The association of PIM with AE was determined by OR and the χ^2 test or Fisher's exact probability test.

Results Sixty-four patients were treated with HDMTX for 160 cycles with a median HDMTX dose of 11760 mg (IQR 3370–14 207.5 mg). Median age was 66.4 years (IQR 55.6–75.3) and 42.2% were women. Eleven patients were treated for leukaemia and 53 for lymphoma.

Median baseline creatinine was 0.66 (IQR 0.57–0.78) mg/dL. AE was present in 80 cycles (50%). In 91.3% of these, patients were receiving concomitant PIM with methotrexate elimination. In 52 cycles methotrexate elimination was altered only after 72 hours.

PIM associated with AE were: levetiracetam (OR=6.9, 95% CI 1.5–32.4; $p<0.05$), non-steroidal anti-inflammatory drugs (OR=10.9, 95% CI 2.4–49.4; $p<0.05$) and doxycycline (OR=0.5, 95% CI 0.4–0.6; $p<0.05$). There were no significant differences between use of proton pump inhibitors, loop diuretics, amphotericin B, penicillin and derivate, aminoglycosides, ciprofloxacin or p-glycoprotein/ABCB1 inhibitors.

Conclusion and relevance There was a high prevalence of patients with AE of HDMTX. Potentially interacting medications with HDMTX are frequently used during treatment. Only levetiracetam and non-steroidal anti-inflammatory drugs were associated with methotrexate AE in our patients.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

5SPSQ-045 OLARATUMAB: WHAT IS THE ECONOMIC IMPACT ON THE NATIONAL HEALTH SYSTEM?

¹C Migliazzi*, ²C Della Costanza, ²E Aliprandi, ²C Tirone, ²M Galassi, ²V Ladisa. ¹School of Specialisation in Hospital Pharmacy-University of Milan, Pharmacological Sciences, Milan, Italy; ²Fondazione Irccs Istituto Nazionale Dei Tumori, Pharmacy, Milan, Italy

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Background and importance The US Food and Drug Administration (FDA) granted olaratumab (human anti-PDGF α monoclonal antibody) fast track authorisation in November 2016 to treat advanced soft tissue sarcoma (STM). Also, the European Medicines Agency (EMA) allowed conditional marketing authorisation for this drug after the phase 1b/2 trial. In the post-authorisation phase III trial ANNOUNCE, data were limited because of the small number of patients included and the lack of confirmation of efficacy and clinical benefit. Consequently, the EMA banned the treatment of new patients with olaratumab.

Aim and objectives We studied the economic impact of olaratumab on the National Health Service (NHS) for our hospital patients, from its introduction in our country (November 2017) to the EMA ban (January 2019).

Material and methods A retrospective analysis was conducted. In our hospital 17 patients, 11 of which were women (64.7%), with a mean age of 54.7 ± 24.5 years, were treated with olaratumab. Data (weight and doses prescribed) were extracted from our chemotherapy prescriptions and preparations database software. We selected patients treated with olaratumab.

Results An olaratumab vial cost € 1375 (€ 2.75/mg). The recommended dose was 15 mg/kg on days 1+8 of each 21 day cycle. Between November 2017 and January 2019, in our

hospital, 17 patients completed 79 total cycles for a total cost of € 457 035.

The primary outcome of the authorisation study showed a better progression free survival (6.6 months). Only five of our patients exceeded this period and had to discontinued treatment because of progression of disease. The total cost of their therapy was € 294 596 (48 total cycles for 5 patients). For the other 12 patients, the cost was € 162 439 (31 total cycles). The average cost of administration to the NHS was € 2815/patient.

