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HEALTH TECHNOLOGY BRIEFING AUGUST 2020

Abemaciclib for early breast cancer – adjuvant treatment

NIHRIO ID	23786	**NICE ID**	10340
Developer/Company	Eli Lilly and Company Ltd	**UKPS ID**	655496

Licensing and market availability plans	Currently in Phase III clinical trials.

SUMMARY

Abemaciclib is in clinical development as an adjuvant treatment for patients with early breast cancer who have undergone surgery. Early breast cancer is where the disease is limited to the breast region and has not spread to other parts of the body. Symptoms include swelling of breast regions, breast or nipple pain, nipple retraction, change in texture of skin covering the breast, nipple discharge and swollen lymph nodes. Treatment of early stage breast cancer usually involves surgery. Most patients will often receive some treatment after ('adjuvant') the surgery to improve the success rate of the treatment.

Abemaciclib is an oral cancer medicine. It works by blocking the activity of certain enzymes known as cyclin-dependant kinases (CDK) 4 and 6, which play a key role in regulating the way cells grow and divide. By blocking these enzymes, abemaciclib slows the growth of breast cancer cells. If licenced, abemaciclib will provide an additional treatment option for patients with early breast cancer who have undergone surgery.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

PROPOSED INDICATION

Early stage breast cancer following surgery.[1]

TECHNOLOGY

DESCRIPTION

Abemaciclib (Verzenio, LY2835219) is a potent and selective inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6), and most active against Cyclin D1/CDK4 in enzymatic assays. Abemaciclib prevents retinoblastoma protein (Rb) phosphorylation, blocking cell cycle progression from the G1 to the S-phase of cell division, leading to suppression of tumour growth.[2]

Abemaciclib is currently in phase III clinical development for the adjuvant treatment for patients with hormone receptor positive (HR+), human epidermal receptor 2 negative (HER-) early breast cancer who have previously received surgery.[1] In the phase III clinical trial (monarchE; NCT03155997) patients received abemaciclib at a dose of 150mg orally, twice daily as long as patient derives clinical benefit, until dose adjustments or until two years of treatment has been achieved.[a]

INNOVATION AND/OR ADVANTAGES

A phase III clinical trial indicated that when used in combination with standard adjuvant endocrine therapy, as opposed to standard adjuvant endocrine therapy alone, it significantly reduced the risk of breast cancer recurrence and death.[3]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Abemaciclib is currently licenced in the UK for the treatment of women with HR+, HER2- locally advanced or metastatic breast cancer in one of the following combinations; with an aromatase inhibitor, with fulvestrant as initial endocrine-based therapy, or with fulvestrant in women who have received prior endocrine therapy.[4]

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.[4]

The most common side-effects of abemaciclib (which may affect more than 1 in 10 people) are diarrhoea, alopecia, pruritus, rash, pyrexia, infections, neutropenia, leukopenia, anaemia, thrombocytopenia, dizziness, dysgeusia, fatigue, nausea, vomiting and decreased appetite.[5]

Abemaciclib is in phase II and phase III development, as a monotherapy or in combination therapy for several indications including head and neck squamous cell carcinoma (HNSCC), biliary tract carcinoma, soft tissue sarcoma, osteosarcoma and chondrosarcoma.[6]

[a] Information provided by Eli Lilly and Company Ltd

PATIENT GROUP

DISEASE BACKGROUND

Breast cancer is the most common cancer in the UK, and mainly affects women, although men can also have the condition. It usually starts in the cells that line the ducts of the breast.[7] Early stage breast cancer is defined as disease confined to the breast with or without regional lymph node involvement and the absence of distant metastatic disease.[8] There are different immune/pathological subtypes of breast cancer, among which is human epidermal growth receptor 2 (HER2). HER2 is a transmembrane receptor protein that is overexpressed in about 20% of breast cancers and associated with more aggressive disease in the absence of HER2 directed therapy. HER2 plays a role in cell growth and differentiation. Those with cancer cells with HER2 are HER2+ diagnosed, whereas those without are diagnosed HER2-.[9,10]

Breast cancers can also be hormone receptor positive (HR+), which means that hormones such as oestrogen or progesterone can bind to the cancer cells and promote cell growth. Approximately 70% of breast cancers are oestrogen receptor positive (ER+).[10]

The exact aetiology is unknown, but family history is a strong risk factor (hereditary factors).[11] Other risk factors for breast cancer include increased age, reproductive history and hormone exposure, lifestyle factors, medical history and radiation exposure.[12]

One of the first noticeable symptom of breast cancer amongst women is a lump or an area of thickened tissue in their breast. Other common signs and symptoms include a change in the size or shape of one or both breasts, nipple discharge, dimpling on the skin of your breasts, and a rash on or around the nipple.[13,14]

CLINICAL NEED AND BURDEN OF DISEASE

In the UK in 2017, breast cancer was the most common cancer accounting for 15% of all new cancer cases.[15] In England, in 2017 there were 46,109 registrations of newly diagnosed cases of malignant neoplasm of breast (ICD-10 code C50), and the direct age-standardised rate per 100,000 population was 166.7 among females and 1.3 among males.[16] Incidence rates among females are projected to rise by 2% in the UK between 2014 and 2035, from 205 per 100,000 (54,833 cases) to 210 per 100,000 (71,022 cases).[17]

In England, in 2018-19 there were 219,885 finished consultant episodes (FCEs) for malignant neoplasm of breast (ICD-10 code C50), and 215,644 admissions resulting in 80,435 bed days and 183,828 day cases.[18]

