**5. Microbiology**

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**112 Can vancomycin injection be nebulised successfully?**

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**Aim:** To evaluate whether off label nebulised vancomycin (Vancocin®) injection can be delivered via Par i LC Plus™ and e-flow rapid™ nebulisers.

**Objectives:** To measure particle size, proportion of drug remaining in the nebuliser, degradation of product and percentage of drug delivered.

**Method:** Vancomycin 250 mg (50 mg/ml-500 mg vial dissolved with 9.6 ml water for injection) were nebulised via both nebuliser systems. Particle size distributions were measured using a HELOS KF particle sizer (Sympatec, Germany) at 4 representative flow rates for children and adults. The proportion of drug remaining and percentage delivered were calculated by measuring residual volume and concentration. Sample degradation was evaluated by HPLC.

**Results:** Par i LC PlusTM — median particle sizes ranged from 1.75–2.18 µm across the 4 flow rates; 61.6–73.9% of particles were between 1–5 µm in size. Of the nebulised dose, 81.2% was delivered with 18.8% remaining in the nebuliser. The residual concentration was 62.1 mg/ml compared to 50 mg/ml at initiation. There was no degradation after nebulisation.

**Conclusion:** It is possible to nebulise vancomycin injection via both the Par i LC Plus™ and e-flow rapid™ nebulisers. The characteristics of the inhalation vary depending on the nebuliser used. It is not known if this is clinically significant.

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**114 Aspergillus fumigatus susceptibility to itraconazole in adult patients with cystic fibrosis**

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**Background:** Aspergillus fumigatus frequently colonizes the respiratory tract of patients with CF and was isolated from specimens of 56% of patients at our CF centre. Itraconazole (ITRA) is frequently prescribed in CF, especially in case of allergic bronchopulmonary aspergillosis.

**Objective:** We hypothesised that A. fumigatus from CF patients who had been treated with ITRA might have minimal inhibitory concentration (MIC) higher than those from CF patients who had received no antifungal treatment.

**Methods:** From June to December 2010, patients with CF at our adult CF centre had a systematic examination of sputum samples for the detection of fungi. In all patients with A. fumigatus, susceptibility to ITRA was prospectively tested.

**Results:** We have tested 79 isolates of A. fumigatus from 79 patients (one sample per patient). The proportion of A. fumigatus isolates with MIC for ITRA >2 µg/ml was 36% (5/14) in the treated group versus 6% (4/65) in the untreated group (p = 0.05). Interestingly the highest MICs (>32 µg/ml) were all observed in treated patients (4/14) (29%) versus 0/65 untreated patients.

**Conclusion:** Our results demonstrate that the development of resistance of A. fumigatus to ITRA in adult patients with CF is clearly favored by prior antifungal treatment. To avoid the emergence of resistant isolates of A. fumigatus to ITRA in CF patients, it remains crucial to assess the real benefit of prolonged treatment with ITRA.

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**113 Safety, tolerability and pharmacokinetics of novel liposomal ciprofloxacin formulations for inhalation in healthy volunteers (HV) and non-cystic fibrosis bronchiectasis (BE) patients**

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Ciprofloxacin (CP) for inhalation (CFI – [ARD-3100]) is an aqueous sustained release liposomal formulation for respiratory infections in cystic fibrosis (CF) and non-CF BE patients. Dual release CP for inhalation (DRCFI – [ARD-3150]) is a new inhaled formulation that matches the duration of release of CP from CFI, supporting 1 × day administration, while providing higher initial concentration of CP in the lung to potentially provide enhanced concentration-dependent antimicrobial effect. Inhaled CP in HV was safe and well tolerated resulting in plasma PK with an absorption-limited half life of 10.5 hr, compatible with 1 × day administration.

A reduction in P. aeruginosa sputum density (p < 0.01) and an increase in FEV1 in CF patients were found. The current study evaluated the ability to modulate the PK of CFI to provide a higher Cmax while maintaining the duration of release.

A single dose, cross-over trial comparing the safety, tolerability and plasma PK of two inhaled formulations (CFI vs. DRCFI) was conducted in 8 adult HV and DRCFI also in 6 BE subjects. Both formulations were safe and well tolerated in all subjects.

In HV, the mean CP Cmax for CFI (169 ng/mL) was 2.5 times greater than for DRCFI (67 ng/mL) and the Tmax was faster for DRCFI (20 min vs. 1.8 hr). In BE and HV, the mean half-life of CFI was 9.7 and 9.4 hr, respectively, vs. 10.8 hr for CP in HV. DRCFI matches the duration of release of CP from CFI, supporting 1 × day dosing, while providing a spike of CP in the lung to potentially enhance antimicrobial effects. High concentrations of CP was found in the sputum of BE subjects. Ongoing clinical trials evaluating CFI (ARD-3100) and DRCFI (ARD-3150) in CF are warranted.

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**115 Comparison between voriconazole and posaconazole in treatment of Aspergillus infections in cystic fibrosis (CF) patients**

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**Background:** Voriconazole is recommended drug for treatment of Aspergillus infections in patients with CF and primary ciliary dyskinesia (PCD). It was difficult to motivate patients to take voriconazole due to side effects.

**Methods:** Data were initially collected from patients’ records and the last two years prospectively. Antifungal drugs were given to 34 patients (3 PCD) after having at least two positive sputum cultures with Aspergillus sp.

**Results:** Comparisons of voriconazole and posaconazole were made in 32 patients (21 CF and 11 non-CF patients). Main side effects for voriconazole is phototoxicity, sometimes leading to pemphigus-like skin lesions with blisters, also after short periods of sun exposure. Others are vomiting, vertigo, tachycardia, vision disturbances, photosensitivity, hallucinations, fever, shivering and nightmares. Side effects for posaconazole were gastrointestinal symptoms. Tiredness and nausea were side effects in both groups. Three patients who relapsed on voriconazole also relapsed on posaconazole.

**Conclusions:** Treatment length is shorter, side effects and number of relapses are fewer with posaconazole. Time to relapse is shorter with posaconazole. The total cost per treatment is lower with posaconazole.