MEDICAL UPDATE – MANAGEMENT OF SECONDARY BREAST CANCER IN YOUNGER WOMEN

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INTRODUCTION

Consultant Clinical Oncologist at Bristol Haematology and Oncology Centre

- Specialize in both radiotherapy and systemic treatments for breast cancer

AIMS & OBJECTIVES

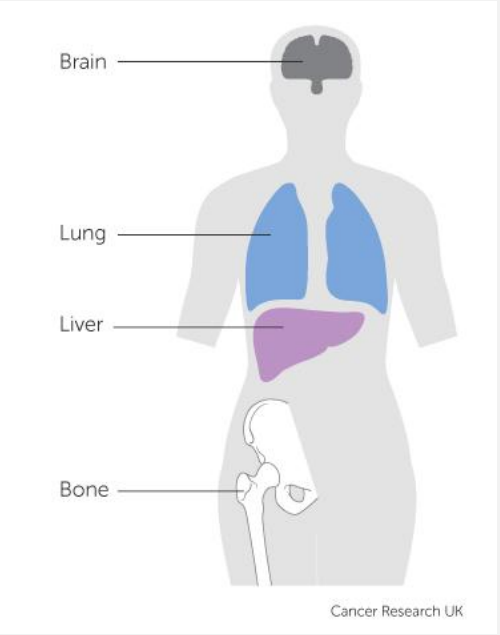
- To increase understanding of metastatic breast cancer

- What is metastatic breast cancer
- Treatment aims
- Overview of current treatments
  - Chemotherapy
  - Radiotherapy
  - Hormone treatment
  - Targeted therapies

- Recent advances in medical management

WHAT IS METASTATIC BREAST CANCER?

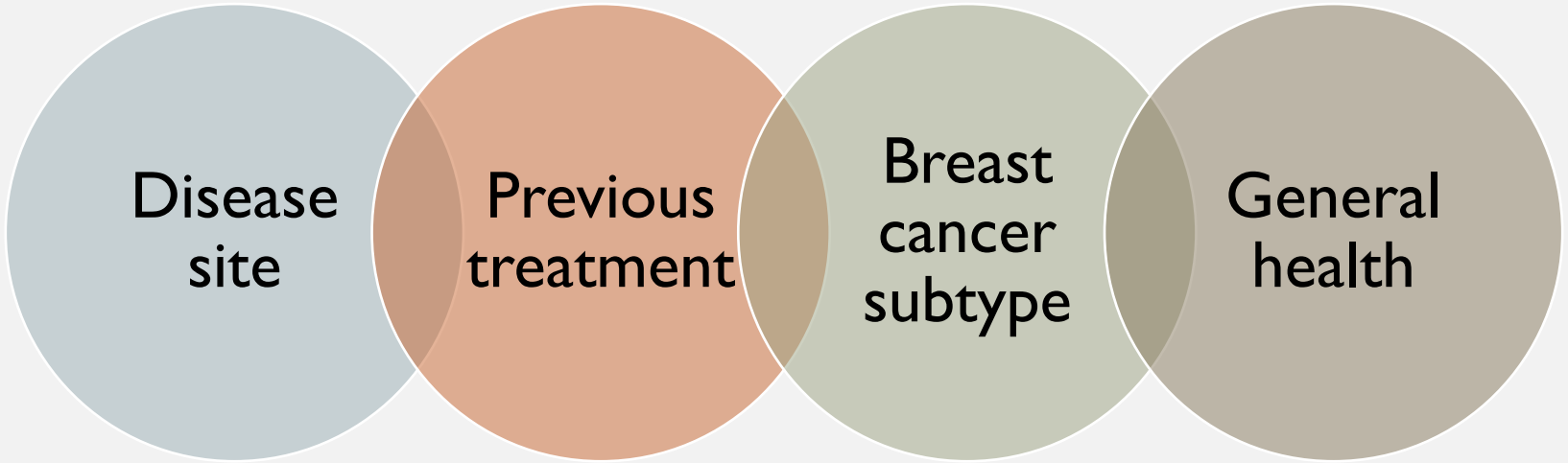
- Cancer from the breast which has spread to other parts of the body
- Is also called stage 4 breast cancer, advanced cancer or secondary breast cancer
- Can be the first presentation of disease or follow previous treatment for early breast cancer



TREATMENT AIMS

- Due to its advanced nature it is not possible to eliminate all disease
- Aims of treatment are to control the cancer and treat any symptoms that are caused by it
- Several factors are taken into account when deciding what is the best treatment with the aim of choosing the therapy most likely to provide the greatest benefit with as few side effects as possible

FACTORS WHEN DECIDING TREATMENT



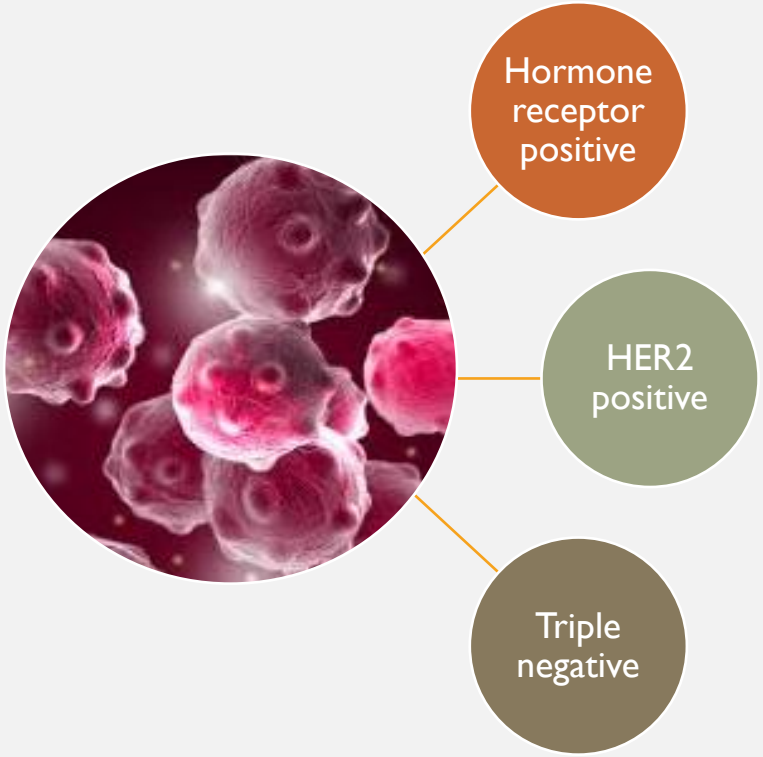
DISEASE SITE

- Bone
  - Need for bone strengthening medications(e.g. Denosumab)
  - Role for prophylactic surgery?
  - Radiotherapy for pain control?
- Brain
  - Involvement of neuro-oncology MDT ?surgery/radiotherapy(e.g. Gammaknife)
  - Choice of treatment – some drugs work better in the brain that others
- Liver
  - Impact on liver function and treatment choice
- Lung/ Peritoneal
  - Need for drainage of fluid

