IQWIG CASE STUDY: PLANNING TRIALS

Prepared by Ascenian Europe
GERMANY

Patient-reported outcomes: duration of measurement is often too short to demonstrate value

Breast cancer

A briefing from an IQWIG critical assessment of study planning

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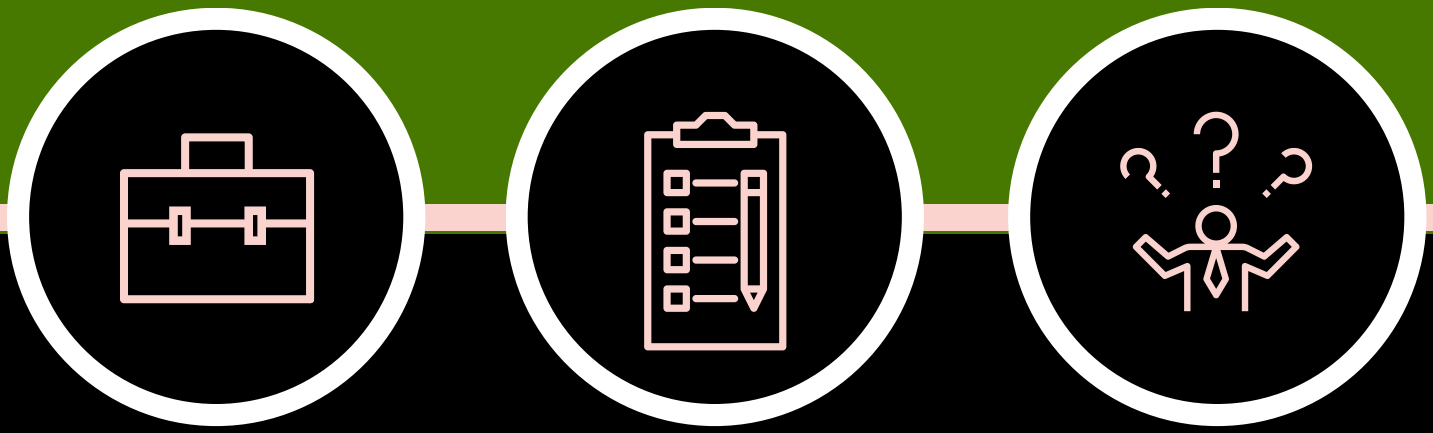
GERMANY: THE IQWIG CASE

Abemaciclib in advanced breast cancer. Duration of measurement of quality of life, symptoms and side effects data was too short for early benefit assessment.



1. BACKGROUND

What was Abemaciclib's data?

2. ASSESSMENT

What were IQWiG's considerations?

3. WHAT IT MEANS

What was IQWiG'S advice?

OBJECTIVE

European HTA results over the last 24 months show that value demonstration doesn't stop with the targeted treatment position. Rather, manufacturers need to show what happens with the patient and treatment pathway once intervention with the new treatment has stopped. In this new paradigm, think beyond!

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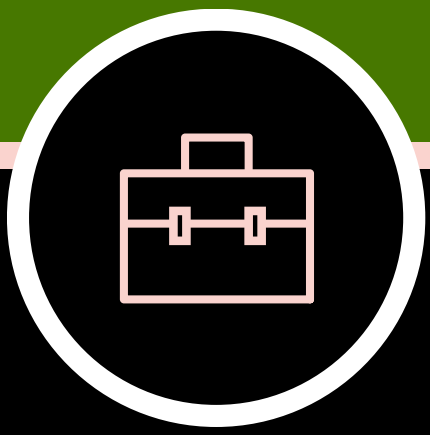
BACKGROUND

Abemaciclib in advanced breast cancer



1. CONTEXT

Abemaciclib in combination with fulvestrant is used for the treatment of postmenopausal patients with hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer.
After the expiry of the limitation of a decision by the Federal Joint Committee (G-BA), the Institute for Quality and Efficiency in Health Care (IQWiG) has reexamined the added benefit - with mixed results.

The manufacturer prepared data from its study MONARCH plus a data analysis by type of pre-treatment, so that corresponding data from two studies (MONARCH 2 and MONARCH plus) were available for the assessment.

An added benefit over fulvestrant alone was not proven for women who have not yet received endocrine therapy. If endocrine therapy has already been completed, there is a proof of a considerable added benefit in the case of visceral metastases - primarily due to a statistically significant prolongation of overall survival. However, survival of patients with non-visceral metastases is not statistically significantly longer with abemaciclib than without, so that the disadvantages in other outcomes shape the result here: There remains an indication of lesser benefit compared to treatment with fulvestrant alone.

SITUATION

Proof of considerable added benefit in populations who completed endocrine therapy and in case of visceral metastases, but not for the non-visceral metastases patients due to non statistically relevant OS - hence other data has to be considered!