Conclusion and relevance After conditional marketing authorisation, further research costs of the approved drug are necessarily at the expense of the NHS. This was the case for olaratumab, that resulted in it not being effective. For this reason, for fast track authorisation, the reimbursement price of the drugs should be taken into account in the post-authorisation costs. Furthermore, it is important to provide hospital monitoring of the clinical effects of the drug and consequent cost.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

5SPSQ-046 PREVALENCE OF NIVOLUMAB ADVERSE EVENTS IN ROUTINE CLINICAL PRACTICE

G Miralles Andreu*, M Pomares Bernabeu, M Llinares Esquerdo, L Soriano Irigaray, AC Murcia López, A Navarro Ruiz. Hospital General Universitario De Elche, Hospital Pharmacy Department, Elche, Spain

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Background and importance Nivolumab was authorised in Spain in 2015. It is a human immunoglobulin monoclonal antibody that binds to PD-1 receptor and blocks its interaction with PD-L1 and PD-L2. It is indicated in adjuvant or metastatic melanoma (MC), metastatic non-small cell lung cancer (NSCLC), renal cell carcinoma (RC) and squamous cell carcinoma of the head and neck (HNC), among others. Its recent commercialisation means there are no data on adverse events (AE) following long term treatment in routine clinical practice.

Aim and objectives To assess the tolerability of nivolumab, to identify and calculate the prevalence of AE related to nivolumab and to compare its frequency with the that described on the data sheet (DS).

Material and methods A descriptive, retrospective, observational study was carried out from March 2016 to September 2019 in a tertiary hospital. It included all patients treated with nivolumab since it was commercialised. Medical records and blood tests of all treated patients were reviewed from the start of nivolumab treatment. Information was collected from the applications Abucasis, Mizar, Farmis-Oncofarm and Gestlab. Variables collected were sex, age, diagnosis, number of nivolumab doses, AE, if the patient died, nivolumab start/end date and reason for stopping treatment. AE were classified according the prevalence described on the DS: very common ($>10\%$), common (1–10%), not common (0.1–1%), rare (0.01–0.1%) and very rare ($<0.01\%$).

Results A total of 48 patients were included, 77% were men and median age was 63 years. The main diagnoses were NSCLC (40%), followed by RC (29%), MC (21%) and HNC

(10%). The median dose received was 7. If the number of doses was calculated according to diagnosis, RC patients received 11 doses, 9 for MC, 4 for LC and 4 for HNC. During the study period, 84.2% of LC patients, 60% of HNC, 20% of MC and 50% of RC died.

Regarding AE, very common (>10%) ones were an increase in lactate dehydrogenase (25%), hypothyroidism (14.6%), eruption (10.4%) and increases in gamma-glutamyl transferase and glutamic-oxaloacetic transaminase (10.4%). The remaining AE were classified as common according its frequency (1–10%): pneumonitis (6.3%), nephritis (4.2%), hepatitis (4.2%), increase in alkaline phosphatase (6.3%), diarrhoea (2.1%), colitis (2.1%), liver failure (2.1%) and arthritis (2.1%). Comparing AE frequency obtained with those reported on the DS, we found that the prevalence of hypothyroidism, colitis, hepatitis, nephritis and arthritis was higher in routine clinical practice than expected.

We found that 77% of patients interrupted nivolumab due to progression of disease (78.4%), AE (16.2%) or ending treatment (5.4%).

Conclusion and relevance Relevant AE that occurred during the study period were hypothyroidism, pneumonitis, hepatitis, nephritis and colitis. Their prevalence was higher than expected and they caused interruption of treatment. The increased prevalence of AE in routine clinical practice highlights the need for strict monitoring of analytical parameters to detect AE as early as possible.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

5PSQ-047 RIBOCICLIB SAFETY IN METASTATIC BREAST CANCER

MC Sánchez Argaiz, M Ruiz De Villegas García-Pelayo, T Chinchilla Alarcón, I Muñoz Castillo*, B Mora Rodríguez. *Hospital Regional Universitario De Málaga, Hospital Pharmacy, Málaga, Spain*

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Background and importance Treatment goals for advanced or metastatic breast cancer include not only delaying the progression of disease and extending survival, but also maintaining or improving quality of life for the patient. CDK4/6 inhibitors, such as ribociclib, in combination with hormonal therapy, is a new standard firstline and secondline treatment for women with advanced or metastatic hormone receptor positive (HR+/HER2-) breast cancer. The starting dose is 600 mg/day for 3 weeks followed by 1 week off, combined with hormonal therapy, aromatase inhibitor and/or luteinising hormone releasing hormone agonists. Management of severe adverse drug reactions (ADRs) may require temporary dose interruptions, dose reductions or discontinuations of treatment.