PREVIOUS TREATMENT

- How long ago was it used
- How well did this work.
  - Disease free interval? Treatment resistance?
- How was this tolerated
- Any lasting side effects e.g. peripheral neuropathy

BREAST CANCER SUBTYPE

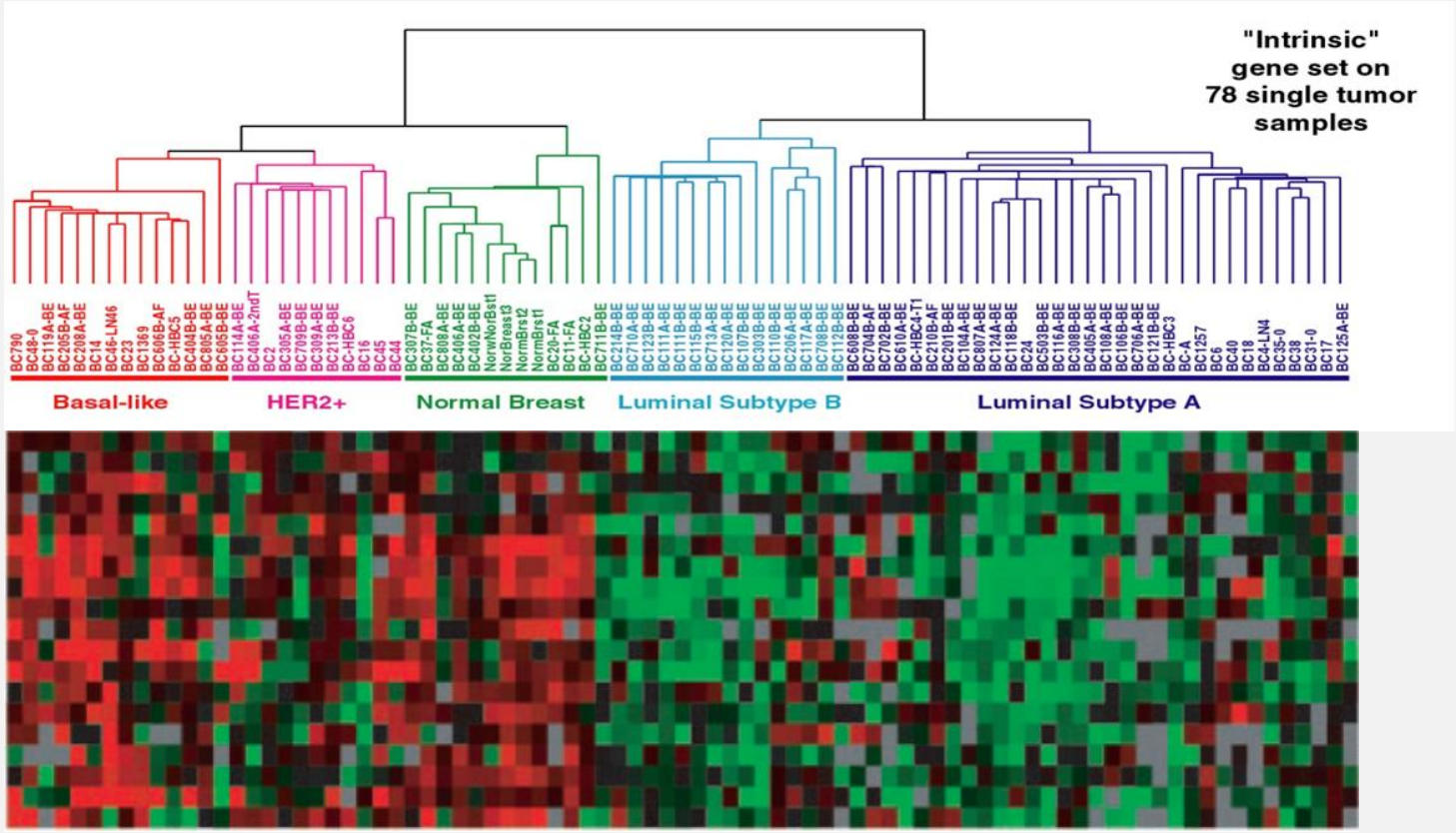


Most prevalent subtype – 70% of all patients. Expression of estrogen and /or progesterone receptors

20% of patients. Overexpression of HER2 receptor

10% of patients. More common in younger women and associated with BRCA mutations

DNA PROFILING IS INCREASING OUR UNDERSTANDING



Sørlie T *et al. Proc Natl Acad Sci* 2001; 98: 10869-10874.

GENERAL HEALTH

- Fitness
- Symptoms
- Other heath conditions
- Organ function incl liver, kidneys, heart
- Social situation

WHAT IS IMPORTANT FOR YOU? (AND YOUR FAMILY/FRIENDS)

- What impact will it have on me?
  - Length of Life? Quality of Life?
  - What symptoms might I get?
- Type of treatment - Oral / IV
- Side effects of treatment –hair loss, fatigue, infection, nausea, diarrhoea
- Practical impact -time in hospital, travel, finances
- Complementary treatment?
- Support available?

TEAM APPROACH TO CARE

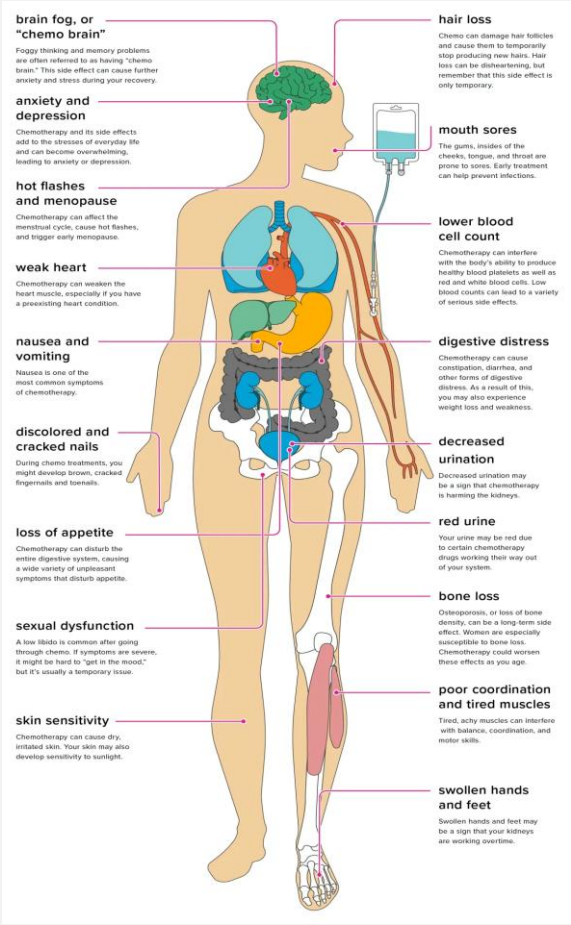
OVERVIEW OF CURRENT TREATMENTS

CHEMOTHERAPY

- Can be intravenous or oral
- Causes DNA damage to stop cancers growing
- Is given in ‘cycles’ of treatment to allow recovery in between treatment, typically once every 3 weeks

SIDE EFFECTS

- Can effect all body systems
- Common side effects include fatigue, hair loss, mouth ulcers, nausea/vomiting, digestive upset
- Most serious side effect is reduced immune system – risk of neutropenic sepsis
- Other side effects can be drug specific – peripheral neuropathy, palmar-plantar erythema etc.



