UK Charity for Triple Negative Breast Cancer

Focus on triple negative breast cancer (TNBC)

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Disclosures

1. I have received fees from pharmaceutical companies, including those making drugs I will discuss
2. The opinions I will state are mine, and not those of a pharmaceutical company, the University of Leeds, Leeds Teaching Hospitals Trust or the National Institute for Health and Care Research
3. **I am a Trustee of the UK Charity for Triple Negative Breast Cancer**

https://www.ukcharityfortnbc.org

What is Triple Negative Breast Cancer?

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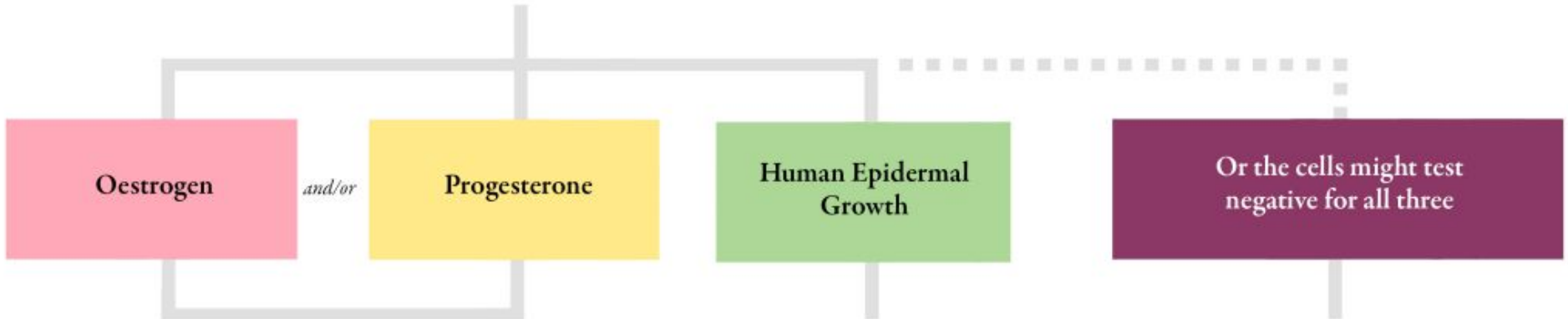
After the whole tumour, or part of it, has been removed by an operation or biopsy it is sent to the laboratory where the pathologist will confirm (i) that it is a breast cancer and (ii) what type of cancer it is.

The type of breast cancer is decided by whether there are certain "receptors" on the cancer cells.



This type of breast cancer is known as hormone receptor (HR) positive

These cancers are generally treated with hormonal drugs such as tamoxifen

This type of breast cancer is known as HER2 positive

These cancers are generally treated with targeted drug therapies such as trastuzumab

This type of breast cancer is known as Triple Negative or TNBC

These cancers are generally treated with chemotherapy but also newer drugs such as sacituzumab govitecan or in some people immunotherapy such as atezolizumab and pembrolizumab

TNBC Background

Overall, 15% - 20% of all breast cancers

- In the U.S., more common in African American and Hispanic women
- More common in younger women

Outcomes are less good than for women with other molecular phenotypes of breast cancer

- Higher risk of recurrence and metastasis after treatment for early disease
  - But many such women are cured
- Survival following development of metastatic disease is less good
  - But metastatic TNBC is not “terminal

Local treatment of TNBC (surgery, RT) essentially the same as other types of breast cancer

But systemic treatments (neo/adjuvant and/or metastatic) differ from HR+ve and HER2+ve disease

- Historically, systemic treatment for TNBC limited to chemotherapy
- But new treatments are emerging specifically for people with TNBC

