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Title: Pulmonary arterial hypertension in patients treated with interferon

Dr. Laurent 24871 Savale laurent.savale@gmail.com MD ¹, Dr. Sven 24872 Gunther sven.gunther@bct.aphp.fr MD ¹, Dr. Marie Camille 24873 Chaumais mcamillechaumais@gmail.com ², Dr. Xavier 24888 Jais xavier.jais@bct.aphp.fr MD ¹, Dr. Caroline 24874 Sattler caroline.sattler@free.fr MD ¹, Dr. Elise 24875 Artaud Macari eliseartaudmacari@yahoo.fr MD ¹, Dr. David 24892 Montani david.montani@bct.aphp.fr MD ¹, Prof. Gerald 24893 Simonneau gerald.simonneau@bct.aphp.fr MD ¹, Prof. Marc 24904 Humbert marc.humbert@bct.aphp.fr MD ¹ and Prof. Olivier 24918 Sitbon olivier.sitbon@bct.aphp.fr MD ¹. ¹ Service Pneumologie, CHU Bicêtre, Le Kremlin Bicêtre, France and ² Service Pharmacie, Hôpital Antoine Bécère, Clamart, France .

Body: Background: Cases of pulmonary arterial hypertension (PAH) in patients treated with interferon (IFN) α or β have been reported in the literature. Additional data are however needed to better evaluate whether IFN can trigger PAH. Objective and methods: This study was designed to describe retrospectively all cases of PAH patients with a history of IFN exposure identified in the French referral centre for pulmonary hypertension. Results: Fifty-three patients (32 males) with PAH and a history of IFN therapy were identified between 1998 and 2012 (mean age 46 ± 6 years). Forty-eight patients were treated with IFN α for chronic hepatitis C (median duration of treatment 7.8 months). Most of them had portal hypertension (90%) and 26/48 (54%) had a HIV co-infection. Five additional patients were treated with IFN β for multiple sclerosis. The delay between initiation of IFN treatment and PAH diagnosis was exactly determined in 42 patients of whom 29 (69%) had a diagnosis made within three years of initiation of IFN therapy. Sixteen patients with known PAH patients were treated with IFN for chronic hepatitis C. Hemodynamic follow-up was available in 12 of them. Increased pulmonary vascular resistance (PVR) of more than 20% was observed in 10/12 cases (median increase of PVR of 43%, IQR 32-67%) in a median delay of 7.4 months after IFN initiation. In half of these patients (5/10), IFN withdrawal resulted in marked hemodynamic improvements. Conclusion: This retrospective analysis suggest that IFN therapy may be a trigger for PAH. However, most of these patients had other risk factors for PAH. A prospective case control study is mandatory to definitively establish a link between IFN exposure and PAH.