RWD94

Healthcare Resource Utilization Associated With Acute Pancreatitis in Patients with Familial Chylomicronemia Syndrome Treated with Olezarsen: A Post-Hoc Analysis of Balance Study Data

Asia Sikora Kessler[1], Montserrat Vera Llonch[1], Veronica J. Alexander[1], Catrina Richards[2], Quratul Ann[2], Catalina Mejía Herrera[3], Spyros Paparrodopoulos[4], Shuting Xia[1], Sotirios Tsimikas[1,5], Seth J. Baum[6]

1. Ionis Pharmaceuticals, Inc, Carlsbad, CA, US; 2. IQVIA Ltd, London, UK; 3. IQVIA Ltd, Frankfurt, Germany; 4. IQVIA Ltd, Athens, Greece; 5. Vascular Medicine Program, Sulpizio Cardiovascular Center, University of California San Diego, La Jolla, CA, US; 6. Flourish Research, Boca Raton, FL

BACKGROUND

- Olezarsen is a triantennary N-acetyl galactosamine-conjugated antisense oligonucleotide that targets hepatic apolipoprotein (Apo) C-III messenger RNA for degradation. It is approved in the US by the Food and Drug Administration and in the European Union at a recommended dose of 80 mg as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS), a rare genetic disorder characterized by severe hypertriglyceridemia and a high risk of acute pancreatitis[1-4]
- The Balance study, a phase 3, international, multicenter, randomized, double-blind, placebo-controlled trial, assessed olezarsen versus placebo in 66 patients with FCS and fasting triglyceride levels ≥880 mg/dL at screening[5]
- This analysis evaluated adjudicated pancreatitis (AP)- and AP- or abdominal pain-related healthcare resource utilization (HCRU) among patients from the study.

METHODS

- This was a post-hoc analysis of the Balance study
- **Intervention**: Patients were randomized 2:1 to receive olezarsen (50 mg or 80 mg) or placebo, administered by subcutaneous injection every 4 weeks for 53 weeks
- **Analyses**: The analyses were conducted separately to assess hospitalizations, total inpatient days, intensive care unit (ICU) admissions, length of hospital stay (LOS), and emergency room (ER) visits in each olezarsen dose group (50 or 80 mg every 4 weeks) and the pooled group (50 mg and 80 mg) versus placebo over a 53-week treatment period
  - Negative binomial regression models were used to estimate annualized adjusted least-squares mean rates (LSMRs) and mean rate ratios (MRRs) with 95% confidence intervals.
  - ANCOVA was used to compare inpatient days.

RESULTS

Table 1. Baseline Patient Characteristics[5]

	Placebo N=23	Olezarsen 50-mg N=21	Olezarsen 80-mg N=22
Mean (SD) age, years	44.0 (14.7)	43.2 (12.1)	47.7 (13.3)
Male, n (%)	11 (47.8)	6 (28.6)	11 (50.0)
Mean (SD) BMI, kg/m^2	24.2 (4.1)	22.4 (3.5)	25.1 (6.0)
Type 1 or 2 diabetes, n (%)	6 (26.1)	3 (14.3)	7 (31.8)
AP in previous 10 years, n (%)	15 (65.2)	15 (71.4)	17 (77.3)
Had previous treatment with volanesorsen, n (%)	10 (43.5)	8 (38.1)	8 (36.4)

AP, acute pancreatitis; BMI, body mass index; N or n, number of patients; SD, standard deviation

Table 2. Reasons for Hospitalization and ER visits

	Treatment Arm				
	Overall N=66	Placebo N=23	Olezarsen 50-mg N=21	Olezarsen 80-mg N=22	Pooled Olezarsen N=43
Hospitalization (n, %)					
Abdominal pain/non-AP	3 (4.55)	2 (8.70)	0 (0.00)	1 (4.55)	1 (2.33)
AP	9 (13.64)	7 (30.43)	1 (4.76)	1 (4.55)	2 (4.65)
ER (n, %)					
Abdominal pain/stomach pain	4 (6.06)	2 (8.70)	0 (0.00)	2 (9.09)	2 (4.65)

N = number of randomized patients in each treatment group; n = number of patients in the specified category; A patient can be included in more than one category if there are multiple reasons for events are recorded.

