ABSTRACT

- **Title**

Use of Erythropoiesis Stimulating Agents (ESA) in Patients With Non-myeloid Malignancies Receiving Myelosuppressive Chemotherapy 2014 – 2021

- **Keywords**

Aranesp, Epogen/Procrit, Darbepoetin alfa, Epoetin alfa, Erythropoiesis Stimulating Agents (ESA), non-myeloid malignancy, anemia

- **Rationale and Background**

The Food and Drug Administration (FDA) requested a postmarketing commitment (PMC) to submit periodic reports based on review of relevant data, including United States (US) electronic medical record (EMR) and claims databases. The PMC will assess the utilization of Aranesp or Epogen/Procrit for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy.

- **Research Question and Objectives**

The primary objectives are: 1) To estimate the proportion of patients with non-myeloid malignancies receiving an ESA over a 180-day follow-up period after initiation of myelosuppressive chemotherapy by calendar year, overall and stratified by specific tumor types including patients with breast cancer, adjuvant breast cancer, metastatic breast cancer, colorectal cancer (CRC), lung cancer, non-small cell lung cancer (NSCLC), and lymphoma; and 2) To describe the hemoglobin (Hb) levels and estimate the proportion of patients with Hb values greater than 10 g/dL immediately preceding ESA treatment initiation in patients with non-myeloid malignancies after initiation of myelosuppressive chemotherapy by calendar year, overall and stratified by specific tumor types (listed in objective 1).

- **Study Design**

We conducted 2 parallel retrospective cohort studies using data from the Truven MarketScan® claims database and the US-based Oncology Services Comprehensive Electronic Records (OSCER) database. Both the MarketScan and OSCER databases were used to evaluate the use of ESAs after the initiation of myelosuppressive chemotherapy among patients diagnosed with non-myeloid malignancy. Patients were further categorized into the following specific tumor types: breast cancer, breast cancer receiving adjuvant therapy, metastatic breast cancer, CRC, lymphoma, lung cancer, and NSCLC. All breast cancer populations were limited to females. In addition, the OSCER database was used to describe Hb levels before the initiation of ESAs. Data were analyzed in cohorts based on calendar year.

- **Setting**

The study evaluated claims and EMR data for US patients in inpatient and outpatient settings. 15 June 2017 (start of data collection).

- **Subjects and Study Size, Including Dropouts**

The number of eligible patients for calendar year cohorts 2014 and 2015 who had received myelosuppressive chemotherapy in the calendar year and had been diagnosed with a non-myeloid malignancy were 48,936 and 32,453 in MarketScan and 66,684 and 73,783 in OSCER database, respectively. The decrease in the number of patients diagnosed with non-myeloid malignancy in the Marketscan database is a result of overall decrease in number of lives covered from 43 million in 2014 to 25 million in 2015. The

decrease in number of lives covered was a consequence of fewer providers contributing data to Marketscan in 2015 compared to 2014.

- **Variables and Data Sources**

Eligible patients in the Truven MarketScan claims database and the OSCER database were evaluated for the following outcome variables or covariates:

- use of an ESA
- age
- gender
- comorbidities (MarketScan only)
- most proximal hemoglobin value within 7 days preceding (and including) the date of first ESA administration (OSCER only)

- **Results**

The analysis of the MarketScan database included a total of 81,389 patients with non-myeloid malignancies initiating myelosuppressive chemotherapy (48,936 patients in 2014 and 32,453 patients in 2015). The most frequently reported individual tumor type was breast cancer (12,583 patients in 2014 and 8,526 patients in 2015). Overall, approximately 61% of patients were women, ranging from 42% in lymphoma to 100% in breast cancer. The mean (SD) age varied by tumor type, ranging from 56 (10) years in patients with breast cancer receiving adjuvant therapy to 66 (10) years in patients with NSCLC. Baseline characteristic including age, gender, and comorbidities were generally consistent by year overall and across tumor types.

The incidence (95% confidence interval [CI]) of ESA use among patients diagnosed with non-myeloid malignancies during the 180-day period following initiation of myelosuppressive chemotherapy in MarketScan was 4.5% (4.3, 4.7) and 3.7% (3.5, 3.9) in 2014 and 2015, respectively. The incidence (95% CI) of ESA use was highest in patients with NSCLC (8.7% [7.9, 9.4] in 2014 and 6.7% [5.8, 7.5] in 2015) and was lowest in patients with breast cancer receiving adjuvant therapy (1.2% [0.9, 1.5] in 2014 and 1.1% [0.7, 1.4] in 2015). Across tumor types, the incidence of ESA use generally declined from 2014 to 2015 (with the exception of CRC, which was similar across years).

The analysis of the OSCER database included a total of 140,467 patients with non-myeloid malignancies initiating myelosuppressive chemotherapy (66,684 patients in 2014 and 73,783 patients in 2015). The most frequently reported individual tumor type was breast cancer (13,722 patients in 2014 and 15,396 patients in 2015). Across all tumor types, approximately 57% of patients were women, ranging from 44% in lymphoma and colorectal cancer to 100% in breast cancer. The mean (SD) age varied by tumor type, ranging from 58 (12) years in patients with breast cancer receiving adjuvant chemotherapy to 68 (10) years in patients with NSCLC. The age and gender distributions were generally consistent over time within tumor types.

The incidence (95% CI) of ESA use among patients diagnosed with non-myeloid malignancies during the 180-day period following initiation of myelosuppressive chemotherapy in the OSCER database was 9.1% (8.9, 9.3) and 7.4% (7.2, 7.6) in 2014 and 2015, respectively. The incidence (95% CI) of ESA use was highest in patients with NSCLC (14.9% [14.2, 15.6] in 2014 and 11.6% [11.0, 12.2] in 2015), and was lowest in patients with breast cancer receiving adjuvant therapy (2.8% [2.5, 3.1] in 2014 and 1.9% [1.6, 2.1] in 2015). For all tumor types, the incidence of ESA use declined from 2014 to 2015.

In the OSCER database, the mean (SD) hemoglobin concentration preceding the first administration of an ESA was 9.1 (0.9) g/dL in 2014 and 9.0 (0.9) g/dL in 2015. Results

were similar by tumor type. Overall, the proportion (95% CI) of patients with Hb value > 10 g/dL before their first administration of an ESA was 6.6% (5.9, 7.2), and 6.4% (5.7, 7.1) in 2014 and 2015, respectively. The proportion of patients with a Hb value > 10 g/dL in 2014 and 2015 varied by tumor type: breast cancer (8.2% and 7.9%), metastatic breast cancer (8.7% and 7.5%), breast cancer with adjuvant therapy (7.9% and 8.6%), CRC (11.3% and 10.1%) lung cancer (5.3% and 5.5%), NSCLC (5.4% and 5.8%), and lymphoma (6.5% and 6.8%).

- **Discussion**

This analysis of real-world data from the MarketScan and OSCER databases indicates that the use of ESAs decreased from 2014 to 2015 in patients with a variety of tumor types who initiated myelosuppressive chemotherapy. The age, gender, and comorbidity profiles of patients initiating myelosuppressive chemotherapy were not divergent between the 2 calendar year cohorts. Overall, greater than 90% of patients had a hemoglobin level < 10 g/dL at the time of ESA initiation (in accordance with the United States Package Insert [USPI]) in both 2014 and 2015.

- **Marketing Authorization Holder**

Amgen Europe B.V.

- **Names and Affiliations of Principal Investigators**

Not applicable.