

## **NIS REPORT SYNOPSIS**

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### **A non interventional, retrospective study on AECOPD treatment status in China**

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#### **Study sites, number of patients and countries**

In this study, it was planned to enroll approximately 5000 patients, from about 50-60 sites of China. A total of 5067 patients were enrolled at 43 sites in China.

#### **Study period**

First patient in: 1 Jan 2014

Last patient out: 29 Sep 2014

#### **Objectives of this Non-Interventional Study**

To observe clinical practice including glucocorticoids treatment in AECOPD in China.

#### **Study design**

This was a retrospective, multi-centre, non-interventional study.

#### **Inclusion/exclusion criteria**

The subject population observed in the NIS fulfilled all of the following criteria:

1.  $\geq 40$  years old;
2. Hospitalization treatment due to AECOPD since Sep, 2013;
3. Diagnosed by GOLD 2013 as COPD at least 3 months before AECOPD based on treating physician's judgment;
4. Provided informed consent or informed consent waiver.

Patients were not eligible to participate if any of the following exclusion criteria were present:

1. Participation in any interventional clinical study within 3 months before being recruited in the study;
2. Ongoing AECOPD during recruitment timeline;
3. The patients whose symptoms haven't recovered and then discharge by themselves;
4. The primary diagnosis of hospitalization was not AECOPD.

### **Study variables**

Primary variable: the percentage of glucocorticoid treatment for AECOPD.

Secondary variables:

Hospitalization

- Percentage of oral /intravenous/ inhaled steroid therapy in patients treated with glucocorticoids, mean dosage, regimen and treatment duration via different administration route in hospital;
- Percentage of antibiotics treatment for AECOPD by clinicians during the hospitalization;
- Percentage of antibiotics treatment via different administration route ( for example, iv, oral) for AECOPD, mean treatment duration via different administration route in hospital;
- Mortality caused by AECOPD and recorded as primary cause of death by clinicians;
- Endotracheal intubation rate in treatment of AECOPD;
- Pneumonia rate at the diagnose of AECOPD and in treatment of AECOPD;
- Hospitalization duration and treatment cost due to AECOPD as primary cause;
- Percentage of treatment category before AECOPD and at discharge (for example, ICS/LABA, LAMA, theophylline, etc);
- Complication due to AECOPD or AECOPD treatment.

### **Statistical methods**

All results were descriptively analyzed. In general, the descriptive statistics (number, mean, and median, standard deviation, minimum and maximum) were performed for continuous variables. The frequency tables (number and percentage of subjects) were performed for categorical variables. Where appropriate, 95% confidence intervals were constructed for the efficacy in proportions of interest.

Linear regression method was used to analyze the factors which might affect the cost for hospitalization, including whether treated with glucocorticoids or not, whether treated with antibiotics or not, whether applied endotracheal intubation or not and whether complication occurred or not.

Survival analysis was used to analyze the duration of hospitalization. Kaplan-Meier method was used to estimate the percentage of patients and their median duration of hospitalization; Cox regression method was used to analyze the factors which might affect the duration of hospitalization, including whether treated with glucocorticoid or not, whether treated with antibiotics or not, whether applied endotracheal intubation or not and whether complication occurred or not, etc.

All hypotheses (if not specified) were addressed by an analysis of two-sided test, with 0.05 significance level.

According to an unpublished market research made in early 2013, among 1000 AECOPD patients, 33% received nebulised corticosteroid. With sample size of 5000 patients, it was estimated that the length of 95% confidence intervals was  $\pm 1.3\%$ .

### **Results and conclusion**

In this study, 5091 patients were screened, and 5067 patients were included in FAS.

Results related to the treatment of glucocorticoids:

Most patients (4569 patients, 90.17%) received glucocorticoids during AECOPD treatment.

The percentage of patients received nebulised glucocorticoid was the highest (3587 patients, 70.79%); followed by intravenous (2463 patients, 48.61%) and relatively lower percentage of patients received oral glucocorticoid (776 patients, 15.31%).

The most common nebulised glucocorticoid was Budesonide (3514 patients, 69.35%) with an average daily dosage of 3.5mg (mean value) for the treatment duration of 9.31 days (mean value); the most common intravenous glucocorticoid was Methylprednisolone sodium succinate (2296 patients, 45.31%) with an average daily dosage of 45.15mg (mean value) for the treatment duration of 6.37 days (mean value); the most common oral glucocorticoid was Prednisone acetate (603 patients, 11.90%) with an average daily dosage of 18.43mg (mean value) for the treatment duration of 6.25 days (mean value).

