

IQWiG Reports – Commission No. D13-02

Determination of antigen expression levels of uPA and PAI-1 in primary breast cancer with intermediate recurrence risk after R0 primary surgery¹

Executive Summary

¹ Translation of the executive summary of the final report *Bestimmung der Antigenexpressionslevel von uPA und PAI-1 beim primären Mammakarzinom mit intermediärem Rückfallrisiko nach R0-Primäroperation* (Version 1.0; Status: 22 August 2014). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:

Institute for Quality and Efficiency in Health Care

Topic:

Determination of antigen expression levels of uPA and PAI-1 in primary breast cancer with intermediate recurrence risk after R0 primary surgery

Commissioning agency:

Federal Joint Committee

Commission awarded on:

3 January 2013

Internal Commission No.:

D13-02

Address of publisher:

Institute for Quality and Efficiency in Health Care
Im Mediapark 8 (KölnTurm)
50670 Cologne
Germany

Tel.: +49 (0)221 – 35685-0
Fax: +49 (0)221 – 35685-1
E-Mail: berichte@iqwig.de
Internet: www.iqwig.de

This report was prepared in collaboration with external experts.

The responsibility for the contents of the report lies solely with IQWiG.

According to §139 b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received". The Institute received the completed *Form for disclosure of potential conflicts of interest* from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts and external reviewers is presented in Appendix E of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

External experts:

- Patrick M. M. Bossuyt, Academic Medical Center of the University of Amsterdam, Netherlands
- Rolf Kreienberg, Women's Hospital, University of Ulm, Germany
- Anne W. S. Rutjes, Institute of Social and Preventive Medicine, University of Bern, Switzerland

IQWiG thanks the external reviewers for their collaboration in the project.

IQWiG employees:²

- Martina Markes
- Dorothea Gechter
- Charlotte Guddat
- Elke Hausner
- Inger Janßen
- Julia Kreis
- Fueloep Scheibler
- Stefan Sauerland

² Due to legal data protection regulations, employees have the right not to be named.

Executive summary

On 3 January 2013, the Federal Joint Committee (G-BA) wrote to the Institute for Quality and Efficiency in Health Care (IQWiG) to commission the assessment of the determination of antigen expression levels of the urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 in primary breast cancer with intermediate recurrence risk after R0 primary surgery.

Research question

The aim of this study was to assess the benefit of a uPA- and PAI-1-based strategy for the decision for or against systemic adjuvant therapy in comparison with a decision strategy independent from uPA and PAI-1 in patients with invasive breast cancer and intermediate recurrence risk after R0 primary surgery with regard to patient-relevant outcomes. In the included study, the systemic adjuvant therapy was chemotherapy.

Randomized controlled trials (RCTs) with a minimum duration of one year were included that investigated a uPA- and PAI-1-based strategy (determined by ELISA [enzyme linked immunosorbent assay]) for the decision for or against systemic adjuvant therapy in patients with invasive breast cancer and intermediate recurrence risk after R0 primary operation with regard to

- overall survival
- disease-free survival (the patient relevance for this outcome should be checked using the concrete operationalization in the included study)
- health-related quality of life
- adverse events both as a consequence of the diagnostic test and as a consequence of the subsequent interventions

For this purpose, a systematic literature search was performed in the following databases: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, a search for relevant systematic reviews took place in the databases MEDLINE and EMBASE in parallel with the search for relevant primary studies. Searches were also conducted in the databases Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The last search was conducted on 21 March 2014.

Systematic reviews and publicly available trial registries were also searched. Furthermore, documents sent by the G-BA and publications that had been provided in the hearing procedure for the preliminary report plan were also screened. Finally, the authors of the relevant study publication were contacted in order to clarify important questions.

The selection of relevant studies was performed by 2 reviewers independently of each other for the result from the bibliographic literature search, from the search in publicly accessible trial registries and from documents sent by the G-BA.

Data extraction was conducted in standardized tables. To evaluate the certainty of results, the risk of bias at study and outcome level was assessed and rated as low or high respectively.

Results

One study in total was identified as relevant for the present benefit assessment. This study was a study with a hybrid design (enrichment design with additional follow-up of the non-randomized subpopulation) investigating whether patients with high concentrations of uPA/PAI-1 in their tumour tissue, who could be allocated to the group with an intermediate recurrence risk by clinical-pathological factors, survived longer after adjuvant chemotherapy with CMF than without chemotherapy. A study with this design is primarily suitable to answer one aspect of the research question, that is the question concerning the effect of chemotherapy in the group of patients chosen based on high uPA/PAI-1 concentrations.

To do this, the patients were differentiated in a group with high and a group with low recurrence risk based on their uPA and PAI-1 concentrations. The patients with high recurrence risk were randomized: They were either allocated to treatment with chemotherapy or observed. The patients with high recurrence risk who did not agree to randomization were analysed separately. Patients with a low recurrence risk based on their uPA/PAI-1 concentrations were observed – and hence received no chemotherapy.

In the intention to treat analysis of this study, no statistically significant difference between the 2 treatment options – chemotherapy or no chemotherapy – could be determined for overall survival or disease-free survival in the randomized group of patients with high uPA/PAI-1 concentrations. The study provided no proof of a patient-relevant benefit of uPA- and PAI-1-based strategy for the decision for or against systemic adjuvant therapy.

Conclusions

The patient-relevant benefit or harm of uPA- and PAI-1-based strategy for the decision for or against systemic adjuvant therapy in primary breast cancer with intermediate recurrence risk after R0 primary operation is unclear because of the lack of suitable studies.

Keywords: urokinase-type plasminogen activator, plasminogen activator inhibitor 1, breast neoplasms, benefit assessment

The full report (German version) is published under <https://www.iqwig.de/de/projekte-ergebnisse/projekte/nichtmedikamentoes-verfahren/d13-02-bestimmung-der-antigenexpressionslevel-von-upa-und-pai-1-beim-primaren-mammakarzinom-mit-intermediarem-ruckfallrisiko-nach-r0-primaroperation.3221.html>.