Systemic treatment: Chemotherapy

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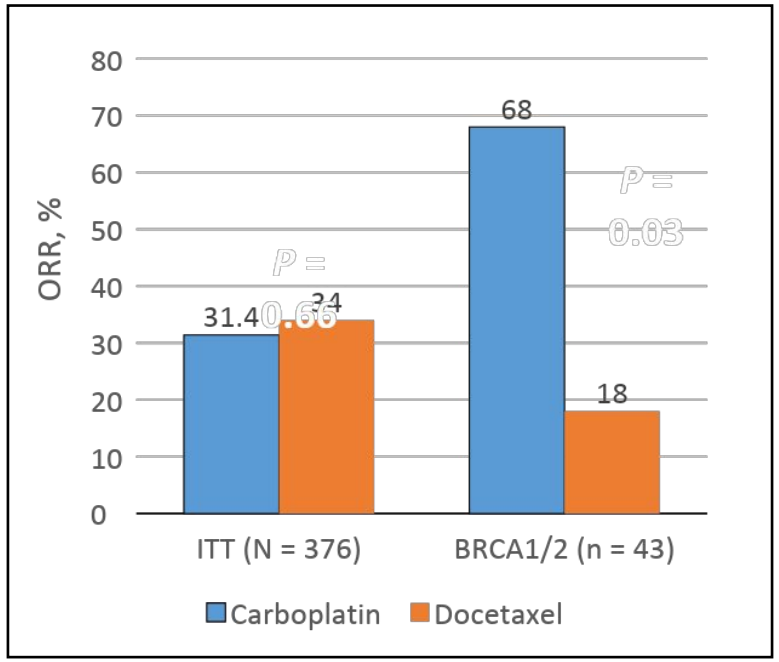
Metastatic TNBC

- Standard cytoxics are effective (right), but some appear more effective than others in TNBC
  - Platinum (below left)
  - Eribulin (below right)

Preferred Single Agents			
Anthracyclines	**Taxanes**	**Antimetabolites**	**Other Microtubule Inhibitors**
Epirubicin	**Paclitaxel (q1w)**	**Capecitabine**	**Eribulin**
Doxorubicin	Docetaxel	Gemcitabine	Vinorelbine
Pegylated/liposomal doxorubicin	*nab*-paclitaxel		
Other Single Agents			
Cyclophosphamide	Etoposide (po)	Fluorouracil	
Mitoxantrone	Vinblastine (iv/po)	(Ixabepilone)	
etc			



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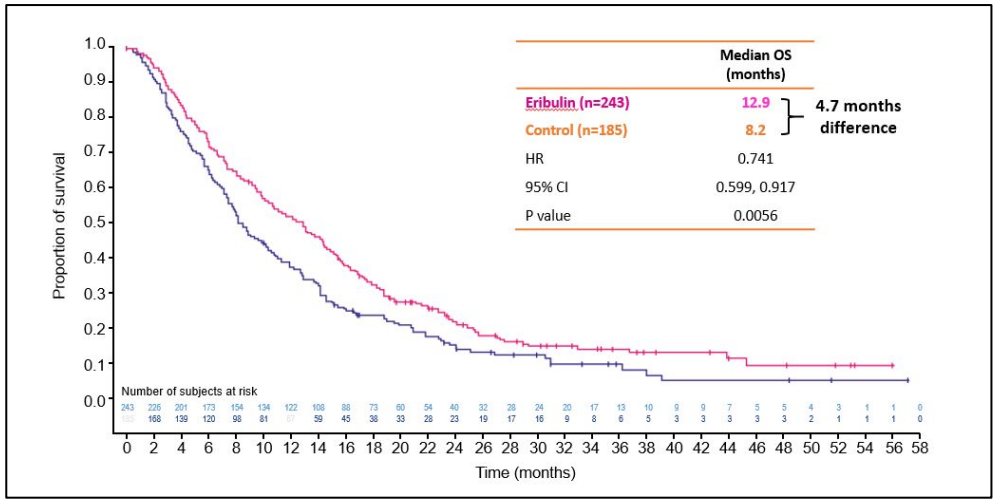

Cortes J. Lancet 2011; 377 (9769): 914-923
Kaufman PA, *et al. J Clin Oncol*. 2015;33(6):594–601