Aim and objectives To assess the safety of ribociclib and analyse the ADRs and severe toxicity that cause dose reductions, dose interruptions and permanent discontinuations.

Material and methods A retrospective observational study was conducted in a tertiary hospital. We analysed the safety of ribociclib by reviewing medical and pharmaceutical records of all patients treated with ribociclib from January 2018 until September 2019. Collected data were age, ECOG, cancer stage, metastatic location, treatment line and dose reduction/interruption. ADRs were collected for the safety profile assessment.

Results Forty-two patients were included, median age 58 years (range 40–72). ECOG at the beginning of the treatment was 0 in 67% (28) of patients, 1 in 31% (13) and 2 in 2% (1). A total of 98% of patients were in stage IV disease and the main metastatic location was bone (76%). Ribociclib combined with hormonal therapy was prescribed as firstline treatment in 79% (33) of patients. One of two patients suffered first dose reduction (400 mg/day) by adverse events due to ribociclib and one of 10 suffered second dose reduction (200 mg/day). The most common ADR grade 3 (severe) was neutropenia (n=11), followed by skin and subcutaneous tissue disorders such as rash, pruritus and erythema (n=5), and gastrointestinal disorders (n=3) that caused delays and dose reduction. There were no permanent discontinuations due to toxicity.

Conclusion and relevance In spite of the manageable safety profile of ribociclib by dose modifications and delays in cycles, it was necessary for close monitoring of side effects and toxicity due to interpatient variability, to find the optimal dose for each patient.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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5PSQ-048 ANALYSIS OF DRUG INTERACTIONS BETWEEN ORAL ANTINEOPLASTIC AGENTS AND CONCURRENT MEDICATIONS

¹A Narrillos-Moraza*, ¹V Escudero-Vilaplana, ¹R Collado-Borrell, ¹A Hoyo-Muñoz, ¹A Gimenez-Manzorro, ¹MA Amor-García, ²S Osorio-Prendes, ³A Calles-Blanco, ¹A Herranz-Alonso, ¹M Sanjurjo-Saez. ¹Hospital General Universitario Gregorio Marañón, Pharmacy, Madrid, Spain; ²Hospital General Universitario Gregorio Marañón, Haematology, Madrid, Spain; ³Hospital General Universitario Gregorio Marañón, Oncology, Madrid, Spain

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Background and importance The development and commercialisation of oral antineoplastic agents (OAAs) to treat cancer has increased significantly in recent years. Drug interactions are the most frequent drug related problems with regard to these drugs.

Aim and objectives To analyse the potential drug interactions (PDIs) of OAAs with concurrent medication.

Material and methods A cross sectional observational study was carried out in outpatients who started treatment with OAAs between December 2015 and May 2019. PDIs were analysed using the Lexicomp and the database About Herbs of the Memorial Sloan Kettering Cancer Centre. PDIs were classified according to severity (major, moderate, minor), risk (X, D, C) and reliability (excellent, good, fair, poor) ratings and mechanism (pharmacokinetics and pharmacodynamics).

Results A total of 881 patients were included (56.2% men) with a median (range) age of 67.8 years (22.5–94.4). The most frequent types of tumours were prostate cancer (16.8%), multiple myeloma (13.6%), hepatocellular carcinoma (13.3%), breast cancer (11.5%), renal carcinoma (n=90; 10.2%) and non-small cell lung cancer (9.9%). Thirty-seven different OAAs were assessed. A total of 860 PDIs were identified. The targeted OAAs involved in more PDIs were: enzalutamide (PDI=231, PDI/patient=2.8), thalidomide (PDI=91, PDI/patient=2.7), everolimus (PDI=77, PDI/patient=1.0), imatinib (PDI=75, PDI/patient=1.8) and sorafenib (PDI=68, PDI/patient=0.6). The most frequent severity and risk ratings were major (55.3%) and C (42.8%), respectively. In total, 61.7% of