Keynote presentation

LIVING BEYOND
BREAST CANCER®

Updates by subtype

HER2-positive, hormone receptor-positive, and triple-negative MBC

Speaker: David Cescon, MD, PhD

2026 Conference on Metastatic Breast Cancer

Updates In HER2+ and Triple Negative Metastatic Breast Cancer

David Cescon MD PhD
Princess Margaret Cancer Centre/UHN
Toronto, Canada

EVERY MOMENT COUNTS

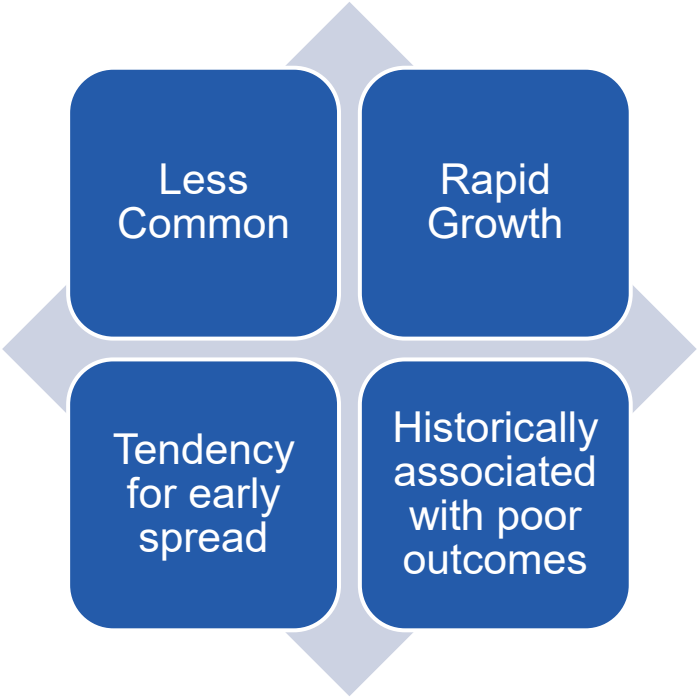
Key Takeaways

HER2+ and Triple Negative Breast Cancer tend to be more aggressive and historically had a poor prognosis

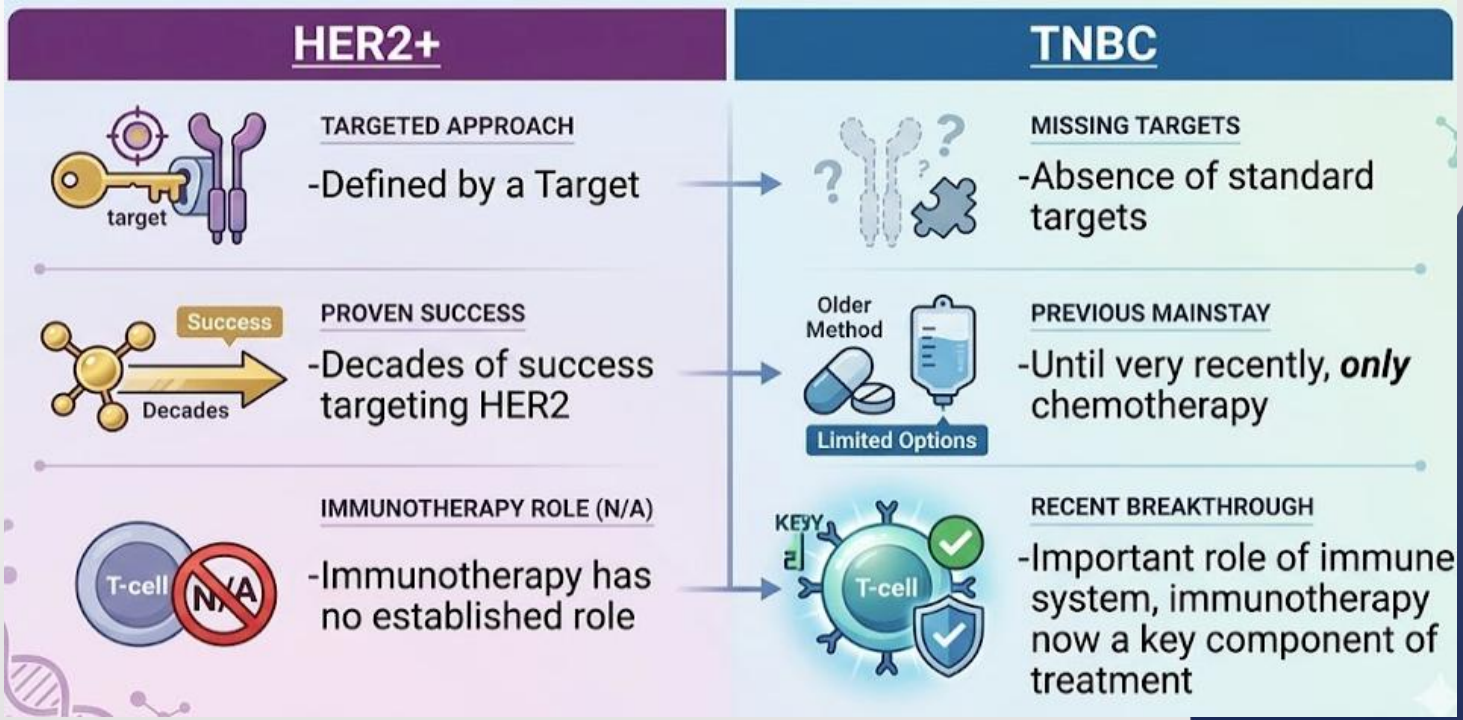
Many treatment advances have been made, creating new options and improving clinical outcomes

“Antibody Drug Conjugates” (ADCs) have emerged as important therapies for treatment of metastatic disease