Systemic treatment: Immunotherapy

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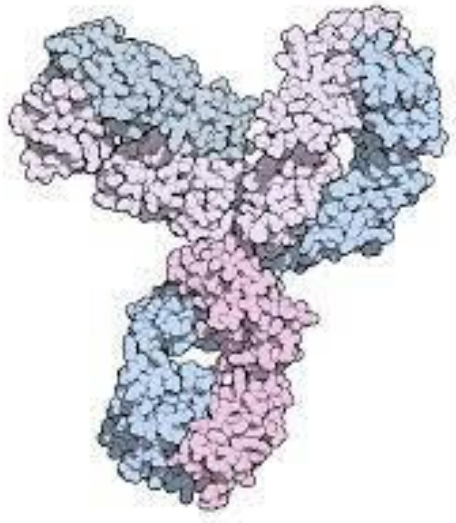
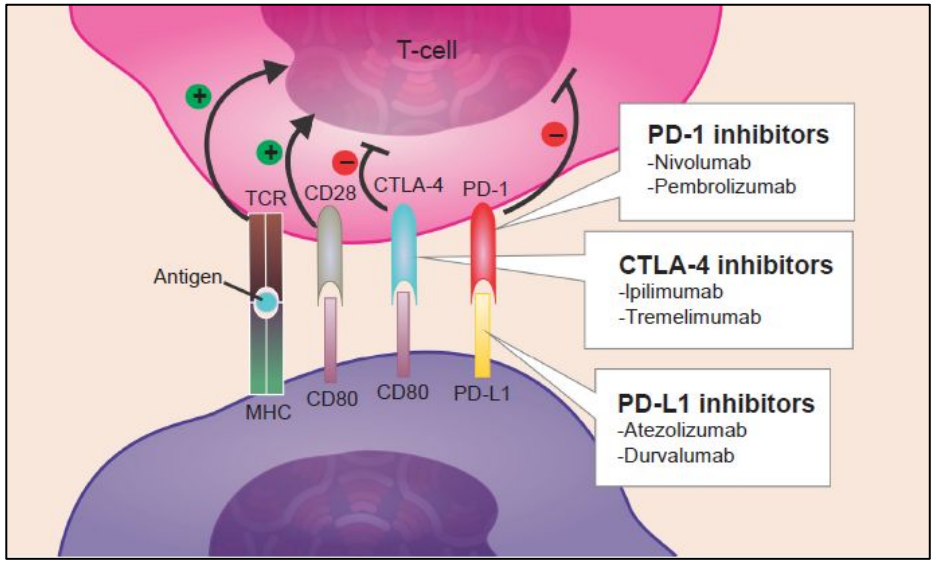
Metastatic TNBC

- Immunotherapy is more effective in PDL-1 +ve TNBC than other types of breast cancer as 1st line treatment





