: Vallecula and sinus piriformis
  - Swallowing process timepoints: After intake, after swallowing, after rinsing

Gloup Zero 250 mg 500 µm,



Objectives and endpoints

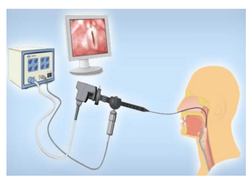
Primary objective
Investigator-reported safety
↓
Primary endpoint
PAS [1] ≤ 2: considered safe

Secondary objective (a)
Investigator-reported acceptability
after rinsing
at vallecula and sinus piriformis
↓
Secondary endpoint
YPRSRS [2] ≤ 2: considered acceptable

Exploratory objective
Investigator-reported acceptability
after intake and after swallowing
at vallecula and sinus piriformis

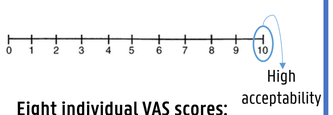
Secondary objective (b)
Participant-reported acceptability
↓
Secondary endpoint
Mean eight-item summary VAS difference ≥ 4: considered clinically relevant

Evaluation via **Fiberoptic Endoscopic Evaluation of Swallowing (FEES)**



✓ Penetration-aspiration Scale (PAS) [1]
✓ Modified Yale Pharyngeal Residue Severity Rating Scale (YPRSRS) [2]

Evaluation via **Visual Analogue Scales (VAS)**



Eight individual VAS scores:
✓ Taste
✓ Perception pellets in mouth and pharynx
✓ Perception residual pellets in mouth and pharynx
✓ Swallowability
✓ Stickiness
✓ Visual aspect

[1] Penetration-aspiration Scale (Rosenbek, J. C, Robbins, J. A, Roecker, E. B, Coyle, J. L, & Wood, J. L. (1996). A penetration-aspiration scale. Dysphagia, 11(2), 93–98)
[2] Modification of the Yale Pharyngeal Residue Severity Rating Scale (Neubauer, P. D., Rademaker, A. W, & Leder, S. B. (2015). The Yale Pharyngeal Residue Severity Rating Scale: An Anatomically Defined and Image-Based Tool. Dysphagia, 30(5), 521–528)

4. Results

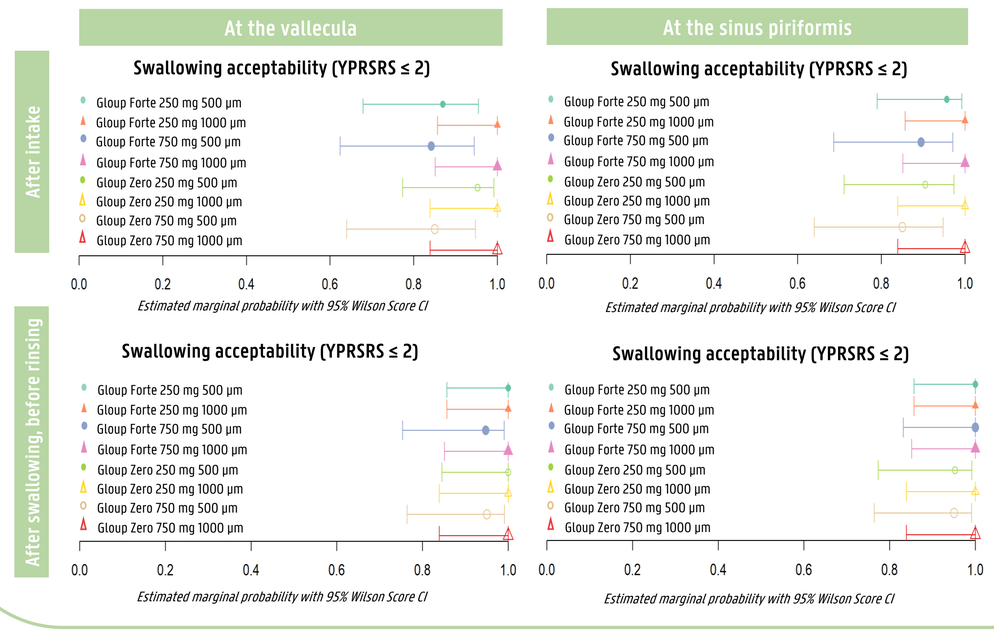
Baseline patient characteristics (N=34)

