PRO-C3 and PRO-C6 fibrogenesis biomarkers in connective tissue disease-associated interstitial lung disease: results from the Phase IIb RECITAL trial

Filipa B. Simões[1], Jannie M.B. Sand[2], Morten A. Karsdal[1], Diana J. Leeming[1], Philip L. Molyneaux[2], Toby M. Maher[2,3]

[1]Nordic Bioscience, Herlev, Denmark, [2]National Heart and Lung Institute Imperial College London, London, United Kingdom, [3]Keck School of Medicine University of Southern California, Los Angeles, California

Background

- ILD is a major cause of morbidity and mortality in connective tissue disease (CTD)
- Cyclophosphamide is an effective treatment for **CTD-ILD**, but limited by side effects
- Rituximab was tested as an alternative in the **RECITAL phase IIb trial** (NTC1862926)
- Both drugs **improved lung function** with **rituximab showing fewer adverse events** (Maher, 2022. Lancet Resp Med)

Cyclophosphamide
- Effective therapy in CTD-ILD
- Side effects

Rituximab
- Rescue therapy in CTD-ILD
- Alternative?

Severe or progressive CTD-ILD
- Systemic sclerosis
- Idiopathic inflammatory myositis
- Mixed CTD

Rituximab (1000 ng at weeks 0 and 2)

Cyclophosphamide (600 mg/m^2 every 4th week for 6 doses)

Aim & Methods

Evaluate the effect of cyclophosphamide and rituximab on fibrogenesis in CTD-ILD

Measure fibrogenesis biomarkers in serum from subjects enrolled in RECITAL at baseline, 12, 24 and 48 weeks after treatment

Biomarker	Description	Target
nordicPRO-C3™	Collagen formation	Type III collagen pro-peptide
nordicPRO-C6™	Collagen formation	Type VI collagen C-terminal

Contact: Filipa B. Simões, fils@nordicbio.com

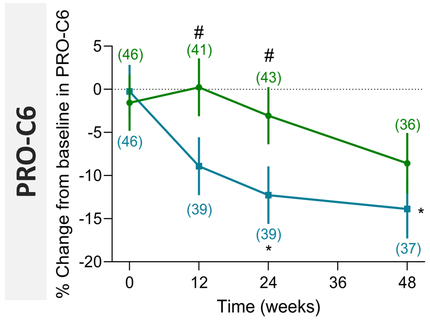
Disclosures: FILS, JSA, MAK, and DJL are employed at Nordic Bioscience and may be shareholders

Imperial College London

NORDIC BIOSCIENCE

Results

Longitudinal change in fibrogenesis biomarkers

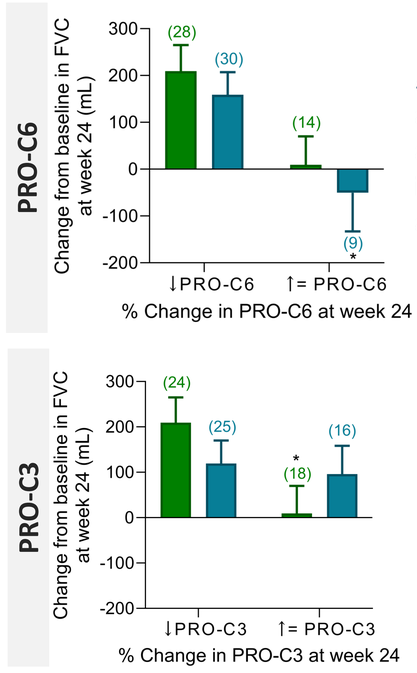


Rituximab **reduced PRO-C6** levels at weeks 24 and 48

Data analysed by linear mixed models adjusted for age, sex and diagnosis and are shown as mean ± standard error.

* significant difference compared to week 0, # significant difference compared to rituximab (p-value < 0.05).

Change in fibrogenesis biomarkers and FVC



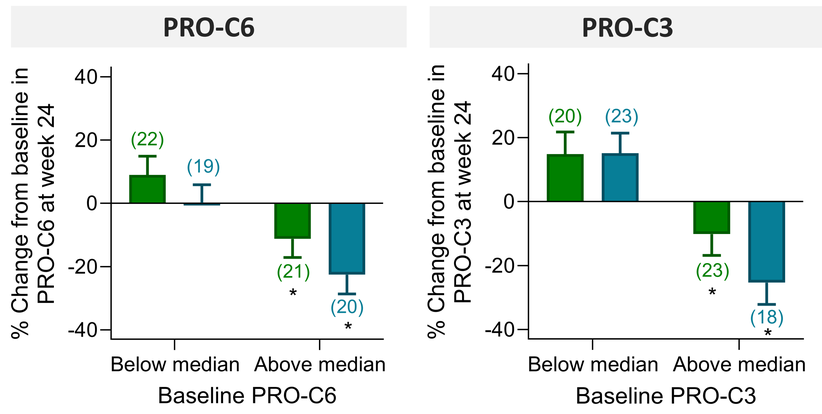
A **decrease** in **PRO-C6** and **PRO-C3** is associated with an **improvement in FVC** at week 24

Patients divided according to the % change from baseline (% CFB) in the biomarker level at week 24:
↓ PRO-C6/C3 (% CFB <0)
↑= PRO-C6/C3 (% CFB ≥ 0)

Data analysed by linear models adjusted for age, sex and diagnosis and shown as mean ± standard error.

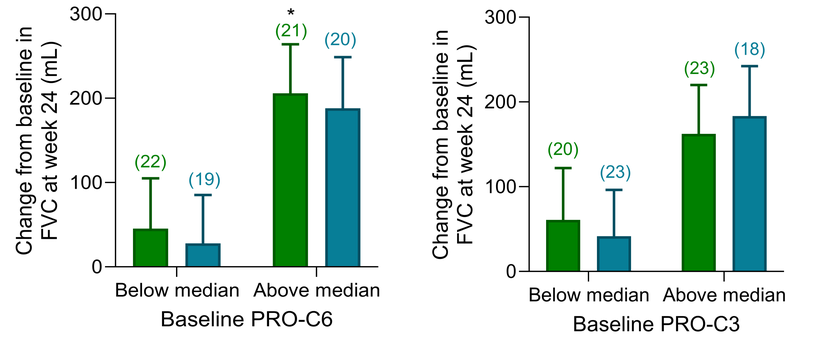
* significant difference compared to ↓ PRO-C6/C3 group (p-value < 0.05).

Baseline fibrogenesis biomarkers and FVC response



Patients divided according to median baseline biomarker levels in two groups: below median and above median. Data analysed by linear models adjusted for age, sex and diagnosis and shown as mean ± standard error. * significant difference compared to "Below median" group for the respective treatment

Patients having higher **baseline PRO-C3** and **PRO-C6** display a **greater biomarker reduction** at week 24



Patients divided according to median baseline biomarker levels in two groups: below median and above median. Data analysed by linear models adjusted for age, sex and diagnosis and shown as mean ± standard error.
* significant difference compared to "Below median" group for the respective treatment

Cyclophosphamide Rituximab

A higher **baseline PRO-C3** and **PRO-C6** is associated with a **higher FVC increase** at week 24

Key Messages

- The decrease in PRO-C6 and PRO-C3 suggest that, besides their immunomodulatory effects, these drugs may also reduce fibrogenesis
- PRO-C3 and PRO-C6, measured at baseline and as % change from baseline, are associated with FVC response

These findings highlight PRO-C3 and PRO-C6 as promising biomarkers for progressive CTD-ILD