Systemic treatment: Immunotherapy

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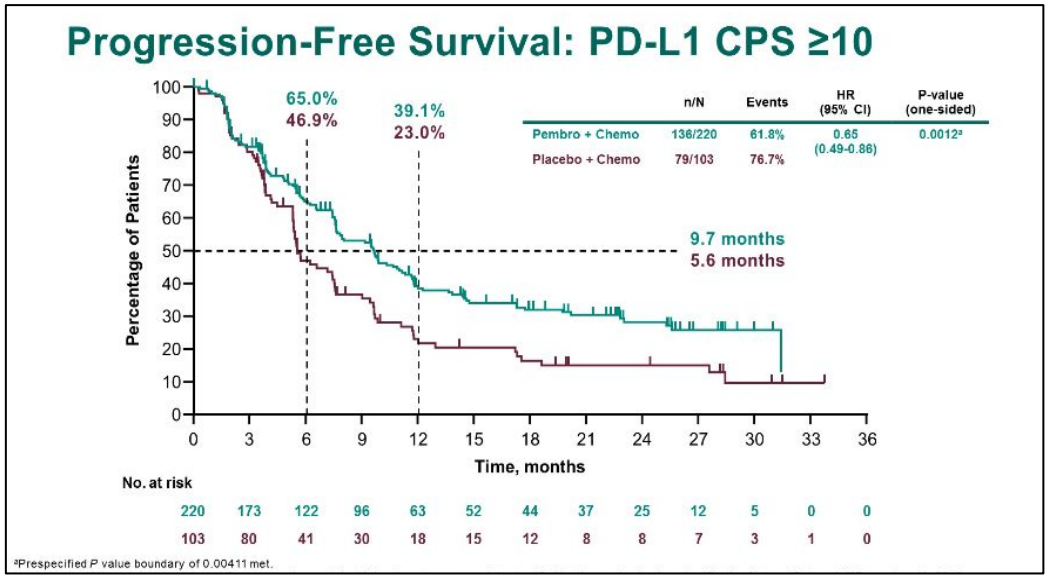
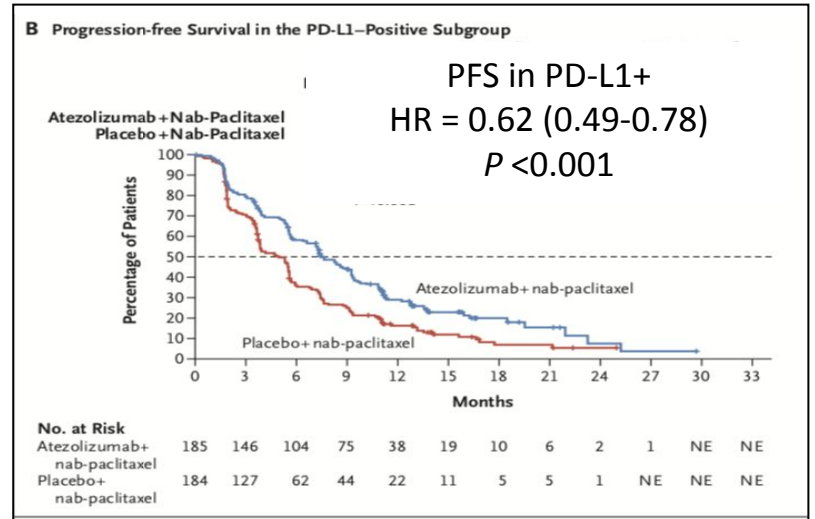
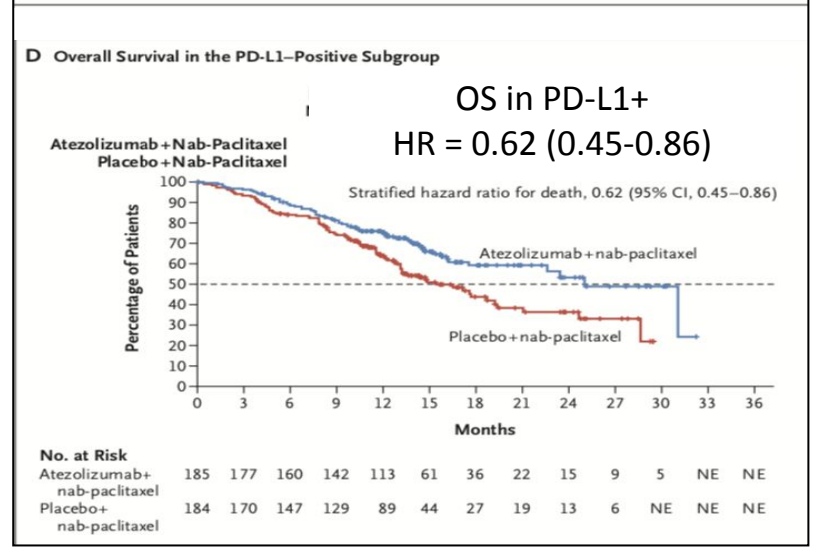
Metastatic TNBC

- Immunotherapy prolongs PFS and OS in PDL-1 +ve TNBC as 1st line treatment
  - 22C3 +ve: Atezolizumab plus *nab*-paclitaxel (right)
  - SP142 +ve: Pembrolizumab plus paclitaxel or *nab*-paclitaxel (below)



Cortes J et al
Lancet 2020





Schmid P, et al. *N Engl J Med.* 2018;379:2108-2121;
Schmid P, et al. *Lancet Oncol.* 2020;21:44-59.

