

## ACP Northern California Chapter Annual Regional Scientific Meeting

# Update in General Medicine

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# Background

- Type 2 DM is the leading cause of kidney failure in the U.S.
- Standard approach to prevent DM nephropathy is with blockade of the renin-angiotensin-aldosterone system (i.e. with ACE-I or ARB)

# CREDENCE Trial



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“Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation” trial

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### Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

V. Perkovic, M.J. Jardine, B. Neal, S. Bompoint, H.J.L. Heerspink, D.M. Charytan, R. Edwards, R. Agarwal, G. Bakris, S. Bull, C.P. Cannon, G. Capuano, P.-L. Chu, D. de Zeeuw, T. Greene, A. Levin, C. Pollock, D.C. Wheeler, Y. Yavin, H. Zhang, B. Zinman, G. Meininger, B.M. Brenner, and K.W. Mahaffey, for the CREDENCE Trial Investigators\*

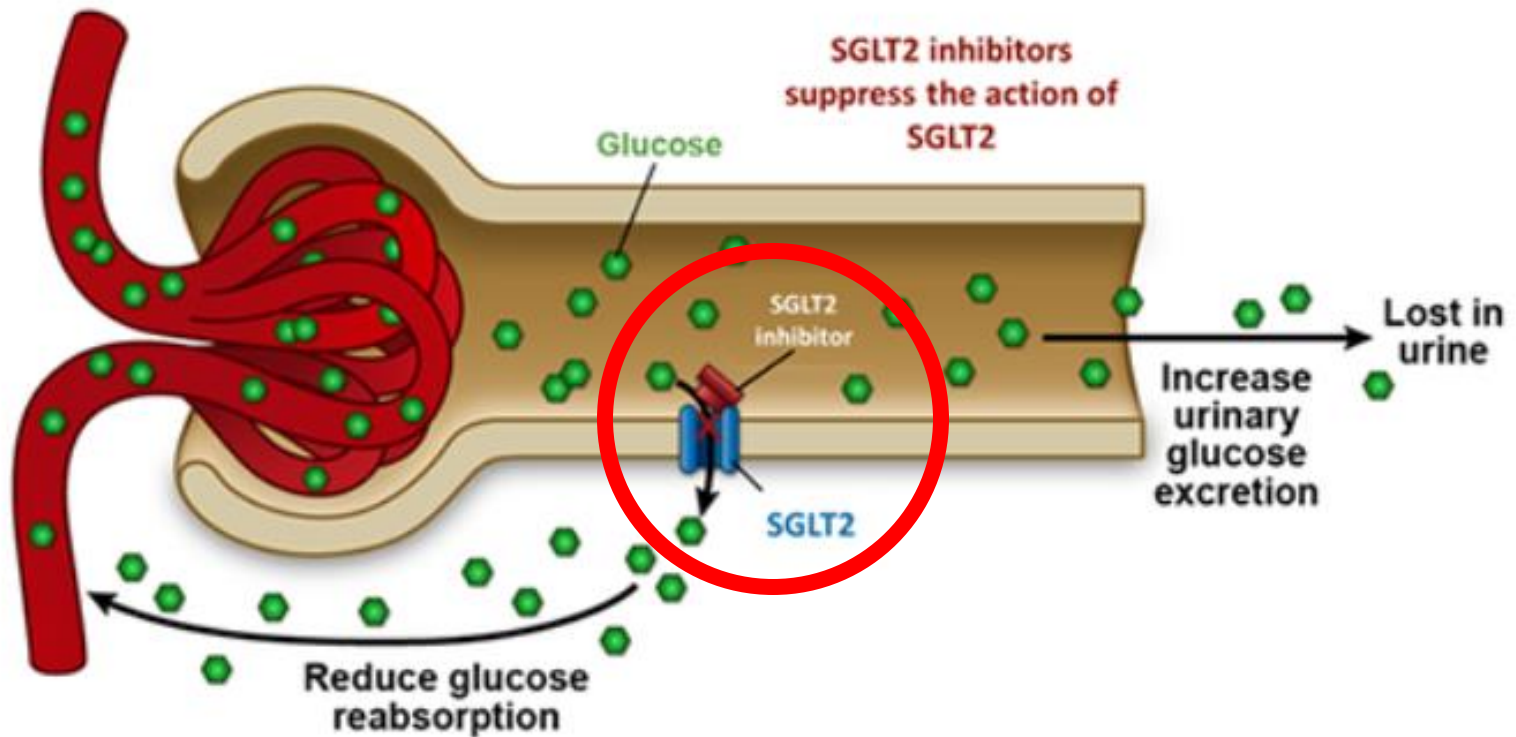
# Background



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## *SGLT2 Inhibitors*



Wright EM, et al. *Physiol Rev.* 2011;91:733-794.