Shared Features of TNBC and HER2+ Breast Cancer



Differences in Biology → Different Treatment



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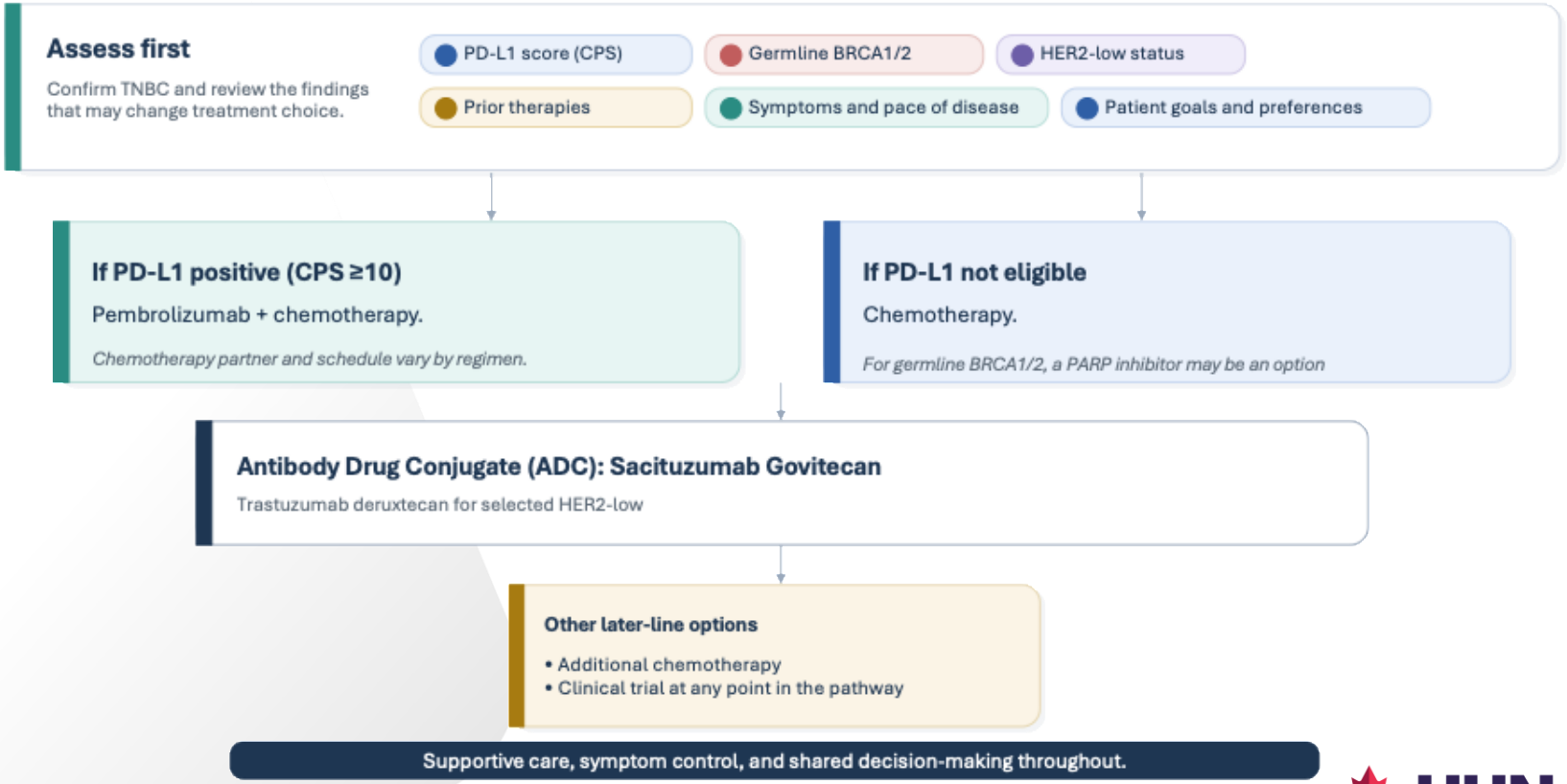
TNBC in 2025



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HER2+ Breast Cancer in 2025

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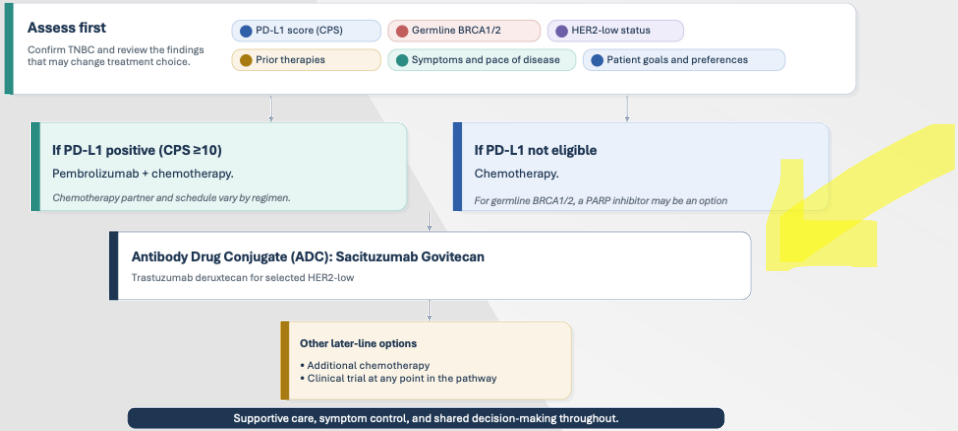

