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A1364
JACC March 17, 2015
Volume 65, Issue 10S

Prevention

TWO YEAR ANALYSIS OF THE SAFETY AND TOLERABILITY OF EVOLOCUMAB: THE OSLER-1 STUDY

Oral Contributions
Room 6B
Monday, March 16, 2015, 11:45 a.m.-11:57 a.m.

Session Title: Highlighted Original Research: Prevention and the Year in Review
Abstract Category: 21. Prevention: Clinical
Presentation Number: 914-10

Authors: *Michael J. Koren, Robert Giugliano, Frederick Raal, David Sullivan, Michael Bolognese, Gisle Langslet, Fernando Civeira, Andrew Lowy, Ransi Somaratne, Thomas Liu, Scott Wasserman, Robert Scott, Marc Sabatine, Amgen Inc., Thousand Oaks, CA, USA*

Background: The OSLER-1 study previously reported that SC evolocumab, a monoclonal antibody against PCSK9, markedly lowered and maintained LDL-C levels with a favorable safety profile, over 52 weeks. We now evaluate the efficacy, safety and persistence of evolocumab treatment over ~2 years (y).

Methods: OSLER randomized patients (pts) who completed short-term, double-blind, controlled studies of evolocumab to standard of care (SOC) vs SOC plus evolocumab 420 mg monthly (QM) for one year. After Y 1, all pts were to receive QM evolocumab. We analyzed persistence of therapy and AE rates for pts initially randomized to evolocumab and stratified by achieved LDL-C (<25, <50, or ≥50 mg/dL).

Results: Of 1104 OSLER pts initially enrolled, 734 were randomized to evolocumab on or prior to July 1, 2012. At the end of Y 2, 590 were still receiving evolocumab -- a persistence rate of 80% for this period. As of July 1, 2014, the median exposure was 28 months. LDL-C lowering was sustained for over two years (54% at week 52, 52% at week 124). Of pts on evolocumab during Y 1 and 2, 34 (4.5%) discontinued due to an AE. Safety and tolerability were comparable regardless of achieved LDL-C (Table).

Conclusion: In the longest term data reported to date with a PCSK9 inhibitor, monthly evolocumab therapy was effective and well tolerated with high rates of treatment persistence for over two years indicating excellent patient acceptance of and response to parenteral therapy for hypercholesterolemia.

Table. OSLER-1 Safety Over 2 Years

Patient incidence, n (%)	Minimum Post Baseline LDL-C Values			All subjects (N = 734)
	LDL-C < 25 mg/dL (N =233)	LDL-C < 50 mg/dL (N = 534)	LDL-C ≥ 50 mg/dL (N = 198)	
SAE	35 (15.0)	73 (13.7)	40 (20.2)	113 (15.4)
AE leading to discontinuation	3 (1.3)	14 (2.6)	19 (9.6)	33 (4.5)
Fatal AE	1 (0.4)	4 (0.7)	0 (0)	4 (0.5)
Injection site reaction*	14 (6.0)	31 (5.8)	24 (12.1)	55 (7.5)
Muscle-related AE	0 (0)	1 (0.2)	0 (0)	1 (0.1)
Neurocognitive AE	2 (0.9)	8 (1.5)	2 (1.0)	10 (1.4)
Creatine kinase > 5X ULN	7 (3.0)	11 (2.1)	4 (2.0)	15 (2.0)
ALT or AST > 3X ULN	3 (1.3)	10 (1.9)	9 (4.5)	19 (2.6)

Data cutoff date July 1st, 2014
Abbreviations: SAE, serious adverse event; AE, adverse event; ULN, upper limit of normal; ALT,alanine aminotransferase; AST, aspartate aminotransferase
*Annualized event rates: 2.5% (LDL-C < 25 mg/dL), 2.5% (LDL-C < 50 mg/dL), 5.5% (LDL-C ≥ 50 mg/dL), 3.0% (total)
Study Funding: Amgen, Inc.