never experienced angina pectoris, and 5 had no personal history or risk factors of cardiovascular disease except age and hypertension in 2. All seven patients had additional examinations in the following hours and/or later. ECG and myocardial enzymes remained normal. Three of 4 patients had a normal exercise ECG; in one case this was followed by coronary by-pass and the patient died after surgery, but he had an history of diabetes mellitus and myocardial infarct. None of these 7 patients was readministered with the drug. One patient required hospitalisation because she experienced general (vagal malaise) and locoregional (pain and superficial phlebitis) reactions related to extravasation of verteporfin within few hours following PDT. The 27 remaining patients experienced isolated lumbar pain, and all reactions subsided within minutes or hours after discontinuation of the infusion. Several patients experienced recurrence of lumbar pain on rechallenge. Based on the number of patients treated during this period, the estimated incidences of systemic AE associated with verteporfin and of thoracic pain were respectively 11.6% and 2.3%.

Conclusion: Verteporfin-associated systemic AE are not rare, and could be potentially severe as shown in some of our patients. The interpretation is however difficult because the treated population consisted of elderly patients. In case of thoracic pain, the decision was made to avoid further administrations of verteporfin, even though the clinical symptoms resolved rapidly and subsequent examinations were reassuring. Additional evaluation is needed to better evaluate the benefit/ risk ratio of verteporfin, and to define the most adequate management in case of clinical symptoms strongly evocating anger.

P058. Clinical use of statins after cerivastatin withdrawal: report from a small community

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Introduction: Cerivastatin was withdrawn from commerce in August 2001, due to reports of an increased rate of fatal rhabdomyolysis in patients treated with this drug. The withdrawal of cerivastatin was intensively covered by international and Italian media for various months, causing important problems to physicians and also to general population. In the past years statins have deeply modified the management of serum lipid disorders and they have always been thought to be safe.

Aim of the Study: We decided to verify if the alert caused by the cerivastatin's withdrawal has affected the prescription of other statins.

Methods: We analyzed the number of prescriptions of statins in an area localized in the south of Sardinia (Italy) in two different periods of time: January-March 2001 versus October-December 2001.

Results: The total number of inhabitants living in the examined area was 476.127. The total number of prescriptions was 31.440 in the first period versus 38.647 in the second (+22.9%). The ratio of prescriptions × 1000 inhabitants was 66.01 versus 81.14. The DDD (Defined Daily Dose) was 72.18 in the first period compared to 76.17 in the second period (+5.5). The report of adverse events somehow related to statins increased from zero to eight in the second period.

Conclusions: Our data suggest that the report of an increased rate of fatal rhabdomyolysis caused by cerivastatin did not modify the clinical use of statins but, at least in the studied area, the level of attention on adverse events possibly related to statins was increased. The details of statins prescriptions dispensed in the monitored area will be discussed.

P059. Selective serotonergic vasoconstrictors in suspected association with pain activation.

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Introduction: Imigran (sumatriptan), Zomig (zolmitriptan) and Naramig (naratriptan) belong to the group of serotonergic vasoconstrictors, indicated for acute treatment of migraine. The Netherlands Pharmacovigilance Centre Lareb and the New Zealand (NZ) Intensive Medicines Monitoring Programme (IMMP) have received reports of aggravation or activation of pain at sites of previous injury in suspected association with the use of these products.

Aim of the study: Our aim was to demonstrate a plausible relationship between the use of serotonergic vasoconstrictors and the phenomenon of pain activation at sites of previous trauma.

Methods: Relevant case reports were identified in the databases of the Netherlands Phamacovigilance Center and the NZ IMMP. These reports were examined individually to assess the relationship of pain activation at sites of previous trauma following the use of the serotonergic vasoconstrictors. We screened other sources of information to find out whether the assumed association was already described in literature and looked into the pharmacodynamics of these products to seek a plausible mechanism.

Results: Lareb received a total of 33 reports of adverse events of zolmitriptan, 1 of which refers to pain activation. For sumatriptan 6 out of 254 reports refer to pain activation and for naratriptan 1 out of 20. In the NZ IMMP there were 6 reports of pain activation identified with sumatriptan out of a total of 2344 reports.

