Extended-Release Versus Immediate-Release Triamcinolone Acetonide For Knee Osteoarthritis With Comorbid Diabetes

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Disclosures

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

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Purpose

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

~14%

of patients with osteoarthritis have diabetes[2]

~30%

of patients with diabetes have osteoarthritis[2]

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

- Intraarticular corticosteroids may result in severe 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 OAK 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

OAK, osteoarthritis of the knee; 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 June 16, 2023; 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.

Study Design

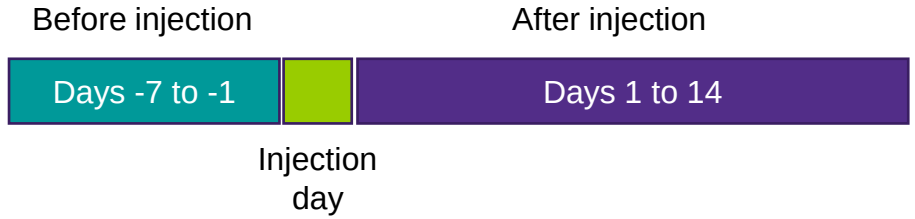
Inclusion criteria

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

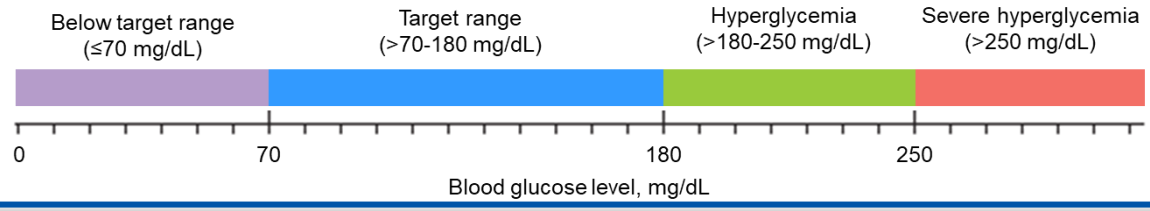
Outcome measures

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

Study design



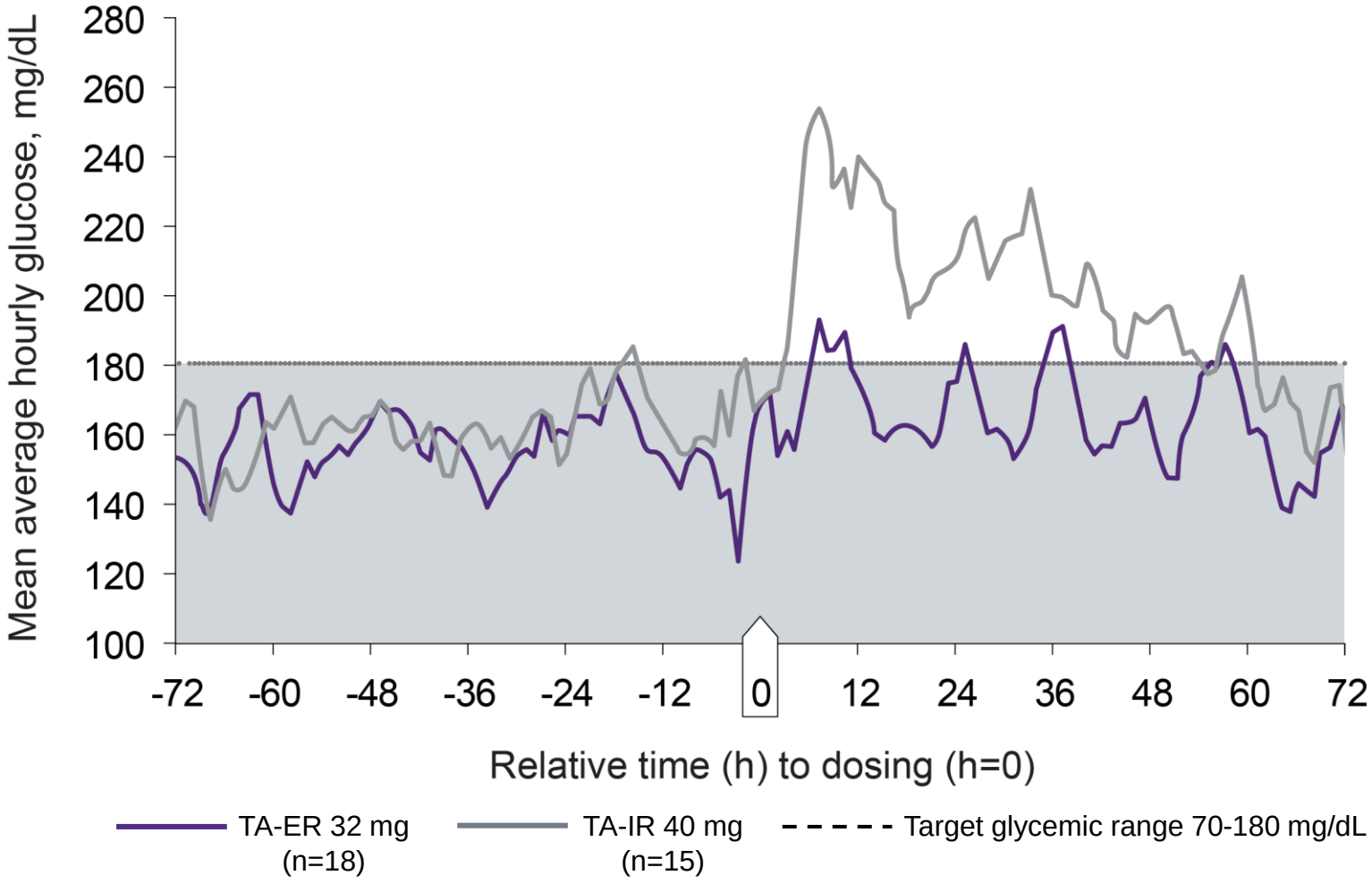
- Participants were randomized to receive an intraarticular injection of TA-ER or TA-IR
- Patients received injections over a 24-hour period
- Participants were monitored using a continuous glucose monitor
- An ambulatory glucose profile summarized blood glucose levels hourly 7 days before injection through 14 days after injection
- Blood glucose levels were defined as



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

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

TA-ER Has a Minimal Effect on Blood Glucose in Patients With Type 2 Diabetes Compared With TA-IR