Table 3. Rate Ratios for ICU Admission Rates*

	Rate Ratio (95% CI)
Any patients hospitalized for AP	
Olezarsen 80-mg	1.25 (0.70 - 2.24)
Olezarsen 50-mg	N.C.
Pooled Olezarsen	0.50 (0.30 - 0.83)
Any patients hospitalized for AP or abdominal pain	
Olezarsen 80-mg	1.25 (0.70 - 2.24)
Olezarsen 50-mg	N.C.
Pooled Olezarsen	0.50 (0.30 - 0.83)

* Reference group: Placebo; N.C.: Not calculable

Figure 1a. AP-related Hospitalizations Annualized Rate

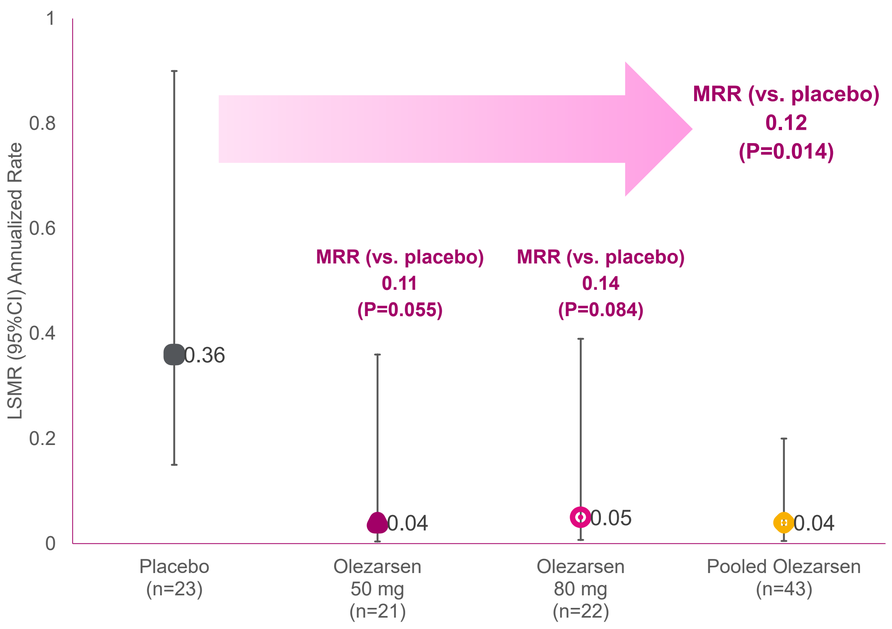
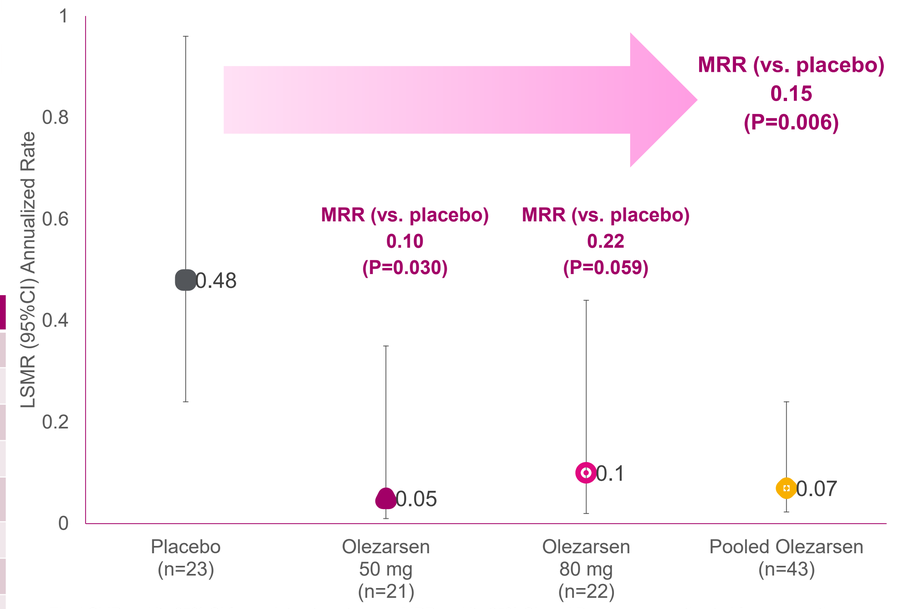
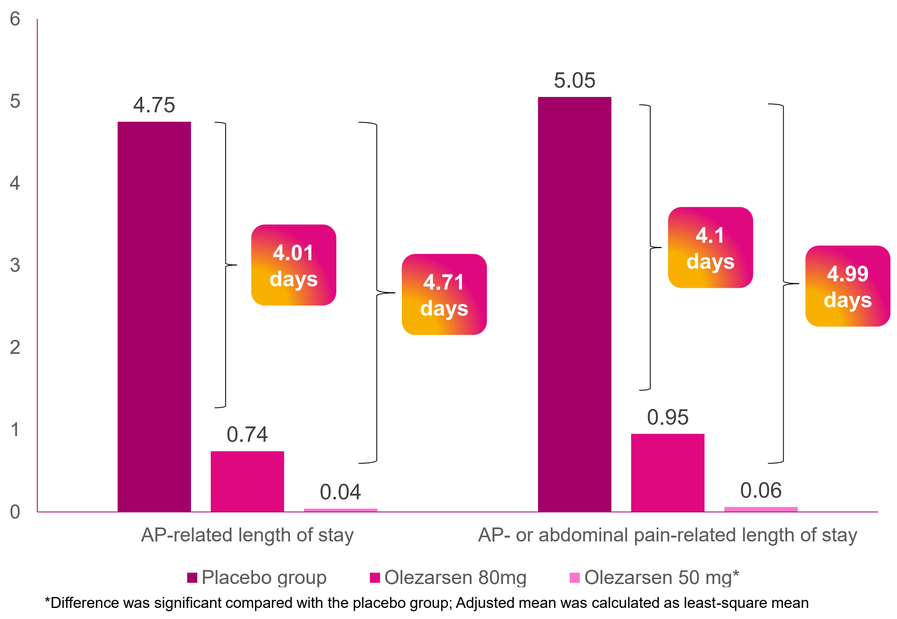