Of the patients who received nebulised glucocorticoids, nearly one-third (1153 patients, 22.76%) received nebulised glucocorticoids alone during the whole treatment. The oral glucocorticoid were all used as a part of sequential or combination treatment. The main route of nebulised with systemic (intravenous and oral) glucocorticoids treatment was nebulised and intravenous sequential or combination treatments, including nebulised/intravenous combination then nebulised dosing alone (222 patients, 4.38%), nebulised/intravenous combination (151 patients, 2.98%) and nebulised dosing alone then nebulised/intravenous combination then nebulised dosing alone (103 patients, 2.03%). In these 3 common routes, the highest nebulised Budesonide average daily dosage and longest treatment duration was found in the route of nebulised dosing alone then nebulised/intravenous combination then nebulised dosing alone (Mean: 4.05mg, 11.78 days) followed by the route of nebulised/intravenous

combination then nebulised dosing alone (Mean: 3.71mg, 10.12 days). Budesonide average daily dosages and treatment duration in these two routes were both higher and longer than that in nebulised Budesonide alone (Mean: 3.69mg, 9.09 days). The lowest nebulised Budesonide average daily dosage and the shortest treatment duration were found in the route of nebulised/intravenous combination (Mean: 3.03mg, 7.91days).

For the 2296 patients who received Methylprednisolone sodium succinate injection, the most common daily dosage was 40mg (2078 patients, 90.51%). For the 177 patients who received Methylprednisolone tablet, the most common daily dosage was 20mg (61 patients, 34.36%). For the 3514 patients who received nebulised Budesonid, the most common daily dosage was 2 mg (1493 patients, 42.49%).

The discharge rate of the patients treated with glucocorticoids (98.75%) was similar with that of the patients without glucocorticoid treatment (98.80%), but the median hospitalization duration for the patients treated with glucocorticoid was slightly longer (11 days vs 10 days).

Other results:

There were 4903 (96.76%) patients received antibiotics and 164 (3.24%) patients didn't receive antibiotics treatment. Intravenous antibiotics were given to 4880 (96.31%) patients, in which 4531 (89.42%) patients received intravenous antibiotics alone; oral antibiotics were given to 354 (6.99%) patients, in which 22 (0.43%) patients received oral antibiotics alone; 331 (6.53%) patients received both intravenous and oral antibiotics.

During AECOPD treatment, 113 (2.23%) patients received endotracheal intubation.

The complicated pneumonia rates were similar at AECOPD diagnosis (1255 patients, 24.77%) and at discharge diagnosis (1227 patients, 24.23%). In the patients with pneumonia, 97.88% patients showed improvement in pneumonia condition at discharge.

There were 63 (1.24%) patients died during hospitalization, in which 56 patients died primarily of AECOPD.

The factors that whether treated with glucocorticoid or not, whether treated with antibiotics or not, whether applied endotracheal intubation or not and whether experienced complication or not were the effect factors on the cost for hospitalization: for the patients treated with glucocorticoid, the average cost was 3134.91 RMB higher compared to the patients without glucocorticoid; for the patients treated with antibiotics, the average cost was 5549.66 RMB higher compared to the patients without antibiotics; for the patients with endotracheal intubation, the average cost was 34384.68 RMB higher compared to the patients without endotracheal intubation; for the patients with complications, the average cost was 2734.98 RMB higher compared to the patients without complications.

Compared to the treatments before AECOPD onset, the percentages of patients received the following treatments at discharge were increased obviously: ICS+LABA (before AECOPD vs

at discharge: 552 patients, 10.89% vs 1230 patients, 24.27%), ICS+LAMA+LABA (before AECOPD vs at discharge: 467 patients, 9.22% vs 1487 patients, 29.35%) and theophylline (before AECOPD vs at discharge: 774 patients, 15.28% vs 1219 patients, 24.06%).

There were 931 (18.37%) patients experienced complications related to AECOPD or the treatment of AECOPD. The most common complications were congestive heart failure (218 patients, 4.30%) and arrhythmia (158 patients, 3.12%).

#### Conclusion:

The results from this study support glucocorticoids to be the essential medication for AECOPD management. In the treatment routes of glucocorticoids, 90.17% Chinese patients received nebulised glucocorticoids during AECOPD treatment.