ANNUAL MEETING ON WOMEN'S CANCER

ADVANCING SCIENCE
EMPOWERING TEAMS
EMBRACING CHANGE

SAN JUAN, PR | APRIL 10-13, 2026 | WWW.SGO.ORG

ANNUAL MEETING ON WOMEN'S CANCER

Impact of GLP-1RA plus Progestin Therapy on Fertility-Sparing Management of Endometrial Intraepithelial Neoplasia and Endometrial Cancer

Tina Yi Jin Hsieh, MD MPH MS
Postdoctoral research fellow
Beth Israel Deaconess Medical Center, Boston, MA
Future OBGYN residency applicant
April 11th, 2026

Unlabeled/Investigational Uses

I will not be discussing any unlabeled or investigational uses of any pharmaceutical products or medical devices.

Disclosures

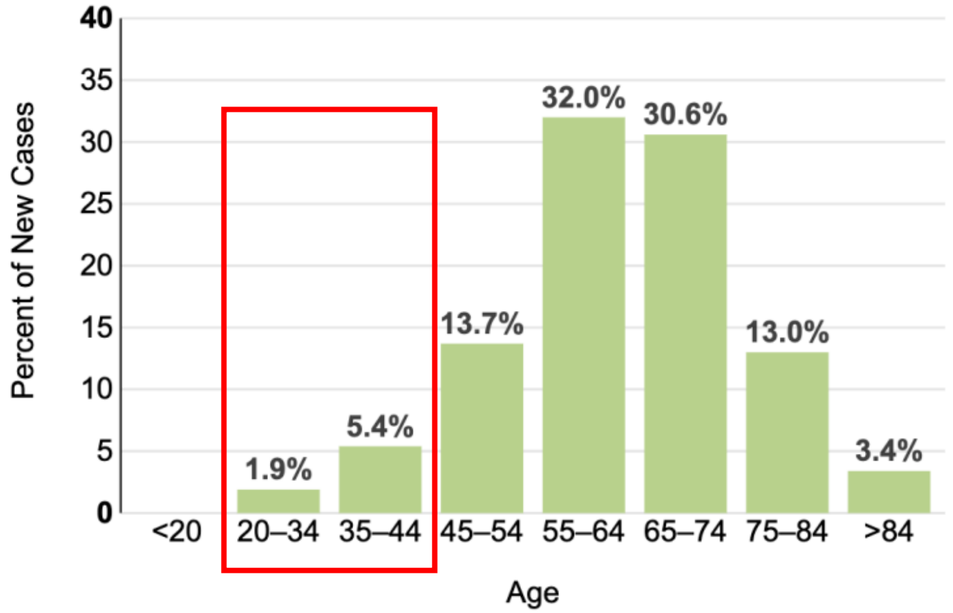
I have no disclosures

Increased EC and EIN incidence in reproductive-age women

- **Endometrial cancer (EC)** and **endometrial intraepithelial neoplasia (EIN) incidence** is rising among reproductive-aged women
  - ↑ 4.5% for age 20-29
  - ↑ 3.0% for age 30-39

- **Fertility-sparing treatment** often selected over definitive surgery for pregnancy considerations

Over 67,000 new cases of EC per year, 12% are premenopausal



AJOG, 2021. PMID: 33412129; National Cancer Institute. Surveillance, Epidemiology, and End Results Program Cancer Stat facts: Uterine Cancer (Accessed June 3rd , 2025)

Current conservative management and potential risk modifiers

- **Progestins**
  - Levonorgestrel-releasing intrauterine device (LNG-IUD)
  - Megestrol acetate (MA)
  - Medroxyprogesterone acetate (MPA)

→ ***Have demonstrated high rates of disease regression***

- **Potential modifiable risk factors**
  - Obesity
  - Type 2 diabetes mellitus (T2DM)
  - Metabolic syndrome
  - Polycystic Ovarian Syndrome

→ ***Critical for improving outcomes***

Obstet Gynecol, 2023. PMID: 37590985

Potential role of Glucagon Like Peptide-1 Receptor Agonists (GLP-1RA)

