TREATMENT PERSISTENCE AND ADHERENCE TO IBRUTINIB IN PATIENTS WITH WALDENSTRÖM MACROGLOBULINEMIA: A GERMAN CLAIMS DATA ANALYSIS

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Background: Waldenström macroglobulinemia (WM) is an incurable condition characterized, in most patients, by symptomatic recurrences that affect the quality of life. Until recently, ibrutinib, a first-generation Bruton tyrosine kinase inhibitor, was the only agent approved in the EU for the treatment of WM. Previous research suggests that adherence to this orally-administered agent is directly related to clinical outcomes. Even if adherence to ibrutinib was reported to be high in particularly monitored clinical trial settings, the rate of ibrutinib adherence and persistence in real-world populations has hardly been investigated so far.

Aims: This study aimed to describe treatment persistence and adherence to ibrutinib in German patients with WM.

Methods: This retrospective study was conducted using anonymized claims data covering the period January 1, 2010, to June 30, 2020, provided by a regional German statutory health insurance fund (AOK PLUS) that insured approximately 3.4 million individuals in Saxony and Thuringia.

Individuals were included in the analysis if at least one inpatient diagnosis with WM (ICD-10-GM code C88.0) and/or two confirmed outpatient WM diagnoses made in different quarters were observed between January 1, 2011, and June 30, 2020. To ensure incident disease, patients had to show a diagnosis-free period of ≥12 months prior to the first observable WM diagnosis. Patients were followed from the first ibrutinib prescription (ATC-code: L01XE27) until either death, loss to follow-up, or June 30, 2020.

Non-persistence (NP) was defined as a supply gap of >90 days, with supply provided by each prescription being derived based on the defined daily dose (DDD by WHO/WIdO) of ibrutinib. Adherence was assessed by calculating the proportion of days covered (PDC) in the period where a patient was generally considered to still continue treatment with ibrutinib (i.e., no supply gap >90 days). A patient was considered non-adherent if the PDC was <80%. Adherence and persistence were assessed under the assumptions that a patient was stockpiling in case of overlapping prescriptions and that there was ongoing drug coverage during a hospitalization (base case; sensitivity scenario analysis regarding different assumptions was conducted). The sensitivity analysis also considered different gap definitions to account for the uncertainty of the concordance between the prescribed daily dosage (treating physician) and DDD (WHO/WIdO definition related to an average patient).

Time to NP was assessed using the Kaplan-Meier estimation. The PDC and rate of non-adherence were analyzed by means of descriptive statistics.

Results: A total of 483 patients with incident WM were identified during the study period, of which 23 patients initiated ibrutinib treatment (mean age: 71.8 years, females: 47.8%). Patients had an average follow-up of 321.5 days after treatment initiation. Based on the Kaplan-Meier estimates, 77.1% (95%-CI: 34.5-93.9%) of patients were still on treatment after one year. The mean PDC was 77.4% (95%-CI: 68.7-86.1%), and the proportion of patients considered non-adherent to ibrutinib accounted for 42.9% (95%-CI: 19.8-65.9%; see the base case in Table 1).

Image:

Table 1: Results of treatment adherence analysis using PDC approach and sensitivity analysis with different assumptions regarding continuation period, coverage during inpatient stays, and stockpiling

	Model assumptions			Results (assessment based on 23 patients who started treatment with ibrutinib)		
	Gap definition determining the assessment periods (periods of general therapy continuation)	Hospitalization periods considered to be covered by ibrutinib	Stockpiling allowed	Kaplan-Meier estimation of the percentage of patients with persistence to ibrutinib (treatment continuation) after one year [95% confidence interval]	Mean Proportion of Days Covered (PDC) in % [95% confidence interval]	Percentage of patients considered non-adherent (PDC<80%) [95% confidence interval]
Base Case Scenario	**90**	**Yes**	**Yes**	**77.1% [34.5% - 93.9%]**	**77.4% [68.7% - 86.1%]**	**42.9% [19.8% - 65.9%]**
Scenario 1	90	Yes	No	77.1% [34.5% - 93.9%]	74.1% [65.8% - 82.5%]	61.9% [39.3% - 84.6%]
Scenario 2	90	No	Yes	88.6% [60.7% - 97.1%]	79.6% [72.6% - 86.7%]	40.0% [16.5% - 63.5%]
Scenario 3	90	No	No	88.6% [60.7% - 97.1%]	76.4% [69.6% - 83.3%]	60.0% [36.5% - 83.5%]
Scenario 4	60	Yes	Yes	78.6% [43.0% - 93.4%]	81.4% [75.1% - 87.8%]	40.0% [16.5% - 63.5%]
Scenario 5	60	Yes	No	78.6% [43.0% - 93.4%]	77.9% [71.6% - 84.1%]	60.0% [36.5% - 83.5%]
Scenario 6	60	No	Yes	76.9% [48.8% - 90.8%]	81.0% [74.6% - 87.4%]	40.0% [16.5% - 63.5%]
Scenario 7	60	No	No	76.9% [48.8% - 90.8%]	77.6% [71.3% - 83.9%]	60.0% [36.5% - 83.5%]
Scenario 8	180	Yes	Yes	100.0% [.]	77.4% [68.7% - 86.1%]	42.9% [19.8% - 65.9%]
Scenario 9	180	Yes	No	100.0% [.]	74.1% [65.8% - 82.5%]	61.9% [39.3% - 84.6%]
Scenario 10	180	No	Yes	93.3% [61.3% - 99.0%]	76.8% [67.9% - 85.7%]	42.9% [19.8% - 65.9%]
Scenario 11	180	No	No	93.3% [61.3% - 99.0%]	73.8% [65.2% - 82.3%]	61.9% [39.3% - 84.6%]
Scenario 12	2 x DDD*	Yes	Yes	74.0% [41.3% - 90.2%]	83.0% [77.8% - 88.2%]	35.0% [12.1% - 57.9%]
Scenario 13	2 x DDD*	Yes	No	63.4% [29.9% - 84.2%]	79.6% [74.3% - 84.8%]	55.0% [31.1% - 78.9%]
Scenario 14	2 x DDD*	No	Yes	61.2% [30.8% - 81.4%]	82.8% [77.7% - 87.8%]	35.0% [12.1% - 57.9%]
Scenario 15	2 x DDD*	No	No	61.2% [30.8% - 81.4%]	79.3% [74.0% - 84.6%]	55.0% [31.1% - 78.9%]

**Gap larger than two times the days supplied with the previous prescription (based on the defined daily dose - DDD)*

Summary/Conclusion: This study suggests that a substantial portion of WM patients have limited adherence and persistence to orally administered ibrutinib. Further nationwide studies with larger sample sizes may be required to confirm the results.