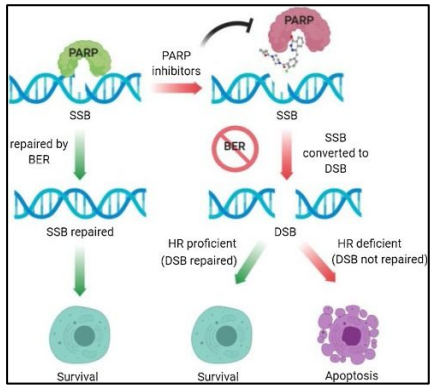
Systemic treatment: Targeted therapies – PARP inhibitors (PARPi)

PARP helps repair damaged DNA

- Blocking PARP may stop cancer cells from repairing damaged DNA leading to cell death.
- gBRCA patients already have deficient DNA repair so their c cancers are more susceptible to PARPi.

Metastatic TNBC

- Increased incidence of *m*BRCA1/2 in TNBC (15 – 25%)
- Less toxicity with PARPi than chemotherapy
  - PARPi response rates similar (60%, 63%) to carboplatin in TNT (68%), and higher than control arms (29%, 27%)
  - Not funded through NHS for MBC



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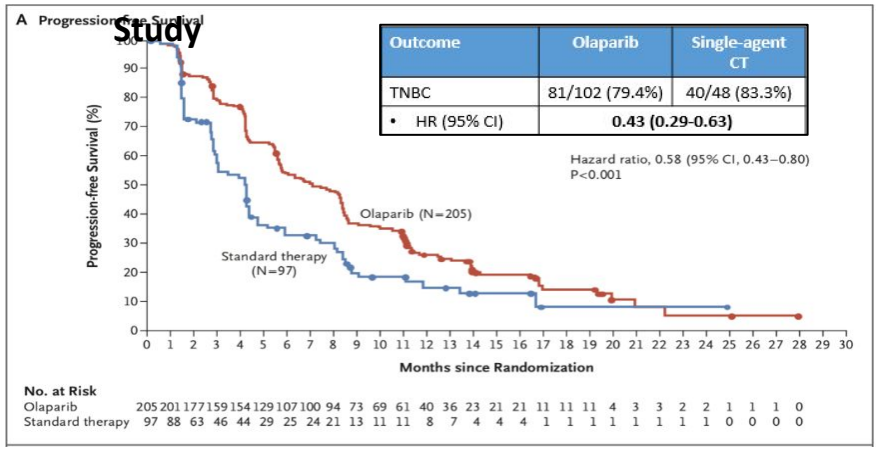
Olaparib: Phase 3 OlympiAD



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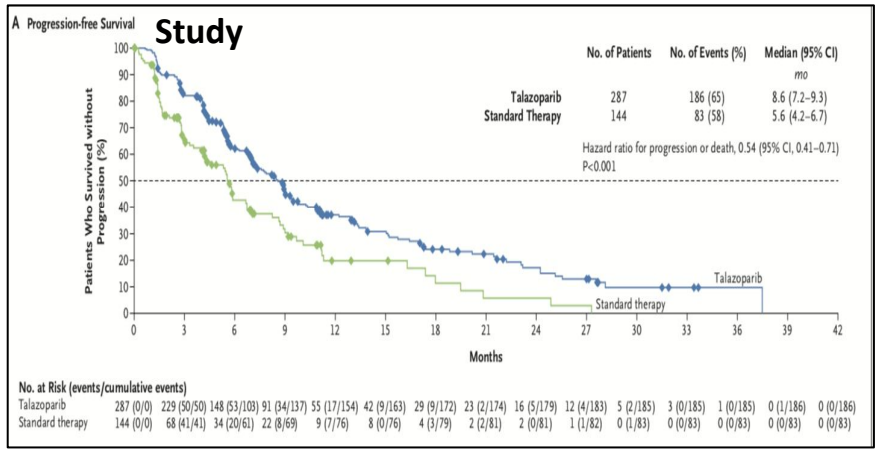
Litton JK, et al. AACR 2020

