Clinical Value of Olezarsen in Preventing the First Acute Pancreatitis Event in Severe Hypertriglyceridemia: A UK Modelling Study

Nana Kragh[1], Zalmai Hakimi[1], Jameel Nazir[1], Michał Pochopień[2], Tobiasz Lemański[2], Wiktoria Miszczyk[2]

[1]Sobi, Sweden; [2]Clever-Access, Kraków, Poland

CONCLUSIONS

Preventing the first AP event in sHTG is **critical in reducing overall disease burden**.

According to the modelling, TG lowering with olezarsen substantially decreases first AP events and **prevents a cascade of subsequent complications** across multiple organ systems.

The greatest clinical benefit is achieved when treatment is initiated prior to the first AP event supporting a proactive treatment approach in high-risk sHTG patients.

INTRODUCTION

- Severe hypertriglyceridemia (sHTG) substantially increases the risk of acute pancreatitis (AP), particularly at triglyceride levels ≥880 mg/dL. The first AP event may trigger recurrent episodes and long-term complications, highlighting the importance of prevention.

OBJECTIVES

To model the clinical value of preventing the first AP event in patients with sHTG treated with olezarsen, measured by:

- The number of first and recurrent AP events prevented.
- The number of downstream AP-related and cardiometabolic complications avoided.
- Outcomes were compared between treatment initiation before and after the first AP event.

METHODS

- **Model type**: A UK population-based Markov cohort model was developed to simulate annual transitions over a 10-year time horizon, comparing olezarsen + standard of care (SoC) with SoC alone in patients with sHTG (TG ≥880 mg/dL).
- **Population:** The model represented a cohort of 10,000 patients with TG ≥880 mg/dL (83.28% male; mean age 51.6 years; 61% with diabetes; no prior history of cardiovascular (CV) events). Patients were stratified into three clinical subgroups: AP-naïve (97.2%), post-first AP (1.05%), and post-recurrent AP (1.75%). The AP-naïve proportion was derived from Patel et al. (2022)[5], while the remaining patients were allocated to the post-first AP and post-recurrent AP subgroups based on AP event distributions observed in the CORE and CORE2 trials[1].
- **Model structure:** The model includes five health states: three stratified by different AP history categories, one for chronic pancreatitis (CP), and one absorbing death state. The cohort was followed annually in both treatment arms. Treatment effects were modelled through changes in TG-category distribution based on the TG reductions observed in the trial, with patients with baseline TG ≥880 mg/dL distributed as 10.8% remaining ≥880 mg/dL, 25.7% reaching 500–<880 mg/dL, 52.0% reaching 150–<500 mg/dL, and 11.5% achieving <150 mg/dL with olezarsen.
- Treatment-specific TG distributions were linked to risks of first and recurrent AP, new-onset diabetes (based on unpublished post hoc analyses of CALIBER data[2]), and TG-category-specific risks of CV events[6], renal events[7,8], and all-cause mortality[5] obtained from published literature. The model also incorporated CP risk conditional on AP history, and the probability of fatal AP. Key clinical inputs are summarized in Table 2.

Table 1: Annual risk of AP depending on the history of AP events (CALIBER[2])

AP history / TG level	< 150 mg/dL	150 – 500 mg/dL	500 – 880 mg/dL	>880 mg/dL
AP naïve	0.04%	0.06%	0.09%	0.66%
After first AP	3.66%	3.66%	4.57%	15.46%
After recurrent AP	10.43%	10.43%	12.90%	38.16%

