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Outcomes in Patients Receiving Oral Octreotide Capsules Related to Time From Last SRL Injection: Analysis From the MPOWERED Phase 3 Study

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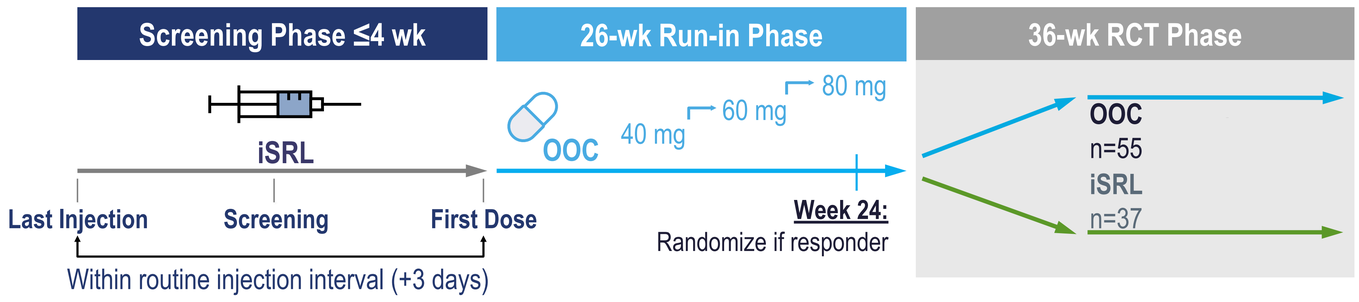
Introduction

- Recent updates to acromegaly treatment guidelines recommend that oral octreotide capsules (OOC) should be initiated circa the time of the next scheduled injectable somatostatin receptor ligand (iSRL) dose, as was performed in the OPTIMAL study[1,2]
- In the MPOWERED phase 3 trial (NCT02685709), OOC could be initiated any time after the last injection up until the time of the next schedule injection +3 days[3]
- The impact of earlier initiation of OOC on safety and efficacy has not been previously investigated
- The objective of this analysis is to describe clinical and safety outcomes based on the time since the last iSRL dose and initiation of OOC during the 26-week Run-in phase of MPOWERED

Study Design

Inclusion criteria
- On a stable dose of iSRL for ≥4 months
- Biochemical response (IGF–I <1.3 × ULN and integrated GH <2.5 ng/mL) at screening



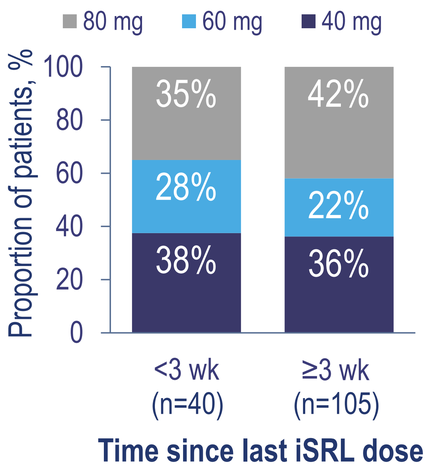
	Populations Assessed	
Time since last iSRL dose	<3 wk (n=40)	≥3 wk (n=105)

GH, growth hormone; IGF-I, insulin-like growth factor I; iSRL, injectable somatostatin receptor ligand; OOC, oral octreotide capsules; RCT, randomized controlled treatment; SRL, somatostatin receptor ligand; ULN, upper limit of normal; wk, week.

