

1. TITLE PAGE

Study Title:	Longitudinal Study on the Epidemiology and Treatment of Auto-Immune Thrombocytopenia (AITP) in Algeria.
Investigational Product:	Not applicable
Indication:	Not applicable
Brief Description:	Epidemiological, national, prospective, longitudinal study on the care of patients with auto-immune thrombocytopenia followed up by hematologists in the public sector in Algeria Initially, the study was supposed to follow up the patients for 18 months after inclusion. As per decision of the Sponsor (20/08/2019), the protocol was modified to include only the data at inclusion. Data from the follow-up that had been collected prior to this decision have not been analyzed.
Study Sponsor:	Amgen Algeria
Study No.:	20160214
EudraCT No.:	Not applicable
Study Phase:	Not applicable
Study Initiation Date:	03 September 2017 (first subject enrolled)
Study Completion Date:	30 August 2018 (inclusion of last subject) The analyses presented in this report are based on a database snapshot date of 18 July 2019.
Principal Investigators:	This study was conducted at 16 centers in Algeria.
Contact Person:	[REDACTED] (AMGEN Medical Responsible), Algeria, [REDACTED]
Good Clinical Practice and Accuracy:	This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and Algerian laws/regulations. Essential documents will be retained in accordance with ICH GCP. The study sponsor declares that the information provided in this report is an accurate representation of the data captured and analyses performed for this study.
Report Date:	24 July 2019

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## 2. SYNOPSIS

**Name of Sponsor:** Amgen Algeria

**Name of Finished Product:** Not Applicable

**Name of Active Ingredient:** Not Applicable

**Title of Study:** Longitudinal Study on the Epidemiology and Treatment of Auto-Immune Thrombocytopenia (AITP) in Algeria

**Investigators and Study Centers** This study was conducted at 16 centers in Algeria.

**Publication(s):** None as of the date of this report.

**Study Period:** 03 Septembre 2017 (first subject enrolled) to 30 August 2018 (inclusion of last subject)

**Development Phase:** Not Applicable

**Previous Reports for This Study:** None

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### Objectives:

The main objective of the study was to assess the incidence of patients aged 16 years and over, diagnosed with AITP in a 12-month period of inclusion.

The secondary objectives of the study were:

1. To assess the incidence by age category of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period;
2. To assess the incidence by gender of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period;
3. To assess the incidence by diagnosis stage (asymptomatic, easy bruising, severe hemorrhage) of AITP diagnosed in patients aged 16 years old and older in Algeria during the inclusion period;
4. To assess the incidence by region (Wilaya) of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period;
5. To assess the prevalence of AITP diagnosed in patients aged 16 years old and over in Algeria;
6. To determine the characteristics of patients aged 16 years and over, AITP diagnosed in Algeria (age, gender, risk factors and comorbidities).

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**Methodology:** This is a longitudinal, prospective, national, epidemiological study on the care of patients with autoimmune thrombocytopenia followed up by hematologists in the public sector in Algeria.

**Number of Subjects Planned:** This study was representative and national. As the primary objective of the study was to estimate the incidence, patient recruitment was open, and no estimate of the sample size was calculated. However, around 1300 AITP patients (incident and prevalent) were expected to be included over the 12-month inclusion period of the study.

**Diagnosis and Main Criteria for Eligibility:** All patients over 16 years old previously diagnosed (prior to inclusion visit) or newly diagnosed (at the time of the inclusion visit) with AITP, treated in the hematology departments in Algeria and who gave their informed consent, were included in the study.

**Investigational Product, Dose and Mode of Administration, Manufacturing Batch Number:** Not applicable

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**Duration of Treatment:** Not applicable

**Study Endpoints:**

Primary endpoint:

Number of new cases diagnosed with AITP and aged 16 years and over, in Algeria during the period of 12 months of inclusion.

Secondary endpoints:

- 1/ Number of new cases diagnosed with AITP and aged 16 years and over, in Algeria during the period of 12 months of inclusion, by age categories.
- 2/ Number of new cases diagnosed with AITP and aged 16 years and over, in Algeria during the period of 12 months of inclusion, by gender.
- 3/ Number of new cases diagnosed with AITP and aged 16 years and over, in Algeria during the period of 12 months of inclusion, by diagnosis stage.
- 4/ Number of new cases diagnosed with AITP and aged 16 years and over, in Algeria during the period of 12 months of inclusion, by Wilaya (Province [Wilaya]).
- 5/ Total number of cases of AITP, aged 16 years and over, previously diagnosed in Algeria during the period of study.
- 6/ Characteristics of patients diagnosed with AITP and aged 16 years and over, in Algeria (age, gender, risk factors and comorbidities).

