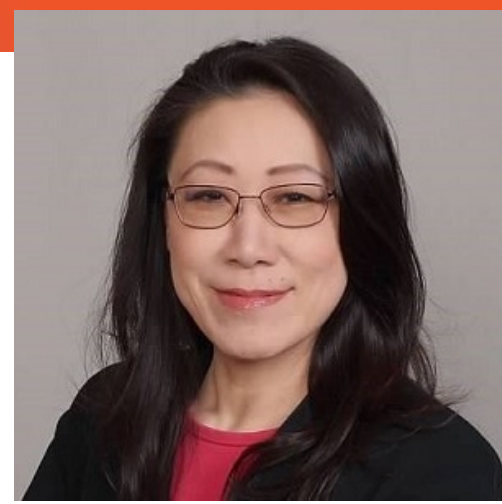


PD-1/PD-L1 Inhibitor Update

Sophia Humphreys, PharmD, MHA, BCBBS, CPGx

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- Pharm.D. from University of Washington in 2000
- MHA from University of Cincinnati 2018
- BCBBS certified in 2022
- Certified pharmacogenomics specialist in 2024
- 24 years of specialized experience in the pharmaceutical industry, involving for-profit and non-profit organizations

**Director, System Formulary Management and Clinical Programs
Sutter Health, Pharmacy Division**

Current PD-1 and PD-L1 Inhibitors

The old and famous:

- Pembrolizumab (2014)
- Nivolumab (2014)

Newer agents

- Cemiplimab-rwlc (2018)
- dostarlimab-gxly (2021)
- Nivolumab & Relatimab-rmbw combo (2022)
- Toripalimab-tpzi (2023)
- retifanlimab-dlwr (2023)
- Tislelizumab-jsgr (2024)

Older PD-1
Inhibitors

- Pembrolizumab (2014)
- Nivolumab (2014)

dostarlimab-gxly (2021)

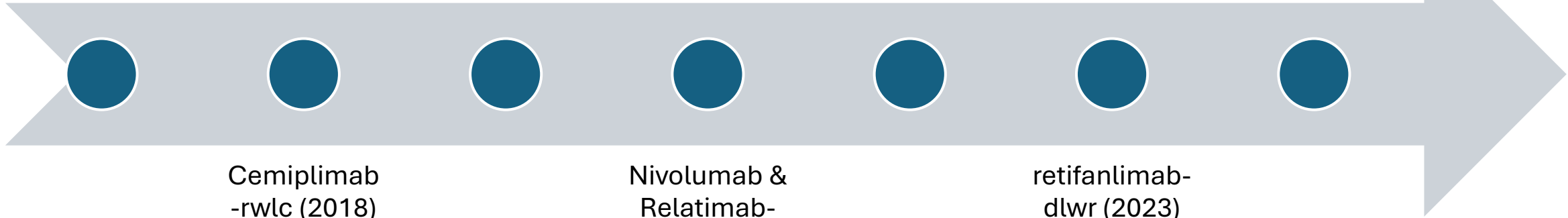
Toripalimab-tpzi (2023)

Tislelizumab-jsgr (2024)

Cemiplimab-rwlc (2018)

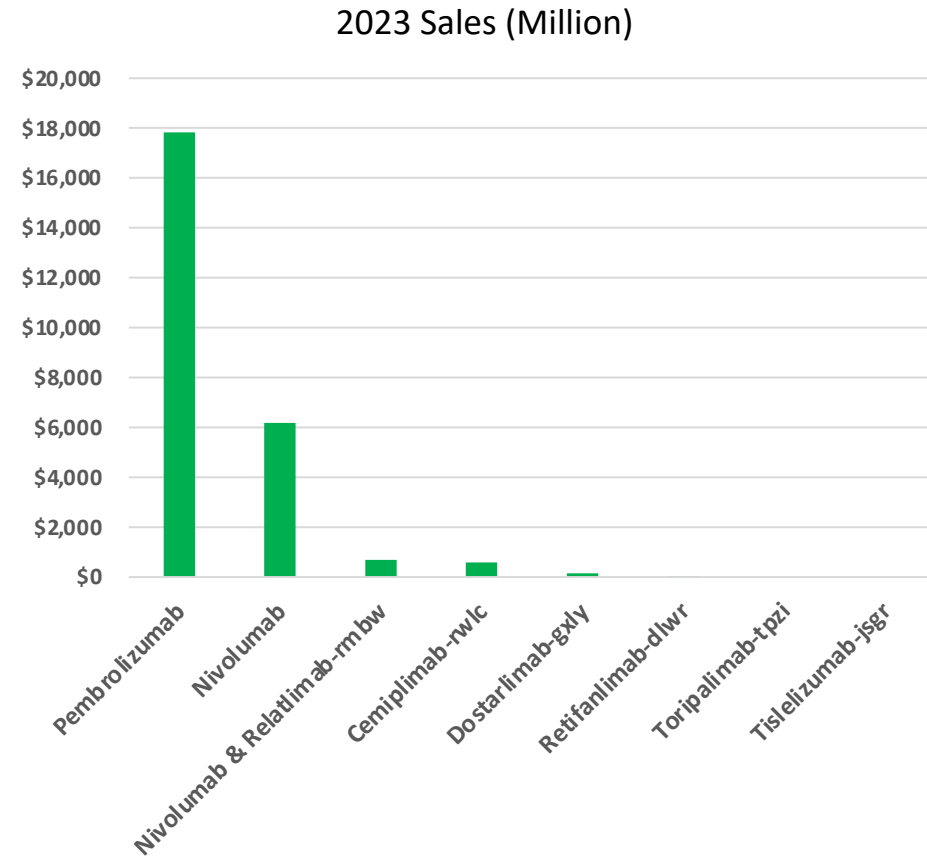
Nivolumab & Relatimab-rmbw combo (2022)