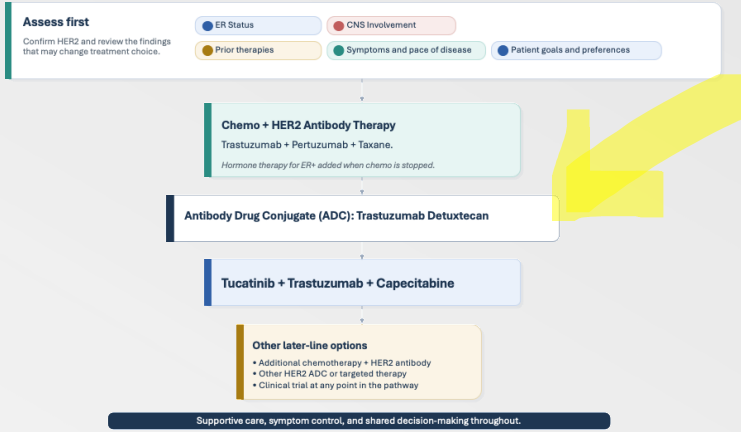

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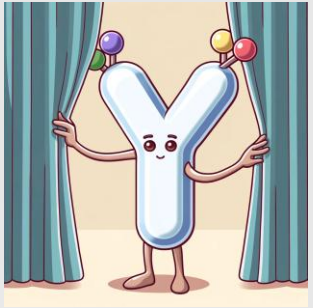
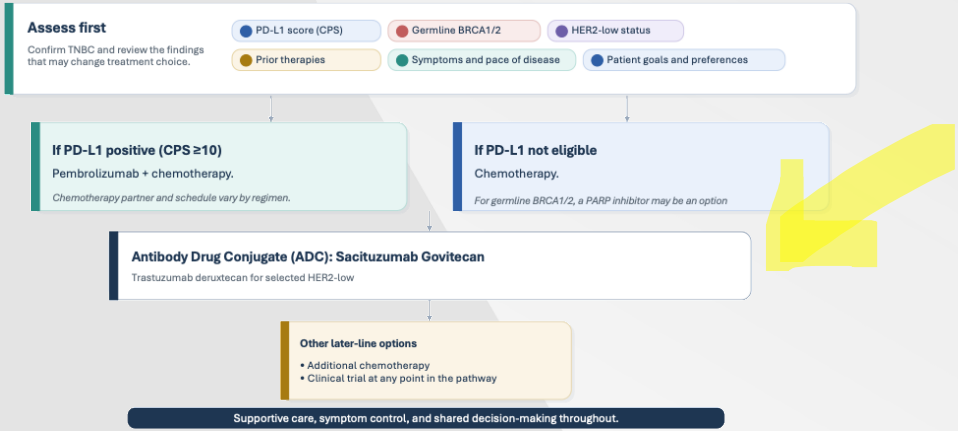
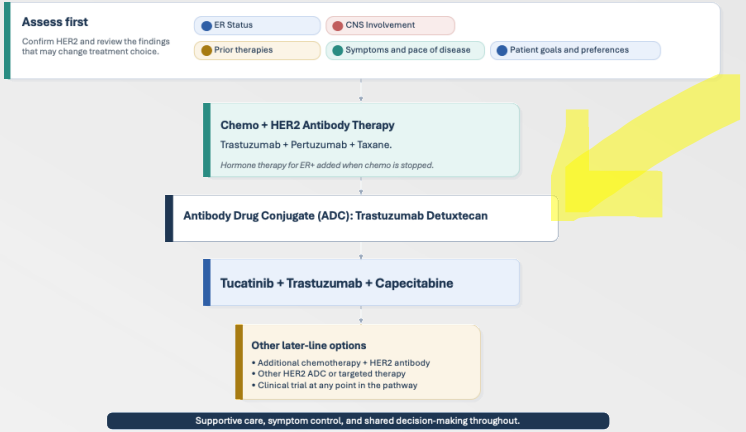
What are ADCs, and where are they headed?







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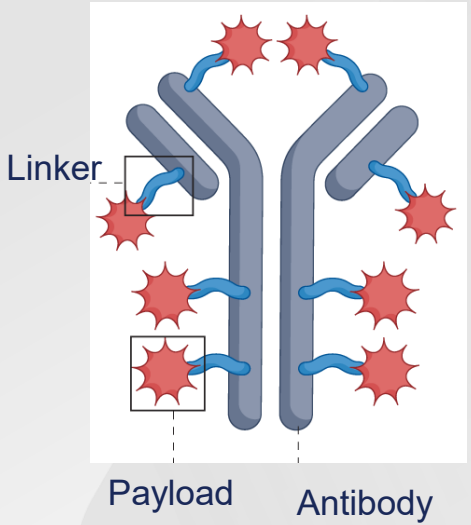
Antibody-drug Conjugates?

- Targeted delivery of potent chemo to tumor cells
- Complex therapy, with 3 main components:
  - Antibody
  - Linker
  - “Payload”



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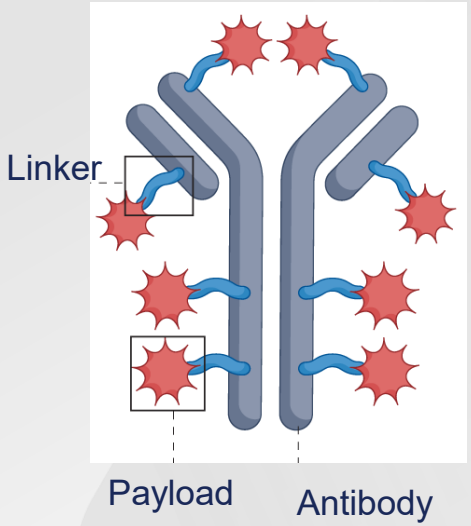
Antibody-drug Conjugates?