Talazoparib: Phase 3 EMBRACA



Systemic treatment: Antibody drug conjugates – sacituzumab govitecan

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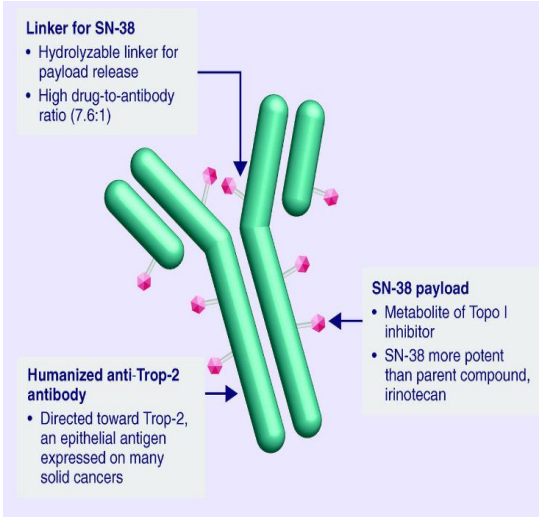
Metastatic TNBC

Antibody targeting Trop-2 conjugated to SN-38, topoisomerase I inhibitor

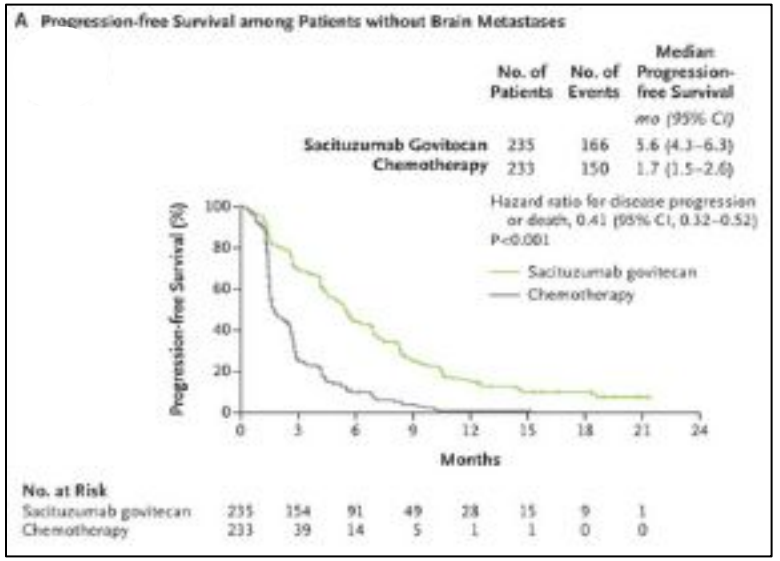


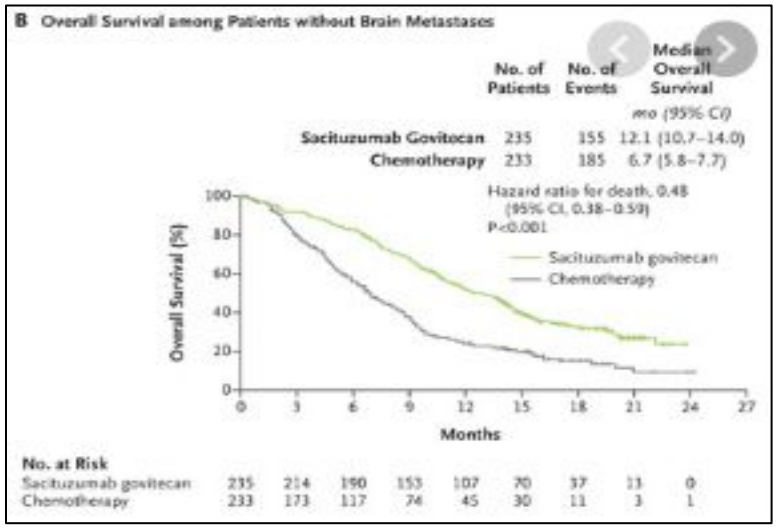
- Trop-2 overexpressed in many solid tumors, including TNBC, with limited expression in normal tissue
- IV days 1 and 8 of 21-day cycle vs TPC
- Toxicities: neutropenia and diarrhea; can be severe
- Prophylactic premedication for infusion reactions and N&V