WHEN IS IT USED

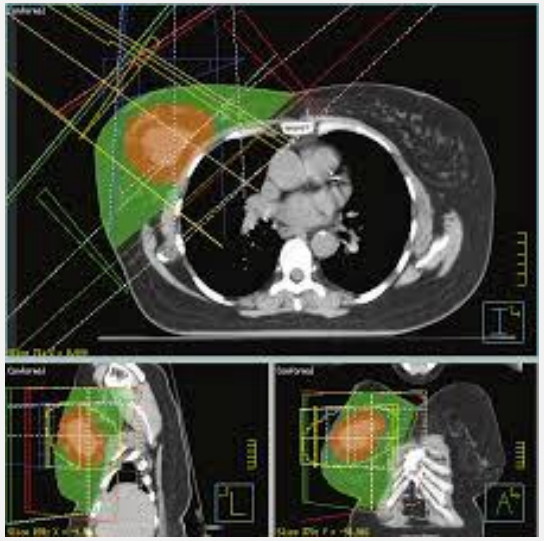
- If hormone or targeted treatments not suitable (either due to being receptor negative or if become resistant)
- If rapid response is needed – for example in visceral disease (liver, lung metastases)

RADIOTHERAPY

- Uses high energy X-rays to kill cancer cells by causing DNA damage
- Targeted at areas of disease to provide symptom control
- Requires a planning scan to design the treatment
- Is given in ‘fractions’ either as a single treatment or over several days

SIDE EFFECTS

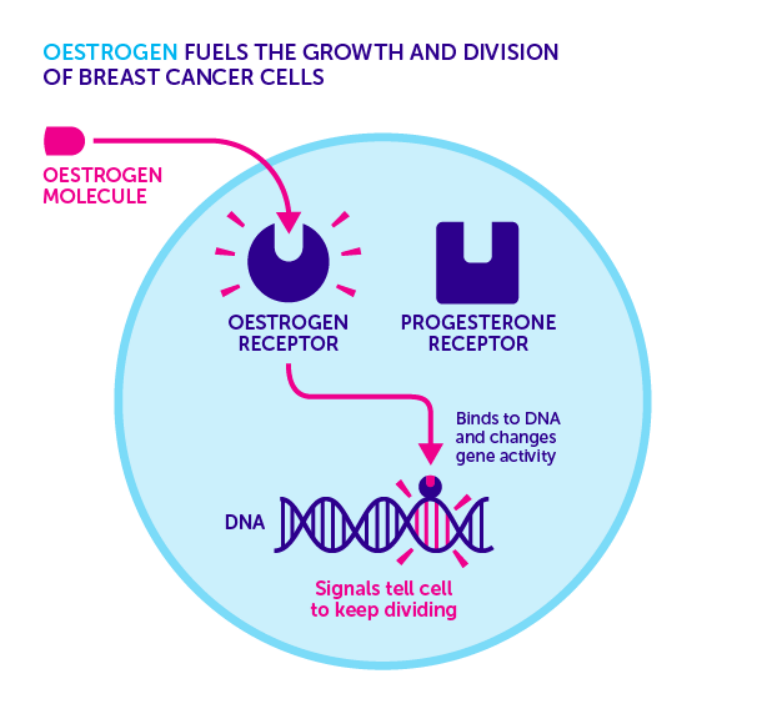
- Depends of where the radiotherapy is targeting
- Fatigue, skin reaction, and an initial symptom flare are common
- There is a maximum safe dose that any area of the body can receive but re-treatments can sometimes be considered



WHEN IS IT USED

- If localized disease or symptoms
- Examples include for bone pain, local disease in breast/lymph nodes and brain metastases

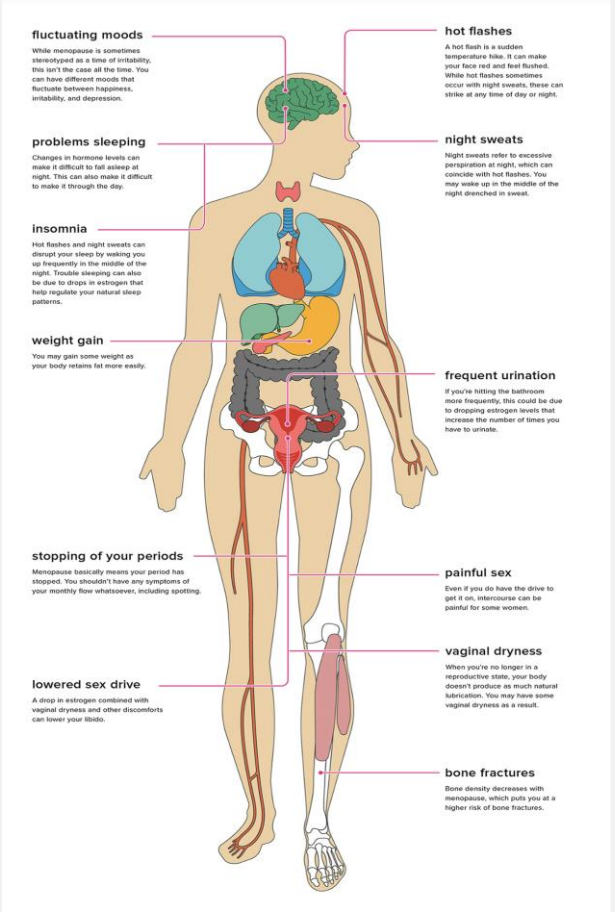
HORMONE TREATMENT



- Work by either blocking the effects of oestrogen on the oestrogen receptor (eg. Tamoxifen/Fulvestrant)
- Or by reducing circulating levels of oestrogen in the body either directly (eg. Anastrazole/Letrozole) or indirectly by suppressing ovarian function (eg. prostap, zoladex)

SIDE EFFECTS

- All can cause the common menopausal symptoms of hot flushes, night sweats and problems sleeping
- Can also affect mood with depression and fluctuating moods
- Will stop periods, lower sex drive as well as causing vaginal dryness and soreness



WHEN IS IT USED

- In patients with hormone receptor positive disease
- Side effects are less than with chemotherapy and therefore used early on in management of disease to minimize impact of treatment on quality of life
- Responses are slower than with chemotherapy therefore not suitable if rapid response needed