1. Antibody binds a tumor target
2. The ADC is taken into the cell
3. Payload is released to damage the cancer cell



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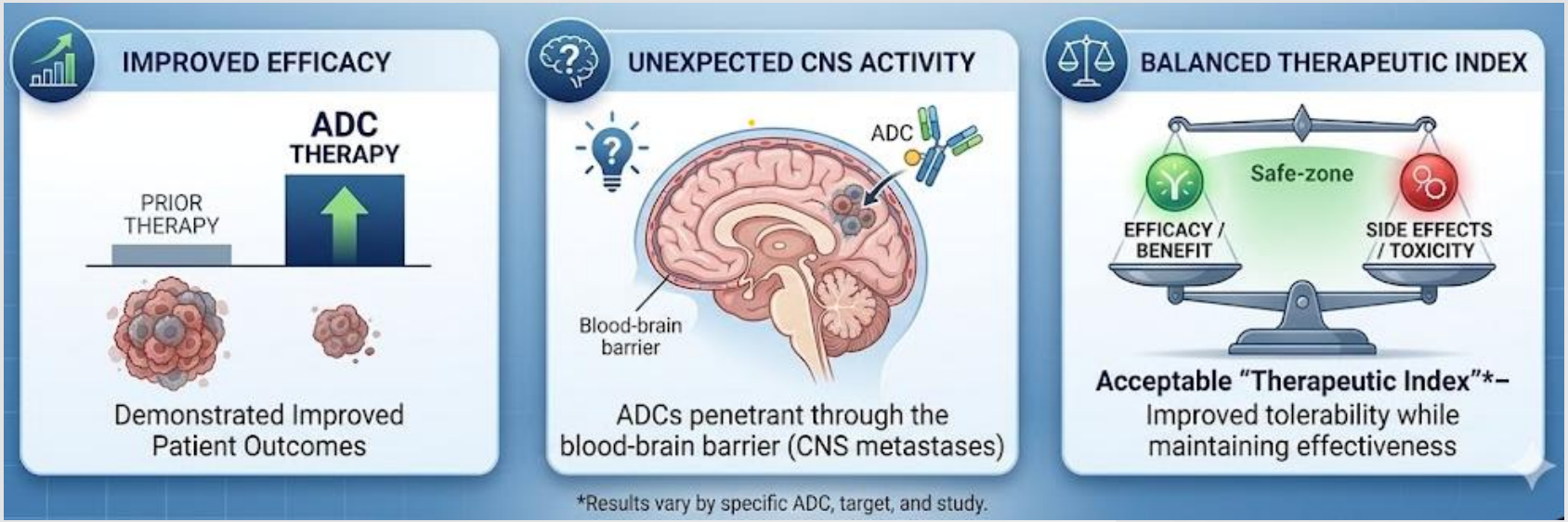
How have ADCs Performed in Metastatic Breast Cancer?



*but important new toxicities

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HER2+ MBC

T-DM1[a] *EMILIA*
T-DM1 was approved as second-line treatment for HER2+ advanced breast cancer

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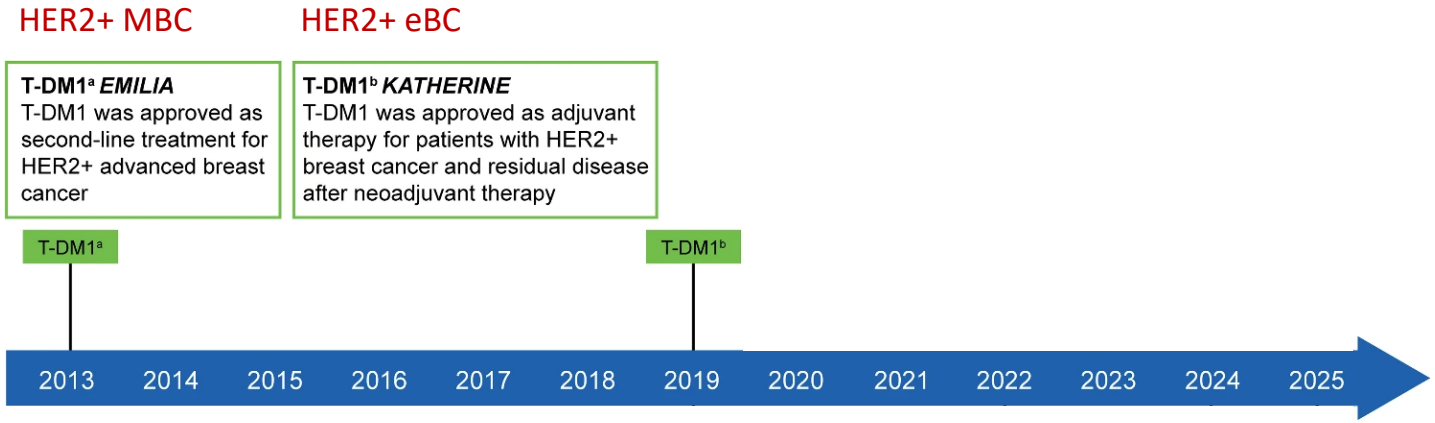
HER2+ MBC
HER2+ eBC
T-DM1[a] EMILIA
T-DM1 was approved as second-line treatment for HER2+ advanced breast cancer
T-DM1[b] KATHERINE
T-DM1 was approved as adjuvant therapy for patients with HER2+ breast cancer and residual disease after neoadjuvant therapy
T-DM1[a]
T-DM1[b]
2013
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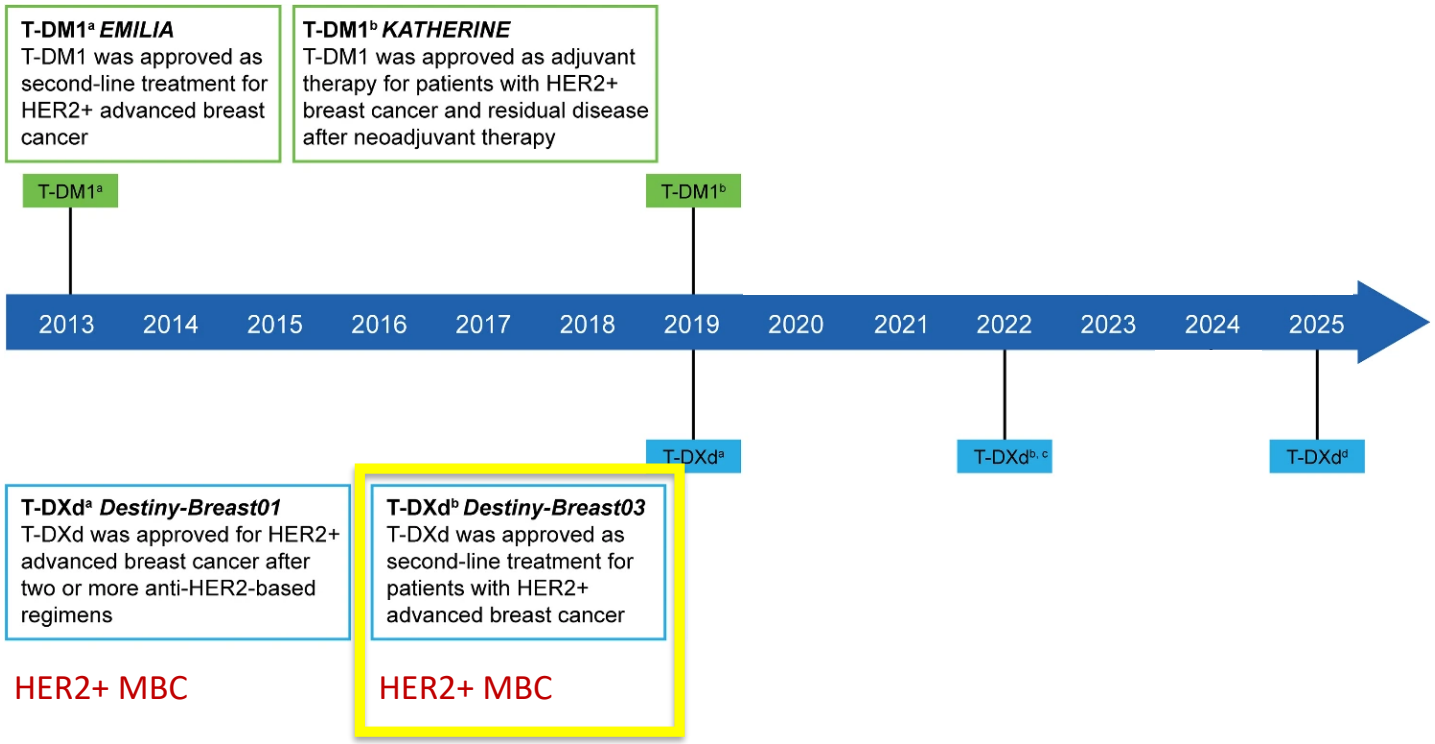
Li et al, 2025