Figure 1b. AP- or Abdominal Pain-related Hospitalizations Annualized Rate



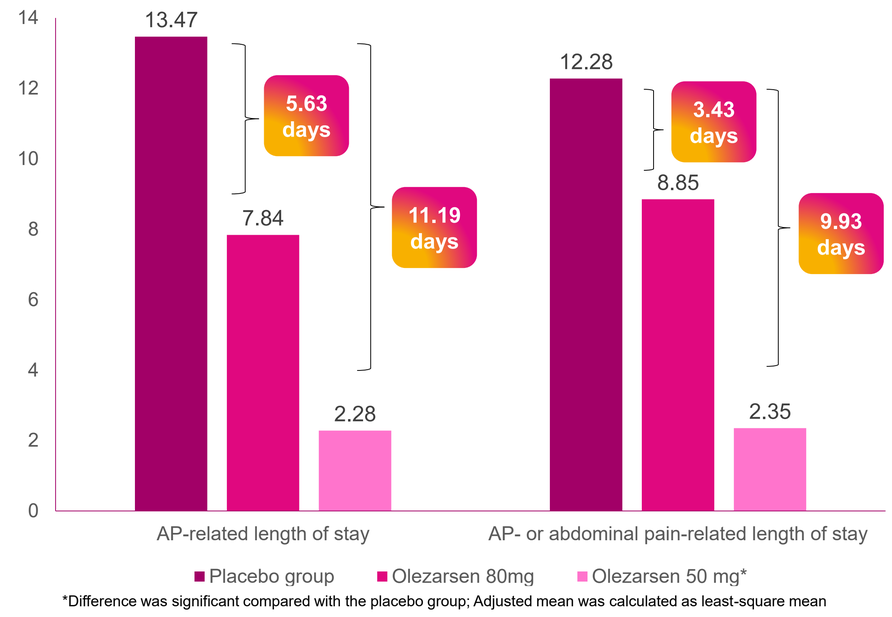
The LSMR and its 95% CI for each treatment group, MRR and its 95% CI, and P-value were estimated from a negative binomial regression model with the treatment group and 2 randomization stratification factors as the fixed effect. The logarithm of time in year that each patient was observed from Week 1 to Week 53 or early termination was used as an offset variable. Abbreviations: CI, confidence interval; LSMR, least squares mean rate; MRR, mean rate ratio.

Figure 2. Adjusted Mean Total Inpatient Days of AP-related and AP- or Abdominal Pain-related Hospitalizations



*Difference was significant compared with the placebo group; Adjusted mean was calculated as least-square mean

Figure 3. Adjusted Mean Length of Stay (days) of AP-related and AP- or Abdominal Pain-related Hospitalizations



*Difference was significant compared with the placebo group; Adjusted mean was calculated as least-square mean

RESULTS

- In the Balance study, two patients in the pooled olezarsen group (one in each dose group) and seven patients in the placebo group were hospitalized for AP.
- The yearly LSMRs of AP-related hospitalizations were significantly lower in the pooled olezarsen group than in the placebo group, consistent with an 88% reduction (0.04 vs 0.36; MRR, 0.12; P=0.014), with fewer total annual inpatient days (−4.36 days, P=0.0274).
  - AP-related and AP- or abdominal pain-related total inpatient days were longer in the placebo group than in the olezarsen treatment groups.
- The annualized ICU admission rate in the pooled olezarsen group was 50% lower (rate ratio: 0.50 [95% CI: 0.30, 0.83]) versus placebo.
- AP-related LOS was longer in the placebo group (12.95 days) than in the pooled olezarsen group (5.29 days).
- Similar results were observed for AP- or abdominal pain-related HCRU.
- ER visits were rare in all treatment groups; no AP-related ER visits were observed.

CONCLUSIONS

- In the Balance study, olezarsen was associated with fewer AP- and AP- or abdominal pain-related hospitalizations and reduced inpatient days versus placebo in patients with FCS, suggesting clinical and economic benefit with olezarsen treatment.
- Findings for inpatient days and LOS should be interpreted with caution due to the small number of events observed in each treatment arm.
- Long-term data from clinical practice is expected to provide additional supportive evidence.

DISCLOSURES

- ASK, MVL, VJA, SX and ST are employees and stockholders of Ionis; CB, QA, CMH and SP are employees of IQVIA Ltd. IQVIA received funding from Ionis Pharmaceuticals for the running of the study; SB is an investigator and consultant for Ionis Pharmaceuticals

REFERENCES

1. Tryngolza highlights of prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218614s000lbl.pdf
2. Brown EE, et al. J Clin Lipidol. 2020;14(4):398–413.
3. Pothoulakis I, et al. Digestion. 2021;102(5):809–13.
4. Davidson M, et al. J Clin Lipidol. 2018;12(4):898–907.e2.
5. Stroes ESG, et al. N Engl J Med. 2024;390(19):1781–92

ACKNOWLEDGEMENT

- Medical writing, layout design and content development support were provided by Weiying Wang, funded by Ionis

contact: MVeraLlonch@ionis.com