# SGLT2 Inhibitors



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- Currently 4 SGLT2 inhibitors are approved in the US:
  - Canagliflozin (Invokana)
  - Dapagliflozin (Farxiga)
  - Empagliflozin (Jardiance)
  - Ertugliflozin (Steglatro)

# Background



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- In CV trials of SGLT2 inhibitors, results have suggested that these drugs may improve renal outcomes in patients with type 2 DM

# Clinical Question



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- **Population** – patients with type 2 diabetes AND albuminuric CKD AND treated with renin-angiotensin system blockade
- **Intervention** – canagliflozin 100mg daily
- **Comparison** – placebo
- **Outcomes** –
  - ESRD
  - Doubling of the serum creatinine level
  - Death from renal or CV causes

# Trial Participants

- **Inclusion Criteria**

- Men and women at least 30 years of age
- Diagnosis of type 2 diabetes with an HbA1c of 6.5% to 12.0%
- Diagnosis of CKD (eGFR of 30 to <90 ml) and albuminuria (urinary albumin-to-creatinine ratio >300 to 5000)
- Treatment with a stable dose of ACE-I OR ARB for at least 4 weeks

- **Exclusion Criteria**

- Suspected non-diabetic kidney disease or type 1 diabetes
- Treatment with immunosuppression for kidney disease
- History of dialysis or kidney transplantation
- Dual-agent treatment with ACE-I and ARB, a direct renin inhibitor, or a mineralocorticoid-receptor antagonist



# Results



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Characteristic	Canagliflozin (N=2202)	Placebo (N=2199)
Age – yr	62.9 ± 9.2	63.2 ± 9.2
Female sex – no. (%)	762 (34.6)	732 (33.3)
Glycated hemoglobin - %	8.3 ± 1.3	8.3 ± 1.3
Estimated GFR – ml/min/1.73 m <sup>2</sup>	56.3 ± 18.2	56.0 ± 18.3
Median urinary albumin to creatinine ratio	923 (459-1794)	931 (473-1868)

