study BI 705564 was administered to 50 male HV at doses from 10 to 80 mg once daily for 14 days. Blood samples were analyzed for BI 705564 plasma concentrations, BTK target occupancy (TO) and CD69 expression in B cells stimulated *ex-vivo* with anti-IgD.

Results All doses of BI 705564 were well-tolerated in both studies. There were no serious adverse events (AEs) and reported AEs were mainly of mild intensity and not dose-limiting. There was no difference in the total number of subjects with AEs (combined data from both trials) between BI 705564 [28/75 (37.3%)] and placebo [8/18 (44.4%)] and no dose-relationship of AEs. The most frequently reported AE was headache (BI 705564: 8.0% vs placebo: 5.6%, combined data). There was no difference in the occurrence of infections (BI 705564: 6.5% vs placebo: 11.1%) or gastrointestinal disorders (BI 705564: 13.3% vs. placebo 11.1%) in both studies (combined data). There were no relevant drug-related changes in vital signs, ECGs and standard safety laboratory tests. Analysis of BI 705564 plasma exposures showed a terminal half-life between 5.7 and 14.2 hour with no relevant accumulation after multiple dosing. Doses of 20 mg and above resulted in an average TO 85% which is expected to result in clinical efficacy based on preclinical studies. After a single dose administration, TO was maintained for at least 48 hour consistent with the mechanism of a covalent irreversible inhibitor. Functional effects on BTK signalling were demonstrated by dose-dependent inhibition up to 100% of CD69 expression on anti-IgD stimulated B cells.

Conclusions BI 705564 was well-tolerated in healthy subjects after single and multiple doses. The favorable clinical safety profile and the high potential based on pre-clinical studies and effects on CD69 support further investigation of BI 705564 in patients with autoimmune diseases like SLE.

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COMPOSITE GOALS PLUS INFLAMMATION: FURTHER RISK ASSESSMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED PULMONARY ARTERIAL HYPERTENSION IN CSTAR-PAH COHORT

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Background Chinese SLE treatment and Research Group (CSTAR) started a multi-center prospective cohort study recruiting SLE patients with pulmonary arterial hypertension (PAH) since 2006. This study aimed to investigate the validity of a multidimensional risk assessment and the prognostic value of it in SLE-associated PAH.

Methods All SLE patients were fulfilled the 1997 revised ACR criteria. PAH was diagnosed based on ESC/ERS guidelines by right heart catheterization. The outcome was all-cause mortality. Two different methods of risk categorization were applied according to baseline data, including low-risk criteria number of none to four and mean score of 1 (low-

risk), 2 (intermediate-risk) or 3 (high-risk). According to first follow-up, patients were further divided into increased risk, remained risk and decreased risk group. A prediction model was used to distinguish SLE-PAH from vasculitic and vasculopathic subtype, based on the time interval between the diagnosis of SLE and PAH and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). KaplanMeier survival curves and Cox proportional hazards analysis were conducted.

Results 282 patients were enrolled. The 5 year survival of patients with none, one, two, three and four low risk criteria were 42.7%, 64.8%, 86.1%, 90.2% and 91.7%, respectively (HR=0.59, 95% CI 0.44–0.78, $p<0.001$). The 5 year survival of patients in low-risk, intermediate-risk and high-risk group were 92.3%, 60.4% and 50.0%, respectively (Log-rank, $p=0.001$). Notably, in low-risk group, patients with vasculitic subtype had better survival than those with vasculopathic subtype (Log-rank, $p=0.044$). The 5 year survival of patients with remained, decreased and increased risk were 65.4%, 88.1% and 23.8%, respectively (log-rank, $p<0.001$).

Conclusions Our study, for the first time, validated the prognostic value of risk stratification strategy at baseline and follow-up visit in patients with SLE-associated PAH. Patients are recommended to have a comprehensive evaluation on PAH and SLE at baseline and every follow-up visit. The SLE disease activity and systemic manifestations predict the phenotype of SLE-associated PAH, which also effect the long-term survival and need to be involved into risk assessment of SLE-associated PAH. Improving to low-risk group can be a future treatment target for SLE-associated PAH patients in clinical practice.

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EVALUATION OF ADVERSE EVENTS AND RELAPSE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS DURING TREATMENT WITH HYDROXYCHLOROQUINE

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Background The antimalarial drug hydroxychloroquine (HCQ) has been widely used in the world to control the disease activity of systemic lupus erythematosus(SLE). In Japan, it has not been approved until September 2015 due to the problem of retinopathy induced by chloroquine. For these reasons, there is insufficient evidence for its effects and adverse events.