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High risk of lung cancer in surfactant-related gene variant carriers

Alexandre Brudon[1,2,43], Marie Legendre[3,4,43], Arthur Mageau[5,6], Julien Bermudez[7,8], Philippe Bonniaud[9], Diane Bouvry[10,11], Jacques Cadranel[12,13], Aurélie Cazes[14,15], Bruno Crestani[15,16], Tristan Dégot[17], Céline Delestrain[18,19], Rémi Diesler[20,21], Ralph Epaud[18,19], Quentin Philippot[15,16], Nathalie Théou-Anton[22,23], Caroline Kannengiesser[22,23], Ibrahima Ba[22,23], Marie-Pierre Debray[23,24], Pascale Fanen[19,24], Efrosine Manali[25], Spyros Papiris[25], Nadia Nathan[4,26], Serge Amselem[3,4], Antoine Gondouin[27], Anne Guillaumot[28], Claire Andréjak[29,30], Stephane Jouneau[31], Guillaume Beltramo[9], Yurdagul Uzunhan[10], François Galodé[32], Virginie Westeel[27], Anas Mehdaoui[33], Sandrine Hirschi[17], Sylvie Leroy[34,35], Sylvain Marchand-Adam[36,37], Hilario Nunes[10,11], Clément Picard[38], Grégoire Prévot[39], Martine Reynaud-Gaubert[7,8], Paul De Vuyst[40], Lidwine Wemeau[41], Gautier Defossez[42], Gérard Zalcman[1,2], Vincent Cottin[20,21], Raphael Borie[15,16] and the OrphaLung network

[1]Service d'Oncologie Thoracique, Hôpital Bichat, AP-HP, Institut du Cancer AP-HP Nord, Paris, France. [2]Université Paris Cité, Inserm CIC-EC 1425, Paris, France. [3]UF de Génétique Moléculaire, Hôpital Armand Trousseau, AP-HP, Paris, France. [4]Sorbonne Université, Inserm UMR-S 933, Maladies Génétiques d'Expression Pédiatrique, Paris, France. [5]Département de Médecine Interne, Hôpital Bichat, AP-HP, Paris, France. [6]Université Paris Cité, Inserm IAME UMR 1137 Team Descid, Paris, France. [7]Service de Pneumologie, Centre de Compétences de Maladies Pulmonaires Rares et de Transplantation Pulmonaire, CHU Nord, AP-HM, Marseille, France. [8]Aix-Marseille Université, Marseille, France. [9]Department of Respiratory Diseases and Intensive Care, Reference Constitutive Center for Adult Rare Pulmonary Diseases, Dijon-Bourgogne University Hospital, University of Burgundy, Inserm UMR1231, Dijon, France. [10]Département de Pneumologie, Hôpital Avicenne, AP-HP, Bobigny, France. [11]Université Paris 13, Inserm UMR U1272, Bobigny, France. [12]Service de Pneumologie et Oncologie Thoracique, DMU APPROCHES, Hôpital Tenon, AP-HP, Paris, France. [13]Sorbonne Université, GRC04 Theranoscan, Paris, France. [14]Département d'Anatomie Pathologique, Hôpital Bichat, AP-HP, Paris, France. [15]Université Paris Cité, Inserm UMR-S 1152 PHERE, Paris, France. [16]Service de Pneumologie A, Hôpital Bichat, AP-HP, Paris, France. [17]Service de Pneumologie, Groupe de Transplantation Pulmonaire, Hôpitaux Universitaires de Strasbourg, Strasbourg, France. [18]Centre de Référence pour les Maladies Respiratoires Rares RespiRare, Centre Hospitalier Intercommunal de Créteil, Créteil, France. [19]Université de Paris Est Créteil, Inserm IMRB, Créteil, France. [20]Service de Pneumologie, Centre National Coordinateur de Référence des Pathologies Pulmonaires Rares, ERN-LUNG, Hôpital Louis Pradel, Hospices Civils de Lyon, Lyon, France. [21]Université Claude Bernard Lyon 1, Lyon, France. [22]Département de Génétique, Hôpital Bichat, AP-HP, Institut du Cancer AP-HP Nord, Paris, France. [23]Université Paris Cité, Paris, France. [24]Service de Radiologie, Hôpital Bichat, AP-HP, Paris, France. [25]General University Hospital "Attikon", Medical School, National and Kapodistrian University of Athens, Athens, Greece. [26]Département de Pneumologie Pédiatrique, Centre de Référence des Maladies Respiratoires Rares RespiRare, Paris, France. [27]Service de Pneumologie, Centre des Maladies Pulmonaires Rares, Hôpital de Besançon, Besançon, France. [28]Service de Pneumologie, Hôpital de Brabois, Vandoeuvre-les-Nancy, France. [29]Respiratory and Intensive Care Unit, University Hospital Amiens, Amiens, France. [30]EA 4294, AGIR, Jules Verne Picardy University, Amiens, France. [31]Service de Pneumologie, Centre de Référence Maladies Pulmonaires Rares, Hôpital Pontchaillou, CHU Rennes, Inserm UMR1085 IRSET, Université de Rennes 1, EHESP, Rennes, France. [32]Pediatrics Department, Pediatric Pulmonology, CHU Bordeaux, Bordeaux, France. [33]Pneumonology and Thoracic Oncology Department, Eure-Seine Hospital Center, Évreux, France. [34]Service de pneumologie, FHU Oncoage, Hôpital Pasteur – CHU Nice, Nice, France. [35]Université Nice Côte d'Azur, Nice, France. [36]Service de Pneumologie, Hôpital de Tours, Tours, France. [37]Université de Tours, Inserm U1100, Tours, France. [38]Service de Pneumologie et de Transplantation Pulmonaire, Hôpital Foch, Suresnes, France. [39]Service de Pneumologie, Hôpital Larrey, Toulouse, France. [40]Service de Pneumologie, Hôpital Erasme, Brussels, Belgium. [41]Service de Pneumologie et Immuno-allergie, Institut Coeur-Poumon, Lille, France. [42]Université de Poitiers, Poitiers, France. [43]A. Brudon and M. Legendre contributed equally to this work.