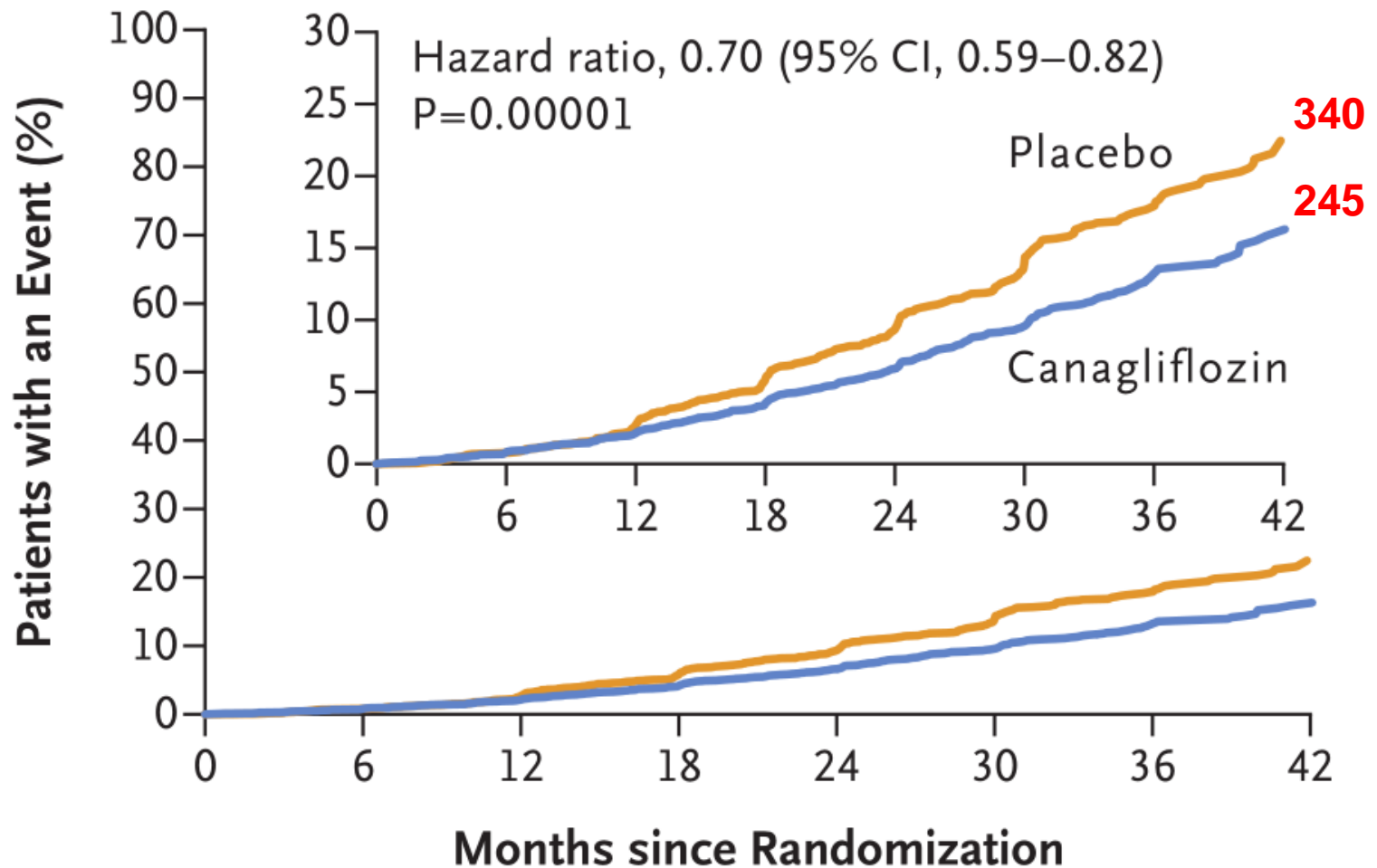
# Results



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## A Primary Composite Outcome



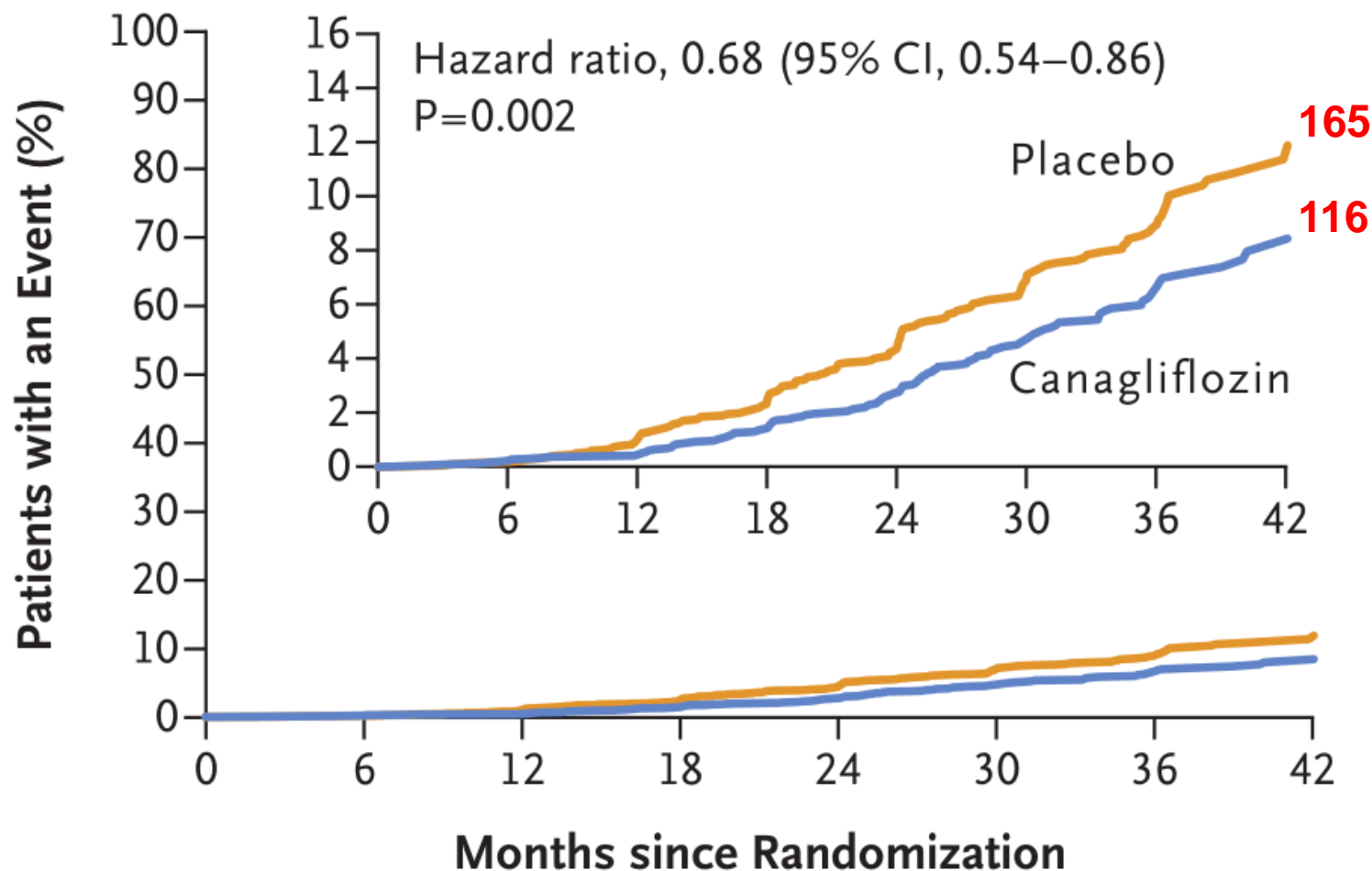
# Results



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## C End-Stage Kidney Disease



