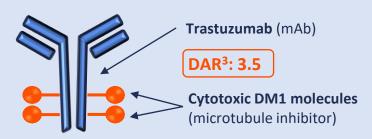


HER2-directed ADCs for BC

Trastuzumab emtansine (T-DM1)¹



EMA approved for:

- Adjuvant treatment of adults with HER2+ early BC with residual invasive disease in breast and/or lymph nodes, after neoadjuvant taxane-based and HER2-targeted therapy
- Adults with HER2+ unresectable locally advanced or metastatic BC who previously received trastuzumab and a taxane, separately or in combination. Patients should have either:
 - Received prior therapy for locally advanced or metastatic disease, or
 - Developed disease recurrence during/within 6 months of completing adjuvant therapy

Trastuzumab deruxtecan (T-DXd)²



EMA approved for:

- Adults with unresectable/metastatic HER2+ BC who have received one or more prior anti-HER2-based regimens
- Adults with unresectable/metastatic HER2-low BC (defined as a score of IHC 1+ or IHC 2+/ISH-) who have:
 - Received prior chemotherapy in the metastatic setting, or
 - Developed disease recurrence during or within 6 months of completing adjuvant chemotherapy

HER2-directed ADCs in late-stage clinical development⁴

Trastuzumab duocarmazine (SYD985)



DAR: 2.7

ARX788



DAR: 1.9

Disitamab vedotin (RC48)



DAR: 4



Monitoring/management of key side effects associated with HER2-directed ADCs for BC

ILD/pneumonitis^{1,2,5}



- Patients should immediately report cough, dyspnoea, fever and/or new or worsening respiratory symptoms
- Patients should be monitored for signs and symptoms of ILD/pneumonitis
- CT or radiographic changes consistent with ILD/pneumonitis warrants immediate treatment interruption and further evaluations
- T-DXd should be permanently discontinued for grade ≥2
 ILD/pneumonitis; T-DM1 should be permanently discontinued for all confirmed cases of ILD/pneumonitis

Nausea/vomiting

 For moderate-emetogenic agents, a two-drug anti-emetic prophylactic regimen can be administered; for high-risk patients or for refractory emesis, an NK1 RA can be added⁶

Advice for patients:7

- Don't force eating; try to eat small meals frequently
- Avoid food smells if they trigger nausea
- Eat cold or room temperature food
- Eat in a cool room
- Sit up or lie back with head raised after eating

Thrombocytopenia



- Platelet count monitoring before each dose; close monitoring of patients with thrombocytopenia or those on anticoagulants¹
- Platelet transfusions if bleeding, or to prevent major bleeds if platelet counts $<10 \times 10^9/L^6$
- Platelet receptor antagonist, romiplostim, if platelet counts $30-50 \times 10^9/L$ (discontinuation when platelet count recovers to $50-100 \times 10^9/L$)⁶

Cardiotoxicity⁶



- BL assessment of cardiovascular toxicity risk factors is important
- Treatment should be interrupted for symptomaticmoderate/severe and asymptomatic-severe CTRCD
- In patients with asymptomatic-mild and -moderate CTRCD, treatment should be continued with the addition of cardioprotective therapy (ACE-I/ARB and beta-blocker)

Neuropathy⁶



- No specific recommendations for prevention/treatment
- No preventive strategies proven effective
- Treatment focuses on reducing pain in patients with chronic PN

Alopecia



- Scalp-cooling can reduce the effect of the drug on hair follicles8
- Initiate scalp cooling 20–45 mins before T-DXd infusions and continue for 20–150 mins after⁸

Neutropenia⁶



- Early assessment and management, including dose reduction, is important
- No dose adjustments for grade ≤2 neutropenia
- **G-CSF prophylaxis** may be given to patients at high-risk of febrile neutropenia or at moderate risk with risk factors
- A short-acting growth factor for 2–3 days can increase ANC