TARGETED TREATMENTS

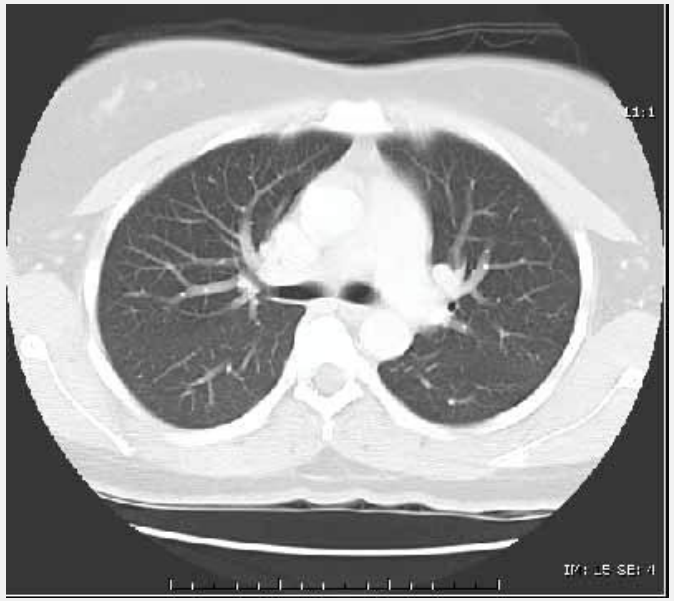
- Act upon specific targets on or in cancer cells which are helping the cancer to grow
- As they are more targeted the side effects tend to be less than with more traditional chemotherapy drugs
- There are tests on the tumour that are done to see whether these drugs are likely to work

EXAMPLES OF TARGETS IN BREAST CANCER

- **CDK 4/6 -** is the target of the oral drugs abemaciclib, palbociclib and ribociclib and improves the effectiveness of hormone treatment
- **HER2** – is overexpressed in some breast cancers causing cancer growth and is the target for drugs such as trastuzumab (herceptin) which block its effects
- **PDL1** – is a protein that helps keep immune cells from attacking cells. If levels in the tumour are high then immunotherapy is more likely to work

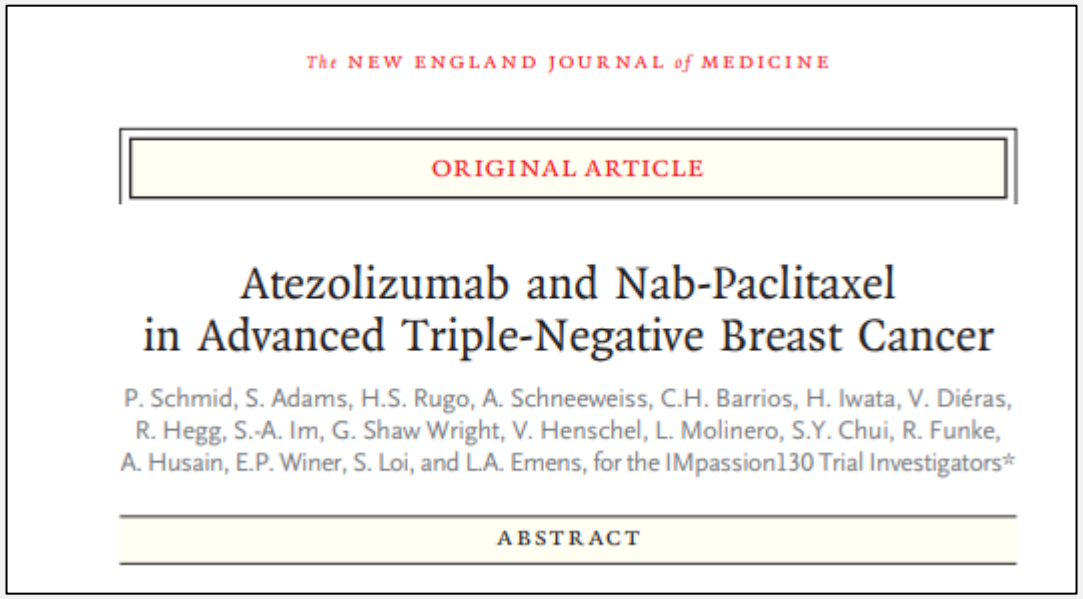
TREATMENT PATHWAYS

- Once a treatment is started then its effectiveness is reviewed regularly and assessed using a combination of scans, blood results and assessment of symptoms
- Providing benefit is maintained then treatment is continued
- Over time treatments can become less effective and when this occurs reassessment is required to choose the next appropriate therapy



RECENT ADVANCES IN MEDICAL MANAGEMENT

TRIPLE NEGATIVE BREAST CANCER



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer

P. Schmid, S. Adams, H.S. Rugo, A. Schneeweiss, C.H. Barrios, H. Iwata, V. Diéras, R. Hegg, S.-A. Im, G. Shaw Wright, V. Henschel, L. Molinero, S.Y. Chui, R. Funke, A. Husain, E.P. Winer, S. Loi, and L.A. Emens, for the IMpassion130 Trial Investigators*

ABSTRACT

THE LANCET

ARTICLES | VOLUME 396, ISSUE 10265, P1817-1828, DECEMBER 05, 2020

Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial

Javier Cortes, MD • David W Cescon, MD • Hope S Rugo, MD • Zbigniew Nowecki, MD • Seock-Ah Im, MD • Mastura Md Yusof, MD • et al. Show all authors • Show footnotes

Published: December 05, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)32531-9 • Check for updates