# Results



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Secondary Outcomes	Canagliflozin	Placebo	HR	P Value
Hospitalization for heart failure	89/2202	141/2199	0.61 (0.47-0.80)	<0.001
CV death, MI, stroke	217/2202	269/2199	0.80 (0.67-0.95)	0.01

# Results



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- Rates of lower limb amputations and fractures were similar in the two groups
- Rates of DKA were low, but higher in the canagliflozin group than in the placebo group

	n/N		Event rate per 1000 patient-years		HR (95% CI)
	Canagliflozin	Placebo	Canagliflozin	Placebo	
Diabetic Ketoacidosis	11/2200	1/2197	2.2	0.2	10.80 (1.39-83.65)

# Study Limitations

- Stopped early
- Excluded patients with advanced CKD (eGFR < 30)
- Excluded patients with nonalbuminuric or microalbuminuric kidney disease

# Practical Implications



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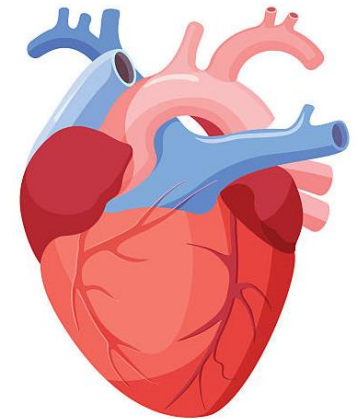
Patient with type 2 DM and A1c  
not at goal

Metformin and comprehensive  
lifestyle change?

CKD (but eGFR > 45) and  
urine albumin/Cr > 300?

ACE-I or ARB?

Consider starting canagliflozin  
100mg once daily





## FDA Approves Invokana (canagliflozin) to Treat Diabetic Kidney Disease (DKD) and Reduce the Risk of Hospitalization for Heart Failure in Patients with Type 2 Diabetes and DKD



RARITAN, N.J., Sept. 30, 2019 /PRNewswire/ -- The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the U.S. Food and Drug Administration (FDA) approved a new indication for [Invokana \(canagliflozin\)](#) to reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes.



# Practical Implications



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- Side effects:
  - Hypotension
  - Increased urination
  - Increased rate of genitourinary infections

# Practical Implications



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## Canagliflozin Invokana

Canagliflozin (Invokana) is an expensive drug used to treat [type 2 diabetes](#). It helps to control blood sugar. This drug is more popular than comparable drugs. There are currently no generic alternatives to Invokana. It is covered by most Medicare and insurance plans, but some pharmacy coupons or cash prices may be lower. The lowest GoodRx price for the most common version of Invokana is around \$493.20, 18% off the average retail price of \$606.96. Compare [SGLT2 inhibitors](#).

Prescription Settings

brand ▾ tablet ▾ 100mg ▾ 30 tablets ▾ [SHARE](#) ▾

**Insurance Coverage:** Many major insurance plans no longer cover Invokana as of 2019. [Learn More](#)

Prices and coupons for 30 tablets of Invokana 100mg

[Set your location](#) for drug prices near you

<a href="#">Costco</a>	\$497.76 <small>with free coupon</small>	<a href="#">GET FREE COUPON</a>
<a href="#">Ralphs</a>	\$512.69 <small>with free coupon</small>	<a href="#">GET FREE COUPON</a>
<a href="#">Safeway</a>	\$519.38 <small>with free coupon</small>	<a href="#">GET FREE COUPON</a>
<a href="#">Vons Pharmacy</a>	\$519.38 <small>with free coupon</small>	<a href="#">GET FREE COUPON</a>

Prices

Medicare

Drug Info

Side Effects

Images

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Google



# Thank you!

# References

- Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. *N Engl J Med* 2019;380:2295-2306.
- Ingelfinger J, Rosen C. Clinical Credence – SGLT2 inhibitors, diabetes, and chronic kidney disease. *N Engl J Med* 2019;380:2371-2373.
- U.S. Food and Drug Administration, *FDA Approved Drug Products*  
<https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=204042> (accessed 10/10/2019)