

mum tolerated dose was approached at 80 to 100 mg due to symptoms of chest discomfort and dyspnea. These results reveal a good safety margin to the highest dose selected for Phase 3 (20 mg).

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### OC016—OFF-LABEL USE AND ADVERSE EVENTS OF BIOLOGIC AGENTS IN PAEDIATRIC PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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**Introduction:** Knowledge of adverse events (AEs) from biologic drugs used in pediatric population is limited. A recent Danish study analyzing AEs submitted to the Danish National Database indicated that off-label use of medicine in general to pediatric patients is associated with increased risk of AEs. The primary objective of the present study was to analyze the safety of off- and on-label use of biologic agents in a clinical sample of pediatric patients over a 3-year period and to identify potential risk factors associated with AEs.

**Patients (or Materials) and Methods:** A retrospective, longitudinal, study conducted in 1 pediatric department at Copenhagen University Hospital. Patients under the age of 18 years who received a minimum 1 treatment with a biologic agent from January 1, 2009, through December 31, 2012, were included if they had been diagnosed with juvenile idiopathic arthritis (JIA) from 2009 to 2012. AEs and off-label uses were identified by medical records review and classified according to the European Medical Agency guidelines. Multivariate logistic regression was used to investigate risk factors associated with an AE, and survival analysis was used to analyze time to an AE.

**Results:** 81 patients were included (65.4% females). Age ranged from 1 to 18 years (mean, 11.5 years). The 81 patients had a total of 133 courses of treatment with etanercept (49.6%), adalimumab (23.3%), infliximab (10.5%), golimumab (8.2%), tocilizumab (5.2%), and abatacept (3.0%). All patients were diagnosed with JIA (26 oligoarticular, 24 polyarticular, 2 systemic, 16 enthesitis-related JIA, and 16 JIA). Totally, 252 AEs were observed in 76% of the patients, 8 (3.2%) of which were severe. 23.8% of the AEs had a treatment consequence (reduction in dose, treatment pause, discontinuation of treatment) in 40.7% of the patients. After 200 days, 70% of all patients had experienced an AE. Gender, off-label use, type of drug, type of JIA, comedication, and comorbidity were not associated with an increased risk of AEs. Older age and severity of illness at time of treatment were the only significant predictors of AEs ( $P = 0.0134$ ,  $P < 0.0001$ ). Off-label use was more likely with increasing number of treatment courses. Off-label use most often comprised of not recommended dose or indication. Time to an AE occurred did not differ with respect to type of drug or numbers of treatment courses.

**Conclusion:** AEs are frequent in this population of pediatric patients with juvenile idiopathic arthritis treated with biologic agents. Off-label use was frequent but not associated with an increased risk of AEs.

**Disclosure of Interest:** None declared.

### OC017—CLINICAL AND NONINTERVENTIONAL TRIALS ASSESSMENT IN CROATIA

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**Introduction:** Clinical trials (CT) and noninterventional trials (NIT) in Croatia are conducted in accordance with local laws (Drug law, and specific acts), and CT legislation is in accordance with European legislation. The Ministry of Health gives a final regulatory approval for CT. Since 2004, all clinical trials in Croatia have had to be reviewed by the Central Ethics Committee (CEC) and a favorable opinion must be issued before a clinical trial commences. Since December 2007, the CEC has also been responsible for issuing opinions on noninterventional trials. During the trial evaluation procedure, CEC assesses scientific and ethical considerations of the trial. The aim of this analysis is to present the procedure of central evaluation and statistics of the CEC.

**Patients (or Materials) and Methods:** The database of the CEC is analyzed, and the trials are presented according to indication (topic), phase, and opinion issued after the first evaluation.

**Results:** According to a defined procedure and discussion, the CEC positive opinion has been given to 702 CT (since May 2004–2012). During the last 5 years, 80 CT per year on average have had a positive opinion from the CEC. The greatest number of CT have been in the field of oncology (147), mental and behavioural disorders (95), and endocrine, nutritional, and metabolic diseases (88), and mostly Phase III trials. During the period of the last 5 years, CEC assessed 67 NIT. The decisions after the first evaluation were conditionally positive or postponed opinion.

**Conclusion:** The model of centralized CT assessment through the Central Ethics Committee, as an independent body, has been confirmed during the investigated period as appropriate for Croatia. Furthermore, CEC assessment of NIT has also been confirmed as useful because this procedure, as a gatekeeper, prevents conducting the trials only for marketing purposes and allows in Croatia only NIT of certain quality and scientific merit.

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### OC018—THE NUMBER OF INCLUDED OLDER PEOPLE IN RECENT PRE-AUTHORISATION TRIALS

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**Introduction:** Older people have often been excluded from pre-authorization trials. Therefore, the regulatory ICH E7 guideline requires a minimal number of older subjects for trials regarding diseases primarily related to aging (>50% of database aged 65+) and for diseases not typical for, but present in old age (>100 subjects 65+). The study objective was to analyze the number of older people in trials of recently authorized drugs indicated for diseases that regularly present in old age.

**Patients (or Materials) and Methods:** Eligible drugs for this descriptive study were registered by the European Medicines Agency between 2008 and 2011. Chosen indications: prevention of venous thromboembolism after replacement arthroplasty (dabigatran, rivaroxaban), osteoporosis (lasofoxifene, bazedoxifene, denosumab), atrial fibrillation (dronedrone, vernakalant), diabetes mellitus type