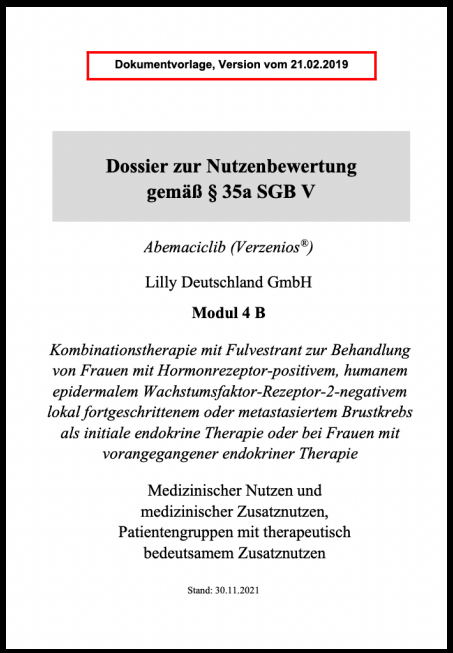
IQWIG ASSESSMENT

Recording of patient-reported outcomes

2. OBSERVATION PERIOD FOR KEY OUTCOMES: TOO SHORT

For the third early benefit assessment of abemaciclib in this indication - after 2019 and 2020 - data on the median treatment and observation periods in the relevant subpopulations from the two studies are now available for the first time. In both studies, the treatment duration is clearly longer in the intervention arm than in the control arm. Moreover, the observation periods for each of the outcomes "morbidity (patient-reported symptoms)", "health-related quality of life" and "side effects" are systematically and significantly shortened, as they were only recorded during and shortly after treatment with the study medication. As the figure shows, these data cover only about a quarter of the median survival time.

See tables 4-15 and 4-16 in Modul 4B of the G-BA dossier. On G-BA: https://www.g-ba.de/downloads/92-975-5286/2021_11_30_Modul4B_Abemaciclib.pdf



Dokumentvorlage, Version vom 21.02.2019

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Abemaciclib (Verzenios®)

Lilly Deutschland GmbH

Modul 4 B

Kombinationstherapie mit Fulvestrant zur Behandlung von Frauen mit Hormonrezeptor-positivem, humanem epidermalem Wachstumsfaktor-Rezeptor-2-negativem lokal fortgeschrittenem oder metastasiertem Brustkrebs als initiale endokrine Therapie oder bei Frauen mit vorangegangener endokriner Therapie

Medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen

Stand: 30.11.2021

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WHAT DID IQWIG ADVISE?

Results must be interpretable and consider what happens after treatment

3. STUDY RESULTS MUST BE INTERPRETABLE

IQWiG notes that the systematic shortening of recording patient-reported outcomes to the duration of treatment is common in dossiers. This gap is particularly important when studies continue for a long time after the end of treatment (e.g., due to disease progression or discontinuation due to severe side effects), because participants often live for years.

The shortened, and unevenly long, data collection time in the study arms severely limits interpretability of study results. For example, it is not possible to tell whether patient-reported disease worsening at the end of treatment is really permanent, or possibly has subsided again shortly afterwards for the - very long - remainder of the study duration. In addition, persistent worsening during treatment in the respective study arm observed for a longer duration (here, the abemaciclib arm) is possible.

THE POINT

Careful planning is required to make data interpretable in the treatment context.

WHAT DID IQWIG ADVISE?

Pos-treatment context must be understood

3.WHAT HAPPENS AFTER TREATMENT

IQWiG concludes that demonstrating the further course of quality of life and symptoms - after the end of treatment and/or progression - is critical information for affected patients and their physicians.

Patients and their physicians have to decide whether - and how - to continue subsequent treatment. To make that decision, for example, they need to balance a possible increase in life expectancy against potential impairments in quality of life.

In the two MONARCH studies, a large proportion of participants made use of at least one further systemic therapy after the end of treatment and observation.

THE POINT

Demonstrate value across treatments. Show impact of the new treatment on follow-on treatment and outcomes.

WHAT DID IQWIG ADVISE?

Prioritize a look beyond the new treatment

3.RESULTS ON SYMPTOMS AND QUALITY OF LIFE ARE RELEVANT FOR PATIENTS

IQiWIG noted that dossiers shared since the advent of AMNOG are often strongly tailored to approval. In such studies, data on patient-reported outcomes are recorded for too short a time, e.g., only until disease progression. But symptoms and quality of life are relevant for those affected after the disease has worsened.

Data on patient-reported outcomes that were recorded over a shortened period do not provide answers to the question of whether patients do better or worse with a drug than with another treatment in the long term. For this reason, the time course of their condition must be recorded for as long as possible, i.e., until the end of the study.

THE POINT

In the future, data with artificially shortened measurement periods will no longer be able to significantly influence benefit assessment.

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Material used in this document was drawn from IQWIG published 3 March 2022:
https://www.iqwig.de/presse/pressemitteilungen/pressemitteilungen-detailseite_62592.html

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