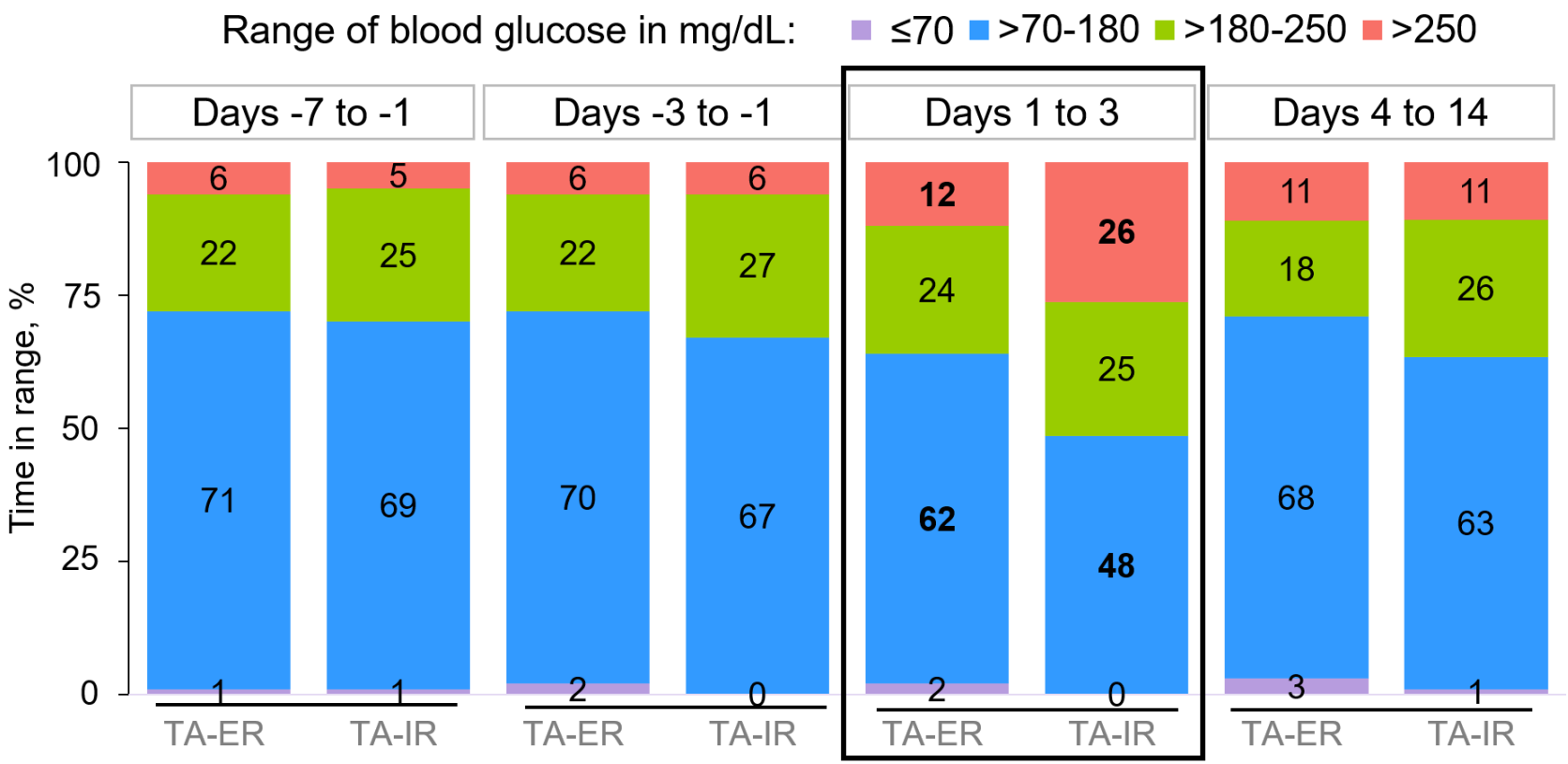


Results based on a study designed to assess the effects of a single intraarticular injection of TA-ER or TA-IR on blood glucose levels in patients with type 2 diabetes mellitus over a 6-day period (72 hours before dosing through 72 hours after dosing; N=33)