In total, the Lareb database contains 8 reports of pain activation syndrome following use of serotonergic vasoconstrictors. Two of these reports refer to aggravation of skin-related pain. Four reports describe aggravation of

pain in recently injured parts of the limbs. The other two reports refer to reactivation of old pain, as was experienced years previously. The NZ reports included two at healing surgical sites, one at the site of a haematoma one at a fracture site and two following skin injury.

Neither the Dutch nor NZ Summaries of Products Characteristics mention the phenomenon described above and no case reports were found in the literature.

The anti migraine effect of zolmitriptan, sumatriptan and naratriptan is ascribed to two effects. Firstly: vasoconstriction in the cranial arteries, inducing reduced blood supply to the meninges. Secondly: inhibition of the trigeminal nerve, reducing the release of several neuropeptides. The mechanism of pain activation is not understood, but 5-hydroxytryptamine (serotonin) is known to be involved with pain sensitising at inflammatory sites and pain processing in the spinal cord.

Conclusion: A plausible association has been demonstrated in two countries of pain activation at sites of previous trauma and the use of serotonergic vasoconstrictors. Tissue injury may be recent or old.

P060. Adverse drug reactions reports of non steroidal anti-inflammatory drugs to the Central Portugal Regional Pharmacovigilance Centre during its first year of operation

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Introduction: Non-steroidal anti-inflammatory drugs (NSAID's) is the most prescribed and dispensed class of drugs in the Central Portugal Health Administration Area. Such therapeutic class is described as responsible for high incidence rates of adverse reactions (ADR) leading to increased iatrogenic morbidity and mortality. Since the establishment of the Central Portugal Pharmacovigilance Regional Centre reported ADR due to NSAID have been monitored.

Aims of the study: The objective is to identify and to characterize preventable situations for further issuing warnings for health professionals.

Methods: Prospective observational study of reported ADR's. Causality assessments were performed using the WHO scale of imputability.

Results: A total of 522 ADR reports have been received over the first 12 months period of operation, of which 102 (19,5%) were due to NSAID's. The distribution of suspected drugs (number of reports) were as follows: acemetacin (3), aspirin (lisine salt)(2), celecoxib (29), cetoprofen (1), clonixine (2), diclofenac (8), etofenamate (2), ibuprofen (5), lornoxicam (2), naproxen (2), nimesulide (16), piroxicam (7), rofecoxib (22) and tenoxicam (1). Of the total number of reported ADR's, 150 were classified as severe after validation and causality assessment. Of these, 41 (27,3%) were due to NSAID's. Increased age, comorbidity and comedications were found to be associated with increased severity of ADR's due to NSAID's. This was observed for both specific and non-specific COX-2 inhibitors. The most affected systems were gastro-intestinal and cardiovascular.

Conclusion: NSAID's were found to be responsible for an high incidence and severity of reported ADR's. Sub-populations at increased risk have been identified. ADR's due to specific COX-2 inhibitors (celecoxib, nimesulide and rofecoxib) are under close monitoring and investigation in the light of this study findings.

P061. Concordance between global introspection and decisional algorithms in the assessment of adverse drug reactions in the presence of confounding factors

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Introduction: Causality assessments of reported adverse drug reactions (ADR's) is a component of pharmacovigilance activities, particularly for it's regulatory implications. The presence of confounding factors in ADR's reports was found to affect causality assessments.

Aim of the study: this study was aimed at comparing the results of imputability from the global introspection method based on the WHO scale of imputability with those obtained from decisional algorithms for ADR presenting identified confounding factors.

Methods: ADR reports with confounding factors were selected. An expert panel assessed causality. The same reports were independently assessed using 15 decisional algorithms.

Results: Low rates of agreements were found. Algorithms rates of concordance with GI varied according to the levels of imputability: 30% for 'Certain', 51% for 'Probable' and 51% for 'Possible'.

Conclusion: Since higher rates of agreement were found in the absence of confounding factors, its presence was found to compromise the specificity of decisional algorithms in causality assessments.