Results: 43.9% of patients achieved a rapid virological response (RVR) and 69.1% of patients had a complete early virological response (cEVR). The serum alanine transaminase (ALT) normalization rates were 70.9% and 86.2% at week 4 and 12. Analyzing IL-28B variation (rs12979860), more proportions of patients with the CC genotype (46.7% or 75.3%) achieved a RVR or a cEVR respectively, compared to patients with the CT/TT genotypes (23.8% or 35.3%). However, in a multivariable logistic regression model, the IL-28B genotype was not shown statistically to be a predictive value for RVR or cEVR. Baseline predictive factors for RVR included the serum HCV RNA <4×10^5 IU/mL (OR: 0.16) and gender (in females, OR: 0.39). The HCV genotype was only a predictive factor for cEVR (2α vs 1b, OR: 8.80). The treatments for 28 patients were discontinued due to adverse events such as anaemia and fatigue.

Conclusion: The recombinant IFN-α2b therapy demonstrated a potent anti-virus effect and a significant biochemical improvement. It has good tolerance and safety profiles. The serum HCV RNA, gender and the HCV genotype were identified as valuable predictors for patients who responded to IFN/RBV treatments in the present study.

OL-008 The Diagnostic and prognostic significance of intrahepatic transforming growth factor-β1, angiotensin converting enzyme-2, alpha smooth muscle actin and endoglin in liver fibrosis associated chronic hepatic infection

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Background: Hepatic fibrosis develops as a response to HCV-related chronic liver injury. Proliferative response of hepatocytes is crucial in HCV infection as hepatocytes are the primary site for HCV replication and receive different cellular stress from surrounding cells.

Objectives: To study intrahepatic expression of transforming growth factor beta-1 (TGF-β1), Angiotensin converting enzyme-2 (ACE-2), alpha smooth muscle actin (α-SMA) and endoglin, a TGF-β receptor in liver biopsies from patients with chronic HCV infection and correlate results with stage of fibrosis and necro inflammatory activity.

Methods: Forty two patients with chronic HCV infection, 20 females, 22 males, median age 34.5 years whose liver biopsy showed different stages of fibrosis were included in this study. Tissue expression of TGF-β1, ACE-2, α-SMA were investigated by immunohistochemistry on paraffin embedded liver tissues and tissue expression of endoglin by immunoblotting. Immuno-reactive semiquantitative score was applied to compare immunohistochemical results with histological findings according to Ishak scoring system for histological activity index (HAI) and stage of fibrosis.

Results: Statistical analysis of data revealed a significant correlation between tissue TGF-β1, ACE-2, α-SMA andendoglin with stage of fibrosis; p<0.001, 0.05, 0.01, 0.001 respectively. Moreover, TGF-β1 correlated significantly with HAI, p<0.05.

Conclusion: Data from this study provide evidence for the implication of ACE-2 and TGF-β receptors in the pathogenesis of hepatic fibrosis as well as a possible role in prognostic and therapeutic management of cirrhosis.

OL-009 Diverse clonal, multidrug-resistant community-acquired, methicillin-resistant Staphylococcus aureus isolated from Chinese children

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Background: Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA), including those encoding Panton-Valentine leucocidin (PVL), are often described more susceptible to most antimicrobial agents except for non-β-lactam antibiotics, than hospital-acquired MRSA. Recently, separate studies have reported the emergence of multidrug-resistant CA-MRSA in certain clones. In this study, the multidrug-resistant CA-MRSA isolates were detected and their distribution was determined in different clones in Mainland China.

OL-007 Synthesis and antimicrobial activity of the novel siderophore sulfactam BAL30072

M.G.P. Page1, E. Desarbre1, K. Gebhardt1, B. Hofer1, C. Mueller2, F. Richalet3, A. Schmitt-Hoffmann1, W.B. Shi4, T. Xie2, H.Y. Xu4, A. Man1* 1Basilea Pharmaceutica International Ltd, 4005 Basel, Switzerland, 2Basilea Pharmaceutica China Ltd, Haimen, PR China

Background: The emergence of serious infections caused by multidrug-resistant Gram-negative bacteria (MDR-GNB) presents a significant therapeutic challenge to clinicians. MDR-GNB can express altered penicillin-binding proteins (PBPs) or produce b-lactamas, which hydrolyse the antibiotic. They can also express efflux systems that actively pump the drug into the extracellular environment or reduce the permeability of the outer membrane by mutation of porins. The growing resistance to carbapenems amongst these strains is causing particular concern and new antibiotics able to overcome these resistance mechanisms are urgently needed.

Methods: Antimicrobial susceptibility testing was performed by broth microdilution according to CLSI recommendations but using Iso-Senstest broth supplemented with 16 mg/L 2,2′-bipyridyl to induce iron uptake. The efficacies of BAL30072 and comparators were tested against MDR-GNB in a mouse model of septicaemia.

Results: The siderophore sulfactam BAL30072 emerged as the most potent compound amongst a series of novel monocyclic beta-lactam derivatives. BAL30072 was active against a wide-range of MDR-GNB including difficult to treat organisms such as P. aeruginosa and Acinetobacter species. It was shown to exploit essential iron uptake systems such as P. aeruginosa and Acinetobacter species to bypass the mutated porins, not to be a substrate for efflux pumps and to be stable towards many beta-lactamases, especially carbapenemases. BAL30072 showed good efficacy against carbapenem-resistant strains in the septicaemia model.

Conclusions: BAL30072 is a novel siderophore sulfactam with potent activity against MDR-GNB. The in-vitro activity translates into a protective effect in an animal model of infection. The compound, which is currently in phase I clinical testing, addresses the growing problems caused by multi-resistant Gram-negative bacteria.

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