

Supplementary information for:

FIRE Study: Real-World Effectiveness and Safety of Ibrutinib in Clinical Practice in Patients

With CLL and MCL

Clinical Hematology International

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Supplementary Table 1 Most common ($\geq 2\%$ all events) severe TEAEs by system organ class and preferred term, split by relationship with ibrutinib: prospective CLL/SLL patients in safety population

System Organ Class			
Preferred Term	Related	Not Related	All Events
At least one severe TEAE, <i>n</i> (%)	72 (35.6)	64 (31.7)	110 (54.5)
Blood and lymphatic system disorders, <i>n</i> (%)	42 (20.8)	20 (9.9)	54 (26.7)
Lymphocytosis	24 (11.9)	3 (1.5)	26 (12.9)
Thrombocytopenia	8 (4.0)	6 (3.0)	14 (6.9)
Neutropenia	9 (4.5)	7 (3.5)	13 (6.4)
Anemia	3 (1.5)	6 (3.0)	9 (4.5)
Hyperleukocytosis	7 (3.5)	1 (0.5%)	8 (4.0)
Infections and infestations, <i>n</i> (%)	8 (4.0)	13 (6.4)	20 (9.9)
Septic shock	3 (1.5)	3 (1.5)	6 (3.0)
Investigations, <i>n</i> (%)	11 (5.4)	2 (1.0)	13 (6.4)
Lymphocyte count increased	8 (4.0)	0	8 (4.0)
Neoplasms benign, malignant and unspecified (including cysts and polyps), <i>n</i> (%)	2 (1.0)	10 (5.0)	12 (5.9)
Richter's syndrome	1 (0.5)	3 (1.5)	4 (2.0)
Respiratory, thoracic, and mediastinal disorders, <i>n</i> (%)	3 (1.5)	9 (4.5)	12 (5.9)
Lung disorder	2 (1.0)	6 (3.0)	8 (4.0)
General disorders and administration site conditions, <i>n</i> (%)	5 (2.5)	5 (2.5)	10 (5.0)
Asthenia	3 (1.5)	2 (1.0)	5 (2.5)
General physical health deterioration	1 (0.5)	3 (1.5)	4 (2.0)

System Organ Class			
Preferred Term	Related	Not Related	All Events
Cardiac disorders, <i>n</i> (%)	5 (2.5)	4 (2.0)	9 (4.5)
Cardiac failure	3 (1.5)	1 (0.5)	4 (2.0)
Nervous system disorders, <i>n</i> (%)	4 (2.0)	5 (2.5)	9 (4.5)
Musculoskeletal and connective tissue disorders, <i>n</i> (%)	2 (1.0)	6 (3.0)	8 (4.0)
Gastrointestinal disorders, <i>n</i> (%)	2 (1.0)	4 (2.0)	6 (3.0)
Injury, poisoning, and procedural complications, <i>n</i> (%)	1 (0.5)	4 (2.0)	5 (2.5)
Skin and subcutaneous tissue disorders, <i>n</i> (%)	3 (1.5)	2 (1.0)	5 (2.5)
Metabolism and nutrition disorders, <i>n</i> (%)	1 (0.5)	3 (1.5)	4 (2.0)
Surgical and medical procedures, <i>n</i> (%)	0	4 (2.0)	4 (2.0)
Vascular disorders, <i>n</i> (%)	2 (1.0)	2 (1.0)	4 (2.0)

CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma; TEAE, treatment-emergent adverse event.

Supplementary Table 2 Most common ($\geq 1\%$ all events) infections and infestation TEAEs in patients with CLL/SLL

System Organ Class			
Preferred Term	Related	Not Related	Total
Infections and infestations, <i>n</i> (%)	26 (12.9)	85 (42.1)	108 (53.5)
Bronchitis, <i>n</i> (%)	3 (1.5)	23 (11.4)	26 (12.9)
Urinary tract infection, <i>n</i> (%)	0	11 (5.4)	11 (5.4)
Influenza, <i>n</i> (%)	0	7 (3.5)	7 (3.5)
Septic shock, <i>n</i> (%)	3 (1.5)	3 (1.5)	6 (3.0)
Sinusitis, <i>n</i> (%)	1 (0.5)	5 (2.5)	6 (3.0)
Erysipelas, <i>n</i> (%)	2 (1.0)	3 (1.5)	5 (2.5)
Fungal infection, <i>n</i> (%)	1 (0.5)	4 (2.0)	5 (2.5)
Rhinitis, <i>n</i> (%)	2 (1.0)	3 (1.5)	5 (2.5)
Ear infection, <i>n</i> (%)	0	4 (2.0)	4 (2.0)
Infection, <i>n</i> (%)	1 (0.5)	3 (1.5)	4 (2.0)
Nasopharyngitis, <i>n</i> (%)	0	4 (2.0)	4 (2.0)
Pharyngitis, <i>n</i> (%)	0	4 (2.0)	4 (2.0)
Sepsis, <i>n</i> (%)	1 (0.5)	3 (1.5)	4 (2.0)
Conjunctivitis, <i>n</i> (%)	0	2 (1.0)	3 (1.5)
Pneumonia, <i>n</i> (%)	0	2 (1.0)	3 (1.5)
Upper respiratory tract infection, <i>n</i> (%)	0	3 (1.5)	3 (1.5)
Cystitis, <i>n</i> (%)	0	2 (1.0)	2 (1.0)
Gastroenteritis, <i>n</i> (%)	0	2 (1.0)	2 (1.0)
Herpes zoster, <i>n</i> (%)	1 (0.5)	1 (0.5)	2 (1.0)