Patient-centred communication tips for optimal breast cancer care⁹

Sharing information

- Information delivery should be guided by patients and build on baseline knowledge and an understanding of beliefs
- Tools to enhance engagement: diaries, information sheets, alert cards, short films, traffic light symptom reporting tools, apps and group patient/carer education

Managing uncertainty

- Patient engagement can be affected by uncertainty and associated fears of disease recurrence, disease progression and potential for limited life
- Nurses can provide clarity on treatment plans, possible side effects and side effect management

Responding to emotions

- Nurses should address patient's concerns before delivering information
- Depression, anxiety and fears about dying can hinder information uptake



Building relationships

 Trusting relationships between patients and nurses are likely to increase patient engagement in self-care activities

Encouraging shared decision-making

- Most patients prefer to make treatmentrelated decisions in partnership with clinicians
- Nurses can support shared decision-making by ensuring patients and their families are well informed about the risks and benefits of treatment

Facilitating self-management

 Nurses can help patients to be active and responsible participants in their care through goal setting and preparing them to manage and monitor symptoms

Insights for nurses caring for people with BC*

Often [being] the first point of contact, it is really important for nurses to listen to patients in order to help improve quality of life

Have a holistic approach to care involving both patients and caregivers as caregivers have a significant role in the patient journey



Communication with patients and their caregivers, using language that is easy to understand is really important

Nurses should educate themselves so they can in turn educate their patients regarding the side effects of ADC therapy



Strategies to help rehabilitation¹⁰

Physical therapy

- Can help patients with pain, stiffness, numbness, limited movement
- Could include: stretching; strength and flexibility exercises; massage and compression bandages to prevent lymphoedema
- Low-impact exercise could aid recovery

Occupational therapy

- Focus on helping with day-to-day tasks
- Techniques include: different ways to do activities, including using adaptive devices; prioritizing tasks; demonstrating ways to adapt lifestyle or home; relaxation techniques to help manage pain/stress

Abbreviations and references

Abbreviations

ACE-I, angiotensin-converting enzyme inhibitors; ADC, antibody—drug conjugate; ANC, absolute neutrophil count; ARB, angiotensin II receptor blocker; BC, breast cancer; BL, baseline; CT, computed tomography; CTRCD, cancer therapy-related cardiac dysfunction; DAR drug—antibody ratio; EMA, European Medicines Agency; G-CSF, granulocyte colony-stimulating factor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; mAb, monoclonal antibody; NK1 RA, neurokinin-1 receptor antagonist; PN, peripheral neuropathy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

References

- 1. EMA. Trastuzumab emtansine SmPC. Available at: https://bit.ly/4avhuvl (accessed 9 July 2024).
- 2. EMA. Trastuzumab deruxtecan SmPC. Available at: https://bit.ly/3URZ2rd (accessed 9 July 2024).
- 3. Liu F, et al. J Cancer. 2023;14:3275-84.
- 4. Zimmerman BS, Esteva FJ. Cancers (Basel). 2024;16:800.
- 5. Rugo HS, et al. JCO Oncol Pract. 2023;19:539-46.
- 6. D'Arienzo A, et al. *EClinicalMedicine*. 2023:62:102113.

- 7. BreastCancer.org. Eating When You Have Nausea and Vomiting. Available at: https://bit.ly/3UNkwFq (accessed 9 July 2024).
- 8. Rugo HS, et al. ESMO Open. 2022;7:100553.
- 9. Oakley C, Ream E. Semin Oncol Nurs. 2024;40:151556.
- 10. Ragland L. Rehabilitation after breast cancer treatment. Available at: https://bit.ly/4bEtrzU (accessed 9 July 2024).

The guidance provided by this practice aid is not intended to directly influence patient care. Clinicians should always evaluate their patients' conditions and potential contraindications and review any relevant manufacturer product information or recommendations of other authorities prior to consideration of procedures, medications or other courses of diagnosis or therapy included here.

Our practice aid coverage does not constitute implied endorsement of any product(s) or use(s). touchONCOLOGY cannot guarantee the accuracy, adequacy or completeness of any information, and cannot be held responsible for any errors or omissions.