FDA-approved for

- **Type 2 diabetes** since **2005**
- **Weight loss** since **2014**

GLP-1RAs' therapeutic potential

- **Weight and glycemic control** influence treatment outcomes
  - Obesity associated with lower remission and higher recurrence during fertility-sparing management
- Potential **anti-tumor, anti-inflammatory,** and **progesterone-sensitizing effects**
  - GLP-1RAs + progestins reduce tumor cell viability in progesterone receptor high- and low-expressing tumors preclinically

FDA, 2005; FDA, 2014; JAMA Netw Open, 2024. PMID: 38967919 ; Cancer Metastasis Rev. 2024. PMID: 38801466

Objective

Knowledge Gap

- Limited real-world data on GLP-1RAs as adjuncts in fertility-sparing EIN/EC management

Aim

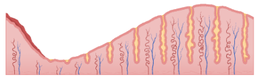
- Evaluate whether adding **GLP-1RAs to progestin therapy** reduces **hysterectomy risk (uterine preserving proxy endpoint)** compared with progestin alone *(histologic regression, livebirth data not available)*

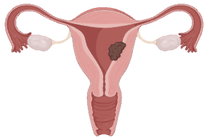
TriNetX: Electronic Health Records (EHR)

- Diagnosis: ICD-9, ICD-10, SNOMED
- Procedures: CPT
- Medications: RxNorm, ATC..etc

Diagnosis

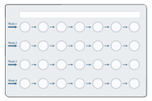
- Endometrial Cancer (EC) - C54, C55
- Endometrial Intraepithelial Neoplasia (EIN) - N85.02





Progestin therapy (P)

- LNG-IUD
- Medroxyprogesterone
- Megestrol acetate



GLP-1RAs

- Older generations (only approved for T2DM)
  - ***dulaglutide,exenatide, lixisenatide, albiglutide***
- Newer generations (also approved for obesity)
  - ***tirzepatide, semaglutide, liraglutide***

TriNetX Research Collaborative (112 HCOs)
N=165,188,322

↓

Female patients
N=88,722,552

↓

Female patients with diagnosis of
EIN or **EC** during
1/1/2017~6/1/2024 (allow for 18-month f/u)
N=190,690

↓

Female patients with diagnosis of EIN or EC
under 45 years old
N=19,042

Use of **GLP-1RA + progestins** after diagnosis of EIN or EC **N=574**	Use of **progestins(P)-only** after diagnosis of EIN or EC **N=2,842**

↓

Exclude **hysterectomy** before index date

Created in https://BioRender.com

Main Analysis

GLP-1RAs + P
v.s. P-only

Subgroup Analysis

Endometrial Cancer Only

Younger age (≤ 40 years old)

1:1 Propensity score matching (covariates)

- Demographics
- Age at Index
- **Medications** (estrogen, SERMs, antidiabetic drugs)
- BMI
- HbA1C
- **Healthcare Utilization** (Inpatient, outpatient, emergency, preventive, consultations)
- Comorbidities

Use of **GLP-1RA + P** after diagnosis of EIN or EC
N=554

Use of **P-only** after diagnosis of EIN or EC
N=2,686

1:1 Propensity Score Matching

GLP-1RA + P
N=432

P-only
N=432

Outcome follow-up

Hysterectomy

- 6 month
- 12 month
- 18 month

Censored upon:
1) Earliest hysterectomy
2) **Loss to follow-up** within the system
3) Conclusion of follow-up period **(December 1st, 2025)**

Hazard Ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards model

SGO ANNUAL MEETING ON WOMEN'S CANCER
SAN JUAN, PR
APRIL 10-13, 2026

Created in https://BioRender.com

Results – Baseline Characteristics (1)