retifanlimab-dlwr (2023)



Financial Impact

Generic Name	2023 Sales (Million)	Est. LOE
Pembrolizumab	\$17,818	2028-2029
Nivolumab	\$6,168	12/22/2028
Nivolumab & Relatlimab-rmbw	\$686	03/18/2036
Cemiplimab-rwlc	\$599	09/18/2035 or later
Dostarlimab-gxly	\$150	08/22/2038
Retifanlimab-dlwr	\$1	03/22/2037
Toripalimab-tpzi	0	2036
Tislelizumab-jsgr	0	2038



Biosimilar Pipeline for PD-1 Inhibitors

2 for nivolumab

7 for pembrolizumab

5 in Phase 3 trials

4 pre-clinical trials

Indication:

- 1 melanoma
- 4 NSCLC
- 4 pre-clinical trials no indications available

Non-Small Cell Lung Cancer

- A systematic review and meta-analysis
- 5893 patients with metastatic or locally advanced non-small cell lung cancer
- Single-agent ICI significantly improved overall survival (OS), progression-free survival (PFS), and health-related quality of life, with significantly less Grade 3 or 4 adverse events compared with platinum-based chemotherapy.
- Combination ICI therapy significantly improved OS with no difference in Grade 3 or 4 adverse events compared with platinum-based chemotherapy.
- The effect of combination ICI on PFS, overall response rate, and health-related quality of life was not reported.
- ICIs included in the studies were atezolizumab, avelumab, **cemiplimab-rwlc**, durvalumab, ipilimumab, **nivolumab**, and **pembrolizumab**.

Newer PD-1 & PD-L1 inhibitor indications

Cemiplimab-rwlc (2018, NCCN Category 1; Preferred for NSCLC)

- Cutaneous squamous cell carcinoma (CSCC)
- Skin Cancer (not otherwise classified): Basal cell carcinoma*
- Lung Cancer: Non-small cell lung cancer (NSCLC)

Dostarlimab-gxly (2021, NCCN Category 2a)

- Endometrial cancer
- Solid Tumor
 - accelerated approval
 - 16 types of dMMR tumor, included both endometrial and non-endometrial solid tumors

The PD-1 Inhibitor Subclass is Expanding Fast

Toripalimab-tpzi (2023, Class II a, first-line)

- Nasopharyngeal carcinoma, Metastatic or recurrent locally advanced disease;
 - **First-line** treatment in combination with CISplatin and gemcitabine
 - **Monotherapy** for Progression on or after platinum-containing chemotherapy

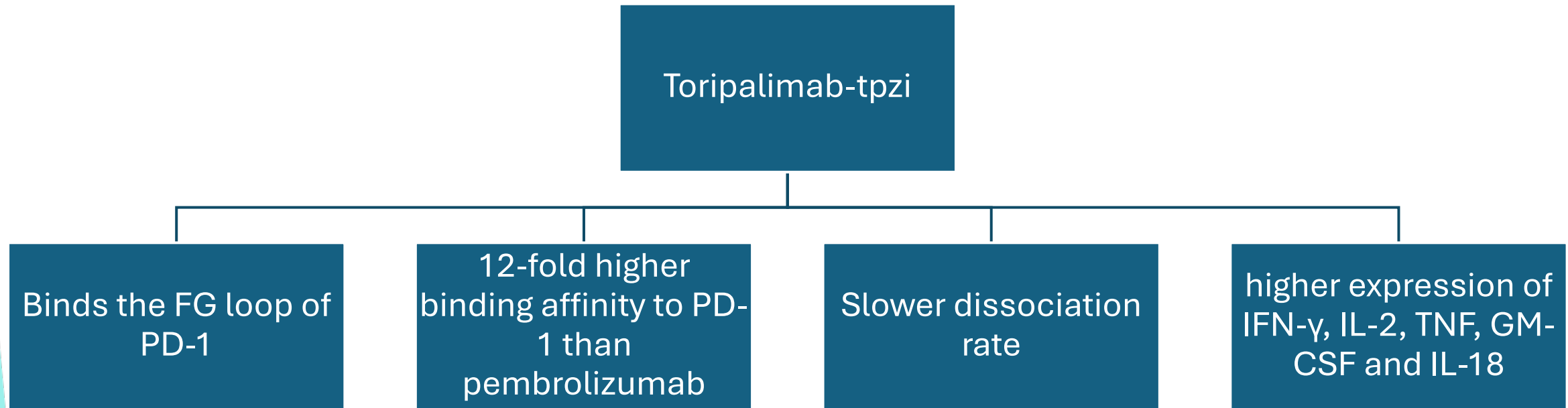
Retifanlimab-dlwr (2023, Class II b)