Table 2: Annual clinical inputs

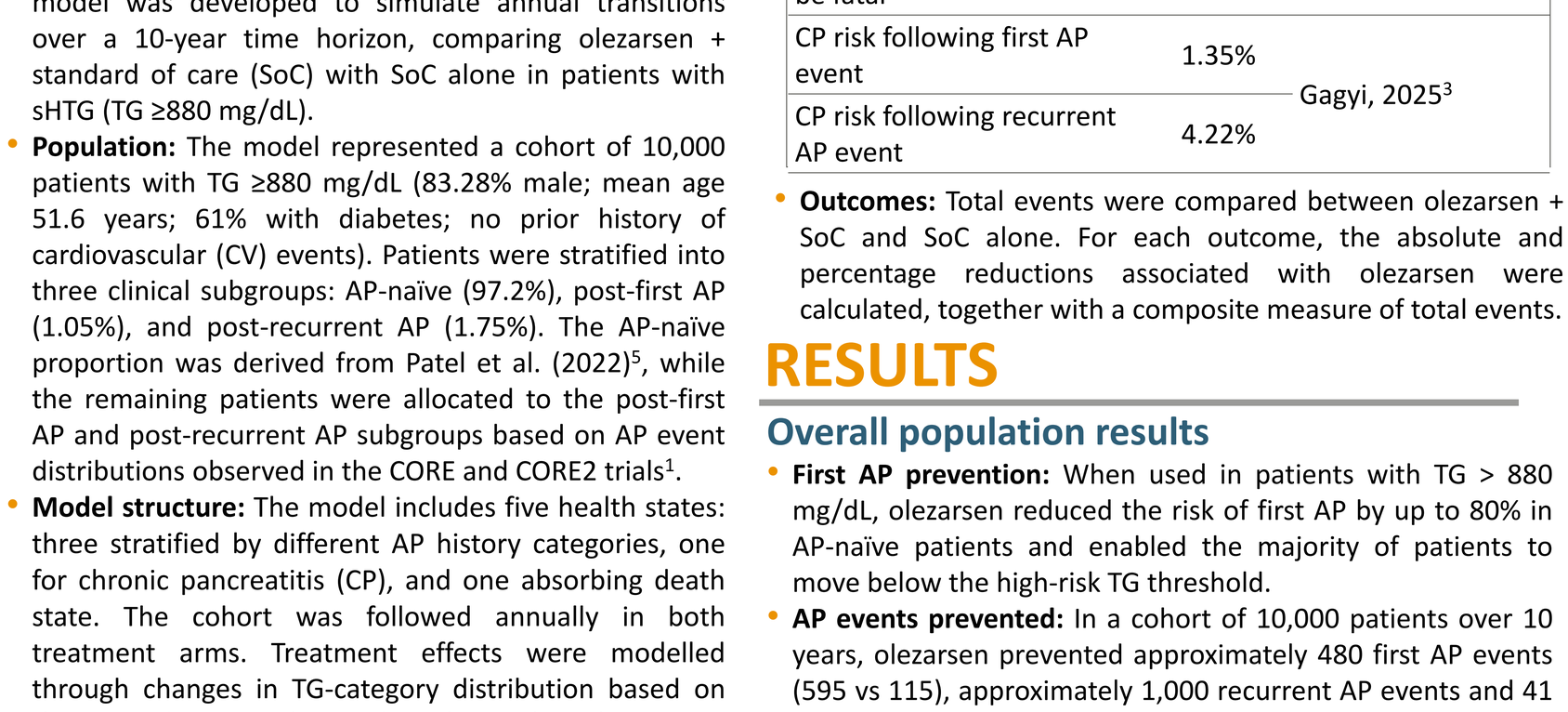
Parameter	Value	Source
TG dependent inputs		
CV events risk	0.33-1.03%	Sikora Kessler, 2025[6]
CKD risk	0.23-0.92%	Qin et al., 2024[8], Weon et al., 2024[7]
Risk of new-onset diabetes in AP-naïve	3.1-26.7%	CALIBER[2]
Risk of new-onset diabetes with prior AP	11-63%	
Increased mortality (HR)	1.00-3.62	Patel, 2022[5]
TG independent inputs		
Probability of AP event to be fatal	6.9%	Roberts, 2014[4]
CP risk following first AP event	1.35%	Gagyi, 2025[3]
CP risk following recurrent AP event	4.22%	

- **Outcomes:** Total events were compared between olezarsen + SoC and SoC alone. For each outcome, the absolute and percentage reductions associated with olezarsen were calculated, together with a composite measure of total events.

