A Double-blind, Randomized, Parallel-Group Comparison of Intraarticular Triamcinolone Acetonide Extended-Release Versus Triamcinolone Acetonide Immediate-Release on Glucose in Patients With Osteoarthritis of the Knee and Type 2 Diabetes Mellitus: a *Post Hoc* Analysis

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Disclosures

The speaker has a consulting relationship with Pacira BioSciences, Inc.

Background

Intraarticular corticosteroid injections can treat pain and improve function in knee OA[1]

~14%

of patients with OA have diabetes[2]

~30%

of patients with diabetes have OA[2]

Intraarticular corticosteroid injection can be associated with hyperglycemia (blood glucose levels >180 mg/dL)[3,4]

- Intraarticular corticosteroids may result in marked hyperglycemia during the first 72 hours after injection; hyperglycemia may last up to 3 weeks after injection[3-5]
- Severe hyperglycemia (blood glucose >250 mg/dL) may lead to negative consequences[6-8]

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- Phase 2 study of patients (n=33) with knee OA and type 2 diabetes mellitus[9]
- TA-ER showed minimal blood glucose disruption compared with TA-IR[9]

The purpose of this *post hoc* analysis was to further characterize the clinical relevance and meaningfulness of the phase 2 study results

OA, osteoarthritis; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

1. American Academy of Orthopaedic Surgeons. https://www.aaos.org/oak3cpg. Published August 31, 2021. Accessed December 8, 2022; 2. Louati et al. *RMD Open*. 2015;1:e000077; 3. Habib and Miari. *J Clin Rheumatol*. 2011;17:302-305; 4. Choudry et al. *JBJS Rev*. 2016;4:e5; 5. Chao and Hirsch. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2000; 6. Battelino et al. *Diabetes Care*. 2019;42:1593-1603; 7. American Diabetes Association. *Diabetes Care*. 2021;44:S73-S84; 8. Gosmanov et al. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2020; 9. Russell et al. *Rheumatology (Oxford)*. 2018;57:2235-2241.

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Study Design

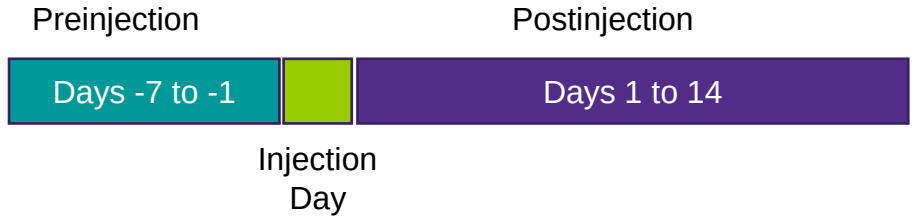
Inclusion criteria

- Symptomatic knee OA ≥6 months
- Type 2 diabetes ≥1 year
- Meet ACR clinical and radiologic criteria for OA
- HbA1c ≥6.5% and <9.0%

Outcomes

- Changes in average daily glucose levels from baseline
- Average time in or above the target range (70-180 mg/dL)
- Time to reach 250 mg/dL
- Glycemic variability

Study design



- Participants were randomized to receive an intraarticular injection of TA-ER or TA-IR
- Participants were monitored using a continuous glucose monitor
- An ambulatory glucose profile summarized blood glucose levels hourly 7 days before injection through 14 days after injection
- Blood glucose levels were defined as
  - Below target range: <70 mg/dL
  - Target range: 70-180 mg/dL
  - Hyperglycemia: >180-250 mg/dL
  - Severe hyperglycemia: >250 mg/dL

ACR, American College of Rheumatology; HbA1c, glycated hemoglobin; OA, osteoarthritis; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

Russell et al. *Rheumatology (Oxford)*. 2018;57:2235-2241.