System Organ Class			
Preferred Term	Related	Not Related	Total
Lung infection, <i>n</i> (%)	0	2 (1.0)	2 (1.0)
Onychomycosis, <i>n</i> (%)	1 (0.5)	1 (0.5)	2 (1.0)
Paronychia, <i>n</i> (%)	0	2 (1.0)	2 (1.0)
<i>Pneumocystis jirovecii</i> pneumonia, <i>n</i> (%)	2 (1.0)	0	2 (1.0)
Pneumonia pneumococcal, <i>n</i> (%)	1 (0.5)	1 (0.5)	2 (1.0)
Viral infection, <i>n</i> (%)	0	2 (1.0)	2 (1.0)

CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma; TEAE, treatment-emergent adverse event.

Supplementary Table 3 Most common ($\geq 2\%$ all events) severe TEAEs by system organ class and preferred term split by relationship with ibrutinib: prospective MCL patients in safety population

System Organ Class			
Preferred Term	Related	Not Related	All Events
At least one severe TEAE, <i>n</i> (%)	12 (20.3)	30 (50.8)	36 (61.0)
General disorders and administration site conditions, <i>n</i> (%)	1 (1.7)	14 (23.7)	15 (25.4)
General physical health deterioration	0	13 (22.0)	13 (22.0)
Asthenia	1 (1.7)	1 (1.7)	2 (3.4)
Blood and lymphatic system disorders, <i>n</i> (%)	4 (6.8)	5 (8.5)	9 (15.3)
Thrombocytopenia	1 (1.7)	3 (5.1)	4 (6.8)
Lymphocytosis	2 (3.4)	1 (1.7)	3 (5.1)
Neutropenia	2 (3.4)	1 (1.7)	3 (5.1)
Anemia	0	2 (3.4)	2 (3.4)
Infections and infestations, <i>n</i> (%)	2 (3.4)	6 (10.2)	8 (13.6)
Respiratory, thoracic, and mediastinal disorders, <i>n</i> (%)	2 (3.4)	4 (6.8)	6 (10.2)
Dyspnea	1 (1.7)	2 (3.4)	3 (5.1)
Lung disorder	0	2 (3.4)	2 (3.4)
Cardiac disorders, <i>n</i> (%)	3 (5.1)	1 (1.7)	4 (6.8)
Atrial fibrillation	2 (3.4)		2 (3.4)

System Organ Class			
Preferred Term	Related	Not Related	All Events
Injury, poisoning, and procedural complications, <i>n</i> (%)	1 (1.7)	2 (3.4)	3 (5.1)
Metabolism and nutrition disorders, <i>n</i> (%)	0	2 (3.4)	2 (3.4)
Tumor lysis syndrome	0	2 (3.4)	2 (3.4)
Nervous system disorders, <i>n</i> (%)	0	2 (3.4)	2 (3.4)

MCL, mantle cell lymphoma; TEAE, treatment-emergent adverse event.

Supplementary Table 4 Infections and infestation TEAEs in patients with MCL

All Events			
System Organ Class			
Preferred Term	Related	Not Related	Total
Infections and infestations, <i>n</i> (%)	5 (8.5)	17 (28.8)	19 (32.2)
Bronchitis, <i>n</i> (%)	0	3 (5.1)	3 (5.1)
Urinary tract infection	1 (1.7)	3 (5.1)	3 (5.1)
Lung infection, <i>n</i> (%)	0	2 (3.4)	2 (3.4)
Pneumonia, <i>n</i> (%)	0	2 (3.4)	2 (3.4)
Bacterial sepsis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Campylobacter gastroenteritis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Conjunctivitis bacterial, <i>n</i> (%)	1 (1.7)	0	1 (1.7)
Enterobacter infection, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Escherichia sepsis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Folliculitis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Gastroenteritis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Herpes zoster, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Hordeolum, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Infection, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Influenza, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Nocardiosis, <i>n</i> (%)	1 (1.7)	0	1 (1.7)
Paronychia, <i>n</i> (%)	1 (1.7)	1 (1.7)	1 (1.7)
Peritonitis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
<i>Pneumocystis jirovecii</i> pneumonia, <i>n</i> (%)	1 (1.7)	0	1 (1.7)

All Events			
System Organ Class			
Preferred Term	Related	Not Related	Total
Sepsis, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Systemic candida, <i>n</i> (%)	0	1 (1.7)	1 (1.7)
Upper respiratory tract infection, <i>n</i> (%)	0	1 (1.7)	1 (1.7)

MCL, mantle cell lymphoma; TEAE, treatment-emergent adverse event.