SGO ANNUAL MEETING ON WOMEN'S CANCER
SAN JUAN, PR
APRIL 10-13, 2026

Characteristics (Selected)	Before PSM			After PSM		
	GLP-1RA + P (N= 554)	P-Only (N= 2,686)	SMD	GLP-1RA + P (N= 432)	P-Only (N= 432)	SMD
Age at Index, mean ± SD	38.5±5.9	35.3±6.1	0.530	37.9±5.9	37.8±5.7	0.022
Race						
White	61.7%	51.4%	0.209	59.7%	59.5%	0.005
Black or African American	14.4%	10.3%	0.127	14.8%	17.1%	0.063
Asian	6.0%	11.6%	0.200	5.8%	3.9%	0.086
Other	5.2%	6.2%	0.042	5.6%	5.1%	0.021
Hispanic	16.6%	16.7%	0.002	17.4%	17.6%	0.006
Socioeconomic Hazards	3.6%	1.2%	0.159	3.5%	2.3%	0.069
EIN (1-year prior index date)	37.7%	34.9%	0.059	38.0%	37.0%	0.019
Type 2 diabetes	43.9%	9.2%	0.852	31.9%	33.3%	0.030
T2DM with complications	38.6%	8.3%	0.768	28.5%	30.3%	0.041
Insulins	19.3%	3.1%	0.532	11.3%	10.2%	0.037
Metformin	33.0%	7.3%	0.679	23.4%	23.8%	0.011
DPP-4 inhibitors	3.1%	0.4%	0.208	2.3%	2.3%	<0.001
SGLT2 inhibitors	5.4%	0.4%	0.304	2.3%	2.3%	<0.001

Before PSM, GLP-1RA+P group was older, higher proportion of T2DM and anti-diabetic drugs

SMD= Standardized Mean Difference
Less than 0.1 → indicated balance between groups

Results – Baseline Characteristics (2)

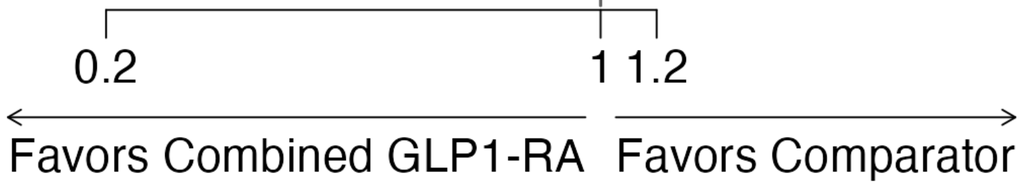
Characteristics (Selected)	Before PSM			After PSM		
	GLP-1RA + P (N= 554)	P-Only (N= 2,686)	SMD	GLP-1RA + P (N= 432)	P-Only (N= 432)	SMD
BMI ≥30kg/m^2 (1 yr before index date)	71.8%	44.9%	0.568	69.4%	68.3%	0.025
HbA1c ≥6.5% (1 yr before index date)	30.9%	4.2%	0.750	19.9%	19.4%	0.012
Comorbidities						
Hypertension	38.4%	13.7%	0.587	31.5%	32.6%	0.025
Hyperlipidemia	26.2%	6.1%	0.568	19.7%	18.5%	0.029
Gastro-esophageal reflux disease	17.5%	6.4%	0.349	13.9%	13.2%	0.020
Healthcare Utilization						
Outpatient	60.1%	40.5%	0.399	56.9%	60.0%	0.061
Preventive medicine	16.4%	9.5%	0.208	14.8%	14.6%	0.007
Emergency department	18.4%	12.4%	0.168	16.7%	15.3%	0.038
Consultations	4.0%	7.1%	0.139	4.4%	4.2%	0.011
Inpatient	9.7%	3.9%	0.231	6.9%	7.2%	0.009

Before PSM, GLP-1RA+P group had higher proportion of obesity, high HbA1C, comorbidities, and outpatient, inpatient, emergency visits

SMD= Standardized Mean Difference
Less than 0.1 → indicated balance between groups

Results – Main Analysis

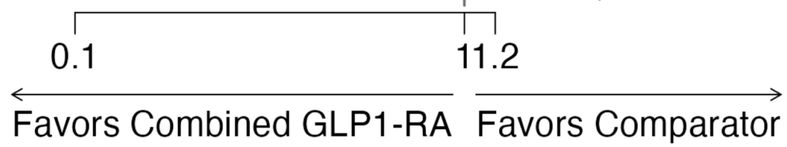
Comparison Groups	GLP-1RA+P Event / Total, N (%)	P-only Event / Total, N (%)	HR (95% CI)
Main Analysis			
Hysterectomy -6 months	28/432(6.5)	77/432(17.8)	0.34 (0.22 to 0.53)
Hysterectomy -12 months	39/432(9.0)	97/432(22.5)	0.38 (0.26 to 0.54)
Hysterectomy -18 months	44/432(10.2)	101/432(23.4)	0.41 (0.29 to 0.58)