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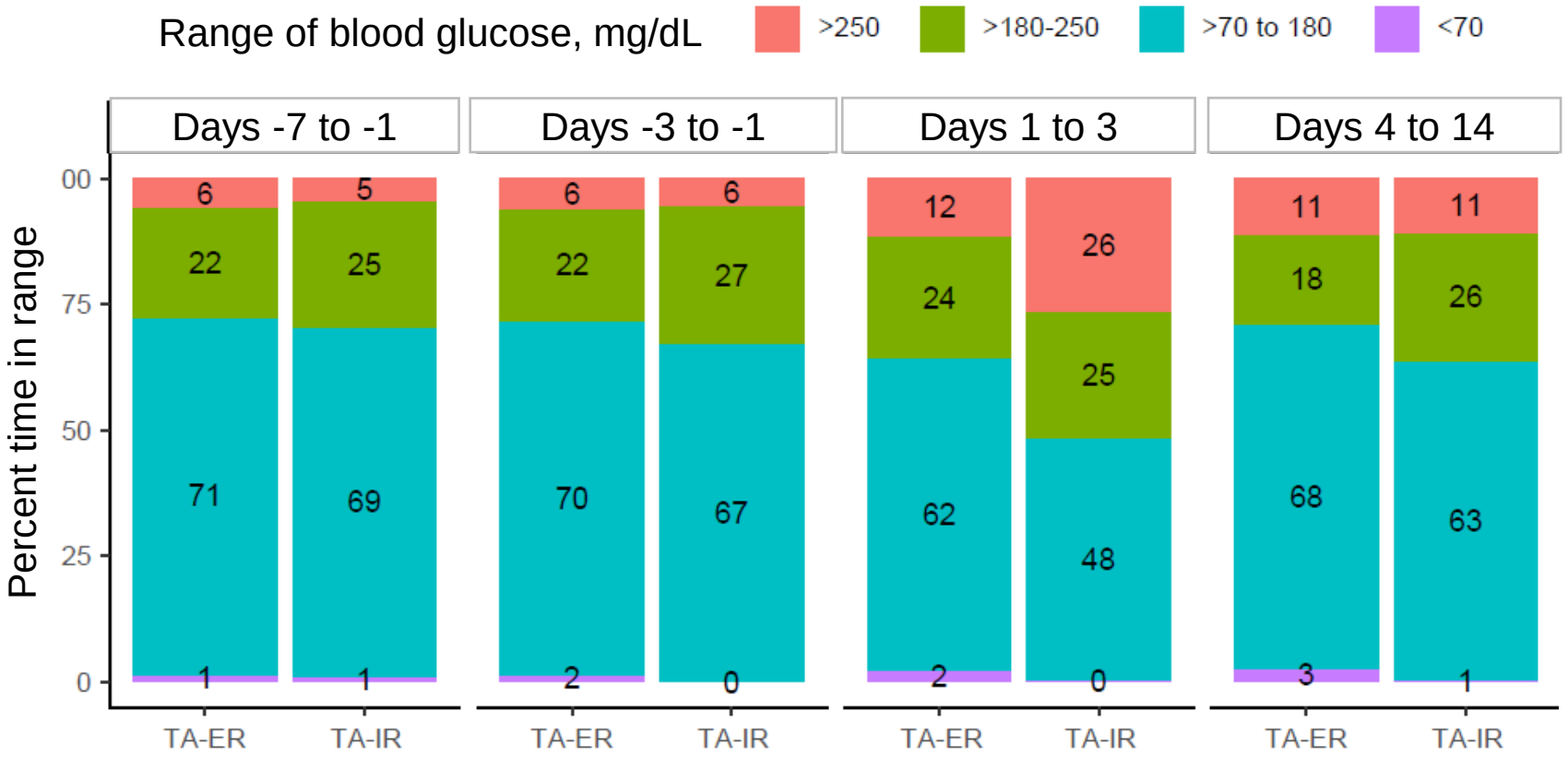
Compared With the TA-IR Group, the TA-ER Group Had Reductions in Postinjection Blood Glucose Levels on Days 1 to 3



Baseline blood glucose levels were comparable between the TA-ER (n=18) and TA-IR (n=15) groups