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**Statistical Methods:**

The data were processed anonymously and confidentially.

Standard descriptive statistics were used:

- Continuous quantitative variables will be summarized by the number of data, number of missing data, mean, standard deviation (SD), median, quartiles 1 and 3, minimum and maximum.
- Categorical variables will be summarized by frequency of missing data, frequencies and percentages of each modality.

New AITP cases and previous AITP cases were defined as follows

- New AITP cases: all patients with an AITP diagnosed during the inclusion period of 12 months from 1<sup>st</sup> September 2017 to 31<sup>th</sup> August 2018.
- Previous AITP cases: All other AITP patients.

The annual incidence of AITP during the 12 months of recruitment period were estimated with the 95% confidence interval of a Poisson distribution.

Statistical analyses were performed using SAS software SAS 9.4 and SAS/STAT 14.3 for Microsoft Windows (SAS Institute, Inc.)

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**Summary of Results:**

Initially, the study was supposed to follow up the patients for 18 months after inclusion. As per decision of the Sponsor (20/08/2019), the protocol was modified to include only the data at inclusion. Data from the follow-up that had been collected prior to this decision have not been analyzed. Results are extracted from the statistical report (Tables and figures) dated on 24<sup>th</sup> July 2019.

**Subject Disposition:**

In total, 1,164 patients were included in the study [Source: Table 3. Patient disposition] between 3 September 2017 and 30 August 2018 [Source: Table 6. First and Last inclusion]. Eventually 1,159 (99.6%) patients were included in the analysis [Table 3. Patient disposition] after exclusion of 5 patients with at least one major protocol deviation [Source: Table 4. Inclusion/Exclusion criteria and protocol deviations]. Among those

patients, 173 (14.9%) patients were newly diagnosed for AITP while 986 (85.1%) patients had been previously diagnosed with the disease [Source: Table 8. Summary of AITP diagnosis].

**Baseline Demographics:** Otherwise specified, data below are described on the overall population of analysis (new and previous AITP cases).

**Sex:** 895 (77.2%) females [Source: Table 9. Summary of demographic data].

**Age:** median age at inclusion was 42 [30;56] years [Source: Table 9. Summary of demographic data] and median age at diagnosis was 36 [25;50] years [Source: Table 11. Summary of AITP assessment].

**Bleeding risk:** low risk; grade 0 for 1,109 (87.9%) patients on the World Health Organization scale [Source: Table 11. Summary of AITP assessment].

**Bleeding score:**  $\leq 8$  for 1,139 (98.3%) patients [Source: Table 11. Summary of AITP assessment].

**Platelet count ( $10^3/\text{mm}^3$ ):** [Source: Table 13. Summary of hematology data]

- Median for new AITP cases: 52 [18;114]
- Median for previous AITP cases: 110 [50;209]

**First-line of AITP treatment:** steroids for 931 (80.4%) patients [Source: Table 18. Summary of first line AITP treatment].

**Last AITP treatment received/On-going AITP treatment (for previous AITP cases only):** steroids for 528 (53.5) patients, 195 (19.8%) patients had received another than steroids AITP treatment and 172 (17.4%) patients had undergone a splenectomy with a median time between diagnosis and surgery of 19.0 [10.9;35.6] months [Source: Table 19. Last AITP treatment received/On-going AITP treatment].

### Primary endpoint results:

Incidence of AITP diagnosed in patients aged 16 years old and over in Algeria is 0.85 [0.75;0.96] cases per 100 000 [Source: Table 20. Incidence of AITP diagnosed in patients aged 16 years old and over in Algeria (primary endpoint)].

### Secondary endpoint results:

Incidence and prevalence are presented as number of cases per 100,000 [95% CI]

1. Incidence by age: Incidence increases with age from 0.54 [0.43;0.68] for the [15-35 years] group to 2.37[1.60;3.51] for patients over 75 years old. Incidence by age is displayed in the table below.