RESULTS

Overall population results

- **First AP prevention:** When used in patients with TG > 880 mg/dL, olezarsen reduced the risk of first AP by up to 80% in AP-naïve patients and enabled the majority of patients to move below the high-risk TG threshold.
- **AP events prevented:** In a cohort of 10,000 patients over 10 years, olezarsen prevented approximately 480 first AP events (595 vs 115), approximately 1,000 recurrent AP events and 41 CP events (123 vs 82).
- **Reduction in downstream complications:** More than 4,800 complications were prevented including 1,940 new-onset diabetes events, 397 CV events, 535 renal events prevented and 416 death (Figure 1).



AP history subgroups comparison

- **Greater benefit in AP-naïve patients**: Larger reduction in complication prevalence in AP-naïve patients and their predominance (97.2% vs 2.8%) translate into a significantly greater total number of avoided events in AP-naïve patients compared to patients with AP history (4,248 vs 585, respectively, Table 3).
- Olezarsen reduced the number of events in patients with a history of AP, although the reduction was lower than in AP-naïve patients (52% vs 57%, respectively). This difference is mainly driven by the substantial reduction in first AP events among AP-naïve patients (81% reduction). **By preventing these initial episodes, olezarsen also markedly reduced the occurrence of subsequent AP events, resulting in a 95% reduction in recurrent AP events.**
- In patients with AP history, olezarsen reduced the number of recurrent AP by 64% and fatal AP by 64%.
- The reduction in the incident cases of CP and new-onset diabetes was −1.3% and −5%, respectively, compared with −85% and −54% in AP-naïve patients.
- CV and renal benefit was comparable between the two groups (stroke/MI: −36% vs −40%; CKD: −59% vs −62%).

Table 3: Summary of outcomes by AP history

Outcome	Without AP history			With AP history		
	Without olezarsen	With olezarsen		Without olezarsen	With olezarsen	
First AP	595	115	**-81%**	-	-	-
Recurrent AP	538	30	**-95%**	808	292	**-64%**
Fatal AP	78	10	**-87%**	56	20	**-64%**
CP	49	8	**-85%**	75	74	**-1.3%**
New-onset diabetes	3,583	1,649	**-54%**	118	112	**-5%**
CV events	966	579	**-40%**	25	16	**-36%**
Renal events	846	324	**-62%**	22	9	**-59%**
Deaths	777	470	**-39%**	25	20	**-22%**
Total	7,431	3,183	**-57%**	1,129	543	**-52%**

REFERENCES

1. Sobi. CORE and CORE2 trials' data. Data on file.
2. Akcea. Data on file: CALIBER
3. Gagyi E-B et al. Ther Adv Gastroenterol. 2024;17. doi:10.1177/17562848241255303.
4. Roberts SE, et al. BMC Gastroenterol. 2014;14:153.
5. Patel RS et al. Cardiovasc Diabetol. 2022;21:102. doi:10.1186/s12933-022-01525-5.
6. Sikora-Kessler A et al. Lipids Health Dis. 2025;24:252. doi:10.1186/s12944-025-02658-8.
7. Weon B et al. PLoS One. 2024;19(4):e0299605. doi:10.1371/journal.pone.0299605.
8. Qin K et al. BMC Public Health. 2024;24:3519.
9. Major RW et al. PLoS Med. 2019;16(11):e1002955. doi:10.1371/journal.pmed.1002955.

ACKNOWLEDGEMENTS

This analysis was funded by Sobi. The authors also wish to acknowledge Emma Ismail from Clever-Access (Tunis, Tunisia), for medical writing and editorial support, funded by Sobi, based on the authors' input and direction, and in accordance with Good Publication Practice (GPP) 2022 guidelines (https://www.ismpp.org/gpp-2022).

DISCLOSURES

NK, ZH, JN: Employees of Sobi. **MP, TL, WM**: Employees of Clever-Access, which received consultancy fees from Sobi for the analyses presented in this poster.

Copies of this poster obtained through QR code are for personal use only.

Nana Kragh| Nana.Kragh@sobi.com