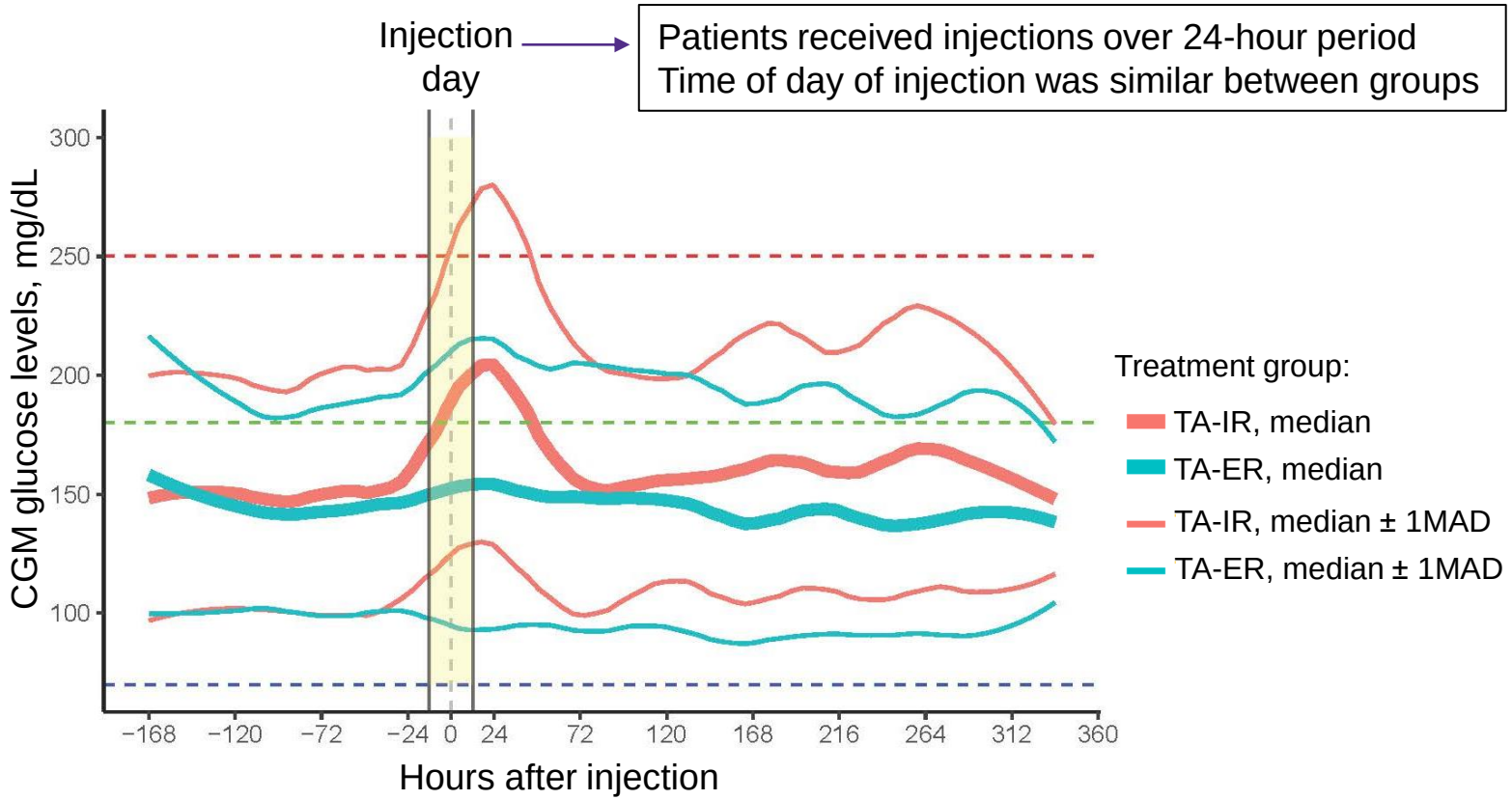
Median change from baseline in maximum glucose levels for days 1 to 3 was lower for the TA-ER group compared with the TA-IR group (92.3 vs 169.1 mg/dL; *P*=0.0011)

2-fold reduction in average time above target range of >250 mg/dL (orange portion of bars) for the TA-ER group compared with the TA-IR group (12% vs 26%; *P*=0.047) for days 1 to 3

Larger percentage of time in target range of 70-180 mg/dL (cyan portion of bars) **for TA-ER group** compared with the TA-IR group (62% vs 48%; *P*=0.123) for days 1 to 3

TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

Better Glucose Control and Lower Glucose Spikes With Triamcinolone Extended Release



Median glucose levels (thick lines), median glucose levels ± 1MAD (thin lines), target range limits (dashed lines), and injection day (yellow shading) are indicated. The red dashed line indicates the severe hyperglycemia threshold, while the green and blue dashed lines indicate the 180-mg/dL and 70-mg/dL thresholds, respectively.

Ambulatory glucose profile analyses demonstrated more consistent blood glucose levels and lower glucose spikes for the TA-ER group compared with the TA-IR group.

Similar trends were observed for 7:00 AM fasting glucose levels.

CGM, continuous glucose monitoring; MAD, mean absolute deviation; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

Median Time to 250 mg/dL and Time to Maximum Glucose Levels Were Significantly Prolonged With TA-ER

Median time to 250 mg/dL glucose

44 h TA-ER

6 h TA-IR

P=0.003

Median time to maximum glucose levels

34 h TA-ER

13 h TA-IR

P=0.007

IQR for maximum glucose levels

114-194 mg/dL TA-ER

131-212 mg/dL TA-IR

Estimated mean GMI levels were lower in the TA-ER group versus the TA-IR group for days 1 through 14 (7.1 vs 7.5; LSM difference [standard error], -0.41 [0.41]; 95% CI, -1.24, 0.42), although this difference was not statistically significant (*P*=0.3241).

CI, confidence interval; GMI, glucose management indicator; IQR, interquartile range; LSM, least squares mean; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

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Conclusions

1. Reduced spikes in glucose for the TA-ER group, which may lead to fewer short-term hyperglycemia-related adverse events in the TA-ER group
2. Increased time in range (70-180 mg/dL) likely to improve glucose management in patients with diabetes, especially in patients undergoing repeat intraarticular injections to manage OA pain
3. Reduced time with glucose levels above 250 mg/dL should improve patient quality of life and reduce healthcare resource utilization
4. Decreased glucose management indicator levels (estimated HbA1c based on mean glucose) for the TA-ER group might result in reduced risk of long-term complications
5. Future studies should include larger sample sizes, patients with broader clinical characteristics, and additional clinically meaningful endpoints

This *post hoc* analysis suggests that TA-ER was associated with a clinically meaningful reduction in hyperglycemia compared with TA-IR

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