Corresponding author: Raphael Borie (raphael.borie@aphp.fr)

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Among 99 adult patient carriers of surfactant-related gene variants, 20 patients developed lung cancer. Regarding the risk of lung cancer in this population, systematic evaluation of familial pulmonary fibrosis relatives by CT scan should be considered. https://bit.ly/48xJKwq

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Abstract

Background Several rare surfactant-related gene (SRG) variants associated with interstitial lung disease are suspected to be associated with lung cancer, but data are missing. We aimed to study the epidemiology and phenotype of lung cancer in an international cohort of SRG variant carriers.

Methods We conducted a cross-sectional study of all adults with SRG variants in the OrphaLung network and compared lung cancer risk with telomere-related gene (TRG) variant carriers.

Results We identified 99 SRG adult variant carriers (*SFTPA1* (n=18), *SFTPA2* (n=31), *SFTPC* (n=24), *ABCA3* (n=14) and *NKX2-1* (n=12)), including 20 (20.2%) with lung cancer (*SFTPA1* (n=7), *SFTPA2* (n=8), *SFTPC* (n=3), *NKX2-1* (n=2) and *ABCA3* (n=0)). Among SRG variant carriers, the odds of lung cancer was associated with age (OR 1.04, 95% CI 1.01–1.08), smoking (OR 20.7, 95% CI 6.60–76.2) and *SFTPA1*/*SFTPA2* variants (OR 3.97, 95% CI 1.39–13.2). Adenocarcinoma was the only histological type reported, with programmed death ligand-1 expression ⩾1% in tumour cells in three samples. Cancer staging was localised (I/II) in eight (40%) individuals, locally advanced (III) in two (10%) and metastatic (IV) in 10 (50%). We found no somatic variant eligible for targeted therapy. Seven cancers were surgically removed, 10 received systemic therapy, and three received the best supportive care according to their stage and performance status. The median overall survival was 24 months, with stage I/II cancers showing better survival. We identified 233 TRG variant carriers. The comparative risk (subdistribution hazard ratio) for lung cancer in SRG patients *versus* TRG patients was 18.1 (95% CI 7.1–44.7).

Conclusions The high risk of lung cancer among SRG variant carriers suggests specific screening and diagnostic and therapeutic challenges. The benefit of regular computed tomography scan follow-up should be evaluated.