✓ Age: 37.3 (SD: 13.1; [20 - 64])
✓ Gender: male (n=14, 41.2%), female (n=20, 58.8%)
✓ EAT-10 total score: 0.26 (SD: 0.62; [0 - 2]); EAT-10 score of 0 (n=28, 82.4%), EAT-10 score ≥ 1 (n=6, 17.6%)

Primary endpoint: investigator-reported safety

✓ All formulations were considered safe (PAS ≤ 2) (relative frequency of 99.51%, 203/204)
✓ 1 swallowing event with PAS > 2 for 'GF 750mg 1000µm' formulation (relative frequency of 96,15%, 1 out of 26 administrations of 'GF 750mg 1000µm')

Exploratory endpoints: investigator-reported acceptability

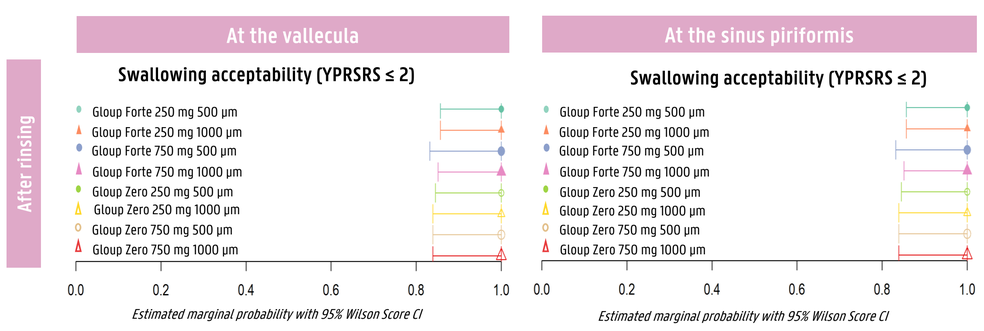


Smaller pellet size: negative impact on residue score

Swallowing: positive impact on residue score

Secondary endpoint (a): investigator-reported acceptability

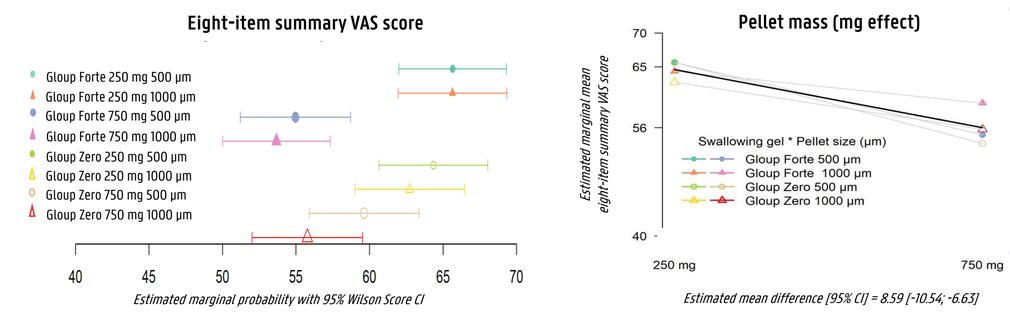
✓ All formulations are considered acceptable (YPRSRS ≤ 2)



After rinsing: complete clearance

Secondary endpoint (b): participant-reported acceptability

✓ All formulations are considered acceptable



Smaller pellet mass: positive impact on acceptability

5. Conclusion

✓ **From safety perspective**
- All formulations are considered generally safe for administration in healthy participants
- The formulation with 1 swallowing event with PAS > 2 is not included in further investigations among patients with swallowing difficulties

✓ **From acceptability perspective**
- All formulations are considered acceptable by both investigator and healthy participants
- Smaller pellet mass has a statistically and clinically relevant positive impact on the mean participant-reported acceptability

✓ **Residue score**
- Negative impact: smaller pellet size
- Positive impact: additional swallowing or swallowing after intake
- Complete clearance after rinsing with water

✓ **Broad applicability for populations with swallowing difficulties, including paediatric patients**

✓ **Future perspective**
- Follow-up palatability study: evaluation of swallowability of oral administration of placebo pellets with a swallowing gel compared to placebo tablet and/or capsule in adult patients with dysphagia *(currently under review by the Ethics Committee)*

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