Approved specifically in TNBC; no Trop-2 testing

TABLE 1: ASCENT Analysis by Trop-2 Expression

Endpoint	Trop-2 High		Trop-2 Medium		Trop-2 Low	
	SG	Control	SG	Control	SG	Control
PFS	6.9 mo	2.5 mo	5.6 mo	2.2 mo	2.7 mo	1.6 mo
OS	14.2 mo	6.9 mo	14.9 mo	6.9 mo	9.3 mo	7.6 mo
ORR	44%	1%	38%	11%	22%	6%





Bardia A, et al. *N Engl J Med.* 2019;380:741-751

Systemic treatment: Antibody drug conjugates – trastuzumab deruxtecan

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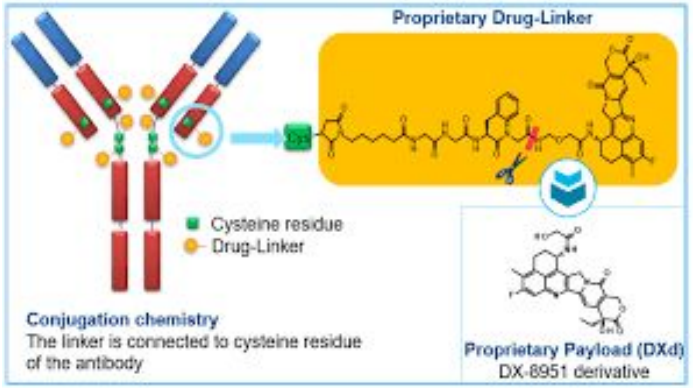
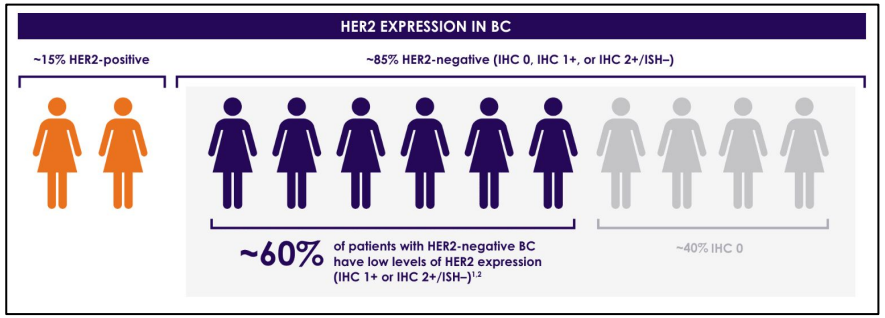
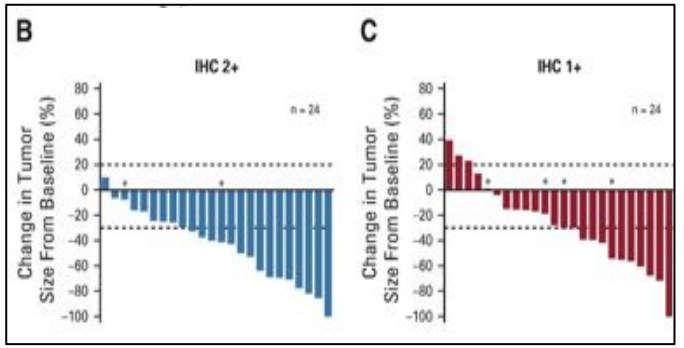
Metastatic TNBC

- HER2-targeted antibody drug conjugate
- Cleaved by lysosomal cathepsins with bystander effect
- Approved in HER2+ve MBC
- 54 patients with pre-treated <u>HER2-low</u> MBC
  - ORR (37.0%; 95% CI, 24.3% to 51.3%)
  - Similar in 1+ and 2+ (36% vs 38%)
  - But lower in ER-ve than ER+ve (14% vs 40%)
  - Median duration of response 10.4 months
- Generally well tolerated but some concerns over interstitial lung disease
- Phase III trials vs TPC ongoing







Modi et al, J Clin Oncol 2020

State of the art of advanced/metastatic TNBC management

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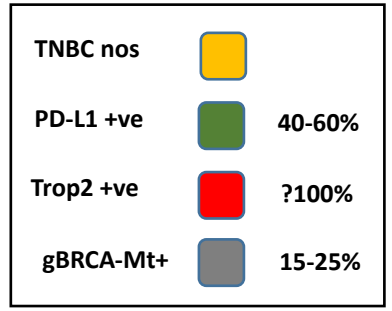
Patients with metastatic/advanced TNBC have an increasing number of approved therapies

