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ABSTRACTS

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risk between individual monoclonal antibodies and the potential underlying mechanism.

Objective/Aim: To quantify and characterize spontaneously reported adverse drug reactions (ADRs) of monoclonal antibodies related to depression and suicidal ideation and behavior. Furthermore, to explore the association between the mechanism of action of the monoclonal antibodies and these ADRs.

Methods: ADRs reported until December 2017 in VigiBase, the WHO global database of Individual Case Safety Reports, were included. Reports related to depression and suicidal ideation and behaviour (MedDRA standardized search) for monoclonal antibodies were extracted. Monoclonal antibodies that had been authorised by any global regulatory authority (e.g. FDA, EMA) for at least 3 years were included. Associations were tested by estimating reporting odds ratios (RORs) for the monoclonal antibodies separately (using bevacizumab as a reference) as well as grouped on their influence on the immune system (not influencing the immune system (reference), suppressing the immune system, and stimulating the immune system). Monoclonal antibodies suppressing the immune system were further stratified according to their intended indication (autoimmune diseases, cancer).

Results: A total of 44 monoclonal antibodies were included for which a total of 2924,319 adverse drug reactions were reported. For these 44 monoclonal antibodies, 9455 (0.3%) reports related to depression and 1770 (0.1%) reports related to suicidal ideation and behaviour were analysed. For both depression and suicidal ideation and behaviour, natalizumab and belimumab showed the highest ROR relative to bevacizumab, i.e. for depression 5.7 (95% CI 5.0–6.4) and 5.1 (95% CI 4.2–6.2), for suicidal ideation and behaviour 12.0 (95% CI 7.9–18.3) and 20.2 (95% CI 12.4–33.0) respectively. Monoclonal antibodies suppressing the immune system showed higher ROR relative to monoclonal antibodies not influencing the immune system, i.e. for depression 1.9 (95% CI 1.8–2.0) and for suicidal ideation and behaviour 3.6 (95% CI 3.0–4.4). This difference was only seen in the monoclonal antibodies suppressing the immune system that are used for treating autoimmune diseases.

Conclusion: Adverse neuropsychiatric effects are seen in patients exposed to monoclonal antibodies. Two antibodies peaked relative to bevacizumab (i.e. natalizumab, belimumab) regarding reporting of depression and suicidal ideation and behaviour. Furthermore, monoclonal antibodies used for treating autoimmune diseases showed higher RORs compared to monoclonal antibodies not influencing the immune system. For the interpretation of these data the indications for use and other population characteristics need further consideration.

Disclosure of Interest: None declared.

ISoP18-1272 Comparison of Reported Adverse Events of Premature and Term Born Infants Following Childhood Vaccinations in the Netherlands

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Background/Introduction: Most reported common adverse events (AEs) following infant vaccination are well-known. In The Netherlands infants receive two different vaccines; a pneumococcal vaccine and a diphtheria, tetanus, pertussis (acellular, component) hepatitis B, poliomyelitis and Haemophilus influenzae type b vaccine (DTaP/IPV/Hib/HepB) at the gestational age of 2, 3 (only DTaP/IPV/Hib/HepB), 4 and 11 months. Some of the reports on AEs received concerned premature babies. This raised the question whether or not there was a difference between reported AEs of preterm and term born babies.

Objective/Aim: To determine differences between the pattern of reported AEs of spontaneous reports following infant vaccinations between premature and term born babies.

Methods: Retrospective analysis of reported AEs to pharmacovigilance centre Lareb of reports following infant vaccinations between a premature and term born babies. Reports concerning AEs after infant vaccinations between December 2011 and May 2017 were selected. The AEs were listed for premature and term born babies. Odds ratios were calculated to compare the AE pattern for both groups.

Results: The most reported well known AEs in both methods were comparable. Table 1 shows the frequencies of occurrence of these reported AEs in spontaneous reports of term and preterm babies. Statistically significant differences were found for apnoea (OR = 90; 95% CI 36–224), apnoeic attack (OR 109; 95% CI 51–232), decreased oxygen saturation (OR = 86; 95% CI 30–249) and syncope (OR = 2.8; 95% CI 1.5–5.1), which were more frequently reported for premature babies.

Table 1: Percentage of reported AEs in premature and term born babies

Reported AE	% of reports premature infant (n=92)	% of reports term infant (n=5633)
Crying	54,3	40,4
Pyrexia	52,2	66,1
Injection site inflammation	20,7	22,2
Apnoeic attack	19,6	0,2
Vomiting	14,1	10,3
Syncope	12,0	4,5
Apnoea	12,0	0,1
Hypotonic-hyporesponsive episode	8,7	6,0
Oxygen saturation decreased	8,7	0,1

Conclusion: This study shows that the pattern of reported AEs is comparable between both groups for well-known common AEs. Apnoeic attacks and comparable symptoms like bradycardia and a decreased oxygen saturation are events also known to occur in premature born babies not being vaccinated. These events are described as rare AE in the SmPC, especially in premature children.

Disclosure of Interest: None declared.