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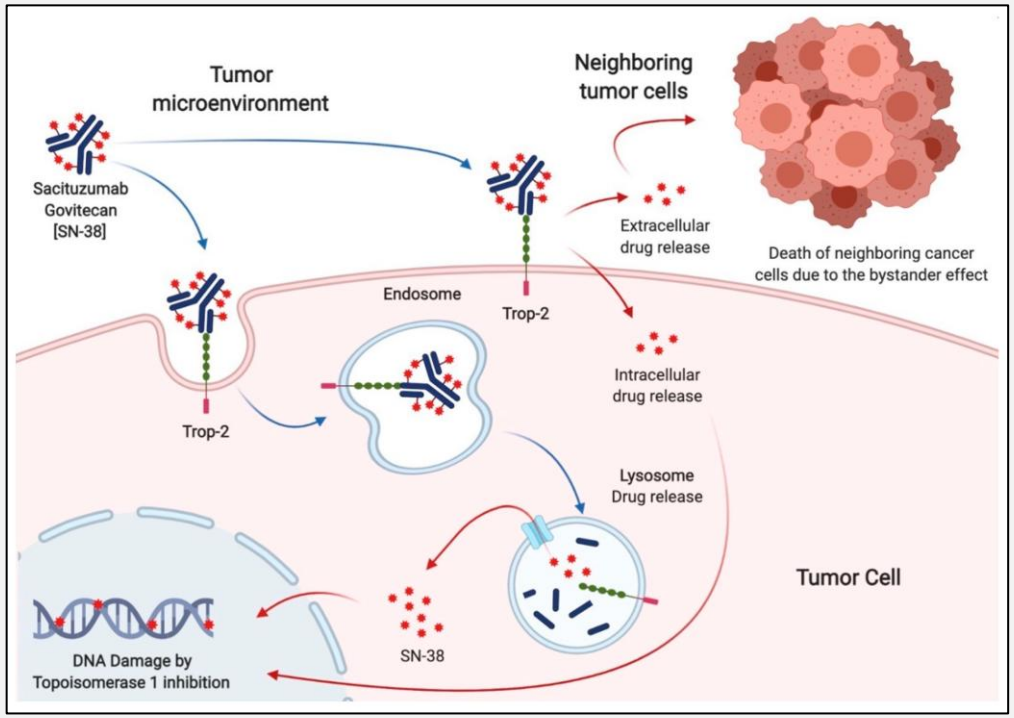
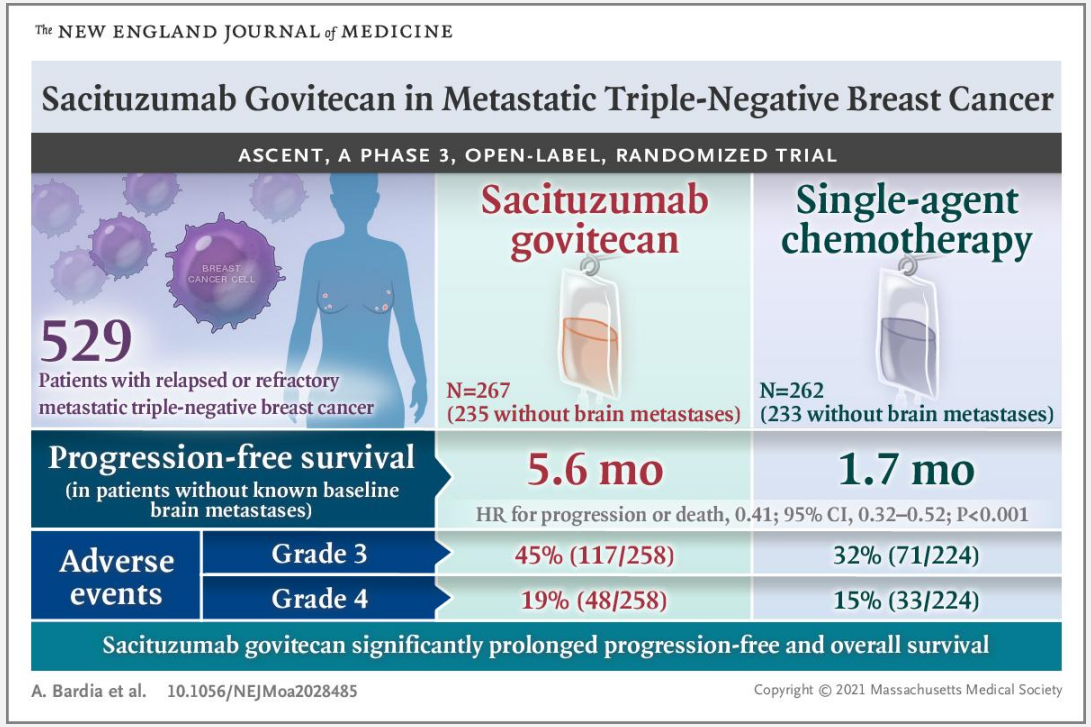
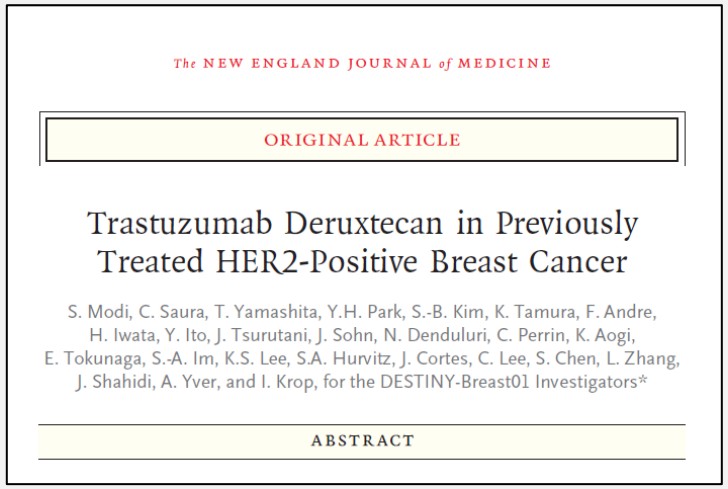




HER2+ BREAST CANCER



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer

S. Modi, C. Saura, T. Yamashita, Y.H. Park, S.-B. Kim, K. Tamura, F. Andre, H. Iwata, Y. Ito, J. Tsurutani, J. Sohn, N. Denduluri, C. Perrin, K. Aogi, E. Tokunaga, S.-A. Im, K.S. Lee, S.A. Hurvitz, J. Cortes, C. Lee, S. Chen, L. Zhang, J. Shahidi, A. Yver, and I. Krop, for the DESTINY-Breast01 Investigators*

ABSTRACT

THE LANCET

ARTICLES | VOLUME 401, ISSUE 10371, P105-117, JANUARY 14, 2023

Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial

Sara A Hurvitz, MD • Roberto Hegg, MD • Wei-Pang Chung, MD PhD • Seock-Ah Im, MD PhD • William Jacot, MD PhD • Vinod Ganju, MD • et al. Show all authors

Open Access • Published: December 07, 2022 • DOI: https://doi.org/10.1016/S0140-6736(22)02420-5 •

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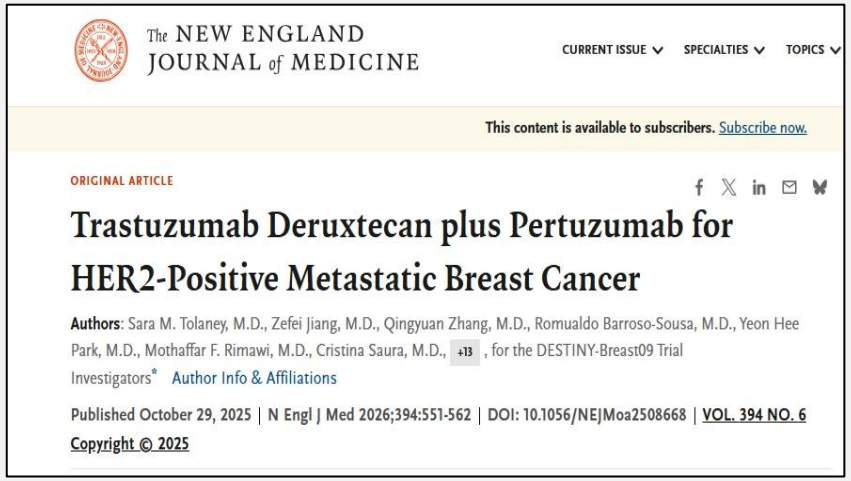