T-DM1[a] EMILIA
T-DM1 was approved as second-line treatment for HER2+ advanced breast cancer
T-DM1[b] KATHERINE
T-DM1 was approved as adjuvant therapy for patients with HER2+ breast cancer and residual disease after neoadjuvant therapy
T-DM1[a]
T-DM1[b]
2013
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2022
2023
2024
2025
T-DXd[a]
T-DXd[b, c]
T-DXd[d]
T-DXd[a] Destiny-Breast01
T-DXd was approved for HER2+ advanced breast cancer after two or more anti-HER2-based regimens
HER2+ MBC
T-DXd[b] Destiny-Breast03
T-DXd was approved as second-line treatment for patients with HER2+ advanced breast cancer
HER2+ MBC

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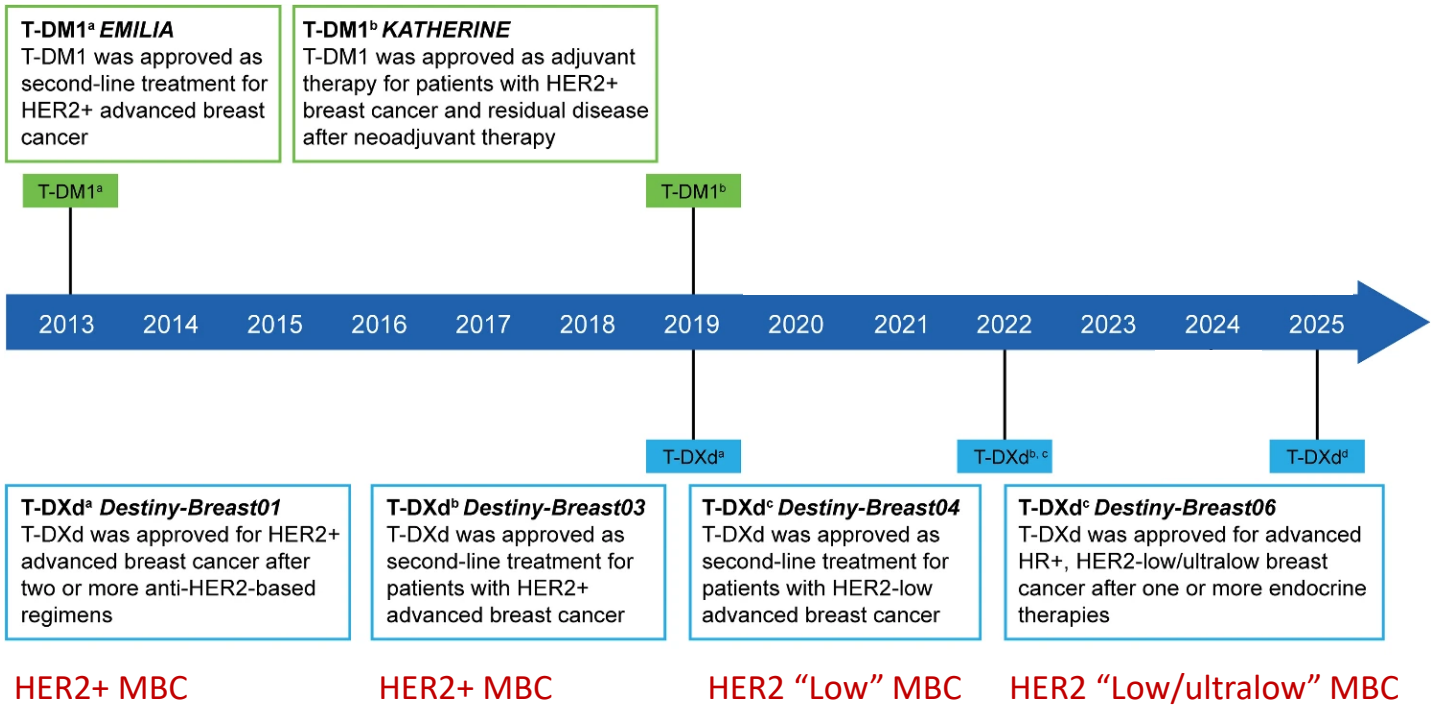
T-DM1[a] EMILIA
T-DM1 was approved as second-line treatment for HER2+ advanced breast cancer
T-DM1[b] KATHERINE
T-DM1 was approved as adjuvant therapy for patients with HER2+ breast cancer and residual disease after neoadjuvant therapy
T-DM1[a]
T-DM1[b]
2013
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2024
2025
T-DXd[a]
T-DXd[b, c]
T-DXd[d]
T-DXd[a] Destiny-Breast01
T-DXd was approved for HER2+ advanced breast cancer after two or more anti-HER2-based regimens
T-DXd[b] Destiny-Breast03
T-DXd was approved as second-line treatment for patients with HER2+ advanced breast cancer
T-DXd[c] Destiny-Breast04