ISoP18-1274 Gynecomastia and Galactorrhea: Unlabeled Adverse Drug Reactions of Retinoids used in Dermatology

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Background/Introduction: Gynecomastia and galactorrhea are rare adverse drug reactions (ADRs) mainly associated with exogenous estrogens, antiandrogens, 5 alpha-reductase inhibitors, spironolactone and cimetidine. Several case reports of gynecomastia and galactorrhea have

been reported in the literature with retinoids [1, 2]. However, these ADRs are not listed in the Summary of Product Characteristics of retinoids.
Objective/Aim: The aim of this study was to describe cases of gynecomastia and galactorrhea concomitant with the use of retinoids in the French Pharmacovigilance database (FPVD).
Methods: All cases corresponding to the MedDRA term "breast disorder" (High Level Group Term) and associated with oral or topical retinoid use for a dermatological purpose were extracted from the FPVD between 1985 and May 2018. Cases were excluded if another drug- or non-drug etiology was finally retained based on the French method for causality assessment.
Results: Thirty-one cases were included. Among them, there were 22 cases associated with oral isotretinoin use (14 cases of gynecomastia, 6 of galactorrhea and 2 of both gynecomastia and galactorrhea), 8 cases of isolated gynecomastia with oral acitretin use and one case of gynecomastia with topical tretinoin use. The indications were mostly acne and psoriasis. Patients' median age was 22 years [Interquartile range (IQR) 19–35]. Gynecomastia and/or galactorrhea were unilateral for almost half of the cases with known clinical description (7/15). The median time of onset was 90 days (IQR 39–347, n = 26). The outcome was known for 27 patients and a total recovery after withdrawal of retinoid was observed for 63% of them. There were two cases of positive rechallenge. Only two cases were considered as serious: one hospitalization and one case that needed surgery.
Conclusion: Gynecomastia and/or galactorrhea could be associated with the retinoid treatment for cutaneous disease. Physicians should be aware of these potential ADRs and inform their patients. For most of the cases, gynecomastia and galactorrhea resolved after withdrawal of the treatment.
References:

1. Larsen GK. Iatrogenic breast discharge with isotretinoin. Arch Dermatol 1985;121:450-1
2. Carmichael AJ, Paul CJ. Reversible gynaecomastia associated with etritinate. Br J Dermatol. 1989;120:317

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ISoP18-1275 Reactogenicity and Safety of the Measles–Mumps–Rubella Vaccine: A Prospective Observational Real World Study

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Background/Introduction: Measles outbreaks are spreading in many European countries due to parents' refusal to vaccinate their children. The highest number of measles cases in Europe during 2017 was reported in Romania [1].
Objective/Aim: To assess the reactogenicity and safety of MMR vaccine as reported by parents of vaccinated children, in real-world general practice.
Methods: Children vaccinated with MMR according to the national immunization schedule (1st dose at 1 year old and 2nd dose at 5 years old) in 2 general practitioners' (GPs) offices from Romania during March 2016–May 2017 were followed-up for 6 months. Demographic characteristics, medical history, history of adverse events (AEs) after previous vaccination and prior use of medication were recorded. We collected the solicited symptoms (Table) within 4 days after vaccination via an online questionnaire, and any AEs urging medical visit within 6 months after vaccination via follow-up phone calls.
Results: A total of 216 children, 123 aged 9–17 months (Group 1) and 93 aged 4–7 years (Group 2) received 219 MMR vaccine doses alone or together with other pediatric vaccines. 3 children in Group 1 received 2 MMR vaccine doses (at 9 and 12 months) due to change in the national vaccination schedule. The incidence of solicited symptoms is presented in the Table 211 AEs urging medical visit were recorded during the 6 months after vaccination in Group 1 and 49 AEs in Group 2. The most frequent unsolicited AEs urging medical visit were upper respiratory tract infections, tonsillitis, bronchiolitis, diarrhea and otitis media. No death was reported.

Table 1 : Incidence of solicited symptoms during 4 days after vaccination (% of doses)

Solicited symptom	**Group 1 (N=126),** % MMR alone (% MMR co-administered)	**Group 2 (N=93),** % MMR alone (% MMR co-administered)
Pain	11.9	16.12
Redness	1.59	1.07
Swelling	1.59	0
Fever	6.52 (26.47)	3.89 (6.25)
Fussiness	22.82 (41.17)	3.89 (6.25)
Drowsiness	17.39 (47.05)	5.19 (12.5)
Loss of appetite	10.86 (17.64)	2.60 (6.25)
Diarrhea	3.26 (17.64)	3.89 (0)
Vomiting	1.08 (2.94)	1.30 (0)

N, total number of MMR vaccine doses. For the general symptoms, N=92 doses of MMR alone and N=34 doses of MMR co-administered with other pediatric vaccines in Group 1 and to N=77 doses of MMR alone and N=16 doses of MMR co-administered in Group 2.

Conclusion: Incidences of both solicited and unsolicited AEs were generally higher in 9–17 months age group, as expected. Likewise, incidence of solicited general symptoms was higher when MMR vaccine was co-administered with other vaccines.
References:

1. European Centre for Disease Prevention and Control. Measles in the EU/EEA: current outbreaks, latest data and trends—January 2018. Available from https://ecdc.europa.eu/en/news-events/measles-eueea-current-outbreaks-latest-data-and-trends-January-2018 [AccessedJuly 2018]

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ISoP18-1276 What is Risky about Risk Communications: a Case Study on Dengue Vaccine

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Background/Introduction: Dengue is a tropical disease that affects large populations and creates a heavy burden of disease. While there are public health strategies like vector control, intensive surveillance, clinical monitoring and intervention, these approaches are often inadequate in hyper-endemic areas. In late 2015, the first Dengue Vaccine was made available and became part of a critical intervention for poputlations at risk. The Philippines licensed this vaccine in December 2015 and adopted it for a pilot public health intervention in three regions of the country with heavy burden of disease. The cases of dengue were particularly high and rising since 2012. In some localities, a state of calamity was declared. There were brewing objections about this immunization program by some quarters. On the 29th November 2017, Sanofi Pasteur informed the Philippine government of their retrospective analysis that those with seronegative status and vaccinated woudl have a trend risk for sever dengue and increased hospitalization after 3 years of protection.