Compared with progestin-only, **GLP-1RA plus progestin therapy** was associated with a **consistently lower risk of hysterectomy** across all follow-up windows

Results – Subgroup Analysis (Age & EC)

Comparison Groups	GLP-1RA+P Event / Total, N (%)	P-only Event / Total, N (%)	HR (95% CI)
Subgroup (Age)			
Younger (<40 yrs)			
Hysterectomy -6 months	13/307(4.2)	47/307(15.3)	0.26 (0.13 to 0.49)
Hysterectomy -12 months	22/307(7.2)	56/307(18.2)	0.37 (0.23 to 0.61)
Hysterectomy -18 months	27/307(8.8)	65/307(21.2)	0.40 (0.25 to 0.62)
Subgroup (Diagnosis)			
EC			
Hysterectomy -6 months	15/192(7.8)	44/192(22.9)	0.31 (0.17 to 0.56)
Hysterectomy -12 months	19/192(9.9)	55/192(28.6)	0.31 (0.18 to 0.52)
Hysterectomy -18 months	22/192(11.5)	58/192(30.2)	0.33 (0.20 to 0.55)



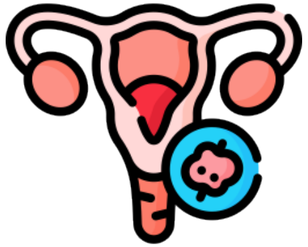
Compared with progestin-only, **GLP-1RA plus progestin therapy** was associated with a **consistently lower risk of hysterectomy** across the younger cohort, and patients with EC

Strengths & Limitations

Strengths

- The first study using a large real-world EHR database with PSM to examine this association

Limitations



Limited baseline clinical granularity

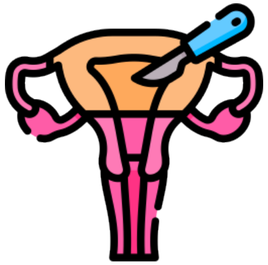
Lack of detailed **tumor** & **treatment data**

No key intermediate or reproductive outcomes

Complete response & **regression rates, reproductive outcomes** could not be evaluated

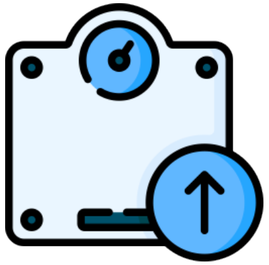
Unknown treatment duration/effects

GLP-1RA duration, weight loss effects and **discontinuation patterns** were not accessible



Unknown hysterectomy intent

Indications: treatment failure, progression, or patient preference could not be determined



Unknown longitudinal effects

Impact of **weight/ metabolic rebound** on progression/recurrence remains unclear

Icons from Flaticon.com

Conclusions

- In a large, real-world cohort of EIN and EC patients managed conservatively, **GLP-1RA + progestin** was associated with a **lower risk of hysterectomy** compared with progestin alone

- Findings suggest a potential role for GLP-1RAs as adjunctive metabolic therapy in fertility-sparing management

- Results are observational and hypothesis-generating, **no causality** should be inferred

Future Directions

- **Prospective validation:**
  - A separate multi-institutional retrospective study should replicate/validate our findings assess more granular clinical outcomes and patient-level details
  - Prospective clinical trials to evaluate the effectiveness of the intervention

- **Molecular and metabolic profiling:**
  - Understand impact of molecular (MMRd/MSI-H, p53 abnormal, NSMP, POLEmut) and metabolic profiling for fertility-sparing patient selection

Acknowledgements

Wonderful mentors & coauthors ☺

- Katharine Esselen, MD, MBA
- Joseph Dottino, MD, MPH
- Michele Hacker, ScD
- Ting-Tai Yen, MD

ANNUAL MEETING ON WOMEN'S CANCER

Stay tuned for the full manuscript coming up soon!!

ANNUAL MEETING ON WOMEN'S CANCER

Any Questions?
Thank you!