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

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

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

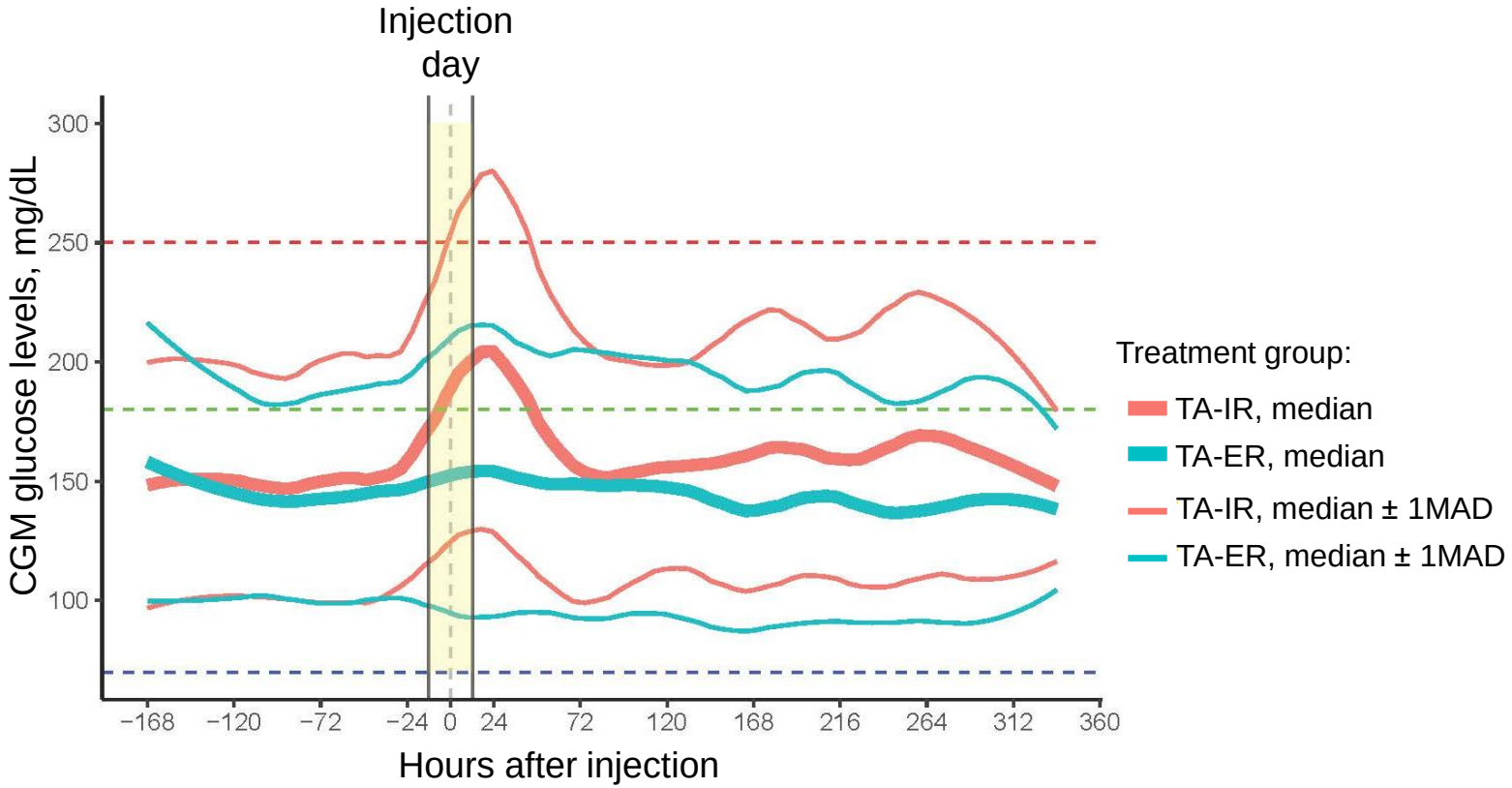
Median change from baseline in maximum glucose levels for days 1 to 3 was lower for the TA-ER group compared with the TA-IR group (92.3 vs 169.1 mg/dL; *P*=0.0011)

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 (blue portion of bars) **for the 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, Lower Glucose Spikes, and Significantly Prolonged Median Time to 250 mg/dL and Time to Maximum Glucose Levels With TA-ER



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.*

Median time to 250 mg/dL glucose

44 hours TA-ER

6 hours TA-IR

P=0.003

Median time to maximum glucose levels

34 hours TA-ER

13 hours TA-IR

P=0.007

*An ambulatory glucose model calculated a smoothed curve for data visualization. CGM, continuous glucose monitoring; MAD, median absolute deviation; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.

Conclusions

1. Reduced spikes in glucose and less time with glucose levels above 250 mg/dL for the TA-ER group may lead to fewer short-term hyperglycemia-related adverse events and decreased healthcare resource utilization
2. Increased time in range (>70-180 mg/dL) is likely to improve glucose management in patients with diabetes, especially in patients undergoing repeat intraarticular injections to manage OAK pain
3. 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
4. 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

OAK, osteoarthritis of the knee; HbA1c, glycated hemoglobin; TA-ER, triamcinolone acetonide extended-release; TA-IR, triamcinolone acetonide immediate-release.