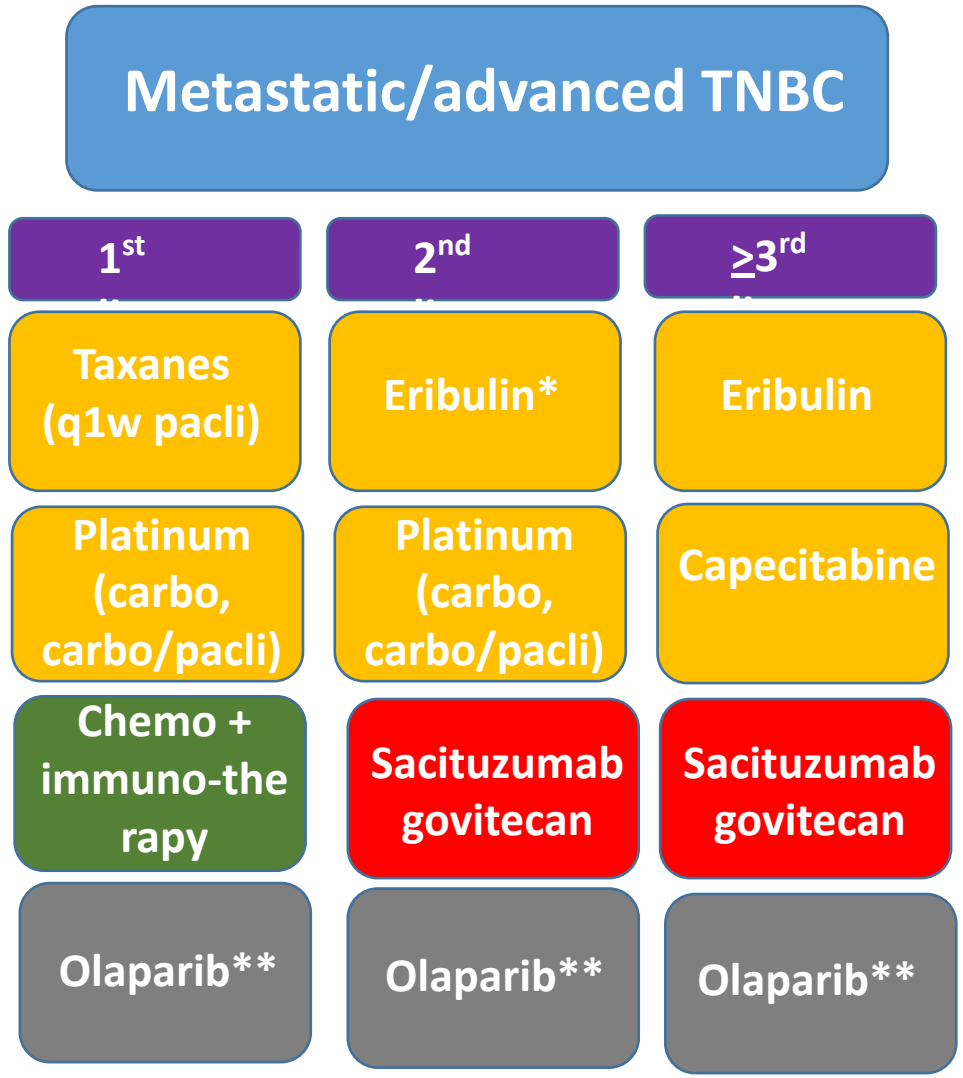
- Specific chemotherapies
- Immuno-oncology
- Targeted therapies
- Antibody drug conjugates

These dugs are achieving meaningful improvements in patient outcomes, including prolonging OS

TNBC on longer a Cinderella cancer, but remains a major unmet need

Opportunities for trial participation





* Approved 2nd line but funded >3rd line in UK

** Approved in EU but not funded through NHS; may be available through manufacturer on individual patient basis

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Thank you for your attention

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