1 ABSTRACT

Title

Post-Authorisation Safety Study (PASS) MA25101: An Observational Cohort Study of the Safety of Brentuximab Vedotin in the Treatment of Relapsed or Refractory CD30+ Hodgkin Lymphoma and Relapsed or Refractory Systemic Anaplastic Large Cell Lymphoma (ARROVEN)

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Keywords

brentuximab vedotin, Hodgkin lymphoma, systemic anaplastic large cell lymphoma, post-authorisation safety

Rationale and Background

Brentuximab vedotin is an antibody-drug conjugate for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma (HL) or systemic anaplastic large cell lymphoma (sALCL). The European Medicine Agency (EMA) requested this study to better understand the safety profile of brentuximab vedotin in a real-world setting.

Research Question and Objectives

The objectives were to evaluate serious adverse events (SAEs) and adverse events of special interest (AESIs), in patients treated with brentuximab vedotin in routine practice, and to identify potential risk factors for peripheral neuropathy.

Study Design

This was a multi-centre, international, prospective, observational study of patients with relapsed or refractory CD30+ HL or sALCL, treated with brentuximab vedotin in routine clinical care.

Setting

Routine care by oncologists and haematologists.

Subjects and Study Size

Safety analyses included 310 patients (prospective: 156 and retrospective: 154) including 58 patients with sALCL. The median age at enrolment was 44.0 (range: 18 - 87) years, with 24.5% aged ≥65 years.

Variables and Data Sources

- Demographics, medical history, co-morbidities, disease and treatment history
- Brentuximab vedotin dosage regimen

- Other treatments and concomitant medications
- SAEs
- AESIs defined in the protocol per EMA's request: peripheral neuropathy, neutropenia (including febrile neutropenia), infections (including opportunistic infections), hyperglycaemia, and hypersensitivity reactions (including infusion-related reactions and allergic reactions)
- Survival status
- Potential risk factors for peripheral neuropathy
- Sub-population evaluations include: elderly (≥65 years), long-term treatment (>16 cycles), disease (CD 30+ HL or sALCL).

Results

Patients received a median of 6.0 treatment cycles (interquartile range [IQR]: 4.0, 9.0; range: 1.0-41.0 cycles); 9 patients received >16 cycles.

Of the 310 patients, 230 (74.2%) reported an SAE and/or AESI. This included 109 patients with an SAE (35.2%) and 213 patients with an AESI (68.7%), including: peripheral neuropathy (n=131, 42.3%), infections (n=97, 31.3%), neutropenia (n=54, 17.4%), hypersensitivity reactions (n=34, 11.0%), and hyperglycaemia (n=4, 1.3%).

Treatment-related SAEs and/or AESIs occurred in 186 (60.0%) patients, two thirds were Grade 1-2 (n=124, 40.0%); this included 68 SAEs (21.9% of patients), and 177 AESIs (57.1% of patients). There were 3 (1.0%) deaths due to treatment-related events.

SAEs and/or AESIs led to treatment discontinuations for 42 (13.5%) patients, of which 32 (10.3%) were serious; and led to study discontinuation for 16 patients, representing 5.2% of the study population. Dose modifications occurred for 15 (4.8%) patients due to SAEs.

Risk of peripheral neuropathy increased with body mass index (BMI) (OR=1.067 [95% CI 1.023, 1.113] per unit; p=0.003); compared to patients with a normal BMI, overweight patients had an OR of 1.520 (95% CI 0.897, 2.577) and obese patients had an OR of 1.849 (95% CI 0.971, 3.523).

Discussion

These results are consistent with the known safety profile of brentuximab vedotin, with the frequency of AESIs generally lower than in previous monotherapy clinical trials. No new important risks were identified. Increased BMI was identified as a potential risk factor for the development of peripheral neuropathy. This final analysis supports the favourable safety profile in line with the established benefit/risk profile of brentuximab vedotin in patients with relapsed or refractory CD30+ HL and sALCL.

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