In England in 2017, there 10,219 registrations of death from malignant neoplasm of breast,[19] and the direct age-standardised death rate per 100,000 population was 0.3 and 33.3 among males and females respectively.[16]

The latest published survival statistics for breast cancer for women in England (patients diagnoses 2013-2017) reported a 1-year survival rate of 95.8% and a 5-year survival rate of 85% (age-standardised).[19]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Treatment of breast cancer should be carried out in specialised breast units/centres and provided by a multidisciplinary team specialised in breast cancer, consisting of at least medical oncologists, breast surgeons, radiation oncologists, breast radiologists, breast pathologists and breast nurses (or similarly trained and specialised health care practitioners).[20]

The management of breast cancer requires different approaches and involves the use of different therapies. The main treatments for breast cancer include surgery, radiotherapy, chemotherapy, hormone therapy, biological therapy (targeted therapy). Patients may have one of these treatments or a combination. The type or combination of treatments will depend on how the cancer was diagnosed and the stage of the disease.[21]

Adjuvant systemic therapy should be started without undue delays, as data show an important decrease in efficacy when it is administered >12 weeks after surgery. The decision on adjuvant systemic therapies should be based on an individual's risk of relapse (which depends on tumour burden and tumour biology), the predicted sensitivity to particular types of treatment, the benefit from their use and their associated short- and long-term toxicities, the patient's biological age, general health status, comorbidities and preferences.[20]

CURRENT TREATMENT OPTIONS

The following are recommended in the treatment of early breast cancer:

Chemotherapy[22]

- Anti-cancer drugs that destroy cancer cells. These can be used on their own or in combination with two or three other chemotherapy drugs. Examples of chemotherapy for early breast cancer include docetaxel – cyclophosphamide, epiribicin - cyclophosphamide (EC), doxorubicin - cyclophosphamide (AC), paclitaxel, and cyclophosphamide - methotrexate - fluorouracil (CMF)

Bisphosphonate therapy[21]

- Zoledronic acid or sodium clodronate as adjuvant therapy for postmenopausal women to reduce the risk of cancer spreading to other areas of the body

Hormone therapy[21]

- Tamoxifen as a treatment for ER-positive breast cancer
- Aromatase inhibitors, such as anastrozole, exemestane and letrozole for postmenopausal women with ER-positive breast cancer

PLACE OF TECHNOLOGY

If licenced abemaciclib will provide an additional option for the adjuvant treatment of patients with early breast cancer that have previously undergone surgery.[1,3]

CLINICAL TRIAL INFORMATION

Trial	**NCT03155997; 2016-004362-26; A Randomized, Open-Label, Phase 3 Study of Abemaciclib Combined With Standard Adjuvant Endocrine Therapy Versus Standard Adjuvant Endocrine Therapy Alone in Patients With High Risk, Node Positive, Early Stage, Hormone Receptor Positive, Human Epidermal Receptor 2 Negative, Breast Cancer** **Phase III – Active, not recruiting** **Location(s): EU (including UK), USA, Canada and other countries** **Primary completion date: 12th April 2021**
Trial design	Randomised, open label parallel assignment.
Population	n= 5637[b]; adults aged 18 and older; has confirmed HR+, HER2, early stage resected invasive breast cancer without evidence of distant metastases; must have undergone definitive surgery of the primary breast tumour; must have tumour tissue from breast (preferred) or lymph node for exploratory biomarker analysis available prior to randomisation.
Intervention(s)	• Abemaciclib tablet at a dose of 150mg orally, twice daily as long as patient derives clinical benefit, until dose adjustments or until two years of treatment has been achieved[b] • Standard adjuvant endocrine therapy administered according to package label
Comparator(s)	Standard adjuvant endocrine therapy administered according to package label.
Outcome(s)	Invasive Disease Free Survival (IDFS) [Time Frame: Baseline to Recurrence or Death from Any Cause (Approximately 10 Years)] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

ESTIMATED COST

Abemaciclib is already in marketed in the UK. The NHS indicative price for abemaciclib tablets are as follows:[23]

- Abemaciclib 50mg, 100mg and 150mg tablets; 28 tablets (prescription only medicine) cost £1475.00 (Hospital only)
- Abemaciclib 50mg, 100mg and 150mg tablets; 56 tablets (prescription only medicine) cost £2950.00 (Hospital only)

[b] Information provided by Eli Lilly and Company Ltd

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal guidance in development. Pertuzumab with trastuzumab emtansine for adjuvant treatment of early HER2-positive breast cancer (ID2711). Publication date: TBC
- NICE technology appraisal guidance. Trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer (TA632). June 2020
- NICE technology appraisal guidance. Pertuzumab for adjuvant treatment of HER2-positive early stage breast cancer (TA569). March 2019
- NICE technology appraisal guidance. Intrabeam radiotherapy system for adjuvant treatment of early breast cancer (TA501). January 2018
- NICE clinical guideline. Early and locally advanced breast cancer: diagnosis and management (NG101). July 2018
- NICE quality standard. Breast cancer (QS12). June 2016
- NICE diagnostics guidance. Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer (DG34). December 2018

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard contract for Cancer: Chemotherapy (Adult). B15/S/a
- NHS England. 2013/14 NHS standard contract for Cancer: Radiotherapy (All ages). B01/S/a

OTHER GUIDANCE

- Early Breast Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. October 2019[20]
- Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update. August 2018[24]
- Healthcare Improvement Scotland. SIGN 134 – Treatment of primary breast cancer – A national clinical guideline. September 2013[25]

ADDITIONAL INFORMATION

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