JOURNAL CLUB SUMMARIES

What's hot that the other lot got

Janice Ward

RAPID DIAGNOSIS OF SECOND-LINE DRUG RESISTANCE IN TB

Rapid diagnosis of the gene mutation associated with rifampicin resistance using GeneXpert MTB/RIF has improved the speed of diagnosis of multidrug-resistant TB; however, there are no established rapid techniques to assess for resistance to fluoroquinolones and injectable drugs. Xie *et al* (*N Engl J Med* 2017;377:1043–54)have conducted a multicentre, prospective, blinded study in Korea and China to determine the sensitivity and specificity of a GeneXpert compatible assay which detects genes associated with resistance to isoniazid, moxifloxacin, ofloxacin, amikacin and kanamycin. A total of 405 patients were enrolled from June 2014 to June 2015 with 304 suitable samples included in the final analysis. The sensitivity of the assay for detection of *Mycobacterium tuberculosis* was 98%, which equalled GeneXpert MTB/RIF. The WHO recommended performance for molecular tests of drug resistance is a sensitivity of 95% and specificity of 98%. Sensitivity for resistance gene detection compared with DNA sequencing ranged from 92.7% for kanamycin to 98.1% for isoniazid; specificity was 99.6% for kanamycin and 100% for the other antibiotics. However, assay performance against phenotypic resistance characterisation was less accurate with sensitivities ranging from 71% for amikacin to 88% for ofloxacin and specificities from 84% for moxifloxacin to 100% for amikacin. The performance of the assay is not sufficient to be used in isolation to guide clinical decisions.

STATIN EFFECT ON MORTALITY IN CANADIAN COPD POPULATION

Data on the effect of statins in patients with COPD are equivocal. Raymakers *et al* (*Chest* 2017;152:486-493) add to this with a retrospective population study from the Canadian pharmaceutical database. Patients with COPD were identified by at least three prescriptions of anticholinergic or short-acting beta agonist inhalers. Statin exposure was registered during the following year. Mortality data were collected in the subsequent year. Up to 39 678 patients were included in the analysis, 19.6% of which received at least one statin prescription. Adjustment was performed for age, sex, health authority and regional income quintile; but not smoking status, lung function or presence of established cardiovascular disease. The multivariate analysis demonstrated a significant reduction in all-cause mortality with a HR 0.79 (95% CI 0.68 to 0.92; p=0.0016). For lung-related mortality the adjusted HR was 0.55 (95% CI 0.32 to 0.93; p=0.0254). The study provides data to suggest a potential benefit of statins in patients with COPD but the significant limitations of the study prevent any definitive conclusion that could influence clinical practice.

PREDICTING OCCULT NODAL DISEASE IN T1A LUNG CANCER

The expanded use of stereotactic body radiation therapy and development of minimally invasive and lung-preserving surgical techniques has widened the treatment options for T1a N0 M0 lung cancers. Ghaly *et al* (*Ann Thorac Surg* 2017;104:1153–60) aimed to aid decision-making by looking for clinical predictors of nodal metastasis in peripheral stage 1 lung tumours. Data collected retrospectively from 449 patients who underwent positron emission tomography (PET/CT) imaging and lobectomy between 2000 and 2015 at a single centre in New York. All patients had N1 and N2 node dissection; 80% of patients had video-assisted thoracoscopic surgery or robotic-assisted thoracoscopic surgery. Postsurgical staging found pN1 disease in 4.5% of patients and pN2 metastasis in 5%. The only measured characteristic that was significantly different between pN0 and pN+ groups was SUVmax on PET/CT imaging (mean SUVmax pN0=2.5 vs pN+=3.9; p=0.003). A cut-off for SUVmax of 3.3 was found to give optimal sensitivity (58%) and specificity (64%) but which provided a poor positive predictor value (15%). Despite multivariate analysis indicating that an SUVmax of above 3.3 was the only independent factor associated with pN+ (p=0.016), it had poor clinical utility with pN+ demonstrated in 24/169 patients with an SUVmax>3.3 and 19/280 with an SUVmax≤3.3. Median follow-up was 48.5 months (range, 22–83 months) and 5-year survival was 85% in pN0 patients vs 81% in nodal metastasis patients (p=0.746). The data does not support use of an SUV limit in isolation but may support decision-making in some patients.

SEARCHING FOR A SECOND-LINE CHEMOTHERAPY FOR MESOTHELIOMA

Mesothelioma continues to have a poor prognosis with no second-line regimens of proven efficacy. The DETERMINE trial (Maoi *et al*. *Lancet Oncol* 2017; 18: 1261–73) assessed the efficacy of tremelimumab (a cytotoxic T-lymphocyte-associated antigen 4) as a second-line or third-line treatment option in patients with pleural or peritoneal mesothelioma that failed standard platinum and pemetrexed regimens with a performance status of 0 or 1. The double-blind, placebo-controlled, phase 2b trial was conducted at 105 centres in 19 countries. Recruitment was between May 2013 and December 2014 with data censored at January 2016. Treatment was with tremelimumab by intravenous infusion at 10 mg/kg (or matching placebo), every 4 weeks for seven doses as induction treatment, followed by maintenance dosing every 12 weeks. 382 patients were randomised to tremelimumab and 189 to placebo; 95% of patients had pleural disease and 93% had stage III or IV disease. There was an expected high mortality at 80% in the tremelimumab group and 82% in the placebo group. Median overall survival was 7.7 months (95% CI 6.8 to 8.9) in the tremelimumab group and 7.3 months (95% CI 5.9 to 8.7) in the placebo group (HR 0.92, 95% CI 0.76 to 1.12, p=0.41). Adverse events of grade 3 or worse occurred in 246 (65%) patients in the tremelimumab group and 91 (48%) patients in the placebo group. Principal toxicity related to gastrointestinal effects in line with published data. The study demonstrates no significant survival benefit with tremelimumab over placebo.

Competing interests None declared.

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