T-DXd was approved as second-line treatment for patients with HER2-low advanced breast cancer
T-DXd[c] Destiny-Breast06
T-DXd was approved for advanced HR+, HER2-low/ultralow breast cancer after one or more endocrine therapies
HER2+ MBC
HER2+ MBC
HER2 “Low” MBC
HER2 “Low/ultralow” MBC

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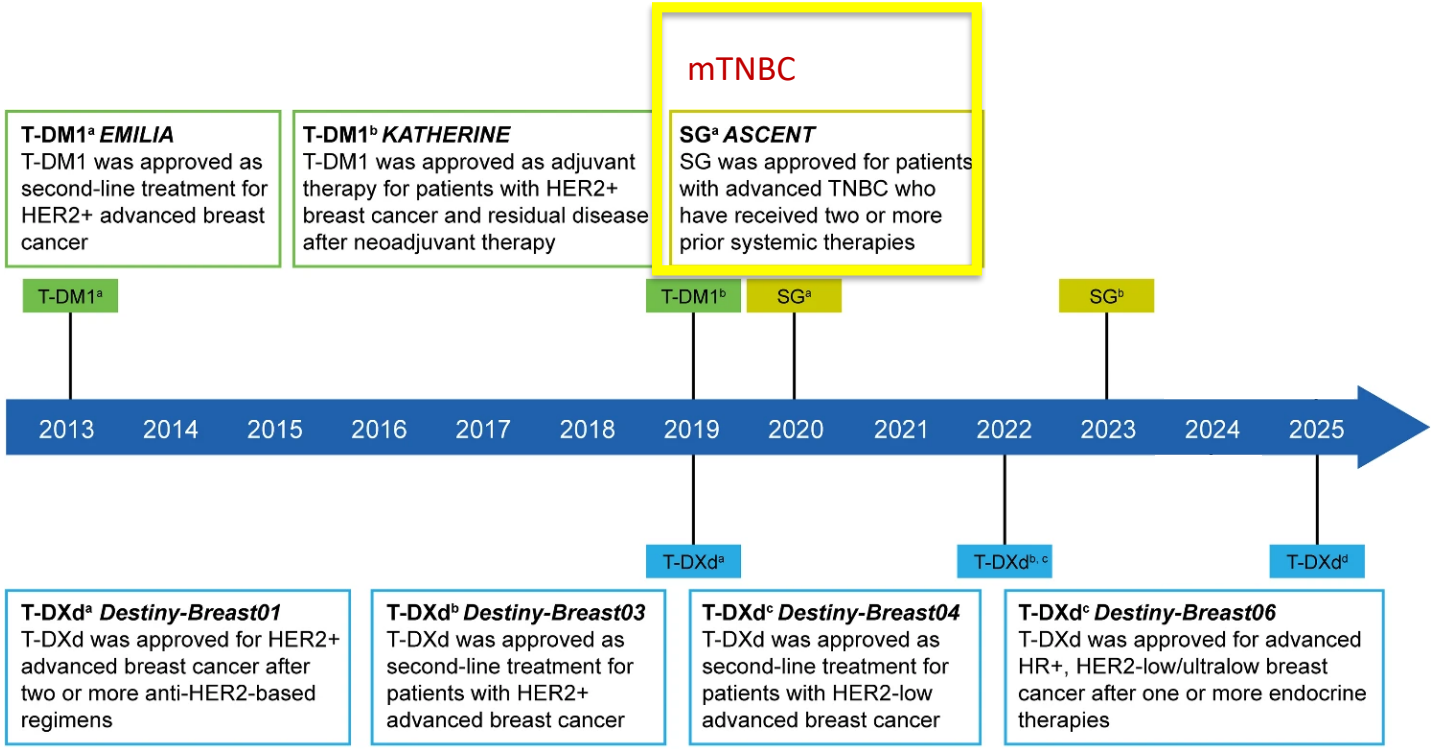
mTNBC
T-DM1[a] EMILIA
T-DM1 was approved as second-line treatment for HER2+ advanced breast cancer
T-DM1[b] KATHERINE
T-DM1 was approved as adjuvant therapy for patients with HER2+ breast cancer and residual disease after neoadjuvant therapy
SG[a] ASCENT
SG was approved for patients with advanced TNBC who have received two or more prior systemic therapies
T-DM1[a]
T-DM1[b]
SG[a]
SG[b]
2013
2014
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2021
2022
2023
2024
2025
T-DXd[a]
T-DXd[b, c]
T-DXd[d]
T-DXd[a] Destiny-Breast01
T-DXd was approved for HER2+ advanced breast cancer after two or more anti-HER2-based regimens
T-DXd[b] Destiny-Breast03
T-DXd was approved as second-line treatment for patients with HER2+ advanced breast cancer
T-DXd[c] Destiny-Breast04
T-DXd was approved as second-line treatment for patients with HER2-low advanced breast cancer
T-DXd[c] Destiny-Breast06
T-DXd was approved for advanced HR+, HER2-low/ultralow breast cancer after one or more endocrine therapies