- Merkel cell carcinoma, Locally advanced, metastatic or recurrent

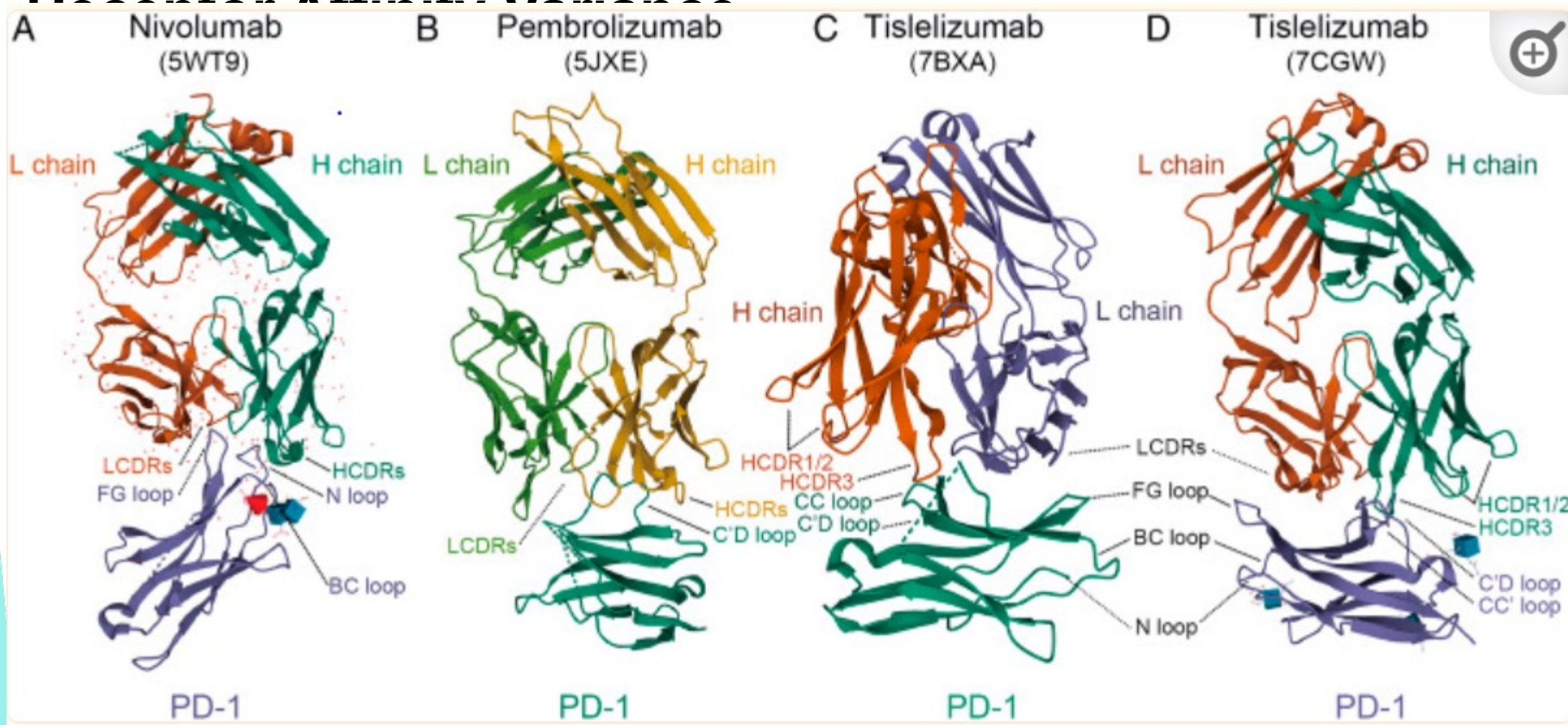
Tislelizumab-jsgr (March 2024, Class II a, second line)

- Unresectable or metastatic **esophageal squamous cell carcinoma** (ESCC) after prior therapy systemic chemotherapy that did not include a PD-1 or PDL-1 inhibitor.
- 1st line ESCC and gastric/gastric esophageal junction cancers (PDUFA 2H 2024)

Are All PD-1 Inhibitors Created Equal?



Receptor Affinity Variants



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Take Aways

PD-1 inhibitors may not have been made equal

More studies are necessary

More indications may come soon

Competition = price reduction?

Biosimilars to older PD-1 inhibitors are in the pipeline

Thank you and stay in touch

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