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CURRENT ISSUE SPECIALTIES TOPICS

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ORIGINAL ARTICLE

Trastuzumab Deruxtecan plus Pertuzumab for HER2-Positive Metastatic Breast Cancer

Authors: Sara M. Tolaney, M.D., Zefei Jiang, M.D., Qingyuan Zhang, M.D., Romualdo Barroso-Sousa, M.D., Yeon Hee Park, M.D., Mothaffar F. Rimawi, M.D., Cristina Saura, M.D., +13, for the DESTINY-Breast09 Trial Investigators* Author Info & Affiliations

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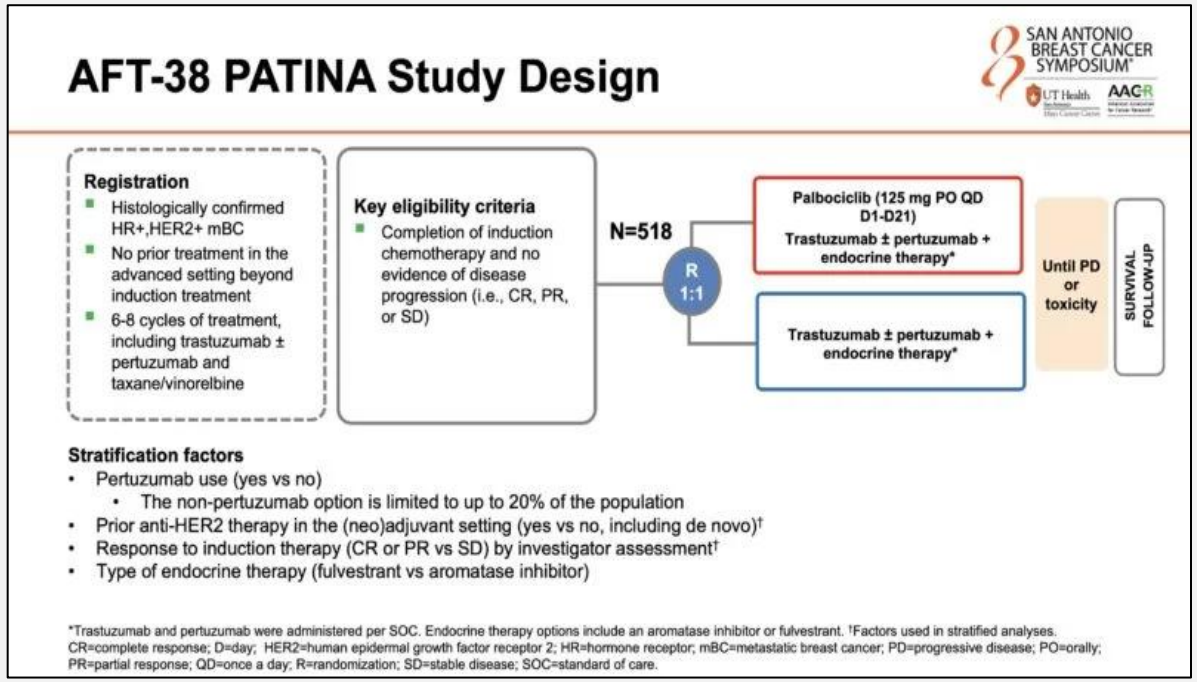
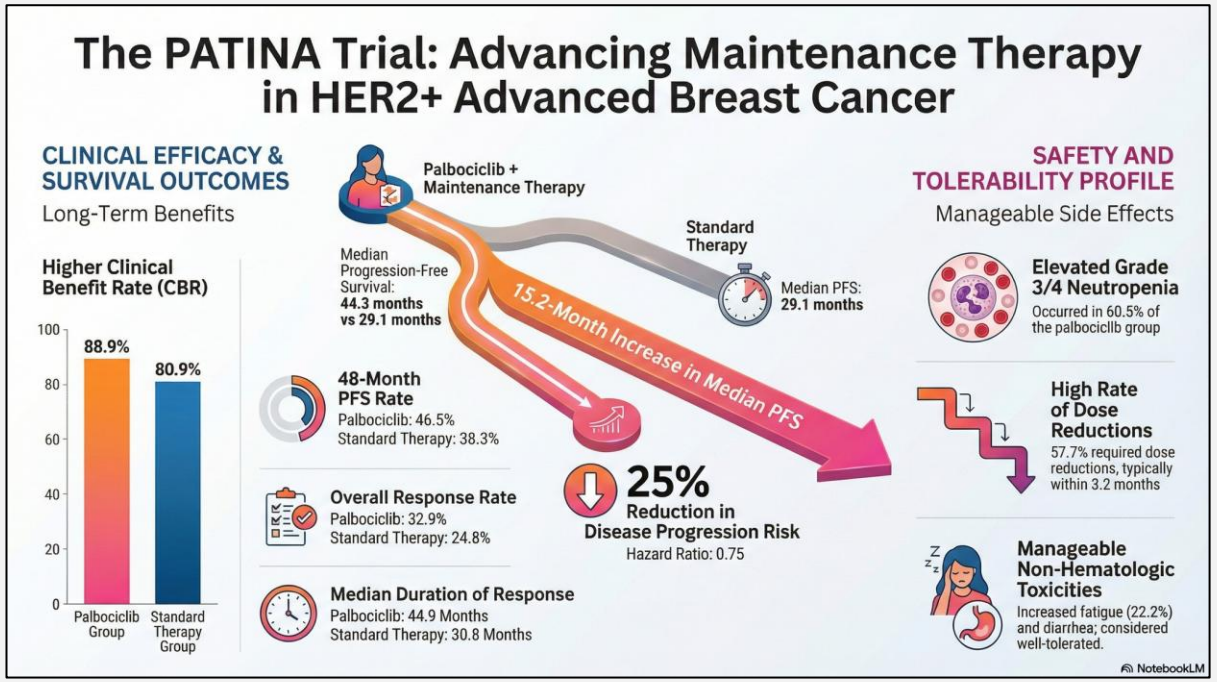
HR+/HER2+


AFT-38 PATINA Study Design
SAN ANTONIO BREAST CANCER SYMPOSIUM
Registration
Histologically confirmed HR+,HER2+ mBC
No prior treatment in the advanced setting beyond induction treatment
6-8 cycles of treatment, including trastuzumab ± pertuzumab and taxane/vinorelbine
Key eligibility criteria
Completion of induction chemotherapy and no evidence of disease progression (i.e., CR, PR, or SD)
N=518
R 1:1
Palbociclib (125 mg PO QD D1-D21) Trastuzumab ± pertuzumab + endocrine therapy*
Trastuzumab ± pertuzumab + endocrine therapy*
Until PD or toxicity
SURVIVAL FOLLOW-UP
Stratification factors
Pertuzumab use (yes vs no)
The non-pertuzumab option is limited to up to 20% of the population
Prior anti-HER2 therapy in the (neo)adjuvant setting (yes vs no, including de novo)†
Response to induction therapy (CR or PR vs SD) by investigator assessment†
Type of endocrine therapy (fulvestrant vs aromatase inhibitor)
*Trastuzumab and pertuzumab were administered per SOC. Endocrine therapy options include an aromatase inhibitor or fulvestrant. †Factors used in stratified analyses.
CR=complete response; D=day; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; mBC=metastatic breast cancer; PD=progressive disease; PO=orally; PR=partial response; QD=once a day; R=randomization; SD=stable disease; SOC=standard of care.