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Now in 2026: ADCs to First Line

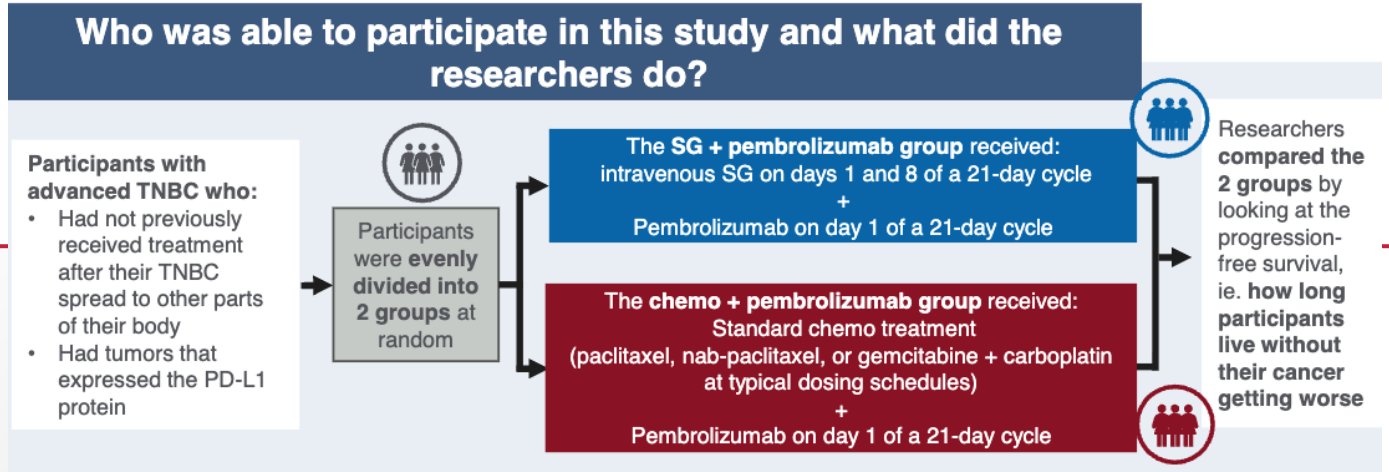
TNBC:

- Sacituzumab Govitecan + Pembro vs Chemo + Pembro (ASCENT-04)
- Sacituzumab Govitecan vs Chemo (ASCENT-03)
- Datopotamab Deruxtecan vs Chemo (TROPION Breast-02)

Now in 2026: ADCs to First Line

TNBC:

- Sacituzumab Govitecan + Pembro vs Chemo + Pembro (ASCENT-04)



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Now in 2026: ADCs to First Line

TNBC:

- Sacituzumab Govitecan vs Chemo (ASCENT-03)
- Datopotamab Deruxtecan vs Chemo (TROPION Breast-02)

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What else is under investigation in TNBC?

More TROP2 ADCs

New ADCs and new payloads

More Immunotherapy

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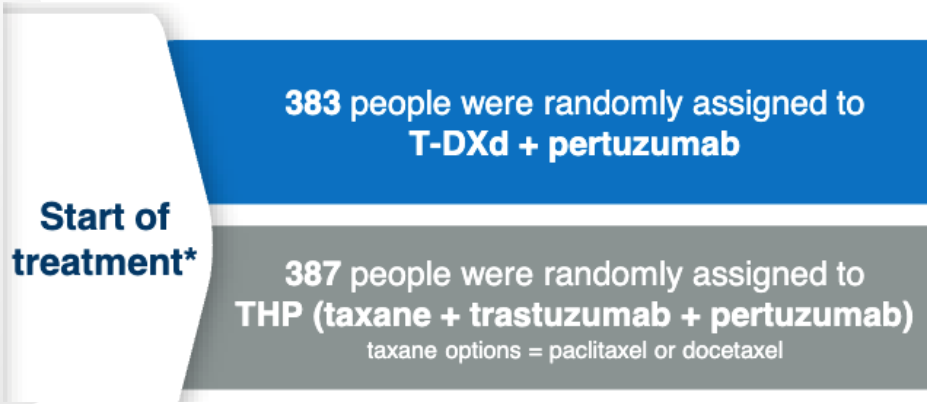
Now in 2026: ADCs to First Line

HER2+

- Trastuzumab Deruxtecan + Pertuzumab vs Taxol +Trastuzumab + Pertuzumab (DESTINY Breast09)