	Number of cases per 100000 [95% CI]
[15-25 years]	0.44 [0.30 ; 0.64]
[25-35 years]	0.63 [0.47 ; 0.84]
[35-45 years]	0.91 [0.70 ; 1.19]
[45-55 years]	1.17 [0.88 ; 1.55]

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[55-65 years[	1.01 [0.70 ; 1.47]
[65-75 years[	1.52 [1.01 ; 2.29]
[75-85 years[	1.71 [1.01 ; 2.89]
>= 85 years	3.38 [1.69 ; 6.75]

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**[Source: Table 21.Incidence of AITP by age]**

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2. Incidence by gender: 0.54 [0.43 ; 0.67] for male and 1.18 [1.02 ; 1.37] for female [Source: Table 23.Incidence of AITP by sex].
3. Incidence by diagnosis stage: 0.37 [0.31 ; 0.45] for asymptomatic patients; 0.14 [0.10 ; 0.19] for easy bruising patients and 0.09 [0.06 ; 0.13] for severe hemorrhage patients [Source: Table 24.Incidence of AITP by diagnosis stage].
4. Incidence by Wilaya: Incidence varies depending on the Wilaya of residence from 0.13 [0.02 ; 0.92] in Tebessa to 1.64 [0.93 ; 2.89] in Sidi Bel Abbès [Source: Table 25.Incidence of AITP by Wilaya].
5. Global prevalence: 5.65 [5.39 ; 5.93] [Source: Table 26. Prevalence of AITP]
6. Prevalence by age: Prevalence by age is displayed in the table below.

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	Number of cases per 100000 [95% CI]
[15-25 years[	3.19 [2.78 ; 3.67]
[25-35 years[	4.60 [4.13 ; 5.11]
[35-45 years[	5.63 [5.06 ; 6.27]
[45-55 years[	7.06 [6.30 ; 7.91]
[55-65 years[	8.38 [7.37 ; 9.53]
[65-75 years[	11.25 [9.68 ; 13.08]
[75-85 years[	8.20 [6.45 ; 10.42]
>= 85 years	7.60 [4.79 ; 12.06]

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**[Source: Table 27.Prevalence of AITP by age].**

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7. Prevalence by gender: 2.58 [2.34;2.85] for males and 8.80 [8.33;9.29] for females [Table 28.Prevalence of AITP by gender].

**Safety Results:** Not Applicable

**Conclusions:**

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The study was able to address all the objectives that were planned in the protocol.

Primary objective:

To assess the incidence of patients aged 16 years and over, diagnosed with AITP in a 12-month period of inclusion:

- 0.85 [0.75;0.96] cases per 100 000.

Secondary endpoints:

1/ To assess the incidence by age category of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period:

- Incidence increases with age from 0.54 [0.43;0.68] for the [15-35 years] group to 2.37[1.60;3.51] cases per 100 000for patients over 75 years old.

2/ To assess the incidence by gender of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period:

- 0.54 [0.43 ; 0.67] for male and 1.18 [1.02 ; 1.37] cases per 100 000 for female.

3/ To assess the incidence by diagnosis stage (asymptomatic, easy bruising, severe hemorrhage) of AITP diagnosed in patients aged 16 years old and older in Algeria during the inclusion period:

- 0.37 [0.31 ; 0.45] for asymptomatic patients; 0.14 [0.10 ; 0.19] for easy bruising patients and 0.09 [0.06 ; 0.13] cases per 100 000for severe hemorrhage patients.

4/ To assess the incidence by region (Wilaya) of AITP diagnosed in patients aged 16 years old and over in Algeria during the inclusion period:

- Incidence varies depending on the Wilaya of residence from 0.13 [0.02 ; 0.92] in Tebessa to 1.64 [0.93 ; 2.89] cases per 100 000 in Sidi Bel Abbès.

5/ To assess the prevalence of AITP diagnosed in patients aged 16 years old and over in Algeria:

- 5.65 [5.39 ; 5.93] cases per 100 000.

6/ To determine the characteristics of patients aged 16 years and over, AITP diagnosed in Algeria (age, gender, risk factors and comorbidities):

- 1,159 patients (264 [22.8%] males and 895 [77.2%] females) with a median age at inclusion of 42 [30;56] years.
- 966 (83.3%) patients had no comorbidities that can confer a bleeding risk or risk of injury.