



What's hot that the other lot got

Simon Rolin

P2X3: A NEW TARGET FOR TREATING CHRONIC COUGH

A substantial proportion of patients with chronic cough (lasting longer than 8 weeks) have no obvious cause after extensive investigation and their symptoms persist despite commonly prescribed antitussive medication. P2X3 receptors are expressed by airway vagal afferent nerves and contribute to the hypersensitisation of sensory neurons. This randomised, double-blind, placebo-controlled UK based phase II study (*Lancet*, doi: 10.1016/S0140-6736(14)61255-1) aimed to investigate the efficacy of a first-in-class oral P2X3 antagonist, AF-219, to reduce cough frequency in patients with refractory chronic cough. After 2 weeks of treatment, cough frequency was reduced by 75% when patients were allocated to AF-219 compared with placebo ($p=0.0003$). Taste disturbance was reported by all patients taking AF-219, leading to six patients withdrawing from the study. Inhibition of P2X3 receptors, by antagonists such as AF-219, seems to have significant effect on cough neuronal hypersensitivity and is a promising new target for antitussives.

ANTIBIOTICS IN FETAL AND EARLY LIFE AND SUBSEQUENT ASTHMA

A rise in the rates of childhood asthma has coincided with the increasing use of antibiotics. Previous studies investigating a possible association have reported conflicting results, potentially due to bias. This nationwide prospective population based cohort study (*BMJ* 2014;349:g6979) followed a cohort of Swedish children from the start of their mother's pregnancy up to school age. Sibling controls were used to adjust for familial factors. Antibiotic exposure in fetal and early life was associated with an increased risk of asthma in

cohort analyses (HR 1.28, 95% CI 1.25 to 1.32), but not in sibling analyses (HR 0.99, 95% CI 0.92 to 1.07). In the sibling analyses, the excess risks after exposure to antibiotics for respiratory infections decreased, and disappeared for antibiotics for urinary tract and skin infections. This would indicate that the positive association was confounded by genetic and environmental factors shared by siblings.

POTENT ANTITUMOUR ACTIVITY OF CRIZOTINIB IN ROS1-REARRANGED NON-SMALL-CELL LUNG CANCER

Chromosomal rearrangement of the gene encoding *ROS1* proto-oncogene receptor tyrosine kinase (*ROS1*) occurs in approximately 1% of patients with non-small-cell lung cancers (NSCLCs). *ROS1* may represent another therapeutic target of the small-molecule tyrosine kinase inhibitor of anaplastic lymphoma kinase, crizotinib. This study (*NEJM* 2014;371:1963–71) enrolled 50 patients with advanced NSCLC who tested positive for *ROS1* rearrangement to treatment with crizotinib at a standard oral dose of 250 mg twice daily. Median progression-free survival was 19.2 months, with 25 patients still in follow-up for progression. Crizotinib showed marked antitumour activity in patients with advanced *ROS1*-rearranged NSCLC, and was associated with grade 2 or lower toxic effects. These results highlight the importance of screening for this genetic alteration in patients with advanced NSCLC.

CLINICAL MANAGEMENT OF ATYPICAL CARCINOID AND LARGE-CELL NEUROENDOCRINE CARCINOMA

In 2012, the European Society of Thoracic Surgeons created the Lung Neuroendocrine Tumours Working Group to develop a database of patients diagnosed with such rare forms of cancer. This study (*Eur J Cardiothorac Surg*, doi:10.1093/ejcts/ezu404) retrospectively collected data on 261 patients in seven

institutions in Europe evaluating variables affecting patient survival and disease-free survival. Five-year overall survival rates for atypical carcinoids (ACs) and large-cell neuroendocrine carcinomas (LCNCs) were 77% and 28% ($p<0.001$), respectively. For ACs, age ($p<0.001$), tumour size ($p=0.015$) and sublobar surgical resection ($p=0.005$) were independent negative prognostic factors; for LCNCs, only pTNM stage III tumours ($p=0.016$) negatively affected outcome in the multivariate analysis. LCNC affects more predominantly men and smokers, and occurs in patients older than those with ACs. Local recurrences and distant metastases developed in 93 patients and were statistically more frequent in LCNCs.

CHEST CT FINDINGS IN HIV-INFECTED INDIVIDUALS IN THE ERA OF ANTIRETROVIRAL THERAPY

Advancements in antiretroviral therapy (ART) have led to chronic comorbidities of HIV becoming more common as the life expectancy of those with HIV has increased. Studies in HIV-infected individuals before the introduction of ART reported a high prevalence of radiographic abnormalities such as nodules, ground-glass opacities and intrathoracic lymphadenopathy. Often, these abnormalities were associated with past or chronic infections. This study (*PLOS One*, doi:10.1371/journal.pone.0112237) assessed the prevalence and nature of radiographic abnormalities on chest CT examinations in a HIV-infected population, without acute respiratory illness, in the current ART era. The majority of participants (5.4%) had a radiographic abnormality with the most common being emphysema (26.4%), nodules (17.4%) and bronchiectasis (10.7%). Age, smoking history and pneumonia were significant predictors of having any radiographic abnormality, but HIV-specific factors (use of ART, CD4 cell count, HIV viral load) did not seem to predict risk.

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Correspondence to Dr Simon Rolin, Heart and Lung Unit, Acute and Respiratory Medicine, South Devon Healthcare NHS Foundation Trust, Torbay Hospital, Newton Road, Torquay, Devon TQ2 7AA, UK; drsrolin@aol.com