Results

Time since last iSRL dose did not impact final OOC dose in the Run-in phase

Final OOC Dose in Run-in Phase

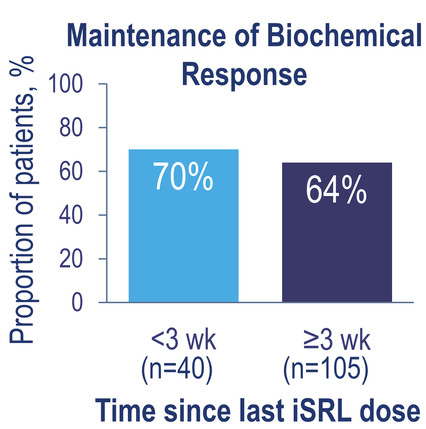


Time since last iSRL dose

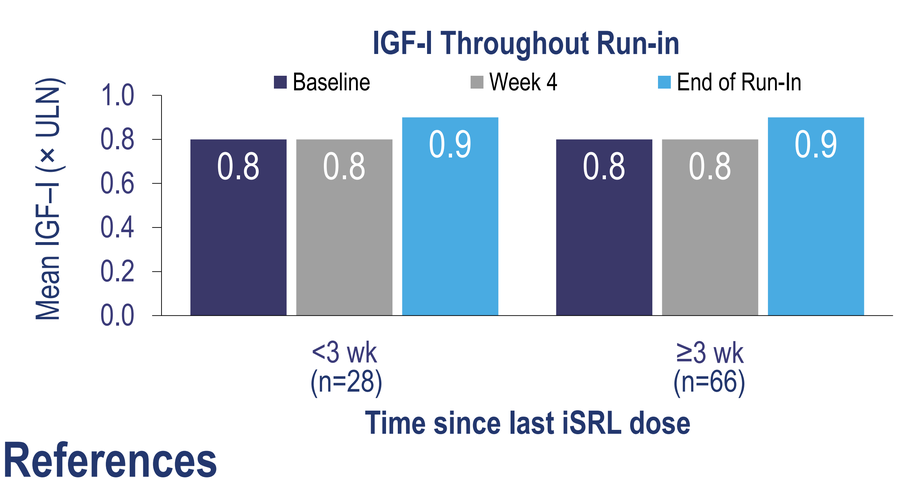
	<3 wk (n=40)	≥3 wk (n=105)
Completed Run-in phase, n (%)	35 (87.5)	81 (77.1)
Reasons for discontinuation, n (%)		
AE	1 (2.5)	13 (12.4)
Treatment failure	2 (5.0)	5 (4.8)
Withdrawal by subject	2 (5.0)	4 (3.8)
Protocol deviation	0	1 (1.0)
Investigator request	0	1 (1.0)

AE, adverse event.

IGF-I levels and maintenance of biochemical response (IGF-I <1.3 × ULN) were comparable during the Run-in phase, regardless of timing of OOC initiation



- Biochemical response was maintained in similar proportions in each group
- When evaluating the population of biochemical responders at the end of Run-in, mean IGF-I values remained within the normal limit at week 4 and week 26 of the Run-in in both groups



No differences were seen in acromegaly symptoms or patient-reported outcomes

- No significant differences in the Acromegaly Treatment Satisfaction Questionnaire (Acro-TSQ) domain scores were observed during the Run-in phase, regardless of OOC initiation timing
- Overall Acromegaly Index of Severity (AIS) scores decreased after the first month and at the end of the Run-in phase for both groups
  - –0.5 change from Baseline for the <3 weeks group and –0.4 for the ≥3 weeks group after the first month
  - –0.7 change from Baseline for the <3 weeks group and –0.2 for the ≥3 weeks group at the end of the Run-in phase

No new or increased safety signals were identified with a shorter time to initiation of OOC

Time since last iSRL dose

	<3 wk (n=40)	≥3 wk (n=105)
Patients with any TEAE, n (%)	26 (65)	79 (75.2)
AEs by System Organ Class (≥10%), n (%)		
General disorders and administration site conditions	5 (12.5)	15 (14.3)
Infections and infestations	9 (22.5)	30 (28.6)
Musculoskeletal and connective tissue disorders	1 (2.5)	20 (19.1)
Nervous system disorders	6 (15)	20 (19.1)
Respiratory, thoracic and mediastinal disorders	5 (12.5)	3 (2.9)
GI disorders	17 (42.5)	54 (51.4)
Related GI AEs by preferred term, n (%)		
Abdominal pain	2 (5)	17 (16.2)
Diarrhea	5 (12.5)	13 (12.4)
Flatulence	3 (7.5)	9 (8.6)
Nausea	9 (22.5)	22 (21)

GI, gastrointestinal; TEAE, treatment-emergent adverse event.

Conclusions

In this post hoc analysis of MPOWERED data, earlier initiation of OOC relative to the last dose of iSRL was not associated with differences in biochemical response or quality-of-life measures in patients who previously tolerated and responded to SRLs

No new or increased safety signals were identified, including drug-related GI events, with a shorter time to initiation of OOC

Further investigation is warranted to validate these results, which may support flexibility in the timing of OOC initiation relative to the last iSRL dose

References

1. Fleseriu M, et al. *Pituitary.* 2021;24:1-13.
2. Samson S, et al. *J Clin Endocrinol Metab.* 2020;105(10):1-13.
3. Fleseriu M, et al. *Lancet Diabetes Endocrinol*. 2022;10:102-111.

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