

## **'Peripheral oxidative burst correlates with VEGF serum levels in IPF: modulation by anti-fibrotic treatments'**

**Giorgio Emanuele Polistina**<sup>1</sup>, Serena Zanotta<sup>2</sup>, Gaetano Rea<sup>3</sup>, Antonietta Coppola<sup>1</sup>, Domenico Galati<sup>2</sup>, Marialuisa Bocchino<sup>1</sup>

*1Department of Clinical Medicine and Surgery - Federico II University Of Naples, Naples, Italy, 2Department of Hematology and Innovative Therapies - Pascale Foundation National Institute of Cancer, Naples, Italy, 3Department of Radiology - Monaldi Hospital, Naples, Italy*

Oxidative stress is a key feature in IPF pathogenesis. Despite anti-oxidant treatment has been disappointing, targeting oxidant-dependent mechanisms is a challenging issue along with the identification of suitable biomarkers. Aim of this prospective study was to measure peripheral oxidative burst (OB) in a cohort of newly diagnosed patients with clinically stable mild to moderate IPF (n=25) in comparison with 25 age and sex-matched healthy volunteers and 25 IPF cases treated with currently available anti-fibrotic drugs (nintedanib and pirfenidone).

Quantitative determination of leucocyte OB was measured by flow cytometry (Phagoburst, BD) along with serum levels of IL-2, IL-4, IL-6, IL-10, TNF-alpha, IFN-gamma and VEGF (BD Cytometric Bead Array). The median MIF (mean fluorescence intensity) of OB was significantly higher in naive IPF patients (14183) as compared to controls (11264, p=0.0002) and treated cases (13267, p=0.03). Also, serum levels of VEGF were higher in naive IPF patients in comparison to controls (137.3 vs 35.8 pg/ml, p<0.0001). Similar results were observed with IL-6 (5.24 vs 1.41 pg/ml, p<0.0001), IL-10 (1.28 vs 0.84 pg/ml, p=0.004), and TNF-alpha (0.35 vs 0.01, p=0.02). Interestingly, only VEGF concentrations were reduced upon treatment (68 pg/ml, p=0.02). Levels of IL-2, IL-4 and IFN-gamma were unremarkable. Interestingly, oxidative stress correlated with VEGF levels both in naive (r=0.43; p=0.04) and in treated (r=0.59, p=0.004) IPF patients. We provide evidence for a constitutive increase of peripheral oxidative burst in IPF at diagnosis that correlates with a fibrosis related biomarker, both being influenced by anti-fibrotic therapy.