The PATINA Trial: Advancing Maintenance Therapy in HER2+ Advanced Breast Cancer
CLINICAL EFFICACY & SURVIVAL OUTCOMES
Long-Term Benefits
Higher Clinical Benefit Rate (CBR)
100
80
60
40
20
0
88.9%
80.9%
Palbociclib Group
Standard Therapy Group
Palbociclib + Maintenance Therapy
Standard Therapy
Median Progression-Free Survival: 44.3 months vs 29.1 months
Median PFS: 29.1 months
15.2-Month Increase in Median PFS
48-Month PFS Rate
Palbociclib: 46.5%
Standard Therapy: 38.3%
Overall Response Rate
Palbociclib: 32.9%
Standard Therapy: 24.8%
Median Duration of Response
Palbociclib: 44.9 Months
Standard Therapy: 30.8 Months
25%
Reduction in Disease Progression Risk
Hazard Ratio: 0.75
SAFETY AND TOLERABILITY PROFILE
Manageable Side Effects
Elevated Grade 3/4 Neutropenia
Occurred in 60.5% of the palbociclb group
High Rate of Dose Reductions
57.7% required dose reductions, typically within 3.2 months
Manageable Non-Hematologic Toxicities
Increased fatigue (22.2%) and diarrhea; considered well-tolerated.
NotebookLM

HORMONE RECEPTOR POSITIVE BREAST CANCER

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Alpelisib for *PIK3CA*-Mutated, Hormone Receptor–Positive Advanced Breast Cancer

F. André, E. Ciruelos, G. Rubovszky, M. Campone, S. Loibl, H.S. Rugo, H. Iwata, P. Conte, I.A. Mayer, B. Kaufman, T. Yamashita, Y.-S. Lu, K. Inoue, M. Takahashi, Z. Pápai, A.-S. Longin, D. Mills, C. Wilke, S. Hirawat, and D. Juric, for the SOLAR-1 Study Group*

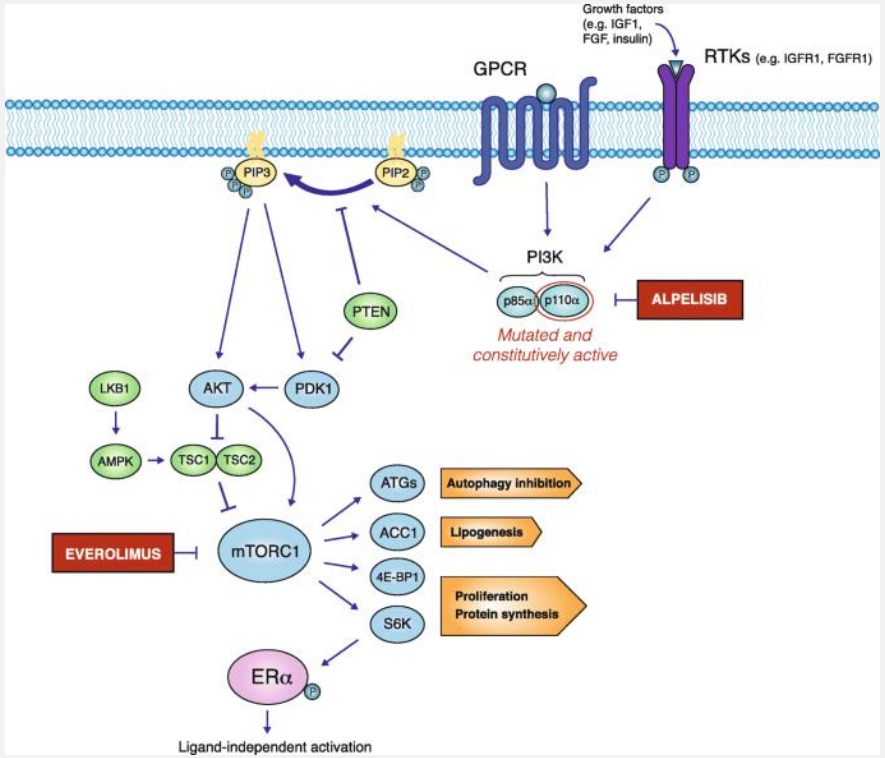
The NEW ENGLAND JOURNAL of MEDICINE

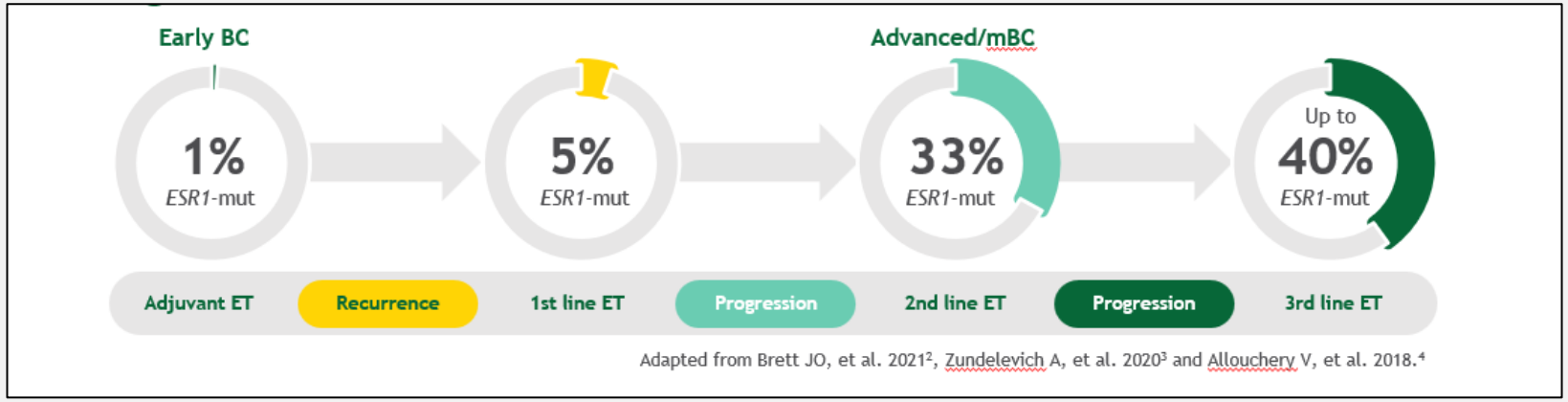
ORIGINAL ARTICLE

Capivasertib in Hormone Receptor–Positive Advanced Breast Cancer

N.C. Turner, M. Oliveira, S.J. Howell, F. Dalenc, J. Cortes, H.L. Gomez Moreno, X. Hu, K. Jhaveri, P. Krivorotko, S. Loibl, S. Morales Murillo, M. Okera, Y.H. Park, J. Sohn, M. Toi, E. Tokunaga, S. Yousef, L. Zhukova, E.C. de Bruin, L. Grinsted, G. Schiavon, A. Foxley, and H.S. Rugo, for the CAPItello-291 Study Group*