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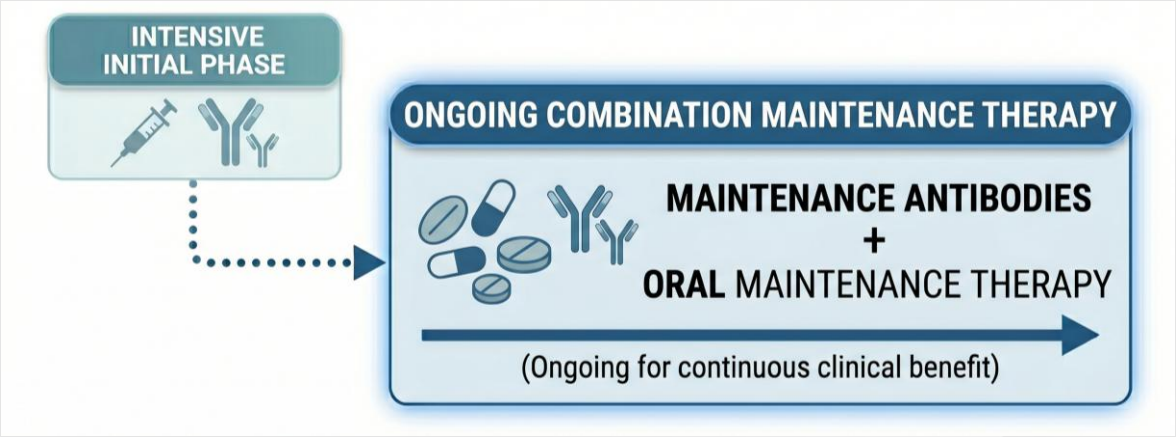
What else is Happening? HER2+

Maintenance Strategies



For HR+: Palbociclib+endocrine therapy: PATINA

Tucatinib: HER2CLIMB-05

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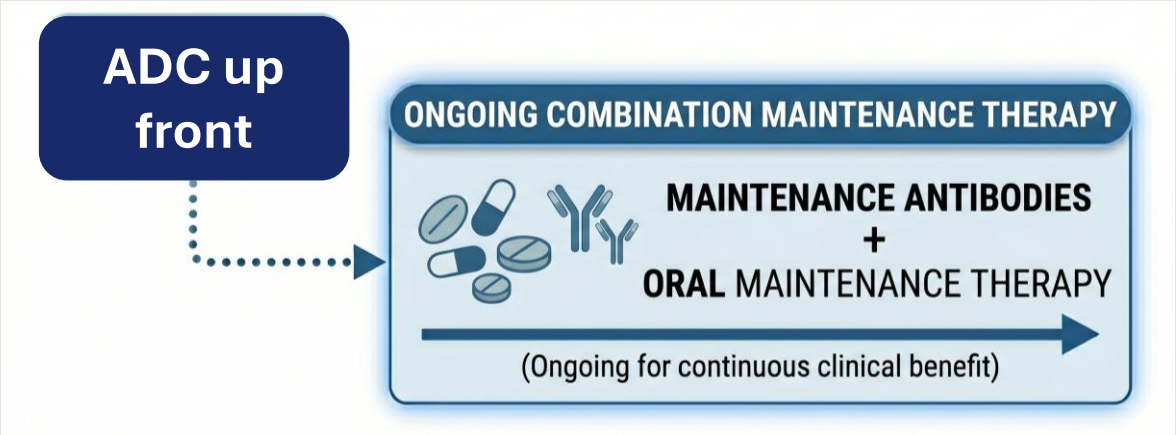
Upfront ADC vs Chemo → Maintenance?

ADC up front →

vs.



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New Treatments under investigation for HER2+ Disease

- Pathway targets (e.g. PIK3CA)
- New HER2 inhibitors
- Next-generation ADCs
- Other biologically selected strategies

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Summary

- Continued advancements are being made for treatment of metastatic HER2+ and TNBC
- A subset of people experience complete and durable disease control
  - How to identify?
  - Possibility of stopping treatments?
- Ongoing efforts to:
  - Use existing treatments for optimal outcomes
  - Develop new treatments where existing are ineffective
  - Understand role of existing or new treatments in later line treatment as ADCs move to first line

More Options, More Decisions – Right Information?

- How will treatment affect my day-to-day life, both now and in the future?
- What type of cancer do I have, and what stage is it? (How far has it spread?)
- What can I do to support my recovery and improve my chances of a good outcome?
- How many people in my situation are cured, and how many live longer with treatment? How long might I live?
- Is my cancer considered curable or incurable?
- What other treatment options are available, including clinical trials, and doing nothing for now?

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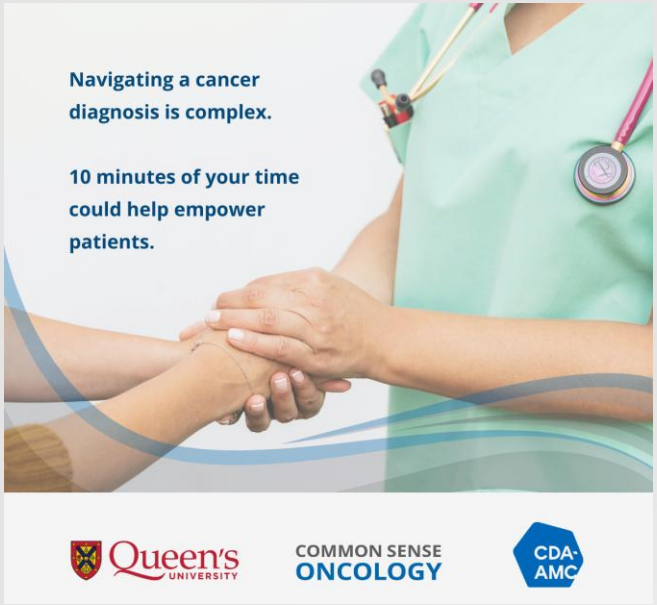
More Options, More Decisions – Right Information?

“Questions to ask your oncologist”



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