ABSTRACT





Adapted from Brett JO, et al. 2021[2], Zundelevich A, et al. 2020[3] and Allouchery V, et al. 2018.[4]

KORSERDU binds to ERα, inducing its blockage and degradation, enabling inhibition of cancer growth and metastasis[1,2]

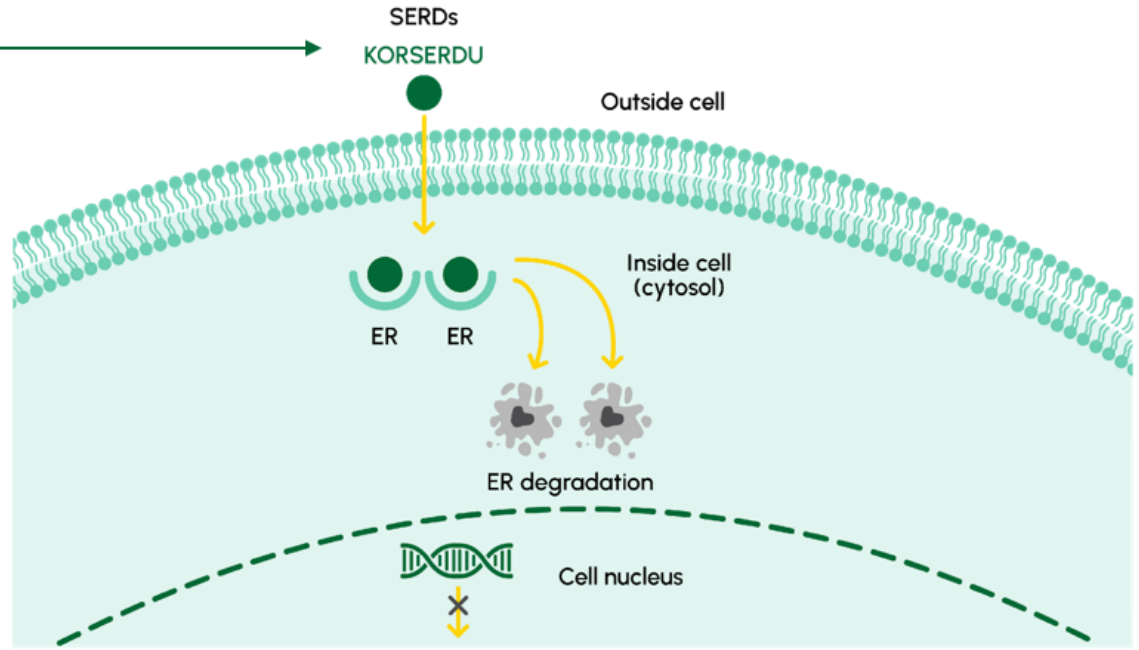


Figure adapted from Bhatia N and Thareja S 2023[3]

BRCA +

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CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation

Authors: Jennifer K. Litton, M.D., Hope S. Rugo, M.D., Johannes Ettl, M.D., Sara A. Hurvitz, M.D., Anthony Gonçalves, M.D., Ph.D., Kyung-Hun Lee, M.D., Ph.D., Louis Fehrenbacher, M.D., +10 , and Joanne L. Blum, M.D., Ph.D. Author Info & Affiliations

Published August 15, 2018 | N Engl J Med 2018;379:753-763 | DOI: 10.1056/NEJMoa1802905 | VOL. 379 NO. 8

The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

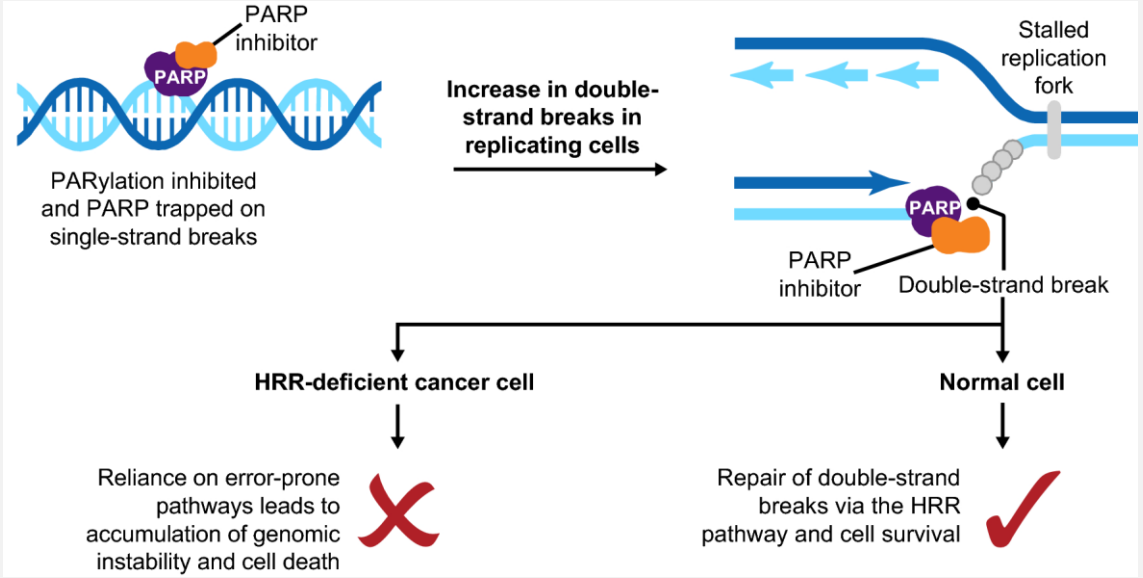
ORIGINAL ARTICLE

Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation

This article has been corrected. VIEW THE CORRECTION

Authors: Mark Robson, M.D., Seock-Ah Im, M.D., Ph.D., Elżbieta Senkus, M.D., Ph.D., Binghe Xu, M.D., Ph.D., Susan M. Domchek, M.D., Norikazu Masuda, M.D., Ph.D., Suzette Delaloge, M.D., +6 , and Pierfranco Conte, M.D. Author Info & Affiliations

Published August 10, 2017 | N Engl J Med 2017;377:523-533 | DOI: 10.1056/NEJMoa1706450 | VOL. 377 NO. 6



SUMMARY

- There are many different treatment options which will have their own advantages and disadvantages
- Individual treatment preferences will differ and therefore important to explore these with your health care team

QUESTIONS?